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Possible pregnancy-associated complications among diabetic patients

Abstract

Background: Diabetes Miletus (DM) is a serious complex condition which can affect the entire body. DM that develops during pregnancy is known as gestational diabetes (GD), which carries health risks for both the mother and fetus. Therefore, the aim of this study was to assess the possible complications among pregnant diabetic patients (cases) compared to non-diabetic pregnant ladies (controls) in Sudan.

Materials and Methods: This was prospective case-control study conducted in Sudan during the period from September 2014 to March 2015. Two hundreds individuals (100 were cases and 100 were controls) were investigated using different clinical and laboratory measures.

Results: Clinical complications when compared to normal pregnant women (control group), diabetic pregnant women (case group) showed significant increase in incidence of persistent glycosuria (GU), urinary tract infection (UTI), hypertension, GD in previous pregnancy, abortion/stillbirth and asymptomatic bacteriuria (AB), (P value <0.001, 0.001, 0.001, 0.001, 0.030 and 0.007 respectively). GU (98% in cases versus 1% in controls), UTI (94% in cases versus 49% in controls), hypertension (23% in cases versus 1% in controls), GDM in Previous Pregnancy (98% in cases versus none in controls), abortion/stillbirth (14% in cases versus 5% in controls) and AB (53% in cases versus 34% in controls).

Conclusion: Several complications are commonly associated with pregnant diabetic patients including; glycosuria (GU), urinary tract infection (UTI), hypertension and lipid profile disorders. Pregnant diabetic ladies should undergo more medical care and follow up than non-diabetics for early management of expected complications.

Keywords: complications, diabetes, sudan, pregnant, women, glycosuria, urinary tract infection, foetal, dm, macrosomia

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Abbreviations: DM, diabetes miletus; GD, gestational diabetes; UTI, urinary tract infection; ER, endoplasmic reticulum; GTT, glucose tolerance test; HIV, human immunodeficiency virus; HPW, health pregnant women

Introduction

Diabetes mellitus (DM) is associated with substantial morbidity and mortality worldwide and its prevalence is increasing in each year.[1] Type 2 DM is the most common type of diabetes with dramatically increasing global prevalence. Many factors have been suggested to reduce the burden of type 2 diabetes, such as, suitable diet, regular exercise along with pharmacotherapy, education of patients and other life style modifications.[2] The prevalence of DM is growing secondary to augmented consumption of food and declined physical activity worldwide. Hyperglycaemia, insulin resistance and hypertrophy of pancreatic beta cells happen in the initial stage of DM. However, with the development of DM, dysfunction and loss of beta cells happen in both types 1 and 2 DM. Programmed cell death is also found to be linked to DM, and apoptosis of beta cells might be the chief process of relative insulin deficiency in DM. endoplasmic reticulum (ER) also acts as a cell sensor to monitor and conserve cellular homeostasis. ER stress has been found to be associated with autophagy and apoptosis. These mechanisms can occur in both physiologic and pathologic settings in DM.[3]

DM is a major health problem in Africa. The prevalence of DM is likely to rise at upsetting rate in Africa. It is estimated that about 20million Africans are now living with diabetes, encompassing a current and future challenge for health systems.[4] DM is a major health problem in Sudan and is a leading cause of morbidity and mortality. The prevalence of uncontrolled type 2 diabetes was found to be 85% in Sudan.[5,6] The great financial burden and adverse social influence on individuals with DM and their families in Sudan, request urgent need for development of evidence-based policy and program strategies, with a stress on low-resource communities.[7]

Genetic susceptibility to type 2 DM is multifactorial. An increasing number of genes have been recognized as risk factors for type2 DM across multiple ethnicities in trans-ancestry meta-analysis of large-scale genome wide association studies. Limited studies have observed at these genes in Sub-Saharan African populations.[8] In Sudan, it was reported a prevalence of 3.4% and recognized DM as the commonest cause of hospital admission and morbidity due to a non- communicable disease.[9] The highest prevalence is described in northern Sudan[10] and the lowest in the western regions,[11] with statistics described in the International Diabetes Federation Diabetes Atlas[12] proposing prevalence varying from 6-10% and 60% of deaths due to diabetes happening in people below 60 years of age.[8]

