IJPSR (2021), Volume 12, Issue 4 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 03 April 2020; received in revised form, 09 October 2020; accepted, 11 October 2020; published 01 April 2021

EVALUATION OF THE SERUM LEVELS OF SOME TRACE ELEMENTS AND ANTIOXIDANT LEVELS IN APPARENTLY HEALTHY INDIVIDUALS WITH FAMILY HISTORY OF TYPE 2 DIABETES IN NNEWI, NIGERIA

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Keywords:

Trace elements, Antioxidants, Plasma glucose, Type2 diabetes mellitus, Family history of type2 diabetes mellitus, Body mass index

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ABSTRACT: There is a paucity of data on studies evaluating trace elements and antioxidant levels and susceptibility of offspring of diabetic parents to type 2 diabetes in Nigerian population. This study evaluated the serum level of some trace elements and antioxidants among apparently healthy individuals with a family history of type2 diabetes mellitus (FH-T2DM). This was a cross-sectional study involving 122 Students (aged between 18-30 years) consisting of 60 apparently healthy subjects with FH-T2DM and 62 apparently healthy subjects without FH-T2DM. Serum levels of Cr, Zn, Se, and Mn and catalase and superoxide dismutase of these subjects were measured using atomic absorption spectrophotometric technique and spectrophotometric technique, respectively. The plasma glucose, body mass index (BMI), waist circumferences, and a waist-to-hip ratio of these subjects were also determined using standard methods. Results from this study showed that mean fasting plasma glucose level was significantly higher (p=0.001); serum levels of Cr was significantly lower (p=0.04) while serum levels of Zn, Mn, Se, SOD and Catalase did not differ significantly (p>0.05) in those with FH-T2DM when compared with those without the FH-T2DM. There were no significant differences in the BMI (*P* = 0.236), WHR (P=0.794) between FH-T2DM and those without FH-T2DM. However, selenium was significantly higher in male offspring of diabetic mothers compared to female offspring of diabetic fathers (p=0.015), and catalase was significantly lower in males from diabetic mothers compared to males from diabetic fathers (p=0.009). This finding may imply that males from diabetic mothers may be at a greater risk of developing diabetes in the future, considering the respective roles of the trace elements and antioxidants in glucose metabolism.

INTRODUCTION: Family history of specific diseases reflects the consequences of genetic susceptibility, shared environment, and common behaviors [1, 2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(4).2108-16

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(4).2108-16

Family history is a non-modifiable risk factor for diabetes mellitus, which, when present, might influence the probability of a suspected diagnosis [3, 4]. Family history taking is essential in the practice of preventive medicine to assess disease risk and influence early detection and prevention strategies [5]. Professional guidelines for clerking of patients usually include family history to assess health risk, initiate interventions, and motivate behavioral changes [6]. It may provide a useful screening tool for detection and prevention of diabetes [5].

In a study among adult Chinese, it was reported that sufficient physical activity and negative family history of diabetes might jointly reduce the risk of developing hyperglycemia and T2DM [7]. In the US population, family history of diabetes showed significant, independent, and graded association with the prevalence of diabetes [8]. This association points to the possibility of formally adding family history to public health strategies aimed at detecting and preventing the disease [8].

Diabetes mellitus is a metabolic disorder that affects carbohydrate, fat, and protein metabolism, which could result from defects in insulin secretion, insulin action, or both [9]. It is a chronic metabolic disease resulting from the diminished or absent secretion of insulin or due to reduced tissue sensitivity to insulin and has a global health burden especially in developing countries like Nigeria [9, 10].

International Diabetes Federation (IDF), in 2017, estimated that 425 million adults were living with diabetes, and further, it is estimated to affect up to 629 million people by the year 2045 [11]. Diabetes Mellitus has become a major public health problem in Nigeria, accounting for a prevalence of 2.4%, with a total number of mortality amounting to 3028 deaths in 2017 [11], with type 2 diabetes making up about 90% of the cases. This indicates a pandemic in full flight, and the greatest increase in rates is expected to occur by the year 2030 [12].

