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Exploring the Intersection of Nutrition and Medical Sciences: A Journey from Food to Health

For centuries, the wisdom of "food as medicine" has echoed through various cultures. However, the scientific exploration of this connection has only recently gained significant momentum. The intersection of nutrition and medical sciences is a rapidly expanding field, fuelled by advancements in biochemistry, genomics, and our understanding of the gut microbiome. Nutrition plays a pivotal role in maintaining health and preventing various diseases, making it an indispensable component of medical sciences. Our first Paper in this issue (A Research Report) aims to shed light on this dynamic interface, highlighting key areas of research and their potential impact on healthcare.

Nutrition is a fundamental aspect of human life, influencing growth, development, and overall health. Food is more than sustenance; it is a powerful tool for promoting health, preventing disease, and even managing chronic conditions. There exists an intricate relationship between nutrition and medical sciences; researchers are exploring how dietary choices interact with the human body's biological processes to influence health outcomes. Over the years, advancements in medical sciences have elucidated the complex mechanisms through which nutrients exert their effects on human health, paving the way for innovative approaches to disease prevention and treatment. The evolving landscape of nutritional science, its integration with medical research, and the exciting advancements shaping personalized medicine through dietary interventions is being examined by scientists. Interdisciplinary collaboration between nutritionists and healthcare professionals is playing a major role in ascribing due importance of nutrition in the prevention and management of various medical conditions.

Nutritional Science: From Basic Principles to Personalized Strategies

Nutritional science underpins our understanding of how food nourishes the human body. It delves into the essential nutrients – carbohydrates, proteins, fats, vitamins, minerals, and water – and their roles in maintaining physiological functions. Traditionally, research focused on identifying deficiencies and recommending specific nutrients to address them. However, the field has broadened its scope, acknowledging the complexities of dietary patterns and their influence on overall health.

The ancient proverb, "Let food be thy medicine and medicine thy food," resonates deeply within the field of nutritional science. This field delves into the intricate relationship between food, nutrients, and human health. Its historical journey began with the identification of essential nutrients that prevent deficiency diseases. Today, nutritional science has evolved significantly, encompassing a holistic approach that considers dietary patterns, individual variations, and the impact of food on chronic disease prevention and management.

The Six Pillars of Nutrition: A Foundational Framework

Our understanding of how food fuels the body rests upon the six core principles of nutrition:

1. Adequacy: This principle emphasizes consuming a variety of foods from all food groups to ensure the intake of all essential nutrients: carbohydrates, proteins, fats, vitamins, minerals, and water. These nutrients fulfil vital physiological functions, from energy production to building and repairing tissues.
2. Balance: A balanced diet ensures the consumption of these essential nutrients in appropriate proportions. This balance can be achieved by incorporating a variety of fruits, vegetables, whole grains, lean protein sources, and healthy fats into the diet.
3. Moderation: Nutritional science promotes the concept of moderation, where no single food group is demonized. Instead, it advocates for mindful eating and portion control to prevent overconsumption and nutrient imbalances.
4. Variety: Consuming a diverse array of foods ensures a broader spectrum of nutrients, including essential vitamins, minerals, and phytochemicals with health-promoting benefits. A varied diet also

enhances the sensory experience of eating and promotes overall dietary satisfaction.

5. Nutrient Density: This principle focuses on selecting foods that provide a high concentration of nutrients relative to their caloric content. Fruits, vegetables, and whole grains are excellent examples of nutrient-dense foods, offering an abundance of vitamins, minerals, and fiber with relatively fewer calories.
6. Individuality: Recognizing that individual needs and preferences vary, nutritional science emphasizes tailoring dietary recommendations to accommodate activity levels, health conditions, and cultural backgrounds.

Beyond Nutrients: The Significance of Dietary Patterns

While the six core principles focus on individual nutrients, modern nutritional science recognizes the importance of dietary patterns. A dietary pattern refers to the overall combination of foods and beverages consumed over time. Research has shown that specific dietary patterns, such as the Mediterranean diet or the DASH diet, can significantly influence health outcomes.

This shift towards dietary patterns acknowledges the synergistic effects of various nutrients within food and across a person's overall diet. For instance, fruits and vegetables not only provide vitamins and minerals but also offer antioxidants and fiber that interact with other dietary components to exert their health benefits.

Personalized Nutrition: A Tailored Approach to Dietary Wellness

The future of nutritional science lies in personalization – crafting dietary strategies that cater to each individual's unique needs and genetic makeup. With advancements in genomics, researchers are exploring how variations in our genes can affect nutrient absorption, metabolism, and susceptibility to chronic conditions.

Personalized nutrition aims to leverage this knowledge to develop customized dietary recommendations. For example, individuals with a genetic predisposition for type-2 diabetes may benefit from a low-glycemic index diet that helps regulate blood sugar levels. Similarly, those with a specific gene variant associated with high cholesterol may benefit from a dietary plan that emphasizes plant-based sources of protein and minimizes saturated fat intake.

Personalized nutrition is still in its nascent stages, but its potential to revolutionize healthcare is undeniable. By considering an individual's genetic makeup, medical history, and lifestyle factors, this approach has the potential to optimize dietary strategies for preventing chronic diseases, managing existing conditions, and promoting overall well-being.

Nutrition and Disease Prevention: A Powerful Alliance

Chronic diseases, such as cardiovascular disease, type-2 diabetes, and certain cancers, are a growing global burden. Research has consistently demonstrated the significant role of diet in both the prevention and management of these chronic diseases, characterized by long-term progressive health deterioration.

Mechanisms of Diet-Disease Link

The connections between diet and disease are multifaceted and complex. Several mechanisms underlie how dietary patterns influence disease risk:

- Nutrient Deficiencies: Deficiency in essential vitamins and minerals, such as vitamin B12 and folate, can contribute to various health problems, including anemia, neural tube defects, and impaired immune function. These deficiencies can increase susceptibility to infectious and chronic diseases.
- Nutrient Imbalances: Excessive intake of certain nutrients, like saturated fats and added sugars, can disrupt metabolic processes. This can lead to an increased risk of chronic diseases like obesity, type-2 diabetes, and cardiovascular disease.
- Inflammation: Chronic low-grade inflammation is a common underlying factor in many chronic diseases. Diets rich in processed foods, saturated fats, and added sugars can promote inflammation, whereas diets rich in fruits, vegetables, and whole grains have anti-inflammatory properties.
- Gut Microbiome: The trillions of microorganisms residing in the gut, collectively known as the gut microbiome, play a crucial role in digestion, nutrient absorption, and immune function. Dietary patterns

can significantly influence the composition of the gut microbiome, and an altered microbiome composition has been linked to various health problems, including obesity, inflammatory bowel disease, and even certain cancers.

Dietary Patterns and Chronic Disease Prevention

Beyond individual nutrients, research suggests that specific dietary patterns are associated with a reduced risk of chronic diseases:

- Mediterranean Diet: This dietary pattern, characterized by a high intake of fruits, vegetables, whole grains, legumes, olive oil, and fish with moderate intake of poultry, dairy, and red meat, has been consistently linked to a reduced risk of cardiovascular disease, neurodegenerative disorders, and certain cancers. The abundance of antioxidants, fiber, and healthy fats in this diet offer various protective benefits.
- DASH (Dietary Approaches to Stop Hypertension) Diet: This diet emphasizes fruits, vegetables, whole grains, and low-fat dairy products with a limited intake of red meat, added sugars, and saturated fats. The DASH diet has been shown to lower blood pressure, a major risk factor for cardiovascular disease.
- Plant-Based Diets: Vegetarian and vegan diets, rich in fruits, vegetables, legumes, whole grains, and nuts, have been associated with a lower risk of type 2 diabetes, heart disease, and certain cancers. These diets are generally lower in saturated fat and cholesterol and often higher in fiber, which can benefit metabolic health.

Specific Nutrients and Food Groups in Disease Prevention

While dietary patterns offer a comprehensive approach, specific nutrients and food groups play crucial roles in disease prevention:

- Fruits and Vegetables: Rich in vitamins, minerals, antioxidants, and fiber, fruits and vegetables offer protection against various chronic conditions. Antioxidants help mitigate oxidative stress, which can damage cells and contribute to the development of chronic diseases. Fiber promotes gut health, supports healthy blood sugar management, and contributes to satiety.
- Whole Grains: Whole grains, such as brown rice, quinoa, and whole-wheat bread, provide a steady source of energy due to their complex carbohydrate content. They are also rich in fiber and essential vitamins and minerals, aiding in gut health, blood sugar control, and weight management, thus reducing the risk of chronic conditions like type 2 diabetes and heart disease.
- Healthy Fats: While saturated fats should be limited, unsaturated fats, particularly those found in oily fish, nuts, seeds, and olive oil, offer significant health benefits. These fats are essential for maintaining cell membranes, promoting heart health, and reducing inflammation.
- Calcium and Vitamin D: These nutrients are crucial for bone health and can help prevent osteoporosis. Dairy products are a good source of calcium, while vitamin D can be obtained from fatty fish, egg yolks, and sun exposure.

Nutritional Interventions in Disease Management

Beyond prevention, dietary modifications play a crucial role in managing various chronic conditions.

- Cardiovascular Disease: Dietary patterns high in saturated and trans fats, cholesterol, and refined carbohydrates contribute to the development of atherosclerosis, a major risk factor for heart disease. Conversely, diets rich in fruits, vegetables, whole grains, and lean protein have been shown to lower blood pressure, improve cholesterol levels, and reduce inflammation, thereby mitigating cardiovascular risk. In patients with existing heart disease, therapeutic diets can help manage cholesterol levels, blood pressure, and weight, thereby reducing the risk of complications.
- Type-2 Diabetes: Dietary management is a cornerstone of type 2 diabetes treatment. By focusing on blood sugar control, these diets promote healthy weight management and include foods with a low glycemic index, complex carbohydrates, and fiber-rich options. A diet high in sugar and refined carbohydrates can lead to insulin resistance, a hallmark of type 2 diabetes. Diets promoting a balanced blood sugar level include whole grains, legumes, fruits with a low glycemic index, and healthy fats. These dietary components help regulate insulin release and improve glucose utilization, potentially

preventing or delaying the onset of diabetes.

- Cancer: The link between diet and cancer is complex, with specific nutrients and food groups playing both protective and detrimental roles. Research suggests that diets rich in fruits, vegetables, and whole grains provide antioxidants and fiber, potentially reducing the risk of some cancers. Conversely, diets high in red meat, processed meats, and added sugars have been linked to an increased risk of certain cancers. While diet alone cannot cure cancer, it can be a valuable adjunct therapy alongside conventional treatments. Specific dietary strategies may help manage side effects of treatment, improve overall health, and potentially enhance the efficacy of some cancer therapies.

The Gut Microbiome: A New Frontier in Nutritional Medicine

The human gut microbiome, a complex ecosystem of trillions of microorganisms, has emerged as a significant player in health and disease. Research suggests that the gut microbiome composition is influenced by our diet, and in turn, it impacts nutrient absorption, immune function, and even our risk of developing certain diseases.

Studies have linked an altered gut microbiome to various conditions, including obesity, inflammatory bowel disease, and even neurodegenerative disorders. This burgeoning field paves the way for the development of prebiotics and probiotics – dietary interventions that target the gut microbiome to promote health and potentially prevent or manage specific diseases.

Nutritional Genomics: Precision Medicine through Diet

The concept of "one size fits all" in healthcare is rapidly becoming outdated. The rise of personalized medicine, which tailors treatment strategies to individual characteristics, is transforming the way we approach health and disease. Nutritional genomics stands at the forefront of this revolution, harnessing the power of genetics to create personalized dietary advice. The field of nutritional genomics explores the intricate interplay between genes, nutrients, and health. There exists an exciting potential of nutritional genomics to revolutionize healthcare by enabling personalized dietary recommendations based on an individual's unique genetic makeup.

This field investigates the intricate relationships between an individual's genetic makeup, nutrient intake, and their health outcomes. By understanding how an individual's genes influence their response to different dietary components, nutritional genomics aims to provide targeted dietary recommendations that optimize health and minimize disease risk.

The Foundation: Genes and Nutrient Metabolism

Nutritional genomics builds upon the fundamental understanding of how genes dictate the production of enzymes involved in nutrient metabolism. These enzymes are vital for various processes, including:

(a) Nutrient Absorption: Genes influence the efficiency with which our bodies absorb nutrients from food. For example, variations in the gene encoding the enzyme lactase can affect lactose tolerance.

(b) Nutrient Metabolism: Genetic variations can affect how our bodies convert nutrients into usable energy or building blocks. For instance, variations in genes related to cholesterol metabolism can influence an individual's response to dietary fat intake.

(c) Nutrient Response: Genes can influence our physiological responses to specific dietary components. For example, some individuals may experience increased blood sugar levels due to genetic variations affecting insulin sensitivity, necessitating dietary modifications for blood sugar control.

Identifying Gene-Nutrient Interactions: The Quest for Personalized Strategies

The core objective of nutritional genomics is to identify specific gene-nutrient interactions that influence health outcomes. This involves a multi-pronged approach:

- Genome-Wide Association Studies (GWAS): These studies analyze the genomes of large populations to identify genetic variants associated with specific health conditions or responses to dietary components.
- Candidate Gene Studies: Researchers may focus on specific genes known to be involved in nutrient metabolism or disease pathogenesis to investigate their interaction with dietary factors.
- Nutritional Intervention Studies: These studies evaluate the effects of specific dietary modifications on

individuals with different genetic backgrounds, providing valuable insights into personalized dietary responses.

Precision Medicine through Personalized Diets

The knowledge gleaned from these studies has the potential to revolutionize healthcare through personalized dietary recommendations. Here are some potential applications:

- Disease Prevention: Identifying individuals with genetic variants that increase their risk for chronic diseases may allow for proactive dietary intervention strategies to mitigate their risk. For example, individuals with a genetic predisposition for type 2 diabetes may benefit from a low-glycemic index diet to regulate blood sugar levels.
- Nutrient Optimization: Nutritional genomics can help personalize dietary recommendations to ensure optimal intake of essential nutrients based on an individual's genetic needs. This could be particularly beneficial for individuals with specific nutrient absorption challenges or those with higher requirements due to their genetic makeup.
- Pharmacogenomics & Nutrigenomics Integration: Nutrigenomics can be integrated with pharmacogenomics, which studies the effect of an individual's genes on drug response. This combined approach can inform dietary modifications to optimize the efficacy and minimize the side effects of medications.

The Future of Personalized Nutrition

For decades, dietary advice has relied on broad population-based guidelines. However, the future of nutrition is poised for a paradigm shift towards personalization. This shift is driven by the convergence of advancements in genomics, metabolomics, and the microbiome, collectively known as multi-omics. By integrating these diverse datasets with an individual's health history, lifestyle, and preferences, a more precise and effective approach to nutrition – personalized nutrition – is emerging.

Genomics plays a crucial role by revealing how an individual's genetic makeup influences nutrient metabolism and susceptibility to diet-related diseases. For instance, variations in genes associated with folate metabolism can impact an individual's need for this vital B vitamin. Metabolomics, the study of small molecules within cells, offers real-time insights into an individual's metabolic response to dietary changes. This allows for the tailoring of diets to optimize metabolic pathways and potentially prevent chronic diseases. Finally, the microbiome, the trillions of microbes residing in our gut, is increasingly recognized as a key player in digestion, immune function, and overall health. Personalized nutrition can leverage the microbiome by recommending prebiotics and probiotics that foster a beneficial gut microbiota composition, potentially improving nutrient absorption and reducing the risk of inflammatory bowel disease.

Technological advancements are instrumental in facilitating the transition to personalized nutrition. The proliferation of affordable wearable biosensors allows for continuous monitoring of physiological parameters like blood glucose and heart rate variability. This data, coupled with dietary intake tracked through mobile applications, provides a rich tapestry of information for nutrition professionals to decipher. Artificial intelligence (AI) algorithms can then analyze this complex data to generate personalized dietary recommendations and even predict potential health outcomes based on dietary choices.

The future of personalized nutrition lies in a collaborative approach. Interdisciplinary teams comprised of nutritionists, geneticists, data scientists, and behavioural psychologists will be essential for developing evidence-based and sustainable dietary plans.

Personalized nutrition has the potential to revolutionize healthcare by shifting the focus from disease treatment to proactive health optimization. By leveraging the power of technological advancements, we can create a future where individuals are empowered to make informed dietary decisions, leading to a healthier and more vibrant population.

Nutritional genomics represents a paradigm shift towards personalized medicine based on an individual's unique genetic blueprint. As the field evolves, we can anticipate advancements in:

- Next-generation Sequencing: Cost-effective and faster genetic testing methods will enable wider application of personalized dietary recommendations.
- Integration with Other 'Omics' Sciences: The integration of nutritional genomics with other 'omics' sciences can provide a more holistic understanding of individual health and responses to dietary interventions.
- Development of Precision Nutrition Apps: User-friendly applications leveraging genetic data and dietary preferences can empower individuals to make informed dietary choices.

Nutritional medicine encompasses the use of dietary interventions, nutritional supplements, and lifestyle modifications to prevent and treat various medical conditions. Integrative approaches that combine conventional medical therapies with nutrition counselling have shown promise in optimizing patient outcomes and reducing healthcare costs. From personalized nutrition plans tailored to individual genetic profiles to targeted interventions for metabolic syndrome and autoimmune disorders, nutritional medicine offers a multifaceted approach to health promotion and disease management. Moreover, the incorporation of culinary medicine, which emphasizes the therapeutic potential of whole foods and culinary techniques, represents a paradigm shift in medical education and practice. By empowering patients to make informed dietary choices and adopt healthier lifestyles, nutritional medicine holds the potential to revolutionize healthcare delivery and improve population health.

The intersection of nutrition and medical sciences represents a dynamic field with far-reaching implications for human health and well-being. By elucidating the intricate relationships between dietary factors, physiological processes, and disease outcomes, researchers and healthcare professionals can develop evidence-based strategies for disease prevention and management. From understanding nutrient metabolism to implementing personalized dietary interventions, the integration of nutrition into medical practice holds the key to promoting optimal health across the lifespan. Moving forward, interdisciplinary collaboration between nutritionists, physicians, and other healthcare providers will be essential for translating scientific knowledge into effective clinical interventions and addressing the growing burden of chronic disease worldwide. By embracing the principles of nutritional medicine, we can pave the way towards a healthier future for generations to come.

(Ravindra Bangar)

Editor

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Research Report

Nutrient Analysis of Raw vs. Processed Chickpea (Cicer arietinum) and Development of Value Added Products

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ABSTRACT

Chickpea (Cicer arietinum) is a pulse crop. It occupies an important place in human nutrition and is a valuable source of protein, fiber and minerals. Being nutritionally important it was taken for the present study for bio chemical analysis of nutrients and development of value added products.

Raw seeds were grounded along with husk to obtain chickpea flour which was analyzed biochemically for the nutrients i.e. moisture, ash, crude-fiber, protein, carbohydrate, fat, calcium, phosphorous, iron, zinc and folic acid.

Whole seeds were subjected to various treatments like roasting, soaking for 10 hrs. and germinating the soaked seeds for 24 hrs. and 48 hrs. They were then dried, powdered and nutrients analyzed.

Khakra, bread, pizza-base and bun are commonly consumed market products by all age groups in states of Rajasthan and Gujarat. These are made of flour which is not high in fiber. Such low fiber diets are reported to be a major cause of diseases like obesity, diabetes, cardiovascular etc. Enhancement of fiber in diet led to the development of value added products. Being high in fiber the chickpea powder (raw) was used for this investigation.

Two types of incorporations were done for bread, pizza base and bun:

(a) Refined flour and chickpea flour in the ratio 70:30

(b) Wheat flour, refined flour and chickpea flour, in ratio 40:30:30

For Khakra, chickpea and wheat flour were used in ratio 40:60

Sensory evaluation of these products was done, which showed that the acceptability of both the types of developed products in terms of texture, taste, appearance and overall acceptability remained same as compared to that of market products.

Statistical analysis of results of biochemical analysis and sensory evaluation was done using ANOVA.

Nutrient analysis /100g of the developed products done using Nutritive Value of Indian Foods suggests that the products made of 40:30:30 ratio (wheat flour, refined flour, chickpea flour) were higher in protein and fiber so were more acceptable than products with 70:30 ratio (refined flour, chickpea flour).

It may therefore be concluded that the use of chickpea flour substantially increased the protein and fiber content. To obtain better nutrients the consumption of these value added developed products may be recommended. This would also help to prevent the life style diseases like obesity, diabetes, cardiovascular etc.

KEYWORDS: Bengal grams, Dietary fiber, Life style diseases

INTRODUCTION

Life cannot be sustained without adequate nourishment. Food is that which nourishes our body. Man needs food for growth, development and to lead an active and healthy life. It may be defined as anything eaten or drunk, which can be absorbed by our body to be used as an energy source. In other words, it is the raw material from which our body is made. Intake of the right kind and amount of food ensures good health, which reflects our physical appearance, emotional well being and energy to perform daily activities[1]. The word "Nutrition" comes from the Latin word "Nutr." meaning "to nurture or to nourish". Nourishment is that which sustains life. A broader definition includes the social, economical, cultural and psychological implication of food and eating[2].

The science of nutrition had its beginning during the late eighteenth century with the discovery of the respiratory gases and especially the studies on nature and the qualification of energy metabolism by Lavishers, referred to as the "Father of the science of nutrition". In a survey in the nineteenth century many chemists and physiologists added important information on the need for protein and some other minerals like calcium, phosphorous and iron. Knowledge of vitamins has been gained in the twentieth century. Indeed more knowledge concerning nutrition has been gained during this century. Nutrition is the finest need of man: his general health and well-being are much dependent on his nutritional status[3]. It is the contribution of processes by which the living organism receives, utilizes the materials necessary for the maintenance of its function, for growth and renewal of its components. It is the science that interprets the relationship of food to the function of the living organization and also the processes by which our body uses the food. Good health is a state of complete physical, mental, social well being and not merely the absence of disease or infinity.

Swaminathan[4] classified food into eleven groups on the basis of their nutritive value:

(1) Cereals

(2) Pulses and legumes

(3) Nuts and oil seeds

(4) Vegetables

(5) Fruits

(6) Milk and milk products

(7) Egg, meat, fish and other animal foods

(9) Fats and Oil

(10) Sugar and other carbohydrate foods

(11) Spices and condiments

Chickpea

Chickpea commonly called gram or Bengal gram is the most important pulse crop. It is a cool season crop i.e. Rabi crop, ranks second in area and third in production among pulses in the world. It is the world's third most important grain legume after beans and peas[5]. It covers an area of 5.81 million hectares with the production of 3.62 million tons in India. It represents about 27% of total area under pulses production in our country.

The scientific name of chick pea is Cicer arietinum. Cicer name is of Latin origin and genus Cicer belongs to family Leguminosae. Legumes are next in importance to cereals as sources of human and animal food and are widely grown throughout the world. They are rich sources of protein in our diets which is about 20-40%. From the point of nutrition they are very important as protein content in pulses is double than that of wheat and thrice than that of rice. For this reason they are called "Poor man's meat". In a vegetarian diet or a diet containing low animal food, they are an important source of protein. Chief protein is globulin called "legumin"[6].

Legumes not only have a dietary value but play an important role in maintaining and improving soil fertility through their ability to fix atmosphere nitrogen. They also serve as economical sources of minerals like calcium, magnesium, iron, zinc and potassium.

There is widespread protein calorie malnutrition in the developing countries and pulses can play an important role in bridging the protein gap.

Figure 1: Flowering Chickpea Plant

Origin and History

The grain is said to be one of the oldest pulses known and cultivated from ancient times both in Asia and Europe. It probably originated in an area of present day south east Turkey and adjoining Syria. Botanical and archaeological evidence show that chickpea was first domesticated in the Middle East and was widely cultivated in India.

Chick pea has been introduced all over the world and is the most important legume grown in India mostly in Madhya Pradesh, Rajasthan, Uttar Pradesh, Maharashtra, Haryana, Karnataka, Bihar and Gujarat.

In Rajasthan, chick pea is cultivated in Ajmer, Jaipur, Dausa, Sikar, Jhunjhunu, Alwar, Bharatpur, Dholpur, Sawai Madhopur, Karauli, Bikaner, Churu, Ganganagar, Hanumangarh, Jaisalmer, Jalore, Pali, Sirohi, Kota, Baran, Bundi, Jhalawar, Tonk, Banswara, Dungarpur and Udaipur. According to the statement of Agriculture Secretariat, Jaipur the production achieved in Rajasthan was 120.0 tonnes in 101.8 hectares area yield on kg/hectare in 2004-2005.

Classification

Cicer was originally classified as tribe vicieae but its portion is sufficiently distinct to consider the genus a tribe of its own, the Cicerae[7]. There are 43 species of Cicer (cultivated and wild) throughout the world.

The Indian gram has been classified into two broad categories:

(1) Desi or brown gram (Cicer arietinum): It is most widely grown. The color often varies from brown to yellow. The flower color may be white, pink or blue. Seed size varies from 5-12 mm. Stem is erect to semi-bending and plant has a good branching ability. Desi type seeds are used in both forms green as well as dry. The green seeds are used as "chhole" for vegetable purpose and "chola" as a roasted form. The dry seeds are puffed and called “chana".

(2) Kabuli or White Gram (Cicerkabuli): Plants of this group have a poor yield potential than desi type. Grains are bold and attractive and usually white in colour. Plants are tall and erect with moderate branching ability.

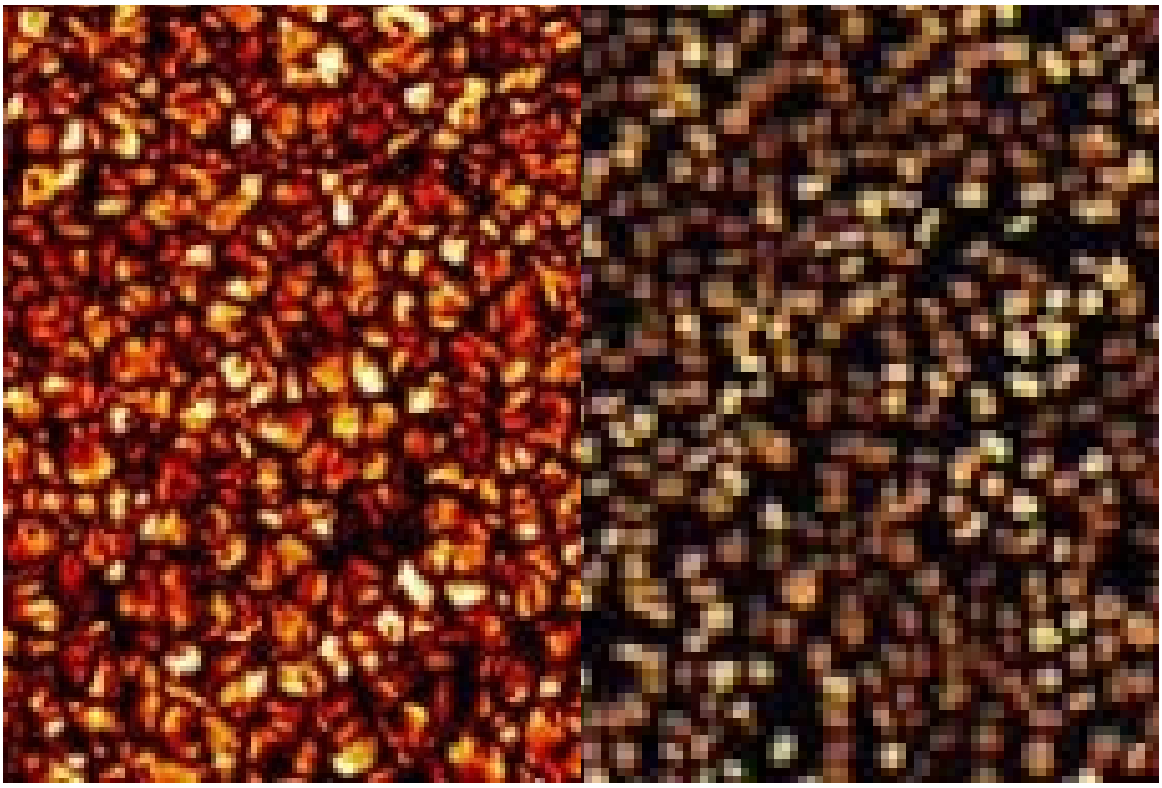

Figure 2: Chickpea Desi
Left: Bengal variety; Right: European variety

Figure 3: Chickpea Kabuli
White and Green Chickpeas

Nutritional Composition

Seed has 38.59% carbohydrate, 3% fiber, 4.8-5.5% oil, 3% ash, 0.2% calcium, and 0.3% phosphorous. Digestibility of protein varies from 76-78% and its carbohydrate from 57-60%[8,9]. Accordingly to the International crops Research Institute for the Semi Arid Tropics (ICRISAT)[10] chick pea seeds contain on an average:

23% - Protein

64% - Total Carbohydrates (47% starch, 6% soluble sugar)

5% - Fat

6% - Dietary Fiber

3% - Ash

Nutrients in Chickpea

(1) Protein and Amino acid

Chickpea seeds contain protein that ranges between 12.6 and 30.5%. The protein content of Dal is higher than that of the whole seed indicating the effect of seed coat on the protein content in chickpea genotypes. They also contain a considerable amount of protein nitrogen (NPN), which also affects true protein content. The NPN and total nitrogen in chickpea are positively correlated[11]. A large variation in NPN would overestimate the true protein content of the sample and would consequently affect the estimated protein intake in the diet. Although genotypes exist with higher protein content no attempt has been made to combine high protein with high yield potential Efforts should be made to develop high protein genotypes since it has been reported that the amount of the protein content may be more than what was previously believed.

Although chickpea is a rich source of protein, quality is limited by sulphur containing amino acids, methionine and cysteine. It generally meets human adult requirement for all the essential amino acids, except methionine and cysteine. Next to sulphur amino acids are tryptophan, threonine and valine since the chemical score for these amino acids were generally below the satisfactorily level in several chickpea genotypes.

However, considerable variation may exist for this amino acid among the chickpea genotypes. Based on the amino acid consumption, the chickpea proteins were found to be of higher nutritive value as compared to other legumes.

(2) Carbohydrates

It is a good source of carbohydrate which together with protein influences the functional properties of chickpea flour and food production. Total seed carbohydrate varies from 52.4-70.9%[12]. Soluble sugars range from 4.80 to 8.5% kabuli types containing slightly higher amount than desi[11]. The bioavailability of carbohydrates is important in terms of calorific value; unfortunately the concentration of non-available

carbohydrates in chickpea is highest (25.6%) among commonly consumed pulses.

(3) Lipids

Among pulses chickpea contains highest amount of lipids, a large variation in fat content (3.8-10.2%) has been reported amongst chickpea genotypes. The fraction is high in unsaturated fatty acids, primarily linoleic and oleic acids. Due to this high content of essential fatty acids particularly linoleic and linolenic acids, the hypocholesterolmic effect of chick pea is high[13].

(4) Minerals and Vitamins

Chick pea is a good source of minerals and vitamins. Consumption of whole seeds of chickpea is desirable since its seed coat contributes about 70% of total seed calcium (190 mg/100 mg). It is high in phosphorous (340 mg/100g), magnesium (140mg/100g), iron (7mg/100mg) and zinc 3mg/100g. It contains a considerable amount of vitamin B1, B2, ascorbic acid and niacin. Its protein digestibility is highest in the dry edible legumes[14].

