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College of Health and Allied Sciences
University of Cape Coast, Ghana

EDITOR'S LETTER

From Setbacks to Comebacks: IHRJ's Journey Ahead

Dear Readers, Authors, and Colleagues,

It is with great honor and enthusiasm that I assume the role of Associate Editor of the Integrated Health Research Journal (IHRJ). As the official journal of the College of Health and Allied Sciences (CoHAS) at the University of Cape Coast (UCC), IHRJ was launched in 2023 with a bold and inspiring vision: to advance global health research and amplify the voices of scholars locally and internationally.

Since its inception, the journal's strategic management has been entrusted to the Biomedical and Clinical Research Centre (BCRC). This partnership was established to uphold rigorous publishing standards and position IHRJ as a premier platform for high-quality, impactful research in health and allied sciences.

Our inaugural year was marked by great promise, with Issues 1 and 2 showcasing outstanding scientific contributions. However, like many emerging journals, IHRJ encountered operational and structural challenges in 2024, which unfortunately resulted in no issues being published during that year. We recognize that delays in manuscript processing caused understandable frustration for many of our valued authors, and for this, we offer our sincere apologies.

To the authors who patiently waited, we extend our deep gratitude for your trust and understanding. To those who, understandably, withdrew their submissions after prolonged delays, we truly regret the inconvenience and warmly welcome the opportunity to collaborate with you again in the future.

Today, under the steadfast leadership of BCRC and with the unwavering support of CoHAS and UCC, IHRJ is embarking on a transformative journey to strengthen its editorial operations. These comprehensive reforms are designed to enhance efficiency, uphold the highest standards of scientific rigor, and restore the confidence and trust of our research community.

As part of this renewal, Volume 2, which was originally scheduled for 2024, will not be published as initially planned. Due to the withdrawal of several manuscripts and the limited number of remaining papers, Volume 2 will now be released in 2025 as a single combined issue (Issues 1 and 2), incorporating both previously accepted and newly submitted manuscripts. This consolidated publication reflects our commitment to transparency while honoring the contributions of authors who remained with us during this transitional period.

Going forward, we are committed to streamlining processing times while maintaining our unwavering dedication to academic integrity and quality. We look forward to a new chapter for IHRJ—one defined by stronger editorial systems, timely publication, and a continued dedication to advancing global health research.

We sincerely appreciate the patience and trust of our contributors, reviewers, and readers as we implement these improvements to better serve the scholarly community.

This is more than a restart—it is a reaffirmation of our mission and a pledge to excellence.

Warm regards,

Emadeldin H. E. Konozy, Ph.D.

Associate Editor

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EDITORIAL

Plant Lectins: The Next Frontier in Precision Glycan-Targeted Medicine

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Precision medicine is revolutionizing healthcare by shifting away from the traditional "one-size-fits-all" approach to treatments. This new approach focuses on developing therapies tailored to each individual. It takes into account a person's unique genetic makeup, environmental factors, and lifestyle choices [1]. To achieve effective precision medicine, highly accurate molecular tools are essential. These tools must be able to detect and target specific disease-related markers with very few errors. Among the promising options in this field are plant lectins. These proteins can bind reversibly to specific sugars [2]. Plant lectins are attracting considerable interest because they can attach accurately to certain sugar structures found on cell surfaces [3].

Glycosylation, the enzymatic process of anchoring glycans to proteins and lipids, is important in cellular communication, immune targeting, and disease progression. Numerous pathological conditions, such as cancer, infectious diseases, and neurodegenerative disorders, are characterized by abnormal glycosylation [4]. Given their notable ability to selectively recognize and bind specific carbohydrate assemblies, plant lectins have emerged as powerful tools to exploit these glycan alterations for both therapeutic and diagnostic applications [3,5]. These proteins present an exciting avenue toward precision medicine by utilizing their high specificity, which enables targeted therapies based on glycan modifications associated with disease [3,6].

The ability to recognize and take advantage of patient-specific molecular signatures is essential for the shift from traditional therapies to precision medicine. Carbohydrate-binding proteins, such as plant lectins, are essential tools for diagnosis and treatment because glycosylation plays a crucial role in disease mechanisms. The high glycan selectivity of these proteins makes them useful for immune modulation [7], targeted drug delivery [8], and biomarker identification [9]. The variety of their structure and function enables accurate interactions with cell-surface receptors, impacting immune responses and signaling pathways—a crucial aspect of tailored treatments. According to their preferences for binding carbohydrates, plant lectins are categorized as follows: lectins that bind mannose, such as Concanavalin A (ConA); lectins that bind galactose, such as Erythrina indica lectin; lectins that bind N-acetylglucosamine, such as *Griffonia simplicifolia* lectin; and lectins that bind fucose, such as *Lotus tetragonolobus* [10]. According to new research, some plant lectins may alter signaling pathways and cellular receptors involved in pain perception and the defense of the stomach mucosa. Lectins' specificity could be used to create customized antinociceptive treatments [11,12] and gastroprotective effects [13-15] that address individual differences in disease mechanisms. For example, lectins that selectively target sialylated glycans—which are overexpressed in neuropathic pain [16]—could deliver localized analgesia with fewer side effects than opioids. *Maackia amurensis* lectins (MAL-I and MAL-II), which bind specifically to α2,3-linked sialic acid (MAL-I) and α2,6-linked sialic acid (MAL-II), illustrate this potential [17]. Patients who take NSAIDs long term may benefit from lectins such as *Calotropis procera* Leaf Lectin (ProLec), which can help increase mucus secretion and protect the digestive tract [14]. This precision-based method may pave the way for new approaches for the treatment of gastrointestinal issues and chronic pain.

In conditions such as cancer, where tumor cells frequently exhibit altered glycan profiles, these proteins exhibit abnormal glycosylation patterns. They are perfect for therapeutic and diagnostic applications because of their binding specificity, which allows for targeted interactions [5]. By attaching to tumor-associated glycans,

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lectins such as ConA and Wheat Germ Agglutinin (WGA) can be used to differentiate malignant tissues for cancer biomarker detection, facilitating early diagnosis [18]. Lectins such as BanLec are used in infectious disease diagnostics to detect pathogen-specific glycans [19], which speeds up the identification of bacterial and viral infections. Using lectin-based assays, neurodegenerative disease screening can identify altered glycans in Parkinson's disease and Alzheimer's disease, potentially leading to early intervention [20]. By selectively binding to glycans specific to neurodegenerative diseases such as Parkinson's disease (PD) and Alzheimer's disease (AD), plant lectins can help with glycan-targeting precision medicine. For example, Concanavalin A (ConA) and Wheat Germ Agglutinin (WGA) can identify tau and amyloid-beta glycans in AD [21,22].

Targeted drug delivery systems are one area where the therapeutic potential of plant lectins is most noticeable. Glycan recognition, in which lectins bind disease-specific carbohydrates; cellular uptake via receptor-mediated endocytosis; and controlled release for intracellular drug delivery that reduces systemic toxicity are all components of their lectin-mediated targeting mechanism [23]. With distinct disease applications, several lectin-based delivery systems, such as lectin-drug conjugates, lectin-coated nanoparticles, and lectin hydrogels, have been created. T/Tn-specific lectins extracted from Artocarpus integrifola are used in cancer treatment to target aberrant O-glycans expressed on the surface of cancer cells [24]. Urtica dioica agglutinin (UDA), which is specific to N',N",N"'-triacetylchitotriose, inhibits SAR-CoV replication by blocking the ability of the virus to bind to the host cell spike protein [25].

To fully utilize plant lectins in clinical settings, several obstacles need to be overcome. The development of hypoallergenic lectins is necessary to address toxicity and immunogenicity concerns [26]. Glycan heterogeneity demands customized glycan profiling, and pharmacokinetic issues necessitate stability and controlled release optimization [27]. To improve clinical applicability, future studies should concentrate on lectin engineering, bioinformatics-driven glycan analysis, and nanotechnology integration [3].

In conclusion, plant lectins have great potential for precision medicine because they provide glycan-specific targeting, accurate diagnosis, and adaptable treatment options. Advances in protein engineering, drug delivery systems, and glycomics could unlock their full potential in treating cancer, infections, and immune disorders. For their clinical translation to be successful, however, issues with safety, bioavailability, and regulatory barriers must be resolved. With further development, plant lectins could soon transform personalized medicine and usher in a new era of patient specific, targeted treatments that harness the power of glycobiology to improve healthcare outcomes.

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INVITED REVIEW

Unconventional Oil Sources: Emerging Nutraceuticals for Integrated Health

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Abstract

Recent scientific research emphasizes the growing importance of functional foods as both nourishment and medicine, leading to the exploration of unconventional oils from plant sources like black seed, hibiscus, black cumin, and insect sources such as melon bug and cochineal. These oils are rich in bioactive compounds—including polyunsaturated fatty acids (PUFAs), antioxidants, phytosterols, and polyphenols—that contribute to anti-inflammatory, cardioprotective, neuroprotective, and immunomodulatory effects. Their unique nutritional profiles support the prevention and management of chronic diseases, metabolic disorders, oxidative stress, and gut microbiome imbalances, while also promoting mental health and longevity. Additionally, they show promise in dermatological applications, offering therapeutic benefits for skin and hair conditions. By integrating traditional knowledge with modern scientific validation, these oils represent a sustainable and innovative approach to holistic health and food product development. However, further research is needed to enhance their stability, bioavailability, and dosage accuracy to ensure clinical efficacy. As nutraceuticals and nutritional supplements, unconventional oils offer exciting potential for future applications in personalized nutrition and disease prevention strategies.

Keywords: Bioactive compounds, health, insect oil, nutraceuticals, unconventional oils.

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Introduction

Unconventional seed oils are oils extracted from the seeds of plants not commonly used for oil production, such as marula kernel oil, Moroccan argan oil, pumpkin seed oil, hibiscus seed oil, apricot kernel oil and insect oils. These oils are often rich in nutrients and beneficial compounds, making them healthy choices for cooking and cosmetics [1]. Unconventional oils add a distinctive flavour to food and offer numerous health benefits. These oils are often cold pressed, contain unsaturated fatty acids that have a positive effect on metabolism.

Conventional vegetable oils are extracted from commonly used sources such as corn, olives, and sunflowers. In contrast, non-conventional vegetable oils are derived from less common sources or processed using different methods, such as fixed oils or oils not typically used in conventional cooking. Conventional oils are known for their diverse nutritional benefits and wide range of applications, whereas non-traditional oils may vary in their nutritional composition, value, and physical properties [2].

Conventional and unconventional vegetable oils are distinguished by their source, scale of production, and typical applications. Conventional oils are from well-established crops and are mass-produced, while unconventional oils are sourced from a wider variety of plants or even other sources like insects and often have specialized uses (Table 1) [3].

For thousands of years, human nutrition has been linked to the use and consumption of oils extracted from various types of plant seeds, in addition to margarine or "ghee" and butter extracted from animal milk and fats [4]. However, through experience and experimentation, humans discovered that the level of cholesterol in these animal derivatives is higher than in vegetable oils. After realizing that high undesirable kinds of cholesterol can lead to atherosclerosis, angina, and heart attacks, humans

turned to consumption of vegetable oils that are virtually cholesterol-free, such as sunflower oil, corn oil, olive oil, palm oil, and the like. These traditional oils have become a staple in human diets [5]. There are unconventional oils that contain unsaturated acids that have a clear effect in lowering blood cholesterol levels (Table 2). Among these acids is oleic acid (Omega9), which is widely used in Mediterranean countries [6].

Unconventional oils have unique flavours and diverse nutrients, and may be more beneficial for some health conditions, but seem to be more expensive or less available than conventional oils. It is that they retain their obvious nutritional benefits.

This review aims to bring together scattered information on some unconventional oil sources for the benefit of researchers and specialists in the food and pharmaceutical industries. It also aims to stimulate further research and interest in unconventional oil sources to diversify the market and enhance the use of untapped plant species.

Methods

The review uses up-to-date data via manual screening of the titles and abstracts of retrieved articles using string foodborne diseases in Sudan and foodborne illnesses as keywords to obtain publications from the electronic databases; Science direct, PubMed, Scopus, and Google Scholar from the year 2000-2025 using the different searching tools, the databases were reviewed from June to September 2025.

Examples of unconventional seed oils and their health properties.

Sclerocarya birrea (Marula)

Sclerocarya birrea (Marula) oil is an oil extracted from the seeds of the fruit of the African marula tree and is widely used in skin and hair care due to its cosmetic benefits. The marula tree is a wild African tree that grows in many African countries. Its components have numerous uses in food and traditional medicine. The fruit juice is richer in vitamin C than orange juice besides containing sesquiterpene hydrocarbons. The fruit seed is soft, white and rich in oil and protein. Oleic, palmitic, myristic, and stearic acids are the major fatty acids in the seed oil, whereas glutamic acid and arginine are the most important amino acids in marula protein. It contains important fatty acids such as oleic and linoleic acid, which help moisturize the skin and hair. Marula oil contains antioxidants that protect the skin from damage caused by free radicals. The tree extracts contain high level of phenolic compounds of high free radical scavenging capacity, and antioxidant activity. The tree has various medicinal uses for diabetes and inflammation, as well as for analgesic, antiparasitic, antimicrobial, and hypotensive purposes [7, 8]. Marula oil helps moisturize the skin, fight signs of aging, lighten scars, reduce inflammation, and treat some skin problems such as acne and dryness. It nourishes the hair, reduces breakage, adds shine and strength, and helps treat dry and cracked scalps [9].

Black Mahlab Seed Oil

Black mahlab (*Monechma ciliatum*) is a species of the genus Monechma belonging to the family Acanthaceae. It is a well-known tropical medicinal herb, long used extensively in Africa for food and medicine. Also known as "black mahlab" among Sudanese people, due to its small, dark brown seeds. The plant is used in traditional dishes, medicinal treatments, and perfumes. The black mahlab seed contains good level of protein with appreciable amount of amino acids. The dry seeds contain different kinds of major elements (Ca, K, and Mg) and of minor elements (Al, Pb Ni, Mn, Cu, Cr, Co, and Fe) [10].

Black mahlab is used as a spice to add a distinctive flavour to dishes, especially baked goods and sweets. It is used in traditional medicine to treat digestive problems such as diarrhea and vomiting. Black mahlab seeds are used in traditional perfumery. in hair care as natural hair moisturizer where they help strengthen hair follicles, reduce hair loss, and stimulate new hair growth [11]. The oil yield of dried seed is about 13.1%, with dominant fatty acids of palmitic (4.5%), stearic (16.0%), oleic (47.3%), and linoleic (31.4%). This unconventional oil was found rich in tocopherols (45.2 mg/100 g) [12].

The plant leave extract has a strong antioxidant effect based on its content of flavonoids, phenols, alkaloids and other metabolites. The black mahlab plant is used in Africa to treat body and liver pain, colds and diarrhea, and it is also traditionally used to treat infertility in women [10]. Studies have shown that the antimicrobial activity of mahlab includes a wide spectrum of bacteria and fungi compared to known antibiotics [11]. Abdel Karim et al. [13] examined the antimicrobial activity of the seeds oil of M. ciliatum and reported that it has a significant effect on Aspergillus niger, Candida albicans fungi and Staphylococcus aureus bacteria. The oil was found to be partially active against Escherichia coli and Pseudomonas aeruginosa

Black cumin seed oil

Black cumin seed oil, also known as black cumin oil, is an oil extracted from the seeds of the plant "Nigella sativa" and has numerous health benefits and diverse uses. The oil is used in traditional medicine to treat a wide range of ailments, and in skin and hair care products [14]. The seed oil contains bioactive compounds such as thymoquinone, which have anti-inflammatory properties. The use of the oil helps fight free radicals and protect cells from damage. It also help relieve symptoms of asthma and bronchitis, alleviate digestive problems such as bloating and gas, lower LDL cholesterol levels, and improve cardiovascular health [15]. In addition to the previous properties, the seed oil can help improve nervous system health and treat certain neurological conditions such as Alzheimer's and Parkinson's diseases, as well as improving urinary tract health conditions such as cystitis and kidney inflammation [16].

Argan Oil

The Argan tree, Argania spinosa, is a natural plant that grows abundantly in Southern Morocco, Southwest Algeria, Mexico, and USA, although the plant bears no fruits with the latter two countries. This tree has lived for millions of years and has a tremendous ability to resist drought and combat desertification [17].

There are two types of Argan oil: Food-grade, which is commonly used in food preparation and is the main ingredient in amlou, is dark brown in colour with a strong flavour [18] due to the roasting of Argan tree nuts before extracting the oil. The second type is golden yellow in colour, as the oil is extracted from the almonds of the Ar gan tree without roasting. It is used as a skin moisturizer and as an important ingredient in high-end cosmetics. It is more expensive than the food grade one due to its high demand18. Argan oil contains 42.8% oleic acid (Omega 9), 36.8% linoleic acid (Omega 6), 6.0% stearic acid, 12.0% palmitic acid, and less than 0.5% linolenic acid (Omega 3). In addition to these fatty acids, it contains tocopherol, squalene, steroids, carotenes, and phenols. The oil is usually prepared using cold pressing as an optimal method for preserving the nutrients and vitamins in the product intended for cosmetic use. Such oil, being rich in vitamin A and fatty acids, and distinguished by its golden yellow colour and distinctive, light aroma, is more expensive, and has moisturizing and nourishing benefits for hair and skin [19]. Amazigh women in Morocco have used this oil since ancient times as a moisturizer for dry skin and as an anti-wrinkle agent, due to its essential fatty acids, omega-6, omega-9, and antioxidants content. In cosmetics, Argan oil is used as an anti-acne, anti-psoriasis, and anti-redness agent [20.] It is easily absorbed and leaves no trace. It moisturizes the skin, softens and smooths it, and treats dryness, cracks, and roughness [20,21]. Argan oil is useful in cleansing the skin of acne scars and impurities, leaving it soft and radiant, and it's particularly beneficial for treating stretch marks and cracks. The oil is also known to nourish the hair and scalp, eliminate dandruff, and gives the hair a lustrous, shiny, and silky texture [22]. The Argan oil helps prevent and treat stretch marks on the abdominal skin. It restores overall freshness and vitality to the skin within just a few days of use by stimulating the vital functions of skin cells [23].

Pumpkin seed oil

Pumpkin seed oil is a vegetable oil extracted from pumpkin seeds. It is rich in unsaturated fatty acids, including the Omega6 linoleic acid (52%), the Omega9 oleic acid (18%), in addition to vitamins, minerals, and antioxidants 24,25. Pumpkin seed oil has many benefits for skin, hair, and seems to help improve heart and prostate health [26].

The bioactive compounds, such as gamma tocopherol and linoleic acid. in pumpkin seed oil contribute to a balanced immune response, reducing the risk of inflammatory and chronic diseases [27]. It helps reduce internal inflammation that weakens the immune system, through its anti-inflammatory and tissue-soothing properties [28].Vitamin E in pumpkin seed oil helps protect immune cells from damage, enhances their strength, and ensures their continued efficient functioning. The seed oil was found rich in powerful antioxidants that combat free radicals, naturally and safely boosting the immune system's response to various infections and diseases [29,30]. The oil contains zinc, essential for the function of immune cells, enhancing the body's natural defenses and increasing its ability to resist infections and viruses [31]. More of these studies showed that pumpkin seed oil is beneficial in treating benign prostatic hyperplasia, as it stops the enlargement of the prostate caused by testosterone hormone. Consuming such oil for more than three months confirmed treatment and alleviation of the symptoms of benign prostatic hyperplasia (BPH), including reduction of inflammation and the urge to urinate, thereby improving the patient's quality of life. Furthermore, the oil was found to prevent the conversion of testosterone to Dihydro-testosterone (DHT) and hence avoiding the negative effects on the prostate. Consumption of pumpkin seed oil has no side effects, making its long-term use safe and largely effective [32,33].

