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Risk Factors associated with Diabetes in Pregnancy: The Nigerian perspective using the new World Health Organization (WHO) criteria

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Abstract

Diabetes Mellitus encompasses a group of metabolic diseases characterized by defective insulin activity. Gestational Diabetes Mellitus (GDM) is classified as type IV Diabetes Mellitus. It is defined as glucose intolerance with first onset or recognition during pregnancy. It is estimated that 7% of all pregnancies are complicated by Gestational Diabetes resulting in more than 200,000 cases annually. Gestational Diabetes is associated with perinatal and obstetric complications. WHO has recently developed new criteria for screening for Gestational Diabetes Mellitus. The aim of this study is to determine factors associated with the development of GDM among antenatal attendees in two health facilities in Niger Delta region of Nigeria. This was a cross sectional study comprising 132 antenatal clinic attendees. The participants of the study were screened for Gestational diabetes using oral glucose tolerance test (OGTT) after appropriate history had been taken. The prevalence of Gestational Diabetes was found to be 15.2%. The mean age of occurrence was 30.45± 4.30. The risk factors associated with GDM were family history of DM in first degree relative, past history of GDM, previous history of stillbirth and higher pre-pregnancy BMI The prevalence of Gestational diabetes is increasing and more likely to be found in older mothers. There is need to screen all pregnant women for Gestational Diabetes Mellitus in Africa.

Keywords: Gestational, Diabetes, WHO, New criteria.

INTRODUCTION

Gestational, Diabetes, WHO, New criteria Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. The definition applies whether insulin or only diet modification is used for treatment and whether or not the condition persists after pregnancy.

It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy. Gestational Diabetes Mellitus is classified as type 4 DM [2]. The diagnosis of gestational diabetes according to the new guideline by the world health organization (WHO) in 2013 is based on any one of the following values: Fasting plasma glucose - 5.1-6.9mmol/l (92-125mg/dl); 1hour post 75g oral glucose load > 10.0mmol/l (180mg/dl); 2 hours post 75g oral glucose load-8.5-11.0mmol/l (153-199mg/dl) [2].

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Epidemiology of gestational Diabetes

Approximately 7% of all pregnancies are complicated by GDM, resulting in more than 200,000 cases annually [2]. The prevalence may range from 1 to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed [3,4]. Using a new diagnostic criterion, an international, multicenter study of gestational diabetes, the hyperglycemia and adverse pregnancy outcome (HAPO) study found that 18 percent of the pregnancies were affected by gestational diabetes [5]. Recent data shows that gestational diabetes mellitus (GDM) prevalence has increased by 10–100% in several race/ethnic groups during the past 20 years [6]. The frequency of GDM usually reflects the frequency of type 2 diabetes in the reference population [7].

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In sub Saharan Africa, the prevalence of GDM just like other types of Diabetes is on the rise and this is thought to be due to urbanization and adoption of western life and increase in the prevalence of obesity [3]. Studies done in South Africa and Ethopia using the old WHO criteria showed prevalence rates of GDM to be 8.8% and 9% respectively [8,9]. In Nigeria, the prevalence of GDM in Jos University Teaching Hospital (JUTH), Jos using the old WHO criteria in a study done in 2009 was 8.3% [10]. Another study done comparing the 75g and 100g OGTT showed a prevalence rate of 11.6% and 4.5% respectively in Lagos University Teaching Hospital (LUTH) in a cohort study done between 1997 and 1999 [11]. The prevalence rate of GDM was 2.98 per 1000 pregnancies (0.3%) in University of Port Harcourt Teaching Hospital using the O'Sulllivan criteria in a study done in 2001 [12].

Associated risk factors for Gestational Diabetes

Classical risk factors for developing gestational diabetes are: Polycystic Ovary Syndrome, a previous diagnosis of gestational diabetes or prediabetes, (impaired glucose tolerance, or impaired fasting glycaemia), family history in first-degree relative with type 2 diabetes, maternal age >35yrs, ethnic background -those with higher risk factors include African-Americans, Afro-Caribbeans, Native Americans, Hispanics, Pacific Islanders, and people originating from South Asia), being overweight or obese, previous delivery of a macrosomic infant (high birth weight: >90th centile or >4000 g (8 lbs 12.8 oz,) and previous poor obstetric history [13]. These risk factors can be classified into very high risk, moderate and low risk for the development of GDM shown in the table 1.