(5) Dietary Fiber

They are the remnants of plant cells, resistant to hydrolysis by human alienating enzymes, vary to a large extent among chickpea genotypes particularly between desi and kabuli genotypes Large variations in crude fiber content has been reported among the commonly grown cultivars .The concentration of dietary fiber is directly related to seed coat content and a large variability in the seed coat of chick pea cultivars has been reported. Dietary fiber content of kabuli genotype varies between 10.6 and 15.2% where as that of desi between 19.0 and 22.7[15].

This study further reported that cellulose and hemi cellulose accounted for about 60-70% of the total seed dietary fiber. Hemicelluloses accounted for about 55% of the dietary fiber whereas cellulose contributed about 10% in both desi and kabuli cultivars. Cellulose has been reported to be the least digestible component of dietary fiber whereas hemicelluloses produce a considerable amount of gas when ingested by human (El Faki et al, 1983). Kabuli cultivars have the best food technological qualities because of their lower content and thickness of seed coat suggesting that cultivars with reduced seed coat thickness would improve grain quality[16,17].

Major Sources:

Total Dietary fibre (TDF) content in food of plant source may vary. (Table 1)

Table 1: Major Sources of Total Dietary Fiber

Source	Fiber %
Cereal	
Wheat grain	16.9
Wheat Bran	47.1
Oat bran	17.2
Barley	19.1
Jowar	8.5
Legumes	
Cow pea	30.7
Lima beans	21.2
Kidney beans	23.3
Spices	
Pepper	27.8
Coriander	36.4
Cumin	23.1
Fennel	28.7
Fenugreek	33.5
Red Chilli	43.3

Source: Prosky et.al.[18]

Medicinal Uses

Medicinal applications include use for aphrodisiac, bronchitis, catarrh, catamenia, cholera, constipation, diarrhoea, dyspepsia, flatulence, snakebite, sunstroke, and warts. Acids are supposed to lower the blood cholesterol levels. Seeds are considered antibilious[19].

Food Uses

- Chick pea seeds are eaten fresh as green vegetable, parched, fried, roasted and boiled as snack. Seeds are ground and the flour can be used as soup, dhal, to make bread, or prepared with pepper, salt and lemon and served as a side dish[20].
- Sprouted seeds are added to salads. Young plants and green pods are eaten as leafy vegetable. Chickpea is canned and used in Turkey and Latin America to produce fermented food.
- Dhal is the split chickpea without the seed coat. It is dried and cooked into a thick soup or ground into flour for snacks and even sweet meats[20,21]. Animal feed is another use of chick pea in many developing countries. Green grain husks or green, dried stem and ears are used for stock feed. Whole seeds may be milled directly for feed.
- An adhesive may also be prepared from chickpea: although not water resistant. It is suitable for plywood.
- Leaves are said to yield an indigo like dye.
- Acid exudates from leaves can be applied medicinally or used as vinegar.
- In Chile cooked chick pea milk (4:1) mixture was good for feeding infants and was effective in controlling diarrhoea.
- Chick pea yields 21% starch suitable for textiles, giving a light finish to silk, wool and cotton cloth[19].

Table 2: Nutritional Composition of Chickpea

Nutrients	Nutritive value of Chickpea/ 100g
1. Moisture	9.8g
2. Protein	17.1g
3. Fat	5.3 g
4. Minerals	3.0 g
5. Fiber	3.9g
6. Carbohydrates	60.9 g
7. Energy	360 Kcal
8. Calcium	202 mg
9. Phosphorous	312 mg
10. Iron	4.6 mg.
11. Carotene	189 mg
12. Thiamine	0.30mg
13. Riboflavin	0.15 mg
14. Niacin	2.9 mg
15. Folic acid	186.0 mg.
16. Vitamin –C	3 mg
17. Choline	194 mg
18. Magnesium	119 mg
19. Sodium	37.3 mg
20. Potassium	808 mg
21 Zinc	6.1 mg

Source: Nutritive value of Indian foods[6]

Significance of the Present Study

Chickpea chosen for our study has many health benefits. It is a valuable source of proteins, carbohydrates, minerals, vitamins and is very high in dietary fiber. So it is a healthy source of carbohydrate for people with insulin sensitivity or diabetes. It contains 7.6 gm of dietary fiber. It is therefore planned to develop products using chickpea. The initiation of chickpea flour to substitute refined flour in the market products was because chickpea has many health benefits:

- Regular consumption may reduce risks of coronary heart diseases. They not only lower cholesterol, but the folate in this legume also lowers homocysteine levels. Homocysteine is a compound found in the body that in high concentrations is directly linked to heart disease. Magnesium is also vital for the heart. This mineral allows blood vessels to relax, which improves circulation, and increases oxygen and nutrient transport throughout the body.
- Preliminary evidences suggest that consumption of chickpea may be beneficial for correcting dyslipidemia.
- The fiber in chickpea helps to decrease blood cholesterol levels by binding bile acids in the small intestine and preventing re-absorption[47].
- Participants took part in a study to compare the effects of chickpea supplemented diet and that of a wheat supplemented diet on human serum The introduction of chickpea in the diet resulted in lower serum levels, total and low density lipoprotein and cholesterol levels.
- Chickpea is an important source of macro nutrients containing twice the amount of protein compared to cereal grains.
- In a study to determine the Glycemic Index of foods, it was concluded that chick pea have a low GI 28-32.
- Chick pea is an excellent source of essential trace element molybdenum. They are a very good source of fiber, folic acid, manganese and a good source of protein, as were as minerals such as iron, magnesium copper.
- Molybdenum is a trace mineral that helps to detoxify sulfites, compounds which are found in many prepared food products, dried fruits, and in wine. Some people are exquisitely sensitive to sulfites and develop headache, dizziness, rapid heart rate, and other unpleasant symptoms when they eat them, Sulfites can be difficult to completely avoid and the molybdenum found in chickpeas may help to offset some of the unpleasant symptoms.
- Chickpea also contains phytoestrogens which are weak plant versions of real oestrogen. There's evidence that these may modulate the body's own production of the hormone in a way that could lower the risk of breast cancer, protect against osteoporosis and minimize hot flushes in post menopausal women.
- Chickpea is an excellent source of soluble fiber. Being high in both soluble and insoluble fiber and with a low glycemic index, chickpeas can help people to feel fuller for longer, thereby helping appetite and manage weight control.
- It also contains fructo-oligosaccharides, a type of probiotics carbohydrate fiber, which supports healthy gut flora. Maintaining a healthy balance of friendly bacteria in the colon is necessary to optimize digestive function and strengthen immunity.

OBJECTIVES

The objectives of the present study were:

- Bio-chemical estimation of various nutrients like moisture, ash, crude-fiber, protein, carbohydrate, fat, calcium, phosphorous, iron, zinc and folic acid in raw chickpea
- To study the effect of various types of processing like roasting, soaking and germination on the nutrient content of chickpea
- Development of value added products using raw chickpea and sensory evaluation of the developed products
- To analyze the obtained data statistically and draw conclusion

Sensory Evaluation

Sensory evaluation of food relies upon evaluation through the use of our senses (Odours, taste, texture, temperature, pain etc.). Only by applying exact scientific testing methods reproducible results can be obtained and analyzed statistically.

Main applications of sensory evaluation are:

1. Quality control of raw products, material and finished
2. Storage test
3. Analysis of competitive products
4. Development of value added product
5. Investigation of factors influencing the odour and flavour of the food, aroma, research market test and hedonic test

LITERATURE SURVEY

From the beginning of time, man has been interested in food and its relationship to him. Poor man's "Meat" is a term used to describe pulses, or food grains that are grown in regions where the consumption of live stock products (animal protein) is limited. Pulses and legumes were amongst the earliest food crops to be cultivated by man[12]. Pulses belong to family Leguminosae and sub-family Papilionacea occupy the most demanding and essential place in Indian Agriculture System because of their valuable peculiar qualities. Pulses are important not only because of their high protein content which is three times as much as in cereals but also to their amino acid composition[4,5]. The amino acids in pulses have been found to be methionine, cysteine and tryptophan.

The crop chosen for the present study was chickpea (Cicer arietinum). Among food legumes, chick pea is a valuable source of proteins, carbohydrates, minerals and vitamins. It occupies an important place in human nutrition in many developing countries[19,22].

Chick pea is a highly nutritious crop. It is an important winter seed legume crop in Indo-Pakistan subcontinent. It contains about 22% protein[11]. It is fed to animals to obtain animal protein. It is the most important pulse crop in India, where it accounts for two, third of the world area and production[23]. Nutritional quality of raw chick pea seed has shown to contain 38-39% carbohydrate, 3% fiber, 4.8- 5.5% oil and 3% ash. The digestibility of protein varies from 76-78% and its carbohydrate from 57-60%.

Nutritional quality of chick pea (raw) as studied by Duke[10] stated that raw whole seeds contain per 100g:

357 Calories, 4.5-15.6% moisture, 14.9-24.6g protein, 8- 16.4g fat, 2.1-11.7g fiber, 2-4.8 g ash, 140-440 mg Ca, 190- 382 mg P. 5.0-23, 9 mg Fe, 0-225 mg b-carotene equivalent, 0.21-1.1 mg thiamine, 0.12-0.33 mg riboflavin, and 1.3-2.9 mg niacin. Further it was observed that boiled and roasted chick pea also contain similar amounts.

Sprouting is said to increase the proportionate amount of ascorbic acid, niacin, available iron, choline, tocopherol pantothenic acid, biotin, pyridoxine, inositol and vitamin-K. Malic acid and oxalic acid exudation from leaves may damage trousers and shoes. Wild species often have similar glandular secretions[10].

The amino acid composition of seeds with 19.5% protein: 5.5% oil (per 16g N) is: 7.2g lysine, 1.4g methionine, 8.8g arginine, 4.0g lysine, 2.3g histine, 4.4g isoluecine, 7.6g leucine, 6.6g. phenylalanine, 3.3g tyrosine, 3.5g threonine, 4.6g valine, 4.1g alanine, 11.7g aspartic acid, 16.0g glutamine, acid 6.0 g hydroxyl proline. 4.3g proline. The leaves contain 4-8% protein[9,10].

Shahid et.al. conducted a study on nutrition and composition of desi chick pea (Cicer arietnium L.) cultivars grown in Punjab, Pakistan. They found that potassium and manganese were noted as being present in higher and lower concentrations respectively. It was found that in these cultivars all the essential amino acids were present. Fatty acid profile indicated that saturated fatty acids were major fatty acids in all cultivars. The levels of some of the anti nutritional factors were also determined. The analysis should almost similar proportions of bio-chemical constituents among all cultivars. The data showed that in terms of quality and quantity. The desi chick pea cultivars can serve as a significant source of essential amino acids, essential fatty acids and trace minerals to meet the demand of population living in Punjab province of Pakistan.

Attia et.al., studied the effect of cooking on the physical properties, chemical composition and nutritive value of chick pea. Their findings were significant and marked losses in ash (34-40%), sugar (32-42%). oligosaccharide (30-34%) and anti nutritional factors content occurred on cooking the seed.

A study on the physio-chemical, nutritional and micro structural characteristics of chick pea following pressure cooking and microwave cooking was conducted by Marconi and associate. They found that the solid loss released in cooking water, were significantly less after microwave cooking than after conventional cooking (6.5 V/S 10.6g /100g of dry pea). They also concluded that in chick pea both types cooking methods increases the digestibility of protein and starches[24].

Khan and the group conducted a study on nutrition evaluation of desi and kabuli chickpeas commonly consumed in Pakistan. They concluded that the hydration capacity per seed of desi (0.16g) was lower than kabuli types (0.26g). The mean cooking time of dry desi and kabuli seed (124.5 V/S 113.8 minute) was reduced to 37.5 V/S 32.8 minute and to 28.8 V/S 22.5 minute, when soaked overnight. The mean value of protein (25.4V/S 24.4), fat (3.7 V/S 5.1%), carbohydrates (47.4 V/S 55%), crude fiber (11.2 V/S 3.9%), ash (3.2 V/s 2.8%) and caloric value (327 V/S 365 Kcal) per 100g were for desi/ kabuli chick peas respectively.

Onrakova and Menkor reported a study conducted on the moisture absorption characteristic of chick pea flour. In this moisture equilibrium data (adsorption and desorption) of chick pea flour were determined using static gravimetric method of saturated salt solution at 4° storage temp: 10, 20, 30, 40° C. The range of aw for each temperature was between 0.11 and 0.85. Equilibrium moisture content decreased with the increase in storage temperature at any given aw.

Khatoon and Prakash in 2006 conducted a study on the nutritional quality of microwave cooked and pressure cooked legumes. They found that the range of nutrient in 100g of cooked samples one as follows: moisture - 62.8 - 69.79%, protein- 14.7 - 24.3g; fat- 0.9 - 5.9 g, 1.7 - 4.6g. They also stated that the cooking methods did not affect the nutrient composition of chick pea, however altered the dietary fiber. in-vitro starch and protein digestibility of pressure cooked samples were higher than microwave cooked[24,25].

Saxena et.al. conducted a study on the nutrients and anti nutrients in chick pea cultivars after soaking and pressure cooking. Results show that soaking for 12 hours in distilled water decreased protein content from 22.4- 20.9% in different cultivars and pressure cooking at 15 lb/in² pressure for 15 and 30 minutes following soaking for 12 hours in distilled water results a further decrease in protein content[14].

Adawy conducted a study on the nutritional composition and anti nutritional factors of chick pea undergoing different cooking methods like boiling, autoclaving, microwave cooking and germination. He concluded that cooking treatments and germination caused significant decrease in fat, total ash, carbohydrate fractions, anti-nutritional factors, minerals and B-vitamins. Germination resulted in greater retention of all minerals and B- vitamins compared to cooking treatments. He also stated that microwave cooking appears to be the best alternative for legume preparation in house hold

purposes[26].

Niti et.al., in 2002 studied the effect of various home procuring methods on the nutritive quality of legumes. Results show that the decrease in total protein content was observed on germination, pressure cooking and frying but increases the digestibility, deduction in carbohydrate content by soaking and heat processing was also observed.

Total reducing sugar content was increased on soaking but cooking decreases it content.

Sharareh conducted a study on the effect of various processing conditions on nutritional qualities of legumes. She concluded that peas are a good source of complex carbohydrates, dietary fiber and protein are low in fat and sodium. She highlighted the importance of cooking method to improve textures palatability and digestibility of the legumes and also described some important methods of cooking like boiling, roasting, electric heating, microwave radiations, micronization and extrusion cooking. In the reference of cooking and soaking she concluded that flatulence effect of beans can be reduced by simply boiling them for a couple of minutes, soaking them for an hour in water and then changing water.

Removal of flatulence factors (galacto oligosaccharides) from chick pea (Cicer arietinum) by germination and mold fermentation was also studied. In this study the flatus producing factors and galacto oligosaccharides were identified in chick pea (Cicer arietinum var. Pant G-114) by descending paper chromatography. Four sugars galactose, sucrose, raffinose and stachyose were identified of which the latter two were galactose-containing sugar. Traditional methods like germination and fermentation by mold (Rhizopusoligosporus NRRL-2710) were employed to reduce galacto oligosaccharide level in seeds, while increasing its digestibility. Germination of seeds for 72 hrs. resulted in almost complete removal of galactose- containing sugars along with the accumulation of sucrose during early stages of germination[27].

Among the various methods available to reduce the plasma cholesterol, the most suitable would be the one involving a change in dietary regimens. Bengal gram (Cicerarietimum) which forms an important part of Indian diets has been reported to be more hypercholesterolemic than other pulses[28,29].

In another study the physico chemical, cooking, textural and roasting characters of chick pea was evaluated. Seeds of 5 desi (PBG-1, PDG-4, PDG-3, GL-769, GPF2) and one kabuli type (L-550) chick pea cvs. were evaluated for above properties. The results allowed that cultivars having higher seed weight and volume had higher cooking time, swelling and hydration capacity. The inter-relationships between cooking characteristics of seeds from different cvs. showed a significant negative correlation of puffing capacity, puffing index, expansion index with seed weight, volume, swelling and hydration capacity. The kabuli type chickpea cv. had poor roasting and textural properties. Cooking time had a positive correlation with hardness and gumminess and a negative correlation with springiness[30].

Adaway conducted a study on the effect of cooking treatment (boiling, auto-claving and microwave cooking) and germination on the nutritional composition and anti nutritional factors of chick pea. The results show that the cooking treatment and germination caused significant decrease in fat, total ash, carbohydrate fraction, anti- nutritional factor, minerals and vitamin-b group. Germination was less effective than cooking treatment in reducing anti nutritional factors. Based on these results microwave cooking appears to be the best alternative for legume preparation in household[26].

Another study conducted on effect of cooking on the protein quality of chick pea concluded that heat treatment produced a decrease of methionine, cysteine, lysine, arginine and tyrosine. The highest reductions being in cysteine (15%) and lysine (13.2%). Protein content declined by 3.4% and in vitro protein digestibility improved significantly from 71.8% 83.5%. After cooking the decrease of lysine was higher in the cooked chick pea seeds. The structural modification in globulin during heat treatment seems to be the reason for the increase in protein digestibility although the activity of proteolysis inhibitors in the albumin fractions was not reduced results suggests that appropriate heat treatment may improve the digestibility of chickpea protein.

Umaid Singh and associate studied the cooking quality and nutritional attributes of newly developed cultivars of chickpea and concluded that kabuli (cream seed coat) may be generally preferred to desi (brown seed coat) cultivars in terms of cooking time and sensory properties. Calcium content is noticeably higher in desi than in kabuli cultivars where as magnesium, iron, copper and zinc showed no definite trends. Levels of lysine, threonine, methionine and cysteine of these genotypes were within the range of FAO values. The biological value of protein was higher for kabuli than for desi although there was no difference in protein and amino acid of these varieties. Kabuli contained more utilizable protein and may be nutritionally better than desi.

Sood et.al., 2003 studied the effect of processing and cooking on the sugar content of chickpea cultivars HPG-17 and C-235. Different treatments like roasting, soaking germination, parching, pressure cooking and solar cooking were done and total reducing and non reducing sugars were estimated in both These sugars varied non-significantly with respect to various treatments. The sugar content was found to be more in HPG -17 than C-235 and HPG-17 was found to be better than C-235 variety.

A research on the grain quality concluded that the chickpea and pigeon pea are rich in protein but some anti nutritional factors reduced the absorption of nutrients. They can be reduced by simple heat treatments like pressure cooking and microwave cooking[11].

Develop Products by Incorporating Chickpea

Ahmed and associate conducted a research on the biochemical and sensory evaluation of carotene and protein enriched biscuits and found that addition of 18% chick pea flour/ pigeon pea flour to wheat flour biscuits increased the protein content from 10% in market biscuits to 13% in supplemented samples. Addition of carrot powder at 10% (Vitamin A content of 426 RE/100g) to flours incorporated for chick pea supplemented biscuits recorded best preference among people and were significantly (PO.05) better than pigeon pea biscuits. The essential amino acid lysine was significantly (PO.05) improved from 1.26g/100g protein in conventional market with to 3.39g/ 100g protein in chick pea biscuit which higher in vitro protein digestibility (95%) had compared to market biscuits (82.5). The calculated protein efficiency ratio of chick pea biscuits (1.6) was significantly (PO.05) higher than that of market biscuits (0.81).

Thakur and Modal in 2003 conducted a study to investigate the dehydration process of green nature 4D chick pea to use it as a snack food. Sample of green chick pea seeds as well as pods were blanched and dried. The dried chick pea seeds and pods were reconstituted within the range of 60-80 percent. The dehydrated chick pea seeds and pods were organoleptically analyzed for mastication. Studies shows that salt blended dried chick pea pods were preferred more to masticate than dried chick pea pods alone[31].

Ramaswamy and Susheesannia tried to experimentally study the effect of the concentration of butter made from chick pea (Cicer arietinum L) flour on the quality of a deep fried snack and concluded that boondi prepared with 40% solids in the batter had more desirable qualities such as uniformity, crispness and fried grain aroma. Those prepared from batters < 40% solids were more porous, oily and less uniform in shape and gave rise to tear drop shaped boondi. At >40% concentration of solid boondis were more firm and less porous with a slight sandy note although the fat content was low. Principal component analysis revealed that among the six commercial samples three samples were found to be close to optional quality while the other three were less satisfactory. Positive correlations were found for porosity, oily notes and fat content and negative correlations for firmness.

Pedrosillano and Sinoloa researched in 2006 on the effects of the chick pea variety on improving the nutritional value of bread and bakery products and concluded that legume flours, due to their amino acid composition and fiber content are ideal ingredients for improving the nutritional value of bread based bakery products. The influence of the total or partial replacement of wheat flour by chick pea flour on the quality characteristics of two kinds of cake was analysed. The effects of chick pea variety and the kind of flour used (white or whole) was also considered. Volume, symmetry, aroma, crust and crumb diminished on increasing the amount of chick pea flour. The replacement of wheat flour by chick pea flour also induced an increase in the initial firmness but cohesiveness and resistance diminished increasing the tendency to hardening.

Rababah and Ereify in their study evaluated the effectiveness of substituting different concentrations of chick pea, flour, broad, bean flour or isolated soy protein (ISP) on the physics chemical and sensory properties of biscuits. Results indicated that fortification decreased spread factor compared with the control. Sensory and instrumental color results showed that fortification with chickpea increased the lightness while fortification with broad bean or ISP increased the darkness. Descriptive results showed that as the fortified ISP and chick pea ratios increased most of liking area about right (JAR) attributes decreased, while they increased for fortified broad beans. Descriptive analysis also showed that 3% of fortified ISP and chick pea or 12% of broad bean provided the best quality ratio within each type of fortification. Consumer results showed that no significant differences of fortification of soy protein isolate (3%), chick pea (3%) or broad bean (12%) and the control. Sensory quality attributes of drinking and JAR were formed except for overall flavour and colour, fortification of chick pea and broad bean flour as well as ISP could be used in production of high protein biscuits[32].

Another study was conducted by Rababah and Ereify on the ability of chick pea flour to enrich pasta products (e.g., lasagne). On addition the influence of protein and other components upon the biological properties of the dough and the cooking quality of the wheat chick pea blends were determined. Supplementing lasagna with 5-20% W/W (weight/weight) chick pea flour improves the physical characteristics of dough which achieves optimum strength and extensible properties thus allowing the lasagna to maintain a firm and elastic form. Organoleptical properties (color, flavour and over all acceptability) improved with a low proportion of chick pea flour especially for 5% W/W substitution. So durum wheat can carry 5-10% (W/W) of chick pea flour and still meet the specification of pasta products in terms of firmness, cooking quality and sensory evaluation[32].

Nutritional Reviews and Health Implications

Regular intake of 40 g of chick pea has been shown to reduce low density lipoprotein cholesterol quickly. Geminated seeds are often recommended to prevent scurvy. Among the food legumes chick pea has the most hypo- cholesterolemic agent i.e. lowers blood cholesterol levels. Germinated chick pea was reported to be effective in controlling cholesterol level in rats[34,35].

Rababah and Ereify studied the improved effects of diets of chick peas on rats V/S cereal diet. Dyslipidemia and insulin resistance were examined. Chick pea treatment also induced a favourable plasma lipid profile reflecting decreasing TAG (total available glucose), LDL cholesterol (LDL-C), HDL-cholesterol levels (P<0.05). HFD (high fat diet) fed rats had higher TAG concentration in muscle and liver whereas the addition of chick pea to the HFD drastically lowered TAG concentration (muscle 39%, liver 23%). The activities of lipoprotein lipases (LPL) in eipdidynal adipose tyrosine and hepatic TAG bypass in liver recorded a 40% decrease and 23% increase respectively in HFD rats compared with those in NFD

rats. Dieting chick peas completely normalized the levels. Furthermore, chick pea- treated obese rats also showed a markedly lower lipids and <P< m RNA content in epididynal adipose tissue. An insulin tolerance test, oral glucose tolerance test showed that chick peas significantly improved insulin resistance and prevented postprandial hyper glycerin and hyper insulin induced by the chronic HFD. The present finding provides a rational basis for the consumption of chick peas as a functional food ingredient which may be beneficial for correcting dyslipidemia and preventing diabetes[33,34].

Chickpea are a valuable source of slowly digestible starch, which is beneficial to health as it results in relatively low post-meal blood glucose. Hawkins and Johnson studied the in vitro carbohydrate digestibility of whole-chickpea and chickpea products to determine levels of slowly digestible starch, rapidly digestible starch (RDS), resistant starch total starch and rapidly available glucose (RAG) of Whole chickpea and Chickpea products.

Nutritional and Sensory Evaluation

Most of nutritionists agree that on an average it is beneficial to plan daily intake fiber content of 30gm fiber on 12g/100Kcal by a normal healthy person. The proportion of soluble to insoluble fiber should be 1.2 and the intake is preferred to be through diet made up of varied sources preferred[18].

It is advisable to derive 50% each of the daily requirements from cereals, fruits and vegetables sources. For better effect American diabetes association (1994) has recommended 25/38g of fiber per day for person suffering from diabetes.

Sensory Evaluation

When the quality of food product is assessed by means of human sensory organs, the evaluation is said to be sensory of subjective or organoleptic. Every time food is eaten a judgment is made.

Sensory quality is a combination of different sense of perception combination into play in choosing and eating food. Appearance, flavour and mouth feel decides the acceptance of the food.

The effective characteristic is not a property of the food, but the subject's reaction to the sensory quality of foods. The reaction is highly conditioned by a variety of physiological and social factors and plays a vital role in the final analysis, in the acceptance and preference of the foods[27].

MATERIALS AND METHODOLOGY

The present study was undertaken to analyze nutritional composition of chickpea, develop various chickpea products and evaluate acceptability of these products. The methodological aspects in which this study was conducted are as follows:

- Selection of samples
- Preparation of powder
- Bio-chemical estimation of nutrients in the selected samples
- Development of value added chickpea based products
- Sensory evaluation of the products
- Calculation of nutrients in the developed products
- Statistical analysis of the results

Selection of Sample

Selected chick pea seeds for experimentation were procured on the basis of variety (desi and kabuli) available in the market. Out of the two, desi type chickpea was selected for the present study. The chickpea was purchased from a general store in Jaipur. Chick pea comes under the food group of pulses and legumes which is a common food source for economically weaker section. The selected variety i.e. desi was divided into four groups:

Group I: Whole (raw)

Group II: Roasted

Group III: Soaked for 10hrs and germinated for 24 hrs.

Group IV: Soaked for 10 hrs and germinated for 48 hrs.

Roasting

Roasting was done in a wok at medium heat till the chickpea sample was light pink in color and gave a good aroma.

Soaking

Common household method for soaking was done. Chick pea samples were soaked for 10 hrs. at room temperature in aqua guard purified water.

Germination

The soaked samples were then germinated at room temperature with a variation in timing for 24 hrs. and 48 hrs.

Drying

The samples were dried in a hot oven at 80°C for 24 hrs and then taken for biochemical analysis.

Preparation of the sample

The dried chickpeas from all the groups were grinded to make a powder. 100 g of the powdered sample was passed through sieve (1.00-mm) and transferred to a well stopper glass bottle.

Biochemical Estimation of Nutrients in the Selected Samples

The aim of biochemical estimation was to evaluate altered state nutrients in the raw and processed chick pea sample by using the standard biochemical techniques. The quantitative analysis of protein, fat, ash, crude-fiber, moisture, carbohydrate, iron, phosphorous, calcium, zinc, folic acid sodium and potassium was done in accordance to Indian Standard Method Tests for Animal feeds and Food Stuffs.

Development of Value Added Products and Standardization of Recipes

By incorporating chickpea (raw) powder four products were developed. Khakra was developed using chickpea and wheat flour whereas other three products formulated using refined flour and chickpea flour were bread, pizza-base and bun. Different cooking methods were used; khakra was cooked on tawa while the others were baked.

The products were chosen keeping in mind the following reasons:

- Are highly popular among people of all age groups
- Have a good shelf life
- High palatability
- Easy to carry and store

Recipes were selected keeping in mind the target group i.e. all age groups. Due to change in life style people are consuming more of market based foods. These products are low in protein and fiber, high in carbohydrate and calories and are reported to be a major cause of life style diseases like obesity, diabetes, dyslipidemia and cardiovascular diseases.

Market available products were coded as:

1. Khakra A1
2. Bread B1
3. Pizza base C1
4. Bun D1

The developed products were coded as:

1. Khakra A2 (Wheat flour 60%, Chickpea Flour40%)
2. Bread B2 (Refined flour70%, Chickpea flour 30%), B3 (Wheat flour 30%, Refined flour 40%. Chickpea flour 30%)
3. Pizza base C2 (Refined flour 70%, Chickpea flour 30%), C3 (Wheat flour 30%, Refined flour 40%, Chickpea flour 30%)
4. Bun D2 (Refined flour 70%, Chickpea flour 30%), D3 (Wheat flour 30%, Refined flour 40%, Chickpea flour 30%)

A. Khakra: This product was developed by incorporating chickpea flour with wheat flour (Tables 3 and 4).

Table 3: Recipe: Basic-Ingredients

Ingredients	Amount
Wheat flour	100g
Salt	Pinch
Water	30-40ml
Oil	2.5ml

Table 4: Recipe: Developed-Ingredients

Ingredients	Amount
Wheat flour	60g
Chickpea flour	40g
Salt	Pinch
Water	30-40ml
Oil	2.5ml

Method

- Oil and salt were added to wheat flour.
- It was kneaded into soft dough using water and rested for 5-10minutes.
- Then the dough was divided into small balls.
- With a rolling pin they were rolled on a board into very thin chapattis.
- Meanwhile a tawa was heated on gas burner.
- One of the rolled chapatti was then roasted on tawa till half done on medium flame.
- This chapatti was then removed from heat and cooled for 2 minutes.
- After cooling it was roasted again on very low flame till crisp.
- The other chapattis were made in the similar way.

B. Bread: Value added product was made using chickpea flour. Further variations were done in amount and type of flours. Wheat flour, refined flour and chickpea flour were used to make different breads (Table 5)

Table 5: Proportion of refined flour, wheat flour, and chickpea in developed products

Products	Wheat flour	Refined flour	Chick pea
B2	70% (210g)	-	30% (90g)
B3	40% (120g)	30% (90g)	30% (90g)

Table 6: Recipe: Basic-Ingredients

Ingredients	Amount
Refined flour	300g
Sugar	20g
Salt	7g
Water	210ml
Oil	7g
Yeast	7g

Method

- In a vessel sugar, salt, yeast was dissolved in water.
- They were then mixed well in a food processor jar using a kneading blade
- To this refined flour was added.
- This mixture was kneaded in a food processor for 10-12 minutes with the oil being added little by little.
- The dough was then taken out from the processor, rolled and kept covered with moist cloth for fermentation till it doubled in volume.
- The kneaded flour was then rolled into a chapatti and its edges were folded.
- This was placed in a greased mould. On the upper surface slight marks were made with a knife and some oil was applied.
- Finally it was baked at 200°C for 40 minutes in a preheated oven and sliced after cooling.

C. Pizza base: This product using chickpea flour was developed and variations were done in proportion and type of flour (Table 7).

Table 7: Proportion of refined flour, wheat flour, and chickpea in developed pizza base

Products	Refined flour	Wheat Flour	Chick flour pea
C2	70% (210g)	-	30% (90g)
C3	40% (120g)	30% (90g)	30% (90g)

Table 8: Recipe: Basic-Ingredients

Ingredients	Amount
Maida	300g
Sugar	20g
Salt	7g
Oil	7g
Water	215ml
Yeast	7 g

Method

- In a vessel sugar, salt and yeast were dissolved in water and mixed well in a food processor jar using a kneading blade.
- To this, refined flour was added and kneaded in the processor for 10-12 minutes, with the oil being added little by little.
- The dough was then taken out, rolled and kept covered with a moist cloth for fermentation till it doubled up in volume.
- Again it was kneaded lightly with hands and 15 balls were made.
- The balls were kept covered with moist cloth for 15 minutes.
- Meanwhile the electric oven was preheated at 200°Cand a baking tray was greased.
- On a rolling board with a rolling pin the balls were rolled into discs of diameter 5-6inches.
- They were then pricked with a fork, placed in the greased tray and baked in oven for 15-20 minutes till upper surface became slight pink in color.

