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The Effect of Duration of Diabetics Type2 on Superoxide Dimutase Status of Diabetic Patients Attending Clinics in Yenagoa, Nigeria.

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Abstract: *This study was done to determine the extracellular superoxide dismutase (SOD) levels in Type 2 diabetic according to their duration of disease in Yenagoa, Bayelsa State. A randomized observational study design was adopted to collect blood samples and demographic data from 100 diabetics and 50 non-diabetic subjects aged 30 years and above. Questionnaire was administered to each subject to obtain data for their socio-economic and demographic after an informed consent. Body weight and height were measured using standard techniques and body mass index (BMI) calculated. Blood samples were collected after subjects have fasted over-night. Blood glucose, glycated haemoglobin and SOD levels were determined photometrically. Results showed an age and sex distribution of 45%/55% male to female among the diabetics with a mean age of 49.14±13.81 and a male to female ratio of 25%/25% among the non-diabetics with a mean age of 49.42±17.14. Mean BMI values were 25.45±27.84 and 26.06±27.70 for the non-diabetics and the diabetics respectively. EC-SOD was significantly lower ($p<0.05$) in the diabetics than the control group when compared. Comparison of EC-SOD in diabetics with their duration of disease showed a statistically significant differences ($p<0.05$) between early and late diabetics. We therefore conclude that EC-SOD levels were lower in diabetics compared with their sex and age matched controls and with increase in disease duration. We recommend a routine EC-SOD test in diabetics to avoid complications that may arise due to their deficiency.*

Keywords: *Diabetes type 2, antioxidant, superoxide dismutase,*

I. Introduction

Type 2 diabetes is considered as the disease with the highest morbidity and mortality among the non-communicable diseases (NCDs) in Africa and constitute about 3.5-15% of all medical admissions in Nigeria (Agoucha*et al*., 2013). In Africa, incidence of type 2 diabetes is on the increase with a projected growth of 98% to occur between 2010 and 2030 in the region as against the world's projected increase of 54% (Mbanya*et al*., 2010). This is reported to be due to effects of globalization, nutritional transitions, epidemiological transitions and "westernized" lifestyles especially, in the urban populations within the region (Maiyaki and Garbat, 2014; Levit, 2008; Adogu*et al*., 2015; Idemayor, 2010; Beran and Yudkin, 2006).

Mortality indices related to diabetes in Africa ranges between 7.6%-41% probably as a result of late diagnosis coupled with advanced complications which are sometimes diagnosed during hospital emergencies. The disease is characterized by microvascular and macrovascular complications arising from oxidative stress the cells are exposed to (Mohammedi *et al*., 2015). The increase glucose concentration in type 2 diabetes generates excessive reactive oxygen species (ROS) with consequent damage to cells (Tiwari *et al*., 2013). Fatmah*et al*., (2012), reported that several studies have unequivocally established that ROS generation not only increases in type 2 diabetes, but is also related to the onset of the disease. In healthy non-diabetic individuals, levels of ROS are under tight control by the protective action of enzymatic and non-enzymatic antioxidants that are derived from diet or produced endogenously. Therefore, excess production of ROS in diabetes is induced by the hyperglycemic condition. While Renuka and Naveen (2014), reported a significant increase in the levels of antioxidants activity in type 2 diabetics, especially in the levels of superoxide dismutase (SOD) enzymes which is considered a primary enzyme as it is involved in direct elimination of ROS, several other studies have established a decrease in the activities of this antioxidant enzyme in type 2 diabetics (Hisalkar*et al*., 2012; Rahbani-Nobar*et al*., 1999; Vivian, 2011 and Tiwari *et al*., 2012).

However, according to some reports, the increase in the generation of free radicals and oxidative stress in diabetics vary probably as a result of different effects in the individual antioxidant system. Akram*etel*., (2015); Ankush*et al*., (2009); Barbagallo and Dominguez, (2015), reported that while some of these differences are related to the status of the diabetic complications, others are dependent on the disease duration. Thus, Renuka and Naveen, (2014); Vivian, (2011) and Rahbani-Nobar*et al*., (1999), reported a decrease in SOD

activities with increase in the duration of the disease probably due to SOD inactivation by H_2O_2 as a result of the autoxidation of glucose. However, according to Hisalkar*et al*., (2012), there is no sufficient data regarding the actual status of antioxidant enzymes in diabetic patients.