Some of these risk factors have also been implicated in the recurrence of GDM. McNeill *et al* in a retrospective longitudinal study of 651 women with GDM reported a recurrence rate of 35.6% [14]. However, previous studies demonstrated a higher recurrence rate of 68–70% [15-17]. Contributing risk factors for recurrence of GDM were parity ≥ 1, BMI ≥ 30, GDM diagnosed at ≤24 weeks, insulin requirements, weight gain, inter pregnancy interval of ≤24 months, hospital admissions, and older age.

Older Maternal Age

One of the best-studied and well-documented risk factors for GDM is older maternal age. Multiple studies have shown that older maternal age is a risk factor for GDM, with age cutoffs ranging from 30 to 35, and up to 40 years of age [18-20]. The average age gap between a gravid diabetic and a nondiabetic pregnant woman is approximately 2.2 years. In a retrospective study of 2,574 pregnant women Jiménez-Moleón *et al* were able to demonstrate that 41.8% of the women with GDM were older than 30 years, and only 26.2% were younger than 25 years [18].

Xiong *et al* in a retrospective analysis of 111,563 deliveries in Canada, found that 22.4% of patients with GDM were older than 35, compared to only 10.3% in nondiabetic controls (OR 2.34, 95% CI 2.13–2.58) [20]. Similar results were also reported by Lao *et al* those pregnant women aged 35–40 are at an increased risk for GDM compared to younger women (OR 2.63, 95% CI 2.4–2.89).

Higher Parity

Several studies have shown that increasing parity is an independent risk factor for GDM, not age related [18,22,23]. Egeland *et al* demonstrated that the age-adjusted risks for women with two, three, or more deliveries were 1.5 (95% CI 1.2–1.9), 1.9 (95% CI 1.4–2.5), and 3.3 (95% CI 2.1–5.1), respectively, compared to women having only one delivery [23]. Jang *et al* in two large retrospective studies, previously described, have demonstrated that the mean parities of GDM and normal controls were 0.6 ± 0.9 and 0.4 ± 0.5, respectively ($p < 0.05$) [19]. Also, their studies demonstrated that 9.8% of women with GDM had given birth at least twice, compared to only 2.6% of the non-diabetic controls ($p < 0.001$).

Past history of delivery of a macrosomic baby

Jang *et al* also reported that a previous birth of a macrosomic baby is a risk factor for GDM [19]. They found that 9.3% of GDM patients had a macrosomic baby in their previous pregnancy, compared to only 2.5% of patients who gave birth to an appropriate for age baby in their previous delivery (or 5.8, 95% ci 1.98–17.02). Jiménez- moleón *et al* also reported an odds ratio of 5.8 for GDM in women with previous delivery of a macrosomic baby [18].

Pre-pregnancy body mass Index (BMI) and weight

The most studied factor in the issue of maternal weight and its relation to GDM is the prepregnancy BMI. Jang *et al* found that the prevalence of GDM increases with rising BMI; 8.8% of the GDM patients were overweight (BMI > 27 kg/m^2), compared to only 1.1% of controls ($p < 0.001$) [19]. Bo *et al* described the mean BMIs in GDM and normal controls to be 25.4 ± 5.3 and 23.6 ± 4.6 kg/m^2, respectively ($p < 0.02$) [24]. Solomon *et al* also found that prepregnancy BMIs 25–30 kg/m^2 and ≥30 kg/m^2 are associated with an increased risk for GDM [25].

Pre-pregnancy weight is another risk determinant of GDM. In a study done by Xiong *et al* found that 15.8% of women with GDM were obese prior to pregnancy (defined as weight ≥ 91 kg), compared to only 7.3% of normal controls (OR 2.4, 95% CI 2.06–2.98) [20]. Isaacs *et al*, in a retrospective study from 1994, showed that women weighing over 300 pounds have a significantly higher incidence of GDM versus a nonobese control group (mean weight 160 ± 21 pounds) [26].