Research has shown that an imbalance of some essential metals might adversely affect pancreatic islet and cause the development of diabetes [13]. It has also been reported that there is a relationship between diabetes mellitus and trace elements in many with an alteration in the metabolism of these minerals [14]. Insulin action has been shown to be influenced by some trace elements like chromium, magnesium, vanadium, zinc, manganese, molybdenum and selenium [14]. Proposed mechanisms of enhancement of insulin action by trace elements include activation of insulin receptor sites [15], serving as cofactors or components for enzyme systems that are involved in glucose metabolism [16], increasing insulin sensitivity, and acting as antioxidants for preventing tissue peroxidation [17].

Zinc activates β cells for the production of insulin and increases insulin signals in the muscle through activation of phosphatidylinositol 3-kinases (PI3-KAKT) pathway and Glucose transporter4 GLUT4 [18]. Zinc is essential for insulin synthesis and release, and its deficiency seems to impair release of insulin [19]. Growing evidence suggests that chromium supplementation, particularly at higher doses and in the form of Chromium Picolinate, may improve insulin sensitivity and glucose metabolism in patients with glucose intolerance and type 1, type 2, gestational, and steroid-induced diabetes and in some individuals without diabetes [20, 21]. Selenium has been known to possess cytoprotective properties as a result of its ability to upregulate antioxidant selenoenzymes. Thus, it was believed that Se supplementation could prevent the onset of metabolic diseases, such as type 2 diabetes (T2D), by counteracting oxidative stress [22, 23]. Several studies have revealed selenium to be an insulin-mimetic, because it plays roles in the regulation of enzymes in the insulin signaling cascade, the expression of lipogenic enzymes, and carbohydrate metabolism in the liver [24, 25].

Manganese (Mn) has an important role in the phosphorylation reactions of glucose and its metabolism. Its deficiency has been implicated in insulin resistance, carbohydrate intolerance, dyslipidaemia, and complications of diabetes [26]. It is an essential micronutrient required for normal carbohydrate, lipid, and protein metabolism. As a major antioxidant due to its mitochondria matrix localization, MnSOD plays a critical role in protecting mitochondria and islets from elevated reactive oxygen species (ROS), which may serve as an important trigger of insulin resistance and type 2 diabetes [26, 27].

Oxidative stress has been shown in some experimental models to negatively impact insulin secretion, thus increasing insulin resistance. This may play a causal role in the pathogenesis of diabetes [28].

Overweight and obese individuals are at increased risk for many diseases and health conditions, including the following: Hypertension, Dyslipidemia, and Type 2 diabetes. Increased waist circumference is also closely associated with an increased risk of diabetes [29]. Therefore, high waist circumference (WC), waist-hip ratio (WHR), body mass index (BMI), and age are risk factors as well as predictors of type 2 diabetes mellitus [30].

The development of type 2 diabetes is caused by a combination of lifestyle and genetic factors [9]. Although some of the risk factors of diabetes mellitus, such as diet and obesity, could be modifiable through dietary management and physical activity, others such as increasing age and genetics non-modifiable risk factors. Oxidative stress impacts negatively on insulin secretion resulting in insulin resistance, and may thus play a causal role in the pathogenesis of diabetes [28]. The pancreatic islets contain relatively small amounts of the antioxidant enzymes, Copper-Zinc Superoxide Dismutase (CuZn-SOD), Manganese Superoxide Dismutase (Mn-SOD), catalase, and glutathione peroxidase (GPx). This unusual situation sets up the β-cell as an easy target for ROS, whether generated by interactions with cytokines or too much glucose [31]. Research has shown that the imbalance of some essential metals might adversely affect pancreatic islet and cause the development of diabetes [32, 33]. Therefore, this study was designed to investigate and compare the glucose, trace elements, antioxidant levels, and BMI of those healthy individuals with a family history of DM Type 2 and that of those without a family history. This study will provide information on the way to reduce or ameliorate the conditions that predispose individuals to alterations of mineral elements and oxidants that may lead to the development of diabetes in the future, especially for individuals with a family history of Type 2 diabetes.

MATERIALS AND METHODS:

Study Design: This is a cross-sectional study that was designed to evaluate the serum levels of some trace elements and antioxidant levels in apparently healthy individuals with a family history of type2 diabetes in Nnewi, Nigeria.

Target Subjects: The subjects were students (aged between 18-30 years) consisting of 122 individuals, 60 apparently healthy subjects with a family history of type 2 diabetes (35- fathers and 25- mothers diabetics), and 62 apparently healthy subjects without a family history of type 2 diabetes.

