AJMAS
https://journal.utripoli.edu.ly/index.php/Alqalam/index eISSN 2707-7179

Original Article

Evaluation of Anticardiolipin Antibodies and Lupus Erythematosus Cell in Type 2 Diabetes Nigerian Population

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ARTICLE INFO

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Received*: 27-03-2023*
Accepted*: 23-04-2023*
Published*: 25-04-2023*

Keywords*. Anticardiolipin Antibodies, Lupus Erythematosus Cell, Type 2 Diabetics, Hypertension.*

ABSTRACT

Background and aim. *Diabetes mellitus, a chronic medical disorder characterized by persistent elevation blood glucose and, glycosuria together with its most common co morbidity still have so many mysteries that needs unravelling. This study was thus designed to evaluate serum anticardiolipin antibodies and the presence of lupus erythematosus cell in both treated and untreated uncomplicated and complicated type 2 diabetes.* ***Methods.*** *This study included 26 uncomplicated type 2 diabetes subjects, 15 were treated, 11 were untreated (newly diagnosed) and 31 complicated type 2 diabetes subjects, 17 were on treatment, 14 were untreated (newly diagnosed) and the remaining 17 were apparently healthy individuals which served as control. A total of 74 subjects were thus assessed. Determinations of blood pressure, Plasma glucose, BMI and anticardiolipin antibodies (ACA) was carried out on all subjects and the values seen in each of the groups compared with one another, however, this study also assessed the effect of treatment, gender and age on all estimated parameters. Results obtained were subjected to statistical analysis using Statistical Package for Social Sciences version 23 (SPSS 23). All parameters were expressed as mean ± SD, ANOVA was the tool of choice in comparing means and values were statistically significant at* $p<0.05$. ***Results.*** *Fasting blood glucose was significantly higher in treated and untreated uncomplicated and complicated type 2 diabetes with hypertension when compared to control respectively. In uncomplicated and complicated type 2 diabetes with hypertension, body mass index was significantly increased when treated and untreated were compared to control respectively. Lupus erythematosus test positivity of 5.8% and 7.1% were seen in treated complicated and untreated complicated diabetes respectively. Anticardiolipin antibody was also significantly higher in treated and untreated uncomplicated and complicated diabetics compared to control respectively. ACA was still higher in untreated compared to treated diabetics.* ***Conclusion****. This research found that ACA hence the likelihood of antiphospholipid syndrome is associated with type 2 diabetes mellitus. This can be more serious if there is vascular complication or when diabetes and its complications are poorly managed.*

Cite this article. *Odewusi O, Abbey A, Obadire O, Olaniyan O, Ogunyemi O, Omon E. Evaluation of Anticardiolipin Antibodies and Lupus Erythematosus Cell in Type 2 Diabetes Nigerian Population. Alq J Med App Sci. 2023;6(1):193-200.*
https://doi.org/10.5281/zenodo.7864673

INTRODUCTION

Diabetes mellitus can be referred to as a group of metabolic disorders with significant high blood sugar levels over a prolong period of time. Diabetes occurs due to either insufficient insulin production by beta cells of islet of Langerhans in the pancreas, or the cells of the body not responding properly to the insulin produced [1]. World Health Organization classified diabetes mellitus into three main types; they are; Type 1 diabetes mellitus which results from insufficient insulin production from the pancreas due to loss of beta cells of islet of Langerhans. Type 1 diabetes mellitus was previously referred to as insulin dependent diabetes mellitus (IDDM) or juvenile diabetes. This form of diabetes mellitus include cases due to autoimmune process and those for which beta dependent diabetes mellitus (NIDDM) or adult-onset

diabetes, is a condition in which the cells of cell destruction is unknown. The second is Type 2 diabetes mellitus the body fail to respond properly to insulin produced. The third main type of diabetes mellitus is gestational diabetes which is referred to as glucose intolerance with onset or first recognition during pregnancy [2].

Hypertension also known as high blood pressure is a long-term medical condition in which the blood pressure in arteries is persistently elevated. About 60% of Nigerian diabetics are hypertensive, as found in many other areas of the world. Females appear to have a slightly higher incidence of concomitant type 2 diabetes and hypertension. Two-third of patients with type two diabetes mellitus have arterial hypertension. Hypertension in turn increases the incidence of both macro and microvascular complications. The coexistence of diabetes and hypertension is possible due to the fact that they show similar risk factors which include; following unhealthy diet, being overweight, and living an inactive lifestyle. Diabetes increases blood pressure by; decreasing the blood vessels' elastic ability, increasing the amount of fluid in the body and changing the way the body manages insulin [3].

As a biomarker, also known as a biological marker, will generally be a substance used as an indicator of a biological state. In practice, a biomarker will always be measured and evaluated to examine normal biological processes, pathogenic processes, or pharmacological response to a therapeutic intervention [4]. Some examples of autoimmune biomarkers include: Anticardiolipin, Lupus erythromatosus cell, C- reactive protein, Antinuclear antibodies, Rheumatoid factor, Anti-centromere. The biomarkers of interest in this research work are anticardiolipin antibodies and Lupus erythematosus cell (LE cell) [5].