II. Materials And Method

2.1 Study Design

The study design was a randomized, cross sectional observational study. The study population comprised one hundred (100) clinically confirmed diabetics attending clinics in Yenagoa and fifty (50) apparently healthy subjects as control, all aged 30years and above.

2.2 Ethical Consideration

Ethical approval was gotten from the Research and Ethics Committee of the NDUTH, Okolobiri, Bayelsa State and informed consent from the patients and control subjects before samples were obtained.

2.3 Sample Collection

Blood samples were collected from the participants after an over-night fast into sodium fluoride ad EDTA containers for the estimation of the fasting blood sugar and their SOD levels respectively. Also, structured questionnaire were administered to the patients simultaneously to obtain their demographic, socio economic and clinical data after an informed consent. Standard techniques were used to take measurements for height, weight and blood pressure readings and their body mass indexes (BMI) calculated. Fasting plasma glucose, HbA1c, and SOD levels were determined following standard operating procedures.

III. Results

Table 1 and Fig. 1 shows age and sex distribution of the diabetic (study) group. Results shows 45% were males and 55% females. The highest number of diabetics were recorded within the age bracket of 30-39 years (27%) in the entire study population whereas, according to sex, in males, 12(26.7%) were recorded as the highest number within ages 50-59 years and in females, 16(29.1%) were recorded as the highest number within ages 30-39 years.

Table 1 Showing Age and Sex Distribution of the Diabetic (Study) Group

Age (yrs.)	**Sex**		**Total**	**Percentage**
	Male	**Female**		
< 30	1	3	4	4.00
30-39	11	16	27	27.00
40-49	7	14	21	21.00
50-59	12	11	23	23.00
60-69	9	9	18	18.00
70 & above	5	2	7	7.00
TOTAL	**45**	**55**	**100**	**100.00**

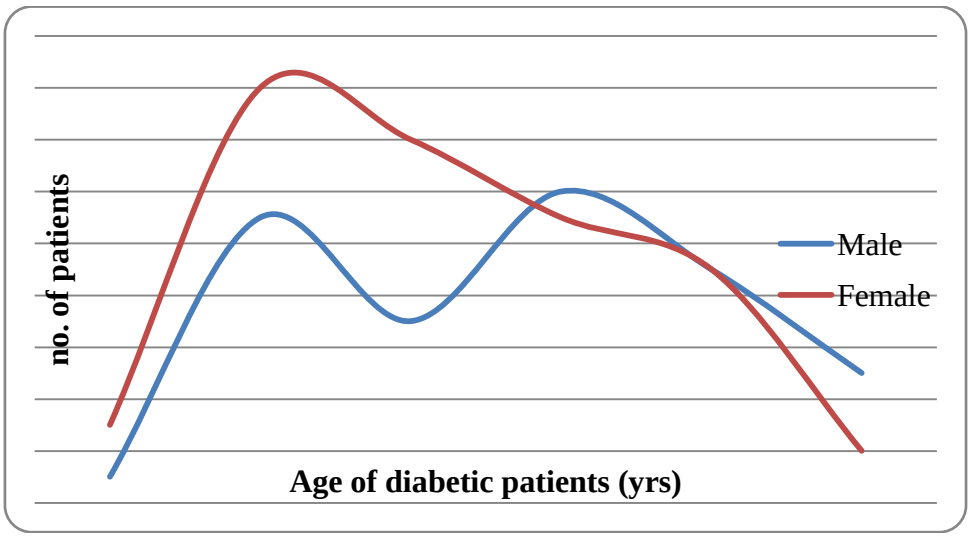

Fig. 1 Showing the Distribution of Diabetics According to Sex and Age

Table 2 shows results of the characteristics of the study group (diabetics) and the control group (non-diabetics). The mean ± SD of age in 100 type 2 diabetic patients was 49.14±13.81 (yrs) and non-diabetic controls was 49.42±17.14 (yrs). The mean age of the diabetic males were 52.36±13.85 (yrs), diabetic females were 46.51±13.32 (yrs), and mean age of control males was 42.40±14.46 (yrs) and control females was 56.44±16.97 (yrs). The mean BMI was 27.24±4.42 for diabetic males and 26.59±3.93 for diabetic females, while the non-diabetic (control) was 26.2±3.73 for males and 27.09±4.66 for females. Distribution according to BMI categories showed the highest occurrence within 25-29.9 BMI categories with a male to female ratio of 24/21 for the diabetics and 9/10 for the non-diabetics respectively. The results also showed a higher number of diabetics within the disease duration of 1-5yrs among all sexes (32/38) male to female ratio.