Hyperglycemia, the common characteristic of both type 1and 2 DM, has the potential to cause severe complications due to its insidious and chronic nature.[13] The most common complications include oxidative stress,[14] Diabetic Neuropathy, Diabetic Nephropathy, Diabetic Retinopathy, Macrovascular Complications, and other Miscellaneous Complications.[13] Gestational diabetes (GDM) has significant maternal

and foetal consequences. Screening permits an active involvement, which considerably improves pregnancy endings. An ideal screening mean should go before disease complications, which is the innovative aim of screening.[15] GDM is associated with substantial maternal and foetal consequences. The maternal risk of GDM includes an augmented risk of caesarean delivery, post-partum haemorrhage and more significantly a 40% risk of evolving diabetes in future. The foetal risk includes foetal macrosomia, birth trauma, shoulder dystocia, stillbirth, neonatal jaundice and neonatal hypoglycaemia.[16] Latest evidence has revealed the importance of guaranteeing that all pregnancies with GDM are identified and managed suitably. However, there leftovers a lack of consensus as to how to best find these women.[17]

Usually, undetected DM patients are more prevalent than detected DM, even in Western County.[18] In Sudan, there are many pregnant ladies with undetected and uncontrolled DM, which in most occasions lead to development of several complications. Therefore, the aim of the present study was to evaluate the burden of complications violation among diabetic pregnant ladies in Sudan.

Materials and methods

This is a prospective, case-control hospital-based study carried out in Omdurman Maternity Hospital and Omdurman Military Hospital in Khartoum State, Sudan. The study conducted during the period from September 2014 to March 2015. The cases sample included a full coverage of all diabetic pregnant women attended to the medical centers during the study period. All cases were post-diagnosed with DM. Controls were selected form healthy pregnant women with normal glucose tolerance, after they were universally screened with non-fasting 2hour 75gm glucose tolerance test (GTT) (<140mg/dl). Pregnant women with GDM diagnosed 2hour 75gm GTT was ≥140mg/dl were advised for medical supervision. Pregnant women with previous history of other medical illness like anemia, smoking, alcoholism, human immunodeficiency virus (HIV), cardiac, renal disease, other chronic diseases and medical treatment were excluded. Adolescents and those over age 45 were also excluded because pregnancy in those age groups is considered to be high risk.

Blood was drawn from the diabetic and health pregnant women (HPW) after overnight fasting (8hrs). 5ml of fasting venous blood was collected from the antecubital vein, through routine method applied under aseptic precaution and tourniquet for a short time as needed, from each subject into plain bottles. So blood was then centrifuged after clotted blood has retracted by the centrifugation machine at 4000rpm for 5minutes and the serum removed and stored at 4°C pending assay for lipid profile with other samples as batches - total cholesterol, triglycerides, HDL- cholesterol, LDL-cholesterol and very LDL (VLDL)-cholesterol. Biochemical assays on the serum were performed with Bio Systems BTS -305 analyzer.

Statistical analysis

SPSS version 16 statistical software was used for statistical analysis. The numeric results (AgNOR counts and tumor markers) were expressed as mean±SD, and the 95% confidence intervals (CIs) of the means were calculated. The X2 test was used to compare the differences in categorical variables between the groups. Relationships between variables were analyzed using Pearson's correlation analysis. AP<0.05 was considered statistically significant.

Ethical consent

Informed written consent was taken from all women who were willing to participate. The study was approved by the Khartoum Ministry of Health ethics committee dated 09/08/2014.

Results

In the present study we investigated 200 pregnant ladies (100 were cases and 100 were controls), their ages ranging from 40 to 18years with a mean age of 28years. The proportions of cases and controls among different age groups were as follow: 36(36%) and 29(29%) for age of 31years or more, 31(31%) and 41(41%) for age of 26-30years, 31(31%) and 22(22%) for age of 21-25years and 2(2%) and 8(8%) for age of 20years or less, as shown in Figure 1.

