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ASSESSMENT OF ERYTHROCYTE SEDIMENTATION RATE AND C-REACTIVE PROTEIN IN ELDERLY DIABETES MELLITUS PATIENTS IN PORT HARCOURT, RIVERS STATE

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ABSTRACT

Background: Diabetes mellitus (DM), a metabolic condition, chronic in nature commonly linked to high levels of inflammatory indicators such as C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR). Inflammation is thought to play a vital role in the pathogenesis and complications of diabetes. Hence, estimating these indicators may provide additional insight into the inflammatory state in diabetic patients.

Aim: This research aimed to assess the levels of C-reactive protein and erythrocyte sedimentation rate (ESR) among the elderly diagnosed with diabetes mellitus in Port Harcourt, Nigeria. This is a cross-sectional study which assessed a total of 88 subjects within the ages of 60-80 years for Erythrocyte sedimentation rate and C-reactive protein in elderly diabetes in Port Harcourt. Subjects were recruited, seven (7) mls of whole blood was collected from each subject via standard venipuncture.

Materials/Methods: Fasting blood sugar (FBS), ESR and CRP were examined using Glucose oxidase method, Westergren and Immunoturbidometric ELISA methods respectively. Statistical package for Social Sciences (SPSS) t-test was used for comparison between two groups with, $p \leq 0.05$ being considered statistically significant.

Results: The CRP level in diabetic patients (10.95±2.78 ng/ml) was statistically significantly higher (p=0.033) than in non-diabetics (7.63±3.57 ng/ml). correspondingly, FBS levels were significantly higher (p=0.026) in diabetics (11.77±2.34 ng/ml) compared to the controls (5.08±3.77 ng/ml). The ESR for female diabetics (70.00±21.21.3mm/hr) was seen in the study. This is suggestive of a raised inflammatory response. Incorporating CRP and ESR tests into the routine management of elderly diabetes patients are proffered to monitor inflammation more efficiently to prevent possible diabetics complications. Given the increasing prevalence of diabetes among older adults, routine screening, early intervention, and lifestyle modifications should be prioritized to prevent the onset and progression of the disease.

Conclusion: The study therefore, advocates regular monitoring of CRP in diabetic patients to help identify those at a higher risk of cardiovascular complications and guide the implementation of preventive strategies, such as anti-inflammatory therapies and lifestyle modifications.

Keywords: C-reactive protein, Diagnosed, Diabetes, Erythrocyte Sedimentation Rate and Elderly.

INTRODUCTION

Diabetes mellitus (DM), results from defects in insulin secretion, it is a disorder with a prolonged metabolic condition characterized by hyperglycemia.

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Its prevalence, globally, increases at a disturbing rate, particularly among the elderly population (International Diabetes Federation, (IDF), 2023). As people get older, the risk of developing type 2 diabetes mellitus (T2DM) heightens as a result of combination of factors such as insulin resistance, decreased beta-cell function, and alteration in body composition (Shah and Vella, 2021). The elderly being more susceptible to diabetes – related complications, frequently experience a subtle inflammatory state, which can intensify these complications (Singh *et al*., 2022).

In the pathogenesis of both diabetes and its complications, including cardiovascular diseases, neuropathy, nephropathy, and retinopathy inflammation plays a fundamental role (Santos and Lima, 2021). Hence, C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) are frequently used biomarkers in the assessment of systemic inflammation in varying diseases, as well as diabetes. CRP is an acute – phase protein produced by the liver in response to pro-inflammatory cytokines, such as interlukin -6 (IL-6) and tumor necrosis factor- alpha (TNF- α) (Ridker *et al*., 2018). Raised values of CRP have been linked to insulin resistance, poor glycemic control, and an increased risk of cardiovascular disease in diabetic patients (Pfutzner and Forst, 2019). ESR, a non – specific indicator of inflammation that estimates the rate at which red blood cells sediment over a given period. Though less specific than CRP, it is generally used to detect inflammation and monitor disease progression in chronic conditions such as diabetes (Sharma *et al*., 2020). Research has shown that diabetic patients are prone to having a raised ESR values, which is indicative of an underlying chronic inflammatory state contributing to the progression of complications (Khafaji *et al*., 2021). The process of inflammation, more often exhibited by the elderly population is due to a low-grade, chronic inflammatory response that develops with aging (Franceschi *et al*., 2018). This age-related inflammation is often seen in elderly diabetic patients, increasing the risk of both metabolic and cardiovascular complications. Going by the rising prevalence of diabetes among the elderly and the established relationship between inflammation and diabetes-related complications, it is imperative to evaluate markers such as CRP and ESR in this population to monitor inflammatory status and potentially guide therapeutic interventions (Gupta and Singh, 2022). Though CRP and ESR as viable indicators of inflammation, their use in the routine management of elderly diabetic patients has not been widely studied. This study aimed to assess the levels of CRP and ESR in the elderly with diabetes mellitus and explore their potential role in identifying those at increased risk of developing complications. By estimating these indicators, Health care workers may gain valuable awareness into the inflammatory burden in elderly diabetics and improve strategies of managing this disease.