Hibiscus (Hibiscus sabdarifa) is a plant widely grown in tropical regions and today, over 300 species of hibiscus are found worldwide. The oil content in hibiscus seeds ranges between 20% and 24% of the dry seed weight. The oil is considered a fixed oil suitable for human consumption and is characterized by its low saturated fatty acid content [34]. The seed oil was reported rich in some fatty acids such as oleic, linoleic, palmitic, and stearic as well as antioxidants. Its high level of unsaturated fatty acids makes it useful for use in cosmetics, skin care, and hair care industries [35]. Some studies suggest that hibiscus seed oil seems to help lower blood pressure, reducing the risk of heart disease [36]. It also helps protect the liver from damage and promotes its health. The oil has anti-inflammatory properties, which help reduce inflammation in the body [37]. The oil also help improve digestion, alleviate some digestive disorders and help lower harmful cholesterol levels in the blood [38].

Further work on this oil found it to revitalize dormant hair follicles, stimulate new hair growth, strengthen hair roots, and prevent hair loss. It acts as a natural conditioner, making it softer and shinier and hence helps maintain natural hair colour and prevent premature graying [39].

Regular use of hibiscus seed oil improves the health of the scalp and its follicles, helps combat dandruff, and nourishes the scalp and follicles, which support healthy hair growth [40]. Hibiscus seed oil helps moisturize the skin, make it more radiant, tighten the skin, and improve its elasticity. It can be used to even out skin tone and eliminate dark spots. The oil possesses antibacterial properties that may help fight acne [41].

Both conventional and non-conventional vegetable oils are analyzed concerning their safety, toxicity, allergenicity, and clinical evidence. High monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA) in vegetable oils may offer health benefits, such as lower cancer risk, yet evidence remains uncertain [42]. Toxicity issues arise from refined oils, containing harmful chemicals like polycyclic aromatic hydrocarbons (PAHs), trans fats, and metals, particularly with reused oil leading to lipid peroxidation risks. High omega-6 oil consumption can increase inflammation, while

some oils may adversely affect gut health [43]. Generally, highly refined oils pose low allergy risks, unlike unrefined oils which retain more proteins. Sustainability is crucial in oil production, as high-impact palm oil alternatives could worsen environmental issues. Non-conventional oils lack solid safety data and may have higher allergic reaction risks due to residual proteins. Scalability challenges stem from geographical limitations and expensive extraction processes, while scaling could lead to new environmental concerns [44].

Insect oils, such as those derived from watermelon bug, sorghum bugs, and black soldier fly larvae, show promise as safe protein sources in animal diets, with potential health benefits noted in some studies. However, concerns exist regarding microbial contamination and allergenicity, particularly for individuals with existing allergies [45]. In contrast, plant oils, while generally low-risk, can pose safety issues when unrefined. The production of insect oils offers significant sustainability advantages, requiring less land, water, and feed, and can utilize waste materials. Conversely, conventional plant oils face increasing environmental challenges despite established safety profiles. Overall, while insect oils may provide nutritional and environmental benefits, their scalability and allergenic risks necessitate further research before broad adoption [46].

Watermelon seed oil

Watermelon (Citrullus vulgaris) is grown in most tropical, subtropical, and arid regions of the world. It is a cash crop that serves as a source of water during the long summer season for both animals and humans [47]. Watermelon seeds are an important agricultural crop in many countries. They are collected from certain watermelon varieties and known for their high protein content and quality. Watermelon seeds contain 18–22% protein, 18–28% oil, 38–47% fiber, 7-8% carbohydrates, moisture 4-5% and 557 calories in 100 grams [48].

Watermelon seeds represent between 4% and 6% of the annual crop production in Sudan and are mainly used as snacks for local consumption and export. The seed oil was reported to be used in a variety of industries, including cosmetics, food, and pharmaceuticals [49,50]. The seed oil is rich in essential fatty acids such as linoleic acid, as well as vitamins and minerals that make it an effective moisturizer and nourisher for the skin and hair [51].

The oil helps hydrate the skin and prevent moisture loss, making it beneficial for dry skin. It contains antioxidants that help fight free radicals and reduce signs of aging such as wrinkles and fine lines. It also moisturizes hair, protecting it from breakage and damage, and helps increase its shine and softness [52]. It helps cleanse pores and reduce the appearance of acne, especially for oily and blemish-prone skin. The oil has anti-inflammatory properties, making it useful in soothing irritated skin [53].

Watermelon seed oil was found effective as diuretics, helping to purify the body of toxins and eliminate excess fluids and salts, which helps regulate blood pressure [54]. Watermelon seed oil plays a major role in strengthening the immune system, due to its high vitamin E content. This enhances the body's ability to fight free radicals, thanks to its antioxidant properties, which reduce the risk of chronic diseases [55]. The seed oil was found important for liver health. It helps enhance its vital functions and protect it from cirrhosis, as it contains nutrients that contribute to reducing its enzymes in the blood [56]. Watermelon seed oil is characterized by its content of fatty acids, such as palmitic and oleic acids, which work to reduce levels of harmful cholesterol in the blood, LDL, and increase good cholesterol, HDL, which helps prevent heart diseases, such as atherosclerosis [50]. Massaging the body with watermelon seed oil helps relieve stress and anxiety, calm the nerves, relax the muscles, and improve sleep. The seed oil can be used as a natural skin cleaner, to remove the dirt and grime that accumulates on the skin's surface. It also provides fatty acids that maintain moisture and protect it from dryness. Applying the oil to the skin is an effective way to reduce the risk of certain conditions, such as psoriasis and eczema [51].

Watermelon seed oil helps reduce oily skin secretions, which clog pores and lead to acne. The oil also delays the appearance of signs of aging on the skin, such as wrinkles and fine lines, because it reduces oxidative stress that threatens skin cells with damage. The oil was found an effective treatment for dry and frizzy hair, as it moisturizes it and makes it soft and shine [52].

Insect oils

Edible insects are rich sources of protein, dietary fiber, fatty acids, minerals, and vitamins. Their most important characteristic is their low carbon footprint, and their production and farming require less land, water, and food resources than livestock. Insect oils are extracted from insects, although they are not as common as those extracted from plants [57]. Examples include cochineal oil (carmine oil), which is used as a food colouring [58].

Cochineal dye is a natural red dye extracted from the cochineal insect, also known as carmine. This dye is used in many applications, including food colouring, cosmetics, and medicines. The cochineal insect is a scale insect that lives on cactus plants, especially in tropical and subtropical regions. Carmine dye is extracted from dried and ground female cochineal insects. It contains carminic acid, which is red in colour. Carmine dye is used to colour variety of foods and beverages, such as desserts, ice cream, soft drinks, processed meats, sauces, and much more. The dye is also used in lipstick, eye shadow, blush, and many other beauty products, and is used in some medications to impart the colour. Cochineal oil is a natural oil extracted from the cochineal insect and used as a natural red dye in food, cosmetics, and medicines. This oil is also known as carmine and assigned E120 as certified additive [59,60].

Watermelon bug oil

The watermelon bug (Aspongopus viduatus) is found worldwide, infecting plants of the cucurbit family, cucumber, cantaloupe and mainly watermelon, and other plants, for example vegetables, c, and wheat. It is called the melon bug, or the shield bug. It resembles the green bug in

size and shape, except that its colour is brown with a bluish tinge, and the basal parts of the wings are dark red [61].

The adult stage of melon bug has been used in a powdered form after drying and grinding as appetizer with different meals. Watermelon bug oil contains a range of fatty acids, including oleic, palmitic, linoleic, and linolenic acids. The insect's protein also contains approximately 16 known amino acids, including all essential amino acids making the bugs good and suitable source of edible oil and protein. The proximate analysis of the dry matter of adult watermelon bugs revealed a moisture content of 8.3%, crude protein of 27%, fat of 54.2%, and ash of 3.5%. Watermelon bug oil was proved to be suitable for cooking and biofuel production [62].

Edible insects are rich in minerals and vitamins. They provide the human body with fat- and water-soluble vitamins A, B1 and B12, C, D, E, and K which are required for normal growth, health and recovering the deficiencies resulted from improper intake of mineral and vitamins [60]. Melon bug fats are composed of saturated and unsaturated fatty acids, with a total saturated fatty acid content of 37.87%, including myristic acid (0.34%), palmitic acid (31.33%), and stearic acid (3.47%). The total monounsaturated fatty acid content, based on dry weight, is 56.78%, including palmitoleic acid (10.62%) and oleic acid (45.53%) [63].

Camel herders in some Sudanese regions make the tar smear by burning dried bugs and then using it to treat some skin diseases in their animals. The effect of crude bug oil and oil stripped of phenolic compounds on a range of bacterial species was studied. Both oils exhibited high antibacterial activity against some of the tested bacteria, while the oil purified by a silicic acid column showed no antibacterial activity. This study suggests the use of bug oil as a food preservative [64].

Sorghum bug oil

Sorghum bug is one of the insect pests that feed on Sorghum plants and many other crops. It is one of the main pests of this crop in Sudan. The bug is mechanically controlled by collection and burying. In nomadic Botana regions, Sudan, people use tar smear received from notably heated bugs for their camels to treat dermatological infections [65].

Mariod, [66] determined the oil content of dried ground sorghum bug adults and found it 60%, almost higher than in commercial oil seeds such as groundnut, soybean, sunflower or rapeseed. Further analysis showed that the main fatty acids in sorghum bug oil are palmitic, stearic, oleic, and linoleic acids with lower content of saturated fatty acids (20.8%) and higher content of unsaturated fatty acids (77.8%).

Research Gaps

Future directions for traditional vegetable oils focus on improving sustainability, nutritional value, and processing efficiency. Researchers are exploring precision breeding and gene-editing technologies like CRISPR to develop oilseed crops with enhanced fatty acid profiles and resilience to climate stress [67]. Innovations in green extraction methods aim to reduce energy use and chemical solvents, while circular agriculture practices seek to repurpose oilseed byproducts for food, feed, and bioenergy. Additionally, reformulating oils to meet specific dietary needs—such as increasing omega-3 content—is gaining traction, alongside efforts to integrate digital tools for better crop and supply chain management [68].

Future directions for insect oils as unconventional oils focus on enhancing sustainable production, expanding applications, and improving consumer acceptance. Advances in eco-friendly extraction methods and bioreactor technologies aim to boost yield and purity, while research explores their use in functional foods, aquafeed, cosmetics, and pharmaceuticals due to favorable lipid profiles and antimicrobial properties [69]. Efforts to blend insect oils with conventional oils and develop hybrid formulations are gaining traction, alongside initiatives to establish safety regulations and educate consumers to overcome cultural barriers. These developments position insect oils as a promising alternative in the quest for sustainable and versatile lipid sources [70].

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REVIEW ARTICLE

The Role of Protein Carbonylation in Various Diseases: A Review

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Abstract

Protein carbonylation is a post-translational modification that involves the addition of a carbonyl group (-C=O) to a protein, resulting in the formation of a carbonylated protein. This modification can occur through various mechanisms, including oxidative stress, enzymatic reactions, and non-enzymatic reactions. Protein carbonylation can have significant consequences, including loss of protein function, protein aggregation, and cellular stress and damage.Recent studies have highlighted the importance of protein carbonylation in understanding the pathogenesis of various diseases, including neurodegenerative disorders, cancer, and metabolic disorders. Protein carbonylation has been implicated in the development of cancer, where it can contribute to the promotion of cell growth and survival. This review provides a comprehensive overview of the mechanisms, consequences, and detection methods for protein carbonylation. We discuss the various mechanisms by which protein carbonylation can occur, including the role of reactive oxygen species (ROS) and other oxidants. We also review the role protein carbonylation, including the loss of protein function, protein aggregation, and cellular stress and damage in several diseases. Therapeutic interventions and protein carbonylation are also considered. Furthermore, we discuss the various methods that have been developed to detect and quantify protein carbonylation, including the use of 2,4-dinitrophenylhydrazine (DNPH) and mass spectrometry. Finally, we highlight the advantages and limitations of the different methods used in the measurement of protein carbonylation.Understanding the mechanisms, role in disease, and detection methods for protein carbonylation is essential for the development of therapeutic strategies to prevent or treat diseases associated with protein carbonylation.

Keywords: Protein Carbonylation, Post-translational Modification, Oxidative Stress, Protein Aggregation, Quality Control

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Introduction

Protein carbonylation is a result of protein oxidation (post-translational modification) that is irreversible and precipitated by reactive oxygen species. This can occur in both animal and plant cells and is non-enzymatic, leading to the proteasomal breakdown of proteins by the proteasome system [1-2]. Protein carbonylation can result from metal-catalyzed oxidation (MCO) of Lys, Arg, Pro, and The side chains or through the Michael incorporation of lipid peroxidation-derived α,β-unsaturated aldehydes and ketones into the side chains of cysteine, lysine, and histidine residues [1].Reducing sugars have also been implicated in protein carbonylation [3]. The role of protein carbonylation spans the growth and development of animals and plants, oxidative stress, associated pathologies such as cellular damage, aging, age-related disorders, and cell signaling transduction [1,2,4-5]. The exact mechanisms and implications of protein carbonylation are still unclear, as an increase in carbonylated proteins is observed in conditions of stress, gradual decline in functional characteristics in human aging, ultimately leading to cell death [1].

The first proximal step of protein carbonylation involves hydroxyl radicals (HO), which largely originate from the Fenton reaction or the Haber-Weiss reactions of superoxide radicals (O_2), H_2O_2, and a transition metal such as iron (Fe) or copper (Cu). This suggests that the presence of Fe may determine the prevalence of protein carbonylation in living organisms [1,6-9]. Respiratory surge produces reactive oxygen species (ROS) such as superoxide anions, hydroxyl radicals, singlet O_2, and hydrogen peroxide in large

quantities. This increased production of inducible nitric oxide synthetase and pro-inflammatory cytokines leads to elevated levels of reactive nitrogen species (RNS) such as nitric oxide, nitrites, nitrates, and pro-inflammatory cytokines. ROS and RNS play a crucial role in eliminating microbes and have a beneficial effect on the host. However, excessive amounts of ROS and RNS can damage host tissues [10-11]. Protein carbonyl content in blood and tissues is a valuable indicator of protein oxidation due to its long-lasting stability under appropriate storage temperatures, specifically -80 degrees Celsius. It is the most frequently used and common indicator of oxidative protein damage [10,12-13]. However, it appears to be undervalued and underutilized in general practice settings to the best of our knowledge.

Importance of Studying Protein Carbonylation

Protein carbonylation evaluates the state of oxidative stress by measuring the extent of protein carbonyls present. This process is important for biomarking in disease and aging, as it can impact protein structure, function, and contribute to the development of various pathologies and age-related changes in the human body [14]. Carbonylation can disrupt the conformation of polypeptide chains, leading to partial or complete inactivation of proteins. It can also affect the chemical and biological activities of enzymes and other functional proteins, such as their ability to attract DNA transcription factors. Proteins involved in insulin signaling may also be weakened, disrupting the insulin signaling pathway. Additionally, protein carbonylation can slow down proteasomal activity, which is responsible for breaking down cellular proteins and recycling amino acids, serving as a form of protein quality control14. There is need to also understand the irreversible and reversible products of protein oxidation (Figure 1).

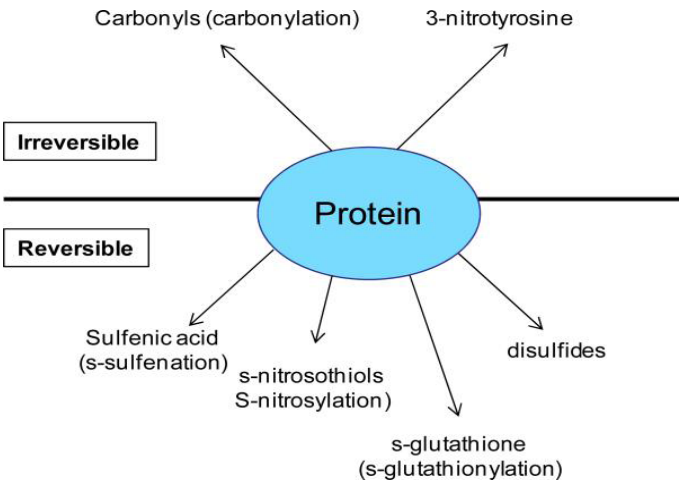

Figure 1: Irreversible and reversible protein oxidation products as described [29].

Protein carbonylation can be a useful tool for evaluating certain diseases, such as pre-eclampsia (a pregnancy-related hypertensive disorder), neurological diseases like Parkinson's and Alzheimer's, hematological cancers such as multiple myeloma, multiple sclerosis, myasthenia gravis, sarcopenia, and renal disease [14,15-16]. In terms of storage, protein carbonylation has been used for evaluations, particularly in stored blood samples [17-18]. With respect to dietary and nutrition practices, concerns have been raised about the toxic effects of consuming oxidized lipids. Lipid-derived carbonyls, like malondialdehyde (MDA), possess mutagenic and cytotoxic properties that can disrupt cellular equilibrium and contribute to health issues. Studies have explored these concerns and their implications on anatomical structures using animal models [19].

Role of Iron in Protein Carbonylation

All forms of life require iron as a vital element. The productivity of photosynthetic organisms is dependent on iron, even though it may not be easily attained and can also be toxic [1,20]. Cellular processes such as respiration, cellular differentiation, and photosynthesis rely on iron as helper molecules. In fauna populations, there is a balance between iron absorption, storage, utilization (effective use), and movement across cell membranes as a result of cellular iron metabolism. Cellular iron metabolism in fauna populations is affected by: (1). Soil acidity or alkalinity and the presence of iron - The optimal pH values for iron absorption by plants is 5.6, which improves iron solubility in the soil. Also required are iron concentrations that promote iron absorption by plants. (2). Iron chelators and transporters such as FRO3 and IRT1 facilitate iron absorption from the soil into the root cells of non-graminaceous plants like tomatoes and peas. In graminaceous plants like maize, iron-chelating phytosiderophores are released into the rhizosphere to form Fe^{3+}MA (Mugineic acid) complexes absorbed by a unique high-affinity transport mechanism. (3). Phytohormones such as auxin, ABA, and ethylene also influence iron metabolism. The association of these phytohormones has been well described [1,21-25].

When iron is in surplus, it can become harmful or toxic to plants, leading to oxidative stress through the Fenton reaction. Available mechanisms to mitigate this effect involve the effective usage of various antioxidant systems, which could be enzymatic and non-enzymatic. The enzymatic antioxidants are catalase (CAT), peroxidase (POD), and superoxide dismutase (SOD), which prevent the Fenton reaction by mopping up ROS and transforming it into less harmful molecules. The non-enzymatic antioxidants are glutathione, tocopherol (vitamin E), and ascorbate, which directly counteract the negative effects of ROS, thereby preventing oxidative stress.Other mechanisms of preventing free Fe^{2+} from initiating the Fenton reaction include: (1) Production of metal chelating agents. (2) Induction of iron storage proteins such as ferritins, which eliminate the Fenton reaction by binding Fe and sequestering it into a secure, readily absorbable form. Large amounts of Fe can be sequestered in this manner, not exceeding 4500 atoms, improving release to the plant cell matrix as needed [1,26-27].In humans, the role of iron in protein carbonylation is somewhat similar. Diseases such as hematological malignancies have found Fe chelators useful. Iron homeostasis plays a crucial role in

the treatment of various hematological tumors, especially myelodysplastic syndrome (MDS). In this context, patients with MDS experience transfusion dependence, which does not eliminate elevated oxidative stress parameters. Iron chelation, mainly by deferasirox (DFX), appears to improve the lifespan of patients with low-risk MDS and in stem cell transplant settings. Additionally, it can reduce mortality and cytopenia while enhancing the hematological response [15].

Deferasirox is an iron chelator commonly used as a therapy for patients with MDS who rely on blood transfusions. It is a powerful NF-kB inhibitor in myelodysplastic cells, acting independently of cell iron starvation through chelation and ROS scavenging. It eliminates the production of free radicals by suppressing the active redox forms of iron. Iron chelation therapy in myeloid leukemia promotes the differentiation of leukemia blasts and normal bone marrow precursors into monocytes/macrophages, requiring the regulation of ROS expression. However, the cytotoxic effects of iron chelation treatment on myeloid blast cells have been observed in vitro, in vivo, and ex vivo, showing synergy with acute myeloid leukemia drugs like decitabine and 5-azacitidine [15]. In multiple myeloma, intracellular iron chelation leads to cell death in myeloma cells. Deferasirox also induces apoptosis in myeloma cells by targeting the oncogenic Pyk2/β-Catenin signal transduction pathway. It is important to note that oxidative stress is a major factor in the development of multiple myeloma. For over two decades, there has been an imbalance in oxidant/antioxidant parameters in the disease, creating a persistent inflammatory environment in the tumor microenvironment. This oxidative state increases the likelihood of genetic mutations, leading to the acquisition of a malignant phenotype and cancer progression [15]. On the other hand, iron overload inhibits cell proliferation in multiple myeloma and enhances the effectiveness of bortezomib, as iron promotes lipid oxidation and inhibits proteasome function [28].