D. Bun: Using chickpea flour value added product was developed. Then variations were done in amount and type of flour (Table 9).

Table 9: Proportion of refined flour, wheat flour, and chickpea in developed buns

Products	Refined flour	Wheat Flour	Chick flour pea
D2	70% (210g)	-	30% (90g)
D3	40% (120g)	30% (90g)	30% (90g)

Table 10: Recipe: Basic-Ingredients

Ingredients	Amount
Maida	300g
Sugar	20g
Salt	7g
Oil	7g
Water	215ml
Yeast	7g

Method:

- Water was taken in a vessel and sugar, salt, yeast were dissolved in it. They were mixed well in a food processor jar using a kneading blade.
- Refined flour was added and kneaded in the processor for 10-12 minutes. Along with this oil was added little by little.
- The dough was then taken out, rolled and kept covered with a moist cloth for fermentation till it doubled in volume.
- A baking tray was greased and electric oven was preheated at 220°C for 10 minutes.
- Again the flour was kneaded lightly and balls were made.
- These balls were kept on the greased tray; some oil was applied on the upper surface and baked in oven at 220°C for 25-30minutes till the upper surface was brown in color.

Sensory Evaluation of the Products

Standardization of chickpea products were carried out through sensory evaluation. Sensory evaluation is concerned with the physical and chemical properties of the stimulus by the reaction it produces in humans acting as a measure apparatus. Chickpea products were evaluated for their sensory characteristics like colour, flavour, texture, taste, quality and overall acceptability by selected panel of judges.

The seven products formed were analyzed through sensory analysis and best products in each category were selected.

The panel was selected on the basis of threshold test. To check their perception for taste each of them were given 2 types of solutions to taste.

- Sugar solution (sucrose) prepared in 2 concentrations:

  0.4g and 0.6g/ 100 ml solution

- Salt solution (sodium chloride) in 2concentrations:

  0.08g and 0.15g / 100ml solution

Besides these solutions, each set had one glass of plain water. The panel members were given these solutions in a row in similar set of disposable glasses. They were then asked to compare the respectable concentrations in increasing order of sweetness or salinity and jot these observations in the score card given to them. Out of 10 members called to judge this threshold test 6 passed the test. Other factors like experience, knowledge, willingness, interest, availability and sincerity on the part of panel members were also considered. To evaluate the products made for the present study the six panel members which were enlisted (appendix) comprised of staff members of the International College for Girls, Jaipur.

For assessing the palatability and acceptability of chickpea products, score cards were developed on the basis of certain qualities generally looked for the in the product. These include color, flavour, taste, texture, acceptability (appendix). Three types of score cards were used:

1. Ranking test (for taste, colour, flavour, texture, quality)

2. Numerical scoring test

3. Hedonic scale test

The developed chickpea products were served to the judges separately in similar plates with different codes. Along with this necessary accessories were given to them to conduct the evaluation in an undisturbed environment. The objectives of the study were explained to the judges before the evaluation. All the panel members were asked to score the product on the basis of the given score cards. The mean scores for each of the sensory character as well as each of the products were calculated from the score cards in the form of percentage.

Statistical Analysis

The results of bio-chemical nutrient analysis and sensory evaluation were analyzed statistically by ANOVA (Analysis of Variance).

Value Added Developed Products

Figure 4: Khakra (A2)

Figure 5: Bread (B2, B3)

Figure 6: Pizza base (C2, B3)

Figure 7: Bun (D2, D3)

Figure 8: A1 Khakra (Wheat flour), A2 Khakra (Wheat flour, chickpea flour)

Figure 9: Bread B1, (refined flour), B2 (refined flour chickpea flour), B3 (wheat flour, refined flour, chickpea flour)

Figure 10: Pizza base C1 (refined flour). C2 (refined flour, chickpea flour), C3 (wheat flour, refined flour chickpea flour)

Figure 11: BUN D1 (refined flour), D2 (refined flour, chickpea flour), D3 (wheat flour, refined flour, chickpea flour)

RESULTS AND DISCUSSION

The objectives of the present study were:

- Nutrient analysis of whole (raw), roasted, soaked and germinated chick pea
- Development of new products using raw chick pea
- Sensory evaluation of the newly developed products by a panel of six judges
- Statistical analysis of the nutrient analysis and sensory evaluation by applying test ANOVA

Chickpea was subjected to various types of treatments, so it was divided into four groups.

Group-1: This group was analyzed raw for its nutrients.

Group-II: The chickpea in this group were roasted and nutrients analyzed.

Group-III: This group was soaked for 10 hrs. then germinated for 24 hrs and nutrients analyzed.

Group-IV: In this group chickpea were soaked for 10 hrs. germinated for 48 hrs and nutrients analyzed.

Bio-chemical analysis of nutrients was done according to Indian Standard Methods of Tests for Animal Feeds and Feeding Stuffs.

Table 11 : Analysis of chickpea at different conditions

Attributes	Whole (I)	Roasted (II)	Soaking 10 hrs Germination (24 hrs) (III)	Soaking 10 hrs Germination (48 hrs) (IV)
Moisture	9.48%	4.02%	-	-
Ash	1.84%	1.57%	2.27%	2.27%
Crude Fiber	7.63%	6.05%	7.57%	7.57%
Acid insoluble ash	0.10%	0.08%	0.06%	0.06%
Fat	5.32%	3.76%	3.93%	3.93%
Protein	25.89%	26.59%	27.89%	28.42%
Carbohydrate	60.37%	61.95%	60.28%	57.38%
Calcium	0.45%	0.47%	0.45%	0.45%
Phosphorous	0.07%	0.07%	0.07%	0.07%
Iron	0.01%	0.01%	0.01%	0.01%
Zinc	0.01%	0.01%	0.01%	0.01%
Folic Acid	0.01%	0.01%	0.01%	0.01%

From the above table it is evident that Moisture content at 105°C was maximum i.e. 9.48% in group I and minimum in group II. This is due to the effect of roasting.

Ash at 600°C decreased from 1.84% in group I to 1.57% in group II. The reason may be attributed to the effect of roasting. Similar results are reported in studies by Allial et.al. (1999).

Crude fiber content found to be 7.63% was maximum in group I, followed by 7.57% in group III and 7.51% in group IV. With the advancement in time of germinating hours, crude fiber decreases. Soaking and germination have been reported to cause this decrease in similar studies by Badshah and Sattar (1991).

Acid insoluble ash was 0.01% in group I whereas it decreased to 0.08% in group IV. This is due to soaking and germination.

Fat content was found to be maximum in raw (group I) i.e. 5.32%.It decreased to 3.76% in roasted (group II), 3.93% in 24 hrs. germination (group III) and 3.99% in 48 hrs. germination (group IV). Roasting reduced the fat content to a greater extent in comparison to soaking and germination. Similar results are reported in studies by Adawy (2002).

Protein in group IV i.e. 28.42% was maximum and minimum in group I i.e. 25.89%. Similar results are reported in studies by Badshah and Sattar (1999). This marked increase may be due to activation of enzymes on soaking and germination and most of the enzymes are proteins.

Soaking and germination have caused a significant decrease in

carbohydrate content of chickpea from 60.37% in group I to 57.68% in group IV. The studies by Frias et.al. (1999) support this result.

There was a negligible decrease in the calcium content from 0.45% in group I, to 0.47% in group III and 0.48% in group IV. Phosphorous also showed a slight decrease from 0.07% in group I, II, III to 0.08% in IV .These results are similar to those reported in studies by Nestares et.al. (1999).

The effect of roasting, soaking and germination had no effect on the zinc content .It was 0.01% in all groups.

Iron and folic acid contents were same 0.01%in group I. II, III. There was a negligible change 0.04% for iron and 0.03% for folic acid in group IV.

New products like khakra, bread, pizza base and bun were developed using raw chickpea in comparison to already existing market products. These products were coded as:

Khakra - A2 (60%Wheat flour, 40% chickpea flour).

Bread - B2 (70% refined flour, 30% chickpea flour). B3 (40% refined flour, 30% wheat flour, 30% chickpea flour).

Pizza-base - C2 (70% refined flour, 30% chickpea flour). C3 (40% refined flour, 30% wheat flour, 30% chickpea flour).

Bun - D2 (70% refined flour, 30% chick flour), D3 (40% refined flour, 30% wheat flour, 30% chickpea flour).

Sensory evaluation of the newly developed products was done by a panel of six judges in terms of color, texture, taste, salt content, quality, overall acceptability, numerical scoring, difference of the developed products from the market products and nutrition composition. The scores given by the judges to the above performances were analyzed using ANOVA.

Table 12: Performance: Texture

Code	Very good	Good	Fairly good	Fair
A 2	-	81.60%	-	-
B2	-	82.50%	-	-
B3	85.33%	-	-	-
C2	-	-	80.83%	-
C3	-	-	80.83%	-
D2	-	83.33%	-	-
D3	88%	-	-	-

A2 - Wheat flour 60%, chickpea flour 40%
B2 - Wheat flour 70%, chickpea flour 30%
B3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
C2 - Wheat flour 70%, chickpea flour 30%
C3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
D2 - Wheat flour 70%, chickpea flour 30%
D3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

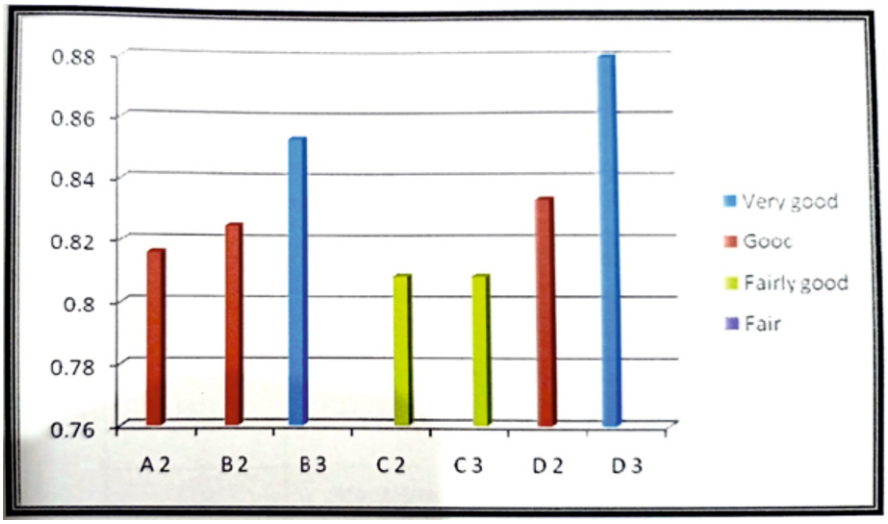

Figure 12: Texture Scores

For texture the scores of the judges were categorized as very good, good and fairly good:

Very good	-	85-90%
Good	-	80-85%
Fairly good	-	75-80%
Fair	-	Below 75%

The table 12 and figure 12 show that in terms of texture D2 scored highest 90% followed by B3 with 89.16% score. They were categorized as very good. D3 with 85% score.
A2 and B2 with 84.16% each were categorized as good. C2, C3 with 81.66% and 79.16% respectively were categorized as fairly good in texture. As the fiber content increases there occurs a change in texture still the developed products obtained good scores.

Table 13 : Performance: Quality

Code	Superior	Equal	Inferior
A2	100%	-	-
B2	66.66%	33.33%	-
B3	83.33%	16.66%	-
C2	33.33%	33.33%	33.33%
C3	50%	16.66% %	33.33%
D2	83.33%	-	16.66%
D3	100%	-	-

A2 - Wheat flour 60%, chickpea flour 40%

B2 - Wheat flour 70%, chickpea flour 30%

B3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

C2 - Wheat flour 70%, chickpea flour 30%

C3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

D2 - Wheat flour 70%, chickpea flour 30%

D3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

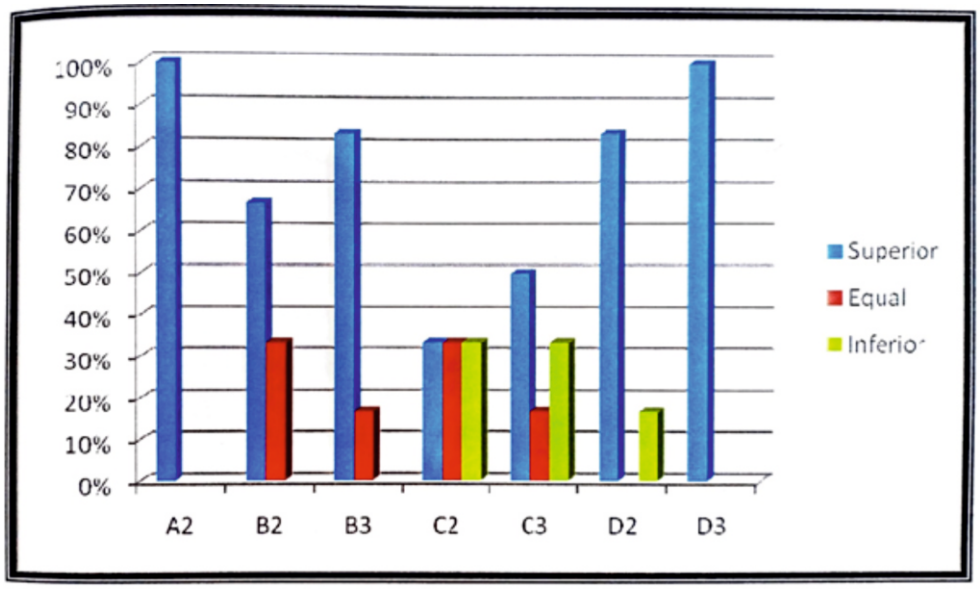

Figure 13: Quality Performance

The scores were graded into superior, equal and inferior as compared to their market counterparts (A - khakra, B - bread, C - pizza base and D - bun).
The table 13 and figure 13 indicate that A2 and D3 were found to be superior in quality by 100% judges. B2 was ranked superior by 66.66% judges while 33.33% stated it to be equal B3 was judged superior by 83.33% judges rest 16.66% graded it equal in quality.C2 was found to be superior by 33.33% judges. 33.33% said it was equal while the remaining 33.33% found it to be inferior.C3 was categorized superior by 50% judges, equal by 16.66% and inferior by 33.33%.D2 was grouped in superior category by 83.33% judges and inferior by 16.66% judges.

Table 14: Performance: Salt content

Code	Optimum	Low	High
A2	100%	-	-
B2	33.33%	66.66%	-
B3	33.33%	66.66%	-
C2	50%	50%	-
C3	33.33%	67%	-
D2	66.66%	33.33%	-
D3	83.33%	16.66%	-

A2 - Wheat flour 60%, chickpea flour 40%
B2 - Wheat flour 70%, chickpea flour 30%
B3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
C2 - Wheat flour 70%, chickpea flour 30%
C3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
D2 - Wheat flour 70%, chickpea flour 30%
D3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

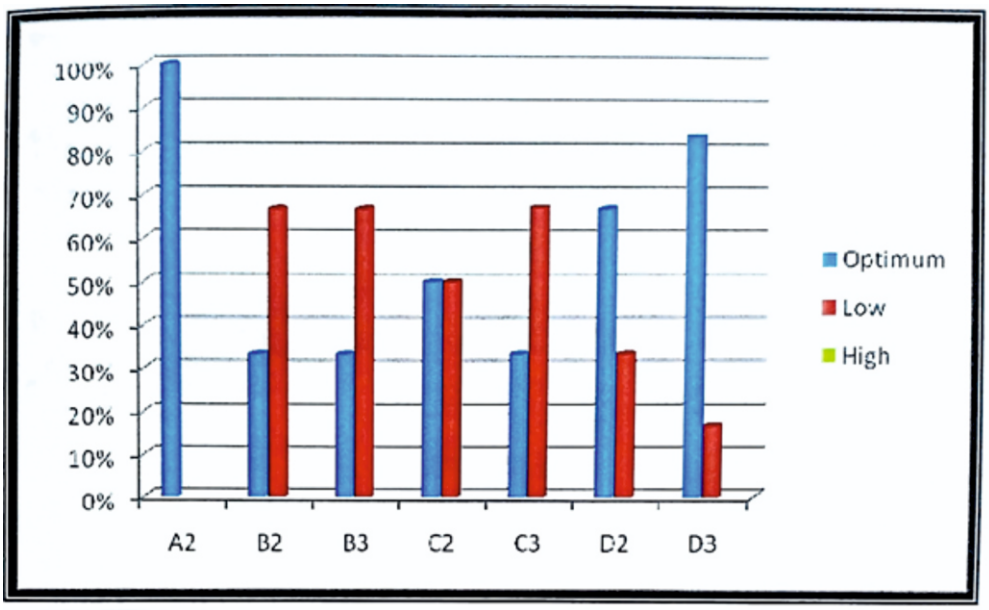

Figure 14: Comparative Assessment of Salt Content

Table 14 and figure 14 show that in case of A2 100% judges stated the salt content to be optimum. For B2 and B3, 66.66% judges found the salt content to be low whereas 33.33% found it to be optimum. In case of C2, 50% judges it was found to be low while the rest said it was optimum. Salt content in C3 was low for 67% judges whereas it was optimum for 33.33%. For D2 33.33% judges said it was low but 66.66% found it to be optimum. 83.33% judges said that in D3 it was optimum and only 16.66% reported it to be low.

Table 15: Performance: Colour

Code	Very Good	Good	Not Good
A 2	-	83.33%	-
B2	-	80.33%	-
B3	-	-	66.66%
C2	-	83.33%	-
C3	90%	-	-
D2	-	84.16%	-
D3	89.16%	-	-

A2 - Wheat flour 60%, chickpea flour 40%
B2 - Wheat flour 70%, chickpea flour 30%
B3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
C2 - Wheat flour 70%, chickpea flour 30%
C3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
D2 - Wheat flour 70%, chickpea flour 30%
D3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

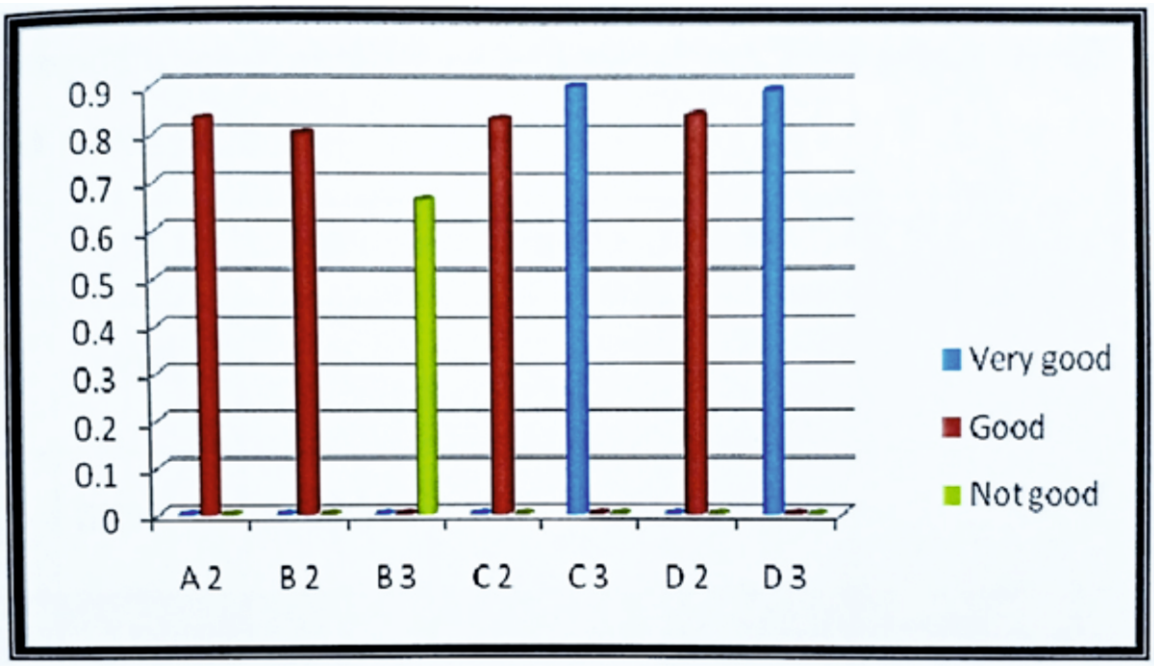

Figure 15: Colour Scoring

Color determines the quality of product at first step without even being tasted. Color was judged and scores were given. These scores were grouped into very good (85-90%), good (80-85%), not good (below 80%). Table 15 and figure 15 indicate that C3 scored 90% followed by D3 89.16% and were categorized as very good. A2, C2 with 83.33% score, B2 with 80.33% and D2 with 84.16% score were categorized as good.B3 was not good in color and scored lowest i.e., 66.66%.

Table 16: Overall acceptability of products on hedonic rating

Code	1	2	3	4	5	6	7	8	9
A2	-	100%	-	-	-	-	-	-	-
B2	-	67%	33.33%	-	-	-	-	-	-
B3	-	50%	50%	-	-		-	-	-
C2	-	16.67%	66.66%	16.67%	-	-	-	-	-
C3	-	50%	16.67%	-	33.33%	-	-	-	-
D2	-	33.33%	16.67%	16.67%	-	16.67%	-	-	-
D3	-	33.33%	50%	16.67%	-	-	-	-	-

A2 - Wheat flour 60%, chickpea flour 40%
B2 - Wheat flour 70%, chickpea flour 30%
B3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
C2 - Wheat flour 70%, chickpea flour 30%
C3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
D2 - Wheat flour 70%, chickpea flour 30%
D3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

Hedonic Scale:
1- Like Extremely
2- Like very much
3- Like moderately
4- Like slightly
5- Neither like nor dislike
6- Dislike slightly
7- Dislike moderately
8- Dislike very much
9- Dislike extremely

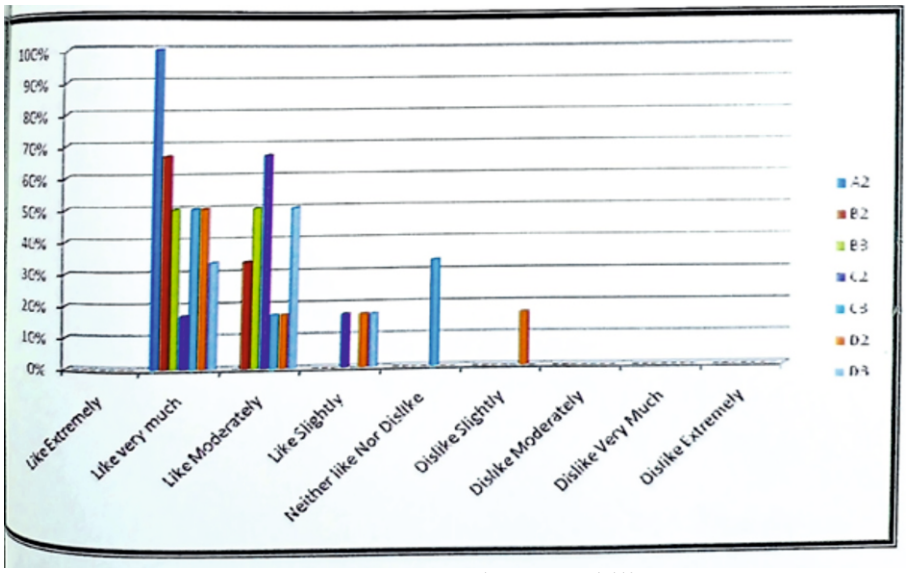

Figure 16: General Acceptability

General acceptability of any product is determined by the overall impression of sensory characters. The judges were asked to view the overall acceptability on hedonic scale. The results are depicted in the table 16 and figure 16. The table shows that the most acceptable product is A2 which was given hedonic rank 2 by all the judges. B2 was given hedonic rank 2 by 66.66% judges while 33.33% Judges gave hedonic rank 4 B3 was given rank 2 by 50% judges while the rest 50% grouped it in rank 4. C2 was given rank 2 by 16.66% judges while 66.66% judges gave rank 4.C3 was grouped in rank 2 by 16.66% judges but D2 scored hedonic rank 2 by 50% judges, 16.67% gave hedonic rank 3, 17% gave hedonic rank 4 and rest 16.67% grouped it in rank 5. D3 was given hedonic rank 3 by 50% judges.33% gave rank 2 and rest 16.66% gave rank 4.

Table 17: Difference of the developed product from the market product

Code	Slight	Moderate	Large	Equal	None
A2	16.66%	83.33%	-	-	-
B2	50%	-	16.66%	-	33.33%
B3	33.33%	50%	-	-	16.66%
C2	33.33%	50%	-	-	16.66%
C3	33.33%	50%	16.66%	-	-
D2	33.33%	67%	-	-	-
D3	33.33%	50%	16.66%	-	-

A2 - Wheat flour 60%, chickpea flour 40%
B2 - Wheat flour 70%, chickpea flour 30%
B3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
C2 - Wheat flour 70%, chickpea flour 30%
C3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
D2 - Wheat flour 70%, chickpea flour 30%
D3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

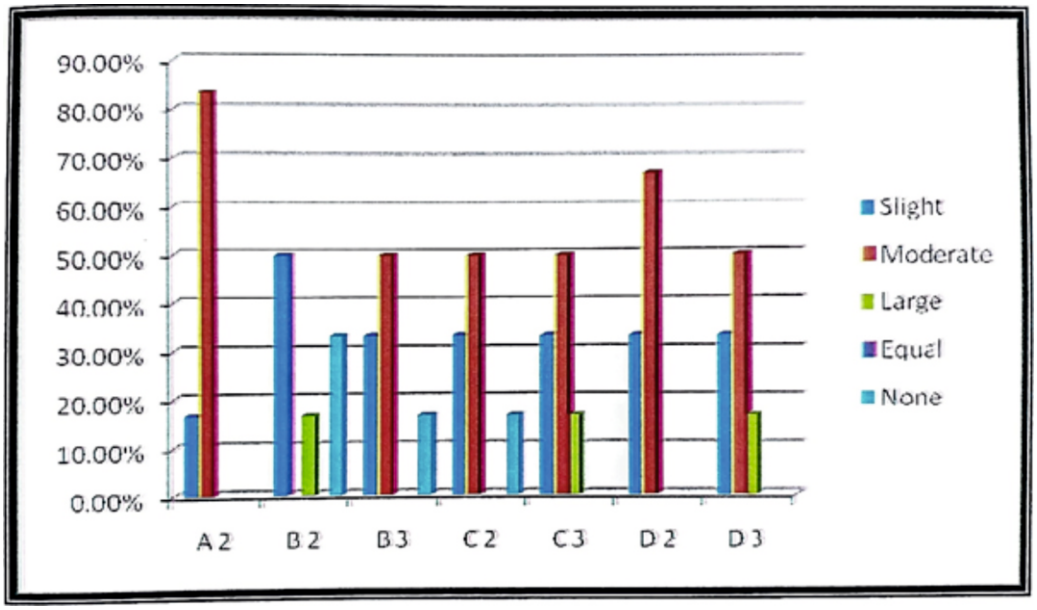

Figure 17: Comparison of Developed Product from Market Product

These developed products were then judged for their difference from the market products. (A - khakra, B - bread, C - pizza base, D - bun) as depicted in table 17 and figure 17. Sensory evaluation by the judges indicate that 16.67% judges graded A2 as superior to the market product and 83.33% said that there was a moderate difference from the market products. For B2 50% judges found a slight difference, 33.33% said there was no difference whereas 16.67% judges stated a large difference. B3 and C2 were judged and 33.33% found a slight difference, 50% found a moderate difference and 16.66% found no difference from their market counterparts.
In C3 and D3, 33.33% judges stated a slight difference, 50% said a moderate difference and 16.66% found no difference.
67% judges stated a moderate difference for D2 whereas 33.33% found a slight difference in the developed products.

Table 18: Numerical scoring of the developed product

Code	Rank 1	Rank 2	Rank 3	Rank 4
A2	88.33%	-	-	-
B2	-	87.50%	-	-
B3	90.83%	-	-	-
C2	-	-	-	85%
C3	-	87.50%	-	-
D2	-	-	86.66%	-
D3	-	-	86.66%	-

A2 - Wheat flour 60%, chickpea flour 40%
B2 - Wheat flour 70%, chickpea flour 30%
B3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
C2 - Wheat flour 70%, chickpea flour 30%
C3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%
D2 - Wheat flour 70%, chickpea flour 30%
D3 - Wheat flour 30%, refined flour 40%, chickpea flour 30%

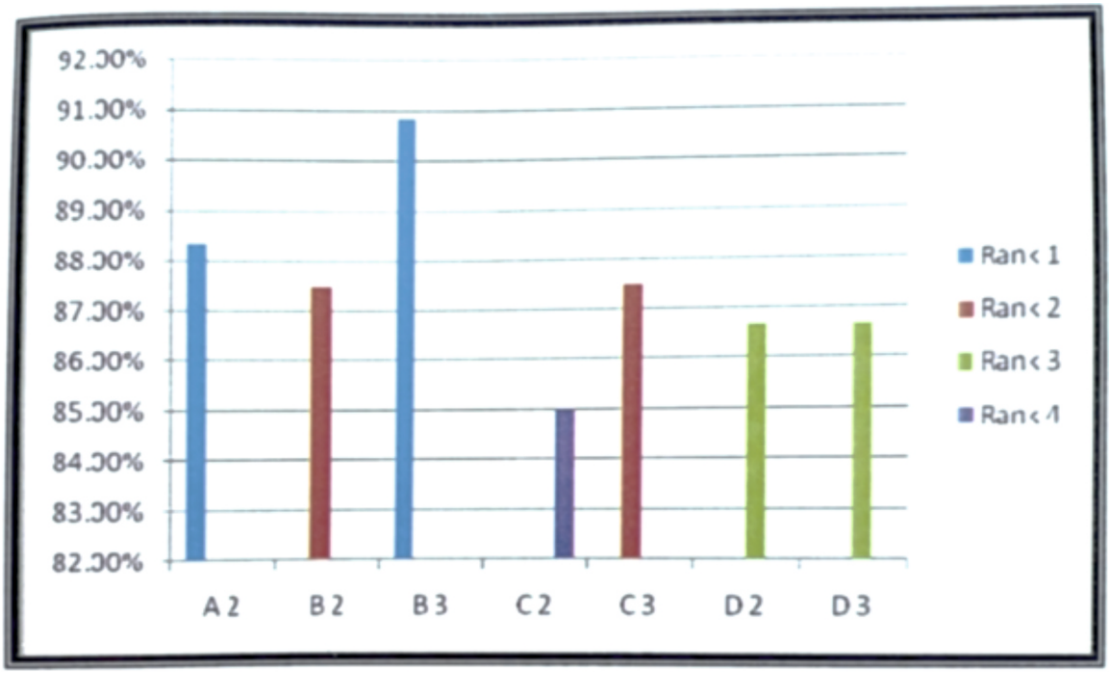

Figure 18: Ranking of Developed Product

Table 18 and figure 18 show that on comparing the developed products B3 scored 90.83% and was ranked 1st A2 scored 88.33% with rank 2nd, B2 and C3 ranked 3rd with 87.50% score each. D2 and D3 ranked 4th with 86.66% score whereas C2 scored least i.e., 85%. The low scores may be attributed to the incorporation of wheat and chickpea flour.

