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Assessment of Serum Bilirubin and Uric Acid Antioxidant Levels in Acne Patients

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Abstract

Objectives:Assessing the serum bilirubin and uric acid [UA] levels as oxidative stress markers in acne patients. Background: UA levels and serum bilirubinhave a role in pathogenesis of acne.Data Sources: Using Medline resources [Pub Med and Medscape] and information about the significance of serum bilirubin and UA levels in acne that is up to date through 2023.Study Selection:For inclusion, each study underwent an independent evaluation. They were involved if they matched the following requirements: 1. Published in English language. 2. Published in peer-reviewed journals.3. Discuss serum bilirubin and UA levels role in pathogenesis of acne.Data Extraction:Studies were disqualified if they didn't meet the criteria for inclusion. Evaluation of the quality of the study involved determining whether it had received ethical approval, eligibility criteria that were clear, proper controls, adequate information, and established assessment strategies. Employing a data collection form, data from each eligible study were independently abstracted to gather details on the study results we were interested in. Conclusions: We can safely conclude that bilirubin and UA may have a possible function in acne vulgaris [AV] pathogenesis.

Keywords: Acne vulgaris; Bilirubin; Uric acid.

1. Introduction

The majority of people who suffer with AV, a chronic inflammatory condition of the pilosebaceous unit, are teens and young adults. Noninflammatory, open or closed comedones as well as inflammatory papules, pustules, and nodules are its defining features **[1].** It has been discovered that acne vulgaris etiology is influenced by microbes, genetic predispositions, and different environmental variables. It has become clear in recent years that acne patients have higher systemic and cutaneous oxidative stress.**[2].**

Oxidative stress is a pathological condition brought on by high amounts of excessively reactive oxygen species in comparison to the body's antioxidant capability. As a result, there may be an increase in apoptotic residues and cell death, autoantibodies production, and an autoimmune cascade response **[3].**

The harm brought on by oxidant molecules is neutralized by antioxidant molecules, which are both endogenous and exogenous components. They achieve this through both extracellular and intracellular defense. Numerous molecules, including UA, transferrin and albumin are involved in extracellular defense. The primary antioxidant defense is provided by enzymes that scavenge free radicals inside the cell. Copper, zinc, and selenium are necessary for these enzymes to act normally **[4].**

Long recognized as the cytotoxic byproduct of iron porphyrin, bilirubin also exhibits a variety of biological properties, including anti-inflammatory, anti-oxidant, neuroprotective, immunomodulatory and cytoprotective action**[5].** Uric acid interacts with superoxide and nitrogen radicals to form a natural metal-chelating antioxidant **[6].**Because of this, serum bilirubin and UA not only reduce overall oxidative stress but also demonstrate the body's antioxidant status**[7].**

2. Materials and methods

Data Sources: By searching and reviewing Medline databases [Pub Med and Medscape] andtherole of serum bilirubin and UA levels in the pathogenesis of acne available till 2023.

Study Selection: For inclusion, each study was evaluated independently. If they met the following requirements, they were included: 1. Published in English language. 2. Published in peer-reviewed journals.3. Discuss serum bilirubin and UA levels function in acne pathogenesis.

Data Extraction: Studies were disqualified if they didn't meet the criteria for inclusion. Evaluation of the quality of the study involved determining whether it had received ethical approval, eligibility criteria that were clear, proper controls, appropriate information, and established assessment measures. Using a data collection form, data from every eligible study were separately summarized to gather details on the study results we were interested in.

Review of literature

Acne vulgaris

The pilosebaceous unit is affected by the AV condition, which results in noninflammatory lesions

[open and closed comedones], inflammatory lesions [papules, pustules, nodules, and cysts], and variable levels of scarring. AV can remain throughout adulthood, with a 50.9 percent prevalence rate of acne in women aging 20 to 29 years versus 26.3 percent in women aging 40 to 49 years. Two thirds of all dermatology office visits for acne are from female patients, and one third of these visits are from women older than 25 years**[8]**.

Acne causes severe morbidity, including persistent scarring and psychological issues like low self-esteem, sadness, and anxiety, all of which have a detrimental effect on quality of life**[9]**.

- **Etiopathogenesis of AV**

Propionibacterium acnes colonization of the follicles, altered follicular keratinization that results in comedones, enhanced and changed sebum expression under androgen regulation, and complex inflammatory processes involving both innate and acquired immunity are the four main pathogenic methods that cause acne lesions. The pathogenesis of acne is also influenced by environmental factors, diet involving dairy and chocolate usage and genetics **[10]**.

Androgens have a significant impact, as shown by the reaction of adult female acne to hormonal therapies, particularly in the context of hyperandrogenism abnormalities like polycystic ovary syndrome [PCOS] and hormone-based therapies usage like oral contraceptives and anti-androgen medicines in women with normal androgen levels. Dehydroepiandrosterone sulphate levels rising in connection with the beginning of acne in premenarchal girls and a subgroup of PCOS patients, as well as the absence of acne in androgen-insensitive women, also play a significant impact. Through androgen receptors on the sebaceous glands, androgens promote the synthesis of sebum**[11]**.

- **Clinical Features and Grading Severity of AV**

Women can develop acne at any age, and the severity of their cases can vary. Lesions on the lower region of the face, particularly on the chin and jawline, are more likely to appear in female patients. However, a more epidemiologic study by **Heng and Chew, [12]**demonstrated that the most typical clinical manifestation of acne in adult women may not be this hormonal distribution.