MATERIALS AND METHODS

Study Design

This cross-sectional study assessed erythrocyte sedimentation rate and C-reactive protein in elderly with diabetes mellitus residents in Port Harcourt.

Study Area

The study was conducted in Port Harcourt, the State capital of Rivers State, Nigeria, which is situated between latitudes $4^{0}53'$N and longitude $6^{0}54'$E. Nigeria's Niger Delta region has the state of Rivers. It was created in 1967 after the former Eastern Region was divided. To the North, it borders the States of Imo, Abia and Anambra, and to the East, it borders the State of Akwa Ibom, and to the West, it borders the States of Bayelsa and Delta. Port Harcourt, the state capital is considered as the commercial hub of Nigeria's oil industry. With estimated populations of over 7 million, Rivers State is a multicultural and multitribal territory with over 26 ethnic tribes in 23 local government areas.

Study Population

The study enrolled 88 participants between the ages of 60 and 80 years; 62 participants were known diabetes, while the remaining 26 were none diabetes as (control subjects). The subjects were informed, and interested parties provided their informed consent. A meticulously designed survey was used to collate the demographic details of study participants.

Collection of Blood Samples, Storage and Transportation

Having obtained informed consent from the study subjects and how the samples will be collected. From the antecubital fossa of the subjects, seven (7) milliliters of venous blood was drawn using vacutainer as described by Chesbrough (2010). Three milliliters of the blood samples was placed in lithium heparin bottles, two milliliters of the blood sample was placed in fluoride oxalate and two milliliters of the blood was placed in EDTA-anticoagulant bottles. Several mild inversions were made to mix the anticoagulant with the blood that was added to the anticoagulant bottles. Centrifugation was performed for five minutes at 2400 rpm in order to separate the serum into the plain bottle.

METHODOLOGY

Determination of Erythrocyte Sedimentation Rate (ESR)

Method: Westergren method as described by Chesbrough, (2010) was employed.

The EDTA-anticoagulated blood was drawn into the Wintrobe tube until it reached the 100mm mark from EDTA. After that, the tube was placed vertically upright at room temperature for an hour in a rack. Using millimeters, the rate at which red blood cells depleted after one hour was recorded.

Determination of Serum C-reactive protein (CRP) Level

Method: Latex Particle-enhanced Immunoturbidometric ELISA

By combining 1mL of reagent 2 with 4mL of reagent 1, the reagent volumes were prepared. The working reagent was prepared and then allowed to come to room temperature. Two test tubes were labeled "Test" and "Standard". 7µL of the sample and 7µL of the C-reactive protein standard were placed in test tubes marked "Test" and "Standard" respectively. Following a thorough mixing and a 10-minute standing period, 1mL of the working reagent was added to each test tube. The absorbance at 540nm was then measured. The microplate reader used for the ELISA process provided the C-reactive protein concentration.

Statistical Analysis

Version 24 of Statistical Package for Social Sciences (SPSS) was used to analysed data. $P \leq 0.05$ was considered statistically significant.

RESULTS

Demographic Details of Study Population

There were 31 male and 31 female diabetic subjects, with average age of 70 ± 3 years. There were 10 male control subjects and 16 control female subjects, with average age of 63 ± 4 years as shown in Table 1.