Anti-cardiolipin antibodies (ACA) are antibodies that are often against cardiolipin. They are a form of anti-mitochondrial antibody. Anti-mitochondrial antibodies are autoantibodies that consist of immunoglobulins formed against mitochondria, especially the mitochondria of the cells in the liver. Normally, the healthy immune system strategizes various mechanisms such as activation-induced cell death, anergy, or clonal ignorance, which play a protective role in order to prevent the activation of self-reactive lymphocytes [6]. When self-reactive lymphocytes are not subjected to the aforementioned tolerance mechanisms, thereby raising the possibility of the survival and activation of auto-reactive T cells and B cells upon encounter with self, it results in autoimmune condition [7]. Clinical conditions where Anticardiolipin can be quantified in appreciable amounts include, systemic lupus erythematosus (SLE) [8], anti-phospholipid syndrome, syphilis.

An LE cell (Lupus Erythematosus cell) is a neutrophil or macrophage that has phagocytized (engulfed) the denatured nuclear material of another cell. Autoantibodies are a characteristic feature of systemic lupus erythematosus and their presence is suggestive of an autoimmune pathogenesis. LE cells are not usually found in the peripheral blood but could form in the buffy coat of peripheral blood after a period of incubation [9].

As diabetes mellitus have been known to be a chronic disorder with a genetic background and a high impact from environmental factors with three kinds of characteristic manifestations: a metabolic syndrome consisting of hyperglycaemia, glycosuria, polyphagia, polydipsia, polyuria and alterations of the lipid and protein metabolisms due to a complete or partial deficiency of the action of insulin and/or a peripheral resistance to the insulin effect. Second but not of less effect is a vascular syndrome including (a) macroangiopathic alterations affecting all organs, particularly heart, brain and peripheral circulation, kidney and retina, and (b) a microangiopathic component involving the microcirculation producing mainly endothelial dysfunction; (3) a peripheral or autonomous neuropathic syndrome causing vascular dysfunction [10. This study was aimed at assessing markers of autoimmunity in patients with complicated and uncomplicated type 2 diabetes mellitus.

METHODS

Study Area

This study was carried out in Federal Medical Centre, Ado-Ekiti, Ekiti State and its immediate environments, Ido-Ekiti which is located in Ido-Osi Local Government Area of Ekiti state, Nigeria.

Study Design

The study design is a cross sectional study using a stratified random sampling method. Stratification was by age, height, weight, body mass index and therapy.

Ethical Approval

Ethical approval was sought and obtained from Federal Medical Centre, Ido-Ekiti, Ekiti State. The nature and purpose of research was explained to each participant using an informed consent for literate participants and verbal explanation for illiterate participant. Participants were not forced to answer questions, they responded according to their free will. The participants were assured of confidentiality and voluntary participation was assured.

Inclusion Criteria
Male and Female patients who were confirmed type 2 diabetics and type 2 diabetics complicated with hypertension were included in the study.

Exclusion Criteria
Pregnant women, nursing mothers and those with underlying disease conditions were excluded from this study.

Subjects
A total number of seventy-four (74) individuals were recruited for this study, comprising of twenty-six (26) subjects with uncomplicated diabetics; thirty-one (31) subjects with hypertensive diabetics and seventeen (17) subjects that does not have history of diabetes and hypertension (control). Treatment in this study was in the form of oral hypoglycemics plus diet restrictions and lifestyle modifications.

Sample Collection
After an overnight fast of 10 hours, venous blood sample of about 6ml was collected from the cubital fossa using a 22G needle and syringe. The whole blood collected was divided into 3 parts of 2 ml each in a plain bottle, a fluoride oxalate bottle and a sterile universal container. The blood in plain bottle was allowed to clot undisturbed at room temperature. The tubes (the plain and anticoagulated blood fluoride oxalate sample) were centrifuged at 12000rpm for 5 minutes. The resultant serum (for Anti-Sarcosine Dehydrogenase-Anti-M7 analysis) and plasma (for glucose analysis) samples respectively were transferred into another well labelled bottles and stored at -20^{O}C until analysis. The remaining 2ml whole blood was dispensed into a universal bottle containing beads, was slightly agitated and used for Lupus Erythematosus Cells (LE Cells) identification.

Analytical Methods
Blood pressure was determined with a digital sphygmomanometer (OMROS, Japan). Body mass index (BMI) was then derived from the height and body weight readings using the formula: BMI=Weight (kg)/Height (m^2). Plasma glucose level was estimated spectrophotometrically using GOD/POD based Randox® glucose kit. Anticardiolipin antibodies were determined using Enzyme Linked Immunosorbent Assay (ELISA).

Statistical Analysis
The data generated was expressed as mean ± SD. Analysis was done using SPSS version 23. The student's t-test was the tool of choice used to compare the serum levels of all variables between hypertensive diabetic and known diabetic hypertensive subjects. Values were compared and significance was tested at P<0.05.