Cellular Sources of Oxidants

The mitochondria is a major production site for reactive oxygen species aside other systems localized within the cell. Moreso, there are several enzymes that are capable of producing ROS and are NADPH oxidase, xanthine oxidase , α-ketoglutarate dehydrogenase complex , d –amino acid oxidases and dihydrolipoamide dehydrogenase [29]. For nitric oxide production invivo, this is made successful by nitric oxide synthase even though deoxygenated myoglobin or xanthine oxido reductase or cytochrome C oxidase can be utilized in nitric oxide (NO) release in very specific conditions which presumably could be in hypoxic conditions or during infections [29]. NO is a gaseous molecule , water soluble with very significant role in signaling processes and has a very short half life with a physiological relevance that is concentration dependent much more restricting its role to a target site [30]. Its production, signaling and roles in human physiology and diseases are as described [30].

Protein carbonylation and Diseases

Protein carbonylation commonly occurs as a result of reactive species-induced protein modification. As mentioned earlier, it specifically targets proteins for degradation, leading to a loss of protein function [31]. Various reports by researchers have linked protein carbonylation to different disease conditions, including neurological and metabolic disorders [32]. Some of these conditions include pre-eclampsia, hypertension, Parkinson's disease, Alzheimer's disease, diabetes mellitus, sickle cell disease (SCD), and malaria infection. These diseases and their effects are often associated with oxidative stress, either directly or indirectly. In this article, we will explore the implications of protein carbonylation in some of these diseases.

Protein Carbonylation and Pre-eclampsia

In pre-eclampsia, when levels of reactive oxygen species (ROS) are elevated and antioxidant concentrations are reduced, it contributes to the progression of the condition. In this context, protein carbonyl could serve as a useful diagnostic tool for assessing protein damage caused by ROS [33]. A study investigating protein carbonyl levels in the decidua and placenta of pre-eclamptic women as markers of oxidative stress found that levels were higher in pre-eclampsia with HELLP (haemolysis, elevated liver enzymes, low platelets) compared to normal pregnancy. This suggests the presence of disturbances mediated by ROS in this disorder. Additionally, urinary protein carbonyl concentration was found to be elevated in pre-eclamptic women, although it was only partially associated with protein misfolding [34].

Also, as described by Ayub et al., their investigation concluded that elevated serum protein carbonyl levels and diminished antioxidant capacity indicate high levels of oxidative stress in women with pre-eclampsia, leading to endothelial dysfunction and the development of preeclampsia. Serum protein carbonyl levels were assessed using the 2,4-dinitrophenylhydrazone (DNPH) assay, which showed a significant association in pre-eclamptic women compared to normal pregnant women. The use of adjunct antioxidant therapies could potentially slow the progression of pre-eclampsia [35]. Pre-eclampsia has an unknown etiology, with some authors suggesting it is a disease based on theories but characterized by hypertension (>140/90 mmHg), proteinuria (>300 mg/d), and edema [35]. The presence of reactive oxygen species (ROS) in pregnancy arises from basal oxygen consumption, leading to mitochondrial stress and ROS production, which is associated with the development of oxidative stress and maternal vasculopathy [35]. Initially, the human placenta is hypoxic, creating an environment that supports maternal homeostasis. However, as the placenta vascularizes, an oxygen-rich environment is established, promoting the generation of ROS [35].

The presence of pre-eclampsia in developed countries is less than 3% of all pregnancies, while developing countries have a higher occurrence, with about 8,500,000 cases globally. This is associated with very high maternal and fetal mortality and morbidity. Protein-linked carbonyls

are identifiers of worldwide protein oxidation caused by various reactive oxygen species in blood, tissues, and cells. This leads to the formation of numerous products due to alterations in a large number of amino acids, damaging both sulfur-containing aromatic and aliphatic amino acids. It is important to note that oxidants disrupt the normal structure of amino acids in proteins, resulting in the formation of both protein-linked and liberated carbonyl groups. The presence of carbonyl proteins is responsible for cellular damage in the placenta [35].

Protein Carbonylation and Malaria

Malaria is a disease caused by five main species of Plasmodium, a vector-transmitted parasite that has been present for the past 70,000 years. It has had a unique influence on the human genome, resulting in erythrocyte polymorphisms that are both quantitative and structural, particularly in its haemoglobinopathies [36-37]. Vital proteins, including enzymes within the parasite, are mostly alkylated by endoperoxidases, specifically the cysteine residue of cysteine proteases. This activity within the parasite enables the uptake and digestion of hemoglobin, supporting the disintegration of red blood cells. Related concerns are as described [36]. Malaria is a communicable disease and a significant threat to life, particularly in tropical and subtropical countries where it is prevalent, leading to high morbidity and mortality rates. Factors contributing to the burden of malaria include population movement of non-immune individuals to endemic areas, lack of access to healthcare, gaps in the medication supply chain, and loss of human capital [38].

Oxidative stress is a significant immune defense system in malaria infection that affects its progression and clinical outcomes [37]. During the acute phase of infection, there is an increase in the rapid production of reactive oxygen species (ROS), leading to a decrease in parasitemia. Additionally, oxidative stress induced by antimalarial agents like artemisinin and chloroquine helps in clearing the malaria parasite. However, excessive ROS production can be harmful to host tissues, resulting in red cell breakdown, metabolic acidosis, and respiratory distress [36,37,39-40]. A pro-oxidant-rich environment favors the survival of the malaria parasite but also makes it susceptible to oxidative stress. Maintaining redox equilibrium is crucial for the parasite's survival. Studies on oxidation using Plasmodium yoelii-infected blood from mice showed reduced protein carbonylation compared to uninfected cells [41]. In a pediatric study on the oxidant and antioxidant status of severe malaria, it was observed that protein carbonyl levels, along with other oxidant and antioxidant markers, were significantly elevated ($p < 0.001$). The increased protein carbonyl levels indicate the extent of oxidative stress, providing valuable insights into the changes in these markers and their implications in the pathogenesis of severe malaria in children. Relevant associations have been elucidated [42].

Protein Carbonylation and Diabetes Mellitus

Diabetes mellitus is a metabolic disease identified by elevated blood glucose concentration. The increased blood glucose concentration, along with heightened levels of glucose-associated reactive products, accelerates the progression of diabetic complications, which can affect the kidneys, nerves, blood vessels, and eyes43. It is projected that 1.31 billion people worldwide will be affected by 2050 [44]. Currently, there is no cure for diabetes, but with proper clinical management, it can be successfully controlled. Sedentary lifestyle, poor diet, obesity, smoking, and excessive alcohol consumption are modifiable risk factors for type 2 diabetes, which increases the likelihood of developing diabetes mellitus [44]. It is important to note that diabetes is caused by either the lack of insulin secretion, insulin action, or both [45-46]. The origins of diabetic complications have been linked to various factors, including oxidative stress, pseudohypoxia, true hypoxia, carbonyl stress, activation of the polyol pathway, increased activity of protein kinase C, advanced glycation end products, changes in lipid metabolism, and alterations in cytokine or growth factor availability [45,47]. The impact of protein carbonylation in metabolic systems and cell signaling, reactive carbonyl stress, and the interaction of glucose with free radicals are explained in detail [43, 45, 47].

Protein Carbonylation and Sickle Cell Disease

The elements of oxidative damage in individuals with sickle cell disease include damage induced by free radicals during vaso-occlusion induced ischemia-reperfusion injury, as well as reduced antioxidant capacity in erythrocytes and in the circulation [48]. It has been established that plasma protein modification can be evaluated by measuring protein carbonyl levels, which have a wide range of associations with different disease conditions and have been identified as a factor that can contribute to disease pathology. In sickle cell disease, carbonyl-modified plasma proteins have been shown to cause endothelial disturbances, which are reported to be a concern in the progression of the disease. Elevated protein oxidation through carbonyl modification has been reported in sickle cell disease [48]. Additionally, carbonyl levels have been found to correlate with plasma iron and hemolysate zinc concentrations [48]. While post-translational modifications due to oxidative stress have been identified, the effects on protein function and quantity are not yet certain.

Protein Carbonylation and Hypertension

Hypertension is a leading cause of morbidity and premature death worldwide. It can affect two or more organs in the body and has a complex and multifactorial etiology [49-50]. The guideline for defining hypertension is a systolic blood pressure of > 130mmHg and/or a diastolic blood pressure of > 80mmHg. Children may have varying blood pressure numbers, and ambulatory measurements throughout the day seem to provide more accurate results than office-based measurements [50,51-52]. Various gender-based classifications have been developed and stratified 50. The etiology of hypertension has been identified in 5% of individuals (secondary hypertension), while 95% of individuals have no known cause (primary or essential hypertension) [53]. Risk factors are diverse and include environmental factors, genetics, and interactions among physiological organs [50,51].

Lifestyle factors can be modified in conjunction with the use of appropriate medication to lower blood pressure. Identifying risk factors early could lead to necessary interventions. Approximately one million people worldwide

are determined to suffer from hypertension, with 9 million deaths attributed to it annually. This number continues to rise at an alarming rate. Projections suggest that 1.56 billion people will be suffering from hypertension by the year 2025 [54]. Urgent and strict interventions are needed as soon as possible.

Vascular dysfunction, cardiovascular remodeling, immune system disturbances, and other issues are associated with hypertension and have been summarized [50]. Oxidative stress has been implicated in these disturbances through redox-reactive and responsive mechanisms, leading to vascular damage [50,55]. In a study using animal models to assess protein carbonylation using the oxyblot method, levels of protein carbonyl were found to be increased. Various concerns are described [56]. Similarly, Wong and Suzuki [57] presented noteworthy results, including mechanisms and approaches. It is important to note that there has been limited research on protein carbonylation in hypertension of different classes. The existing research could serve as a foundation for further insights into the role of carbonylation in hypertension.

Protein carbonylation and liver disease

The liver is the largest internal organ of the body and is exposed to reactive oxygen species activity [58]. The disequilibrum between production of free radicals and its elimination by the liver antioxidant defence system is what is responsible for the extensive damage. Some of the outcome from the extensive damage are induction of irreversible changes in cell ligands including proteins and DNA and these directly affect metabolic mechanisms that regulate appropriate biological functions [58]. Some key aspects of liver disease are alcoholic liver disease, non alcoholic fatty liver disease and alcoholic steatosis and liver cirrhosis which is the final stage and so far no pharmaceutical or nutrient based treatment for managing individuals with alcoholic liver disease [59]. Major and minor alcoholic liver process is described (Figure 2). In a publication by Pomacu et al. [60] pathological features that are useful in liver cirrhosis are varied and those include hepatocyte degradation and neo-fibrotic crosis, substitution of liver parenchyma by fibrotic tissues and nodules capable of regeneration , then loss of liver function. In any case, exposure of the liver to increase quantity of ethanol undergoes structural and functional changes due to oxidative stress and inflammation. Ethanol (Ethyl alcohol) elevates the release of reactive oxgen species with an attendant production of pro –fibrotic cytokines and the liberation of multiple inflammatory markers and collagen production when liver fibrosis progresses [60]. Depending on the type of liquor, the amount of ethyl alcohol varies between 20 -30%. It should be noted that the liver receives blood from the stomach and small intestine through the portal vein and its volume of ethyl alcohol is much more with only 2 – 5 % of it lost unchanged through urine and breath with the majority of its excretion taking place through hepatic metabolism61. The parenchymal cells of the liver which makes up more than 70 % of the liver tissue metabolises alcohol and has the largest number of enzymes that oxidizes ethanol. Chief among these enzymes are alcohol dehydrogenase and aldehyde dehydrogenase alongside cytochrome p4502E (CYP2E1) and catalase . In chronic alcohol consumption , oxidative stress leads to elevated peroxidation of polyunsaturated fatty acids to form highly reactive electrophillic α/β unsaturated aldehydes that brings about post translational protein modification altering capability [62]. In a study by Shearn et al. [62] using immunohistochemistry and western blotting, there was an elevated protein carbonylation in end stage alcoholic liver disease which occurred basically in the hepatocytes . Of the 1224 carbonyalted proteins in normal hepatic and end stage alcoholic cirrhosis , 411 have been identified to be unique to cirrhotic alcoholic liver disease, 261 unique to normal hepatic tissue and 552 common to both groups. Bioinformatic pathway analysis of these carbonylated proteins within the liver are as documented [62]. In a related study, age realted increases in reactive oxygen species and protein carbonylation have been identified in the liver but no report on the functional impact has been described and research that showed a functional effect of the oxidative stress did not identify targets of carbonylation. Moreso, elevated carbonylation of endoplasmic reticulum resident proteins takes place in the liver with age. These resident proteins are endoplasmic reticulum chaperone protein GRP78 and calreticlin . The reactivity of these proteins by carbonylation in the liver could interfere with protein folding and quality assurance [63]. Liver disease associated with elevated proetein carbonylation are alcoholic liver disease, non alcoholic fatty liver disease, non alcoholic steatohepatitis with fatty liver supplying the much needed ecosystemfor the generation of reactive lipid species and the protein modification that follws afterwards [63]. Also, alcohol down regulates antioxidant enzymes such as glutathione peroxiadse and upregulates hydrogen peroxidase [64].

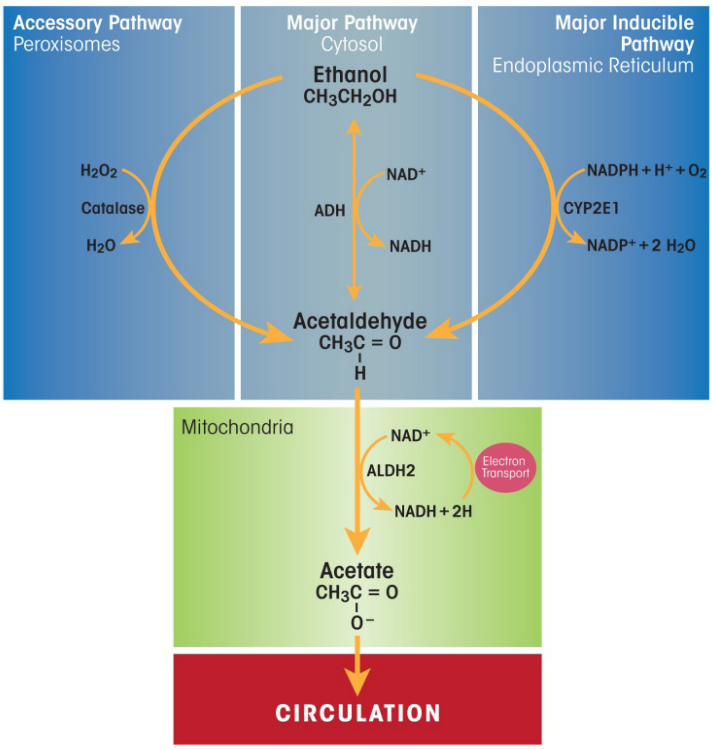

Fig 2: Major and Minor Alcohol Metabolic Process in the Liver [59].

Protein Carbonylation and Peptic Ulcer Disease

Peptic ulcer disease (PUD) is a gastro intestinal disease that is influenced by gastric acid or pepsin secretion . There is a discontinuation in the interior mucosal linning of the gastrointestinal tract (GIT). This alteration continues into the muscularis propria layer of the gastric epithelial surface. The stomach and the proximal duodenum are target sites. However, the lower eosophagus , distal duodenum or jejunum may be affected [65]. Pain within the epigastric region of the abdomen is symptomatic within half an hour following a meal in individuals with agastric ulcer. Also, pain with a duodenal ulcer becomes evident 2 – 3 hours after a meal . Besides , gastric acid secretion, *Helicobacter pylori* infection has been implicated in peptic ulcer disease alongside non steroidal anti-inflammatory drug accounting for most of the disease origin [65]. Rarer causes of PUD are Zollinger–Ellison syndrome, malignancy , stress , viral infection , vascular insufficiency, radiation treatment, chron disease and chemotherapy. Other agents that may be involved in peptic ulcer disease are smoking and alcohol consumption. Some of the complications that could arise from from PUD are upper gastrointestinal bleeding, gastric outlet obstruction, perforation , penetration and gastric ulcer. A 2015 report by Ashrafrezaei et al. [66] 68 out of 150 cases showed that protein carbonyl levels were significantly elevated in cases of H. pylori infection compared to controls. This therefore confirms oxidative damage by H. pylori. The pathogenesis of H. pylori infection is the production of alkaline mileu by urease enzymes and oxidative stress [66]. However, more work needs to be done in respect of carbonylation given the dearth of information on protein carbonylation associated with peptic ulcer disease.

Protein carbonylation and vitamin B12 deficiency

Vitamin B12 or cobalamin is a B group water soluble vitamin and lready implicated in neuronal health and haem production. It is mostly present in animal tissues and generally not available in plants and this may be the reason why vegetarians are a risk group for vitamin B12 deficiency [67-68]. In developed countries, clinical B12 deficiency is limited and primarily as a result of genetic aberrations and often leads to myeloneuropathy or megaloblastic anaemia, a disease where there is presence of megaloblast). Megaloblast becomes apparent when restriction of DNA production causes asynchronous maturation between the nucleus and the cytoplasm with symptoms being properly identified neurological symptoms [69]. B12 could possess antioxidant properties with subclinical B12 deficiency contributing to oxidative stress and the start of age associated diseases68. Subclinical B12 deficiency has been indicated to be serum B12 levels between 119 – 200 pmol/L with the possibility of long term destruction to nucleic acids, proteins and lipids even though individuals may be symptom free [68]. Three general factors have been identified to cause subclinical B12 deficiency and are inadequate intake, increased demand and malabsorption [68]. It is already established that the imbalance between pro-oxidant such as ROS and antioxidant lead to oxiadative stress. Eukaryotic cells constantly eliminate free radicals via endogenous antioxidant . The nuclear factor – erythroid -2-related factor (NrF2) is a major modulator of endogenous antioxidant defenses [68]. Once oxidative stress occurs , excess of the ROS promotes inflammation and subsequent cytokine production which brings about more ROS production. Inflammatory responses mediates tissue repair in response to aggressors but also with a deleterious effects if it continues longer than necessary [68]. Also ROS can destroy functional molecules and tissues through the transformation of carbohydrate, proteins , lipids, DNA and these activity alongside antioxidant properties of B12 have been summarized [68] (Figure 3). Currently, there is limited work done on investigations between protein carbonylation and vitamin B12 deficiency. This, most likely remains an area to be examined explicitly to further push the frontiers in vitamin B12 related conditions.