Statistical Analysis of the Results of Biochemical Analysis

Statistical Analysis was done on the data obtained. ANOVA (analysis of variances) was used for analysis (Table 19).

Table 19: Statistical analysis

Attributes	Whole (I)	Roasted (II)	Germination (24 hrs) (III)	Germination (48 hrs) (IV)	GM	SE	SD 5%	CoV
Moisture	9.47±0.0049	4.02±0.005	-	-	6.75±2.98	0.003	0.013	0.09
Ash	1.83±0.005	1.56±0.005	2.26±0.05	2.23±0.005	1.97+0.30	0.003	0.01	0.29
Crude Fiber	7.62±0.005	6.04±0.006	7.56±0.005	7.50±0.005	7.18±0.689	0.003	0.01	0.08
Fat	5.31±0.01	3.75±0.005	3.96±0.005	3.98±0.005	4.24±0.64	0.002	0.009	0.17
Protein	25.88±0.0076	26.58±0.006	27.89±0.007	28.41±0.005	27.19±1.03	0.0032	0.009	0.02
Carbohydrate	60.366±0.0133	61.94-0.0003	60.2750-0.0003	56.72±0.02	58.11±8.34	3.7501	-	12.91
Calcium	0.44	0.46±0.005	0.45±0.000	4.47±0.005	0.46±0.01	0.01	0.04	1.09
Phosphorous	0.06±0.005	0.07-0.00	0.06±0.005	0.08±0.00	0.07±0.006	0.0024	0.007	5.76
Iron	0.01±0.005	0.01±0.005	0.01±0.006	0.01±0.005	0.013±0.004	0.003	0.01	43.3
Zinc	0.01±0.005	0.01±0.005	0.01±0.005	0.01±0.005	0.013±0.004	0.003	0.01	43.3
Folic Acid	0.01±0.005	0.01±0.005	0.01±0.005	0.01±0.005	0.01±0.007	0.003	0.01	34.64

GM - General Mean

SE - Standard Error

SD 5% - Standard Deviation at 5%

CoV - Co efficient of Variance

The ANOVA for moisture revealed that moisture content in roasted sample is significantly less (4.03%) than the control (9.48%). The difference between treatments was significant.

The highest ash content observed in 10 hrs soaking 24 hr germination (group III) was 2.27% followed by 2.23% in 48 hr germination group (IV) then 1.83% in whole (group I) and 1.56% in roasted sample (group II). The difference between all treatments was significant.

Crude fiber was 7.62% in whole which was significantly higher than 7.56% in 24 hrs germination, 7.50% in 48 hrs germination and least in roasted. Difference between all the products was significant.

ANOVA on fat content revealed that fat was significantly higher 5.31% in whole (group I) than the other treatments which were 3.76%, 3.96%, 3.98% in roasted 24 hrs germination and 48 hrs germination showing significant difference between treatments.

Protein content analysis shows that it is significantly higher in

group IV (48 hrs germination) 28.49% respectively whereas it is low in other treatments Difference between all the treatments being significant.

Carbohydrate content is significantly higher in whole 60.36%, 61.94% in roasted and 24 hrs germination 60.27%, and56.72% in group IV revealing that difference between treatments was not significant.

ANOVA for calcium and phosphorous reveal that there is no significant difference for all treatments. There was no difference between the products for zinc, iron and folic acid.

Statistical Analysis of Sensory Evaluation

Mean Values for Different Characters

The analysis of variance reveals no significant difference between treatments for all characters. This indicates that numerical scoring of the products, color, texture, flavour, text, quality and overall acceptability of the products developed were at par to the market products.

Although there was no significant difference in the sensory evaluation of the developed products but the incorporation of wheat flour, chickpea flour in refined flour has increased the nutrient values.

Nutrient analysis of developed products

Nutrient Analysis of the prepared products was done in accordance with Nutritive Value of Indian Foods[36].

Table 20: Estimated nutrient content of market available (A) and developed khakra (A2)/ 100g

Products	Protein	Fat	Carbohydrate	Energy	Crude Fiber
A	12.1g	1.7g	69.4g	391Kcal	1.9g
A2	13.5g	2.g	66.7g	381.7Kcal	2.5g

The above table gives a detailed account of protein, fat, carbohydrate, energy and crude fiber of khakra. The prepared product was good in nutritive values i.e. higher in protein and fiber, low in carbohydrate and energy as compared to standard. This was due to the high nutrient content of chickpea flour.
The market available products bread, pizza base and bun were taken as B, C and D.
The nutrient values of these market available products are given in the following table.

Table 21: Estimated nutrient content of market available products bread, pizza base and bun (B, C, D)/ 100g

Products	Protein	Fat	Carbohydrate	Energy	Crude fiber
B/C/D	7.8g	63g	51.9g	245 Kcal	0.2g

Products B2, C2, D2 were prepared using 70% refined flour and 30% chickpea flour. The nutritive values are given in table/ 100 g

Table 22: Estimated nutrient content of Value added Products
Bread, pizza base, bun (Refined flour 70%, chickpea flour 30%)/ 100g

Products	Protein	Fat	Carbohydrate	Energy	Crude fiber
B2/C2/D2	12.8g	63g	70.1g	352 Kcal	1.36g

Products B3, C3, D3 were prepared using 40% refined flour, 30% wheat flour, 30% chick pea flour. The calculated nutritive values are as given in table.

Table 23: Estimated nutrient content of Value added products Bread, pizza base, bun (wheat flour 30%, refined flour 40%, chickpea 30%)/ 100 g

Products	Protein	Fat	Carbohydrate	Energy	Crude fiber
B3/C3/D3	13.2g	63g	68.5 g	349 Kcal	1.8g

The products B3/C3/D3 (bread, pizza base and bun) made using 40% wheat flour, 30% refined flour and chickpea flour 30% are nutritionally better due to high protein (13.2g), fiber (1.8g),carbohydrate (68.5g) and energy (349Kcal). B2, C2, D2 made of 70% refined flour and 30% chickpea flour have protein (12.8 g), crude fiber (1.35g), carbohydrate (70.1g) and energy (352.2 Kcal). The developed products A2, B3, C3 and D3 had more protein, fiber and low carbohydrate than the commercial products.

It may therefore be recommended that the use of these products instead of available products in daily life may be beneficial. This is because today people are consuming more of these market products in spite of the fact that they have low fiber and protein, but are rich in carbohydrate and calories. Fiber is particularly important in diet as lack of fiber causes obesity, constipation, diverticulous disease, cardio vascular diseases, diabetes etc.

The initiation of chickpea flour to substitute refined flour in the market products was because chickpea has many health benefits:

Heart disease: regular consumption may reduce risks of coronary heart diseases.

Dyslipidemia: Preliminary evidences suggest that consumption of chickpea may be beneficial for correcting dyslipidemia.

Cholesterol: The fiber in chickpea helps to decrease blood cholesterol levels by binding bile acids in the small intestine and preventing re-absorption. The introduction of chickpea in serum levels, total and low the diet resulted in lower density lipoprotein and cholesterol levels.

Protein: Chickpeas are an important source of macro nutrients containing twice the amount of protein compared to cereal grains.

Glycemic Index: In a study to determine the GI of foods, it was concluded that chick pea have a low GI 28-32.

Nutrients: Chick peas are an excellent source of essential trace element molybdenum. They are a very good source of fiber, folic acid, manganese and a good source of protein, as were as minerals such as iron, magnesium copper.

SUMMARY AND CONCLUSION

The present investigation was done on chickpea. Chickpea (Cicer arietinum) chosen for this study is a pulse crop belonging to family Leguminosae and has many health benefits. It is a valuable source of proteins, carbohydrates, minerals, vitamins and very high in dietary fiber. Therefore it is a healthy source of carbohydrate for people with insulin sensitivity or diabetes. Out of the two varieties desi and kabuli, desi was chosen for investigation.

Nutrient content of raw chickpea/100g:

Moisture- 9.8 gm, Protein-17.1 gm, Fat- 5.3 gm, Carbohydrate-60.9 gm, Fiber-3.9 gm, Energy-360 Kcal, Calcium- 202 mg, Phosphorous- 312 mg, Iron- 4.6 mg, Folic acid- 186.0mg, Zinc- 6.1 mg.

This study was undertaken under following heads:

- Procurement of raw chickpea
- Bio-chemical analysis of chickpea
- Development of products
- Sensory evaluation of the developed products
- Statistical analysis of the results of biochemical analysis and sensory evaluation using ANOVA (Analysis Of Variance)
- Nutrient calculation of the developed products

Variety chosen for Chickpea was procured from market in Jaipur. For bio-chemical analysis it was divided into four groups:

Group I - It was analyzed raw

Group II - Chickpea was roasted and nutrients analyzed

Group III - This group was soaked for 10 hrs. and germinated for 24 hrs. and nutrients analyzed

Group IV- It was soaked for 10 hrs. germinated for 48 hrs. and then analyzed for nutrients

Group II, III, IV were dried in electric oven at 80°C for 24 hrs. They were cooled, grinded and sieved. The powdered chickpea was then stored in bottles with names of their respective groups and analyzed

Bio-chemical analysis was done in accordance to Indian Standard Method Tests for Animal feeds and Food Stuffs for moisture, ash, crude-fiber, protein, carbohydrate, fat, calcium, phosphorous, zinc, iron and folic acid

Raw chickpea powder was used to develop products available in the market

Products were divided as:

Market available products;

Product made by using refined flour and chickpea flour in the ratio 70:30;

Products made by using wheat flour, refined flour and chickpea flour in the ratio 30:40:30;

Khakra, bread, pizza-base and bun were developed using the basic recipe;

In case of khakra wheat flour and chickpea flour were used in the ratio 60:40

Sensory evaluation of the developed products was done by a panel of six judges. Judges were chosen on the basis of sensory evaluation test and comprised of staff of International College of Girls. For evaluation following types of score cards were given to the judges:

(a) Ranking scores cards for color, flavour (salt and sugar content), texture, taste, quality, hedonic rating, and difference from the market product.

(b) Numerical scoring of the products.

(c) Hedonic Scale Test

Bio-chemical estimations and results of sensory evaluation were statistically analyzed using ANOVA.

The results of bio-chemical analysis revealed that moisture content maximum in group I and minimum in group II decreased due to the effect of roasting.

Ash at 600°C was higher in group I than in group II. The reason may be attributed to the effect of roasting.

Crude fiber content found to be was maximum in group I. followed by group III and then group IV. With the advancement in time of germinating hours, crude fiber decreases.

Acid insoluble ash was more in group I whereas it decreased in group IV due to soaking and germination.

Fat content was found to be maximum in raw (group I). It decreased in roasted (group II) more as compared to in 24 hrs. germination (group III) 48 hrs. germination (group IV). Roasting reduced the fat content to a greater extent in comparison to soaking and germination.

Protein was maximum in group IV and minimum in group I. This marked increase may be due to activation of enzymes on soaking and germination and most of the enzymes are proteins.

Soaking and germination have caused a significant decrease in carbohydrate content of chickpea from group I to group IV. The difference between all the treatments was significant.

There was a negligible decrease in the calcium content from group I, in group III and then to group IV. Phosphorous also showed a slight decrease from group I, II, III to group IV.

The effect of roasting, soaking and germination had no effect on the zinc content .It was same in all groups.

Iron and folic acid contents were same group I, II, III. There was a negligible change for iron and folic acid in group IV. There difference was not significant.

The analysis of variance for sensory evaluation reveals no significant difference between treatments for all characters. This indicates that numerical scoring of the products, color, texture, flavour, texture; quality and overall acceptability of the products developed were at par to the market products.

Although there was no significant difference in the sensory evaluation of the developed products but the incorporation of wheat flour, chickpea flour in refined flour increased the nutrient values.

Nutrient Analysis of the prepared products was done in accordance with Nutritive Value of Indian Foods.

The prepared product khakra was good in nutritive values i.e. higher in protein and fiber, low in carbohydrate compared to standard. This was due to the high nutrient content of chickpea flour.

The market available products bread, pizza base and bun available in the market were taken as B, C and D.

The products B3, C3, D3 (bread, pizza base and bun) made using 30% wheat flour, 40% refined flour and chickpea flour 30% are nutritionally better due to high protein (13.2g), fiber(1.8g), carbohydrate (68.5g) and energy (349Kcal). B2, C2, D2 made of 70% refined flour and 30% chickpea flour had protein (12.8 g), crude fiber (1.35g), carbohydrate (70.1g) and energy (352.2 Kcal). The developed products A2, B3, C3 and D3 had more protein, fiber and low carbohydrate than the commercial products.

It is widely accepted that foods have many beneficial properties. It not only performs nutritional role but also is a powerful medicine. An effort was made to make high fiber products by incorporating chickpea flour, wheat flour and refined flour. On sensory evaluation these products were found to be same as market products.

Nutritionally the products made using wheat flour, refined flour and chickpea flour in the ratio 40:30:30 were better than the products made of refined flour and chickpea flour in the ratio 70:30. Therefore the use of these products is highly recommended.

It may therefore be recommended that the use of these products instead of available products in daily life may be beneficial. This is because today people are consuming more of these market products in spite of the fact that they have low fiber and protein, but are rich in carbohydrate and calories. Fiber is particularly important in diet as lack of fiber causes obesity, constipation, diverticulous disease, cardio vascular diseases, diabetes etc.

The initiation of chickpea flour to substitute refined flour in the market products was because chickpea has many health benefits:

1. Heart disease: regular consumption may reduce risks of coronary heart diseases.
2. Dyslipidemia: - Preliminary evidences suggest that consumption of chickpea may be beneficial for correcting dyslipidemia.
3. Cholesterol: The fiber in chickpea helps to decrease blood cholesterol levels by binding bile acids in the small intestine and preventing re-absorption. The introduction of chickpea in the diet resulted in lower serum levels, total and low density lipoprotein and cholesterol levels.
4. Protein: Chickpeas are an important source of macro nutrients containing twice the amount of protein compared to cereal grains.
5. Glycemic index: In a study to determine the GI of foods, it was concluded that chick pea have a low GI 28-32.
6. Nutrients: Chick peas are an excellent source of essential trace element molybdenum, also a very good source of fiber, folic acid and minerals such as iron, magnesium copper, and manganese.

CONFLICT OF INTEREST: None

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Cross Sectional Study

The Spectrum of Psychiatric Morbidities in the Caregivers of Patients with Alcohol Use Disorder - A Cross Sectional Study

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ABSTRACT

Background: Alcohol use disorder not only impacts the individual affected but also imposes adverse consequences on their family members, who are highly vulnerable to developing significant psychiatric disorders due to the intimate dynamics of their relationship. Recognizing and addressing these challenges is paramount, as caregivers serve as essential sources of moral support and assistance in facilitating the substance user's path towards abstaining from alcohol.

Method: An assessment was conducted on 250 caregivers of patients diagnosed with Alcohol Use Disorder based on DSM-5 criteria. The evaluation involved the use of clinical instruments corresponding to both level 1 and level 2 of the DSM-5 cross-cutting measures. The data was analysed using SPSS 26.

Results: The study comprised mainly middle-aged caregivers, with the largest group aged 36-45 (44.0%), followed by those over 45 (25.6%), 26-35 (22.4%), and under 25 (8.0%). Most had completed secondary or senior secondary education, often self-employed or housewives from middle or lower-middle-class backgrounds. Caregivers were primarily wives of patients, predominantly Hindu. Urban residency and extended nuclear families were common. Sleep disturbances (33.2%), depression (25.2%), anxiety (20%), anger (12.4%), and somatic symptoms (9.2%) were prevalent psychiatric issues. Some participants exhibited moderate to severe levels of anger (6.8%, 5.6%), anxiety (17.6%, 1.6%), depression (8.0%, 14.8%, 2.4%), sleep disturbances (14.0%, 14.8%, 4.4%), and somatic symptoms (3.2%, 6.0%).

Conclusion: The study proposes the necessity to raise awareness among psychiatrists regarding the assessment and treatment of caregivers of individuals dependent on alcohol.

KEYWORDS: Alcohol use disorder, caregivers, psychiatric morbidities

INTRODUCTION

Alcohol use disorder (AUD) stands as an alarming global public health challenge, characterized by profound alterations in neurochemical systems that manifest in both acute and chronic forms[1-3]. The widespread consumption of alcohol precipitates substantial individual suffering across diverse areas such as physical, psychological, economic, and social dimensions[4]. According to the World Health Organization (WHO), AUD accounts for 1.4% of the global disease burden, leading to 3.2% of all deaths (approximately 1.8 million) and a loss of 4% of disability-adjusted life years (DALYs), equating to 58.3 million DALYs lost annually[5]. In particular, countries like India, where alcohol usage is prevalent among 33% of the populace, ranking second globally, witness a notable impact, with 20% of DALYs lost attributed to associated health complications, pronounced nutritional deficiencies, and a heightened prevalence of alcohol addiction[6].

In families where someone struggles with alcohol problems, the people taking care of them become really

important. They're often at the centre of family issues caused by the person's drinking. This affects the whole family and leads to lots of problems[7,8]. Frequent arguments, conflicts and financial troubles become common because of patient's alcohol use, which makes life tough for the caregivers[9]. They have persistent feeling of sadness and hopelessness, helplessness which makes them susceptible for, many mental health issues like sleep disturbances, depressive illness, anxiety problems, anger issues, as well as other health and social problems[10,11].

Despite the multitude of challenges faced by caregivers, there is a lack of substantial research investigating the impact of these challenges on their mental health. There are only a few studies on this topic. So, we need to pay more attention to how taking care of someone with alcohol problems affects caregivers' mental health. This study aims to understand this better and find ways to help caregivers cope better with their situation.

Therefore, AUD is a complicated problem that affects not only the person who has it, but also their family. To deal with this problem, we need to use comprehensive strategies that recognize the different aspects of AUD and give importance to the needs of both the people with AUD and their caregivers.

MATERIAL AND METHODS

A cross-sectional study was carried out in the Department of Psychiatry at Pacific Medical College and Hospital in Udaipur, Rajasthan. The study received ethical approval from the Ethics Review Committee of the institution. All participating subjects provided informed written consent prior to their involvement in the study. Subjects were recruited for the study over a span of 1.5 years.

Study Population

The caregivers of Alcohol Use Disorder patients attending Psychiatric health services at Pacific Medical College & hospital were included in the study. A total of 250 participants were recruited by consecutive sampling method.

Inclusion Criteria

- Patients of AUD (as per DSM-5 diagnostic criteria) and their caregivers (living with them for at least one year)
- Who gave consent to participate in the study
- Caregivers with age group above 18 to 55 years
- Comorbidity in husbands with Nicotine dependence syndrome only.

Exclusion Criteria

- Those who have a major psychiatric disorder diagnosed or treated in past
- Living with the patient for <1 year
- Age group below 18 yrs.

Instruments Used in the Study

- DSM-5 cross cutting questionnaire level 1 and level 2 to assess psychiatric morbidity among caregivers.

Participants, Procedure and Study Design

- Patients of Alcohol use disorder as per DSM-5 diagnostic criteria and their caregivers (living with them for at least one year) were assessed. These caregivers are not having any other psychiatric disorder and their family members were under treatment as outpatient or inpatient for AUD. All the subjects recruited for the research underwent following:
- Details of the study protocol were explained to the subjects.
- Informed consent was obtained.
- Detailed history was taken including demographic details and details regarding alcohol consumption
- DSM-5 cross cutting level 1 and 2 scale: to make diagnoses of psychiatric disorders according to DSM-5
- **Statistical Analysis**
- All statistical calculations were done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 26.

RESULTS

Most of the people in the study were between 36 and 45 years old (44.0%), followed by those over 45 years old (25.6%), 26 to 35 years old (22.4%), and under 25 years old (8.0%), as indicated in Table 1.

The majority of the participants had completed secondary or senior secondary education and had graduated. In terms of occupation, most were either self-employed or housewives. Many of them belonged to the middle class or lower middle class, as shown in Tables 2, 3, and 4.

The study included mostly Hindus, and most of the caregivers were wives of the patients, as shown in Tables 5 and 6.

A large portion of the study participants were from urban areas and belonged to extended nuclear families, as shown in Tables 7 and 8.

The most common psychiatric issues observed were sleep disturbances (33.2%), followed by depression (25.2%), anxiety (20%), anger (12.4%), and somatic symptoms (9.2%), as detailed in Table 9.

Among the participants, 6.8% showed moderate anger and 5.6% showed severe anger. For anxiety, 1.6% showed mild symptoms and 17.6% showed moderate symptoms. In terms of depression, 2.4% showed mild symptoms, 8.0% showed moderate symptoms, and 14.8% showed severe symptoms. For sleep disturbances, 4.4% showed mild symptoms, 14.0% showed moderate symptoms, and 14.8% showed severe symptoms. Lastly, for somatic symptoms, 3.2% showed moderate symptoms and 6.0% showed severe symptoms, as shown in Table 10.

Table 1: Distribution of study population according to age

Age (years)	Frequency	Percentage
< 25 years	20	8.0%
26-35 years	56	22.4%
36-45 years	110	44.0%
> 45 years	64	25.6%
TOTAL	250	100

Table 2:Distribution of study population according to education level

Education	Frequency	Percentage
Uneducated	40	16.0%
Primary	34	13.6%
Middle	25	10.0%
Secondary/ Senior Secondary	70	28.0%
Graduation	81	32.4%
TOTAL	250	100%

Table 3:Distribution of study population according to occupation

Occupation	Frequency	Percentage
Laborers	44	17.6%
Self-Employed	68	27.2%
Professional	20	8.0%
Agriculture	31	12.4%
Business	14	5.6%
Housewife	73	29.2%
Total	250	100%

Table 4: Distribution of study population according to socioeconomic status

Socio-economic Status	Frequency	Percentage
Upper Middle Class	21	8.4%
Middle Class	126	50.4%
Lower Middle Class	71	28.4%
Lower Class	32	12.8%
Total	250	100%

Table 5: Distribution of study population according to religion

		Frequency	Percent
Religion	Hindu	110	73.3%
	Muslim	40	26.7%

Table 6: Distribution of study population according to relationship with caregiver

Relationship of Caregiver with Patient	**Wife**	**90**	**60.0%**
	Mother	58	38.7%
	Other	2	1.4%

Table 7: Distribution of study population according to area of residence

		Frequency	Percent
Area of Residence	Urban	125	50.0%
	Rural	125	50.0%

Table 8: Distribution of study population according to type of family

Type of the Family	Nuclear	56	22.4%
	Joint	80	32.0%
	Extended Nuclear	110	44.0%
	Living alone	4	1.6%

Table 9: Distribution of study population according to DSM-5 level 1 cross cutting measure

DSM-5 CROSS CUTTING LEVEL 1 (Psychiatric Morbidity)	Frequency	Percent
1 (Anger)	31	12.4%
2 (Anxiety)	50	20.0%
3 (Depression)	63	25.2%
6 (Sleep disturbances)	83	33.2%
7 (Somatic symptoms)	23	9.2%

Table 10: Distribution of study population according to DSM-5 level 2 cross cutting measure

Psychiatric Morbidity Interpretation	Severity	Frequency	Percent
Anger	None	219	87.6%
	Moderate	17	6.8%
	Severe	14	5.6%
Anxiety	None	202	80.8%
	Mild	4	1.6%
	Moderate	44	17.6%
Depression	None	187	74.8%
	Mild	6	2.4%
	Moderate	20	8.0%
	Severe	37	14.8%
Mania	None	250	100.0%
Repetitive Thoughts & Behavior	None	250	100.0%
Sleep Disturbances	None	167	66.8%
	Mild	11	4.4%
	Moderate	35	14.0%
	Severe	37	14.8%
Somatic Symptoms	None	227	90.8%
	Moderate	8	3.2%
	Severe	15	6.0%
Substance Use	None	250	100.0%

DISCUSSION

Demographic Details

In our study, the majority of participants were aged between 36 and 45 years (44.0%), followed by those over 45 years (25.6%), 26 to 35 years (22.4%), and under 25 years (8.0%). Akhilesh et al. found that the average age of caregivers in their study was 41.5 years. In research focused on understanding the burden on families of individuals with alcohol problems[12]. Rospenda et al. noted that most caregivers were females, with an average age of 42.1 years[13]. Regarding education, most participants in our study had completed secondary or senior secondary education, with many also having graduated. The primary occupations were self-employment and housewifery,

and the majority of participants belonged to the middle or lower-middle socioeconomic class. Most of the participants identified as Hindu, and the majority of caregivers were wives of the patients. Urban areas were the predominant residence location, and extended nuclear families were common.

In another study by Kaur et al., the majority of caregivers were housewives, with smaller percentages employed in various occupations such as unskilled employees, semiskilled workers, or being jobless or farmers[14]. The level of education varied, with a significant proportion having completed high school or elementary school, while some were illiterate or had completed middle school. Similarly, Goit et al. found that the majority of caregivers were married, with a large portion being illiterate and most working as housewives[15].

Psychiatric Morbidities

In our study 6.8% of subjects showed moderate anger, while 5.6% showed severe anger. Mild anxiety was demonstrated by 1.6% of subjects, with 17.6% experiencing moderate anxiety. For depression, 2.4% showed mild symptoms, 8.0% showed moderate symptoms, and 14.8% showed severe symptoms. Similarly, 4.4% of subjects experienced mild sleep disturbances, 14.0% experienced moderate disturbances, and 14.8% experienced severe disturbances. Additionally, 3.2% of subjects exhibited moderate somatic symptoms, while 6.0% exhibited severe symptoms.

In a study by Gohil et al., 71% of caregivers were found to suffer from at least one DSM-5 diagnosis, indicating a significant impact of alcohol dependence on caregivers. Among these, 36.4% had dysthymia, 21.8% had major depressive disorder, 8.2% had anxiety disorders, and 4.5% had generalized anxiety disorder. However, 29% showed no psychiatric condition, while 30% showed no psychiatric condition at all[16].

Kishor et al. observed that 65% of spouses of individuals with alcohol use disorder had a psychiatric disorder, with mood and anxiety disorders being the most prevalent. Specifically, 43% of those surveyed had major depressive disorder[15].

In a study conducted by Kumar et al., the findings revealed that 8.8% of participants exhibited symptoms of dysthymia, 29% were diagnosed with major depression, 6.7% experienced social anxiety disorder, and 13.3% were diagnosed with generalized anxiety disorder[17].

Another study conducted by Rajpurohit et al., levels of depression were categorized into normal, mild, moderate, severe, and extremely severe symptoms among caregivers, with percentages of 31%, 19%, 30%, 9%, and 11%, respectively. Likewise, varying degrees of anxiety and stress symptoms were observed, with percentages for each category as follows: normal (53%), mild (10%), moderate (27%), severe (4%), extremely severe (6%) for anxiety, and normal (35%), mild (41%), moderate (13%), severe (10%), and extremely severe (1%) for stress among caregivers[18].

Gupta et al. investigated the occurrence of psychiatric diagnoses in wives of individuals with alcohol and opioid dependence. They found that psychiatric diagnoses were prevalent in 16% and 20% of wives in the alcohol and opioid dependence groups, respectively. Depression and dysthymia were identified as the most frequent diagnoses in both groups[19].

A study by Sekar et al., out of the total, 72% of wives were evaluated for the prevalence of psychiatric disorders, findings unveiled 43% exhibited moderate depression, 12% had mild depressive episodes, and 3% experienced severe depressive episodes. Additionally, 6% suffered from severe anxiety disorders, while 8% had moderate anxiety disorders. Notably, depression emerged as the predominant diagnosis among wives of individuals with Alcohol Dependence Syndrome[20].

CONCLUSION

Psychiatric issues in the caregivers of individuals struggling with alcohol use disorder are frequently overlooked or not given enough attention. The findings of this study highlight the significant mental health challenges in caregivers, underscoring the need for greater awareness and support. Addressing these issues is crucial not only for improving outcomes for the individuals with alcohol dependence but also for mitigating potential risk factors that could adversely affect the caregiver's own health. Therefore, it is essential for treatment programs for those with alcohol dependence to include formal psychological assessments of their partners. This proactive approach will not only cater to the needs of this often-overlooked group but also facilitate their meaningful participation in the treatment journey.

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Clinical Study

Spiritual Beliefs and Health Anxiety as Predictors of Fear of Death among Young Adults

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ABSTRACT

Excessive concern about health and subsequent fear of death play an important role in one's mental health. Spirituality is an essential aspect of human life and is considered to be an important determinant of how successfully people may overcome a variety of problems including fear of death. The present study aimed at exploring the spiritual Beliefs and health anxiety as predictors of fear of death among Young Adults in India. A sample of 395 participants (235 males and 160 females) aged between 18-30 years was collected using convenience and snowball sampling techniques. The informed consent was taken from the participants and data was collected using various measures including Whiteley Index scale, Spirituality Well-being scale and Death Anxiety Scale. The results indicated that health anxiety and spirituality significantly predict fear of death. Furthermore, Health anxiety and spirituality was found to have significant negative correlation. Spirituality and fear of death was also found to have significant negative correlation.

KEYWORDS: Spirituality, Health anxiety, Fear of death, Young adults

INTRODUCTION

Emotional suffering and insecurity brought on by the awareness of one's own health including fears, memories and thoughts of death in general population is a major public health concern. Death anxiety is a complex psychological concept with many facets that can be influenced by several contributing and moderating factors which play a crucial role in the maintenance of this fear and thoughts[1,2]. Spirituality is among one of these factors which is a sense of significance or direction that comes from a

higher power. Spirituality is a component of human existence that is connected to significant structures that give a person's life meaning and direction and assist them in coping with life's ups and downs[3]. The main forces influencing how organisms behave in order to survive are life and death. The basic survival mechanism for humans is "fight or flight," the primary premise of evolutionary theory, as this stress response aids in determining the intensity of danger[4,5]. This conscious awareness of danger increases the likelihood of survival by connecting harmful risks to the risk of dying. This level of self-awareness goes well beyond just survival and exposure to these cues associated with death might result in fear of death[6]. According to existential perspective, the fear of death is viewed as an essential component of human existence and also that humans are unique in their awareness of their own mortality, which can cause worry and fear[7]. The central concept of this perspective is that people must face the truth of their own mortality and the realization that life is temporary[8,9,10]. People may experience existential dread as a result of coming to terms with the truth that they will eventually cease to exist. According to Yalom (2008), if fear of death is a crucial step in the developmental process, teenagers may engage in risk-taking behaviour to deal with death anxiety that has not been appropriately handled[11]. This tendency of avoiding fear of death persists throughout one's entire life since it starts in childhood and continues through adolescence and maturity. According to Sigmund Freud, fear of dying is a natural aspect of human nature and it's a type of defense mechanism to deal with the unconscious conflicts[12,13]. The urge for self-preservation and the acceptance of death's inevitability, in his opinion, are at odds when we are conscious of our own mortality. Death anxiety is a symptom of unconscious struggle rather than a sign of psychopathology[14]. Clinically speaking, concern over dying is a sign that an underlying conflict has arisen. The cognitive viewpoint concentrates on successful death coping, including controlling the emotions associated with fear of dying[15]. According to the cognitive viewpoint, anxiety over dying can be treated therapeutically as a subtype of generalized health anxiety. Our fear of dying is not a basic part of who we are, but rather a factor in health issues[16,17]. Spirituality and the fear of death are closely intertwined, as many people turn to spirituality as a way to cope with their fear of death. Moreno-Montoya (2017) studied relationship between spiritual beliefs, beliefs about death and health among Romani people, a cultural minority in Spain[18]. Findings indicated that supernatural beliefs offer protection from illness. Schuttee et.al, (2016) examined about health anxiety, acceptance of death, and coping mechanism of patients with health anxiety[19]. Result showed that patients with health are more anxious about health and have less acceptance of death than patients with depression. Another study done by Birgit et.al (2018) also showed positive association between Fear of death and Health anxiety[20]. It was a systematic review of literature, but all studies were cross-sectional. Tabei SZ (2016) through non-systematic review examined the effect of spirituality on people's health and discussed about the relation between spirituality and health[21]. In the southern part of Iran, during the COVID-19 outbreak, Khiyali et al. (2023) conducted research on health anxiety and spiritual health in cancer patients receiving chemotherapy[22]. The study's findings led to the conclusion that improving patients' spiritual wellbeing and resilience should be a key component of their care because these traits are effective tools for battling cancer and easing patients' worry, particularly during the COVID-19 epidemic.