RESULTS
Figure 1 showed distribution according to subjects under examination. From the results obtained, a combined total of seventy-four (74) subjects were used in this study comprising twenty-six (26) subjects who had uncomplicated diabetics; thirty-one (31) subjects who were hypertensive diabetics and seventeen (17) subjects who do not have history of diabetes and hypertension were used as control samples (Figure 1).

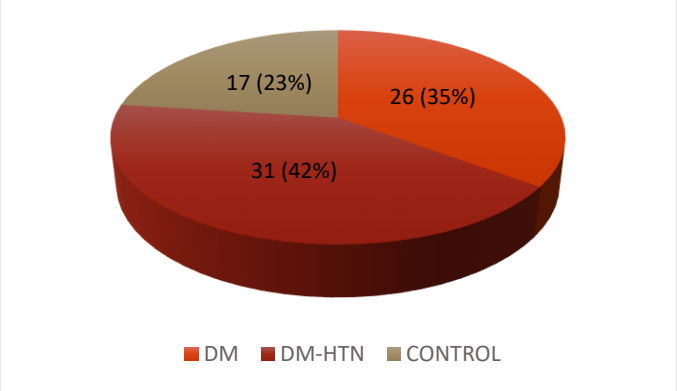

Figure 1: Distribution according to subject category

Figure 2 showed the distribution of the subjects according to gender. The results obtained showed that the study comprise a total of twenty-six (26) diabetic subjects; of which ten (10) were male subjects and sixteen (16) were female subjects, and thirty-one (31) hypertensive diabetic subjects; of which sixteen (16) were male subjects and fifteen (15) were female subjects. The finding shows that the incidence of diabetes is more in females than males and diabetes complicated with hypertension is more in males than females (Figure 2).

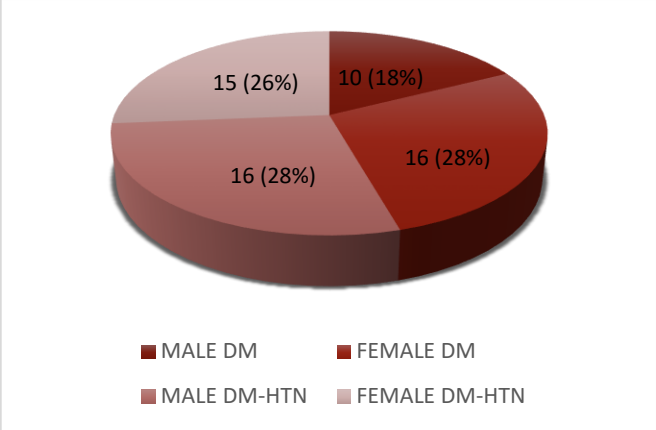

Figure 2: Distribution of subjects according to gender

Figure 3 showed the distribution of the subjects according to treatment. The study comprises a total of twenty-six (26) diabetic subjects and thirty-one (31) hypertensive diabetic subjects of which elevens (11) diabetic subjects were untreated and fifteen (15) diabetic subjects were on treatment, fourteen (14) hypertensive diabetic subjects were untreated and seventeen (17) hypertensive diabetic subjects were on treatment (Figure 3).

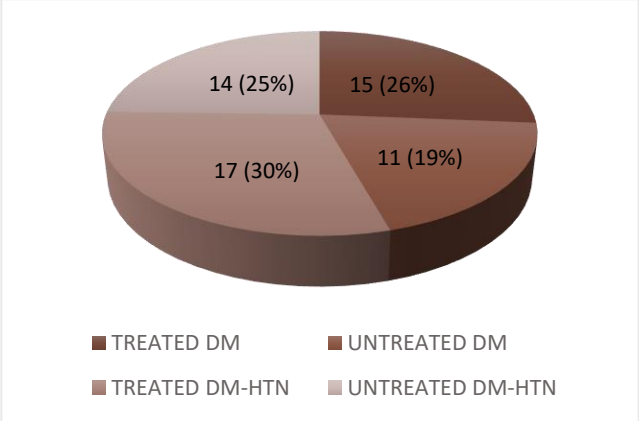

Figure 3: Distribution of subjects according to treatment status

Table 1 showed the Mean ± SD, t-value and p-value of Treated DM subjects compared with control for all parameters (BMI, Glucose and Anticardiolipin). The results obtained showed that the BMI was significantly higher in treated diabetics when compared to control ($p<0.05$), glucose was insignificantly higher in treated diabetics compared to control ($p=0.5652$) and anticardiolipin in treated diabetics was significantly higher when compared to control ($p<0.0001$) (Table 1).

Table 1. Mean ± SD, t-value and p-value of treated DM subjects compared with control for all parameters (BMI, Glucose and Anticardiolipin).