Family history of Diabetes Mellitus

Gestational diabetes mellitus (GDM) aggregates in families. The cause of this clustering with first-degree relatives who have previously had either GDM or another form of diabetes is likely to have genetic, epigenetic, and environmental components associated with the future development of GDM [27]. In a study done by Sang YR *et al* among Korean women, history of T2DM in first-degree relatives was associated with an increased risk of developing GDM [28]. The risk of developing GDM was increased approximately two-fold in cases with a parental history of T2DM, approximately five-fold in cases with sibling history of T2DM, and approximately 6.5-fold in cases with both sibling and parental histories of T2DM [29].

Another study by Williams MA *et al* also showed an increase risk of developing GDM in women with positive family history of type 2 DM [29]. A subset (10%) of women with GDM have an autoimmune- or human leucocyte antigen (HLA)-related condition that more closely resembles type 1 diabetes [30]. This group of women may go on to develop type 1 DM after birth. Other studies have also shown positive relationships with markers for type I DM such as HLA-DR3 or HLA DR4 in women with GDM [31,32].

Polycystic Ovarian Syndrome

The definition of polycystic ovarian syndrome (PCOS) according to the revised rotterdam criteria, a consensus on diagnostic criteria of the American Society for Reproductive Medicine and the European Society of Human Reproduction and embryology: At least two of three criteria must be present: (i) oligoamenorrhoea or amenorrhoea; (ii) hyperandrogenism (clinical/biochemical); and (iii) polycystic ovaries on ultrasound, defined as more than 12 cysts of 2-9mm, or >10ml volume (Rotterdam Eshre/Asrm-sponsored PCOS consensus workshop group, 2004). The revised rotterdam criteria are considered the current standard diagnostic criteria.

PCOS has been documented as risk factor for development of GDM. Ashrafi *et al* reported that pregnant Iranian women with a history of infertility [33] and PCOS who conceived by assisted reproductive technology or spontaneously were at increased risk for developing GDM compared to controls without PCOS [34].

In a meta-analyses of pregnancy outcomes in women with PCOS demonstrated a significantly higher chance of developing GDM for PCOS women (odds ratios of about 2.90) [34,35]. Another study done by Lansone *et al* also reported PCOS as a risk factor for GDM [36].

AIM OF STUDY

To assess factors associated with the occurrence of GDM in antenatal clinic attendees in two health facilities in Port Harcourt.

MATERIALS AND METHODS

This was a prospective cross-sectional study of 132 consenting consecutive pregnant women attending the antenatal clinics of the University of Port Harcourt teaching Hospital with gestational ages of between 24-28 weeks.Those with pre-gestational diabetes mellitus, those on drugs that affect glucose tolerance and those with multiple pregnancies were excluded. Ethical approval for the study was obtained from the Ethical Committee of the University of Port Harcourt Teaching Hospital before commencement of the study. The study was carried out over a period of five months (July to November2014).

Data from the study subjects included biodata, parity, weight, Body Mass Index (BMI), blood pressure. All study subjects underwent a 75g Oral Glucose Tolerance Test. They were asked to fast for at least 8hrs before the test and return in the morning (8am) for the test. They were told to take their last meal before 10pm and bring their breakfast to clinic to eat immediately after the test to avoid hypoglycaemia. They were allowed to rest for 5-10mins before commencement of the test. A fasting plasma sample was collected after which 75g anhydrous glucose dissolved in 250mls of water was given to each subject to drink over five minutes. Time 0 was taken from the time of the first sip. Venous blood samples were collected at fasting, 1hour and 2hours after glucose consumption. During the test subjects were not allowed to do any physical activity or eat or smoke but water could be taken. Plasma glucose estimation was determined according to the method described by Trinder *et al* using the glucose oxidase enzyme solution [37].

The glucose tolerance status for each subject was determined using the new WHO criteria.

The new WHO criteria as stated below are:

Fasting ……5.1mmol/l- 6.9mmol/l (92-125mg/dl)

1 hour…… ≥10.0mmol/l (180mg/dl)

2 hours……..8.5mmol/l-11.0mmol/l (153-199mg/dl)

GDM was diagnosed where one or more threshold value is exceeded.

Statistical Analysis

Data was analyzed using the statistical package for the social sciences (SPSS) version 20.0 and the level of statistical significance was set at $p<0.05$.