METHODOLOGY

A two-group design based on gender i.e., females and males were used in the present study. This study followed a correlational design using online surveys as a method of data collection. In this study fear of death was the dependent variable and Spiritual Beliefs and Health Anxiety were the independent variables. The sample consisted of 429 young adults out of which only 395 participants were included with the age group ranging from18-30 years. The sampling technique used for the study was convenience and snowball sampling. The Whiteley Index[23], Spirituality Well-being scale[24], and Death Anxiety Scale[25] were the three tests used in the study.

RESULT

The statistical analysis encapsulated the various constructs of the study in a nutshell. A total of 429 replies were gathered, but 34 were eliminated during screening. Version 2.0 of IBM SPSS software was used for the analysis.

Table 1: Descriptive Statistics (N=395)

Variable	Mean	Std. Deviation	Minimum	Maximum	Range
Health Anxiety	38.39	8.59	26	58	14-70
Spirituality	42.30	9.39	16	60	12-60
Fear of Death	43.17	7.39	15	63	15-75

Table 2: Group Statistics (Female=235 & Male=160)

Variable	Gender	Mean	Std. Deviation
Health Anxiety	Female	38.96	8.68
	Male	37.56	8.42
Fear of Death	Female	43.18	7.60
	Male	43.16	7.10
Spirituality	Female	42.20	9.28
	Male	42.44	9.58

Table 3: Bivariate Correlation Table

Variable	1	2	3
Health Anxiety	—		
Spirituality	-.176**	—	
Fear of Death	.181**	.321**	—

**significant at 0.01 level

Table 4: Result of Regression Coefficient

Predictor	RSquare	Adjusted RSquare	F		Sig.
Health Anxiety	.119	.114	26.396	.128	0.000
Spirituality				-298	0.000

DISCUSSION

Spirituality is a crucial component of human life and an essential component that enables people to successfully navigate a wide range of difficulties. Health anxiety is a psychological health condition characterized by persistent and excessive fear about having a serious illness, despite medical reassurances that there is no medical evidence of any such illness[26,27,28.]

The results of regression analysis that the independent variables significantly predicted fear of death, (r= -.176, p<.001). Furthermore, the R2 value of .119 suggests that the model accounts for 11.9% of variance in fear of death. The study found out that Health anxiety and Fear of Death has significantly weak positive correlation (r = .181, p<001) and Spirituality and Fear of Death has significant weak negative correlation (r = -.321, p<001).These findings are consistent with previous research which studied the significant relationship between spiritual beliefs, beliefs about death and health among Romani people[18]. Findings indicated that high spiritual belief causes low health anxiety which results in lower fear of death. According to this study, health anxiety and spirituality were among the most significant predictors of fear of death. The study further reveals that the excessive concern for one's health can heighten one's awareness of mortality and enhance one's fear of dying.

Table 4 shows that health anxiety and spirituality have a significantly weak negative correlation (r = -.176, p<.001) which suggests that people who are high on spirituality may have lower levels of health anxiety. These results are in line with earlier research by Tabei and his colleagues (2016), who looked at the relationship between health and spirituality[21]. Table 4 further shows that health anxiety and fear of death has significantly weak positive correlation (r = .181, p<.001) which means that higher the level of health anxiety higher will be fear of death. These findings are similar to previous research that has found significant relationship between health anxiety and fear of death[29,30,31,32]. Another study done by Lebeland his colleagues (2020) found that a common mistrust of how a body functions predisposes to irrational fear of death in health anxiety[33]. They also found strong positive correlation between fear of death and health anxiety. The present study also showed that spirituality and fear of death has a weak negative correlation (r = -.321, p<.001) which means people who have higher levels of spirituality will have less fear of death. This result is consistent with previous study done by Greyson (2006) who studied relation between fear of death and spirituality[34]. His research revealed that having a close encounter with death deepened spiritual consciousness. Many experiencers express the opinions that love is more essential than worldly possessions, that life continues after death, and that everything happens for a reason as they become more empathic and spiritually oriented[35].

CONCLUSION

Spirituality is said to be one of humans' inherent abilities that has favorable impact on health of people[36,37,38]. Spirituality can be a powerful tool for coping with the fear of death by providing a sense of connection, comfort, and acceptance. It can help people come to terms with their mortality and live more fully in the present moment[39]. The present study aimed at studying the effect of spiritual beliefs and health anxiety on fear of death among young adults in India. The study was conducted on a sample of 395 young adults, and data was collected using standardized measures of spiritual beliefs, health anxiety and fear of death. The results of the study indicated that health anxiety and spiritual belief significantly predict fear of death. These results are in line with earlier studies[20,27]. Furthermore, the study found that there was no significant gender difference in all the three variables. Overall, the result of the present study suggests that health anxiety and spirituality are important predictors for fear of death.

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Case Report

Neonatal Respiratory Syncytial Virus Pneumonia: A Case Report and Review of Literature

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ABSTRACT

Respiratory Syncytial Virus (RSV) has been identified as the major causative organism of lower respiratory tract infection (LRTI) in neonates and infants.

***Case Report**: A 7 day old baby girl has born at 36+2 weeks of gestation presents with cough, cold, nasal congestion, difficulty in breathing and poor feeding since last 2 days. On examination, baby was dull, lethargic, had noisy breathing with moderate intercostal and subcostal retractions. X-ray showed bilateral hyper-inflated lung fields suggestive of bronchiolitis. Nasopharyngeal swab sent for respiratory viral panel PCR was positive for Respiratory Syncytial Virus. Baby responded to supportive management in the form of non-invasive ventilator (NIV) supports, nebulisation and chest physiotherapy. Baby was successfully discharged home on room air and exclusive breastfeeding by Day 12 of hospital admission.*

***Virus**: RSV is an enveloped, single stranded, negative strand RNA virus.*

***Epidemiology**: The highest hospitalization rates were seen during the first 6 months of life with peak rates of 25.9 per 1000 children seen in infants between 30 and 90 days of life. Risk factors include - prematurity, low birth weight, male gender, underlying lung or congenital heart disease, maternal smoking, lack of breastfeeding and over-crowding.*

***Pathogenesis**: RSV primarily spreads via air-borne droplets or via indirect contact with contaminated surfaces. Incubation period is between 2-8 days.*

***Clinical Presentation**: Neonates have atypical clinical manifestations and include afebrile cough, nasal congestion, choking on milk, spitting, rapid breathing and apnoea.*

***Diagnosis**: NICE recommends that the diagnosis of RSV infection should primarily be based on detailed history and physical examination. Additional radiological and laboratory investigations should be performed only in severe cases requiring intensive care management.*

***Prevention**: Basic hygiene rules such as frequent hand-washing, keeping surfaces clean and covering mouth and nose while coughing and sneezing is the most effective preventive measure. In inpatient setting, infected patient should be isolated with proper precautions.*

***Treatment**: Neonates with marked respiratory distress, saturation below 92% on room air, clinical dehydration and apnoea should receive inpatient management. Supportive care along with inhaled hypertonic saline and inhaled bronchodilator forms the standard of care.*

***Prognosis**: Most patients recover in 1-2 weeks. However, re-infections are common throughout life as RSV infection do not grant permanent immunity.*

KEYWORDS: Neonate, Respiratory Syncytial Virus, Pneumonia, Bronchiolitis, Palivizumab, Ribavirin

INTRODUCTION

Respiratory Syncytial Virus [RSV] has been identified as the major causative organism of lower respiratory tract infection [LRTI] in neonates and infants[1]. Respiratory Viral Infections [RVIs] in neonates continue to be the most under-diagnosed entity owing to their subtle clinical presentation and the absence of set protocols for viral pathogen testing in most of the NICUs[2]. This leads to increased length of hospital stay, unnecessary antimicrobial exposure and significant short- and long-term morbidity in preterm as well as term neonates[3]. Also, there is scarcity of Indian data on incidence, clinical profile and outcome of RSV pneumonia.

We present a case of Respiratory Syncytial Virus pneumonia in a 7 day old neonate. We also review the literature, discussing the risk factors, diagnosis and treatment of neonatal RSV.

CASE REPORT

A 7 day old baby girl was born at 36+2 weeks gestation to a primigravida mother through emergency caesarean section. Breastfeeding was initiated within 2 hours of birth. Baby was discharged home at 3rd day of life after receiving birth vaccination. At day 5 of life, baby was admitted to an outside NICU for neonatal jaundice and received phototherapy for 48 hours. Baby developed cough, cold and nasal congestion on 6th day of life which progressed in next 24 hours. Baby then developed poor oral intake and breathing difficulty for which baby was admitted to our NICU. Mother is a known case of asthma on SOS inhaled β2-agonist and inhaled corticosteroids. On general physical examination, baby was found to be dull, lethargic and had noisy breathing with moderate subcostal and intercostal retractions. Systemic Examination revealed no significant abnormality other than conducting sounds in bilateral lung fields. Baby was taken on non-invasive ventilation at optimal settings. Intravenous fluids and intravenous empirical antibiotics as per unit's protocol were started. Septic screen revealed thrombocytosis with negative C-reactive protein. X-ray chest showed developing consolidation in right para-cardiac region (Fig.1). Nebulisation with hypertonic saline and chest physiotherapy was started. On day 3rd of hospital stay, repeat X-ray chest showed bilateral hyper-inflated lung fields suggestive of bronchiolitis.

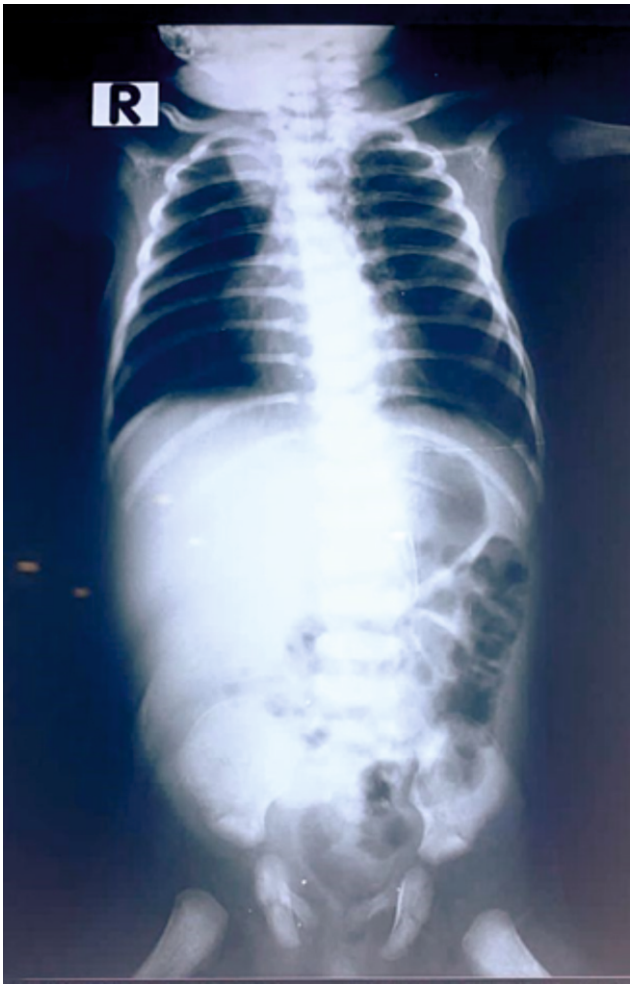

Figure 1: X-ray chest showing consolidation in right para-cardiac region

Intravenous Azithromycin was added. Nasopharyngeal swab sent for respiratory viral panel PCR was positive for Respiratory Syncytial Virus [RSV]. Supportive treatment in the form of non-invasive ventilator [NIV] support, nebulisation and chest physiotherapy was continued. Intravenous antibiotics were stopped after blood culture came out to be sterile. Baby had intermittent episodes of bronchospasm, characterised by worsening subcostal and intercostal retractions and bilateral wheeze on auscultation. These episodes warranted increase in NIV settings and nebulisation with corticosteroid [Budesonide], β2-agonist [Levosalbutamol] and Adrenaline was added. In view of persistent NIV requirement and oro-nasal copious secretion, HRCT-Chest was done which ruled out any associated lung anomaly and H-type tracheo-esophageal fistula. Supportive treatment was continued. Baby showed gradual improvement from 8th day of hospital stay [Day 10 of illness]. NIV support was gradually weaned and baby was taken on room air on day 11th of hospital stay. Baby was then started on breastfeeds which baby accepted well with no worsening respiratory distress. Baby was successfully discharged home by day 12 from admission.

REVIEW OF LITERATURE

Virus

Respiratory Syncytial Virus [Family – Pneumoviridae, Order – Mononegalevirales, Genus - Orthopneumovirus], primarily isolated from a Chimpanzee in 1956, is an enveloped, single-stranded, non-segmented, negative-strand RNA virus[4]. There are two main antigenic groups, A and B, based on surface glycoproteins. Subgroup-A infections are more common, severe, and contagious[5].

Epidemiology

The global annual rate of RSV hospitalization, as per a systematic review, was 4.4 per 1000 children aged <5 years. The highest hospitalization rates were seen during the first 6 months of life with peak rates of 25.9 per 1000 children seen in infants between 30 and 90 days of life6. RSV hospitalization rate was 4.6 per 1000 children in preterm neonates [<37 weeks gestation] which was nearly equivalent to rate of 5.2 per 1000 children for term neonates[7].

The under-developed neonatal airway, along with narrow internal diameter, poor elastic support and a tendency towards increased mucus secretion following inflammation, gets easily blocked as compared to older children. Preterm neonates, owing to their low levels of IgG antibody and immature immune system, are at an increased risk of severe and fatal RSV infections. Other risk-factors include – low birth weight, male gender, underlying lung disease or congenital heart disease, maternal smoking, history of atopy, lack of breast feeding, siblings attending daycare/kindergarten and over-crowding[8].

In India, seasonal outbreaks of RSV infection occur from October to April, with a peak observed in January or February.

Pathogenesis

RSV primarily spreads via air-borne droplets or via indirect contact with contaminated surfaces. Vertical transmission [respiratory tract of mother placenta transient RSV viremia developing foetal lung] as well as hematogenous spread from the primary site of infection to remote extra-pulmonary site can also be seen[9].The incubation period is usually between 2-8 days[10]. Viral shedding lasts for an average of 11 days. However, preterm neonates and immune-compromised hosts can stay infective up to 4 weeks.

RSV primarily infects ciliated cells of the upper respiratory tract, epithelium of the small bronchioles and type 1 pneumocytes. The predominant pathological findings include nasal and pharyngeal mucosal congestion, airway oedema, degeneration and necrosis of alveolar epithelial cells, shedding of necrotic cells and excessive mucus production that leads to bronchial narrowing, excessive aeration and disruption in gas exchange[11].

Both humoral and cellular immunity helps in clearing the RSV infection. Based on the disease severity, the body first mounts an interleukin-8 (IL-8) mediated neutrophil response. Pulmonary CD8+ T-cell response helps in viral clearing and is followed by systemic T-cell lymphopenia. Protective antibodies are produced by B-cell activating factors in the airway epithelium[12]. IFN-γ also plays a protective role but ultimately results in immunopathological injury of the lower respiratory tract.

Neonates can be effectively prevented from RSV infection by maternally transmitted antibodies. However, the degree of protection is directly proportional to the RSV antibody titre of the mother[13].

Clinical presentation in neonates

Clinical manifestation of RSV infection in neonates is often atypical and includes afebrile cough, nasal congestion, choking on milk, spitting, and rapid breathing. Apnoea can be the presenting feature in approximately 20% of neonates. On physical examination, features of rhinitis and pharyngitis along with conjunctival and tympanic membrane congestion may be seen. On auscultation, prolonged expiration, rales, inspiratory rhonchi, decreased lung sounds and increased aeration in lung periphery may be found[14]. Primary RSV infection in neonates causes severe lower respiratory tract infection, including bronchiolitis, bronchospasm and pneumonia. However, disease severity reduces with subsequent infection and LRTI is seen in only 50% of secondary infections[15].

Diagnosis

1. The National Institute for Care and Excellence16 recommends that the diagnosis of RSV infection should primarily be based on detailed history and physical examination. Additional radiological and laboratory investigations should be performed only in severe cases requiring intensive-care or in cases of atypical bronchiolitis.

2. Complete Blood Count is non-specific for RSV infection.
3. C-reactive protein can be mildly elevated.
4. X-ray chest shows hyper inflated lung fields, heterogenous infiltrates, patch-type atelectasis and increased peri-bronchial shadows. It also helps to rule out other differential diagnosis.
5. Serology – Direct Fluorescence Antibody Test with a sensitivity and specificity of 95% can provide results in 2-3 hours. But it has a limited role as a diagnostic tool as seroconversion takes approximately 2 weeks and maternally transferred antibodies are also present up to 6 months of age[17].
6. Rapid antigen diagnostic tests [RADT] have a sensitivity of 80% and a specificity of 97%[18]. They can provide results in shortest time [less than 30 minutes] and thus, can be used as screening tests. However, low sensitivity warrants negative results to be confirmed with PCR-based assays.
7. Reverse Transcriptase Polymerase Chain Reaction [RT-PCR] has a higher sensitivity as compared to rapid antigen detection test and viral culture18. Typically included as a part of multiplex PCR-based assays to detect multiple respiratory pathogens, it provides rapid and reliable results. The only disadvantage is that these assays are more expensive than RADT.
8. Viral Cell Culture demonstrating characteristic plaque morphology with syncytium formation is the gold standard test for the diagnosis of RSV infection. Rapid cell culture [shell vial] results are available within 48 hours as compared to classic cell culture that takes 4-8 days to yield result.

Prevention

A. Pertussis and Influenza vaccination during pregnancy – Maternal vaccination will provide passive immunity to newborn until they are themselves vaccinated. Currently there is no RSV vaccine available. However, preventing avoidable diseases will protect neonate's immune system and make it less vulnerable to RSV infection.

B. Hygiene and behavioural measures – As droplet infection is the major source of RSV transmission, basic hygiene rules such as frequent hand washing, keeping surfaces clean and covering mouth and nose while coughing and sneezing is the most effective preventive measure. Exclusive breastfeeding, not smoking near the child and avoiding exposure to crowded places also reduces the risk of RSV infection. In inpatient settings, infected patients should be isolated with standard and contact precautions.

C. Palivizumab prophylaxis – Palivizumab is a RSV-specific humanized IgG1 monoclonal antibody produced by recombinant DNA technology. It prevents adherence of virus to respiratory epithelium and thus, inhibits viral replication. Prophylactic Palivizumab administration is recommended during RSV season in neonates and infants who are at risk for high mortality and morbidity with RSV infection[19]. It is given intra-muscularly at a dose of 15ml/kg monthly for a total of five doses.

D. Nirsevimab – It is a recently approved monoclonal antibody that targets the RSV F-glycoprotein. It has a longer half-life and a single injection has been shown to prevent RSV-infection and hospitalization for 150 days in a multi-center, placebo-controlled RCTs[20,21].

Treatment

Neonates with marked respiratory distress, oxygen saturation below 92% on room air, clinical dehydration and apnoea should receive in-patient management[16].

A. Supportive Care: It includes respiratory support [ranging from supplemental oxygen via nasal cannula to mechanical ventilation], clearing secretions from airway, maintaining hydration, assisted feeding, chest physiotherapy and close monitoring of the clinical status. This forms the mainstay of treatment.

B. Medications**:**

1) Ribavirin – It is a synthetic nucleoside analogue licensed by FDA in 1993 against severe RSV infections. However, American Academy of Paediatrics (2021) guidelines does not recommend routine administration as it is expensive and must be given early in the disease course. Long-term aerosol administration and concerns for safety [haemolytic anaemia, leukaemia, bronchospasm, conjunctival irritation and teratogenic potential] also precludes routine use of Ribavirin in RSV pneumonia[22].

2) Inhaled hypertonic saline – AAP recommends that nebulized hypertonic saline can be administered to infants and children with RSV infection who require hospitalization[22]. Hypertonic saline increases mucociliary clearance and thereby helps in keeping the airway clean of mucus plugs.

3) Inhaled Bronchodilator [β-2 agonist like Albuterol, Salbutamol and Anticholinergics] –Bronchodilators may be tried if a strong personal or family history of atopy is present and wheezing is predominantly present. Routine use of bronchodilator therapy is not recommended[22].

4) Nebulized Adrenaline – Hartling et al[23] in their recent meta-analysis evaluated nebulized epinephrine vs. placebo in bronchiolitis and found no effectiveness of epinephrine in hospitalized patients on length of stay [LOS] or other inpatient outcomes. A recent, large, multi-center trial further demonstrated a longer LOS when epinephrine was used on a fixed-schedule as compared with an as-needed schedule[24].

Canadian Bronchiolitis Epinephrine Steroid Trial[25]compared hospitalization rates over a period of 7 days in 800 patients with bronchiolitis and found that the group of patients who received epinephrine in combination with corticosteroids had reduced hospital admission by day

7 than the double placebo group. However, the role of epinephrine in out-patient department remains controversial and a formal large, multi-center study is needed before a recommendation in this setting.

5) Inhaled or Systemic Corticosteroids –Although the Canadian Bronchiolitis Epinephrine Steroid Trial[25] showed a reduction in hospital admission rate 7 days after treatment with combined inhaled adrenaline and oral dexamethasone, a recent Cochrane Systematic Review[26] showed that corticosteroids neither reduced outpatient admissions when compared with placebo nor reduced LOS for inpatients.

In summary, infants with bronchiolitis do not benefit significantly with corticosteroids alone. However, there can be a potential benefit from combination of steroids with both α- and β-agonist agents and additional large trials are needed to clarify effectiveness of this therapy.

6) RSV-IVIG – It is a hyperimmune polyclonal immunoglobulin obtained from donors with high RSV neutralising antibodies. It has five-fold greater efficiency in neutralising RSV as compared with IVIG. RCTs showing no benefit along with other disadvantages like need for hospitalization, long-term infusion, high volume doses, sudden cyanotic episodes and necessity to avoid live-attenuated vaccines for at least 9 months precludes its use[27].

Prognosis

Most patients recover in 1-2 weeks. However, reinfections are common throughout life as RSV infection do not grant permanent immunity. Infants who required hospital admission because of RSV infection have been found to have significant long-term pulmonary sequelae, such as asthma, recurrent wheezing and impaired lung function, which may last for 10 years or longer[28].

CONCLUSION

Respiratory Syncytial Virus is the leading agent causing of respiratory illness associated hospital admissions in children under 12 months of age. It can lead to recurrent wheezing and asthma in later life. PCR-based viral detection methods should be considered in neonates with acute respiratory tract infection requiring NICU admission and those who are at high risk of RSV infection. Currently there are no vaccines available for the prevention of RSV infection. Supportive therapy in the form of respiratory support and maintaining hydration forms the mainstay of treatment in the absence of availability of specific treatment.

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

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Case Report

Correction of Lower Crowded Dentition with Fixed Orthodontic Self-Ligating Bracket System – A Case Report

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ABSTRACT

Dental crowding is a prevalent orthodontic issue encountered globally. This case report details the diagnosis and treatment of a 21-year-old male patient presenting with significant crowding, deep bite, and midline deviation. The primary concern reported by the patient was crowding and dissatisfaction with their smile's aesthetics. Clinical examination revealed an Angle Class I malocclusion with severe crowding. Fixed orthodontic appliances were employed to comprehensively address the severe crowding, resulting in successful correction Patient was having dental history of root canal treated teeth with 32, 41, 42 and extracted 31 as he was having periapical cyst I.R.T 31

KEYWORDS: Self ligation, Crowding, Extraction, Periapical abscess

INTRODUCTION

The decision to extract teeth for orthodontic treatment has been a subject of significant discussion throughout history. Over the past century, treatment planning philosophies have shifted between prioritizing non-extraction therapy and extraction of all four premolars. Recently, a single-tooth extraction approach, specifically targeting a lower incisor, has gained popularity. This case series presents three patients with various malocclusions successfully treated using mandibular incisor extraction[1]. Adults with normal molar alignment (Angle Class I) often experience crowding in their front teeth, impacting roughly a quarter of women and a smaller percentage of men.

Determining the necessity of tooth extraction remains a critical decision for orthodontists during treatment planning. The ongoing debate regarding extraction versus non-extraction approaches represents one of the most enduring philosophical controversies in orthodontic practice. This controversy encompasses both biological and mechanical considerations[2]. Historically, orthodontic treatment plans primarily focused on either complete tooth preservation (non-extraction) or extraction of all four first premolars. However, recent years have witnessed a growing interest in an alternative approach: the extraction of a single mandibular incisor. Traditionally reserved for cases with a misplaced or compromised incisor, this strategy is gaining traction as a viable option for achieving optimal outcomes through simplified mechanics in carefully selected patients[4].

This crowding occurs because the jaw size doesn't accommodate all the teeth comfortably, causing overlapping and rotations. Third molars and natural forward pressure on the teeth can worsen this issue. Orthodontic treatment aims to correct such misalignments

and improve facial aesthetics by aligning the teeth with the facial features[5]. This case study successfully treated lower front teeth crowding, a deep bite, and a misaligned midline in an Angle Class I patient using braces after removal of 31 having periapical cyst which cannot be saved due to large pathology.

Figure 1

Figure 2

Figure 3

Figures 1, 2 and 3: Pre-Treatment Extra-Oral Photographs

Extraoral examination revealed a straight facial profile, Mesocephalic head shape (medium skull proportions), and symmetrical facial features. The patient's lips were competent (meeting comfortably at rest), and speech function was unimpaired. (Figures 1, 2 and 3)

The patient demonstrated good oral hygiene. The mucosa, palate, and tongue appeared normal. Examination revealed crowding of the lower incisors with a deep bite of 4.5 mm and an overjet of 2 mm. A midline shift of 0.5 mm to the right was observed on the lower arch. The molar and canine relationship bilaterally was in Class I (normal molar relationship). The transverse relationship (upper and lower arch width) was also normal. (Figures 4, 5 and 6) Discoloration of the lower left central incisor was noted. Further investigation using a periapical radiograph (IOPA) revealed a periapical cyst involving all lower incisors.

Intra oral analysis indicated a -2 mm discrepancy in the upper arch (lack of spacing) and a -6.5 mm discrepancy in the lower arch (greater spacing needed). A positive curve of Spee of 3 mm was present (increased curvature in the lower incisor region). The overall arch shapes of the maxilla and mandible were normal. No clinical signs of temporomandibular joint dysfunction (clicking, discomfort) or limitations/deviations in jaw movements were observed.

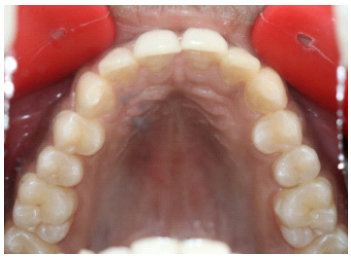

Figure 4

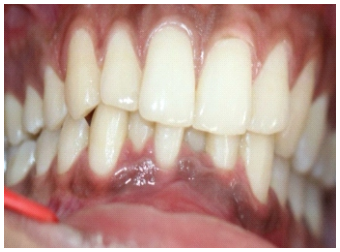

Figure 5

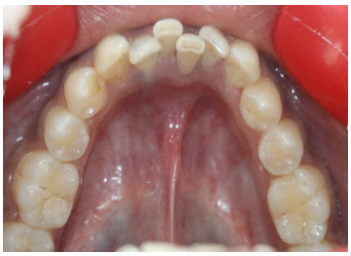

Figure 6

Figures 4, 5 and 6: Pre Treatment Intraoral Photographs

The OPG's patient showed that patient had impacted on the lower third molar. There was Radiolucency seen at the roots of lower incisors (Figure 7 &8).

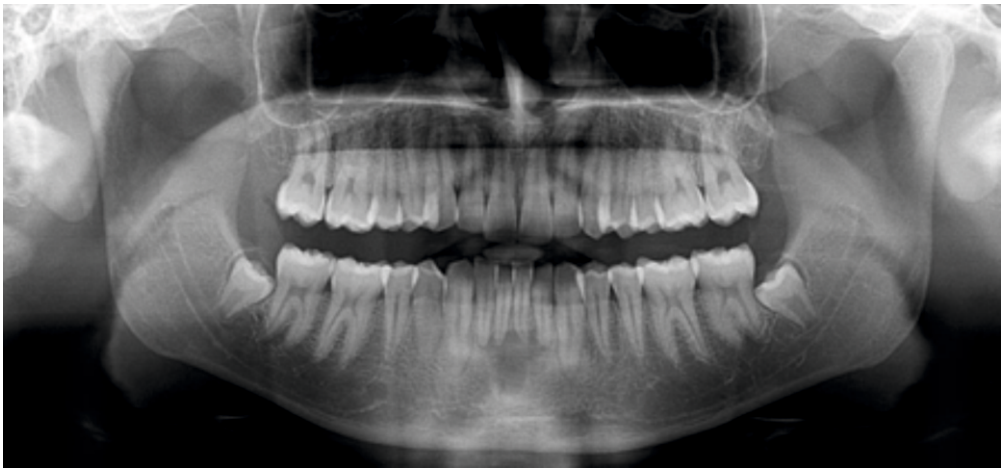

Figure 7 : Pre-Treatment OPG

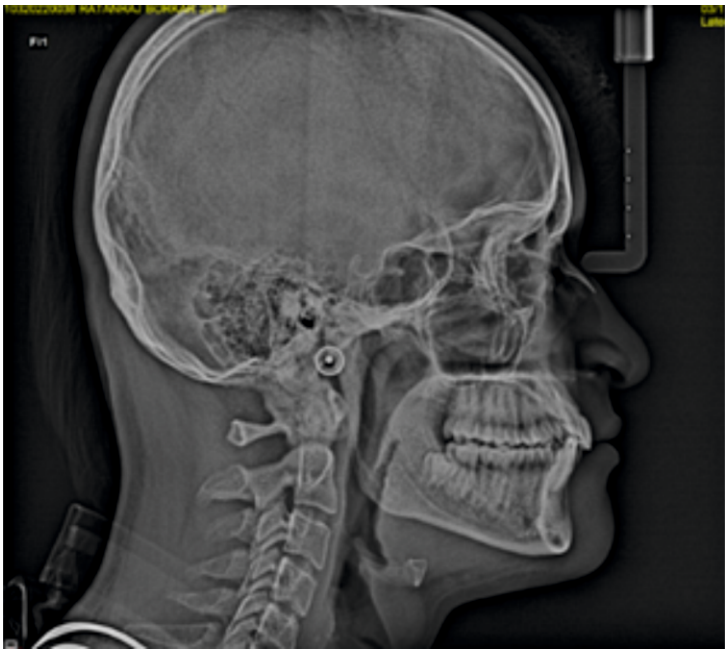

Figure 8 : Pre-Treatment Lateral Cephalogram

DIAGNOSIS

Class I Jaw base with average growth pattern (Figure - 8) having Angle Class I Malocclusion with Proclined Skeletal upper and lower incisors, crowding, deep bite, and midline shifting.

