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PLASMA FIBRINOGEN: A CARDIOVASCULAR RISK BIOMARKER IN TYPE 2 DIABETES MELLITUS SUBJECTS

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ABSTRACT

Diabetes mellitus is a public health disease considered as metabolic and endocrine disorder that has been involved in cardiovascular episode. Fibrinogen, a glycoprotein has been incriminated as a risk factor of cardiovascular disease. This study aims to evaluate the plasma fibrinogen concentration of type 2 diabetes mellitus subjects in Agbor, Nigeria. A total of three hundred and ninety six (396) respondents were recruited into the study which comprises of three hundred and six (306) type 2 diabetes mellitus and ninety (90) age and sex matched apparently healthy subjects as controls. Five milliliters (5ml) of venous blood was collected aseptically with minimum stasis and dispensed into appropriate containers. Plasma fibrinogen concentration was evaluated using standard methods while statistical package for social sciences was employed to determine difference in mean ± standard deviation using student t test. Diabetes mellitus subjects exhibit a significantly ($p<0.050$) higher plasma fibrinogen than apparently healthy subjects when compared. Also, male diabetes mellitus show a significantly ($p<0.05$) higher plasma fibrinogen than female diabetes mellitus subjects when compared. In the same vein, male apparently control subjects show significantly ($p<0.05$) than female apparently control subjects when compared but there is no significant ($p>0.05$) difference observed in the age of all respondents. It is therefore pertinent to state that type 2 diabetes mellitus are prone to cardiovascular disease as well as the male gender. It is therefore recommended that plasma fibrinogen should be done regularly for diabetes mellitus subjects as well as life-style modification to prevent excess mortality.

Keywords: Diabetes mellitus, Plasma fibrinogen, cardiovascular disease, Nigeria

INTRODUCTION

Diabetes mellitus is a metabolic disorder which results from endocrine failure that may be due to absent of insulin or insensitivity of the insulin receptors to glucose thereby leading to hyperglycemia. The global prevalence of diabetes mellitus has risen drastically over the past two decades and this is expected to increase especially type 2 diabetes mellitus due to increase prevalence of obesity, modified nutrition and reduced physical activity (Alvin 2001). A prevalence of 2.2% was reported in 1992 in Nigeria but this rose to 5.77% in 2018 as reported by Uloko et al. (2018) in their systemic review. The highest prevalence of 9.8% was obtained from the south south geopolitical zone while the lowest prevalence of 3.0% was from the North West zone (Uloko et al., 2018).

Fibrinogen is a soluble glycoprotein also known as clotting factor 1 due to its involvement in coagulation process as a precursor of fibrin. It is made up of six polypeptide chains of two alpha (α), two beta (β) and two gamma (γ) chains and linked together by disulphide bond (Chatterjea and Shinde, 2007).

Evidence has shown that diabetes mellitus has a stronger tendencies towards cardiovascular diseases (Adu et al., 2015). Jain and colleagues (2001) observed that cardiovascular complications account for about 50% of death among type 2 Diabetes mellitus and about 25% in type 1 diabetes mellitus subjects. Selvin et al., (2010), opined that people with pre-diabetes and diabetes have a substantially elevated risk for cardiovascular disease. Previous authors in their various studies have observed that diabetes mellitus subjects have higher cardiovascular morbidity than non-diabetes mellitus subjects due to the haemostatic factor hyperfibrinogenemia that is implicated as a source of atherosclerosis and its complications (Wilhelmsen et al., 1984, Thompson and Smith, 1989, Ernst and Ludwig, 1993). Bembde (2012) in his study observed that cardiovascular risk in diabetes mellitus may be linked to fibrinogen due to haemostatic disorders. Earlier authors have observed that blood fibrinogen concentration may be genetically determined and influence by a lot of environmental or life style factors (Cook and Ubben 1990, Ernst 1993). There is paucity of data on plasma fibrinogen level in diabetes mellitus in this locality hence this study aim to evaluate the plasma fibrinogen concentration in type 2 diabetes mellitus subjects and possibly use it a cardiovascular risk biomarker.

MATERIALS AND METHODS

Study area

This study was carried out among patients attending the Diabetic Clinic of Central Hospital, Agbor. Agbor is the administrative headquarter of Ika South local Government area and second largest urban town in Delta North Senatorial District of Delta State in South South, Nigeria.

