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Review Paper

Study of Serum Bilirubin and CRP in Elderly Type 2 Diabetic Patients- A Review

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Abstract

Type 2 Diabetes Mellitus (T2DM) is a complex metabolic disorder marked by hyperglycemia, insulin resistance, and systemic inflammation. In elderly individuals, the disease poses heightened risks due to age-related physiological changes and increased susceptibility to complications. This review explores the roles of serum bilirubin and C-Reactive protein (CRP) as biomarkers of oxidative stress and inflammation, respectively, in elderly T2DM patients. It emphasizes their potential utility in disease monitoring, predicting complications, and guiding therapeutic interventions.

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INTRODUCTION

Diabetes Mellitus (DM) is a significant non-communicable illness that poses a major risk to both international economics and public health. In both industrialized and developing nations, the number of individuals with DM has dramatically grown due to variables like population ageing, urbanization, and lifestyle changes. Hyperglycemia brought on by varying degrees of insulin insufficiency and resistance characterizes type 2 diabetes, an endocrine condition [1]. Renal, neurological, and cardiovascular complications might arise from multiorgan damage caused by chronic hyperglycemia [2]. In the world, 9% of men and 7.9% of women have adult type 2 diabetes [3]. People with diabetes number 415 million. worldwide, and the condition known as diabetes mellitus (DM) has grown to epidemic proportions. It is projected that by 2040, this number would rise to 642 million [4]. India is the country with the highest number of diabetics worldwide; estimates place the country's population with prediabetes at 77.2 million and diabetes at 62.4 million [5]. It is estimated that up to 79.4 million people in India could be affected by DM by 2030 [6]. India has one of the biggest socioeconomic burdens of diabetes worldwide as a result of these staggering numbers [7]. This review focuses on the dual roles of

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these biomarkers in the elderly diabetic population, a group prone to increased morbidity and mortality.

Diabetes Mellitus (DM) in Elderly stage

Globally, the frequency of DM is rising [8, 9], and with its associated social and economic costs, it is turning into an epidemic and endemic issue [10, 11]. Its mortality, co-morbidities, and prevalence, however, are higher in the old than in the young, [12]. The prevalence of DM among the elderly is generally 20%, with an equal number of cases going untreated, [13]. Frequencies that are reported range from 18% to 33%, [14, 15]. This variety can be a reflection of variations in the examined populations' ages, lifestyles, and genetic backgrounds. However, 30% of elderly individuals have poor glucose management, which raises their chance of developing diabetes, [16]. Elderly type 2 diabetes appears to be resulting from several causes, including genetic predisposition, a long life expectancy that reduces insulin secretion, and changes to certain environmental conditions that cause central obesity. The final one is in charge of insulin resistance [17], which is the primary cause both metabolic and type 2 diabetic mellitus syndrome in adults and the elderly.

As there is various complication with reference to type 2 diabetes and various biochemical changes occurs one of the changes is of serum bilirubin and c reactive protein. These parameters holds much of the importance hence this study is to look forward the affiliation with both these parameter in elderly patient of type 2diabetes.

Role of Serum billirubin in Type 2 Diabetes Mellitus patient

Bilirubin, one of the most substantially conserved classes of non-polar molecules, has been demonstrated to possess anti-inflammatory and antioxidant properties [18, 19]. Bilirubin is the byproduct of heme catabolism and a member of a phylogenetically ancient class of tetrapyrrolic chemicals. Heme oxygenase (HO), an enzyme system made up of two forms (HO-1 and HO-2), is accountable for the division of Biliverdin is produced via cyclic tetrapyrrole heme, ferrous The elements iron (Fe2+) and carbon monoxide (CO). Thereafter, biliverdin is converted by biliverdin reductase. to bilirubin. As HO-1 expression rises, bilirubin concentration rises as well [20]. Higher HO-1 expression was revealed to have a protective effect against various illnesses in an animal investigation [21]. Numerous investigations on the HO-1 pathway have examined The connection between bilirubin levels and Numerous illnesses, such as diabetes mellitus, heart disease, and diabetic complications [22–24]. Studies on bilirubin were first mostly concerned with cholestasis, particularly in infants [25]. Recent research on bilirubin has revealed that it could offer defense against vascular disorders. After controlling for several confounding variables, a prospective research showed that, following modification for several confounding factors, the possibility of an ischemic stroke was reduced in the highest bilirubin group (OR: 0.66, ninety-five percent confidence interval (CI): 0.49–0.89) [26]. Furthermore, compared to diabetic individuals with normal bilirubin concentrations, Inoguchi *et al*. showed that the prevalence of vascular problems was decreased in patients with Gilbert's syndrome [27].