Table 1. Distribution of Study Participants by Age

Subjects	Male (n)	Female (n)	Age (Yrs) M± SD or SEM
Diabetic mellitus	31	31	70 ± 3
Control	10	16	63 ± 4

Table 2. Comparison of CRP and ESR Among Study Participants

	CRP (mg/l)	ESR (mmol/L)
Diabetic Subjects	10.95 ± 2.78	11.77 ± 2.34
Control	7.63 ± 3.57	5.08 ± 3.77
p-value	0.033^{s}	0.026^{s}
t-value	15.241	11.811

Key: CRP- C-reactive protein, FBS-Fasting Blood Sugar, s-statistically significant

Table 3. Comparison of CRP and ESR among Diabetic Subjects according to gender

Parameters	Male	Female	t-value	p-value
CRP (mg/ml)	10.55±2.25	11.36±3.44	2.001	0.295^{NS}
ESR (mm/hr)	62.84±25.45	70.00 ±21.31	2.521	0.014^{S}

Key: CRP- C-reactive protein, ESR-Erythrocyte Sedimentation Rate, s-statistically significant, ns- not statistically significant

DISCUSSION

The equal number of male and female diabetic subjects in this study reflects an increasing global trend where diabetes prevalence affects both genders equally. Peters *et al*., (2022) deduced that while the general prevalence of type 2 diabetes mellitus (T2DM) is comparable among both gender, sex-specific differences occur in disease progression, treatment outcomes, and complications. In another light, Chamberlain *et al*. (2022) deduced that Diabetic women are more susceptible to developing cardiovascular diseases, mostly postmenopausal women, as a result of the loss of protective effects of estrogen. This hormonal alteration adds to high insulin resistance, abdominal fat buildup, and dyslipidemia, all these worsen diabetes-related complications in older women.

The age range for both male and female diabetic subjects in this study highlights the importance of implementing age-specific diabetes management strategies. As people get older in age, their ability to manage blood glucose levels become altered due to decline in pancreatic function, reduced insulin sensitivity, and other age-related physiological alteration (Espeland *et al*., 2023). This study therefore, advocates that the age factor be considered in clinical interventions, and more attention should be given to elderly populations to mitigate the risk of complications.

Zhou *et al*. (2022) advocate that aging is a significant risk factor for diabetes, as age-related metabolic changes set in, reduced physical activity, and the buildup of their comorbidities such as hypertension and dyslipidemia raise the possibility of acquiring the disease. Inclines to worsen with age, supporting a higher blood glucose level and the subsequent development of diabetes as people get older in age (Basu & Dutta, 2021). Age is a viable tool in the development of diabetes – related complications, as it does not only affect the chances of chronic inflammation and oxidative stress but also alters the body's ability to regulate glucose and respond to insulin (Wang *et al*., 2023).

In another development, the study found that C-reactive protein (CRP) levels in diabetic patients were significantly higher than in non-diabetic controls, with a p-value of 0.033. This significant difference emphasizes the established relationship between diabetes mellitus (DM) and increase inflammation. Raised CRP levels serve as a reliable pointer of systemic inflammation in such patients (Mahmoud *et al*., 2023). Similarly, a study conducted by Abbasi *et al*. (2022) found that CRP levels in diabetic patients were 1.6 to 2.2 times higher than in non-diabetic controls, further supporting the hypothesis that inflammation plays a serious role in the development and progression of diabetes. The elevation of CRP in diabetic patients could be linked to several mechanisms. CRP is an acute – phase protein produced by the liver in response to pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor- alpha (TNF- α), which are elevated in T2DM (Ridker *et al*., 2020).

Chronic hyperglycemia in diabetic patients induces oxidative stress and inflammation, leading to the activation of immune cells and the release of cytokines that stimulate CRP production (Hameed *et al*., 2021). When this inflammatory environment is activated, insulin resistance is enabled, which explains the elevated CRP levels in the diabetic individuals.

Mahmoud *et al*. (2023) stated that increased levels of CRP in the diabetic group reflect a higher likelihood of cardiovascular complications, which are the leading cause of morbidity and mortality in patients with T2DM. Ridker *et al*. (2020) found that higher CRP levels were associated with a greater risk of cardiovascular events in diabetic patients, independent of traditional risk factors like blood pressure and cholesterol levels.

FBS levels served as an initial pointer of glycemic control, and raised levels indicate both type 1 and type 2 diabetes mellitus (T2DM) (American Diabetes Association, 2023).