Inclusion Criteria: Inclusion criteria included First degree relatives with a family history of type 2 diabetes, individual between the age of 18-30 years, males and females with one parent or more parents being positive to type 2 diabetes who were healthy and not on any special diets were recruited for the study.

Exclusion Criteria: Exclusion criteria included Individuals- males and females whose parents never had type 2 diabetes at the time of this research and who were below the age of 18 and above 30 years of age were also excluded from the study.

Sampling Technique and Administration of Questionnaire: The subjects were selected by simple random sampling technique with Questionnaire which included questions such as age, sex, family history of diabetes, *etc*.

Ethical Approval and Consent: Ethical approval letter (dated 19/10/2016) was obtained from the Ethics Committee of the Faculty of Health Sciences Nnamdi Azikiwe University Nnewi campus. The consent of the participants was sought and obtained before the commencement of the study.

Blood Sample Collection and Storage: Seven milliliters (7ml) of venous blood was collected from each of the participants after an overnight fast of 12 hours. Two milliliters (2mls) of the blood was dispensed into fluoride oxalate bottles for glucose estimation. The remaining sample was dispensed into a plain bottle and allowed to clot, retracted and serum separated and stored at -20 °C for two months until analyzed. The stored aliquots were used for trace elements and antioxidants estimations.

Anthropometric Measurements: Height and weight were measured using a calibrated stadiometer and portable weighing machine (SH 2003B), respectively. The height and weight were recorded to the nearest centimeters and kilograms, respectively. Body mass index (BMI) was obtained through a calculation using the formulae:

$$\text{BMI} = \text{Weight (kg)} \div \text{height}^2 (\text{m}^2).$$

Waist circumference (WC) was also measured using non elastic flexible tape in the standing position. Waist-hip ratio (WHR) was calculated as waist circumference divided by hip circumference.

Quality Control Measures: Quality control sera were run alongside tests in each batch of analysis and their results were compared to the

manufacturer's control range and found to be within the acceptable limit.

Methods of Sample Analysis:

Determination of Plasma Glucose: This was done using **the** Glucose oxidase method (GOD-POD) RANDOX according to the method described by Stein [34].

Determination of Trace Elements: Trace elements (Manganese, Selenium, Chromium, and Zinc) were assayed by Atomic Absorption Spectro-photometry [35].

Determination of SOD Activity: This was determined using the method as described by Misra and Fredovich [36].

Determination of Catalase Activity: Catalase activity was determined using the method as described by Sinha [37].

Statistical Analysis: Statistical Package for Social Sciences (SPSS) version 20 software was used to analyze the data obtained in this study. The statistical tools used to analyze the data obtained in this study were the Student independent t-test, One Way Anova, and PostHoc. Values were expressed as mean ± SD, and the results obtained were considered significant at $p \leq 0.05$.

RESULTS: Table 1 shows the serum levels of Trace elements, Antioxidant levels, and anthropometric characteristics of those with a family history of type 2 diabetes and those without a family history of diabetes. The mean plasma levels of fasting plasma glucose of those subjects with a family history of type2DM and those without a family history of T2DM were (4.5±0.4 and 4.2±0.4) respectively. This result showed that the fasting blood glucose was significantly higher in those with a family history of T2DM (P=0.001) when compared to those without a family history of diabetes type 2. The mean serum levels of Chromium of subjects with a family history of type 2 diabetes and those without family history were (0.16±0.10 mcg/l and 0.25±0.22 µg/L) respectively. This result shows that the mean levels of chromium were significantly lower in subjects with a family history of T2DM (P= 0.004) compared to the control subjects. The mean serum levels of their Zinc were 959.6±94 µg/L and 981.8±95 µg/L, respectively. The result of their zinc levels showed no significant difference when compared (p=0.220). The mean levels of manganese and selenium of the subject with family history of type2DM and the control subjects were (0.8±0.45 µg/L and 0.88±0.52 µg/L) and (109.4±35.7 µg/L and112.8 ±36 µg/L) respectively. The results of their mean levels of Manganese and Selenium showed no significant difference when compared (p=0.768 and p=0.411) respectively. The serum mean levels of Superoxide Dismutase and Catalase of those with family history of T2DM and those without family history are (6.8±1.4 and 6.8±1.5 U/mL) and (27.2±7.2 and 29±10.3) respectively. These results showed no statistical significant difference when compared (p=0.849 and p= 0.270) respectively. The mean values of the BMI of the subjects with family history of diabetes and those without the family history were 25.5±2.5 and 24.9±3.5 respectively. The mean values of WHR of those with family history of diabetes type2 and the control were 0.79±0.04 and0.79± 0.03 respectively. There was no statistically significant difference in the values of the Anthropometrical (BMI AND WHR) assessments between subjects with family history of T2DM compared with those without family history of T2DM (p= 0.236 and 0.794) respectively.