Group	TREATED DM (n=15)	CONTROL (n=17)	t-value	p-value
BMI (kg/m²)	27.26±5.67	24.08 ± 0.66	2.2998	0.0286*
Glucose (mmol/L)	4.75 ± 0.81	4.61 ± 0.54	0.5816	0.5652
Anticardiolipin	2.75 ± 0.55	1.39 ± 0.98	4.7495	<0.0001***

***Note**: * = significant at P<0.05; ** = significant at P<0.005; *** = significant at P<0.0001*

Table 2 showed the mean ± SD, t-value and p-value of Untreated DM subjects compared with control for all parameters (BMI, Glucose and Anticardiolipin). The results obtained showed that BMI, glucose and anticardiolipin levels were significantly higher in uncomplicated treated diabetics when compared control ($p<0.0001$) respectively (Table 2).

Table 2. Mean ± SD, t-value and p-value of untreated DM subjects compared with control for all parameters (BMI, Glucose and Anticardiolipin).

Group	UNTREATED DM (n=11)	CONTROL (n=17)	t-value	p-value
BMI (kg/m²)	30.66± 3.52	24.08 ± 0.66	8.7312	<0.0001***
Glucose (mmol/L)	8.73 ± 1.44	4.61 ± 0.54	10.7720	<0.0001***
Anticardiolipin	7.04 ± 1.38	1.39 ± 0.98	12.6921	<0.0001***

***Note**: * = significant at P<0.05; ** = significant at P<0.005; *** = significant at P<0.0001*

Table 3 showed the mean ± SD, t-value and p-value of Treated DM subjects compared with Untreated DM subjects for all parameters (BMI, Glucose and Anticardiolipin). The results obtained showed that BMI was insignificantly lower in treated diabetics when compared to uncomplicated untreated diabetics ($p=0.0926$), while Glucose and Anticardiolipin were significantly lower in treated diabetics compared to untreated diabetics ($p<0.0001$) respectively (Table 3).

Table 3. Mean ± SD, t-value and p-value of treated DM subjects compared with Untreated DM for all parameters (BMI, Glucose and Anticardiolipin).

Group	TREATED DM (n=15)	UNTREATED DM (n=11)	t-value	p-value
BMI (kg/m²)	27.26± 5.67	30.66 ± 3.52	1.7514	0.0926
Glucose (mmol/L)	4.75 ± 0.81	8.73 ± 1.44	8.9795	<0.0001***
Anticardiolipin	2.75 ± 0.55	7.04 ± 1.38	10.9733	<0.0001***

***Note**: * = significant at P<0.05; ** = significant at P<0.005; *** = significant at P<0.0001*

Table 4 showed the mean ± SD, t-value and p-value of Treated DM/HTN subjects compared with control for all parameters (BMI, Systolic, Diastolic, Glucose and Anticardiolipin). The results obtained showed that BMI, systolic and diastolic blood pressure were significantly higher in treated diabetics complicated with hypertension compared to control ($p<0.0001$). Also, anticardiolipin was significantly higher in treated diabetics with hypertension compared to control ($p<0.05$). However, glucose was insignificantly higher in treated diabetics with hypertension relative to control ($p=0.1872$) (Table 4).

Table 4. Mean ± SD, t-value and p-value of treated DM/HTN subjects compared with control for all parameters (BMI, Systolic, Diastolic, Glucose and Anticardiolipin)

Group	**Treated DM/HTN (n=17)**	**Control (n=17)**	**t-value**	**p-value**
BMI (kg/m²)	28.94± 3.95	24.08 ± 0.66	5.0051	<0.0001***
Systolic (mmHg)	143.94 ± 10.25	111.53 ± 4.91	11.6299	<0.0001***
Diastolic (mmHg)	91.0 ± 5.77	72.65 ± 7.49	7.6830	<0.0001***
Glucose (mmol/L)	4.99 ± 1.01	4.61 ± 0.54	1.3498	0.1872
Anticardiolipin	2.2 ± 1.08	1.39 ± 0.98	2.2245	0.0338*

***Note**: * = significant at P<0.05; ** = significant at P<0.005; *** = significant at P<0.0001*

Table 5 showed the mean ± SD, t-value and p-value of Untreated DM/HTN subjects compared with control for all parameters (BMI, Systolic, Diastolic, Glucose and Anticardiolipin). The results obtained showed that BMI, systolic and diastolic blood pressure, glucose and anticardiolipin levels were significantly higher in untreated diabetics with hypertension when compared to control ($p<0.0001$) respectively (Table 5).

Table 5. Mean ± SD, t-value and p-value of untreated DM/HTN subjects compared with control for all parameters (BMI, Systolic, Diastolic, Glucose and Anticardiolipin).