Sample Size Determination

The sample size was calculated as 299 due to prevalence of diabetes mellitus of 9.8% as reported by Uloko et al., (2018) in southern Nigeria using the formula proposed by Araoye and colleagues (2003).

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

Where:
N = Minimum sample size
Z = Standard normal deviation corresponding to 95% confidence interval =1.96
P = proportion of diabetes from a previous study
q = complimentary probability = (1-p)
d= degree of precision =0.05

$$N = \frac{2\ (1.96)^2 \text{ X } 0.098 \text{ X } 0.902}{(0.05)^2}$$

$$N = \frac{2(3.8416) \times 0.098 \times 0.902}{0.0025}$$

$$N = \frac{7.6832 \times 0.098 \times 0.902}{0.0025}$$

$$N = \frac{0.67916}{0.0025} = 271.66.$$

With 10% attrition of 27.2, therefore minimum sample size will be 299.

Study population

A total of three hundred (396) respondents were recruited for this study which comprises of three hundred and six (306) diabetic subjects attending the diabetic clinic and ninety (90) sex and age matched apparently healthy subjects were used as control.

Ethical clearance and Informed consent

Ethical clearance was obtained from the ethical committee of Central Hospital, Agbor while informed consent was taken from the subjects after properly explaining the procedure and protocol of the study to them.

Inclusion and exclusion criteria

Inclusion criteria includes both male and female who had been confirmed type 2 diabetic patients without any other underline ailment, non- alcoholics, non- smokers and not pregnant women who visited the diabetic clinic of Central Hospital, Agbor while exclusion criteria are alcoholics, Smokers and Pregnant women and those that are not diabetes.

Sample Collection

After an overnight fast and using aseptic precautions, 6ml of venous blood was collected from the medial cubital vein from each of the subjects and controls into a citrated container and fluoride oxalate containers. The blood in citrated containers was used for fibrinogen estimation while the blood sample in the fluoride oxalate containers was used for the analysis of blood glucose immediately to confirm diabetes status of subjects.

Biochemical analysis

Plasma fibrinogen concentration was determined using clot – weight method of Ingram (1952) while fasting blood glucose was analysed using Glucose Oxidase Peroxidase method developed by Trinder (1969) using Randox reagent. Manufacturer's instructions were strictly followed in all procedures with control samples added to ensure quality control.

Statistical analysis

Data generated from analysis were analyzed statistically using Statistical Package for Social Sciences (SPSS) IBM, Chicago, version 21.0. The mean ± standard deviations and student t test was used to evaluate difference in means with significant difference is at <0.05.

RESULTS

Figure 1 shows the distribution of respondents with diabetes mellitus having 77% (306) of the total number while the controls are made up of 23% (90) of the respondents.

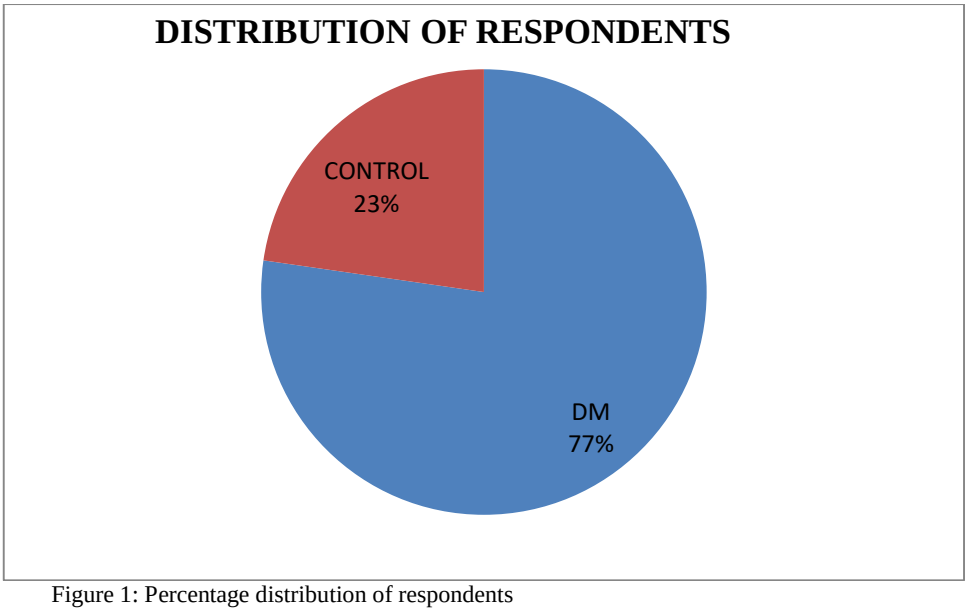

Figure 1: Percentage distribution of respondents

A total of three hundred and six (306) diabetes mellitus with female subjects having 65% (198) and male subjects 35% (108).