Table 2 Showing the Characteristics of the Diabetic Patients and Controls

CHARACTERISTIC	**TYPE 2 DIABETIC PATIENTS (n=100)**	**CONTROLS (n=50)**	**P-VALUE**
Sex (male/female)	45/55	26/24	
Age (yrs) (mean ± SD)	49.14±13.81	49.42±17.14	
Males	52.36±13.85*	42.40±14.46	0.0060
Females	46.51±13.32*	56.44±16.97	0.0059
Height (male/female)	1.64±0.11/1.64±0.11	1.65±0.09/1.58±0.12	
Weight (male/female)	72.82±11.60/71.65±13.55	71.40±11.75/67.60±13.60	
BMI (male/female)	27.24±4.42/26.59±3.93	26.2±3.73/27.09±4.66	
BMI category			
< 18.5 (male/female)	-/-	-/-	
18.5-22.9 (male/female)	10/12	5/7	
23-24.9 (male/female)	4/14	7/3	
25-29.9 (male/female)	24/21	9/10	
≥30 (male/female)	7/8	4/5	
Duration of disease (yrs)			
1-5 (male/female)	32/38	-	
6-10 (male/female)	9/10	-	
11-15 (male/female)	2/5	-	
16-20 (male/female)	2/2	-	

*p < 0.001 vs. controls

Table 3 shows results of the comparison of some biochemical parameters between the control and the diabetic groups. Serum FBS levels were higher in the diabetics (6.15±2.91) than the control groups (4.43±0.97) and was significant (p<0.05) when compared using the student t-test. Also, mean values for HbA1c and EC-SOD for the diabetics were highly significant (p<0.05) 7.91±0.80% and 164.9±21.30u/ml respectively when compared with the mean values in the control group 5.32±0.63% and 184.9 ±17.78u/ml for HbA1c and EC-SOD respectively using the student t- test.

Table 3 Biochemical Parameters in Type 2 DM Patients as Compared with Control

Parameter	**Control**	**Type 2 DM Patient N**	**50**
100			
Male/Female	25/25	45/55	
Age (years)	49.42±17.14	49.14±13.81	
BMI	25.45±27.84	26.06±27.70	
FBG (mmol/l)	4.43±0.97	6.15±2.91***	
HbA1c	5.32±0.63	7.91±0.80***	
SOD (U/ml)	184.9 ±17.78	164.9±21.30***	

***p < 0.001 Type 2 DM patients vs. Controls

Table 4 show results of the comparison of SOD levels with the duration of disease in type 2 diabetic patients using a One-way ANOVA test at p< 0.05 level of significance. Results show a consistent decrease in SOD levels with increase in the duration of the disease generally and according to sexes (F=3.756 & p=0.018 in males, F= 3.176 & p=0.0317in females and F=7.176 & P=0.002 in the entire diabetics).

Table 4 Comparison of SOD levels with duration of diabetes in Diabetic males and Females

Parameter	**1-5yrs**	**6-10yrs**	**11-15yrs**	**16-20yrs**	**F ratio**	**p value**
Male	**170.2 ± 22.90**	**151.69 ± 74**	**145.07± .07**	**138.02 ± 83**	**3.756**	**0.018**
Female	**166.7 2 ± 2.04**	**152.8 1± 0.24**	**148.0 4± .47**	**141.0 1 ± 41**	**3.176**	**0.031**
All diabetics	**168.3 2± 2.34**	**152.2 9 ±74**	**147.1 4 ± 88**	**139.52 ± 52**	**7.176**	**0.002**

IV. Discussion

Oxidative stress and its related consequences in the microvascular and macrovascular complications in diabetes mellitus have been considered widely in recent times among researchers. Fatmah*et al*., (2012), reported that there is convincing experimental and clinical evidence that the generation of ROS increases in type 2 diabetes and is also clearly related to its onset. The level of these antioxidants critically influences the susceptibility of various tissues to oxidative stress; their potentials decreases with progression of the disease (Vivian, 2011) and is associated with the development of complications in diabetes (Shirish*et al*., 2013).