Group	Untreated DM/HTN (n=14)	Control (n=17)	t-value	p-value
BMI (kg/m²)	33.37± 4.36	24.08 ± 0.66	8.6961	<0.0001***
Systolic (mmHg)	152.5 ± 9.54	111.53 ± 4.91	15.4340	<0.0001***
Diastolic (mmHg)	96.79 ± 6.52	72.65 ± 7.49	9.4585	<0.0001***
Glucose (mmol/L)	9.85 ± 2.93	4.61 ± 0.54	7.2511	<0.0001***
Anticardiolipin	4.55 ± 1.11	1.39 ± 0.98	8.4167	<0.0001***

***Note**: * = significant at P<0.05; ** = significant at P<0.005; *** = significant at P<0.0001*

Table 6 showed the mean ± SD, t-value and p-value of Treated DM/HTN subjects compared with Untreated DM/HTN for all parameters (BMI, Systolic, Diastolic, Glucose and Anticardiolipin). The results obtained showed that BMI was insignificantly lower in treated hypertensive diabetics when compared to untreated hypertensive diabetics (p=0.0060). However, systolic and diastolic blood pressure were significantly lower in treated diabetics with hypertension compared to untreated hypertensive diabetics (p<0.05) respectively. Also, glucose and anticardiolipin were significantly lower in treated diabetics with hypertension compared to untreated diabetics with hypertension (p<0.0001) (Table 6).

Table 6. Mean ± SD, t-value and p-value of Treated DM/HTN subjects compared with Untreated DM/HTN for all parameters (BMI, Systolic, Diastolic, Glucose and Anticardiolipin)

Group	Treated DM/HTN (n=17)	Untreated DM/HTN (n=14)	t-value	p-value
BMI (kg/m²)	28.94± 3.95	33.37 ± 4.36	2.9658	0.0060
Systolic (mmHg)	143.94 ± 10.25	152.5 ± 9.54	2.3866	0.0237*
Diastolic (mmHg)	91.0 ± 5.77	96.79 ± 6.52	2.6224	0.0138*
Glucose (mmol/L)	4.99 ± 1.01	9.85 ± 2.93	6.4116	<0.0001***
Anticardiolipin	2.2 ± 1.08	4.55 ± 1.11	5.9544	<0.0001***

***Note**: * = significant at P<0.05; ** = significant at P<0.005; *** = significant at P<0.0001*

Only 2 out of the 57 recruited diabetic subjects were LE positive giving an overall positivity of 3.4%. 1 (5.8%) out of 17 subjects with treated complicated diabetes were LE cell positive and 1 (7.1%) out of 14 subjects with untreated ucomplicated diabetics were LE cell positive. LE cell positivity seems to be higher when diabetes is complicated with hypertension(Table 7).

Table 7. A table showing LE cell positivity between treated uncomplicated and complicated diabetes and untreated uncomplicated and complicated diabetes.

Group	No.	LE cell positivity	Percentage (%)
DMtr	15	0	0
Dmuntr	11	0	0
DMHTNtr	17	1	5.8
DMHTNuntr	14	1	7.1
Control	17	0	0

Treated Complicated Diabetes mellitus (DMHTNtr); Treated Uncomplicated Diabetes mellitus (DMtr); Untreated Complicated Diabetes mellitus (DMHTNuntr); Untreated uncomplicated Diabetes mellitus (DMuntr)

Blood glucose, BMI and ACA appears higher in male diabetics (whether complicated or uncomplicated) (figs 4, 5 and 6). On the other hand, biguanides (metformin) appears to be the preferred drug for diabetics as both glucose and ACA were lower than in patients who were placed on the other drug. Among the diabetics exhibiting high blood pressure, ACE inhibitors yeilded the most desirable results (Figures 7, 8 amd 9).

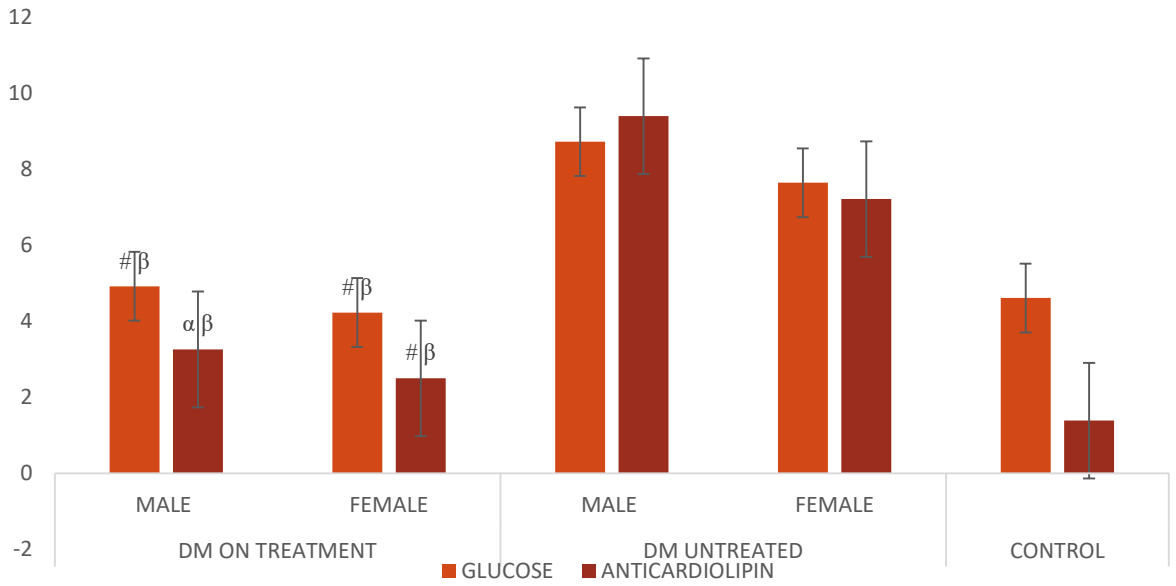

Figure 4. Glucose level and anticardiolipin in subjects according to gender in treated DM relative to untreated DM and control