Bilirubin has long been thought of as a harmful by product of Though further study is needed, heme catabolism is beginning to identify it as a possible endogenous antioxidant in physiological settings [28]. Bilirubin is thought to have anti-inflammatory properties in addition to its capacity to scavenge excess ROS [29]. Several of population-based Serum bilirubin levels and risk have been demonstrated to be adversely connected by research. of diabetes [30], chronic renal disease and coronary artery disease [31, 32], peripheral vascular dysfunction [33], and diabetes-related peripheral neuropathy [34], based on these physiological effects of bilirubin. measurements of blood bilirubin and DR have been linked in a small number of research publications [35–38].

The upkeep of the balance of bilirubin has implications for the risk of metabolic disorders, such as of vascular hypertension, metabolic syndrome, and diabetes, bilirubin, and homeostasis., as well as heart disease (CVD). Numerous factors, such as smoking cigarettes, gender, fasting, consuming a range of medicines and/or plant products, altitude, race, and age, can affect the concentration of serum bilirubin [39]. Each of these elements may have an impact on the biological effects of bilirubin on the human body.

Role of C-Reactive Protein (CRP) in Type 2 Diabetes patients

An increasing amount of research indicates that systemic inflammation at low levels raises type 2 diabetes risk [40]. Anti-inflammatory drugs may also postpone the onset of diabetes or prevent it altogether [41]. It's unclear yet if inflammation has a significant role in diabetes risk. A common indicator of inflammatory illness is C-reactive protein (CRP), which is a marker of acute inflammation. Increases in CRP has lately been connected to type 2 diabetes [42] and obesity [42, 43]. Consequently, Numerous studies are beginning to show that insulin resistance is a long-term, low-grade inflammatory condition [44]. Increased CRP values have been shown in prospective case-control studies [45–49], to be predictive of type 2 diabetes development, suggesting a potential role for inflammation in the onset of diabetes [45,47–49]. Anti-inflammatory drugs possess the ability to decrease C-reactive protein (CRP), a measure of inflammation that is independently linked to the onset of diabetes [50-53].

Circulating CRP levels with incident diabetes mellitus risk have been linked in a number of prospective studies. Studies vary in their findings; some demonstrate an independently positive correlation between CRP and incident diabetes [54–62], while others find no correlation at all considering the effects of obesity and insulin resistance account [63–66]. Furthermore, claims have surfaced of variations in the relationship between sex and CRP and diabetes [67–68]. Additionally, a small number of studies have revealed a negative relationship between blood bilirubin levels and and CRP.

Interplay Role Between Bilirubin and C-Reactive protein CRP

The balance between oxidative stress and inflammation is pivotal in diabetes management in Low Bilirubin and High CRP.

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This combination signifies a pro-oxidative and pro-inflammatory state, indicative of advanced disease or complications. Therapeutic Implications: Interventions aimed at reducing inflammation and oxidative stress (e.g., lifestyle modifications, antioxidant therapy) could improve outcomes.

Implications in Elderly T2 DM Patients

Elderly individuals with T2DM are uniquely vulnerable due to Age-related decline in antioxidant defenses. Chronic low-grade inflammation termed "inflammaging Increased comorbidities like hypertension and cardiovascular disease. Regular monitoring of serum bilirubin and CRP could help identify high-risk elderly diabetic patients. Personalized interventions based on these biomarkers may delay complications.

Challenges and Future Directions

Limitations of Current Research

Most studies are cross-sectional, limiting causal inference. Confounding factors such as medication, diet, and comorbidities need better control.

Areas for Future Research

Longitudinal Studies: To establish causal relationships between bilirubin, CRP, and diabetic complications. Intervention Trials: To assess the impact of therapies targeting oxidative stress and inflammation. Biomarker Thresholds is establishing age-specific reference ranges for bilirubin and CRP in elderly T2DM patients.

CONCLUSION

Serum bilirubin and CRP are promising biomarkers in elderly T2DM patients, reflecting oxidative stress and inflammation, respectively. Their combined analysis can offer insights into disease progression and guide therapeutic strategies. Future research should focus on integrating these biomarkers into clinical practice for better risk stratification and management. Serum bilirubin, with its antioxidant properties, offers insights into oxidative stress and its protective role against diabetic complications. Meanwhile, CRP serves as a reliable indicator of systemic inflammation, a critical factor in the pathophysiology of T2DM and its associated risks. Together, these biomarkers can enhance the early detection of complications, improve risk stratification, and guide personalized treatment strategies. However, further research is essential to validate their clinical utility and establish standardized thresholds for their use in routine practice.

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