Protein Carbonylation and Psoriasis

Psoriasis is a chronic dermal disease that is not contagious and impacts various populations [70]. There is presence of cutaneous aggregation of neutrophils liberating reactive oxygen species [71]. The prevalence rate stands at less than 11.8% across populations. Majority of persons under the age bracket of 35 years are heavily impacted by psoriasis. Genetic, epigenetic and environmental effects contribute to the development of psoriasis [70]. The contributions by these effects lead to altered interactivity between immune elements, cell signaling proteins and dermal cells givig rise to psoriasis. The import of protein carbonylation and its

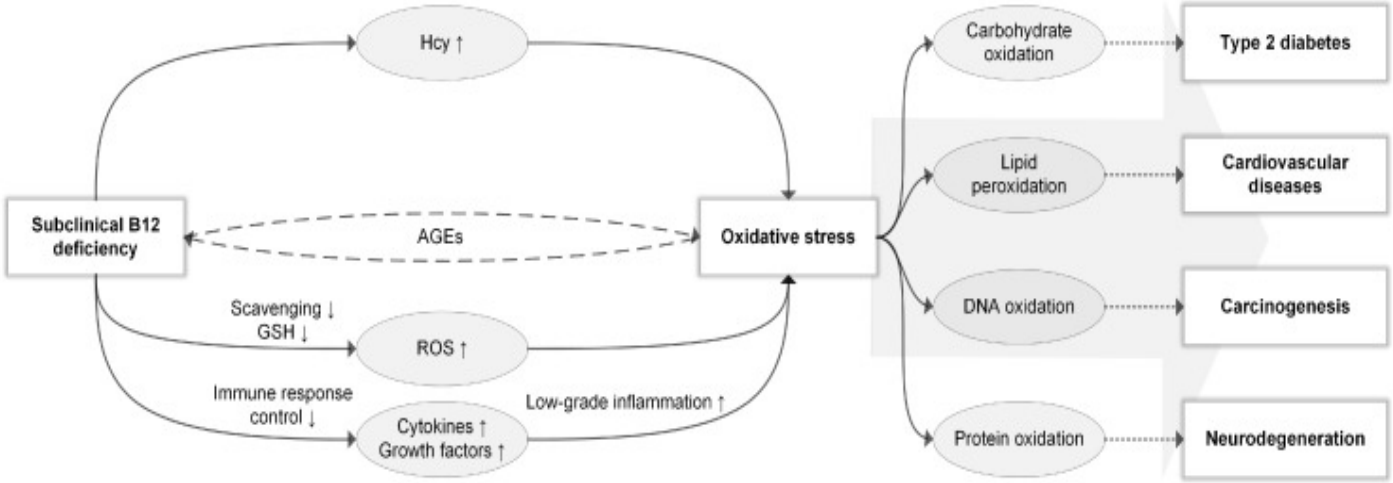

Figure 3: Subclinical B12 Deficiency in relation to Oxiadative Stress [68].

outcome between amino acid residues of proteins and reactive oxygen species or reactive nitrogen species (RNS) are already established and this leads to oxidative stress. Recently , it is established that persons with psoriasis presents with increased level of reactive oxygen species in the dermal stratum [70]. The attack of proteins by reactive oxygen species is a continuous process and this impacts protein molecular structure, net charges, folding and hydrophobicity/hydrophillicity and this certainly produces protein carbonyl groups. Much more, myeloperoxidase present in activated neutrophils releases hypochlorous acid, chloraminated oxidants and chloramines which results in advanced oxidation protein products (AOPPS) which has crosslinked dityrosine. The dual presence of carbonyl groups and AOPPS are identified as early determinants of oxidative stress and can be utilized to assess protein damage caused by oxidation [70]. Myloperoxidase is a basic modulator of anti tumor action of neutrophils [72]. Main functions of activated neutrophils are phagocytosis, liberation of granule contents, neutrophil extracellular traps, antigen presentation , production of reactive oxygen species, role in inflammatory responses and ability for tissue damage especially in chronic inflammatory conditions [72,73]. In psoriasis, those between the ages of 41-55 years, those who are obessed and females with waist circumference greater than 88 cm had significant levels of protein carbonyl and with a negative correlation but not significantly between protein carbonyl with age, duration of psoriasis, BMI and waist circumference in the studied population [70]. In a related study by Yacizi et al. [71] protein carbonyl were found to be higher in psoriasis patients with oxidative stress with findings such as inflammation, phagocytic cells oxidation, MPO–hypochlorous acid oxidation reactions which is shown by increased total/differential leucocytes counts, CRP, ESR, MPO, neopterin, AOPP, Protein carbonyl compound, pyrolised protein, lipid hydroperoxidases (LPH) and reduced thiol levels.

Protein Carbonylation and Therapeutic Interventions

A number of strategies and interventions have been deployed to mitigate the effect of oxidative stress as a result of reactive oxygen species . some of these interventions are enzymatic and non enzymatic in nature. Also, chelators, reducing agents scavengers but non of these have shown impactful delivery in the reduction of oxidative stress with great therapeutic impact [64]. For diabetes mellitus , carbonyl stress can be managed by redox mutation , RCO texofication and inhibition of carbonyl stress. Hypotensive agents such as angiotensin – converting enzyme inhibitor and angiotensin II receptor antagonist are identified as useful therapies because of non production of side effects such as vitamin B6 deficiency and neurotoxicity which have been associated with first generation of carbonyl stress inhibitors such as amino guadine that behaves as RCO trapping agents [12]. For antioxidant therapy, limitations exist and one of such limitation is the significant destruction to macromolecules and tissue injury which afterall leads to cell death In effect , antioxidant therapy can only rescue undamaged macromolecules and surviving cells, a concern that will not be satisfactory to limit symptoms . There is also the concern in utilizing antioxidant therapy which is that clinical experts cannot identify individuals who might benefit from particular antioxidant therapy . So far, optimal daily requirements of usual antioxidants such as α- tocopherol and vitamin C are still being debated and guidelines have not been for less usual though necessarily less significant antioxidants such as γ-tocopherol . It has been identified also that certain groups of individuals might react adversely to specific antioxidants as found in some living cancer patients utilizing β-carotene. In view of these , clinical experts will determine an appropriate method for the type of anti-oxiadant supplementation appropriate for certain individuals and the responsiveness of patients to the prescribed treatment [12].

Protein Carbonylation Procedures

The standard method for quantifying carbonyl groups involves their reaction with 2,4-dinitro-phenylhydrazine (DNPH) to form 2,4-dinitrophenylhydrazone, a stable product. Various techniques can be used to analyze the dinitrophenyl group (DNP) adduct. The interaction of the DNP group with ultraviolet light enables the spectrophotometric quantification of total carbonyl levels in proteins or protein complexes. To shift the absorption maximum of DNP from 370nm (UV) to 450nm (visible region), the medium must be alkalized [14,74-75].The primary protein carbonylation reaction involves the direct oxidation of lysine, arginine, proline, threonine, and other amino acid side chains, resulting in detectable protein products with DNPH. Secondary protein carbonylation reactions can also occur through the addition of aldehydes, such as those generated from lipid peroxidation chemistry [2].

A. Spectrophotometric and HPLC estimations of protein carbonyl following dinitrophenyl hydrazine modification

The original procedure for derivatizing carbonyl groups with various agents to estimate carbonyl availability was described by Levine in 1990. The content of the published document evaluates the reactivity of carbonyls with borohydride , DNPH, fluorescein thiosemicarbazide and fluorescein amine76. This procedure describes how oxidatively modified proteins greater than 0.0005g of protein are processed with 10mM DNPH for 60 minutes. This is followed by a precipitation step using 20% trichloroacetic acid (TCA), then washed with ethanol-ethyl acetate at a ratio of 1:1, and dissolved in 6M guanidine. The process is finalized by measuring at 360-390 nm 76,77. Other methods of derivatization with DNP followed by high performance liquid chromatography (HPLC) estimation and /or immunoblotting have also been described [78].

Limitations of the spectrophotometric procedure

1. It is complex and labour intensive and takes a lot of time.
2. It can't meet up for high throughput estimations.
3. Protein and volume needs are high.
4. Loss of acid soluble protein during wash is between 10 -15% (Result must be expressed in terms of the loss and protein level computed for.
5. Additional carbonyl groups may be added due to the acidic state.

6. DNP may be held in the protein pellet and making it soluble again may be defective which could lead to false reports [76,79].

Other identified concerns that are common include nucleic acid interference because it contains carbonyl groups. It may be advisable to consider a depletion protocol in this regard. Additionally, interference by biologically active compounds such as haemoglobin, myoglobin, and retinoids, which absorb within the visible spectrum of 370nm, can lead to elevated background readings. The lack of commercially available and accessible protein standards and controls makes it challenging to compare results using spectrophotometric measurements between laboratories [76].These limitations can be overcome by using HPLC determination, which offers the advantage of detecting DNP absorbance at 366nm, equivalent to protein absorbance at 280nm. In this case, DNP derivatization should be carried out using sodium dodecyl sulfate (SDS) instead of guanidine-HCL, as the latter is unsuitable for most columns [76].

B. Enzyme linked immunosorbent assay (ELISA) for the estimation of protein carbonyl

In 1971, Peter Perlmann and Eva Engvall developed the first ELISA, using an enzyme-linked antibody to detect rheumatoid factor. In 1997, it was further developed using anti-DNP antibody as described by Buss et al. [80] A standard curve was created using HOCl-oxidized (hypochlorous acid, a weak acid identified by French chemist Antoine Jerome Balard in 1834) and sodium borohydride-reduced BSA. Reduced BSA is used for the blocking step [76]. To proceed with the ELISA procedure, plasma from severely ill patients and healthy patients must be diluted to 4mg/ml and processed with 10mM DNPH for three-quarters of an hour at room temperature. The volume ratio of sample to DNPH is 1:4 (20% dilution). The variable concentration of carbonyl for both severely ill patients and healthy patients is documented [81]. A strong linear correlation (r = 0.70) was determined between the absorbance of the spectrophotometric assay (375nm) and the ELISA for plasma samples (n = 26) [76].

The protocol by Buss et al. [80] has been modified by Alamdari [82]. This procedure requires protein samples to be diluted in phosphate-buffered saline, which are then adsorbed to wells of an ELISA plate and reacted with DNPH. The protein-conjugated DNPH is analyzed by commercially produced anti-DNPH antibody, followed by the addition of a second antibody conjugate with horseradish peroxidase for estimation. Calibration of this procedure necessitates oxidized albumin and 5µg of protein. The valuable aspect of this modification is the elimination of the need to concentrate protein in samples, whether experimental or clinical, with minute amounts of protein. This modification also eliminates the effect of TCA on carbonyl measurement. The standard curve linearity was found to be in the range of 0 – 3.4 nmol carbonyls/mg protein. Aqueous humor and diluted plasma samples have been analyzed for carbonyl content using the modified protocol [82].

Studies utilizing anatomical portions of animal models..... (organ homogenate) as outlined by Augustyniak et al. [83] identified four distinct variants of the protein carbonyl assay across different laboratories. Reports from these laboratories varied in terms of the increase in protein oxidation status over time of irradiation. Reasons for these discrepancies include differences in assays, protein aggregation, and the disappearance of nearly all healthy oxidized proteins during the experiment [83]. Additional concerns that could contribute to the observed differences include dilutions, temperature variations, blocking agents used, washing requirements, sample diluents, and primary antibody requirements [83]. To ensure accurate and reliable results, it is essential for research experts to address these concerns in their technical approaches. The differences in incubation temperature for the ELISA and spectrophotometric methods are well explained [76].

ELISA is an enzyme immunoassay (EIA) procedure with a heterogeneous background used for clinical analysis, and is a modified form of the radioimmunoassay (RIA). Tagged antigens and antibodies are conjugated with enzymes instead of radioactive iodine [84]. In the ELISA method, a reactivity component is adsorbed nonspecifically or covalently bound to the surface of a solid stage. Examples of the solid stage include a microtiter well, plastic bead, or magnetic particle, which aids in easier segregation of the bound and free labeled components in the reaction [84]. The general steps for an ELISA procedure are coating, blocking, detection, and final read, and the four main types of ELISA techniques are as described [84].

Benefits of the ELISA protocol

1. Large number of samples can be estimated.
2. Aliquots of samples can be utilized.
3. Plasma, tissue and cell culture samples can be utilized.

Limitations of the ELISA protocol

1. Estimation of protein concentration is mandatory before executing the assay since assay takes 2 days for sample adsorption to the plate overnight.
2. The wash steps in-between may bring about loss of sample. ELISA plates with varied binding capacities for various requirements are being deployed by companies depending on the hydrophobic, hydrophilic or mixed domain of the molecules involved for estimation.
3. The various monoclonal and polyclonal antibodies present a problem as well since they potentially have a reactivity with different epitopes.
4. There is an absence of available uniform and recognized protein standards which leads to insufficient comparison [76].

There is no information about the molecules being oxidized or the identity of the carbonylation , whether primary or secondary [83].

C. Determination of Protein Carbonyl by Immunoblotting

The immunoblotting method described by Shacter et al. [81], Levine et al. [78] and Keller et al. [85] may not offer

the much-needed accuracy. Additionally, some of the identified problems include issues with reproducibility. If reproducibility is affected, reliability may not be guaranteed at any level of testing. Another concern is the performance of pre- and post-electrophoresis derivatization, specifically the use of nitrocellulose membrane which is not satisfactory for incubation in highly acidic solutions. The pre- and post-electrophoresis derivatization described by Keller et al. [85] is limiting due to lengthy wash steps, making the procedure time-consuming [76,78,81,85]. The results of the immunoblotting method cannot be determined with specific concentration due to its semi-quantitative nature [76]. To address this issue, the utilization of appropriate controls and good laboratory practices should be prioritized. Various variants of immunoblotting (western blot) for cell lines and protein extracts have been described [83]. Currently, carbonyl western blot using the trade name OxyBlot is widely used in educational experiments [3]. Immunoblotting, also known as western blot, was developed in 1979 and is a popular technique routinely used in research, molecular diagnostics, and proteomics studies in laboratories worldwide. It is used for the detection and semi-quantification of proteins with specific amino acids that have undergone post-translational modifications due to physiological changes in both diseased and healthy states. The identified mechanisms for amino acid modifications include phosphorylation, ubiquitination, biotinylation, glycosylation, methylation, acetylation, sumoylation, nitration, oxidation/reduction, nitrosylation, and other variations [86]. The protocol and issues associated with immunoblotting are extensively described [86].

D. Determination of Protein Carbonyl by Gel Electrophoresis

Gel electrophoresis using polyacrylamide for the determination of protein carbonyls has high resolution for protein evaluation and could eliminate impurities of low molecular mass. The reason for utilizing gel electrophoresis for the detection of protein carbonyls is the availability of unreacted DNPH and non-protein carbonyls [79]. The four significant steps using gel electrophoresis for protein carbonyl studies are DNPH derivatization of carbonyl groups at acidic pH (1M HCl), gel electrophoresis, electrotransfer to PVDF membrane, and antibody-based determination [79]. The beauty of the gel electrophoresis methodology, as described by Rogowska-Wrzesinska et al. [79] is the possibility to quantify the extent of carbonylation of each protein in association with its total quantity. It should be noted that various chemical probes for determining protein carbonyls in polyacrylamide gel have been invented and advanced [79]. The specific approaches for when the DNPH derivatization is carried out have been detailed alongside other associated procedures [79].

E. Determination of Protein Carbonyl by Chromatography

Notably, gas chromatography (GC), high performance liquid chromatography (HPLC), and liquid chromatography coupled with tandem mass spectrometry (LC-MSMS) can be used for the determination of protein carbonyls. This provides quantitative knowledge about protein carbonylation and the site of carbonylation. Released protein carbonyls such as formaldehyde, acetone, isobutyraldehyde, and glyoxylic acid, liberated from oxidized amino acids such as alanine, valine, leucine, and aspartic acid, have shown appreciable results following the deployment of reverse phase (RP-HPLC). The differential concerns regarding the use of chromatographic analysis for protein carbonyl determination are properly elucidated [79].

F. Detection of Protein Carbonyl by Mass Spectrometry

This method provides the opportunity to identify protein modifications without the need to understand the specific type of modification present. High-throughput investigations of complex protein mixtures may not be feasible with this procedure due to the labor requirements. Mass spectrometry offers an ideal methodology for evaluating modified proteins because the covalent incorporation or depletion of a chemical moiety from an amino acid results in an increased or decreased molecular mass of that residue. This phenomenon is demonstrated by the oxidation of a methionine residue, which increases the mass from 13Da to 147Da through the incorporation of a single oxygen atom [79]. Different proteins that have undergone oxidative modifications exhibit varying properties, therefore specific approaches tailored to a particular type of modification are necessary and have been clearly explained [79].

Quality Control, Standardisation and Safety Requirement in Protein Carbonyl Analysis

The work by Rogowska-Wrzesinska et al. [79] on the analysis of protein carbonylation is extensive and has indeed highlighted the challenges, assurances, and potentials in commonly used methods. As with any research and clinical investigations, the importance of quality control and standardization cannot be overlooked in order to achieve reliable, relevant, and reproducible results (3R's). In this context, their recommendations for quality control primarily focus on the analytical phase and include the following: 1) Measurements should be conducted promptly. 2) Experimental steps should be minimized to the essentials. 3) Derivatization should be carried out early in the process. 4) Primary chemicals from reputable vendors should be utilized. 5) Working solutions should be freshly prepared to prevent contamination. 6) Optimization and standardization of the entire procedure should be implemented. 7) Control samples and steps should be included to eliminate background noise and signal interference. Additionally, adherence to good laboratory practices and the adoption of a global quality assurance system incorporating ISO 15189, ISO 9001, and ISO 17025, with clearly defined rules for establishing and maintaining quality systems in the laboratory, should be taken into account [87-88].

Reference materials, internal reference samples, and participation in external quality assurance programs define the success of analytical accuracy. Additionally, in light of safety concerns in protocol handling, technical documents should be carefully reviewed to identify various risks, safe handling instructions, properties of reagents,

contact information for vendors and manufacturers, and the date the technical document was detailed according to Occupational Safety and Health Administration guidelines [87]. Pre-analytical considerations in quality control requirements include the sample matrix, buffer composition, quality of chemicals, acidity or alkalinity levels, temperature requirements, atmospheric oxygen, number of steps, stabilizers, presence of other oxidized molecules, elimination of excess reagents or interfering substances, storage conditions, and enrichment protocols. Guidance on modifying any aspect of the procedure should also be provided [79]. Effective healthcare delivery and expert team collaboration are essential. This involves establishing valuable connections between laboratories and in-vitro diagnostic (IVD) manufacturers to test the applicability and standardization of different methods for various sample matrix types and considerations. Interlaboratory evaluations will provide insight into the strengths, weaknesses, opportunities, and threats associated with different methods (reproducibility concerns) and allow participants to assess their competence and status in handling protein carbonyls [79,87].

Conclusion

Protein carbonylation is an intriguing aspect of oxidative protein chemistry. The shared developmental concerns between plants and humans demonstrate that oxidative stress is a persistent issue in all living organisms and must be effectively managed. This paper has presented the progression and outcome trends of protein carbonylation in several common clinical and pathological conditions. By utilizing the methods outlined, the degree of protein carbonylation can be accurately determined, providing insight into which proteins have been modified and where these modifications have occurred. It is recommended that user-friendly methodologies be implemented and that these technologies be advanced to different institutions and hospitals with the necessary expertise.

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RESEARCH ARTICLE

Misuse of dexamethasone for cosmetic purposes boosts hyperthyroidism and hepatotoxicity in albino rats

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Abstract

Background: The use of dexamethasone (Dex) for cosmetic purposes, particularly for skin lighting, is widespread and is associated with a high incidence of skin cancer in several populations. This study aimed to investigate the misuse of Dex for skin whitening, particularly its influence on thyroid, liver, and kidney function in female albino rats.

Materials and methods: In the in vivo comparative experiments I and II, 36 female albino rats, each weighing 140–162 g, were used. Thyroid function, liver enzyme activity, and renal function were assessed using enzyme-linked immunosorbent assay (ELISA). Liver and kidney sections were fixed and stained with hematoxylin and eosin (H&E).

Results: The groups administered high and low doses of Dex exhibited significant increases in thyroid hormone levels, liver enzyme activities, creatinine, and urea levels compared to the control group. In contrast, thyroid-stimulating hormone (TSH) levels were significantly lower ($P < 0.05$). Kidney sections displayed ghost glomeruli, partially necrotic tubular cells, and chronic inflammation at both doses. Liver sections showed binucleated cells, infiltration, and focal necrotic cells relative to the control.

Conclusion: The misuse of Dex for cosmetic purposes influences hyperthyroidism, hepatotoxicity, and renal impairment, with dose- and duration-dependent effects.

Keywords: Thyroid, hepatocyte, kidneys, dexamethasone, cosmetics.

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Introduction

Dex is a widely used synthetic steroid with anti-inflammatory and immune-suppressant properties [1]. In contrast, Dex is commonly used to lighten skin colors and is available in various forms, including creams, lotions, soaps, tablets, and injections. Approximately 25–67% of adult women regularly use skin-whitening cosmetics [2,3]. However, cultural standards and beauty norms can influence the use of cosmetics, and some populations find lighter skin tones more appealing [4,5]. Women use skin lighteners because they are dissatisfied with their natural skin [6]. Despite its potential risks and adverse effects, Dex is often misused as a cosmetic in many African and Asian countries, leading to the illegal distribution of unverified cosmetic products containing Dex [7,8].