This study measured the concentrations of extra cellular superoxide dismutase levels in type 2 diabetics attending clinics in Yenagoa, Bayelsa State with relation to their duration of disease. The results showed a diabetic population of 45% males and 55% females with the highest number of diabetics occurring within the age range of 30-39 years (27%) in all sexes. This is in agreement with the reports of the IDF (2003) and King *et al*., (1998) of 28% prevalence rate of diabetes in sub-Saharan Africa within this same age bracket. However, reports of other studies do not give consistent information on the age range regarding the prevalence of diabetes. According to King *et al*., (1998), the prevalence rates differ between the developed countries and the developing countries; whereas the peak prevalence rate in the developed countries is between 65 years and above, it is between 45 and 64 years in the developing countries while in the sub-Saharan Africa two peak age brackets were identified- 20 to 44 years and 45 to 64 years.

Our findings also showed a significantly low EC-SOD levels among the diabetics compared with the control group ($p<0.001$). These findings are in agreement with the findings of Picchi*et al*., (2010), Song *et al*., (2007), Coyne *et al*., (2005), Arif*et al*., (2010) and Hisalkar*et al*., (2012). Despite the agreement that there is an increase generation of free radicals and oxidative stress in diabetic patients, the level of antioxidants generated in diabetics is reported to vary and with no sufficient data regarding the actual status of antioxidant enzymes in diabetic patients (Hisalkar*et al*., 2012). However, according to Akram*et al*., (2015), the observed differences may be due to the effect of the diabetes on the individual antioxidant systems. Thus, Kimura *et al*., (2003), Palanduz*et al*., (2001), Al-Rawi (2011) reported an increase in SOD levels in diabetics while Arif*et al*., (2010), Hisalkar*et al*., (2012) reported a reduced SOD levels in diabetics. The above results are indicators of decrease in the protective antioxidant mechanism due to an increase production of free radicals and ROS in the diabetic patients.

Our study also demonstrated an inverse relationship between levels of EC-SOD and duration of disease among the Type 2 diabetics in the entire population studied. This finding is in agreement with the findings of Rahbani-Nobar*et al*., (1999); Vivian, (2011), who posited that SOD induction and its activity progressively decreases with an increase in the duration of Type 2 diabetes due to non-enzymatic glycation which predominates as the duration of the disease increases with consequent production of H_2O_2 which further inhibits SOD synthesis. Also, according to Taheri *et al*., (2012), at the early stage of the disease, the antioxidant defense system was able to counter the levels of free radicals generated but not at the later stage when the balance has been compromised.

Our study also considered the levels of the superoxide dismutase enzymes with respect to their sexes within the diabetic's and within the control group. Mean values of the EC-SOD were higher among the males compared with their female counterpart in both the diabetics and the control groups and were significantly different. These results agree in part with the findings of Hisalkar*et al*., (2012).

V. Conclusion

Results from our study show EC-SOD levels are lower in Type 2 diabetic patients than in non-diabetic patients and also decreases with an increase in the duration of the disease state in Bayelsa state of Nigeria. It also demonstrated that EC-SOD values are lower in females than in males. In order to minimize risk associated with low levels of EC-SOD in type 2 diabetes, and recognizing that the increase in morbidity and mortality due to type 2 diabetes can be largely prevented and controlled through collective and multiple level, we recommend that prevention must be the cornerstone of the global response to the reduction of diabetic complications. It may be imperative to focus on improving the EC-SOD level of diabetics as a secondary management strategy.

Consequently, we recommend a reduction in the level of exposure of individuals and populations to the common modifiable risk factors for type 2 diabetes, namely, tobacco use, unhealthy diet, physical inactivity, and the harmful use of alcohol, and their determinants, while at the same time strengthening the capacity of individuals and populations to make healthier choices and follow lifestyle patterns that foster good health, promote access to comprehensive and cost-effective prevention, treatment and care for the integrated management of type 2 diabetes. Also, it is prudent to monitor EC-SOD levels in type 2 diabetic patients periodically to avoid development of complications related to their deficiencies and treat the condition(s) whenever possible.

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