Table 2 shows the serum levels of Trace elements, antioxidants and anthropometric features of the study population of subjects whose fathers have diabetes mellitus type2 and those whose mothers have type2 diabetes mellitus according to history.

The mean plasma levels of glucose in subjects whose mothers have T2DM and those whose fathers have T2DM were (4.5±0.4 and 4.49±0.38) respectively. The result of their mean plasma levels of glucose showed no statistical significance when compared (p=0.936). The mean serum levels of their chromium were 0.15±0.10 and 0.16±0.10) respectively. The result of their chromium levels showed no significance when compared (p=0.732). The mean serum levels of their Zinc were 981±66 µg/L and 983±107 µg/L, respectively. The result of their zinc levels showed no significant difference when compared (p=0.224). The mean levels of manganese and selenium in the subjects whose mothers have T2DM and those whose father have type2 DM are (0.9±0.47 µg/L and 0.7±0.4 µg/L)

and (121.6±35 µg/L and 100.8±34 µg/L) respectively. The results of their mean levels of Manganese and Selenium showed no significant difference when compared (p=0.490 and p=0.278) respectively.

The mean serum levels of Superoxide Dismutase and Catalase of those whose mother were positive to T2DM and those whose fathers were positive to T2DM were (6.6±1.1 and 6.9±1.5) and (24.5±5 and 29±27) respectively. These results showed no statistical significant difference when compared (p=0.440 and p= 0.11) respectively.

The mean values of the BMI of the subjects who have positive mother T2DM and those who have positive father T2DM were 25.2±2.6 and 25.8±2.4 and their mean values of WHR were 0.79±0.05 and 0.79± 0.03 respectively. There was no statistically significant difference in the values when compared (p= 0.332 and 0.656).

Table 3 Shows sex distribution of some parameters of the first generation offspring of type 2 diabetic parents.

The mean plasma levels of fasting blood glucose (FPG) of females from diabetic mothers (fm) (4.5±0.5) and males from diabetic mothers(mm) were 4.48±0.3, and mean plasma levels of fasting blood glucose (Fpg) of females from diabetic fathers (ff) and males whose fathers (mf) were positive to type 2 Diabetes mellitus were (4.5±0.37 and 4.47±0.4) respectively. This result showed no statistical significance when compared (p=0.982).

The mean serum levels of chromium of (Fm) (0.13±0.09) males (Mm) whose mothers were positive to type2 Diabetes mellitus (0.18±0.11) and the mean serum levels of chromium of females(Ff) and males (Mf) whose fathers were positive to type 2 Diabetes mellitus were (0.18±0.10 and 0.15±0.10) respectively. The result of their mean serum chromium levels was significantly lower when compared (p=0.536). The mean serum levels of Zinc of Fm and Mm were 987±56 µg/L and 975±80 µg/L respectively, and that of Ff (942±103 µg/L) and Mf (945±113 µg/L) and the result of their zinc levels showed no significance when compared (p=0.448).

The mean serum levels of manganese of Fm (0.9±0.5mcg/l) Mm (0.9±0.40 µg/L) Ff (0.7±0.4 µg/L) and Mf were (0.73±0.40 µg/L) and selenium of Fm (115±29 µg/L), Mm (130±41 µg/L), ff (95.4±29 µg/L) and mf (105±35 µg/L) respectively. The results of their mean levels of Manganese showed no significant difference when compared (p=0.260). However, the mean serum levels of selenium of mm were significantly higher when compared with ff (p=0.015).