ETIOLOGY

The primary contributing factor in this case is believed to be the eruption of third molars in the lower jaw on both sides (bilaterally). This eruption has resulted in crowding of the lower anterior teeth.

TREATMENT OBJECTIVES

- Achieve proper alignment of crowded teeth in both the upper (maxillary) and lower (mandibular) arches
- Correct the deep bite (excessive vertical overlap of the upper front teeth over the lower front teeth)
- Address the midline discrepancy (misalignment) in the lower arch
- Establish a Class I molar relationship (normal alignment of the molars)
- Achieve an ideal arch form for both the upper and lower

jaws

- Optimize Overjet (horizontal overlap of the upper front teeth over the lower front teeth) and overbite (vertical overlap of the upper front teeth over the lower front teeth) to desired levels

TREATMENT PLAN

Based on a comprehensive evaluation, including clinical examination, dental and orthodontic history, Extraoral and intraoral photographs, and radiographs, a treatment plan was formulated to address the malocclusion. Fixed orthodontic appliances with self-ligating brackets were chosen to achieve the desired tooth movements and alignment in both the maxillary and mandibular arches. Treatment involved the extraction of tooth #31 (lower left central incisor) due to its poor prognosis (non-vital with extensive pathology). This extraction aimed to alleviate crowding in the lower anterior segment. Root canal treatment was performed on teeth #32 (lower left lateral incisor), #41 (upper right canine), and #42 (upper right first premolar) before bonding the lower arch. The treatment concluded with the removal of retainers on both upper and lower arches.

TREATMENT PROGRESS

Informed Consent and Initial Procedures

Following informed consent, a comprehensive medical history was documented for the patient. Scaling (removal of calculus and plaque) was performed as initial treatment to prepare the teeth for bracket placement.

Tooth Extraction and Appliance Placement

Due to a poor prognosis, tooth #31 (lower left central incisor) was extracted. Self-ligating brackets with 0.022" slots were then bonded to all teeth in both arches. Buccal tubes with 0.022" slots were bonded to all first molars.

Alignment and Leveling

Nickel-titanium thermal wires of progressively increasing sizes (0.014", 0.018", and finally 0.016" x 0.022") were employed in both arches to achieve leveling and alignment of the teeth.

Arch Expansion and Refinement

Following alignment, stainless steel wires of size 0.016" x 0.022" were used in conjunction with up and down elastics to establish arch compatibility (proper coordination between upper and lower arches). Subsequently, stainless steel wires of size 0.017" x 0.025" were utilized for finishing and detailing the occlusion (fine-tuning the bite).

Treatment Outcomes

Good profile is achieved (Figures 9, 10 and 11). Orthodontic treatment successfully addressed the initial crowding in the upper arch and spacing in the lower arch. Normal overbite (2 mm) and Overjet (2 mm) were achieved. A Class I molar and canine relationship (ideal alignment) was maintained. Additionally, the curve of Spee was flattened (reduced curvature in the lower incisor region. (Figures 12, 13 and 14)

Debonding and Retention

Approximately one year after treatment initiation, all fixed appliances were removed. Fixed canine-to-canine retainers were placed on both arches, along with removable retainers (Begg's wrap-around retainers) for additional support.

Figure 9

Figure 10

Figure 11

Figures 9, 10 and 11 : Post Treatment Extra -Oral Photographs

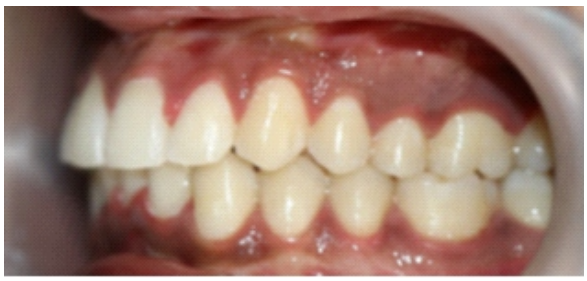

Figure 12

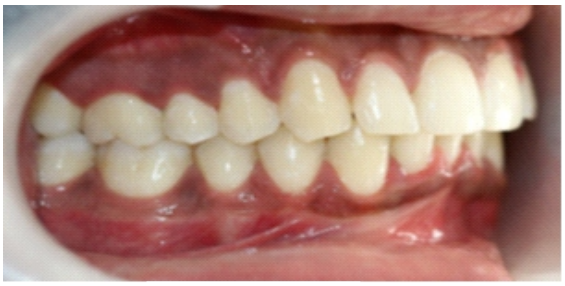

Figure 13

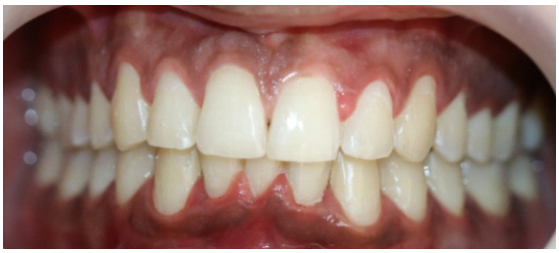

Figure 14

Figures 12, 13 and 14: Post Treatment Intra Oral Photographs

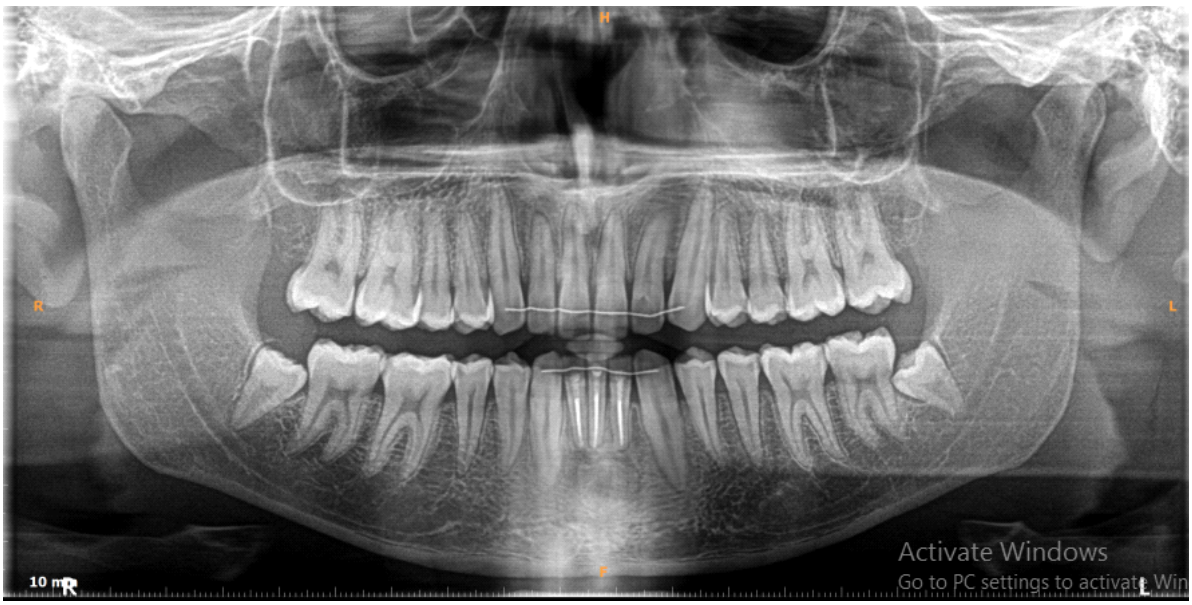

Figure 15 : Post Treatment OPG

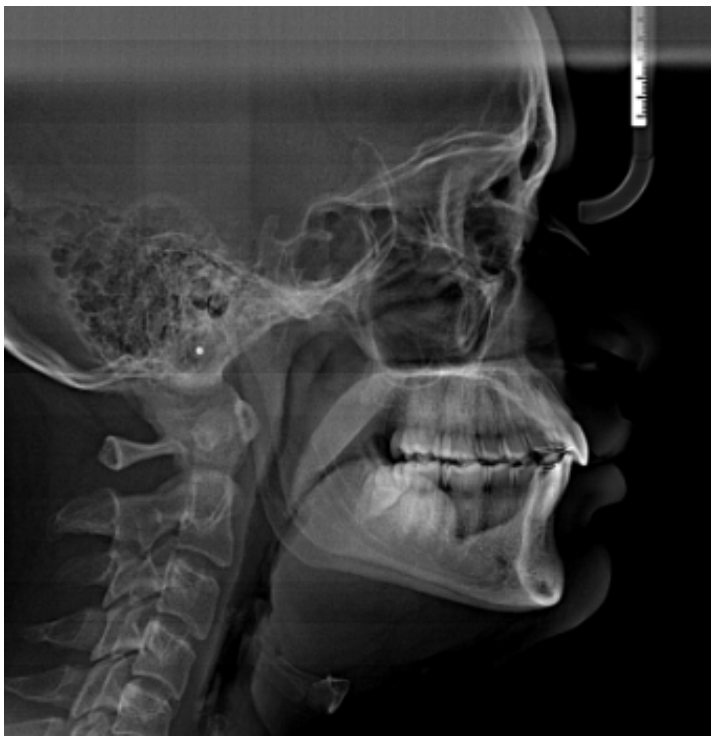

Figure 16: Post Treatment Lateral Cephalogram

DISCUSSION

This case report describes a 20-year-old male patient who presented to Pacific Dental College with the primary concern of lower arch crowding. The patient desired aesthetic improvement through fixed orthodontic appliances and expressed a preference for non-extraction treatment OPG reveals right inclination of all the teeth after treatment (Figure 15) and post-treatment cephalogram indicate straight profile Class I Jaw base (Figure 16) .

Treatment Considerations

The decision to extract or preserve teeth during orthodontic treatment planning involves careful consideration of the entire case complexity. Factors influencing this decision include the patient's medical history, treatment compliance, oral hygiene, susceptibility to cavities, and overall tooth health.

In this specific case, the patient was informed about the poor prognosis of tooth #31 (lower left central incisor) due to a large cyst (Figure 15). Following informed consent, tooth #31 was extracted, and the resulting space was utilized to address the lower arch crowding without further extractions.

Treatment Phases

Leveling and Aligning: A sequence of nickel-titanium (NiTi) thermal round archwires of increasing sizes (0.014", 0.018", and finally 0.016" x 0.022") was employed in both arches to achieve proper tooth alignment and leveling. NiTi wires offer the advantage of shape memory, which enhances their performance during the leveling stage.

Arch Coordination and Finishing: Stainless steel archwires of size 0.016" x 0.022" were used to establish arch compatibility (proper coordination between the upper and lower arches). This was followed by finishing and detailing the occlusion (fine-tuning the bite) using 0.017" x 0.025" stainless steel wires in both arches.

Retention

Following treatment completion, fixed retainers were bonded to the upper and lower anterior teeth for long-term stability. Additionally, Hawley retainers (removable retainers) were provided for both the upper and lower arches.

CONCLUSION

Generally, all treatment objectives were achieved successfully. The treatment successfully corrected crowding in a young adult with a normal bite (Class I) by extracting a lower front tooth due to poor health. It achieved proper alignment and bite without needing additional tooth removal.

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

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Review

The Present Status of Prevalence of Vitamin B12 Deficiency in Hypothyroid Individuals – A Review

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ABSTRACT

It is not uncommon to find the conglomeration of autoimmune diseases in a person. The most common autoimmune hypothyroidism is seen in general population and frequently associated with other autoimmune conditions like pernicious anaemia, celiac disease, rheumatoid arthritis etc. The present short review point towards the common association of hypothyroidism with vitamin B12 deficiency observed by different scientific groups. The symptoms of both the conditions overlap and therefore it is important to consider this common association for better patient management.

KEYWORDS: Autoimmune thyroiditis, Levothyroxin, Cobalamin, TPA

INTRODUCTION

The most prevalent endocrine disorder in developing countries is related to thyroid hormone imbalance. Hypothyroidism is a common endocrine disorder with reduced production of thyroid hormones. It is a common disease with different frequency between countries. However, the common occurrence of hypothyroidism is three times more in women than in men (12.4% versus 3.7%) in developing countries. Sex, geographical factors, age, ethnicity and iodine consumption are the determining factors for the occurrence of thyroid diseases[1]. Out of total patients of hypothyroidism, about 12% with primary autoimmune type disease experience pernicious anaemia. In hypothyroidism vitamin B12 deficiency is observed in up to 40% of patients[2].

Vitamin B12 (also known as cobalamin) is found naturally in animal foods or artificially in fortified cereals. Cobalamin has a complex mechanism of absorption in the terminal ileum that depends on the intrinsic factor (a secretory product of the gastric parietal cells) and eventually releases cobalamin in the blood linked to the plasma binding protein, transcobalamin[3].

The prevalence of B12 deficiency varies depending on the level used to define deficiency and the populations studied. In developed countries, vitamin B12 deficiency (serum B12 level <148 pmol/L) increases with age from 3% in the younger population to reach 10% in the elderly. Borderline B12 levels or subclinical cobalamin deficiency (SCCD), which is defined as a serum B12 level between 148 and 221 pmol/L, is reported in 20% of the elderly population. In developing countries, the prevalence of low and borderline B12 levels is elevated approaching 70% in adults. Furthermore, detection of B12 deficiency depends on the diagnostic strategy and the type of B12 assay used in the measurement[4,5].

In general, poor dietary intake and malabsorption conditions for example, pernicious anemia (PA), are the most common causes of B12 deficiency. The wrongheaded immune response in PA is directed against the gastric parietal cells and the gastric H/K-ATPase resulting in the deficiency of the intrinsic factor and achlorhydria. Vitamin B12 deficiency in PA is not only caused by the loss of the intrinsic factor but is also due to the associated achlorhydria because gastric acid is needed to release cobalamin from its dietary sources [6].

Primary hypothyroidism is a disease of the thyroid gland that results in a reduction of the blood levels of the thyroid hormones (thyroxine [T4] and triiodothyronine [T3]) and a subsequent compensatory rise in the thyroid-stimulating hormone (TSH) levels. Hypothyroidism can be either overt (OH), with elevated TSH and low free T4 levels, or subclinical (SCH), with a normal free T4 level despite the elevated TSH level. Hypothyroidism affects 3% to 5% of adults and is more common in women and the elderly[7].

In iodine-sufficient regions, autoimmune thyroiditis is the most common cause of primary hypothyroidism, and it is usually associated with the antithyroid peroxidase (TPO) and the antithyroglobulin (TG) autoantibodies[8].

The prevalence of B12 deficiency is 10% to 40% among hypothyroid patients. Previous studies showed that 5% to 10% of patients with primary hypothyroidism have pernicious anaemia, whereas 24% of pernicious anaemia patients have thyroid disease[1].

The link between hypothyroidism and PA is related to the common autoimmune aetiology of both disorders. In addition to PA, hypothyroid patients may have other abnormalities that may cause vitamin B12 deficiency such as inadequate dietary intake or decreased intestinal absorption due to slow gut motility and bacterial overgrowth[2].

Another condition that may coexist with hypothyroidism and can cause B12 deficiency is celiac disease which is an autoimmune disease of the gut that occurs in genetically susceptible individuals due to gluten sensitivity. Twenty-six percent of celiac disease patients have autoimmune thyroid disease (AITD). Low serum level of vitamin B12 is seen in about 40% of untreated celiac disease patients[9].

Both B12 deficiency and hypothyroidism can present with symptoms such as depression, memory impairment, dementia, fatigue, numbness, and paresthesia. Due to the non-specificity of symptoms, B12 deficiency may be overlooked in hypothyroid patients[10].

The early recognition and appropriate treatment of B12 deficiency in hypothyroid patients are crucial because it is a reversible cause of peripheral neuropathy (PN), myelopathy, cognitive defects, anaemia, and pancytopenia. However, the significance of B12 deficiency in hypothyroidism and the need to screen hypothyroid patients with serum B12 level measurement is a subject of controversy. Some studies reported a prevalence of B12 deficiency among hypothyroid patients similar to euthyroid patients, while other studies reported a high prevalence of B12 deficiency among hypothyroid patients[11]. The present paper will review the facts concerned with hypothyroidism and B12 deficiency association

REVIEW OF LITERATURE

Hypothyroidism

Hypothyroidism is a chronic disease associated with deficiency in the thyroid hormones, thyroxine (T4) and triiodothyronine (T3). Untreated or inadequately treated hypothyroidism results in musculoskeletal and nurological symptoms, , cardiovascular disease, and infertility[12]. Environmental iodine deficiency is the most common cause of hypothyroidism, worldwide, while in areas of iodine sufficiency, the most common cause of primary hypothyroidism is autoimmune thyroiditis (Hashimoto's disease)[13].

The full implications of hypothyroidism in the population are not completely appreciated or defined. Hypothyroidism affects up to 5% of the population according to European prevalence estimates, while as many as 5% of the population may have undiagnosed thyroid failure[14]. Among the patients who are treated, up to one-third are not receiving adequate treatment. The economic impact of undiagnosed, untreated or undertreated hypothyroidism is therefore not inconsequential, especially with regard to costs associated with maternal and congenital hypothyroidism, or with hypothyroid patients having comorbid conditions such as diabetes mellitus[15].

Hypothyroidism is also associated with decreased quality of life, increased number of sick leave days and even increased mortality[16]. Levothyroxine is the mainstay of treatment for hypothyroidism, and is one of the World Health Organization's essential medicines required for basic health care[17].

Epidemiology and Risk Factors

The prevalence of overt hypothyroidism in the general population varies between 0- 3% and 3-7% in the USA and between 0-2% and 5-3% in Europe, depending on the definition used[14].

A meta-analysis[7] of studies across nine European countries estimated the prevalence of undiagnosed hypothyroidism, including both overt and mild cases, at around 5%. Differences in iodine status affect the prevalence of hypothyroidism, which occurs more frequently both in populations with a relatively high iodine intake and in severely iodine-deficient populations[18].

Hypothyroidism occurs more frequently in women, in older people (>65 years), and in white individuals, although data on ethnic differences are scarce[19].

Hypothyroidism is more common in patients with autoimmune diseases, such as type 1 diabetes, autoimmune gastric atrophy, and coeliac disease, and can occur as part of multiple autoimmune endocrinopathies. Individuals with Downs'

syndrome or Turners' syndrome have an increased risk of hypothyroidism. By contrast, tobacco smoking and moderate alcohol intake are associated with a reduced risk of hypothyroidism[20].

The heritability of TSH and free thyroxine concentrations in serum is estimated to be 65% and 23-65%, respectively[21]. Results from genome-wide association studies have so far explained only a small proportion of thyroid function variability and only three studies have focused on hypothyroidism specifically. The loci most consistently implicated in hypothyroidism include autoimmunity-related genes and thyroid-specific regulatory genes (panel). Most of these loci are also associated with serum TSH concentrations within the reference range[22]. Monogenetic disorders leading to congenital hypothyroidism are rare and include TSH resistance (due to an inactivating mutation in the TSH receptor), thyroid dysgenesis, and thyroid dyshormonogenesis[23].

Causes and Classification

Hypothyroidism can be classified as:

1. Primary (due to thyroid hormone deficiency);
2. Secondary (due to TSH deficiency);
3. Tertiary (due to thyrotropin-releasing hormone deficiency); and
4. Peripheral (extra-thyroidal; panel)

Central hypothyroidism (including both secondary and tertiary) and peripheral hypothyroidism are rare and account for less than 1% of cases[24].

In iodine-sufficient areas, the most common cause of hypothyroidism is chronic autoimmune thyroiditis (also known as Hashimoto's disease). High concentrations of anti-thyroid antibodies (predominantly thyroid peroxidase antibodies and anti-thyroglobulin antibodies) are present in most patients with autoimmune thyroiditis. Raised concentrations of thyroid peroxidase antibodies are also detected in about 11% of the general population[25].

In patients with subclinical hypothyroidism, thyroid peroxidase antibody measurements help to predict progression to overt disease. The exact mechanisms underlying autoimmune thyroiditis are not known, but both genetic and environmental factors are involved. A higher genetic risk score-calculated using five genetic variants for thyroid peroxidase antibodies identified by genome-wide association studies- showed a graded association with higher TSH concentrations and clinical hypothyroidism[26].

Smokers have lower thyroid peroxidase antibody concentrations than non-smokers, and incidence of autoimmune thyroiditis increases after smoking cessation. Other environmental factors implicated in autoimmune thyroiditis are vitamin D and selenium deficiency, and moderate alcohol intake[27].

Central hypothyroidism is rare and affects both sexes equally. It is more often associated with pituitary than hypothalamic disorders but frequently involves both[24].

Biochemically, central hypothyroidism is defined by low or low-to-normal TSH concentrations and a disproportionately low concentration of free thyroxine. Occasionally, TSH concentration is mildly elevated, probably because of decreased bioactivity[28].

Over half of central hypothyroidism cases are caused by pituitary adenomas. Other causes of central hypothyroidism include pituitary or hypothalamic dysfunction due to head trauma, pituitary apoplexy, Sheehan's syndrome, surgery, radiotherapy, genetic, and infiltrative disease. Several drugs are known to affect the hypothalamic-pituitary- thyroid axis (panel)[29].

Consumptive hypothyroidism is caused by aberrant expression of the deiodinase 3 enzyme (which inactivates thyroid hormone) in tumour tissues. Although very rare, such over-expression can induce severe hypothyroidism. Elevated concentration of deiodinase 3 was first described in a newborn baby with infantile hepatic haemangiomatosis, but can also occur in patients with vascular and fibrotic tumours and gastrointestinal stromal tumours[30].

Patients with rare genetic syndromes that lead to a reduced sensitivity to thyroid hormone (panel) usually have normal TSH concentrations, but can also present with tissue-specific hypothyroidism[31].

Clinical Presentations

The clinical manifestations of hypothyroidism range from asymptomatic presentation to life threatening- myxedema coma. Myxedema coma, which was first described in the late 1900s as an outcome of long-standing untreated and severe hypothyroidism, has become a rare condition. Nevertheless, because the disease course is striking, with mortality of 40% despite treatment, early recognition is vital[32].

Myxedema coma leads to an altered mental status, hypothermia, progressive lethargy, and bradycardia and can eventually result in multiple organ dysfunction syndrome and death. Therefore, early initiation of thyroid hormone therapy and other supportive measures is crucial[33].

Although very rare, severe primary hypothyroidism can lead to pituitary hyperplasia with concomitant pituitary pathology (e.g., secondary adrenal insufficiency) and symptoms (e.g., amenorrhoea)[34].

The most common symptoms of hypothyroidism in adults are fatigue, lethargy, cold intolerance, weight gain, constipation, change in voice, and dry skin, but the clinical presentation can include a wide variety of symptoms that differ with age, sex, and time between onset and diagnosis (Table 1)[35].

The symptoms for the diagnosis of hypothyroidism are non-specific, especially in elderly patients who present with fewer and less classic signs and symptoms than younger individuals.

An increase in the severity of symptoms might predict hypothyroidism, since a change in seven or more symptoms in the past year increases the likelihood of hypothyroidism (likelihood ratio 8-7) [36].

However, in a case-control study, none of 34 hypothyroidism-related symptoms could be used to identify patients with hypothyroidism. Furthermore, 15% of patients with autoimmune hypothyroidism are asymptomatic or report only one hypothyroidism- associated symptom, whereas 70% of euthyroid controls have one or more thyroid- associated complaints[37].

Table 1: Clinical presentation and implications of hypothyroidism[35]

	Presentation	Signs and implications
General Metabolism	Weight gain, cold intolerance, fatigue	Increase in body-mass index, low metabolic rate, myxedema*, hypothermia
Cardiovascular	Fatigue on exertion, shortness of breath	Dyslipidemia, bradycardia, hypertension, endothelial dysfunction or increased intima-media thickness*, diastolicdysfunction*,Pericardialeffusion*,hyperhomocysteinemia*, electrocardiogram changes*
Neurosensory	Hoarseness of voice, decreased taste, vision or hearing	Neuropathy, cochlear dysfunction, decreased olfactory and gustatory sensitivity
Neurological and Psychiatric	Impaired memory, paresthesia, mood impairment	Impaired cognitive function, delayed relaxation of tendon reflexes, depression*, dementia*, ataxia*, Carpal tunnel syndrome and other nerve entrapment syndromes*,myxedema coma*
Gastrointestinal	Constipation	Reduced oesophageal motility, non- alcoholic fatty liver disease*, ascites (very rare)
Endocrinological	Infertility and sub-fertility, menstrual disturbance, galactorrhoea	Goiter, glucose metabolism dysregulation, infertility, sexual dysfunction, increased prolactin, pituitary hyperplasia*

Musculoskeletal	Muscle weakness, muscle cramps, arthralgia	Creatine phosphokinase elevation, Hoffman's syndrome*, osteoporotic fracture* (most probably caused by overtreatment)
Haemostasis and Haematological	Bleeding, fatigue	Mild anaemia, acquired von Willebrand disease*, decreased protein C and S*, increased red cell distribution width*, increased mean platelet volume*
Skin and Hair	Dry skin, hair loss	Coarse skin, loss of lateral eyebrows*. yellow palms of the hand", alopecia areata*
Electrolytes and Kidney Function	Deterioration of kidney function	Decreased estimated glomerular filtration rate, hyponatraemia*

*Uncommon Presentation

Vitamin B12

Vitamin B12 (B12) also known as cobalamin has a chemically complex structure. It is the largest of all vitamins[38]. At the centre of a coring ring, it contains an atom of cobalt and is the only active substance in the body. In the mitochondria it exists in 2-deoxyadenosyl (ado) form which is the cofactor for the enzyme L-methyl malonylcoenzymeA (COA) mutase. Methyl cobalamin which is the cofactor of methionine synthase is the other major cobalamin occurring naturally. Purine and pyrimidines synthesis requires methionine synthase. The reaction in which methyl group of methyl tetrahydrofolate is transferred to homocysteine to form tetrahydrofolate and methionine. Megaloblastic anaemia develops due to interruption of this reaction. Transcobalamin II is the active transport protein for vitamin B12. The endogenous forms consist of cobalamin and holotranscobalamin. The reduced state is treated with cyanocobalamin.

Availability

Vitamin B12 is synthesised solely by anaerobic microorganisms. The food of animal origin is the only source available for humans which include fish, meat, poultry, dairy and eggs. There are no naturally occurring active forms of vitamin B12 from plant sources. It is also available in the supplements and fortified foods in crystalline form[39]. The bioavailability of vitamin B12 depends on individual's gastrointestinal absorption capacity. The supplements contain cyano form, which is also found in trace amounts in food. Deficiency results from reduced consumption, reduced absorption, autoimmune states or genetic disorders.

Absorption

Cobalamin absorption consists of two mechanisms, active and passive. Passive mechanism occurs via the buccal, duodenal and ileal mucosa but is inefficient. The active mechanism is the normal physiologic mechanism, occurs through ileum and is mediated by the intrinsic factor (IF). Hydrochloric acid which is produced by the gastric mucosa is required to separate the vitamin B12 which is bound to the protein. This released cobalamin binds to R protein and reaches duodenum where R protein gets separated. Intrinsic factor binds to the free cobalamin and is absorbed by distal ileum. Vitamin B12 is secreted in bile which via the ileal receptors gets reabsorbed into enterohepatic circulation. This process requires intrinsic factor. Intrinsic factor deficiency leads to pernicious anaemia. About 0.1% gets excreted per day. Excess vitamin B12 gets excreted in urine.

Vitamin B12 Deficiency in General Population

3-4% of the general population have vitamin B12 deficiency. The reduced state is very rare in kids and adolescents. Vitamin B12 helps in central nervous system myelination, synthesis of nucleic acids and erythropoiesis. A sufficient contribution of B12 is necessary to support the function[40]. Malabsorption and reduced consumption through diet are not the uncommon reasons for reduced state of B12, which is usually seen in the elderly[41]. Strict vegetarians are prone to B12 deficiency and can meet their requirements from supplements and fortified foods. Vegetarian pregnant and lactating women are at high risk of deficiency and require adequate intake of vitamin B12 supplements. Under nutrition is common among the elderly due to physical capacity, illnesses and inflammation of gastric mucosa. Malabsorption usually occurs due to inability to break free B12 which is present bound to protein. Bariatric surgery patients are at increased risk of developing vitamin B12 deficiency and also require lifelong supplementation through diet.

Patients with both hypothyroidism and vitamin B12 deficiency

also have similar symptoms such as fatigue, dementia, weakness, memory loss, depression, lethargy and tingling. Thus, vitamin B12 deficiency may be ignored in hypothyroidism. Macrocytosis occurs commonly in patients having underactive thyroid. The relationship between TSH and B12 vitamin is not studied in detail. Due to inadequate intake, sluggish bowel motility, bacterial overgrowth, vitamin B12 deficiency can occur in hypothyroidism. Hypothyroid patients on thyroid hormone replacement therapy may not fully recover at times due to vitamin B12 deficiency.

Vitamin B12 Deficiency in Hypothyroidism

The prevalence and clinical features of B12 deficiency in hypothyroid patients were evaluated in one hundred and sixteen hypothyroid patients[2]. Laboratory parameters including Haemoglobin, MCV, Vitamin B12 levels and presence of anti-thyroid antibodies were analyzed. Patients with low B12 levels were treated with parenteral intramuscular vitamin B12 monthly, and monitored for improvement of symptoms. In this study there were 95 females and 21 males.

Forty six (39.6%) hypothyroid patients had low vitamin B12 levels. Males and females had the same prevalence of B12 deficiency. Generalized weakness, impaired memory, depression, numbness and decreased reflexes were more frequently noted in B12 deficient patients, but failed to achieve statistical significance when compared with B12 sufficient patients. The mean Hb was 11.9+/- 1.6 mg/dl in B12 deficient group and 12.4 +/- 1.7 mg/dl in the B12 sufficient group, however the mean MCV did not differ in the two groups. Patients with B12 deficiency did not have a higher prevalence of anaemia. Thyroid antibodies were checked in half the patients and 67% had positive titres for anti thyroid antibodies. Prevalence of vitamin B12 deficiency did not differ in patients with positive antibodies (43.2%) compared to those with negative antibodies (38.9%) (p= 0.759). Twenty four hypothyroid patients with B12 deficiency received intramuscular vitamin B12 injections monthly and improvement in symptoms was noted in 58.3% .Additionally, 21 subjects complained of symptoms consistent with B12deficiency but who had normal range B12, levels and were prescribed monthlyB12 injections and 8 (40%) had good subjective clinical response at 6 months.

The study concluded that there was a high (approx 40%) prevalence of B12 deficiency in hypothyroid patients. Traditional symptoms were not a good guide to determine the presence of B12 deficiency. Screening for vitamin B12 levels should be undertaken in all hypothyroid patients, irrespective of their thyroid antibody status. Replacement of B12 led to improvement in symptoms, although a placebo effect could not be excluded, as a number of patients without B12 deficiency also appeared to respond to B12, administration[2].

A literature search was conducted using multiple electronic databases to assess the prevalence of vitamin B-12 deficiency in thyroid dysfunction. Only original studies assessing the prevalence of vitamin B-12 deficiency in thyroid dysfunction that reported their findings as percentages of the sample were eligible for inclusion. From a total of 7091 manuscripts generated, 6 were included in this review. The prevalence of vitamin B-12 deficiency in hypothyroidism was reported as 10, 18.6, and 40.5% in three separate studies. The prevalence of deficiency in autoimmune thyroid disease was reported as 6.3, 28, and 55.5% in three studies. The prevalence of vitamin B-12 deficiency in hypothyroidism and autoimmune thyroid disease were reflective of the nutrition status of the population. Autoimmune thyroid disease was also associated with the autoimmune disorders pernicious anaemia and atrophic gastritis which might lead to malabsorption of vitamin B-12. Vitamin B-12 screening was recommended upon initial diagnosis with autoimmune thyroid disease and then periodically thereafter. There was not enough evidence to recommend regular screening for patients with hypothyroidism unless the underlying cause was autoimmune thyroid disease[42].