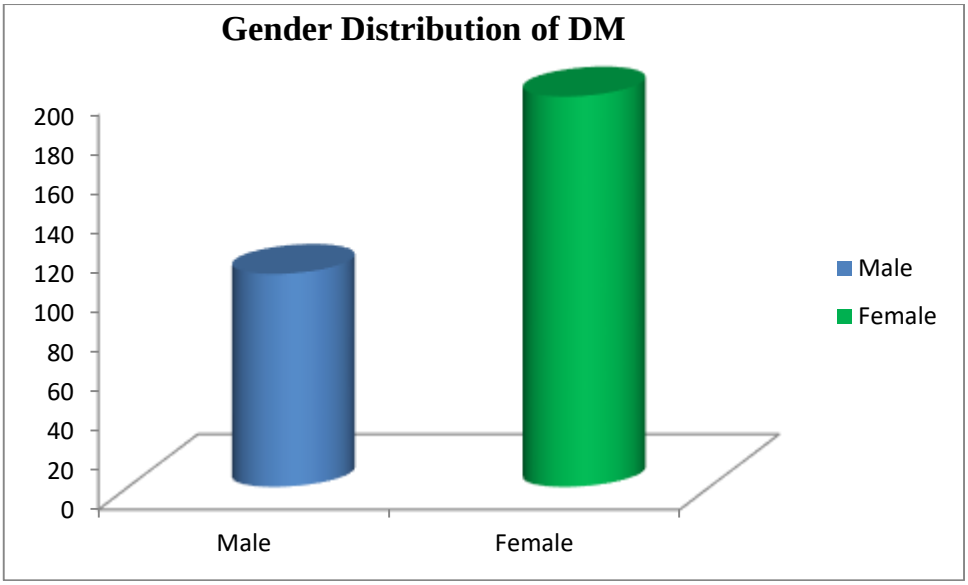

Figure 2: Sex distribution of Diabetes mellitus subjects

A total of ninety (90) of apparently healthy subjects were used as controls with female subjects having 63% (57) and male subjects 37% (33).

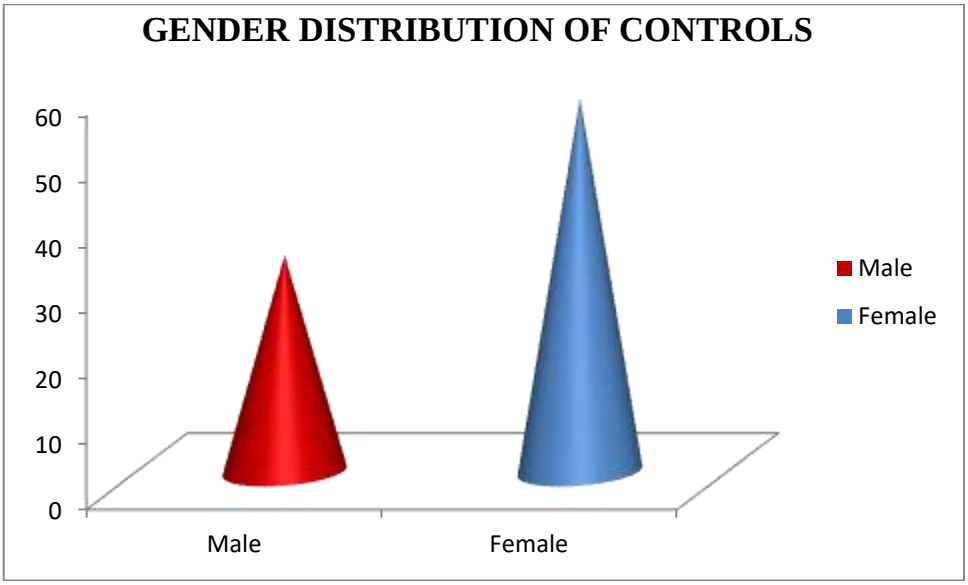

Figure 3: Gender distribution of control subjects

There was no significant (p>0.05) difference observed in the age of both diabetes mellitus and apparently healthy subjects used as controls when compared. However, diabetes mellitus shows a significantly (p<0.05) higher plasma fibrinogen concentration than apparently healthy subjects when compared as shown in table 1 below.