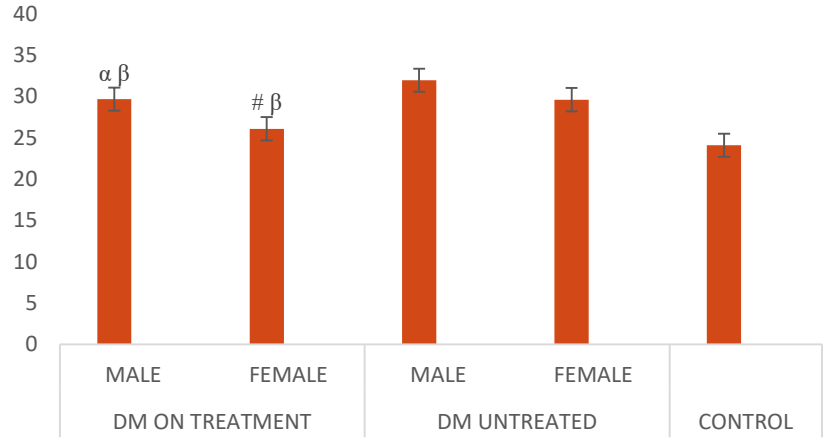

Figure 5. BMI of subjects according to gender in treated DM relative to untreated DM and control

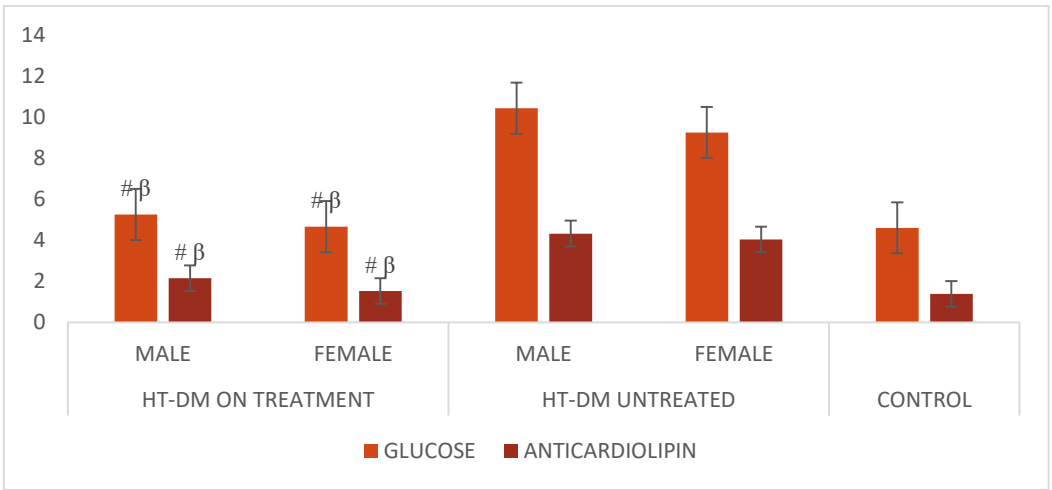

Figure 6. Glucose level and anticardiolipin of subjects according to gender in treated, untreated DM complicated with hypertension (DM/HTN) and control

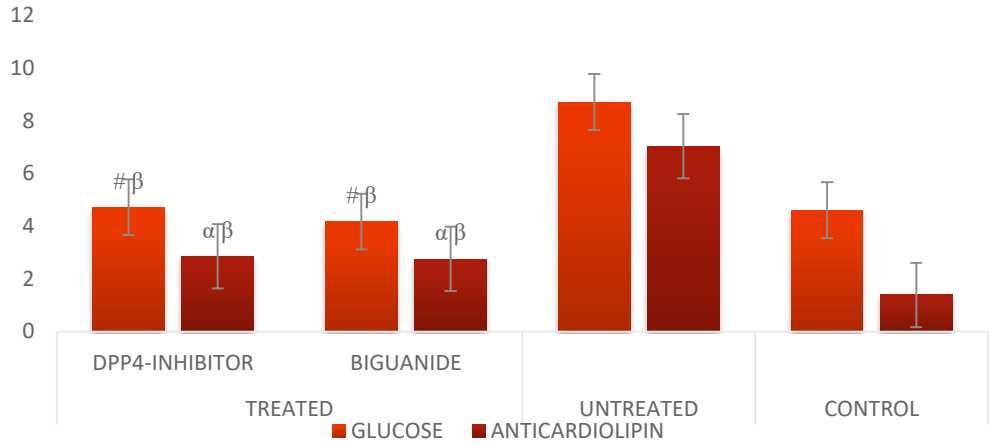

Figure 7. Effect of treatment in glucose and anticardiolipin in treated DM relative to untreated type 2 DM and control