Siddique and associate from Pakistan determined the prevalence of vitamin B12 deficiency in hypothyroid patients. Two hundred and twenty five hypothyroid patients with age range of 30-70 years of either sex willing to participate in study were selected. Estimation of serum vitamin B12 was carried out. Cut off value for vitamin B12 was taken <148 pmol/L. In this study 103 patients (45.8%) were female and rest 122 (54.2%) were males. 54 patients (24%) had Vitamin B12 deficiency while rest 171 (76%) showed negative results. Female gender, malnutrition, lower BMI and socioeconomic status were risk factors linked with vitamin B12 deficiency. Age was not among the risk factors. It was concluded that prevalence of vitamin B12 deficiency was high (24%) in Pakistani patients with hypothyroidism. Female patients with malnutrition and lower BMI should be screened periodically to reduce the complications associated with vitamin B12 deficiency[43].

In another study by Tripathi and associate compared the vitamin B12, Folate and Ferritin with thyroid hormones in hypothyroid individuals. In this study, total 350 samples were included in which 175 were hypothyroid patients and 175 were normal individuals of age group between 15-65 years. Measurements of serum concentrations of Total T3, Total T4, TSH, Vitamin B12, Folate and Ferritin were done using Chemiluminiscence Immunosorbant Assay. Serum TSH levels were significantly increased in Hypothyroidism as compared to normal individual (7.42±1.75 vs. 2.72±1.28, p< 0001*). The total T3 level was significantly decreased in Hypothyroidism in comparison to normal individual (0.43±0.41 vs. 1.30±0.29, p<0001*). Similarly, total T4 level was significantly decrease in Hypothyroidism in comparison to normal individual (3.60±1.38 vs. 6.62±1.11, p<0001*). Level of Vitamin B12 was significantly decreased in Hypothyroidism in comparison to normal individual (210.45±129.30 vs. 483.93+264.74, p< 0001). Folate was significantly decreased in Hypothyroidism as compared to normal (2.51±0.99 vs. 6.67±0.83, p< 0001*). Ferritin was also observed significantly decreased in Hypothyroidism in comparison to normal (23.08±1.18 vs. 63.43±3.30, p< 0001). TSH was observed significantly correlated with Folate (r=0.187* p=0.013). The study

concluded that the lower values of above these parameters in hypothyroidism interpret that thyroid hormones were metabolic hormones and produced impact on metabolic and hormonal balance in which hemopoietic system was highly affected[44].

An observational study was conducted to assess prevalence of anaemia in hypothyroidism and to see if there is any association between vitamin B12 deficiency and anaemia in these patients. All hypothyroid patients attending the medicine OPD or admitted to medicine wards were enrolled for the study. Total 60 patients were included. Data was analyzed to assess the burden of anaemia and B12 deficiency in hypothyroid and to find out any correlation between TSH level, anaemia and vitamin B12 deficiency). About one third of hypothyroid had decreased vitamin B12 levels. TSH level showed significant positive correlation with haemoglobin value. 28% of the hypothyroid patients had vitamin B12 deficiency, but TSH levels itself did not correlate with vitamin B12 level. However, it was seen that those who had combined thyroid and B12 deficiency had significantly higher chances of developing generalized swelling and breathlessness. The study concluded that although there was no correlation between TSH level and B12 deficiency, it might be helpful to determine B12 level in hypothyroid patients who presented with anaemia, generalized swelling and/or breathlessness as B12 supplementation might give better symptomatic relief in them as compared to treating with thyroxine alone. More elaborative studies with larger sample size were required to explore this rather unattended relation of anaemia in hypothyroidism with B12 deficiency[45].

Kumar and associate compared the levels of vitamin B12, Folate and ferritin with thyroid hormones in hypothyroidism patients. The study was carried out among 400 persons in which 200 individuals were normal and 200 were hypothyroid patients. Measurements of serum concentrations of Total T3, Total T4, TSH, Vitamin B12, Folate and Ferritin were estimated using Chemiluminiscence Immunosorbant Assay. In normal individual group, all the serum values were in normal range. The levels of TSH of hypothyroid patients show a significant increase in comparison to normal individuals. Hypothryroid patients had significantly lower levels of serum total T3 and T4. The mean serum vitamin B12 and Folate were also significantly decreased as compared to normal. Serum ferritin level was observed lower in comparison to normal. TSH was observed significantly correlated with Folate. There was no correlation found of TSH with vitamin B12 and ferritin. There was no correlation found between total T3 and Vitamin B12. A negative correlation was observed between total T3 and Folate but it was not significant. No association was found between total T3 and ferritin. Total T4 was observed negatively associated with Vitamin B12 and ferritin but both are not significant. There was no correlation found between Total T4 and Folate. The study concluded that hypothyroid patients were observed to have lower levels of serum Vitamin B12, Folate and Ferritin in comparison to normal individuals[46].

A retrospective study was conducted on130 patients of hypothyroidism. They were investigated for the Vitamin D (Vit-D) and Vitamin B12 (Vit-B12) levels and their correlation with anti-thyroid peroxidase (anti-TPO) antibodies. The patients were divided into two groups as those having Vit- B12 levels below 200 pg/mL (n=60) and Vit-B12 levels equal to or above 200 pg/mL (n=70). These two groups were compared in terms of age, sex, thyroid-stimulating hormone (TSH), free-T4 (FT4), Vit-D, and anti-TPO. The correlation between Vit-B12 and anti-TPO levels was also investigated in these groups. Patients were then divided into four groups according to their Vit-D levels. Patients with normal Vit-D levels (25[OH] D>30 ng/mL; n = 5), those with Vit-D insufficiency (20-30 mg/mL; n=9), those with Vit-D deficiency (10-20 ng/mL; n=43), and those with severe Vit-D deficiency (<10 ng/mL; n=73). These four groups were compared in terms of age, gender, TSH, FT4, Vit-B12, and anti-TPO levels. In addition, the correlation between levels of Vit-D and anti-TPO was also investigated. It was found that Vit-B12 deficiency and Vit-D deficiency were associated with autoimmune hypothyroidism, and that there was a negative correlation between Vit-B12 and Vit-D levels and anti-TPO antibodies in these patients. The study concluded that in patients with autoimmune hypothyroidism, Vit-D and Vit-B12 deficiency should be investigated at the time of diagnosis and periodically on follow-ups[47].

In a prospective study the prevalence of vitamin B12 deficiency in hypothyroid patients was determined. The study was conducted at Medicine / Endocrinology department Lady Reading Hospital Peshawar from January to December 2019. 225 hypothyroid patients from IPD & OPD with age range of 30-70 years of either sex willing to participate in study were included in study. Estimation of serum vitamin B12 was carried out. Cut off value for vitamin B12 was taken < 148 pmol/L. 225 patients were included in our sampled population with mean age 47.15 + 7.210 ranging from 40 to 66 years of age. 103 patients (45.8%) were female and rest of 122 (54.2%) were males. In the study 54 patients (24%) had Vitamin B12 Deficiency and rest of 171 (76%) showed negative results. Female gender, malnutrition, lower BMI and socioeconomic status were risk factors linked with vitamin B12 deficiency, while age was not among the risk factors. The study concluded that prevalence of vitamin B12 deficiency was high 24% in Pakistani patients with hypothyroidism[48].

A hospital-based study was done on patients of hypothyroidism to determine the prevalence of vitamin B12 deficiency (<200 pg/mL). Most of the hypothyroid patients were <50 of age; out of these, 24.5% of patients had vitamin B12 deficiency. While in the age group >50 years, 27.3% of patients had vitamin B12 deficiency. The study concluded that Vitamin B12 deficiency was common in hypothyroid patients. Screening for vitamin B12 deficiency should be undertaken routinely in the diagnosis of hypothyroidism and regularly thereafter[49].

In a retrospective review of patients who presented with memory complaints were assessed in a study conducted at Peru. They were subjected for correlation of thyroid dysfunction, vitamin B12 and Folate deficiencies. Patients had either subjective cognitive decline (SCD), MCI, or dementia. They included 720 patients (330 SCD, 154 MCI, and 236

dementia); the dementia group was significantly older [mean age SCD 69.7 ±4.1, dementia 72.4±3.7 (p = 0.000)] and had lower Folate levels than SCD patients. The MCI group had higher free 13 levels compared with SCD patients. Those with lower TSH had greater dementia risk (OR = 2.91, 95%CI: 1.15-6.86) but not MCI risk in unadjusted models. B12 deficiency or borderline B12 deficiency was present in 34% of the dementia group, yet no clear correlation was seen between neuropsychological test results and B12 levels. There was no association between MCI or dementia and thyroid hormone, B12 or Folate levels in adjusted models. The study concluded that the findings did not support an association between metabolic and endocrine disorders and cognitive impairment in older Peruvians from Lima despite a high prevalence of B12 deficiency[50].

A prospective study on 50 newly detected hypothyroid patients was conducted by Raju and Kumar to evaluate vitamin B12 deficiency. Lab parameters analysed included haemoglobin, thyroid function tests (TFT), vitamin B12 levels and antithyroid peroxidase (anti-TPO) antibody levels. Of the 50 hypothyroid patients evaluated, 23 were males and 27 were females between the age of 18 to 70 years. Anti TPO antibodies were present in 24 patients (48%) out of 50, out of which 17 (70%) patients had vitamin B12 deficiency. Out of 50 hypothyroid patients, 26 patients (52%) had vitamin B12 deficiency. Statistically significant association between autoimmune hypothyroidism and vitamin B12 deficiency was detected. It was found that 26 of 50 (52%) patients had low B 12 levels. Incidence in females (54%) was more than in males (46%). The study distinctly showed association between hypothyroidism and vitamin B12 deficiency and also autoimmune thyroid disease[51].

Prevalence of auto immune thyroid disease and vitamin B12 deficiency was assessed in patients with thyroid disorders in Himalayan region. Study population comprised of patients above 18 years of age. Thyroid function tests (T3, T4, TSH) along with anti thyroperoxidase antibody (ATA) was done by chemiluminescence and vitamin B12 levels were done by chemiluminiscent enzyme immunoassay after serum separation of 120 subjects. ATA level >50ulU/ml was taken as positive and Vitamin B12 deficiency was taken as a value less than 160 pg/ml. Mean age of study population was 42.48 (±12.32) years. Forty hypothyroid and forty hyperthyroid and 40 controls were recruited. ATA positivity was reported in 52.5% (63/120) of the samples. In the present study more than 50% of cases with thyroid disorder and ATA positivity showed deficiency of vitamin B12 (hypothyroidism 63.3% hyperthyroidism, 51.8%). The study concluded that all patients with thyroid dysfunction should be screened for vitamin B12 status and treated accordingly[52].

In another recent study, Aon and associate assessed the prevalence of B12 deficiency among hypothyroid patients and evaluated for pernicious anemia and celiac disease as etiologies. A total 133 patients were included. Thyroid hormones and thyroid peroxidase (TPO) autoantibodies were measured. Serum B12 was measured and if deficient, intrinsic factor antibodies (IFAB) and tissue transglutaminase (tTG) antibodies were evaluated. The study included 45 patients with overt hypothyroidism (OH), 48 patients with subclinical hypothyroidism (SCH), and 40 patients as controls. Mean age was 34.3 years and 82% were females, TPO antibodies were positive in 73.5% of OH and 51.1% of SCH patients. B12 deficiency was detected in 33.3%, 47.9%, and 37.5% of OH, SCH, and controls, respectively with no significant difference (P.334). Borderline-to- low B12 level was more prevalent in the OH and the SCH groups compared to controls (68.9%, 85.4%, and 57.5%, respectively; P=.014). Among B12- deficient hypothyroid patients, 7.5% had positive IFAB and 13.3% had positive tTG antibodies. We did not find a significant association of TPO positivity and B12 deficiency (OR, 0.69; 95% CI 0.3-1.57; P.147). The study concluded that they did not find a higher prevalence of B12 deficiency among hypothyroid patients nor an association with TPO positivity. Borderline B12 levels were more prevalent among hypothyroid patients[53].

The prevalence of vitamin B12 deficiency in cases of subclinical hypothyroidism (SCH) was studied. One hundred patients of subclinical hypothyroidism (26 males and 74 females) and equal number of age and sex matched controls were included in the study. The serum levels of TSH, T3 and T4 were estimated through chemiluminescence by fully automated analyzer (Vitros 5600) to identify cases of SCH. The serum level of Vitamin B12 was estimated through ELISA technique. The collected data were analyzed statistically using unpaired student t-test and were compared by using Pearson correlation coefficient. In SCH patients, both T3 and T4 levels were within normal range, whereas TSH levels were in the range of 4.9-11.2 mlU/lit. Significantly low levels of serum Vitamin B12 were found in cases of subclinical hypothyroidism ($p < .0001$). These levels showed a highly significant negative correlation ($r = -0.2536$; p-value -0.01109) with serum TSH levels. The study concluded that there was a higher prevalence of Vitamin B12 deficiency in SCH patients. Hence, they hypothesized that by routine laboratory testing, early detection of vitamin B12 deficiency, and appropriate therapeutic measures could be helpful[54].

Singh and associate assessed the prevalence of vitamin B12 deficiency, the spectrum of clinical features and to draw attention to the possibility of rare hidden characteristics. The study was a multicenter retrospective, and prospective. All cases of vitamin B12 deficiency of either sex or age were enrolled in this study. Parenteral vitamin B12 was given, and cases were evaluated for the response on follow-up for more than three months. Of 220 cases, 52.27% were males. Maximum cases were reported from the age group 50 to 65 years (27.27%) and belonged to urban areas (59.1%). The majority were strict vegetarian (86.36%). Among comorbidities, diabetes (20.91%) followed by malabsorption (10.45%) were most common. The cutaneous manifestations were revealed at 38.18%. The most frequent neurological manifestation was paraesthesia (98.18%). Head heaviness/ache was the most frequent (95%) psychiatric manifestation. Anemia was revealed in 87.73% of cases with 88.64% macrocytosis. Axonal sensorimotor (52.63%)

neuropathy was a prevalent finding of NCV study. The study concluded that a high index of clinical suspicion was needed in cases with vague manifestations, especially in the pure vegetarian population. Early recognition could prevent further damage as most of its related disorders were generally reversible with treatment[55].

In a nutshell, there still needs larger studies in this direction to know the exact correlation between vitamin B12 levels in hypothyroid individuals. However, at the present time one should be vigilant regarding vitamin B12 deficiency in such patients, because clinically the symptoms of both diseases are common. Treating one condition without consideration of other may not benefit the patient.

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Review

Lymph – The Essence of Life

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ABSTRACT

Lymph is the cream of all we eat and drink. In fact, it is the cream of all creams. Biologically, lymph contains most ingredients of the blood except red pigment. It has same composition as of the interstitial fluid and works for the defense of the body. However, as per Yoga psychology, lymph is a hormone and other glands, use this to manufacture their respective hormones. It is also the food for the brain cells and the cause of psychic change. Most importantly, its formation is affected by physical and psychic environment to which the role of microvita may be further added. The present article deals with the prevailing scientific knowledge, the concept of yoga psychology, the new science of bio-psychology and the microvita, regarding importance of lymph and the possible future scientific research.

KEYWORDS: Immuno-proteins, Thymus, Sentient food, Microvita, Physico-psycho-Spiritual practice.

INTRODUCTION

The streams of spirituality and medical sciences have been flowing for thousands of years without any interrelationship between two. It is only last two or three decades that the synthesis between these two sciences has emerged. It was in fact, the pioneer concepts of microvita and biopsychology coined by Shrii P.R.Sarkar, that the people among all strata have started thinking in terms of synthesizing spiritual science and physical science. In fact, concept of microvita is the link between these two. Whatever he said in his discourses, are entirely logical and rational but still need empirical verifications and acceptance by scientific community. In fact, many of his claims are a way ahead of science in its present state. Hopefully, the intellectual mass will analyze, verify and accept the concepts and utilize them for human welfare. The concept of lymph is one of the examples where the streams of sciences (spiritual and medical) diverge. The present article is an attempt to search interrelation among the physical, psychological, para-psychological and spiritual thoughts about lymph and the possible connection of lymph with microvita

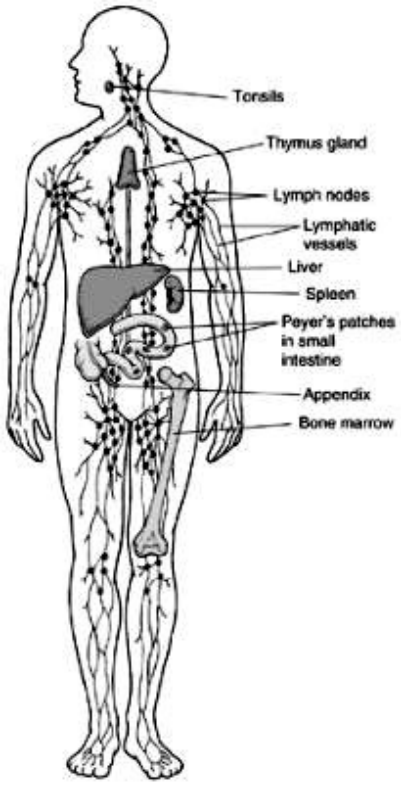

Figure 1 : Lymph nodes and Limphatic vessels

Lymphatic System

The lymphatic system represents an accessory route through which fluid can flow from the interstitial spaces into the blood (Fig. 1). It is important to note that the lymphatics can carry proteins and large particulate matter away from the tissue spaces, neither of which can be removed by absorption directly into the blood capillaries. The return of proteins to the blood from the interstitial spaces is an essential function without which life cannot sustain.

Scientific Concept

Lymph contains most ingredients of the blood except red pigment. It is extracted from the blood, processed and modified by the regional lymph glands before returning to the blood. It is through lymphatics that the lymph is collected from all regions of the body and is poured into the blood. The lymph glands are present all over the body and grouped in certain areas. Superficially they are around the joints e.g. axilla, groin, elbow, knee. The other important groups are in the neck, chest and abdomen. Besides these, lymphatic tissue are present in various other organs e.g. the liver, spleen, gut, tonsils etc. All tissues have lymphatic channels except the brain, spinal cord, bones, deeper parts of the nerve and some parts of the skin and muscles. These tissues do have minute channels called perilymphatics or paralymphatics through which interstitial fluid can flow. This fluid eventually empties either into the lymphatic vessels or in the case of the brain, in the cerebro-spinal fluid and then directly into the blood. This whole system of lymph with lymph glands, lymphatics and scattered lymphoid tissues are called the lymphoid system.

Essentially all the lymph vessels from the lower part of the body eventually empty into the thoracic duct, which empties at the junction of the left internal jugular vein and left subclavian vein. Lymph from the left side of the head, the left arm and the parts of the chest region also enter the thoracic duct. Lymph from the right side of the neck and head, the right arm and parts of the right thorax enters the right lymph duct (much smaller than the thoracic duct) which empties at the junction of the right subclavian vein and right internal jugular vein.

The fluid that returns to the circulation by way of the lymphatics is extremely important because substances of high molecular weight, such as proteins, cannot be absorbed from the tissue in any other way, although they can enter the lymphatic capillaries, almost unimpeded. The reason for this is a special structure of the lymphatic capillaries.

Formation of Lymph

Lymph is derived from interstitial fluid that flows into the lymphatics. Therefore, lymph as it first enters the terminal lymphatics has almost the same composition as of the interstitial fluid. Twenty liters of fluid is filtered per day in the intercellular spaces from the small blood capillaries. Seventeen liters with all its electrolytes is soon reabsorbed back into the venous blood . The remaining 3 liters along with filtered proteins remain in intercellular spaces. The protein molecules,

because of their large size are not reabsorbed through the small pores of venous capillaries. The remaining three liters of fluid in the tissue with its protein content must be continuously removed. If the proteins filtered in the tissues are not removed readily by lymphatics, the tissues will develop edema. This will disturb the dynamics of fluid exchange, which is crucial for the life.

The protein concentration in the interstitial fluid of most tissues averages about 2g/dl, and the protein concentration of lymph flowing from these tissues is near this value. In the liver, lymph formed has a protein concentration as high as 6g/dl and lymph formed in the intestine has a protein concentration as rd high as 3-4g/dl. Because about 2/3 of all lymph is derived from the liver and intestines, the thoracic duct lymph, which is a mixture of lymph from all area of the body, usually has a protein concentration of 3-5g/dl.

The lymphatic system is also one of the major routes for absorption of nutrients from the gastrointestinal tract especially for absorption of virtually all fats in food. Indeed, after a fatty meal, thoracic duct lymph sometimes contains as much as 1-2% fat.

Finally, even large particles; such as bacteria can push their way between the endothelial cells of the lymphatic capillaries and in this way enter the lymph. As the lymph passes through the lymph nodes, these particles are almost entirely removed and destroyed.

It is important to note that proteins are the most essential ingredients of human chemistry and the body conserves them at all costs. In this direction, lymph plays an important role by conserving the protein and thereby maintaining tissue structure. Proteins are present in every cell of the body and provide the skeleton of the cells, thereby maintain the shape and structure of the cells. Proteins also help in carrying the minerals like iron, calcium, magnesium etc. in the body . Furthermore, proteins are made of amino acid molecules which are utilized by some endocrine glands to manufacture their hormones e.g. thyroid, parathyroid and pituitary glands.

Lymph also transports fat, particularly from the regions of the gastrointestinal tract where it is absorbed from the diet. Like proteins, fat is also an important ingredient of the human body and execute important physiologic functions. The cell wall is made up of fat, through which exchanges of various nutrients and minerals occur. Some cells have special fat components for specialized functions. Brain cells for example, are rich in fat, which has special conducting properties for the propagation of nerve impulses. Some endocrine glands such as adrenal and sex glands utilize fat for synthesis of their hormones which are called steroid hormones.

In a nutshell, lymphatic system plays a very important role in the transportation of the two most important biological nutrients, the protein and fat, in the human body. These two ingredients are crucial for the maintenance of structural integrity, hormonal synthesis and sustaining human health.

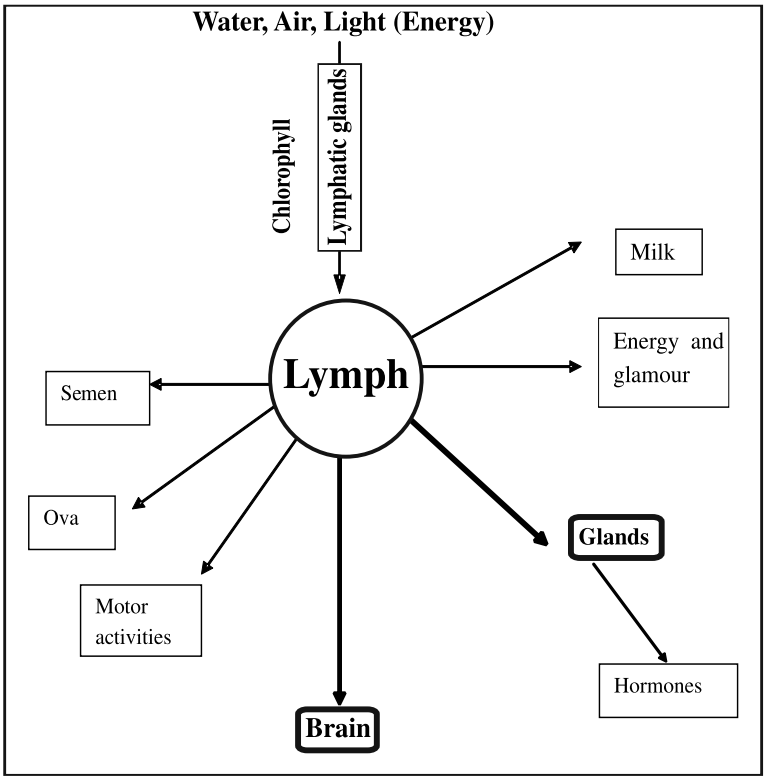

Figure 2 : Lymph for all round development

Circulation of Lymph

Lymph flows at the rate of 120 ml/hr, much slower than the blood. This can be increased about 5 to 15 fold by exercise and decreased by the rest. Valves exist in all the lymphatic channels. The lymphatic pump is enhanced by muscle contraction, movements of the parts of the body, compression and by arterial pulsation. Respiratory movements of the chest and lungs also enhance this pumping effect.

Some organs are located in the remote nooks and corners of the body from which lymph drainage is not easy in the ordinary conditions and therefore the flow of lymph is minimal from these organs. Kidneys, adrenal glands and pancreas are adhered to the back wall of the abdomen where normal day to day activities do not produce a significant movement or compression of these organs. Furthermore, lymph flow from these organs is further reduced in people leading sedentary life styles. To reach every nook and corner of the body, one needs special postures which may not be vigorous, nevertheless; very effective in enhancing the lymph flow from these remotely placed organs. These special postures (a`sana`s or yogic postures) when coupled with coordinated breathing (Pr`ana`ya`m) squeeze the main lymphatic channels in the chest, enhance the lymph flow many fold (Fig. 3).

When lymph flow is decreased in the face of normal lymph formation, the tissue loses its luster and becomes swollen or edematous. This is associated with the loss of energy. On the other hand, when lymph formation is decreased as occurs in dehydration and debilitating conditions, the energy is sapped and glamour is lost.

Lymphoid – the Defense System

A more important function of the lymphoid system is removal of various foreign materials such as dust particles inhaled in lungs, viruses and bacteria which have invaded the tissues. These are removed before they reach the blood. Lymphatics traverse through a number of lymph glands where the lymph is exposed to many kinds of defensive cells, called macrophages that engulf the foreign intruders and digest them out of existence. These scavenger cells are well programmed to recognize what is foreign to the body and which is its own.

In the lymph glands, many cells and proteins are added to the lymph, which plays a very important role in the immune reactions of the body and hence called immuno-lymphocytes and immuno-proteins respectively. These two immune materials are produced by the different regions of the lymph nodes. The region of the lymph node, which produces lymphocytes (T- lymphocytes) is dependent upon the thymus gland. The region of the lymph glands, which have cells that produces immuno-proteins or immuno-globulins are dependent on the signals from the bone marrow (B-lymphocytes) and produce various classes of immunoglobulins (IgG IgM, IgA, IgE). These proteins immobilize and inactivate the intruders while the Tlymphocytes engulf them. Thus after passing through the lymph nodes, the lymph gains (immune cells and proteins) and loses (harmful intruders) something.

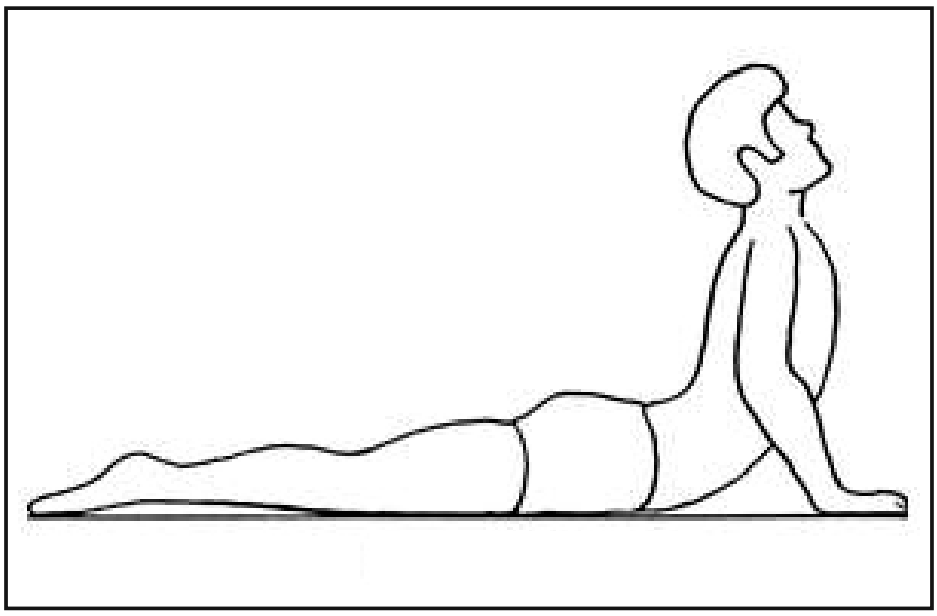

Figure 3 : Yogic a'sana - Cobra Posture

Thymus- heart of Lymphoid System

It is regarded as the heart of the lymphoid system because whatever happens in the lymph glands and in the lymphoid tissues is pre-planned preprogrammed and predetermined in the thymus gland. In the fetus, the thymus gland is very active in sorting out its affairs. It is so choosy in the early stage that 90% of its own cells that multiply are rejected and killed. Only the very 'fit' and 'competent' one are allowed leaving the gland to migrate to the lymph glands. These migrating cells are 'stamped' and primed to recognize between self and non-self. This message stays with them as long as they live and when they multiply in the lymph glands, their off- springs carry this message from generation to generation.

Changes in the Thymus Gland

At birth, the thymus has almost finished all its functions. It weighs about 10-15 g and at puberty, its weight doubles its birth weight to about 30-40 g. The growth of the gland after 5 to 6 years of age is due to the increase in its supporting tissues rather than in the cell mass. In fact, the lymphocytes in the gland progressively decrease after this age.

The androgen hormones secreted by the adrenals and sex glands have an antagonistic relationship between these glands and the thymus. Experimentally, it has been shown that removal of sex glands and adrenal glands delays the normal involution of the thymus glands whereas injection of cortisone or androgen sex hormones, cause shrinking or atrophy of the thymus.

By mid-adult life, the thymus shrinks to about 10 g. The remaining cells in the thymus continue to secrete a hormone called thymopoetin or thymosin whose main function is to keep reminding the migrated lymphocytes in the lymph glands what they have been programmed for. It is because of this hormone that the thymus is classed as an endocrine gland despite being the centre of the lymphoid system. This dual role of the thymus is perhaps suggestive of the close relationship between the lymph and the hormones.

Functions of Lymphoid System

1. Transportation of lymph from all parts of the body to the blood
2. Defense of the body
3. Recognition of self and non-self

Yoga Psychological Concept of Lymph

In Yoga psychology, lymph is considered as an important constituent of the body because many glands and sub-glands in the human body are dependent on lymph. The initial stuff in the manufacture of lymph is the energy and vitality derived from the different quinquelemental factors of the Universe such as, light, water etc. It is the cream of all we eat and drink. It is cream of all creams.

Lymph is a hormone manufactured by lymphatic glands. It is the initial hormone and other glands use lymph to manufacture their respective hormones. The lymphatic glands supply the raw material to glands for hormone production. Lymph also maintains the luster of the skin.

In the male and female bodies, the lymphatic glands become very active at the time of puberty. A special type of nerve sensation occurs in the genitals which creates vigor in a person and gives the feeling in the mind “I shall have to do something”. At that age, one decides or tries to decide one's future.

The testes glands convert lymph into semen. If the testes function properly and if there is no hindrance from the lymphatic glands, intelligence will develop. Without the testes, solar plexus (Ana`hat cakra) will be undeveloped and intelligence will decrease. Lymph is also the food for the brain cells, so a shortage in lymph supply to the brain cells affects the intellectual growth of a person. Human qualities grow along with the growth of lymph. The lymph is converted into semen by the testes. Man should have proper control over the conversion of lymph into semen. This is the principle part of Brahmacarya Sa`dhana`.

When the lymphatic glands and the testes start functioning at the same time, the testes work in a proper manner. The raw material for the testes is the hormone generated by the lymphatic glands. In the female body, ova are created in the ovaries. Some of the lymph helps in maintaining proper energy and glamour in the body, and a certain portion, in the case of females, is converted into milk.