The serum mean levels of Superoxide Dismutase of (Ff) and males (Mf) were (7.±1.6 and 6.8±1.4) U/mL, and serum mean levels of Superoxide Dismutase females (FM) and males (Mm) with positive T2DM mothers were (7.1±1.1 and 6.0±0.9) These results showed no statistical difference when compared (p=0.367). The serum mean levels of Catalase of fm and ff were (25.7±6.7 and 28.±6.5U/L), and the serum mean levels of mm and mf were (23±5 and 30±8) U/L, respectively. Furthermore, the mean serum levels of catalase of mm were significantly decreased compared to mf (p=0.009).

TABLE 1: FASTING PLASMA GLUCOSE, SERUM TRACE ELEMENTS, ANTIOXIDANTS LEVELS AND ANTHROPOMETRIC PARAMETERS OF HEALTHY INDIVIDUALS WITH FAMILY HISTORY OF TYPE2 DIABETES MELLITUS AND THOSE WITHOUT FAMILY HISTORY OF TYPE 2 DIABETES (MEAN AND STANDARD DEVIATION)

Parameters	DM History N=60	CONTROL N=62	t-test	p-value
Fasting plamsa glucose (mmol/L)	4.5±0.4	4.2±0.3	-3.66	0.000
Chromium (µg/L)	0.16±0.10	0.25±0.22	2.969	0.004
Zinc (µg/L)	959±94	981±94	1.234	0.220
Mn (µg/L)	0.88±0.46	0.87±0.55	0.768	0.444
Selenium (µg/L)	109.5±36	112±35.5	0.411	0.682
Superoxide Dismutase (U/ml)	6.8±1.4	6.9±1.5	0.191	0.849
Catalase (U/ml)	27.2±7.2	29±10.3	1.109	0.270
BMI kg/m^2	25.5±2.5	24.9±3.5	-1.109	0.236
WHR	0.79±0.04	0.79±0.03	0.262	0.794

Significance=≤0.05, Mn=Manganese, BMI=Body Mass Index, Fpg=fasting plasma glucose, mcg/l= Microgram per litre, IU/ml= International unit per millitre

The mean values of the BMI of the Fm and Mm were 25±3 and 25.5±2.4, and the mean of their WHR were 0.8±0.05 and 0.79±0.03 respectively, while that of Ff and Mf were 25.3±3.7 and 25.5±2.9 for BMI and 0.79±0.03 and 0.8±0.03 for their WHR. The result showed no statistical significance when compared (p= 0.585 and 0.893).

TABLE 2: FASTING PLASMA GLUCOSE, SERUM TRACE ELEMENTS, ANTIOXIDANT LEVELS AND ANTHROPOMETRIC PARAMETERS OF HEALTHY INDIVIDUALS WITH FAMILY HISTORY OF TYPE2 DIABETES MELLITUS

Parameters	Type2history due to Mother N=25	Type2history due to Father N=35	t-test	p-value
Fasting blood Sugar (mmol/L)	4.5±0.4	4.4.9±0.38	0.080	0.936
Chromium (µg/L l)	0.15±0.10	0.16±0.10	-0.377	0.732
Zinc (µg/L)	981.8±66	943±107	1.682	0.098
Mn (µg/L)	0.9±0.47	0.7±0.4	2.016	0.49
Selenium (µg/L)	121.6±35	100.8±34	50.8	0.278
Superoxide Dismutase (U/ml)	6.6±1.1	6.9.±1.5	-778.	0.440
Catalase (U/ml)	24.5±5	29±7	56.418	0.110
BMI kg/m^2	23.7±3.5	25±3.3	48.652	0.332
WHR	0.78±0.03	0.80±0.03	37.035	0.6567