RESULTS

A total of 132 women between the gestational ages of 24-28 weeks were recruited into this study. The most common age group was 26-30 years and the least common age group was between 41-45 years as shown in table 1. The mean age of the subjects was (31.33±4.33) years with a range of 21-42 years.

Factors associated with the occurrence of GDM

The study population was divided into two groups those with gestational diabetes (GDM) and those without gestational diabetes (NoGDM) based on the new WHO criteria.

Table 1: Sociodemographic data of study population

Variable	**Number (percent) n=132 (100%)**
Age group	
21 – 25	9(6.8)
26 – 30	55(41.7)
31 – 35	44(33.3)
36 – 40	22(16.7)
41 – 45	2(1.5)
Educational level	
Primary	2(1.5)
Secondary	20(15.2)
Tertiary	110(83.3)
Occupation	
Skilled/ professional employment	32(24.2)
Unskilled employment	14(10.6)
Public servants	26(19.7)
Business(traders)	24(18.2)
Unemployed	20(15.2)
Others	16(12.1)
Parity	
0	25(18.9)
1	36(27.3)
1	49(37.1)
2	20(15.1)
3	2(1.5)

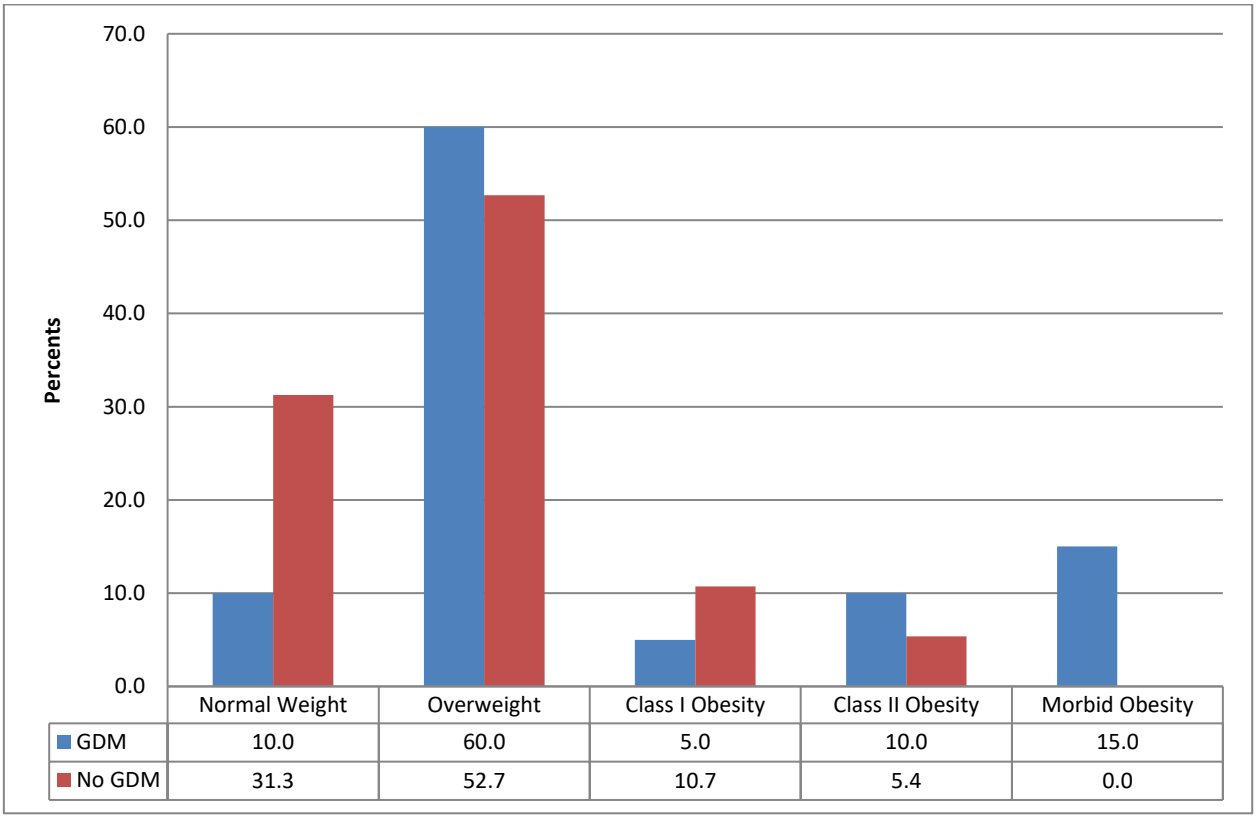
Table 2: Comparision of factors associated with gdm in study population