Table 1: Plasma fibrinogen concentration of Diabetes mellitus and control subjects

	DM (n=306)	Controls (n=90)	Significance
Age (Years)	54.43±7.72	54.13±8.29	p>0.05ǂ
Fibrinogen(g/dl)	5.45±1.86	3.69±0.72	p<0.05*

There was no significant (p>0.05) difference observed in the age of both male and female diabetes mellitus when compared. However, male diabetes mellitus shows a significantly (p<0.05) higher plasma fibrinogen concentration than female diabetes mellitus subjects when compared as shown in table 2 below.

Table 2: Plasma fibrinogen concentration of male and female Diabetes mellitus subjects

	Male DM (n=108)	Female DM (n=198)	Significance
Age (Years)	54.23±3.69	52.46±4.26	p>0.05ǂ
Fibrinogen(g/dl)	5.87±1.48	4.46±1.68	P<0.05*

There was no significant (p>0.05) difference observed in the age of both male and female control subjects when compared. However, male control subjects shows a significantly (p<0.05) higher plasma fibrinogen concentration than female control subjects when compared as shown in table 3 below.

Table 3: Plasma fibrinogen concentration of male and female control subjects

	Male Control (n=33)	Female Control (n=57)	Significance
Age (Years)	53.69±6.42	53.23±5.37	p>0.05ǂ
Fibrinogen(g/dl)	4.50±1.72	3.76±0.51	P<0.05*

DISCUSSION

Diabetes mellitus has been considered a public health concern globally due to its multisystemic nature and the debilitating effect on the individuals. This study seeks to evaluate the plasma fibrinogen in diabetes mellitus and possibly use it as a cardiovascular biomarker. There was no significant (p>0.05) difference observed in the age of both diabetes mellitus and apparently healthy subjects when compared. This is in contrast with the report of Jain et al., (2001) which associated hyperfibrinogenemia with age of the individuals in their study. There was a significantly (p<0.05) higher plasma fibrinogen concentration in diabetes mellitus subjects when compared with non-diabetic apparently healthy subjects. This is in tandem with the previous report by earlier authors (Jain et al., 2001, Bembde 2012 and Gupta et al., 2016) that had similar findings. In an earlier study, previous authors observed that glucose impairment enhances thrombogenic factors like fibrinogen in diabetes mellitus (Kannel et al., 1987) which suggest that there is a linkage between hyperfibrinogenemia and cardiovascular risk. Bruno et al., (1996) observed that fibrinogen plays a role in the early formation of plaque as well as late complications of cardiovascular disease. In earlier studies, it was observed that haemostatic factor such as hyperfibrinogenemia has been incriminated as a source of atherosclerosis and its complications (Wilhelmsen et al., 1984, Thompson and Smith 1989). Vorster and colleagues (1998) in their study observed that fibrinogen level >3.5g/dl is a stronger risk factor for stroke than hypertension. This may be a contributing factor for the high rate of mortality observed among diabetes mellitus subjects.

There was a significantly (p<0.05) higher plasma fibrinogen in male subjects (both diabetes mellitus and controls) when compared with female subjects. This is in a variance with the report of Vorster et al., (1998), though find a higher fibrinogen in female but not statistically significant when compared with their male counterparts. This higher fibrinogen in male subjects may be attributed to increase level of stress, cigarette smoking and intake of alcohol among male subjects especially in Africa setting like Nigeria.

In conclusion, it has been observed that diabetes mellitus subjects have higher plasma fibrinogen levels which may contribute to unexpected high stroke rate and excess mortality among them. Also, male subjects are equally at higher propensity of developing cardiovascular disease due to high fibrinogen concentration in them as a result of increase stress, alcohol intake as well as cigarette smoking. It is therefore, pertinent to recommend that plasma fibrinogen should be added as a routine test menu for diabetes mellitus and there should be modification of life- style for healthy living.

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