In one investigation of post-adolescent acne, two subtypes persistent acne and late-onset acne were detected in 85% of the patients, who had primarily comedonal acne**[13]**. 80 percent of adult female patients have persistent acne, which is characterized as acne that lasts into adolescence into maturity**[14]**. Acne that develops after the age of 25 is referred to as late-onset acne. Women who exhibit symptoms of hyperandrogenism, such as hirsutism or irregular periods, as well as those who have real late-onset acne, ought to undergo additional testing to rule out underlying endocrine conditions like PCOS**[15]**.

Doshi et al. [16]created a worldwide method for evaluating acne [GAGS]. The forehead, each cheek, nose, chin, chest, and back are divided into six parts in this approach, and each area is given a factor based on its size.

Bilirubin

The modification of blood bilirubin levels represents a possible treatment option for a wide range of medical states since bilirubin has a significant function in cardiovascular health, stroke, diabetes, and metabolic syndrome **[17].** Although it is poisonous at high levels, this molecule acts as the serum's most potent antioxidant when consumed within the usual physiologic range**[18].**

- **Antioxidant Activity of Bilirubin**

Modifying serum bilirubin levels can be a possible therapeutic goal for a wide range of medical disorders because it has a crucial function in metabolic syndrome, diabetes, stroke, cardiovascular health, and other conditions**[17].** It has been demonstrated that it can guard against hydrogen peroxide excess 10,000 times its molar level thanks to its strong antioxidant activity. Similar to how renal ischemia reperfusion injury is caused by the strong oxidant peroxynitrite, which is created when nitric oxide [NO] and the superoxide anion combine to generate it, bilirubin prevents nitrosative damage**[19]**.

- **Anti-Inflammatory and Immunomodulatory**

With a focus on reducing the release of damage-associated molecular patterns [DAMPS] and interleukin 1 beta[IL-1 β], bilirubin exerts immunomodulatory properties by damaged pancreatic islet cells, that are important innate immune response stimulants during cell- or organ-transplantation. Bilirubin supplement has even helped to develop tolerance to organ transplants by suppressing these early signals, lowering apoptosis and the production of inflammatory mediators, and eradicating the early signaling that causes allo-recognition and acute or chronic graft rejection**[20].**

Beyond its direct antioxidant activity, bilirubin exerts cytoprotective benefits through inhibiting pro-apoptotic genes and upregulating anti-apoptotic genes, among other mechanisms. In models of pancreatic, intestinal, and heart injury, treatment with bilirubin and biliverdin has also been demonstrated to suppress NF-κB regulated pathways and avoid pro-inflammatory signaling **[21].**

- **Hormone-Like Effects and Signaling**

In a diet-induced rodent model of non-alcoholic fatty liver disease and obesity, bilirubin supplementation can alleviate hepatic steatosis, lessen ketosis, and increase fat consumption. Adipocytes with biliverdin reductase knockout exhibit oxidative stress, lipid accumulation, hypertrophy, and diminished mitochondria **[22].**

Uric Acid

Animals naturally produce the chemical molecule UA as a purine metabolite. It is primarily eliminated by the kidneys and intestines after being produced by the liver. As a result of uricase function loss, that resulted in humans having higher UA levels than other mammals, it is the byproduct of purine metabolism in humans. Uric acid has remarkable antioxidant properties because of its double bonds, and it may account for 2/3 of the total plasma antioxidant capacity**[23]**.

Nephrolithiasis or gouty arthritis are frequently related with uric acid etiology. Poor solubility in the extracellular environment, which causes crystal formation, low affinity [and deposition] to specific tissues, and antigenicity are all factors that contribute to high uricemia pathogenicity [after crystal phagocytosis]. Confounding factors include the mix of quantitative and qualitative etiological factors for hyperuricemia, as some hyperuricemia people may exhibit symptoms whereas others may not. Hyperuricemia is regarded as a predictive marker of renal illness, diabetes mellitus, cardiovascular disease, and inflammation in the clinical setting. Consequently, carrying a [modest] risk of dying**[24].**

- **Uric acid as a protective factor**

It is unknown if UA would serve as an antioxidant defense mechanism against oxidative stress or a causative cause. Acute spikes in UA levels appear to offer antioxidant defense, despite the fact that chronic elevated levels are linked to a higher risk for coronary artery disease. There is a theoretical basis for uric acid's role in reducing oxidative damage through one or more processes since it is a water-soluble antioxidant that inactivates free radicals of oxygen and binds the primary electron transfer medium for free radical formation [iron]**[25].**

More than half of the blood's antioxidant capability is contributed by it. Additionally, due to the stabilizing properties of vitamins C and E, UA protects cells from damage, and its antioxidant impact depends on ascorbic acid levels in plasma. Additionally, it directly affects the suppression of free radicals, safeguarding DNA and the cell membrane. Because of its antioxidant properties, most authors do not believe that UA is harmful to human health**[26].**

- **The antioxidant activity of UA**

The brain is where UA's antioxidant activity happens, protecting against diseases like multiple sclerosis and neurological disorders. Higher concentrations of UA are mainly linked to a lower risk of Parkinson's disease development and a positive impact on the disease progression. The free radical theory of Parkinson's disease pathogenesis had previously proposed such a protective impact because UA is a well-known antioxidant**[27]**.

3. Conclusion

From the present study, we concluded that bilirubin and UA may play a role in pathogenesis of AV.

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