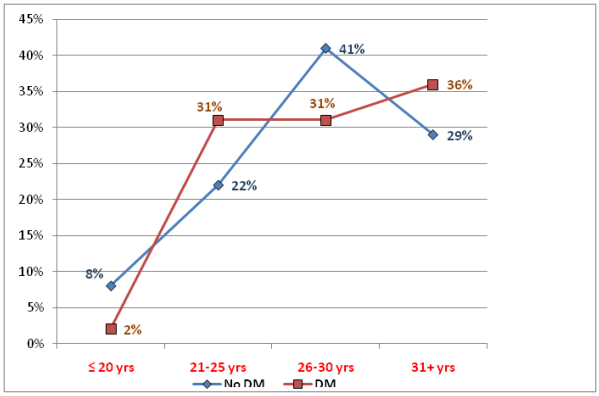

Figure 1: Description of study population by age.

With regard to educational levels, cases and controls were categorized as follows: 51(51%) and 51(51%) were university graduates, 33(33%) and 36(36%) were high school graduates and 16(16%) and 13(13%) were primary school graduates, as shown in Figure 2.

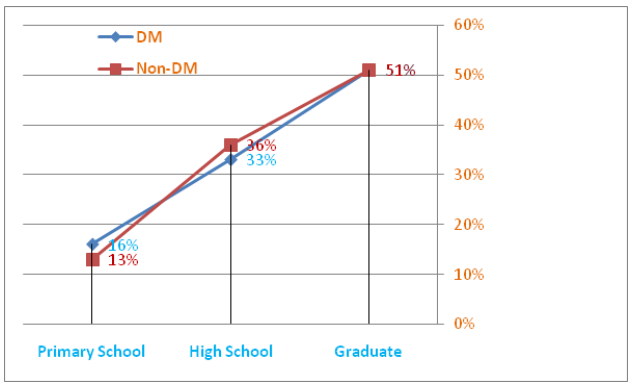

Figure 2: Description of study population by educational level.

For occupations of the study subjects, cases and controls were grouped as follows: 72(72%), 82(82%) were housewives, 24(24%), 15(15%) were employees, whereas 2(2%) were labors in cases and 2(2%) were in medical field among controls, as shown in Figure 3.

According to the residence cases and controls were grouped as follows: 55(55%), 50(50%) reside in Omdurman, 35(35%), 47(47%) reside in Bahry, 9(9%), 2(2%) reside in Khartoum. In regard to pregnancy complications, persistent GU was reported in 98(98%) of the cases versus one woman (1%) in the control group (P < 0.001), UTI was reported in 94(94%) of the cases versus 49(49%) in the controls (P<0.001) and asymptomatic bateruria was reported in 53(53%) of the cases versus 34(34%) of controls (P<0.007), gestational diabetes during previous pregnancies was reported in

98(98%) in the cases versus none in the controls (P<0.001), history of hypertension in 23(23%) in the cases versus one (1.0%) in the control group (P<0.001), while macrosomic baby was reported in one women of each group (1%). Abortion/Stillbirth was reported in 14(14.0%) in the cases versus 5(5.0%) in the controls (P<0.030), as indicated in Table 1 & Figure 4.

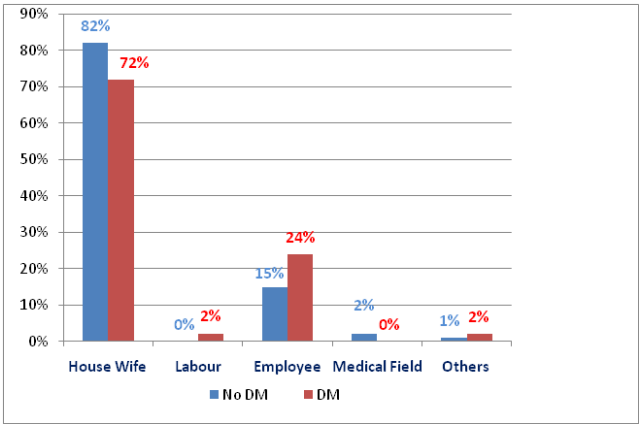

Figure 3: Description of study population by occupation.

Total cholesterol was high in 84(84%) of the cases with mean concentration of (202±17mg/dl) versus none in control group. Triglyceride was high in 96(96%) of the cases with a mean concentration of (180±15mg/dl) versus none in control group. HDL was high in 18(18%) of the cases with a mean concentration of (53±10mg/dl) versus none in control group. LDL was high in 93(93%) of the cases with a mean concentration of (114±17mg/dl) versus 23(23%) of the controls. VLDL was high in 96(96%) of the cases with a mean concentration of (37±15mg/dl) versus none in control group. All lipid profile parameters have shown statistically significant differences between cases and controls (P<0.001), indicating the risk of lipids disorders during pregnancy among diabetic pregnant ladies, as indicated in Table 2.