Dex decreases melanocyte-stimulating hormone production [9], which may make the skin more susceptible to Ultraviolet (UV) radiation from sunlight, consequently increasing the risk of skin cancers such as melanoma [10]. It has been proposed that Dex may cause a decrease in TSH, free triiodothyronine (FT3), and free tetraiodothyronine (FT4) levels due to damage to the pituitary gland, leading to secondary hypothyroidism [11]. Additionally, Dex elevates transaminase activities and creatinine levels [12]. Moreover, steroid drugs cause fatty liver and necrosis, as well as dil-

atation and glomerular congestion [13]. There is a need for immediate research to highlight the discrepancies between previous studies and the increasing improper use of Dex as a cosmetic product. Therefore, we used experimental female albino rats to evaluate the impact of Dex on thyroid, liver, and kidney function at varying doses and durations.

Materials and Methods

Drug Preparation

Dex 0.5 mg was obtained from a local pharmacy in Khartoum State. The tablet was crushed, and 1 mL of 50% methanol was added to form a stock suspension. The mixture was homogenized using an Ultrasonic Sonicator and diluted to achieve the desired concentrations at low and high doses.

Experimental Animals

The study utilized female albino rats, aged 3–4 months and weighing 140–162 g, were obtained from the Pharmacy College Animal House. Rats were acclimated to laboratory conditions for 7 days. The rats were housed under standard conditions and were healthy, fed a nutrient-rich diet. In the in vivo comparative animal study, 36 rats were divided into six groups of six rats each, with 18 rats per experiment, as follows:

In Experiment I, Group I received a placebo and served as the control group. Group II was treated with a low dose of Dex at 8.3 µg/kg/day, while Group III was treated with a high dose of Dex at 24.9 µg/kg/day for 30 days.

In Experiment II, Group I received a placebo once again. Group II was treated with the same low dose of Dex (8.3 µg/kg/day), and Group III received the high dose of Dex (24.9 µg/kg/day) for 60 days. All doses are administered orally.

Ethical Approval and Euthanasia

This study was approved by the local Committee of the Faculty of Medical Laboratory Sciences, Al-Neelain University, and all experiments were conducted at the Pharmacy College of King Abdulaziz University. It adhered to the guidelines set by the US National Institutes of Health and the Declaration of Helsinki for the ethical treatment of animals. After an 18-hour overnight fast, the rats were euthanized using 1.9% diethyl ether in a closed chamber through inhalation, in accordance with the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals: 2020 Edition. Blood samples were collected via cardiac puncture, and the rats were then sacrificed to collect liver and kidney tissues. Liver and kidney tissues were examined histologically, and blood samples were centrifuged at 3000 rpm to obtain serum. Biochemical parameters were measured using an ELISA Dynex Best 2000 analyzer.

Estimation of Thyroid Hormones

TA double-sandwich ELISA was performed using T3 (Cat. No. MBS261285), T4 (Cat. No. MBS704309), and TSH (Cat. No. MBS726442) competitive enzyme immunoassay kit (MyBiosource, Inc., Germany). The T3 assay utilized a specific antibody coated on a surface and an avidin-HRP combination. After incubation, the free components were washed, and the substrate was added. The color intensity was proportional to the T3 concentration. T4 and TSH are coated explicitly with biotin-conjugated antibodies. After incubation, the unbound T4 and TSH were washed. Then, the substrate was added. Color intensity was inversely correlated with TSH and T4 levels.

Estimation of Liver Enzymes

The double-sandwich ELISA method was used to quantify the activities of aspartate transaminase (AST) (Cat. No. MBS264975), alanine transaminase (ALT) (Cat. No. MBS269614), alkaline phosphatase (ALP) (Cat. No. MBS269614), and γ-glutamyl transpeptidase (GGT) (Cat. No. MBS9343646) (MyBiosource, Inc., Germany). The antibodies were tagged with biotin and monoclonal pre-coated antibodies. Samples and biotin-labeled antibodies were added to each well. After rinsing, the avidin-peroxidase conjugates were added. The color was proportional to the activities of AST, ALT, ALP, and GGT.

Estimation of Urea and Creatinine

The ELISA (Cat. No. MBS2600001) (MyBiosource, Inc., Germany) was used to measure the urea levels. Briefly, according to the manufacturer, color development was based on the urea concentration. A competitive enzyme immunoassay (Cat. No. MBS749827) from MyBiosource, Inc. (Germany) was used to measure creatinine levels. Color development was inversely proportional to the creatinine concentration.

Histological Methods

The experimental rats were euthanized, and the liver and kidney organs were excised. Biopsies were obtained for histopathological analysis and fixed in 10% neutral-buffered formalin. The samples were then processed into paraffin wax blocks, and 5µm sections were prepared [14]. These sections were stained with hematoxylin and eosin (H&E), a standard pathological stain. Two experienced pathologists conducted a systematic, anonymous, and blinded analysis of all samples. Findings were reported blindly, without knowledge of the treatment groups, and later matched to the respective rat groups. Once identified, the findings were correlated with specific treatment exposures, and representative histology for each of the four experimental groups was selected and is shown in Figures 4 and 5.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software (version 21.0; SPSS Inc., Chicago, IL, USA). Data are expressed as mean ± standard error of the mean (SEM) and compared with controls using a t-test and analysis of variance (ANOVA). Statistical significance was set at $p<0.05$.

Results

Thyroid Hormones

After 30 days of Dex treatment, TSH levels were significantly decreased in the low-dose (2.17 ± 0.32 mIU/L) and high-dose (0.60 ± 0.15 mIU/L) groups compared to the control

group (4.27 ± 0.37 mIU/L) (p<0.05). The T3 levels were significantly higher in the low-dose (132 ± 5.70 ng/ml) and high-dose (209 ± 20.2 ng/ml) groups than in the control group (103 ± 4.26 ng/ml) (p<0.05). The T4 levels were significantly increased in the low-dose (15.2 ± 0.72 µg/dL) and high-dose (25.0 ± 1.75 µg/dL) groups compared to the control group (9.06 ± 0.43 µg/dL) (p<0.05). After 60 days of Dex treatment, the TSH in the low-dose (1.40 ± 0.40 mIU/L) and high-dose (0.66 ± 0.15 mIU/L) groups decreased significantly compared to the control group (3.11 ± 0.27 mIU/L) (p<0.05). There were significant increases in the T3 levels in low-dose (131 ± 13.05 ng/ml) and high-dose (275 ± 28.49 ng/ml) compared to the control group (103 ± 4.24 ng/ml) (p<0.05. The T4 levels were significantly increased in the low-dose (18.1 ± 0.90 µg/dL) and high-dose (27.1 ± 2.45 µg/dL) groups compared to the control group (9.10 ± 0.53 µg/dL) (p<0.05), as shown in Figure 1.

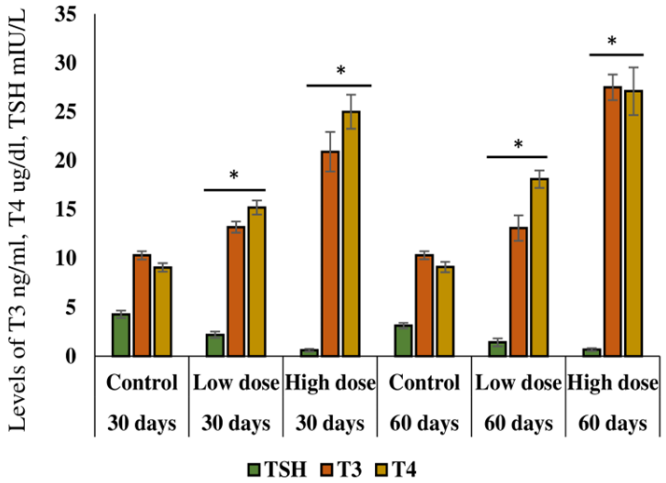

Figure 1. Comparison of mean TSH, T3, and T4 levels among Group II (low-dose Dex), Group III (high-dose Dex), and the control group following Dex administration for 30 and 60 days. (*) Indicates a significant difference (p<0.05).

Liver Enzymes

The administration of Dex for 30 days resulted in significantly increased ALT, AST, ALP, and GGT activities in both the low-dose and high-dose groups compared to the control group (p < 0.05). After administering Dex for 60 days, ALT activities were significantly increased in both the low-dose (56.2 ± 5.60 U/L) and high-dose (126 ± 23.0 U/L) groups compared to the control group (16.2 ± 1.30 U/L) (p < 0.05). The AST activities were significantly increased in the low-dose (71.5 ± 8.60 U/L) and high-dose (144 ± 18.7 U/L) groups compared to the control group (22.5 ± 2.17 U/L) (p<0.05). The ALP activities were significantly higher in the low-dose (105 ± 7.20 U/L) and high-dose (168 ± 20.5 U/L) groups than in the control group (52.6 ± 3.29 U/L) (p<0.05). The GGT activities were significantly increased in the low-dose (61.0 ± 3.66 U/L) and high-dose (98.0 ± 6.40 U/L) groups compared to the control group (16.0 ± 1.18 U/L) (p<0.05), as depicted in Figure 2.

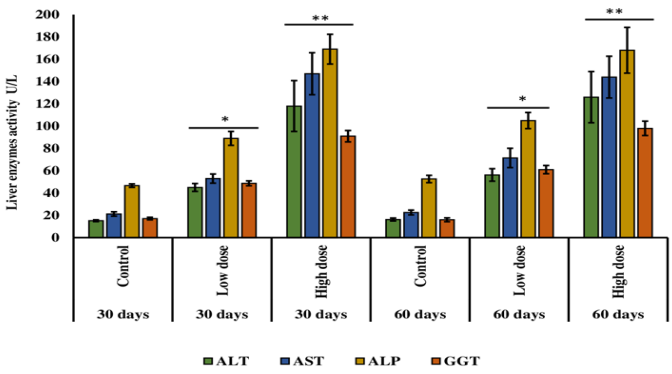

Figure 2. Comparison of liver enzyme activity levels (ALT, AST, ALP, and GGT) among Group II (low-dose dex), Group III (high-dose dex), and the control group over 30 and 60 days. (*) Indicates a significant difference (P < 0.05).

Renal Functions

After administering Dex for 30 days, the mean urea levels were significantly increased in the low-dose (4.18 ± 0.25 mmol/L) and high-dose (7.98 ± 0.63 mmol/L) groups compared to the control group (2.09 ± 0.07 mmol/L) (p<0.05). The creatinine levels were significantly higher in the low-dose (119 ± 12.3 µmol/L) and high-dose (167 ± 10.6 µmol/L) groups than in the control group (53.9 ± 5.30 µmol/L) (p<0.05). Following 60 days of Dex treatment, the urea levels were significantly increased in the low-dose (4.48 ± 0.34 mmol/L) and high-dose (7.80 ± 0.49 mmol/L) groups compared to the control group (2.32 ± 0.11 mmol/L) (p<0.05). The creatinine levels were significantly higher in the low-dose (123 ± 12.3 µmol/L) and high-dose (176 ± 15.0 µmol/L) groups compared to the control group (61.8 ± 7.07 µmol/L) (p<0.05), as shown in Figure 3.

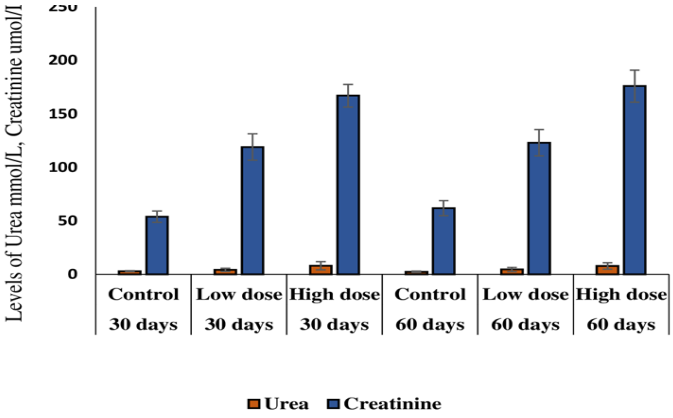

Figure 3. Comparison of mean urea and creatinine levels among Group II (low-dose Dex), Group III (high-dose Dex), and the control group over 30 and 60 days. A significant difference was defined as P ≤ 0.05.

Histological findings

Experiment 1: Control group A displayed normal hepatocytes (Figure 4). Groups B and C showed mild congestion, focal hepatocyte necrosis, nuclear lysis, dilated blood sinusoids with mononuclear inflammatory cells, active hepatocytes with significant numbers of

inflammatory cells (primarily lymphocytes), and numerous apoptotic cells.

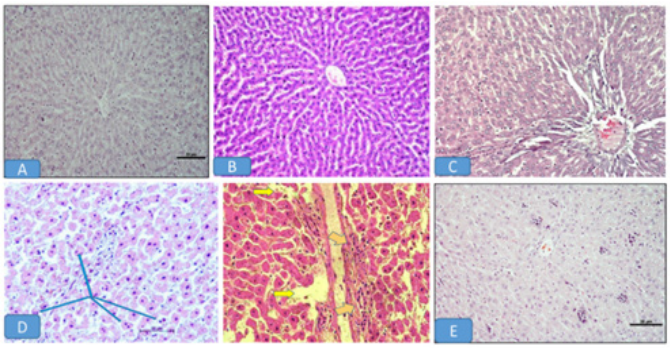

Figure 4. Histological section of liver stained with H and E (×10,40,40,40,20): A: Group I as control, B: Group II, which received low dose Dex for 30 days, C: Group II, which received low dose Dex for 60 days, D: Group III which received high dose for 30 days, E: Group III which received high dose Dex for 60 days.

Experiment 2: Group D showed increased binucleated cells due to hepatocyte toxicity and acute inflammatory cell infiltration (mainly neutrophils) with focal necrotic regions. Group E showed significant central vein congestion, loss of hepatocyte outlines, nuclear lysis, and dilated blood sinusoids filled with mononuclear inflammatory cells.

Experiment 1: A: Normal kidney sections from the control group (Figure 5). B: Mild chronic tubular inflammation with lymphocytic infiltration and tubular necrosis, reduced corpuscle and glomerular size, dilated tubular lumen, and slight parenchymal disorganization. C: Vascular and kidney tubular degeneration with a balanced cellular appearance.

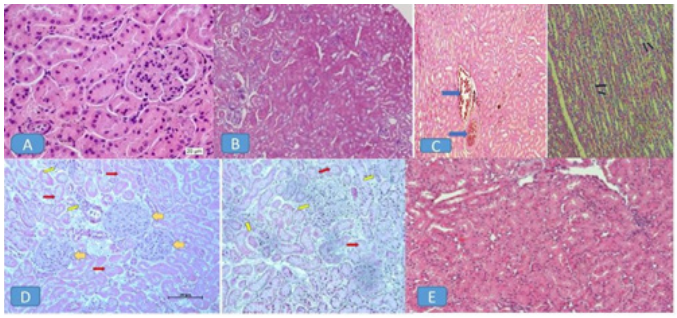

Figure 5. Histological section of kidney stained with H and E (×40, 10, 10, 20, 20): A: Group I Control, B: Group II treated with low dose Dex for 30 days, C: Group II which was treated with low Dex dose for 60 days, D: Group III treated with high dose Dex for 30 days, E: Group III which received high dose Dex for 60 days.

Experiment 2: D: Ghost glomeruli and tubular cells exhibiting necrosis, chronic inflammation, hemorrhage, reduced corpuscle and glomerular size, and a dilated tubular lumen with significant parenchymal disorganization. E: Significant lymphocytic infiltration, tubular necrosis, chronic inflammation, and hemorrhage with reduced corpuscle and glomerular size, dilated tubular lumen, and marked parenchymal disorganization.

Discussion

Despite its many adverse effects, Dex is commonly administered orally for skin lightening in African and Asian countries and has been associated with higher rates of skin cancer, especially in regions with elevated ultraviolet (UV) exposure. However, only a few studies have examined the direct effects of Dex on liver toxicity and thyroid functions. Therefore, this study aimed to investigate the effects of Dex on thyroid, liver, and kidney function in albino rats, simulating its potential misuse for cosmetic purposes. Dex dosages elevated T3 and T4 levels while suppressing TSH levels with dose- and duration-dependent effects. The findings partially align with earlier research that reported elevated levels of T3 and T4 following Dex treatment [15, 16]. However, other studies contradict the notion that Dex treatment leads to secondary hypothyroidism [17]. This contradiction is attributed to the fact that prolonged Dex treatment causes pituitary cell damage, resulting in low TSH levels and subsequently reduced stimulation of the thyroid gland [18,19]. The steroid hormone Dex may account for this inconsistency, as low doses of Dex synergize with thyroid hormones to enhance female fertility, given that estrogen increases the production of thyroid-binding globulin [20].

The cytotoxic effect of Dex on liver function was investigated and compared to that of the control group. Both low- and high-dose treatments resulted in higher activities of AST, ALT, GGT, and ALP. Our investigation indicated the potential hepatotoxic effect of Dex, which may lead to the leakage of transaminases and cholestasis biomarkers into the bloodstream due to hepatocellular damage. Prior research on Dex abuse has revealed liver necrosis, which was attributed to the damaged structural integrity of the liver caused by long-term Dex treatment [21,22]. Furthermore, our findings were supported by histological examination of liver sections, which revealed fatty liver and hepatocyte necrosis, consistent with previous reports that Dex administration leads to increased AST and ALT activities, indicating hepatocellular damage [13,23,24] . Moreover, increased serum ALP activity indicates disturbances in biliary flow, liver damage, or cholestasis [21]. This is further supported by elevated GGT activity, which is known to increase in response to liver injury or biliary obstruction [25]. Hence, previous studies have demonstrated that chronic Dex treatment leads to increased activity of cholestatic biomarkers [26, 27], which results in hepatotoxicity and liver injury [28].

To demonstrate the effect of Dex on renal function, urea and creatinine levels were measured, and kidney histological sections were analyzed. Our findings showed elevated urea and creatinine levels after Dex administration, indicating renal dysfunction [23]. Typically, these increases are associated with impaired renal function resulting from glomerular and tubular damage [27, 29] and a reduction in the number of nephrons 30. These observations were reinforced by histological results, which showed increased

renal corpuscles and glomerular size, along with necrosis, following Dex treatment. Previous studies have also reported that Dex raises urea and creatinine levels [12, 13, 22, 27] and induces renal necrosis [31]. Elevated serum creatinine levels indicate impaired glomerular clearance, whereas increased plasma urea levels may result from impaired renal excretion due to glomerular and tubular damage from prolonged Dex administration [32]. Additionally, another study reported that corticosteroids increase protein catabolism and blood urea nitrogen (BUN) levels [33].

This study provides insights into the misuse of Dex for skin lightening and its effects on thyroid, liver, and kidney function. However, the lack of assessment of FT3 and FT4 levels, which are more specific to thyroid functions, and the absence of clinical data from experimental animals are considered limitations.

Conclusion

The study investigated the effects of oral Dex administration and found that Dex increased T3 and T4 levels while decreasing TSH levels. Dex also increased ALT, AST, ALP, and GGT activities, as well as urea and creatinine levels. The findings indicated marked necrosis and inflammation in the liver and kidney tissues. Thus, oral misuse of Dex for cosmetic purposes has the potential to induce hepatotoxicity, renal dysfunction, and hyperthyroidism in a dose—and duration-dependent manner. Further studies are required to understand the mechanisms underlying these adverse effects.

Authors' contributions

Conception and design F.Y.A., A.M.I.; Supervision A.M.I., A.A.A., S.M.A.; Conducting experiments F.Y.A., S.M.A., A.A., Z.E., A.A.A., A.M.I.; Writing original research F.Y.A.; Writing review and editing A.M.I., F.Y.A., S.M.A., A.A.A., Z.E., A.A., O.A.M. All authors have read and approved the manuscript.

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Disclosure statement

None to declare.

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RESEARCH ARTICLE

Determinants of birth weight: a retrospective analysis at the University of Cape Coast Hospital

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Abstract

Background: Although birth weight continues to be a key factor in determining the future physical and mental development of children, there is little surveillance data, especially in low-income settings where the incidence of low birth weight remains high. This present study aims to examine and model the probable association between maternal obstetric and socio-demographic factors and the birth weight of newborns born to mothers delivering at the University of Cape Coast Hospital in the Central Region of Ghana.