In the case of spiritual aspirants, there is excessive hormone secretion in the solar plexus. Love for children is converted into love for the Supreme. The solar plexus cannot function properly if the supply of the lymph is not perennial or regular. Lymph is thus the cause of psychic change, the transformation of love for the unit into love for the Supreme.

For the manufacture of lymph, chlorophyll is a must. Chlorophyll accelerates the speed of the production of lymph, but it doesn't act as the initial stuff. Those who are vegetarians produce more lymph because they get chlorophyll from green vegetables. Those who take animal proteins suffer from want of lymph.

Food, Lymph and Intellect (Brain)

As per yoga psychology, there is intimate relation with the food consumed, the lymph formed and the development of intellectual faculties. In the case of human being, those who are vegetarians and taking sentient food, will manufacture more lymph and that lymph will nourish the glands and plexii and will be utilized as a food for the brain. Moreover, those who are practicing Brahamcarya Sa`dhana`- more lymph will be directed to the intellectual advancement because less will be converted into semen and finally lost. On the other hand, those who consume static food, more of animal proteins- the lymph formation will be less leading to relative intellectual backwardness. Furthermore, lymph will be converted to semen leading to less availability to nourish brain.

In case of animals, those who are granivorous like cows and monkeys will produce more lymph because of more chlorophyll in their diet and will be more intellectually

advanced and it is possible for them to do sa`dhana` in future. On the other hand, those who are carnivorous like cats, tigers, and dogs, though clever and cunning, but are less intellectual than granivorous. They will manufacture less lymph because of lack of chlorophyll in the diet and their brains will be less intellectually developed, and therefore, they cannot do sa`dhana`.

It is well said that what we think depend on what we eat and the link between eating and thinking, thereby is probably the lymph which nourishes the brain. This is purely the concept of yoga psychology and the modern science has to do research in this direction.

Figure 4 : Sentient food

Lymph, Milk Production and Motor Activities

Lymph is also required for the production of milk. Till women give birth to their children, they can move fast but after their children are born, they can't move so fast. If cows give excessive milk, they can't move fast. Deer can move fast but they give little milk. Tiger and cats are carnivorous, that's why they give little milk. Cows and buffaloes give much milk because they take chlorophyll from green grass and green vegetation.

Catalysts for Lymph Production

There are certain factors which act as positive and negative catalysts in the manufacture of lymph. A good environment, both physical and psychic, acts as positive catalyst. Positive psychic and positive physical environments are positive catalytic agents and negative psychic and negative physical environments are negative catalytic agents. Even if food is sentient, but environment is negative, such condition is detrimental to mental progress. Cinema halls, prostitute houses, busy commercial places are negative physical environments. Bad discussions, bad books and bad thoughts prevailing among the local populations are negative psychic environments.

Positive high grade discussions create positive psychic environment. Where spiritual aspirants gather, where spiritual discussions are held (Dharma Cakra, Dharma Maha Cakra) such environments serve as positive catalyst. That is why Shiva recommended satsanga or good company for the attainment of salvation. Satsanga provides positive psychic environment. It will help in the manufacture of lymph. The creation of hormones in the other glands depends upon these positive and negative catalytic agents.

In case of spiritual aspirants or Sa'dhakas, a major portion of the lymph remains in the body. That is why their intellectual standard is higher than the common people. The surplus lymph goes to the brain and serves as food for the nerve cells.

Figure 5 : Physico-psycho-spiritual meditation

Lymph – for Physical, Mental and Psycho-spiritual Development

Lymph is produced from the energy and vitality acquired from the different quinquelemental factors of the Universe. Chlorophyll accelerates the speed of its production. Lymphatic glands supply lymph to the glands and surplus lymph goes to the brain (Fig. 2). Lymph is therefore responsible for energy and glamour, motor activity and production of milk, ova and semen (Physical process). It also goes to glands and plexii producing appropriate hormonal secretions responsible for psychic and psycho-spiritual development. Finally it nourishes brain, causing intellectual development. Hence, lymph is cause of all round development. Sarkar has rightly said that "Human qualities grow along with the growth of lymph".

The Link between Science and Yoga Psychology

At first instance, it is difficult to link the two divergent concepts of lymph. Medical science accepts it as a system responsible for transportation of proteins and fats from interstitial fluid back to blood along with its immunological functions. Spiritual science, on the other hand, considers lymph as the important element having hormonal function and responsible for intellectual advancement. How lymph can be related with hormone? Yoga psychology proposes that the lymph provides raw material for synthesis of hormones. For example, the sex glands in males and females, when activated, utilize the lymph to form sperms and ova and their respective hormones. Biological science gives no comments on this concept.

An interesting coincidence is the observation of high concentration of Acquired Immuno Deficiency Syndrome (AIDS) virus in the lymph glands and the seminal fluid even though the virus enters the body through the blood stream. Both these organs, lymph glands and testes, probably have tissues, which the AIDS virus has affinity for. It is also possible that the lymph is concentrated in the testes making it more vulnerable to the viruses. Whatever the mechanism may be, there is apparently a close relationship between lymph and the testes.

The contention of Shrii Sarkar that lymph is a hormone seems extremely logical. The parts of the lymphoid system have a structure of glands and their contents, i.e. the lymph, is poured directly into the blood which is the requirement for being an endocrine gland, even though transport channels are involved in this function. Lymph contains the precursor of all hormones in the form of protein and fat as well as its own hormones in the form of immunoglobulin and thymosin. In fact, the lymph is as essential for life as are hormones with the difference that hormones are secreted in minute quantity whereas lymph is produced in copious amounts.

One of the most remarkable assertions of Shrii Sarkar is the influence of physical and psychic environments on lymph formation. Physical environments such as cinema, hotels, halls, commercial counters, gatherings, and crowded shopping centers have negative effect on lymph formation. Similarly the negative psychic environment such as those created in pornographic materials, sexual fantasies and excessive sexual indulgences act as a negative catalyst for lymph formation. On the other hand, spiritual company and spiritual discussions create a positive environment facilitating the lymph formation.

It can be concluded that knowledge of the lymph and lymphoid system in modern science is relatively recent and primitive. It is only since the advent of cancer and AIDS that the lymphoid system has attracted attention of medical researchers. Even now the focus of attention is the lymphocytes and the immune response. The relationship between hormone and lymph is not recognized as yet by medical science and it is in this area that Shrii. P.R. Sarkar has given numerous clues for future research.

Microvita and Lymph Production

Shrii P. R. Sarkar's concept of microvita further adds to the explanation of some un-explained. A positive physical and psychic environment induced by positive microvita, therefore enhances more lymph formation (the food for the brain), which brings higher psycho-spiritual status. That higher mental status proves to be a boon for the progress of human faculties and an asset to move towards the closeness of Supreme desideratum. Generating positive microvita environment, (physical and psychic) by increasing their concentration with the help of sentient food, satsanga, swadhyaya, spiritual practice, collective meditation and kiirtana, in fact, affect the entire human endocrinology because microvita act as positive catalytic agents for the lymph production which is the mother of all hormones (Fig. 4,5,6). Chlorophyll; though, accelerate the speed of lymph formation, yet it does not act as an initial stuff. The initial stuff is the energy and vitality derived from the different quinquelemental factors such as light, water etc. to which we would like to add positive microvita. These positive microvita may act as initial stuff or undoubtedly, as said earlier, they act as positive catalytic agent for lymph formation. It is an assumption, a theoretical proposition which needs further discussion and verification.

Figure 6 : Collective Kiirtana

CONFLICTS OF INTEREST: None

FINANCIAL SUPPORT: None

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New Drug Approvals

S. No.	Treatment Indication	Drug's Name	Company	Description	Date of FDA Approval
1.	Birth Control	Opill (norgestrel) Tablets	Perrigo Company plc	Opill (norgestrel) is a progestin-only, over-the-counter birth control pill for the prevention of pregnancy.	July 13, 2023
2.	Respiratory Syncytial Virus (RSV)	Beyfortus (nirsevimab-alip) Injection	Astra Zeneca	Beyfortus (nirsevimab-alip) is a respiratory syncytial virus (RSV) F protein-directed fusion inhibitor used for the prevention of RSV lower respiratory tract disease in neonates and infants.	July 17, 2023
3.	Anthrax Prophylaxis	Cyfendus (anthrax vaccine adsorbed, adjuvanted) Injection	Emergent BioSolutions Inc.	Vanflyta (quizartinib) is an oral FLT3-ITD (FMS-like tyrosine kinase-3-internal tandem duplication) inhibitor for the treatment of patients with FLT3-ITD positive acute myeloid leukemia.	July 20, 2023
4.	Acute Myeloid Leukemia	Vanflyta (quizartinib) Tablets	Daiichi Sankyo	Qlosi (pilocarpine hydrochloride ophthalmic solution) 0.4%, is a low dose formulation of the approved cholinergic agonist pilocarpine indicated for the treatment of presbyopia in adults.	July 20, 2023

Continued ...

S. No.	Treatment Indication	Drug's Name	Company	Description	Date of FDA Approval
5.	Molluscum Contagiosum	Ycanth (cantharidin) Topical Solution - formerly VP-102	Verrica Pharmaceuticals Inc.	Ycanth (cantharidin) is a topical terpenoid for the treatment of molluscum contagiosum in adult and	July 21, 2023
6.	Warfarin Reversal in Urgent Surgery & Invasive Procedures	Balfaxar (prothrombin complex concentrate, human -lans) Lyophilized Powder for Injection	Octapharma USA, Inc.	Balfaxar (prothrombin complex concentrate, human-lans) is a blood coagulation factor replacement product indicated for the urgent reversal of acquired coagulation factor deficiency induced by Vitamin K antagonist (VKA, e.g., warfarin) therapy in adult patients with need for an urgent surgery/invasive procedure.	July 21, 2023
7.	Demodex Blepharitis	Xdemvy (lotilaner) Ophthalmic Solution - formerly TP-03	Tarsus Pharmaceuticals, Inc.	Xdemvy (lotilaner ophthalmic solution) is an isoxazoline ectoparasiticide indicated for the treatment of Demodex blepharitis.	July 25, 2023
8.	Opioid Overdose	RiVive (naloxone hydrochloride) Nasal Spray	Harm Reduction Therapeutics, Inc.	RiVive (naloxone hydrochloride) is an over-the-counter (OTC) opioid antagonist nasal spray indicated for the emergency treatment of opioid overdose.	July 28, 2023

Continued ...

S. No.	Treatment Indication	Drug's Name	Company	Description	Date of FDA Approval
09.	Postpartum Depression	Zurzuvae (zuranolone) Capsules	Sage Therapeutics, Inc.	Zurzuvae (zuranolone) is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator indicated for the treatment of postpartum depression in adults.	August 4, 2023
10.	Geographic Atrophy	Izervay (avacincaptad pegol) Intravitreal Solution	Iveric Bio, Inc.	Izervay (avacincaptad pegol) is a complement C5 protein inhibitor indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).	August 4, 2023
11.	Multiple Myeloma	Talvey (talquetamab-tgvs) Injection	Janssen Pharmaceutical Companies of Johnson & Johnson	Talvey (talquetamab-tgvs) is a first-in-class, bispecific GPRC5D-directed CD3 T-cell engager for the treatment of patients with heavily pretreated multiple myeloma.	August 9, 2023
12.	Prostate Cancer	Akeega (abiraterone acetate and niraparib) Tablets	Janssen Pharmaceuticals, Inc.	Akeega (abiraterone acetate and niraparib) is a CYP17 inhibitor and a poly (ADP-ribose) polymerase (PARP) inhibitor combination indicated with prednisone for the treatment of adult patients with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC).	August 11, 2023

Continued ...

S. No.	Treatment Indication	Drug's Name	Company	Description	Date of FDA Approval
13.	Uveal Melanoma	Hepzato (melphalan) Lyophilized Powder for Injection	Delcath Systems, Inc.	Hepzato (melphalan) is an alkylating drug used as a liver-directed treatment for adult patients with uveal melanoma with unresectable hepatic metastases.	August 14, 2023
14.	Multiple Myeloma	Elrexfio (elranatamab-bcmm) Injection	Pfizer Inc.	Elrexfio (elranatamab-bcmm) is a B-cell maturation antigen (BCMA) CD3-targeted bispecific antibody (BsAb) for the treatment of patients with relapsed or refractory multiple myeloma.	August 14, 2023
15.	Fibrodysplasia Ossificans Progressiva	Sohonos (palovarotene) Capsules	Ipsen	Sohonos (palovarotene) is a retinoid indicated for the reduction in volume of new heterotopic ossification in adults and pediatric patients aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP).	August 16, 2023
16.	CHAPLE Disease	Veopoz (pozelimab-bbfg) Injection	Regeneron Pharmaceuticals, Inc.	Veopoz (pozelimab-bbfg) is a complement C5 inhibitor indicated for the treatment of adult and pediatric patients 1 year of age and older with CHAPLE disease.	August 18, 2023

Continued ...

S. No.	Treatment Indication	Drug's Name	Company	Description	Date of FDA Approval
17.	Macular Degeneration, Diabetic Macular Edema, Diabetic Retinopathy	Eylea HD (aflibercept) Injection	Regeneron Pharmaceuticals, Inc.	Eylea HD (aflibercept) is a higher dose formulation of the approved vascular endothelial growth factor (VEGF) inhibitor aflibercept indicated for the treatment of patients with neovascular (wet) age-related macular degeneration (nAMD), diabetic macular edema (DME), and diabetic retinopathy (DR).	August 18, 2023
18.	Multiple Sclerosis, Crohn's Disease	Tyruko (natalizumab-sztn) Injection	Sandoz Inc.	Tyruko (natalizumab-sztn) is an integrin receptor antagonist biosimilar to Tysabri, approved for the treatment of multiple sclerosis and Crohn's disease.	August 24, 2023
19.	Hematopoietic Stem Cell Mobilization	Aphexda (motixafortide) Lyophilized Powder for Injection	BioLineRx Ltd.	Aphexda (motixafortide) is a hematopoietic stem cell mobilizer indicated in combination with filgrastim (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with multiple myeloma.	September 8, 2023
20.	Myelofibrosis	Ojjaara (momelotinib) Tablets	GSK	Ojjaara (momelotinib) is a JAK1/JAK2 and activin A receptor type 1 (ACVR1) inhibitor for the treatment of myelofibrosis patients with anemia.	September 15, 2023

Continued ...

S. No.	Treatment Indication	Drug's Name	Company	Description	Date of FDA Approval
21.	Bacterial Infection, Trichomoniasis, Amebiasis	Likmez (metronidazole) Oral Suspension - formerly ATI-1501	Appili Therapeutics Inc. and Saptalis Pharmaceuticals, LLC	Likmez (metronidazole) is an oral liquid suspension formulation of the approved nitroimidazole antimicrobial metronidazole for the treatment of trichomoniasis, amebiasis, and anaerobic bacterial infections.	September 22, 2023
22.	Major Depressive Disorder	Exxua (gepirone) Extended-Release Tablets	Fabre-Kramer Pharmaceuticals Inc.	Exxua (gepirone) is an azapirone antidepressant for the treatment of adults with major depressive disorder.	September 22, 2023
23.	Reversal of Pharmacologically Induced Mydriasis	Ryzumvi (phentolamine mesylate) Ophthalmic Solution - formerly Nyxol	Ocuphire Pharma, Inc.	Ryzumvi (phentolamine mesylate) is an alpha adrenergic blocker indicated for the treatment of pharmacologically-induced mydriasis.	September 25, 2023
24.	Pompe Disease	Pombiliti (cipaglucosidase alfa-atga) Lyophilized Powder for Injection	Amicus Therapeutics	Pombiliti (cipaglucosidase alfa-atga) is a hydrolytic lysosomal glycogen-specific enzyme used in combination with Opfolda (miglustat) for the treatment of adults with late-onset Pompe disease.	September 28, 2023

Continued ...

S. No.	Treatment Indication	Drug's Name	Company	Description	Date of FDA Approval
25.	Rheumatoid Arthritis, Polyarticular Juvenile Idiopathic Arthritis, Juvenile Idiopathic Arthritis	Tofidence (tocilizumab-bavi) Injection	Biogen Inc.	Tofidence (tocilizumab-bavi) is an interleukin-6 (IL-6) receptor antagonist biosimilar to Actemra indicated for treatment of moderately to severely active rheumatoid arthritis, polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis.	September 29, 2023
26.	Primary Hyperoxaluria	Rivfloza (nedosiran) Injection	Novo Nordisk	Rivfloza (nedosiran) is a lactate dehydrogenase A (LDHA) directed small interfering RNA used to lower urinary oxalate levels in patients with primary hyperoxaluria type 1 (PH1).	September 29, 2023
27.	Diagnosis and Investigation	Technegas (technetium Tc 99m carbon) Inhalation Aerosol	Cyclopharm Limited	Technegas (technetium Tc 99m carbon) is a radioactive diagnostic agent for the evaluation of pulmonary embolism.	September 29, 2023

(Ravindra Bangar)
Editor

Call for Papers

Pacific Journal of Medical and Health Sciences (ISSN: 2456-7450) is a quarterly journal of the Pacific Group of Institutions in the Medical and Health Sciences. The subject areas for publication include, but are not limited to, the following fields: Anatomy, Anesthesia, Biochemistry, Biomedical Sciences, Physiology, Pharmacology, Cancer, Cardiology, Community Medicine, Dermatology and Venereal Diseases, Diabetes, Endocrinology, Epidemiology and Public Health, Forensic Science, Gastroenterology, Geriatric Medicine, Hematology, Immunology, Infectious Diseases, Internal Medicine, Microbiology, Nephrology, Neurology, Neurosurgery, Obstetrics and Gynecology, Ophthalmology, Orthopedics, Otorhinolaryngology, Pediatrics, Pathology, Psychiatry, Pulmonary Medicine, Radiology, Toxicology, Dentistry, Nursing, Health Informatics, Occupation Safety and Health. Its key aims are to provide interpretations of growing points in medical knowledge by trusted experts in the field, and to assist practitioners in incorporating not just evidence but new conceptual ways of thinking into their practice.

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The *Pacific Journal of Medical and Health Sciences* invites original research based papers, medical case studies and paper reviews. The manuscripts received are sent to referees and are accepted on their recommendation only.

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Your paper should be approximately 8-15 pages in length, including abstract, all figures and tables and references.

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Number references consecutively in the order in which they are first mentioned. Identify references in text, tables, and captions by Arabic numerals superscripted above the line.

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Only use standard abbreviations. SI units should always be used.

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These should be marked with ® and proprietary drug names should be capitalised e.g. Cifran.

Manuscript Order

- TITLE page
    - Full title of the article
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    - Department and institution to which the work should be attributed
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- STRUCTURED ABSTRACT of no more than 150 words. The abstract headings should include:
    - Introduction or background
    - Sources of data
    - Areas of agreement
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    - Growing points
- KEY WORDS: a minimum of 3 key words which reflect the content of the review
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- TEXT to follow a similar general format to the abstract. Authors should ensure that technical language used is understandable to a scientific but general readership. A glossary may be a useful addendum where appropriate.
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- ACKNOWLEDGMENTS
- REFERENCES listed in numerical sequence according to their order of appearance in the text. Avoid using abstracts as references.

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If there are more than 6 authors of a paper, abbreviate to the first 3 names and then add 'et al'. Use abbreviated journal title as given in Index Medicus.

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The use of figures is strongly encouraged where they can assist the reader in the understanding of the article and replace lengthy passages of text. Number figures consecutively and, where figures are related, number them 1(a), 1(b), 1(c) etc.

Photographs

These should be of sufficiently high quality with respect to detail, contrast and fineness of grain.

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Number tables consecutively and place a descriptive heading above each table. Give each column a short heading. Explain in footnotes all non-standard abbreviations used in a table.

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Captions should be brief descriptions of each figure or illustration (e.g. Fig. 1 The diagram shows…). Where relevant, captions should also include definitions for all symbols used.

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Paper be typed	MS. Word
Font	Times New Roman
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Tables, Graphs and charts etc.	In the text, the references for table should be mentioned as Table-1 and so on, not as above table. Same should be followed in case of graphs and charts. Each table, Graph and chart should have its own heading and source.
Abstract	500 Words
Full length paper	5000 Words
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(Editorial Team)

Peer-Review Policy
Double-blind Peer Review Process

Peer-review is the system used to assess the quality of a manuscript before it is published. Independent researchers in the relevant research area assess submitted manuscripts for originality, validity and significance to help editors determine whether the manuscript should be published in their journal.

In cases where the journal is unable to find sufficient peer reviewers, the Editorial Board may identify suitable reviewers and provide reports to avoid further delays for authors. Manuscripts submitted to Pacific Journal of Medical and Health Sciences are first assessed by our editors.

The aim and objective of the Pacific Journal of Medical and Health Sciences is to ensure the high standards of the original and scientific research papers and articles. With our Journal, a double-blind peer review system is in operation.

In the case of proposed publications, our editorial board will judge and evaluate the proposed manuscript on certain parameters like relevance of the submitted work with the aims and scope of the journal, scientific quality the work and contribution of the work in respective branch of knowledge. If, the proposed work found suitable in quick review by the editorial board than editor will forward copies of an author's work to two experts ("referees" or "reviewers") in the respective field by e-mail or through a web-based manuscript processing system.

These referees or reviewers will return an evaluation of the proposed work to the editor in prescribed format along with weaknesses, problems, and suggestions for improvement. Further, this evaluation will be forwarded by editor after reviewing the comments of referees in context with the scope of the journal to the author for consideration and improvement of the proposed work.

Referees' evaluations usually include an explicit recommendation of what to do with the manuscript or proposed work as per the options available in the prescribed format.

During this peer review process, the role of the referees is advisory, and the editor is typically under no formal obligation to accept the opinions of the referees. Moreover, in the process of scientific publication, the referees do not communicate with each other, do not act as a group, and are not aware of each other's identities or comments.

In particular situations, where the referees disagree considerably about the quality of a manuscript, there are a number of strategies for reaching a decision. When the editor receives positive and negative reviews for the same manuscript by two different reviewers, the editor will ask for one or more additional reviews or on the basis of comments of one reviewer, the edit may take his/her decision about the respective manuscript.

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We recommend that if reviewers suspect any of the following problems with any article that they are reviewing that they contact the journal editor to discuss the situation without delay. Reviewers should keep all information about such matters confidential and not discuss them with colleagues other than the journal editor.

1. If you suspect that the paper has been either published or submitted to another journal.
2. If you suspect that the paper is duplicating the work of others.
3. If you suspect that there might be problems with the ethics of the research conducted.
4. If you suspect that there might be an undeclared conflict of interest attached to the paper (Editors might have more information about this than you do so it is best to check).

We recommend that reviewers should think carefully about their own potential conflicts of interest relating to the paper before undertaking the review. They should also notify the editor if they become aware of the identity of the author during blind peer review. Additionally, reviewers should be careful not to make judgments about the paper based on personal, financial, intellectual biases or any other considerations than the quality of the research and written presentation of the paper.

PURPOSE OF PEER REVIEW

It is widely accepted that Peer Review is the most valid form of research evaluation and it is a cornerstone in the process of bringing academic research to publication in the following ways:

Evaluation - Peer review is an effective form of research evaluation to help select the highest quality articles for publication.

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Quality - The filtering process and revision advice improve the quality of the final research article as well as offering the author new insights into their research methods and the results that they have compiled. Peer review gives authors access to the opinions of experts in the field who can provide support and insight.

TYPE OF PEER REVIEW OF JOURNAL

Double blind peer review - names are hidden from both reviewers and the authors.

HOW TO REVIEW ARTICLES

Referees are sent invitations to review papers by journal editors. These requests are made via email. If you are asked to provide a review, in order to avoid delays, we would be grateful if you could let us know as soon as possible if you are unable to complete it at the time or if a problem arises after the invitation has been accepted. Suggestions for alternative reviewers are always gratefully received!

Below we present some advice and guidance about how to conduct a review and put together a reviewer report that will be effective and beneficial to authors:

ETIQUETTE

Timeliness - We understand that our reviewers are busy so it won't always be possible for invitations to be accepted. Please let us know as soon as possible if they need to refuse a review or if a problem arises after the invitation has been accepted. Most journal editors are grateful to receive suggestions about someone else that might be suitable to do the review if you have to decline the invitation.

Conflict of Interest - it is important to highlight to the journal editor any conflict of interest that you feel might occur if you review the paper. Please do so as discretely and as quickly as possible.

Discussion -- it is important to discuss with the journal editor any concerns that you have about the paper or their specific requirements for review if you are being invited to review for the first time. Editors are usually open to discussing their expectations and journal requirements with reviewers.

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These guidelines include a list of questions and will usually offer the reviewer the chance to make general comments

- Read the paper very carefully.
- Relevance to the publication (most editors will reject at submission those articles that do not match the aims and scope of the journal, but it is worth considering this as you read the paper).
- Significance of the research within the field.
- Originality of the work conducted. It is also important to consider whether the author has ever published a substantially similar paper elsewhere (if you suspect the work may not be original, please view our ethics page for information about how to deal with a variety of situations).
- The methodology employed during the research.
- Technical accuracy.

STRUCTURE AND COMMUNICATION

- Accuracy of references
- Overall Structure of the paper, communication of main points and flow of argument
- Quality of written language and structure of the article
- Effectiveness of the article abstract and introduction (some journals will request
- Whether the argument is clear and logical and the conclusions presented are supported by the results or evidence presented
- Whether the title of the article is suitable or effective
- Whether the abstract is a good summary of the article
- Whether the work meets with the article types accepted by the journal

The accessibility of the paper to a broad readership

Whether the paper is internally consistent

FEEDBACK IN YOUR REVIEWER REPORT - GIVING ADVICE TO AUTHORS AND SUGGESTING REVISIONS

- Be as objective as possible in your comments and criticisms and avoid making negative comments about work referenced in the article

- Be specific and as constructive as possible in your criticism. Be clear about what needs to be added or revised.
- If relevant, make suggestions about additional literature that the author might read to enrich or improve their arguments
- You should ensure that you are clear which of your comments you are happy for the author to see and which are meant specifically for the journal editor in order to avoid confusion or bad feeling
- While peer reviewers should feel free to make general comments on written quality and make suggestions about how articles might be improved by broadening reading of other literature, it is not the job of the peer reviewer to rewrite articles or suggest detailed changes to wording

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> Recommend whether a paper should be accepted, rejected or revised (major or minor revisions)

> Most importantly, keep all activity, content and comments relating to the paper confidential

Most important - keep all activity, content and comments relating to the paper confidential.

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Our publication ethics and publication malpractice statement is mainly based on the Code of Conduct and Best-Practice Guidelines for Journal Editors (Committee on Publication Ethics, 2011).

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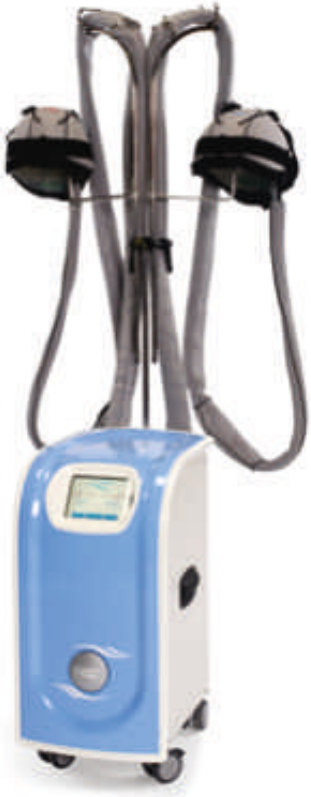

Rajasthan's First Scalp Cooling Machine has been established in Pacific Medical College and Hospital, Udaipur for providing US FDA Approved Scalp Cooling Therapy to Cancer Patients to prevent hair-loss due to Chemotherapy.

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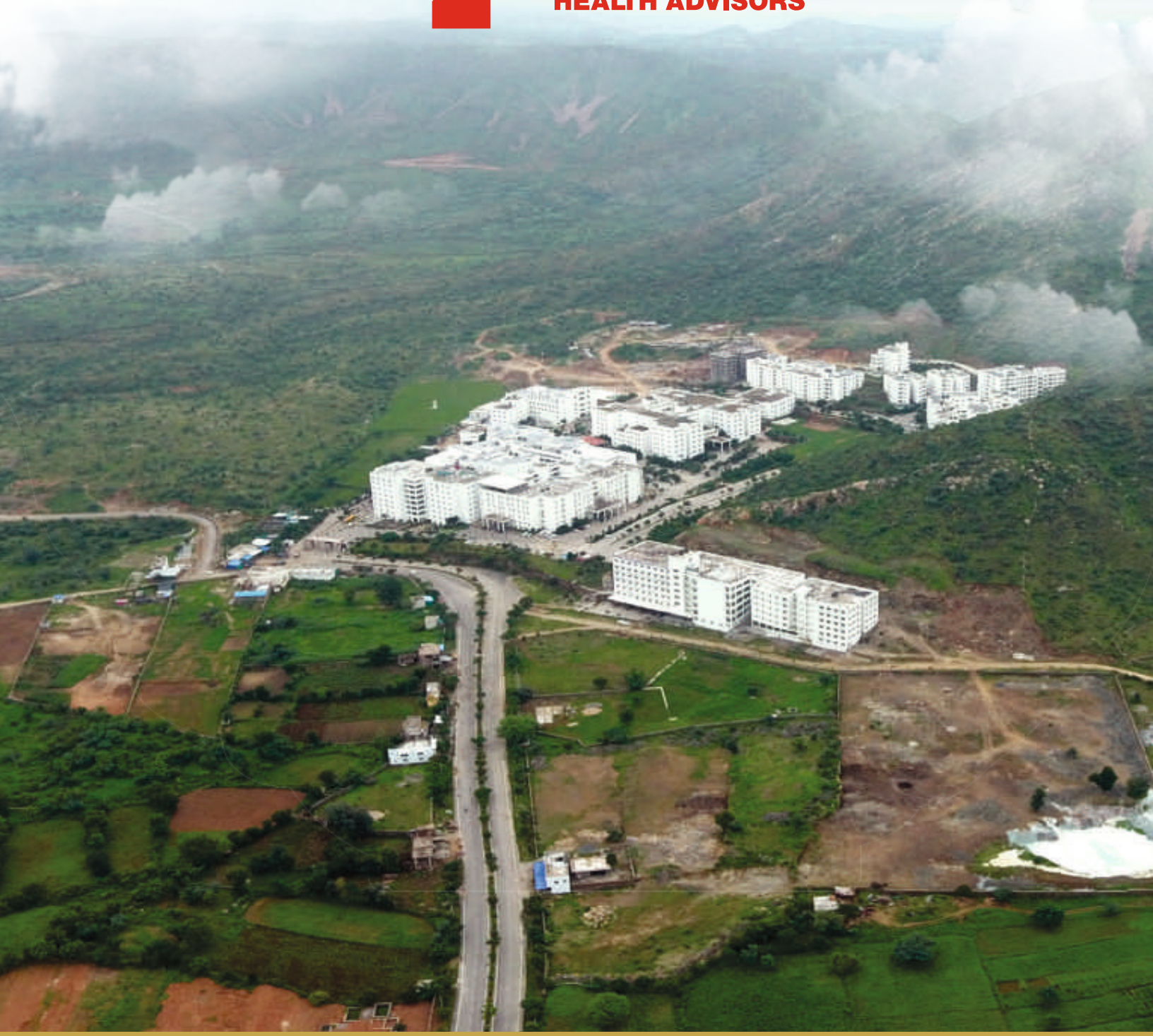

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