It is imperative to note that when FBS values increase, it implies an alteration in glucose absorption owing to malfunction in the availability of insulin. A study by Moradi *et al.* (2021) supports this finding, showing that FBS levels in diabetic, with average values around 11mmol/L, similar to those observed in this study. The significant difference between diabetic and non- diabetic FBS levels found in this study is also in alignment with the results of other researchers, which highlights the role of hyperglycemia in diabetes. For example, a study by Kaul *et al.* (2022) has it that FBS levels in T2DM patients were significantly higher than in healthy controls. Their study also highlights that raised values of FBS can be linked to poor glycemic control and an increased risk of diabetic complications. This supports our findings, which emphasize the importance of monitoring FBS in diabetic patients to reduce the risk of chronic complications.

Worthy of note, in the study, is the variability in FBS levels in non-diabetic patients which could be ascribed to factors such as diet, physical activity, and body weight, which impact glucose metabolism even in non-diabetic individuals. This is in consonance with the findings of Rhee *et al*. (2023), who reported similar variations in FBS levels in non-diabetic individuals, caused by lifestyle factors and occasional episodes of insulin resistance. This variability which advocates for the need to engage in regular monitoring of blood glucose levels at risk populations to detect early diabetic conditions and begin interventional preventive measures (American Diabetes Association, 2023).

Furthermore, the study found that the erythrocyte sedimentation rate (ESR) for female diabetics was statistically significantly higher ($p=0.014$) than that of male diabetics.

This is suggestive of a heightened inflammatory response in female diabetic patients in comparison to the males.

ESR is a nonspecific pointer of inflammation that is raised in response to acute – phase reaction, and often rose in chronic inflammatory states such as diabetes mellitus (Omar *et al*., 2023).The elevated ESR in diabetic patients might reflect inflammatory nature of diabetes, mainly in females, who are prone to raised values of inflammatory markers such as C-reactive protein (CRP) and ESR. A study by Al-Khazraji *et al*. (2021) reported similar findings, noting that female diabetics revealed significantly higher ESR levels in comparison to males, suggestive of hormonal variations, including the impact of estrogen, resulting in raised inflammatory response in females.

Estrogen may have ovulatory impact on the immune system, which could play off negatively on the inflammatory response in women.

Estrogen raises the making of pro-inflammatory cytokines such as interleukin-6 (IL-6), which invariably excites the liver to produce more acute-phase proteins like CRP, causing a raised ESR (Sainz *et al*., 2023).

The gender variance in ESR levels could be due to fat distribution among males and females. A much lower percentage of fat is seen in men than women, which may impact high increase levels of pro-inflammatory cytokines, particularly in adipose tissue (Francois *et al*., 2022).

Besides, the differences in ESR levels among both sexes diabetics could be affected by lifestyle and behavioral factors. From study, it has been shown that women are prone to experience stress; this can result in raise inflammation through the activation of the hypothalamic – pituitary – adrenal (HPA) axis (Luo *et al*., 2023). Inflammation caused by stress has been related to higher ESR and CRP levels. This further explains the higher ESR levels observed in female diabetics in this study.

CONCLUSION

The study observed elevated CRP and ESR levels in elderly diabetic patients, indicating an increased inflammatory response. Incorporating CRP and ESR testing into routine diabetes management may help better monitor inflammation and prevent related complications. Given the rising prevalence of diabetes in older adults, early screening, intervention, and lifestyle changes are crucial for slowing disease progression. Significantly higher ESR levels in female diabetic patients compare to males suggest a stronger inflammatory response in women, possibly influenced by hormonal and metabolic factor.

Recommendations

Considering the increased inflammatory markers (CRP and ESR) and poor glycemic control (FBS) in diabetic subjects, it is recommended that healthcare providers monitor these parameters regularly in diabetic patients. Interventions to manage both inflammation and blood sugar levels should be emphasized in diabetic care, possibly incorporating anti-inflammatory treatment strategies alongside glycemic control. Given the sex differences observed in ESR levels, tailored treatment approaches based on gender may improve management outcomes.

Limitation

Further studies with larger and more diverse populations, as well as additional biomarkers, are needed to confirm these findings. Longitudinal studies are needed to confirm whether elevated CRP predicts complications.

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