P≤0.05 is significant

TABLE 3: SEX DISTRIBUTION OF SOME PARAMETERS OF THE FIRST GENERATION OFFSPRING OF TYPE-2 DIABETIC PARENTS

Groups	FPG	Chromium	Zinc	Manganese	Selenium	SOD	CAT	BMI	WHR
FM n=14	4.5±0.5	0.13±0.09	987±56	0.9±0.5	115±29	7.0±1.1	25.7±6.8	25±3	0.8±0.05
MM n= 11	4.48±0.3	0.18±0.11	975±80	0.9±0.4	130±41	6.0±0.9	23±5	25.5±2.4	0.79±0.04
FF(n=15)	4.5±0.4	0.18±0.10	942±103	0.7±0.4	95.4±29	7.0±1.6	28±6.5	25.5±2.5	0.78±0.03
MF(n=20)	4.4±0.4	0.15±0.10	945±113	0.7±0.4	105±35	6.8±1.4	30±8.0	25.5±2.9	0.79±0.04
FM vs	P=0.846	P=0.270	P=0. 751	P=0. 852	P=0.287	P=0.110	P=0. 348	P=0.549	P=0.613
MM	P= 0.970	P=0. 215	P=0.207	P=0. 144	P=0. 133	=0.720	P=0. 082	P=0.571	P=0.447
FM vs FF	P=0.760	P=0. 665	P=0. 206	P=0. 107	P=0. 406	P=0.857	P=0. 076	P=0.173	P=0.641
FM vs MF	P=0.940	P=0. 432	P=0. 401	P=0. 192	P=0. 058	P=0.121	p=0. 009	P=0. 529	P=0.912
MM vs MF	P=0.725	P=0.361	P=0. 934	P=0. 955	P=0. 425	P=0.	p=0. 371	P=0. 435	P=0.723
FF vs MF	P=0. 817	P=0. 966	P=0. 387	P=0. 236	P=0. 015	837	p=0. 082	P=0. 938	P=0.841
FF vs MM	0.56	0.735	0.821	1.374	2.353	P=0.195	2.727	0.652	0.205
F-Value	0.982	0.536	0.488	0.260	0.082	1.076	0.053	0.585	0.893
p-value						0.367			

Key: FPG; Fasting plasma glucose, SOD: Superoxide dismutase, CAT: Catalase, P≤0.05 is significant, FM: FEMALES FROM DIABETIC MOTHERS, MM; Males from diabetic mothers, FF; Females from diabetic fathers, mf; males from diabetic fathers

DISCUSSION: Family medical history of diabetes is an important factor worthy of consideration in the event to prevent and manage diabetes mellitus. Individuals who have a family history of diabetes tend to have a higher risk of type 2 diabetes (T2DM) compared with individuals with no family history of type 2 diabetes [38-40]. Katulanda *et al.* noted the prevalence of diabetes was 23% higher in patients with a family history of diabetes [41].

Although this study revealed that both subjects with and without a family history of type2 diabetes (T2DM) had normal fasting plasma glucose levels, the plasma means the level of glucose was significantly higher (P=0.0001) in those subjects with a family history of T2Dm (4.5±0.4) when compared with those without a family history (4.2±0.3).

This is in accordance with the work of Marianne *et al.,* who observed that individuals with a family history of diabetes had a significantly higher concentration of glucose than individuals without a family history of diabetes [42].

This increase in plasma glucose level of those with a family history of Type2 diabetes is also in agreement with the work of Allison *et al.,* who demonstrated that non-diabetic offspring of diabetic parents have modest hyperglycemia, even within the normal range, which may contribute to attenuated endothelial function since they have impaired endothelium-dependent vasodilation and lower nitric oxide that lead to cardiovascular risk in advance to the development of overt diabetes [43]. The increase in glucose may be due to insulin resistance, according to Akbar *et al.,* who observed

a high prevalence of insulin resistance among the young subjects with a positive family history of diabetes during the evaluation of cardiac autonomic function in non-diabetic offspring of type 2 diabetes mellitus patients through assessment of heart rate variability [44]. Insulin resistance plays an important role in the pathogenesis of type 2 diabetes; the two principal components of the blood glucose regulation path-way are insulin secretion and insulin sensitivity.

Moreover, a significantly lower mean serum level of chromium was observed in subjects with a family history of type 2 diabetes (0.16±0.10mcg/l) compared with the control (0.25±0.22) (p=0.004). Some researchers have earlier reported chromium to improve insulin receptor /post-receptor signaling [45]. Chromium potentiates the actions of insulin, augments the insulin signaling pathway, blunts the negative-regulators of insulin signaling, enhances AMPK activity, up-regulating cellular glucose uptake, and attenuates oxidative stress [46]. Reduced chromium levels may contribute to explain why those with family history of T2Dm have higher mean glucose level than those without family history of T2D as observed in this study. This also may be a contributing factor to the pathogenesis of insulin resistance and the development of diabetes mellitus as often observed among the offspring of diabetic parents. However, the mean serum levels of selenium of males from diabetic mothers (mm) (130±41 µg/L) were significantly higher (p=0.015) when compared with mean serum levels of selenium of females from diabetic fathers (ff) (95.4±29 µg/L).