Variable	No GDM N=112	GDM N=20	Chi square	P value
Age groups				
21 – 25	6 (5.4)	3 (15.0)	5.245	0.263
26 – 30	50 (44.6)	5 (25.0)		
31 – 35	35 (31.3)	9 (45.0)		
36 – 40	19 (17.0)	3 (15.0)		
41 – 45	2 (1.8)	0 (0)		
Parity				
0	20 (17.9)	5 (25.0)	0.888	0.926
1	31 (27.7)	5 (25.9)		
2	42 (37.5)	7 (35.0)		
3	17 (15.2)	3 (15.0)		
4	2 (1.8)	0 (0.0)		
Family history of DM	25 (22.3)	10 (50.0)	6.672	0.010*
Past History of GDM	11 (9.8)	7 (35.0)	9.135	0.003*
Previous macrosomic baby	18 (16.1)	5 (25)	0.940	0.332
Previous stillbirth	8 (7.1)	7 (35)	13.074	0.000*
Glycosuria				
Nil	111 (99.1)	18 (90.0)	7.633	0.022*
1+	0 (0.0)	0 (0.0)		
2+	0 (0.0)	1 (5.0)		
3+	0 (0.0)	1 (5.0)		
Proteinuria				
Nil	94 (83.9)	18 (90.0)	1.085	0.781
1+	12 (10.7)	1 (5.0)		
2+	4 (3.6)	1 (5.0)		
3+	2 (1.8)	0 (0.0)		

Table 3: Comparison of factors associated with GDM in study population for quantitative variables

Variable	NoGDM N=112	GDM N=20	T Test	P value
AGE (years)	31.40 (4.35)	30.95 (4.30)	.432	0.669
CALCULATED GA (weeks)	26.48 (1.79)	26.50 (1.57)	-.046	0.964
HEIGHT (m)	1.64 (0.06)	1.62 (0.06)	1.333	0.194
PRE-PREGNANCY WEIGHT (kg)	71.54 (10.5)	78.50 (12.23)	-2.668	0.009*
PRE-PREGNANCY BMI (kg /m2)	26.68 (3.83)	30.23 (5.85)	-3.491	0.001*
SYSTOLIC BP (mmHg)	114.02 (12.6)	114.50 (14.7)	-.138	0.891
DIASTOLIC BP (mmHg)	71.61 (10.8)	68.50 (10.9)	1.177	0.250
FPG (mmol/l)	4.34 (0.65)	5.28 (1.5)	-4.646	0.000*
1 HOUR OGTT (mmol/l)	7.08 (1.7)	9.20 (2.8)	-4.609	0.000*
2 HOURS OGTT (mmol/l)	5.76 (1.4)	7.72(2.52)	-5.012	0.000*

Data are expressed as mean (standard deviation)



	Normal Weight	Overweight	Class I Obesity	Class II Obesity	Morbid Obesity
GDM	10.0	60.0	5.0	10.0	15.0
No GDM	31.3	52.7	10.7	5.4	0.0

Figure 1: Column chart showing BMI of GDM and No GDM subjects

The mean age subjects with GDM was 30.95± 4.30 years while those without GDM was 31.40± 4.35years. Gestational Diabetes Mellitus was commoner in those aged between 31-35 years as shown in table 2 There was no statistically significant difference between the parity of those with GDM and those without GDM as shown in table 2

Family history of DM, past history of GDM and previous history of stillbirth was significantly higher in those with GDM compared to those without GDM, *p*-value 0.01, 0.003, 0.00 respectively as shown in table 2. The presence of glycosuria on urinalysis was also significantly more in those with GDM, p value 0.022 as shown in table 2.