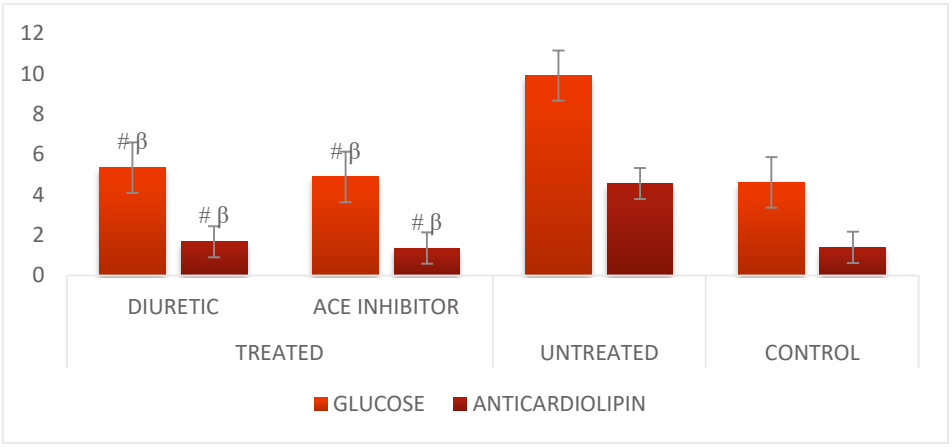

Figure 8. Effect of treatment on Glucose and Anticardiolipin in treated DM/HTN relative to untreated DM complicated with hypertension and control

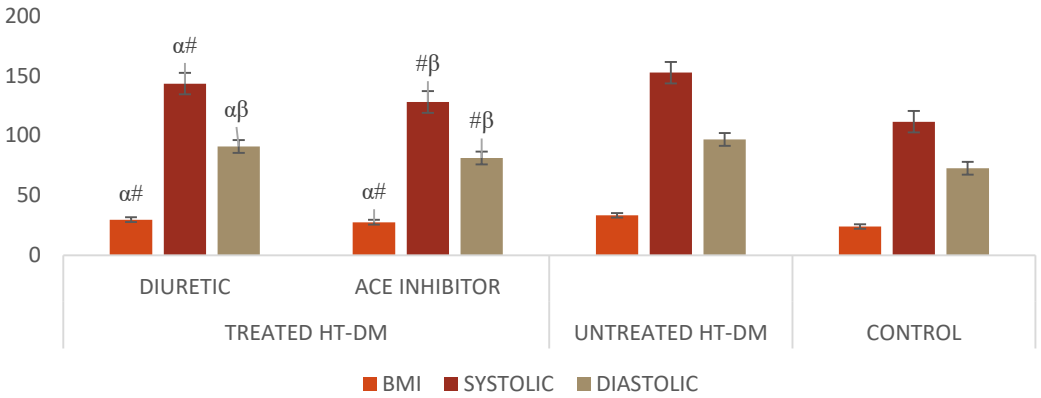

Figure 9. Effect of treatment on BMI, Systolic and Diastolic blood group in treated DM/HTN relative to untreated DM complicated with hypertension and control

DISCUSSION

Diabetes mellitus is a group of metabolic disorders characterized by persistent hyperglycemia [11]. The Global Burden of Disease research estimated 1.4 million deaths worldwide from diabetes in 2016, this gave a 31% result increase from 2006 [12]. Hypertension also known as high blood pressure is a long-term medical condition in which the blood pressure in the arteries is persistently elevated [13] have been known as a common co morbidity of type 2 diabetes. Diabetes increases blood pressure by decreasing blood vessels ability to stretch, increases the amount of fluid in the body and changes the way the body produces and handles insulin [14]. As both type 2 diabetes and coexistence of type 2 diabetes with hypertension has been theorized to have links with autoimmunity [15], this research has been designed to evaluate the serum level of Anticardiolipin Antibodies (ACA) and Lupus erythematosus (LE) positivity in addition to fasting blood glucose (FBG), Body Mass Index (BMI), Systolic blood pressure (SBP) and Diastolic blood pressure (DBP) in uncomplicated and complicated type 2 diabetes mellitus.

Body Mass Index (BMI), an individual's weight in kilograms divided by the square of height in meters (kg/m^2) [16] was seen to be significantly higher in treated and untreated uncomplicated diabetes compared to control. This finding is in line with the works of Medhi *et al*. [17], where body mass index was seen to be significantly higher in treated and untreated diabetics when compared to control. On the other hand, the finding of a higher and significant BMI of treated and untreated hypertensive diabetics compared to control together with a significantly lower BMI seen in treated diabetics with hypertension relative to their untreated counterparts lends credence to the works of Chaudhary *et al*. [18], where BMI was seen to be significantly higher in hypertensive diabetics than non-hypertensive diabetics. Obesity, hence high BMI have been stated as a most important risk factor of both diabetes and hypertension. On the basis of gender, male diabetics, whether complicated or not were seen to have higher BMI than females, a finding which is in line with the works of Zhang *et al*. [19], where male patients had a higher body mass index (BMI) may be due to the influence of sex hormones. BMI showed a fair pattern of increase with advancement in age a finding is in agreement with previous report [20]. This could be caused by a reduction in physical activity as age progresses.