It has been previously shown that an excessive amount of selenium in the body is associated with the pathogenesis of insulin resistance and the development of diabetes mellitus [23]. It is known that selenium at plasma concentrations in the range of 80-120 µg/L [47] acts as an antioxidant and insulin-mimetic nutrient and favors the synthesis and action of insulin. However, at plasma levels above 120 µg/L, selenium may loss its function as an antioxidant as a result of dysregulation of the redox state which can compromise the chemical interactions involved in the insulin signaling cascade. This outcome may elucidate that male offspring from diabetic mothers may have impaired glucose metabolism and increased risk of T2D due to selenium supporting the hypothesis that the risk of T2D is higher in the offspring if the mother rather than the father has type 2 diabetes [48].

The serum mean levels of serum superoxide dismutase and catalase of those with a family history of T2DM and those without family history were (6.8±1.4 and 6.9±1.4) and (27.2±7.2 and 29±10) respectively. These results showed no significant difference when compared (p=0.849 and p= 0.270), respectively. However, the mean serum levels of catalase of males from diabetic mothers were significantly decreased compared to males from diabetic fathers (p=0.009). This further suggests that pancreatic islets of male offspring of diabetic mothers contain a relatively smaller amount of catalase which could further predispose their β-cell as an easy target for reactive oxygen species that may increase insulin resistance and impair pancreatic β-cell function [49]. Given this existing data, it is reasonable to hypothesize that a significant low level of catalase in male offspring of diabetic mothers with type 2 Dm may predispose males more to insulin resistance, glucose intolerance, and subsequent to Diabetics than the females from diabetic mothers.

Demographic and anthropometric characteristics of the study group and the control group without a family history of DM showed that there were no significant differences in any of demographic or anthropometric characteristics between the 2 groups. This is in agreement with the work of Akbar *et al.*, who documented similar results in their study [44].

Obesity is a predisposing factor of importance in diabetes mellitus affecting the population of all age groups and socio-economic levels in both developed and developing countries. It is known to be a contributory risk factor for several disease states, including diabetes mellitus [50]. The mean levels of the anthropometric parameters such as BMI and WHR of the studied population showed no significant difference when compared with the control group, and this may be as a result of the fact that means values showed the individuals were not obese.

CONCLUSION: The trace elements assayed in this study revealed significantly lower chromium levels in subjects with a family history of T2D

compared to non-diabetic history subjects. Male offspring of diabetic mothers showed significantly lower serum levels of catalase and lower serum levels of selenium compared to females from diabetic fathers and males from diabetic fathers, respectively. Males from diabetic mothers may be at a greater risk of developing insulin resistance, glucose intolerance, and subsequently diabetes in the future, considering the respective roles of the trace elements and antioxidants in glucose metabolism.

RECOMMENDATION: Having observed the slight alteration in the levels of glucose and chromium in the subjects with a family history of T2DM and significant changes in serum levels of selenium and catalase of male offspring of diabetic mothers. Maternal diabetic history may be a serious risk factor of diabetes mellitus, and we recommend that more work should be done on male subjects whose mothers are diabetic with a wider and larger population may however, be necessary to collaborate these findings.

ACKNOWLEDGEMENT: The authors wish to acknowledge the sincere efforts, willingness and dedication shown by the participants of this study which was instrumental to the success of this study.

FUNDING: No funding sources

CONFLICTS OF INTEREST: None declared

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How to cite this article:
Okwara JE, Agudi CC, Ogbodo EC, Njoku CM, Analike RA, Amah AK, Eze OO and Meludu SC: Evaluation of the serum levels of some trace elements and antioxidant levels in apparently healthy individuals with family history of type 2 diabetes in Nnewi, Nigeria. Int J Pharm Sci & Res 2021; 12(4): 2108-16. doi: 10.13040/IJPSR.0975-8232.12(4).2108-16.