Materials and methods: This cross-sectional retrospective study analyzed birth records of 1030 deliveries at the Maternity Ward of the University of Cape Coast Hospital for the period of November 2020 through March 2022. The census sampling technique was used. The multiple linear regression method was used to model the association. Data were processed using *SPSS v 22* and *EViews 12* software packages.

Results: A total of 539 (52.33%) male and 491 (47.67%) female neonates were in the study sample. The mean birth weight was 3.21 kg [SD = .5 kg]. Low birth weight prevalence was 5.5%. Male newborns (3.24 kg) were significantly heavier ($p < .001$) than the females (3.18 kg). The best-fit model on the association between newborn birth weight (BW) and maternal obstetric and socio-demographic factors was: BW = 2.988 - .112Gender + .077Tertiary education + .042Sulphadoxine-pyrimethamine (IPTp-SP) dose + .039Parity + .113Gestation.

Conclusion: Public health interventions aimed at improving birth weight should focus on encouraging women education, preventing preterm deliveries and increasing uptake of Sulphadoxine-pyrimethamine prophylaxis against malaria.

Keywords: association, birth weight, maternal factors, Cape Coast

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Introduction

Birth weight is a critical indicator of morbidity and mortality throughout childhood and adulthood stages of human development [1]. It serves as a key anthropometric index reflecting both physical and mental health outcomes in children [2]. Researchers in epidemiology have strongly indicated that the birth weight of a newborn is a precursor to the potential development of the newborn. Studies have shown that the weight of a baby at birth is strongly associated with the risk of mortality in the first year, childhood developmental problems, and the risk of various diseases in adulthood [3]. According to the World Health Organization (WHO), newborns are categorized by birth weight into three main groups: high, normal, and low [4]. The high and low categories are considered abnormal and therefore require special attention and treatment for their survival after birth. Hence, newborns weighing 4.0kg and above are considered high birth weight or macrosomia babies, those weighing 2.5kg to less than 4.0kg are considered normal birth weight whereas those weighing below 2.5kg are classified as low birth weight (LBW) babies [5]. Despite global efforts to reduce the prevalence of low birth weight and improve maternal and child healthcare, many countries in sub-Saharan Africa, including Ghana and Nigeria, continue to report significant rates of LBW [6].

Several studies have demonstrated an association between

birthweight and socio-demographic and/or maternal factors [7-10]. Such associations have been found between birth weight and maternal BMI [8], education, residence, and antenatal care visits[7] and maternal smoking [10]. In Ghana, representative studies on the association of birth weight and socio-demographic and maternal factors were conducted in some specific areas and selected facilities in the country, with only a few being conducted in the central region of Ghana [9,11]. Also, a previous study by Prah et al.[9] conducted in the same setting established empirical support for the link between low birth weight and some maternal factors. Health authorities in this region have introduced many interventions in the past five years to improve maternal health indicators, including birth weight. These interventions have included training on safe motherhood for midwives, doctors, and anaesthetists. There is a need to determine if these interventions have impacted birthweight and its maternal determinants, and to provide surveillance data that reveals factors that continue to significantly affect the birth weight of newborns.

This study aimed to examine and model the probable association between maternal obstetric and socio-demographic factors and the birth weight of babies born at the University of Cape Coast Hospital in the Central Region of Ghana.

Materials and Methods

Study setting

The study was conducted at the University of Cape Coast, a public institution located in Cape Coast, Central Region, Ghana. The university is uniquely positioned on a hill overlooking the Gulf of Guinea. The University of Cape Coast Hospital serves the healthcare needs of the university community and surrounding areas. It offers year-round specialist services in obstetrics and gynecology, including comprehensive antenatal and postnatal care.

Study design and duration

This was a retrospective cross-sectional study carried out in April 2022. It reviewed birth records from the University Hospital's Maternity Ward over a 17-month period, from November 2020 through March 2022. The choice of this design was driven by the need to assess patterns in birth weight without the logistical complexities of prospective cohort studies.

Study population, sample, and data source

The study population included all birth records of mothers who were delivered at the maternity ward of the university hospital for the period of November 2020 through March 2022. Data on neonates and maternal obstetric and socio-demographic factors were retrieved. Data were subjected to rigorous quality checking. Data were retrieved from the delivery register of the maternity ward of the hospital. All birth records in the hospital for the specified period were 1,397 and were all considered for analysis. However, after excluding records which were potential sources of bias, the analysis was finally conducted on a sample of 1,030 remaining birth records.

Potential sources of bias

Birth weight is known to be affected by maternal medical conditions such as sickle cell disease, severe anaemia, HIV and hypertensive disorders of pregnancy which may lead to low birth weight. Whilst maternal pre-gestational and gestational diabetes usually lead to high birth weight babies. Also, multiple pregnancies lead to the birth of babies with smaller weights compared to singleton pregnancies. Fetuses with chromosomal abnormalities may develop abnormal birth weights. In order to address these potential sources of bias, records of all these maternal and fetal conditions were excluded from the study as well as records with missing data.

Study variables

The study design had only one response variable with nine explanatory variables. In this cross-sectional study, the response or dependent variable is a metric scale variable which is the newborn birth weight measured in kilograms (Kg) immediately after the delivery of the baby. The explanatory or independent variables included two dummy variables (gender of baby and locality of mother), one categorical but ordinal variable (maternal educational level), one categorical but nominal variable (maternal occupation), and five metric scale variables: maternal age at delivery, parity, gestation, uptake of Intermittent Preventive Treatment in pregnancy with Sulphadoxine-Pyrimethamine (IPTp-SP), and the number of antenatal care visits.

Statistical analysis

Continuous variables were summarized using means and standard deviations and comparisons between groups were made using the t-tests. Frequencies and percentages were used to summarize categorical variables. The association between babies' weight and maternal obstetric and socio-demographic factors was estimated using multiple linear regression analysis. Adjusted analyses were performed with multivariable linear regression. In dealing with the problem of multicollinearity, the independent variables with a bivariate correlation of more than 0.70 were not included in the multiple regression analysis. The final multiple linear regression model was diagnosed and evaluated for fitness and robustness using a number of indicators and tests. Backward regression analysis was deployed to succinctly eliminate collinear as well as non-significant predictors in the model so as to arrive at the best-fitting model for the data. The data processing was performed using both *EViews 12* and *SPSS v 22* computer software packages. Statistical significance was set at 5% and 95% confidence interval (CI).

Ethical consideration

Ethical approval was obtained from the University of Cape Coast Institutional Review Board (UCCIRB/EXT/2022/03). Additional permission was secured from hospital management. To ensure ethical compliance, privacy, anonymity, and confidentiality were strictly maintained. A coding system replaced personal identifiers, and research staff received training to uphold these standards.

Results

There was a total of 1,397 deliveries during the period under review. After excluding records with missing data (n = 125), maternal medical conditions such as diabetes, pre-eclampsia, HIV, sickle-cell disease, and anaemia (n = 212), and multiple gestations (n = 30), 1,030 records remained available for analysis. A tabular representation of maternal socio-demographic characteristics is displayed in Table 1.

As shown in Table 1 the mean maternal age of the mothers who delivered at the UCC Hospital for the study period was 30.29 years with a standard deviation (SD) of 5.24 years. Twenty-five (2.4%) were teenage mothers, 829 (80.5%) were in the (20–35) year age class, whereas 176 (17.1%) of the mothers were above 35 years of age. In the area of maternal educational status, 21 (2.04%) had no formal education, 26 (2.52%) had primary education, 501 (48.64%) had secondary or high school education, and 482 (46.8%) had tertiary education. Neonatal and Obstetric characteristics of mothers who delivered at the UCC Hospital Maternity Ward for the study period are also presented in Table 2.

As shown in Table 2, a total of 539 (52.33%) male and 491 (47.67%) female neonates were in the study sample. The mean birth weight was 3.21 kg, [SD = .5 kg] for the study period in the given area. Normal birth weight constituted 923 (89.6%) of the newborn population at the facility for the period and about 10% made up for the abnormal birth weight population with a 5.5% prevalence of LBW. Almost all of the women in the study, about 98%, had 4 or more antenatal care visits and 979 (95%) gave birth after 36 weeks of gestation. The mean gestational age at birth was 38.92 (SD = 1.61) weeks. The majority of mothers were para 1-3; 659 (64%), and 257 (25%) were first-time mothers with about 114 (11.1%) of the mothers having 4 or more children. In order to protect and insulate women from getting malaria during pregnancy Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine (IPTp-SP) doses of up to five (5) times are administered to every pregnant woman in the full course of her pregnancy. However, the study results showed that 229 (22.2%) of the women failed to take the medicine, 128 (12.4%) had between 1-3 doses of the medicine, and 673 (65.3%) of the women who were the majority had ≥ 4 doses of the IPTp-SP medicine.

As shown in Table 3, to approach and examine the maternal obstetric and socio-demographic factors associated with newborn birth weight a multiple linear regression analysis was performed to evaluate the prediction of Birth Weight (BW) from gender of the neonate, maternal educational status, maternal occupation, maternal locality, maternal age, antenatal care visits, iptp-sp dose, maternal parity, and gestation. The regression results revealed maternal educational status, maternal occupation, maternal locality, maternal age, antenatal care visits, and IPTp-SP dose not to be statistically significant predictors of the model ($p > .05$). However, the results of the multiple linear regression analysis revealed a statistically significant association between BW and gender of the neonate, maternal parity, and gestation. The predictors explained 18.10% of the variance and a collective significant effect was found. $F(14, 776) = 12.29$, $p < .001$, $R^2 = .181$. Collinearity statistics indicated the phenomenon existed in the model. Hence, a stepwise regression approach that begins with a full

Table 1. Descriptive statistics of maternal socio-demographic factors at UCC Hospital Maternity Ward for the period of November 2020 through March 2022 (N = 1030)

Background Characteristics	Number	Percentage
Maternal age (completed years)		
< 20	25	2.4
20-35	829	80.5
> 35	176	17.1
Mean (SD)	30.29 (5.24)	
Maternal educational status		
No formal education	21	2.04
Primary education	26	2.52
Secondary/High school	501	48.64
Tertiary	482	46.8
Maternal occupation		
Employed (Gov't/Private)	444	43.11
Trader/Self-employed	442	42.91
Farming	2	0.19
Student	62	6.02
Unemployed	65	6.31
Maternal Locality		
Urban	691	67.09
Rural	339	32.91

Table 2. Descriptive statistics of neonates and obstetric characteristics of mothers delivering at UCC Hospital Maternity Ward for the period of November 2020 through March 2022 (N = 1030)

Background Characteristics	Number	Percentage
Newborn's gender		
Male	539	52.33
Female	491	47.67
Birth weight (kg)		
< 2.5 (LBW)	57	5.5
2.5-4.0 (Normal birth weight)	923	89.6
> 4.0 (HBW) or macrosomia	50	4.9
Mean (SD)	3.21 (0.5)	
Antenatal care visits		
< 5 visits	61	5.9
≥ 5 visits	969	94.1
Gestational age (completed weeks)		
< 28 weeks	2	0.2
28-36 weeks	49	4.8
> 36 weeks	979	95
Mean (SD)	38.92 (1.61)	
Maternal Parity		
First-time mother	257	25
1-3 previous deliveries	659	64
≥ 4 previous deliveries	114	11.1
Number of IPTp-SP doses		
None	229	22.2
1-3 doses	128	12.4
≥ 4 doses	673	65.3

(saturated) model and at each step gradually eliminates variables from the regression model to find a reduced model that best explains the data was deployed. Results of the best fit model derived are shown in Table 4.

The final regression model derived indicated that the significant predictors explained 17.10% of the variance and a collective significant effect was found, $F(5, 785) = 32.32$, $p < .001$, $R^2 = .171$. Collinearity statistics indicated the phenomenon did not exist in the model anymore.

The intercept of the simultaneous multiple linear regression model as shown in Table 3 is given as [β = 2.714, 95% CI (2.402, 3.025), p < .001]. This represents the conditional BW mean of a male neonate whose mother had no formal education, unemployed, was a rural dweller, never attended antenatal care, never received Sulphadoxine-Pyrimethamine (IPTp-SP) dose, and was a first-time mother.

After adjusting for the effect of multicollinearity in the model maternal age, antenatal care visits, and maternal locality all remained insignificant predictors of newborn birth weight.

The final multiple linear regression model as shown in Table 4 had a new intercept value of [β = 2.988, 95% CI (2.838, 3.139), p < .001] which represents the conditional BW mean of a male neonate born to a first-time mother who attained tertiary educational level. This value had fallen at the grand mean of gestational age. Hence, the mathematical representation of the best fit model on the association between birth weight (BW) and maternal obstetric and socio-demographic factors at the University of Cape Coast Hospital in the Central Region of Ghana is given as;

$$\widehat{BW}_i = 2.988 - .122\,Gender_i + .077\,Tertiary\ Education_i + .042\,Sulphadoxine\text{ - }Pyrimethamine\ (IPTp\text{ - }SP)\ dose_i + .039\,Parity_i + .133\,Gestation_i$$

The model indicated that there is a significant difference in the conditional BW mean between male and female neonates with female neonates scoring .112 kg lower than their male neonates counterparts [β = -.112, 95% CI (-.175, -.048), p < .001]. Maternal educational status became a significant predictor of BW after the backward elimination regression method was deployed. The coefficient of the tertiary education category [β = .077, 95% CI(.013, .141), p < .05] indicated that the conditional BW mean of the tertiary education category was .077 kg higher than that of the no formal education group and that this difference was statistically significant. The coefficient of Sulphadoxine-Pyrimethamine (IPTp-SP) dose also became a significant predictor of BW. The new coefficient [β = .042, 95% CI(.010, .074), p < .05] indicated that for any additional dose of IPTp-SP the conditional BW mean increased significantly by .042 kg. Similarly, the new coefficient of maternal parity [β = .039, 95% CI(.018, .061), p < .001] indicated that every additional previous delivery made after 28 weeks of gestation, the conditional BW mean increased by .039 kg. This new coefficient is relatively statistically more significant. Finally, the new coefficient of gestational age [β = .113, 95% CI(.094, .133), p < .001] is also relatively statistically more significant. The coefficient indicated that for every additional week of gestational age the conditional BW mean increased significantly by .112 kg.

The standardized beta coefficients which compare the

Table 3. Neonatal and maternal obstetric and socio-demographic factors associated with newborn weight in UCC Hospital Maternity Ward over November 2020 through March 2022 (N=1030)

	Unstandardized Coefficients		Standardized Coefficients	t-stats	p-value	95% Confidence Interval for β		Collinearity Statistics	
Model	B	SE(β)	Beta			LB	UB	Tolerance	VIF
(Constant)	2.714	0.159		17.103	0.000	2.402	3.025		
Gender of Neonate									
Male	Ref								
Female	-0.116	0.033	-0.117	-3.556	0.000	-0.179	-0.052	0.974	1.027
Maternal Educational Status									
No Formal Education	ref								
Primary Education	0.22	0.156	0.067	1.412	0.158	-0.086	0.527	0.473	2.114
Secondary Education	0.177	0.119	0.179	1.485	0.138	-0.057	0.411	0.072	13.829
Tertiary Education	0.208	0.125	0.21	1.667	0.096	-0.037	0.453	0.066	15.078
Maternal Occupation									
Unemployed	Ref								
Student	0.056	0.093	0.028	0.598	0.550	-0.127	0.239	0.489	2.045
Trader/Self-employed	0.067	0.069	0.068	0.971	0.332	-0.069	0.204	0.216	4.633
Employed (Public/Private)	0.11	0.073	0.11	1.501	0.134	-0.034	0.253	0.196	5.095
Farming	-0.089	0.469	-0.006	-0.189	0.850	-1.009	0.832	0.924	1.082
Type of Locality									
Rural	Ref								
Urban	0.047	0.034	0.045	1.361	0.174	-0.021	0.114	0.983	1.017
Maternal Age	0.003	0.004	0.031	0.694	0.488	-0.005	0.011	0.513	1.951
Antenatal Care Visits	0.008	0.011	0.028	0.746	0.456	-0.013	0.029	0.775	1.291
IPTp-SP dose	0.032	0.017	0.065	1.855	0.064	-0.002	0.066	0.858	1.166
Maternal Parity	0.036	0.014	0.11	2.524	0.012	0.008	0.065	0.557	1.794
Gestation	0.112	0.011	0.363	10.387	0.000	0.091	0.133	0.864	1.157
†Dependent Variable: Birth Weight (BW) in kilograms (kg)									

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strength of the effect of each individual predictor variable to the dependent variable presented in Table 4 indicated that for every unit increase in the standard deviation of the IPTp-SP dose the conditional BW mean increased by .08 standard deviations. Similarly, maternal Parity, as well as gestation predictors, would each affect .119 and .369 increments respectively in the standard deviation of the conditional BW mean for every unit increase in their respective standard deviations. Hence, a comparative analysis of the impact of the significant regressor variables on BW revealed that among all the significant predictors, neonatal gender and maternal obstetric factors had the most impact on the anthropometric index BW than maternal socio-demographic factors.

Model Diagnostics

Normality of residuals was performed using both Shapiro-Wilk and Kolmogorov-Smirnov test of normality with Lilliefors Significance Correction. The results were significant ($p < .001$) indicating non-normality of the residual of the model. However, the non-normality of the multiple regression residual is inconsequential considering that the sample size (N = 1030) is very large. The Durbin-Watson statistic (DW = 1.980) is within the acceptable range of $1.5 \leq DW \leq 2.5$ indicating that residuals of the final multiple linear regression model are not auto-correlated. The Breusch-Pagan-Godfrey test of heteroskedasticity in the model was performed. A non-significant chi-squared test statistic for the Breusch-Pagan test [$\chi^2 = 1.1097$, $p = .9532$] was found indicating constant variance. Multicollinearity was also examined using the variance inflation factor (VIF) and Tolerance factor. Problematic if VIF > 10 and Tolerance < .1. However, collinearity statistics results in Table 4 did not show any VIF > 10 nor any Tolerance < .1 for which the assumption of no multicollinearity in the model would be violated. Therefore, model diagnostics indicated that the final regression model is free from auto-correlation, heteroskedasticity, as well as multicollinearity.

Discussion

This study examined the associations between maternal obstetric and socio-demographic factors and birth weight at the University of Cape Coast Hospital, Ghana. The findings provide essential contributions to the existing body of evidence by revealing the nuanced roles of parity, gestational age, maternal education, and IPTp-SP prophylaxis in influencing birth weight in a coastal Ghanaian context.

The mean birth weight observed (3.21 kg) aligns closely with what was found (3.25kg) among the same population in an earlier study [9]. Using nationally representative data, Boateng et al.[12] and He et al.[13] found mean birth weights of 3.15 kg and 3.25 kg, respectively. Notably, the prevalence of low birth weight in this study (5.5%) is significantly below the 2020 WHO global estimate of 14.7%[6], the national average of 14.4% in Ghana [6], and in sub-Saharan Africa, 13.9%[6]. A study by Boateng et al.[12] and He et al.[13] also recorded higher LBW rates of 7.2% and 10.2%, respectively, for Ghana. This may reflect the exclusion of high-risk pregnancies, for example, preeclampsia, and sickle cell

Table 4. Significant Neonatal and Maternal Obstetric and Socio-demographic Predictors of Newborn Birth Weight in UCC Hospital over November 2020 through March 2022 (N = 1030)

	Unstandardized Coefficients		Standardized Coefficients	t-stats	p-value	95% Confidence Interval for β		Collinearity Statistics	
Model	B	SE(β)	Beta			LB	UB	Tolerance	VIF
(Constant)	2.988	0.077		39.021	0	2.838	3.139		
Gender of Neonate									
Male	Ref								
Female	-0.112	0.032	-0.113	-3.466	0.001	-0.175	-0.048	0.991	1.009
Maternal Educational Status									
No Formal education	Ref								
Tertiary Education	0.077	0.033	0.078	2.359	0.019	0.013	0.141	0.974	1.027
IPTp-SP dose	0.042	0.016	0.084	2.554	0.011	0.01	0.074	0.967	1.034
Maternal Parity	0.039	0.011	0.119	3.603	0	0.018	0.061	0.971	1.03
Gestation	0.113	0.01	0.369	11.156	0	0.094	0.133	0.965	1.036

†Dependent Variable: Birth Weight (BW) in kilograms (kg)

disease, from the current study as well as its hospital-based nature, which ensured that all the mothers were antenatal clinic attendants, unlike the population-based nature of the earlier studies. Despite these differences, there is an indication of a positive impact of the many interventions, such as regular training of midwives and doctors on safe motherhood, as the LBW prevalence among the same population has improved from the 7.7% found in an earlier study[9].