Glucose, a simple sugar is released into the blood stream from metabolized food and carried into the cells for energy and storage by insulin [21]. In this research, the finding that glucose level is not only higher in diabetes patients than control but can also be much higher when diabetes is not well treated or managed on one hand supports earlier reports [1, 22-23], where poorer control of blood glucose was observed sequel to non-adherence to the guielines of type 2 diabetes management. On the other hand, the deleterious effect of vascular complications on the control of glucose also goes in line with other reports [24-25], where glucose level of hypertensive diabetics was significantly higher than nondiabetic hypertensive subjects. Diabetes have been associated with remodeling of the blood vessels thereby causing hypertension which in turn limits how the body handles glucose [14]. However, the finding that glucose appear higher in male diabetes subjects supports the finding of a higher BMI in males as seen above. It should be recalled that obesity is a risk factor for diabetes and it should not be surprising if BMI follows the same gender path with glucose. Glycaemic control has a pattern of dwindling with advancement in age in both complicated and uncomplicated diabetes, a finding that agrees with the works of Xiao *et al*. [27], where glucose was found to be higher in age group above 50 in diabetics and diabetic individuals with hypertension.

The systolic blood pressure (SBP) is that due to the pumping of the heart while the diastolic blood pressure is the measurement of forces as the heart relaxes to allow the blood flow into the heart [28]. Both systolic and diastolic pressure were observed to be significantly higher in both treated and untreated hypertensive diabetics when compared to control respectively, also systolic and diastolic blood pressure were significantly lower in treated hypertensive diabetics when compared to untreated hypertensive diabetics, this implies that treatment could be effective enough to reverse elevated blood pressure. This is in line with previous study [29-30], where systolic and diastolic blood pressure was seen to be significantly higher in complicated diabetes relative to control [29-30]. Across gender lines, hypertension was found to be significantly higher in male diabetics. It is noteworthy to state that this research is in line with previous works stating that ageing, obesity and diabetes as risk factors for the development of hypertension. The finding that blood pressure increases with advancement in age which agrees with various works [31-33] due to the fact that as we grow older blood vessels become stiffer and less elastic, resulting in a reduced diameter making the force per unit area inside them to rise. As seen in this research, several studies have demonstrated the linear relationship between systolic and diastolic blood pressure [31,34]. Zhou et al. [34] stated that systolic blood pressure and diastolic blood pressure are not only positively correlated but that the correlation is also linear", while the American Heart Association [31] supports the claim as long as both are within the range of blood pressures not alien to clinical practice [31].

LE cells are referred to as mature polymorphonuclear leukocytes which have phagocytosed the liberated nuclear material of another leukocyte [35]. In this research, it was observed that there is a nil incidence of LE cells in uncomplicated diabetes. contrarily, untreated hypertensive diabetics had a percentage of LE test positivity of 7.1 % as compared to the percentage in treated hypertensive diabetics having 5.8 % positive LE cells. Odewusi *et al*. (2021) [36] reported a

relationship between LE cell positivity and hypertension. As a result of these findings, it can be stated that while complicated diabetes is associated with increased LE positivity. The absence of proper management may accelerate or contribute to autoimmunity.

Anti-cardiolipin antibodies (ACA) are antibodies that are against cardiolipin, an important component of the inner mitochondrial membrane and constitute about 20% 0f its total lipid composition [37]. ACA are routinely found in immunocompromised patients whereby self-antibodies destroys self-antigens. In this research, the finding of a higher Serum ACA levels in treated and untreated as well as complicated diabetes compared to control respectively associates the antiphospholipid syndrome with diabetes. This finding of a higher ACA levels in complicated diabetes agrees with the higher LE cell seen in this group and is in agreement with previous study [37] which described a significantly higher frequency of autoimmunity in patients with types 1 and 2 diabetes than controls. However, serum ACA was seen to be higher in both diabetics and hypertensive diabetic male subjects when compared to females of same group respectively disagrees with Shahin *et al.* [38] where there was no significant association between ACA levels and sex or type of diabetes. Furthermore, it appears serum ACA showed a progressive increase with advancement in age. Moreover, Serum ACA was seen to be lowest in those treated with metformin and ACE inhibitors. Elevated anticardiolipin antibodies, hence a susceptibility to the antiphospholipid syndrome may be a complication of diabetes and its co morbidity. In fact this could be the likely reason why there is a higher likelihood of intravascular coagulation in type 2 diabetes subjects [39]. This could go on to explain the higher incidence of stroke and organ damage in diabetes patients.

CONCLUSION

This research concluded that serum increased ACA levels as well as LE positivity are possible associates of diabetes mellitus. It also found out that ACA levels increase with age, BMI. and being of the male gender as well as complication in type 2 diabetes patients

Conflict of Interest

There are no financial personal, or professional conflicts of interest to declare.

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