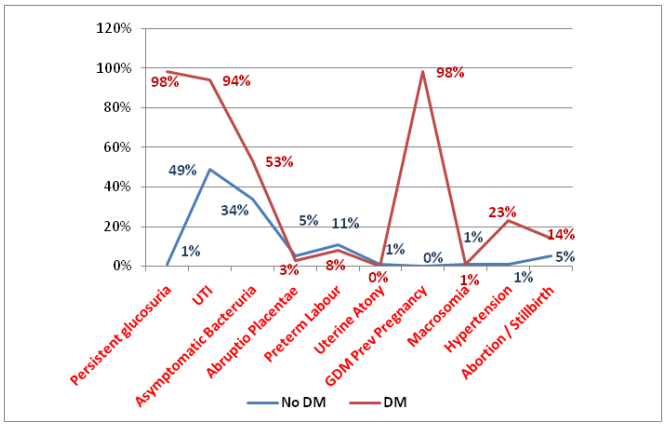

Figure 4: Description of the cases and controls according to frequency of the complications.

Table 1 Distribution of the cases and controls according to frequency of the complications

Antenatal and postnatal complications	Pregnant		Total	P value
	None DM	DM		
Persistent Glucosuria	1(1.0%)	98(98.0%)	99(49.5%)	0
UTI	49(49.0%)	94(94.0%)	143(71.5%)	0
Asymptomatic Bacteruria	34(34.0%)	53(53.0%)	87(43.5%)	0.007
Abruptio Placentae	5(5.0%)	3(3.0%)	8(4.0%)	0.47
Preterm Labour	11(11.0%)	8(8.0%)	19(9.5%)	0.469
Uterine Atony	1(1.0%)	0(0.0%)	1(0.5%)	0.316
GDM Prev. Pregnancy	0(0.0%)	98(98.0%)	98(49.0%)	0
Macrosomia	1(1.0%)	1(1.0%)	2(1.0%)	0.1
Hypertension	1(1.0%)	23(23.0%)	24(12.0%)	0
Abortion/Stillbirth	5(5.0%)	14(14.0%)	19(9.5%)	0.03

Table 2 Distribution of the cases and controls according to frequency of the hyperlipidemia

Hyperlipidemia		Pregnant		Total	P value
		No DM	DM		
Total Cholesterol	Normal total cholesterol	100(100.0%)	16(16.0%)	116(58.0%)	0.001
	High	0(0.0%)	84(84.0%)	84(42.0%)	
Triglyceride	Normal triglycerides	100(100.0%)	4(4.0%)	104(52.0%)	0.001
	High	0(0.0%)	96(96.0%)	96(48.0%)	
HDL	Normal HDL	100(100.0%)	82(82.0%)	182(91.0%)	0.001
	High	0(0.0%)	18(18.0%)	18(9.0%)	

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Table continued...

Hyperlipidemia		Pregnant		Total	P value
		No DM	DM		
LDL	Normal LDL	77(77.0%)	7(7.0%)	84(42.0%)	0.001
	High	23(23.0%)	93(93.0%)	116(58.0%)	
VLDL	Normal LDL	100(100.0%)	4(4.0%)	104(52.0%)	0.001
	High	0(0.0%)	96(96.0%)	96(48.0%)	

Table 3 Distribution of the cases and controls according to mean of the hyperlipidemia

Hyperlipidemia	Mean±SD		P value
	No DM	DM	
Total Cholesterol	134±24	202±17	<0.001
Triglycerides	90±17	180±15	<0.001
Lipoprotein Choles HDL.C	43±8	53±10	<0.001
Lipoprotein Choles LDL.C	73±21	114±17	<0.001
Lipoprotein Choles VLDL.C	18±3	37±15	<0.001