GDM subjects had significantly higher mean pre-pregnancy weight (78.50 ±12.23) and BMI(30.23± 5.85) than subjects without GDM (p value 0.009 and 0.001) respectively as shown in table 3 More of those without GDM were normal weight compared to those with GDM while GDM subjects were more in the overweight group compared to those without GDM as shown in figure 1.

There was no significant difference in the systolic and diastolic blood pressure of subjects with GDM and subjects without GDM as shown in table 3.

The mean fasting plasma glucose was significantly higher in those with GDM (5.28± 1.5) than those without GDM (4.34± 0.68) with a *p*-value of < 0.001. GDM subjects also had significantly higher mean one hour (9.20± 2.8) and two hours (7.72±2.52) post 75g glucose load plasma values than subjects without GDM, *p*-value 0.000. These are shown in table 3.

DISCUSSION

Factors associated with GDM in study population

In this study, there was significant association between family history and the development of GDM as in previous studies done by Anzaku *et al*, Olarinoye *et al* and Wokoma *et al* [10-12]. Fifty percent of GDM subjects had a family history of DM in first degree relative compared to 22.3% of those without GDM (p<0.05). This shows a strong association between family history of DM and the development of GDM which is similar to findings by Sang *et al* in Korea that found a two fold increase in GDM patients that had a parental history of DM [28]. They also found that there was a five-fold increase in development of GDM in cases with sibling history of Type 2 DM and approximately a 6.4 fold increase in those with both parental and sibling histories of Types 2 DM. This suggests that the stronger the family history of Type 2 DM, the more the risk of development of GDM. This could be explained to be due to familial clustering of genes and similar genes implicated in the predisposition to DM and GDM.

A past history of GDM was also significantly associated with the occurence of GDM in this study. Thirty five percent of the subjects with GDM had a past history of GDM as compared with 9.8% of those without GDM (p0.003) which is similar to a high recurrence rate of 35.6% of GDM as reported by MacNeil *et al* in a large retrospective longitudinal study among 651 women with GDM [14].

Previous history of stillbirth was found to be significantly higher in subjects with GDM (35%) than those without GDM (7%) with a pvalue of <0.05. This was also found in previous study done by Olarinoye *et al* in Lagos, Nigeria that reported rate of 21.8 % [11]. Other studies done by Jang *et al* also showed that previous history of stillbirth was a significant risk factor for GDM [22].

Pre-pregnancy weight and body mass Index (BMI) is one of the most studied factors in the relation to GDM. Jang *et al* found that the prevalence of GDM increases with rising BMI [22]. Bo *et al* found that the mean BMIs in GDM and normal controls to be 25.4 ± 5.3 and 23.6 ± 4.6 kg/m^2, respectively ($p < 0.02$) [24]. Solomon *et al* also found that pre pregnancy BMIs 25–30 kg/m^2 and ≥30 kg/m^2 are associated with an increased risk for GDM [25]. These were similar to the findings in this study with the mean pre-pregnancy BMI being (30.23 ± 5.85) among those with GDM which was significantly higher compared to a BMI of (26.68 ±3.83) in those without GDM with a pvalue of 0.001. The mean pre-pregnancy weight of those with GDM was also significantly higher than those without GDM which is similar to a study done by Xiong *et al* that reported that 15% of women with GDM were obese prior to pregnancy compared to 7.3% of normal controls [20].

CONCLUSION

The prevalence of gestational Diabetes like other types of Diabetes is increasing, due to increase in obesity, urbanization and adoption of western lifestyle.

There was significant association between family history of DM, past history of GDM, previous stillbirth and history of delivery of a macrosomic baby and the occurrence of GDM. Pre- pregnancy BMI had a strong association with GDM in contrast to those without GDM. There is need to screen all pregnant women for GDM due to the high and increasing prevalence of GDM. This new WHO should be adopted universally to enable a uniform criteria for the diagnosis of GDM which uses lower thresholds to detect mild degrees of hyperglycaemia that predicts adverse maternal and fetal outcomes.Preventive measures of risk factors for GDM should be advocated such as maintenance of a normal pre-pregnancy body weight and BMI, younger age of child bearing <35 years, lower parity etc. GDM patients should be followed up and advised on preventive measures against any future development of Type 2 DM.

Conflicts of Interest

There is no conflict of interest in this study.

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