Gestational age was the strongest determinant of birth weight, with each additional week of gestation associated with a 113g increase in birth weight. This is consistent with earlier studies in Ghana[14,15] affirming gestation as the most influential modifiable factor for birth weight. These findings underscore the importance of preventing preterm births as a critical public health priority.

Male neonates weighed significantly more than female neonates on average, consistent with established biological patterns observed globally[16,17].

Tertiary education was significantly associated with higher birth weights. An earlier study in the Democratic Republic of the Congo reported that higher maternal education levels were associated with increased utilization of maternal healthcare services, such as antenatal care and skilled birth deliveries[18]. Another study emphasized how maternal education reduced disparities in prenatal care utilization, particularly among disadvantaged groups[19]. Educated mothers may possess greater health literacy, autonomy, and economic empowerment, all of which positively affect prenatal care utilization and nutrition. This reinforces broader evidence supporting maternal education as a social determinant of child health outcomes.

Higher parity was positively associated with birth weight. This aligns with evidence from earlier studies that explored the association between parity and birth weight and found that infants born to nulliparous women had lower mean birth weight compared to that of multiparous women[20,21]. This may be due to some physiological adaptations from earlier pregnancies, which could enhance fetal growth. typically have better obstetric outcomes due to uterine conditioning and experiential knowledge. However, other studies have noted that as parity increases, maternal resources decrease, increasing the risk for low birth weight infants[22].

Malaria Prophylaxis (IPTp-SP): The number of IPTp-SP doses was a significant predictor of birth weight. This confirms the protective effect of malaria prevention during pregnancy on fetal growth, as observed in earlier studies in Papua New Guinea[23] and Ghana[24]. Given Ghana's high malaria burden, this finding reaffirms the necessity of improving compliance with WHO's recommendation of at least three IPTp-SP doses.

Maternal age, locality, antenatal care visit count, and employment status were not significant predictors in the final model. This may be due to the high antenatal coverage (>94% had ≥4 visits), the urban-rural proximity in the Cape Coast municipality, and strong baseline maternal health education in the cohort. Previous studies have shown mixed results on these variables[7,25], often depending on context.

The final model accounted for 17.1% of the variance in birth weight. While this is statistically robust, it suggests that other unmeasured factors such as genetics, environmental pollutants, maternal stress, or detailed nutritional intake also play substantial roles. Because it directly affects intrauterine growth and birth weight, adequate maternal nutrition is essential for fetal development[26]. Detailed dietary assessments, which could have provided a more in-depth understanding of the relationship between nutrition and birth weight, were not included in this study.

It is commonly known that birth weight is heritable, and that both maternal and paternal genetic factors have a major impact on the growth patterns of newborns[27]. Although genetic predisposition was not evaluated in this study, family history information could be used in subsequent studies to enhance prediction models.

It has been demonstrated that reduced birth weight and preterm deliveries are linked to prolonged stress during pregnancy[28]. The dataset's exclusion of mental health evaluations, regrettably, restricted the investigation of psychosocial factors that influence birth weight.

According to research from Ghana's cities, air pollution has a major negative impact on perinatal outcomes[29]. Given the urban-rural mix of Cape Coast, more information on the factors influencing birth weight may be obtained by looking into environmental exposures.

Future research should explore these additional dimensions through longitudinal designs and mixed-methods approaches.

The findings of this study have many public health implications: The findings support continued investments in girl child education, particularly at secondary and tertiary levels. There should be community health campaigns to improve coverage of IPTp-SP. Efforts must be made to detect and manage preterm risks to extend gestational age.

Despite its many strengths, this study has some limitations. The retrospective cross-sectional design restricts conclusions to associations rather than clear causal links, so limiting the capacity to create causality. The study was also done at one site, which could affect its generalizability to other healthcare environments in Ghana where demographic and clinical traits differ. The prevalence estimates of low birth weight may have been affected by the exclusion of high-risk pregnancies, such as maternal conditions and multiple gestations, so they underrepresent extreme cases. Excluded were unmeasured variables such as maternal nutritional status, genetic predisposition, psychosocial stress, and environmental exposures, which could cause birth weight differences outside the ones studied. Future studies should use mixed-method frameworks, longitudinal designs, and multi-center strategies to investigate a more complete spectrum of factors influencing birth weight.

Conclusion

This study contributes valuable empirical evidence to the growing literature on maternal and neonatal health by modeling the specific associations between

maternal obstetric and socio-demographic factors and birth weight in a primary hospital setting in Ghana. By analyzing a substantial dataset of 1,030 births, the study has demonstrated that gestational age, maternal parity, neonatal sex, tertiary education, and IPTp-SP prophylaxis significantly influence birth weight, jointly explaining approximately 17% of its variance.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Contributions

McAdams Abu Bakr and James Kojo Prah: conception, design, acquisition, and interpretation of data and drafting the manuscript; Mary Boadi-Kusi and Beth Offei-Awuku: acquisition of data and reviewing of several drafts of the manuscript. All authors have read and agreed to the final manuscript.

Data Availability

Data is available upon request from the authors.

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RESEARCH ARTICLE

Impact of hemodialysis on nutritional indices in chronic kidney disease patients: A cross-sectional study in Korle- Bu Teaching Hospital

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Abstract

Background: Chronic kidney disease (CKD) is predicted to become the fifth leading cause of global mortalities by 2040. Hemodialysis (HD) is one of the choices for treatment in some countries for CKD patients with end stage renal disease (ESRD). Meanwhile, malnutrition, a well-known CKD-related complication is reported as a non-cardiovascular risk factor associated with mortality in HD patients. Therefore, measures to prevent, screen and manage malnutrition could impact CKD outcomes.

Aim: The aim of the study was to assess the impact of hemodialysis on nutritional indices in CKD patients.

Methodology: The study was a cross-sectional design that enrolled 177 patients with ESRD patients visiting the HD Unit at the Korle Bu Teaching Hospital (KBTH). Medical records of patients were retrieved and a semi-structured questionnaire was administered to obtain demographic, socio-economic data and lifestyle history. The Patient-Generated Subjective Global Assessment (PG-SGA) tool was used to assess the nutritional status of the HD patients.

Results: Majority of the study participants 107 (57.1%) were males, whereas 48 (27.1%) were within the ages of 40 – 49 years and 91 (51.4%) had tertiary education. About 87 (49.2%) were on HD for at least 4 years and 138 (78.0%) had two HD sessions weekly. Exactly 72 (40.7%) and 105 (60.5%) reported fatigue and hypertension as the frequent nutritional symptom and the commonest influencing factor to ESRD, respectively. Also, 57.6% of patients had normal weight [BMI (18.5 - 24.49 kg/m2)] and 52.0% were well-nourished. There was a significant negative correlation between BMI and PG-SGA category rating ($r = -0.325$, $p \leq 0.01$) and 53.1% of HD patients needed the highest triaging intervention.

Conclusion: Whereas more than half (52.0%) of HD patients were well-nourished, 53.1% required highest-level of triaging intervention. Additionally, fatigue was the frequent nutritional symptom and hypertension was the prevalent predisposing factor among the HD patients. Further studies evaluating malnutrition of HD patients with other nutritional status tools are recommended.

Keywords: Chronic kidney disease, hemodialysis, malnutrition, end stage renal disease, cardiovascular disease

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Introduction

Chronic kidney disease (CKD) is a major global public health concern, affecting an estimated 7 billion individuals worldwide and projected to become the fifth leading cause of mortality within the next two decades [1]. The incidence of CKD continues to rise, particularly in low- and middle-income countries (LMICs), where healthcare systems often face resource constraints [2]. Notably, the prevalence of

CKD stages 3–5 in LMICs is comparable to that observed globally, further highlighting the urgent need for targeted interventions.

Hemodialysis (HD) remains a commonly adopted therapeutic intervention for managing CKD and is the standard care provided for many patients with end-stage renal disease (ESRD) [3]. Despite advances in dialysis therapy, mortality rates among HD patients remain high. This has prompted the recommendation of comprehensive strategies to address modifiable comorbidities that contribute to adverse outcomes in CKD populations [3]. One of such comorbidity is malnutrition, a frequent complication of CKD that significantly affects physical and cognitive functioning, quality of life, and survival. Malnutrition in HD patients has been identified as a non-cardiovascular risk factor with strong correlations to morbidity and mortality. It may result from inadequate nutrient intake, impaired absorption, drug interactions, reduced appetite, and dietary restrictions [4]. The condition is frequently characterized by a reduction in both body cell mass and fat-free mass, altering overall body composition [5].

Globally, studies report a high burden of malnutrition among CKD patients. A recent Chinese study, for instance, identified an 87.5% malnutrition prevalence, with socio-demographic variables such as age, gender, weight loss, and decreased food intake being independently associated with the condition [6]. In another study, only 12.7% of CKD patients were well-nourished, while the remaining were classified as either mild-to-moderately (81.8%) or severely malnourished (5.5%) [7]. Nutritional literacy has also been shown to play a protective role; individuals with higher nutritional literacy demonstrate significantly lower malnutrition incidence [8].

To address nutritional challenges in this population, the United States Kidney Disease/Dialysis Outcomes and Quality Initiative (KDOQI) recommends the use of validated screening tools such as the Subjective Global Assessment (SGA) for the diagnosis of malnutrition [9]. The Patient-Generated Subjective Global Assessment (PG-SGA), including its digital form (Pt-Global web tool), is also widely accepted as a reliable tool for nutritional evaluation in CKD populations [10].

While the global burden of CKD and its nutritional implications have been extensively studied, there is a paucity of data from sub-Saharan Africa, particularly Ghana. In Ghana, the prevalence of CKD is increasing, with many patients presenting at advanced stages, often requiring dialysis. However, limited attention has been given to the nutritional status of these patients despite the critical role of nutrition in clinical outcomes. Malnutrition in HD patients may result from inadequate nutrient intake, inefficient absorption, inflammation, and metabolic derangements, and it is often exacerbated by polypharmacy, anorexia, and restrictive dietary recommendations [4]. This condition is marked by changes not only in body weight but also in body composition, particularly a reduction in fat-free mass [5]. A recent study in China reported a malnutrition prevalence of 87.5% among CKD patients, with socio-demographic factors such as age, sex, weight loss, and reduced food intake showing significant associations with malnutrition6. Similarly, another study found that only 12.7% of CKD patients were well-nourished, while 81.8% were mildly to moderately malnourished and 5.5% were severely malnourished [7]. Nutritional literacy has also been identified as a determinant of malnutrition risk, with lower literacy levels associated with higher rates of malnutrition8. To identify and manage malnutrition in CKD patients, especially those on maintenance dialysis, the Kidney Disease Outcomes Quality Initiative (KDOQI) recommends the use of the Subjective Global Assessment (SGA) tool9. In this study, the Pt-Global web tool/PG-SGA which has been validated for use in CKD patients [5] was employed to assess nutritional status.

The lack of research on HD-related malnutrition in Ghana presents a significant challenge to the country's healthcare system. CKD is increasingly prevalent in Ghana, with many patients presenting at advanced stages that require renal replacement therapy such as HD [9]. The rising burden of chronic kidney disease (CKD) in Ghana is evidenced by a national prevalence estimated at 13.3%, with many patients presenting at advanced stages of the disease, often necessitating renal replacement therapy such as hemodialysis (HD) [10]. This late presentation is frequently attributed to factors such as limited awareness, inadequate screening programs, and insufficient access to early nephrology care [11]. Consequently, a significant proportion of patients require immediate initiation of dialysis upon diagnosis, underscoring the pressing need for early detection and intervention strategies in the Ghanaian healthcare system [16]. Furthermore, the high cost of HD and its limited coverage under Ghana's National Health Insurance Scheme often result in irregular treatment sessions and inadequate dietary management. These factors contribute directly to poor nutritional status among patients on maintenance dialysis [10].

Unlike high-income earning countries where nutritional monitoring and support by renal dietitians are integrated into standard care, Ghana lacks the infrastructure and resources to provide such comprehensive services [11]. This gap is particularly concerning because malnutrition in HD patients is linked to adverse clinical outcomes, including increased hospitalization, poor quality of life, and higher mortality rates [4]. Without localized research, treatment protocols may fail to reflect the specific dietary habits, comorbid conditions, and socio-economic realities of Ghanaian patients [12]. Moreover, the absence of empirical data limits policymakers' and healthcare providers' ability to allocate resources effectively and develop evidence-based, context-specific guidelines.

Materials and Methods

Study Design/Area

This descriptive cross-sectional study was conducted among 177 ESRD out-patients who visited the HD Unit at the Korle Bu Teaching Hospital (KBTH). KBTH is the first public healthcare facility in the southern part of Ghana and the third largest and leading center for referral cases in Africa, with over 2000-bed capacity, 21 clinical and diagnostic departments, and 3 national centers. As the largest tertiary referral hospital in Ghana and a central site for dialysis care, KBTH provides a representative setting for understanding the burden and characteristics of HD-

related malnutrition among CKD patients in the country.

Study design

This study recruited 177 end-stage renal disease (ESRD) out-patients attending the hemodialysis (HD) unit of the Korle Bu Teaching Hospital (KBTH) in Accra, Ghana. The sample size was determined using Cochran's formula for sample size estimation, which is suitable for large populations as reported by Nanjundeswaraswamy and Divakar [13] and is widely applied in health research to estimate sample sizes based on desired precision levels. The details of sample size determination using the Cochran [14] formula is presented below:

$$N = \frac{Z^2 pq}{e^2}$$

where,

N = minimum sample size

Z = z value of 1.96 from a 95% confidence interval

p = estimated proportion of the population with CKD, 0.133(13.3%)

q = 1- p

e = margin of error set at 0.05 (5%).

$$N = \frac{(1.96)^2 * (0.133) * (1 - 0.133)}{(0.05)^2}$$

$$N = \frac{3.8416 * 0.133 * 0.867}{0.0025}$$

$$N = \frac{0.4429787376}{0.0025}$$

$$N = 177.191$$

For this study, a CKD prevalence (p) of 13.3% in Ghana was utilized, as reported by Adjei et al. [15] With a 95% confidence level (Z = 1.96) and a 5% margin of error (e = 0.05), the calculated sample size (n_0) was adjusted to account for the finite population of ESRD patients at KBTH, resulting in a final sample size of 177 participants. Eligible participants were adults aged 18 years or older who had been undergoing HD for at least three months..

Inclusion and Exclusion Criteria

This study enrolled patients diagnosed with end-stage renal disease (ESRD) who had been receiving hemodialysis (HD) treatment for a minimum of three months. Patients were eligible if they were 18 years or older and capable of providing informed consent. Exclusion criteria included individuals who were bedridden, had significant physical deformities, or were diagnosed with mental health conditions that impaired comprehension or communication. These exclusions were necessary because accurate anthropometric assessments, which formed part of the study's data collection, required patients to assume specific physical positions and to follow instructions reliably. In cases of physical deformity or cognitive impairment, such measurements could not be performed accurately, thereby compromising the integrity of the data. Additionally, patients who declined to provide informed consent were excluded in accordance with ethical standards.

Ethical Considerations

The study was approved by the Institutional Review Board of the KBTH. More specifically, administrative approval with reference number: KBTH-ADM/00078/2023 was obtained from the administration of the KBTH, of which copies were given to the Heads at the various centers/ units where study participants were selected. Also, results and records of the study participants were strictly kept confidential and anonymous.

Collection of Data

The medical records of the study participants were retrieved from patients' folders and a semi-structured questionnaire was administered to them to obtain their demographic, socio-economic data and lifestyle history. Also, anthropometric parameters (weight and height) were measured using weighing scale and stadiometer respectively. Body mass index (BMI) was calculated as weight in kg divided by the height in m^2. The resultant BMI ranges were used in classifying participants' weight status as follows: severely underweight (below 16.5 kg/ m^2), underweight (below 18.5 kg/ m^2), normal (18.5- 24.9 kg/m^2), overweight (25.0- 29.9 kg/m^2), class I obesity (30-34.9 kg/m^2), class II obesity (35- 39.9 kg/m^2) and class III obesity (above 40 kg/m^2).

The Patient-Generated Subjective Global Assessment (PG-SGA) instrument was used to assess the nutrition status of the participants. The study adopted the English Language version 4.3.20 of the Scored PG-SGA tool which is a modification of the Subjective Global Assessment (SGA). This assessment tool is in two main parts: the first and second parts were completed by the patients and a qualified health practitioner (registered dietitian, nutritionist, medical doctor, and/or physician). The first part has four boxes: boxes 1 and 3 are additive whereas boxes 2 and 4 are not. In box 1, the current and the past month's post-dialysis weight of participants taken from their dialysis chat were used in calculating their percentage weight loss. Box 2 gives information about their food intake during the past month in comparison to their usual intake and specifies specific foods currently being eaten if there are changes. For Box 3, participants indicated nutritional symptoms over the past two weeks irrespective of the number of times they occurred, which has affected their food intake. The activity level of participants during the past month is rated by them in Box 4. On the other hand, the second aspect looks at some specific diseases that can affect overall nutritional status, metabolic demands and physical examination of the muscle status, fat stores and fluid status but the muscle status takes preeminence over the others, each ranging with a score from 0 (no abnormality) to 3 (severe). Category

rating of A, B, or C is given based on the total score: 7 - 10, 11 – 20, 21- 35, which is interpreted as, A (indicating that the participants were well-nourished), B (mild-moderate malnutrition) and C (severe malnutrition) respectively.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed by Statistical Package for Social Sciences (SPSS), version 20.0. Specific outcomes such as socio-demographic characteristics and medical history were analyzed using descriptive statistics (frequencies and percentages). Similarly, categorical and continuous variables (lifestyle characteristics, anthropometric parameters and the nutritional status) of participants using the Scored PG-SGA were analyzed descriptively and presented as percentages, means, standard deviations and graphs. Also, Pearson's correlation was used to analyze the association between BMI and PG-SGA.

Results

Socio-demographic characteristics

The majority, 107 (57.1%), of study participants were males and most of them, 48 (27.1%), were within the age category 40 – 49 years. 109 (61.6%) of the study participants were married, 91 (51.4%) had tertiary education, 145 (81.9%) resided in urban communities, 69 (39%) were unemployed and 56 (31.6%) lived on low salaries (Table 1).

Medical history and lifestyle of participants

With respect to the medical history and lifestyle, there was no family history of ESRD in 149 (84.2%) of study participants. Majority of them, 87 (49.2%) have been on hemodialysis for at least 4 years and most of them, 138 (78.0%), undertook 2 hemodialysis sessions weekly. In most patients, 105 (60.5%), hypertension was the prevalent predisposing factor to ESRD. About 53 (29.9%) were engaged in alcohol drinking and none was a smoker. Likewise, about 90 (50.8%) were engaged in physical activities, among which 38 (21.5%) were physically active for least 3-times in a week (Table 2).

Body mass index (BMI) and dietary habits

Data of anthropometrics and BMI estimation showed that 20.3% were overweight (25.0- 29.9 kg/ m^2) and majority (57.6%) had normal weight (18.5 - 24.49 kg/m^2). The proportion of participants under each category of severely underweight (< 16.5 kg/m^2), underweight (< 18.5 kg/m2), class I (30- 34.9 kg/m^2) and class II (35- 39.9 kg/m^2) obesity was less than 10%. In addition, 36.1% had a percentage weight loss between 0 to 1.9% and 4.5% had no changes in their weight. Most of them (55%) indicated that they were taking normal meals. However, 38.4% indicated eating less than usual over the past month as compared to 22.0% who started taking very little of any meal. (Figures 1- 4).