Discussion

There are enough evidences reported that pregnancy in preexisting diabetic women, is frequently associated with an increased risk of maternal and fetal adverse outcomes.[18] In the present study we found a diverse complication associated with pregnancy among diabetic women compared to non-diabetic healthy women. Women with diabetes, especially type 1, have poorer pregnancy outcomes, as well as greater incidence of spontaneous abortions, pre-eclampsia, fetal macrosomia, preterm delivery, congenital anomalies and perinatal mortality. A study in this context showed a higher incidence of perinatal fetal morbidity (hypoglycemia, jaundice, respiratory distress syndrome) in the patients with type 1, type 2 and gestation diabetes than in the healthy controls.[19] Similar findings to our results were also reported in a study found that Maternal and neonatal outcomes for women with type 2 diabetes were worse than those for nondiabetic controls. Diabetic women have a higher risk for primary caesarean section, pre-eclampsia, infections during pregnancy, large neonatal birth weight, large for gestational age, and macrosomia.[20]

In the observational Hyperglycemia and Adverse Pregnancy Outcomes study, women with hyperglycemia not meeting criteria for GDM were still at increased odds of multiple adverse outcomes, including large-for gestational-age (LGA) birth weight, high cord-blood serum C-peptide levels, primary cesarean delivery, neonatal hypoglycemia, premature delivery, shoulder dystocia or birth injury, intensive neonatal care, hyperbilirubinemia, and preeclampsia.[21,22]

In the present study, the most frequent age among cases was 31years. Such age was previously reported as significantly associated with GDM in comparison to controls (pregnant non diabetic) (P value=0.013), and this disagrees with the current study (P value=0.064).[23] The education level between the two groups showed predomination of educated women; 51% were university graduates in both groups, while primary schools graduates were less representing 16% and 13% in the cases and controls respectively. Yet, most mothers in cases and controls were housewives with percentages of 72% and 82% respectively, followed by employees who represented 24% and 15% respectively. Educated patients were more likely to have positive attitude and practice towards the disease and its management.

Distribution of the study population according to residence showed that participants were mostly from Omdurman in both case and control groups (55% and 50% respectively), followed by those who reside in Bahry (47 and 35 respectively). Also, parity among most of them ranged from 1-3 representing 76% in the case group and 80% in control group. With regard to clinical complications when compared to normal pregnant women (control group), diabetic pregnant women (case group)showed significant increase in incidence of persistent glucosuria (GU), urinary tractinfection (UTI), hypertension, GDM in previous pregnancy, abortion/stillbirth and asymptomatic bacteriuria (AB).

A study by Mardi et al.,[23] found that, one of the strongest predictor of GDM in comparison to controls in Sudanese women is GU (RR=2.39, P value=0.000), but UTI (P value=0. 251) failed to demonstrate significant associations with GDM, and this is compatible with our study regarding GU and opposing our results in UTI. Unexpectedly, macrosomic babies reported at the same frequencies in the two groups (one macrosmic baby for each). And this is not compatible with other study conducted elsewhere,[24] when they found that, diabetes is associated with LGA/macrosomic babies (p value=0.002).

Another study found strong significance linked women with history of still birth (p value=0.0004), relatives having diabetes (OR=8.08, p value=0.004), history of more than two miscarriages (p value=0.0001) to the development of GDM in comparison to control (pregnant women without GDM) which are compatible with the current study.[25] The adverse pregnancy outcome can't be a limited of complications, depending on women conditions and other participating factors, different maternal complication were reported in literature which reviewed that, maternal complications are pregnancy induced hypertension, pre-eclampsia, hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, Cesarean section, hypoglycemia and the worsening of any degree of a pre-existing renal insufficiency and retinopathy.[26,27]

The current findings showed significant increase in lipid profile parameters (P value=0.000) among cases. All lipid parameters

including, total cholesterol (TC), Triglyceride (TG), high density lipoprotein Cholesterol (HDL.C), low density lipoprotein Cholesterol (LDL.C) and low density lipoprotein Cholesterol (VLDL.C) were found significantly higher in cases compared to controls. It was found that dyslipidemia, more specifically high-serum low-density lipoproteins (LDL) and low-serum high density lipoproteins (HDL) are known risk factors for cardiovascular disease.[28]

Conclusion

Diabetes often associated with a significant increase in complications among pregnant diabetic women, which need more care during the pregnancy, as it serve as risk factors for the maternal and fetal.

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

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