Poor nutrition symptoms

In addition, most of the participants experienced more than one nutritional symptom except for those 49 (27.7%) who had no eating problems. Among the symptoms were fatigue: 72 (40.7%), feel full quickly: 52 (29.4%), diarrhea: 45 (25.4%), nausea: 43 (24.3%) and vomiting: 35 (19.8%) were reported by participants. (Table 3).

Table 1: Sociodemographic characteristics of participants (n = 177)

Variable	Frequency	%
Gender		
Male	101	57.1
Female	76	42.9
Age groupings (Years)		
18-29	21	11.9
30-39	31	17.5
40-49	48	27.1
50-59	44	24.9
60 and above	33	18.6
Occupation		
Student	10	5.6
Self-employed	59	33.3
Government worker	39	22.0
Unemployed	69	39.0
Level of education		
Basic	33	18.6
Secondary	49	27.7
Tertiary	91	51.4
No formal school	4	2.3
Marital status		
Married	109	61.6
Single	56	31.6
Divorced	5	2.8
Widowed	7	4.0
Place of residence		
Urban	145	81.9
Rural	32	18.1
Monthly income (GHS)		
Less than 500	56	31.6
500-1000	54	30.5
Between 1000-2000	35	19.8
More than 2000	32	18.1

Patient Generated Subjective Global Assessment (PG-SGA)

More than half (68.9%) of the study participants had a resultant nutritional score of 0-5 (indicative of fewer nutritional symptoms) and a little above 20.0% and below 10.0% had nutritional scores of 6-10 and 11-15 which are indicative of mild and moderate nutritional symptoms respectively. Many of the participants (43.5%) performed general activities without limitations as compared to 3.4% who could not exercise (not feeling up to most things, but in bed or chair less than half of the day). Nutritional status assessment categorized majority (52.0%) of the participants as group A (which indicated the participants were well-nourished) as opposed to 43.5% and 4.5% categorized as B (mild-moderate malnutrition) and C (severe malnutrition) respectively. (Figures 5 - 7).

Correlation between BMI and PG-SGA

Furthermore, there was a significant negative correlation between BMI and PG-SGA category rating ($r = -0.325$, $p \leq 0.01$) and majority of the study participants (53.1%) had the highest triaging category (highest level of intervention)

Table 2: Medical history and lifestyle of participants (n = 177)

Variable	Frequency	%
Family history		
Yes	28	15.8
No	149	84.2
Duration being on dialysis		
3-6 months	18	10.2
7-11 months	19	10.7
1-3 years	53	29.9
4 years and more	87	49.2
Number of sessions		
1 session	10	5.6
2 sessions	138	78.0
3 sessions	29	16.4
Cause of disease		
Diabetes	1	0.6
Hypertension	107	60.5
Both	21	11.9
Other	48	27.1
Lifestyle activity		
Alcohol drinking	53	29.9
Smoking	0	0
Both	0	0
None	123	69.5
Other	1	0.6
Physical activity		
Yes	90	50.8
No	87	49.2
Time spent on physical activity		
Once	21	11.9
Twice	31	17.5
Three times or more	38	21.5

Table 3: Nutritional Symptoms Experienced by Participants (n = 177)

Symptoms	Frequency	%
No problems eating		
No appetite	28	15.8
Nausea	149	84.2
Constipation		
Mouth sores	18	10.2
Things taste funny	19	10.7
Problems swallowing	53	29.9
Pain	87	49.2
Others		
Vomiting	10	5.6
Diarrhea	138	78.0
Dry mouth	29	16.4
Smells bother me		
Feel full quickly	1	0.6
Fatigue	107	60.5

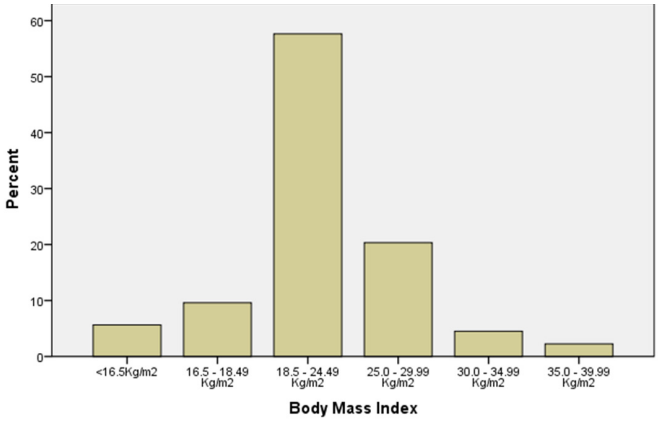

Figure 1: Body Mass Index of participants

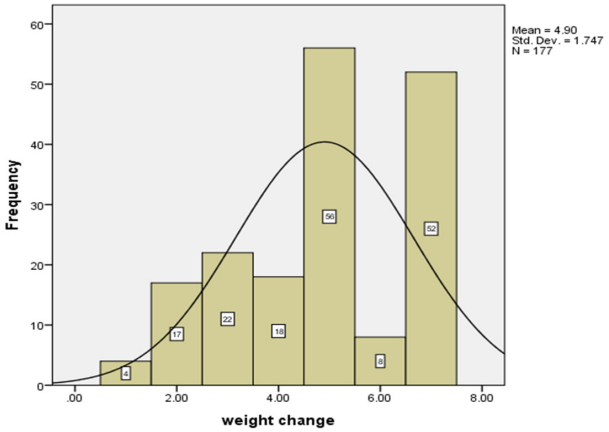

Figure 2: Weight change of participants

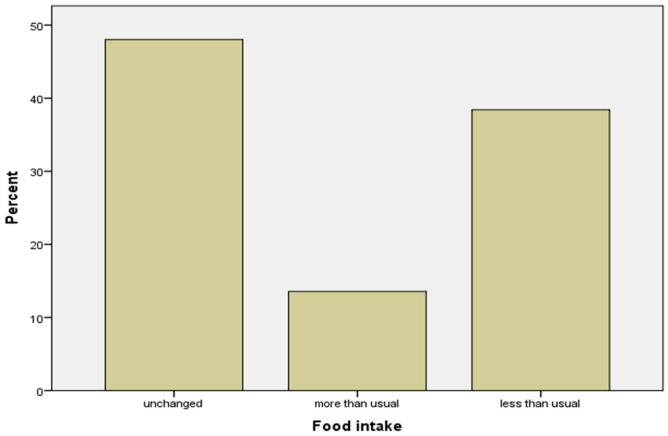

Figure 3: Food intake of participants

as compared to 7.3% in the lowest level (indicating no intervention required). (Table 4 & Figure 8).

Discussion

The prevalence of malnutrition in adult hemodialysis (HD) patients remains highly variable across studies, with recent reports indicating rates from approximately 15% up to over 60%, depending on the assessment methods and populations studied. For example, a cross-sectional study in Iran found a malnutrition prevalence of 63.18% among HD patients, with severity ranging from mild to severe malnutrition [16]. Nutritional status continues to be strongly associated with quality of life (QOL), morbidity, and mortality in HD patients. Recent studies

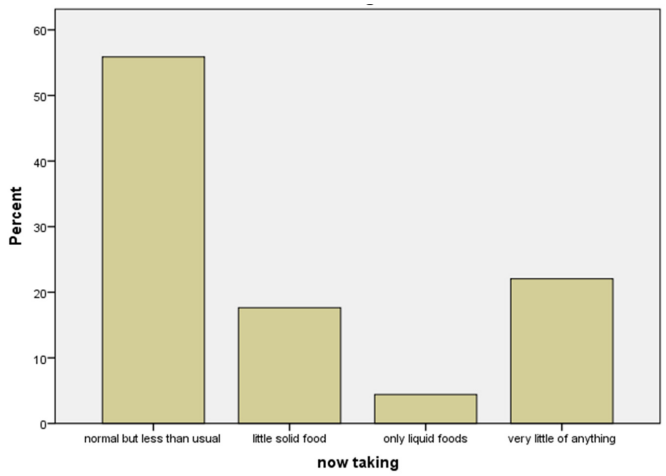

Figure 4: Food intake among participants eating less than usual

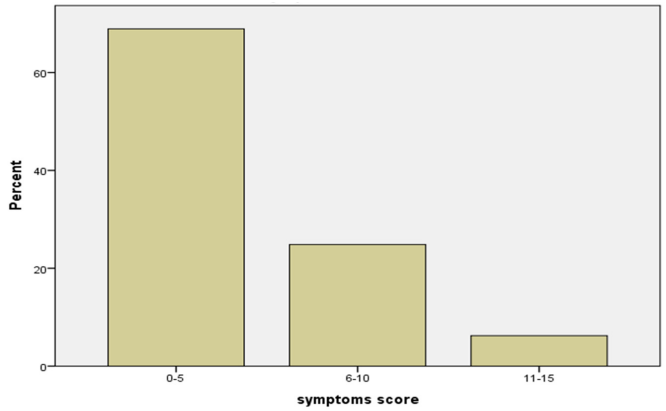

Figure 5: Nutritional symptom score

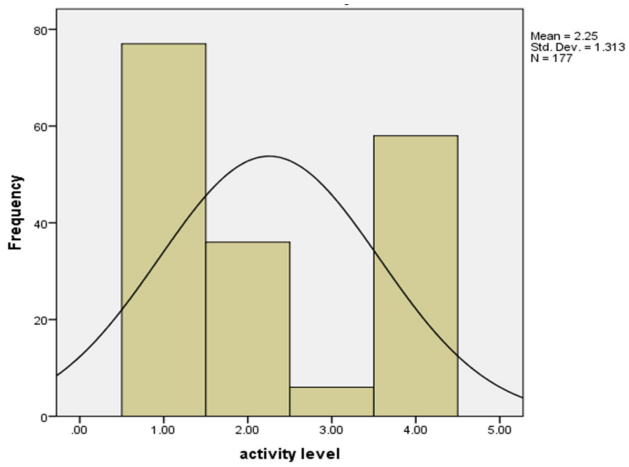

Figure 6: Functional Ability of participants

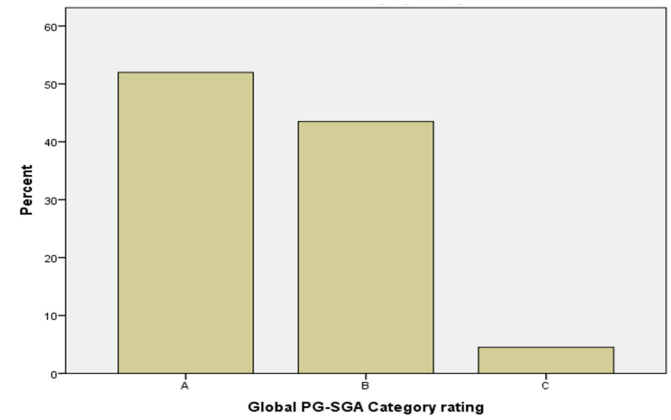

Figure 7: Global PG-SGA category rating among participants

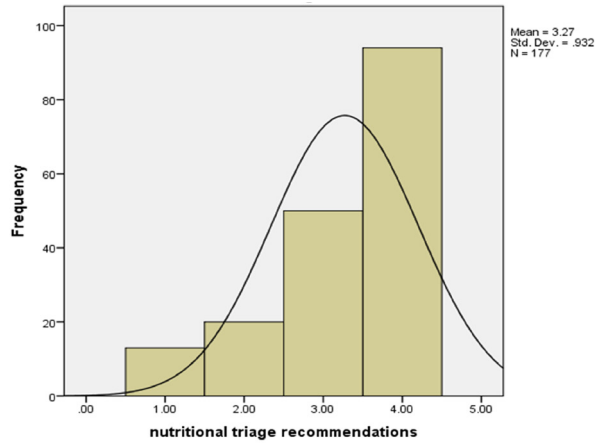

Figure 8: Nutritional triage recommendation

highlight that malnutrition or nutritional risk correlates significantly with lower QOL scores across multiple domains in dialysis patients [17]. Furthermore, malnutrition is identified as a strong predictor of mortality in chronic kidney disease patients on dialysis, particularly in the hemodialysis subgroup [18]. Regarding the Ghanaian population specifically, there remains a paucity of research on nutritional status evaluation in HD patients. Most recent studies focus on other regions such as Iran, India, and Europe, with limited data available from Ghana. This gap underscored the need for focused nutritional assessment studies in Ghanaian HD patients to address this under-investigated area.

In this study, we assessed the nutritional status of HD patients using the Scored Patient-Generated Subjective Global Assessment (PG-SGA), which is a validated tool for identifying malnutrition in clinical settings. According to the results of this study, 52.0% of the HD patients were well-nourished, whereas 43.5% and 4.5% had mild-to-moderate and severe malnutrition, respectively.

Our findings are partially in support of a similar study conducted by Steiber et al. [19] who evaluated the scored PG-SGA as a nutrition assessment tool in HD patients. According to their PG-SGA classification, 80% of patients were well nourished, 20% were moderately malnourished or at risk of malnutrition, and no patients were assessed as severely malnourished. Similarly, a study by Rifai et al. [20] also used PG-SGA to assess nutritional status in hemodialysis patients and found that better nutritional status assessed by PG-SGA correlated with good quality of life, reinforcing the tool's relevance and validity in current clinical practice. Also, in conformity with the findings of this present study is that of Sedhain et al. [21] who even though employed the Modified Quantitative Subjective Global Assessment (MQSGA) criteria, showed that 66.7% of the patients suffered from mild to moderate malnutrition, 33.3% were well nourished and none of the patients were severely malnourished. The differences in

the prevalence of malnutrition observed in these studies partially may be explained by the socio-economic status of the patients, while in their case majority of the patients had high socio-economic status and for that matter, they were able to finance treatment in a private hospital. This was a contrary observation in our study.

Unemployment was reported by 69 participants (39.0%), and 56 (31.6%) lived on low incomes. These socio-demographic characteristics are important in understanding nutritional outcomes among HD patients. For instance, individuals with higher educational attainment may possess better health literacy and dietary knowledge, enabling them to make informed nutritional choices. Conversely, low income and unemployment may limit access to nutrient-dense foods, thereby increasing the risk of malnutrition. Urban residency may offer better access to healthcare and dietetic services, although it may also expose patients to processed food environments, depending on socio-economic status. Marital status may further influence nutritional well-being, as spousal support could play a role in meal preparation, adherence to dietary recommendations, and overall care. Collectively, these factors highlight the complex interplay between sociodemographic characteristics and nutritional status in HD patients. To corroborate these assertions, a 2024 cross-sectional study investigated how socio-demographic factors influence nutritional status and quality of life in adult HD patients and concluded that these factors strongly interfere with nutritional status [22].

Our data showed that nutritional symptoms (NS) were common among the HD patients. Many of them experienced more than one symptom, except for 27.7% who reported no issues related to eating. In contrast, 40.7%, 29.4%, 25.4%, 24.3%, and 19.8% of the patients experienced early satiety, diarrhea, nausea, vomiting, and poor appetite respectively. These outcomes are consistent with findings by Yuan et al. [23] who assessed gastrointestinal symptoms in patients with uremia undergoing hemodialysis and reported a high prevalence of GIS, approximately 79.6%, with symptoms such as dyspepsia, constipation, reflux, and eating disorders being most common. The study highlighted that these symptoms, although mostly mild, seriously affected patients' quality of life and nutritional status. It also discussed factors influencing GIS, such as BMI, age, dialysis duration, and inflammation markers, which can exacerbate nutritional impact symptoms that directly impair dietary intake and overall nutritional status.

Importantly, our findings support previous reports indicating that nutrition impact symptoms (NIS) account for a substantial portion of the PG-SGA score, as they directly affect dietary intake and overall nutritional status [24].

Inflammation is a well-established underlying factor associated with poor appetite, nausea and impaired olfactory function in HD patients. Proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) are elevated in chronic kidney disease (CKD) and have been implicated in appetite suppression and increased resting energy expenditure, contributing to protein-energy malnutrition [25,26]. Additionally, the accumulation of uremic toxins between dialysis sessions contributes to altered taste perception, such as dysgeusia, characterized by enhanced sensitivity to bitter and salty flavors and diminished sensitivity to sweet tastes [27]. These physiological disturbances can reduce the desire to eat, exacerbate food aversion, and further impair nutritional intake.

Furthermore, alterations in appetite-regulating hormones, such as ghrelin and leptin, have been observed in HD patients. Elevated levels of des-acyl ghrelin, an anorexigenic form of ghrelin, and increased leptin levels may contribute to reduced appetite and food intake [28]. Additionally, impaired olfactory function, associated with retained uremic molecules, has been linked to malnutrition in end-stage renal disease (ESRD) patients, further complicating nutritional management [29,30].

Collectively, these factors underscore the multifaceted impact of inflammation and uremic toxin accumulation on the nutritional status of HD patients, highlighting the need for comprehensive assessment and targeted interventions to address malnutrition in this population.

The presence of such symptoms has significant implications for the quality of life of HD patients. Malnutrition-related symptoms can lead to fatigue, physical weakness, and reduced functional capacity, all of which limit patients' ability to engage in daily activities, work, or social interaction. Persistent nausea, poor appetite, and altered taste perception may also contribute to psychological distress, including anxiety and depression, thereby worsening overall well-being. In addition, these symptoms may hinder adherence to dietary recommendations, complicating the clinical management of CKD.

We believe that several factors may underlie the different manifestations of NS among our HD patients, including lifestyle habits such as alcohol consumption, the duration of time spent on dialysis, and the frequency of HD sessions. These variables likely interact with the physiological stressors of ESRD and HD to influence the presence and severity of NIS, ultimately impacting nutritional status and quality of life. Therefore, addressing nutritional symptoms through early identification and multidisciplinary intervention is critical to improving both clinical outcomes and the lived experience of HD patients.

Our finding suggests a significant negative correlation between BMI and PG-SGA category rating ($r = -0.325$, $p \leq 0.01$). This finding agrees with a similar work conducted by Sedhain et al. [21] who assessed nutritional status of patients on maintenance hemodialysis by using the MQSGA tool among a Nepalese population. According to their study, MQSGA showed a more significant negative correlation between BMI and MQSGA ($r = -0.448$; $P = < 0.001$). Nutrition triage recommendations using PG-SGA scores made by Jager-Wittenaar & Ottery [31] suggest initiation of urgent nutrition intervention. Based on the recommendations of Jager-Wittenaar & Ottery [31], 53.1% of the HD patients required the highest level of intervention to improve nutrition symptoms as compared to 7.3% indicating no intervention required in our study.

To the best of our knowledge, the current study is the first to investigate malnutrition screening among HD patients using the Scored PG-SGA in Sub-Saharan Africa of which Ghana is no exception. The potential strength of the present study is its clinical relevance. We strongly believe that, after admission of patients to the KBTH hospital, all HD patients will be screened for malnutrition with the PG-SGA since it has high accuracy and simplicity as a screening method in daily practice. This will facilitate early recognition of nutritional status as well as symptoms among HD patients. However, our study has one major important limitation. Owing to the small sample size, it is not ascertained at this time the general nutritional status of HD patients in the Ghanaian population.

Conclusion

In conclusion, 52.0% of the hemodialysis (HD) patients were well-nourished, yet 53.1% required the highest level of triaging intervention according to the Scored Patient-Generated Subjective Global Assessment (PG-SGA). While the majority of participants had normal body weight, had been on HD for at least four years, and received two dialysis sessions per week, fatigue was the most frequently reported nutrition-related symptom. Hypertension was the most prevalent predisposing factor, and many of the patients were physically active.

These findings underscore the urgent need to integrate routine and systematic nutritional screening into the clinical management of HD patients in Ghana. The PG-SGA has demonstrated utility as a practical and effective tool for identifying nutritional risk and guiding individualized interventions. Early identification and management of malnutrition can help improve health-related quality of life, reduce complications, and enhance treatment outcomes.

Future research should be expanded to include multi-center studies with larger and more diverse patient populations. It is also important to compare various validated nutritional assessment tools, explore biochemical markers of nutritional status, and examine the longitudinal effects of targeted nutritional interventions. Investigating the role of healthcare access, dietary counseling, and socio-economic support systems could also contribute to more comprehensive care for HD patients in Ghana and similar settings.

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Conflicting Interest

The authors declare that there are no other conflicting interests.

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