Evaluation of American and WHO Cut off Limits of Fifty Gram Glucose Challenge Test for Diabetes Mellitus Screening in Pregnant Women

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Abstract:

This is a prospective cross-sectional study included two hundreds gestational Sudanese ladies who were selected with the same inclusion criteria. The study was conducted in Omdurman teaching hospital and Baghdadi charitable center from Jan2008 to Jul 2009.

The aim of this study was to compare sensitivy and specificity of the American cut off limit (≥ 130mg/dl) and the WHO one (≥ 140mg/dl), for fifty gram glucose challenge test as screening test for gestational diabetes mellitus. Also to study the percentages of positive glucosuria with or without GDM (Gestational diabetes mellitus).

Method: 200 venous sampleswere collected and glucose oxidase spectrophotometeric method was used to detect glucose concentration .

Results

After comparing the results of both American cut off limit (≥ 130mg/dl) and the WHO one (≥ 140mg/dl) to the American standard 100g GTT and after statistical analysis, it was found that the American cut off limit was more sensitive (100%) than of the WHO (89%), while the specificity was more or less the same.

Conclusion

In conclusion during screening with 50 gram challenge test (GCT) some cases with gestational diabetes may be missed if WHO cut off limit is not shifted to a lower limit .

Introduction:

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia among other signs. The world health organization recognizes three main forms of diabetes: type 1, type 2, and

gestational diabetes (or type 3, occurring during pregnancy), although these share signs and symptoms but have different causes and population distributions. Type 1 is generally due to autoimmune destruction of the insulin-producing cells (pancreaticbeta cells), while type 2 is characterized by tissue wide insulin resistance and varies widely. Gestational diabetes is due to a poorly understood interaction between fetal needs and maternal metabolic controls.[1]

Since the first use of insulin in 1921 it was found that types 1 and 2 were incurable, but treatable, while gestational diabetes typically resolves with delivery. Asides from acute glucose level abnormalities, are that known as long term complications. These include cardiovascular disease, chronic renal failure, retinal damage, nerve damage, and microvascular damage and poor healing which can lead to gangrene and even amputation.[5]

There is accelerated population growth, urbanization and high prevalence of obesity and an inactive lifestyle. So the number of people with DM is increasing at a rapid speed. About 6% of adults in the world, or 246 million people, have diabetes. These figures were published in December 2006; by the International Diabetes Federation. The federation, a coalition of diabetes associations from more than 150 countries, estimates that the prevalence of diabetes (mainly type 2) is rising and now affects 5.9% of people aged 20-79 years. Almost 80% of affected people live in developing countries.[6]

Before the 1990 ,diabetes was considered a rare medical condition in Africa. Epidemiological studies carried out in that decade, however, provided evidence of a trend toward increased incidence and prevalence of type 2 diabetes in African populations.[12] Africa is experiencing the most rapid demographic and epidemiological transition in world history. It is characterized by a tremendous rise in the burden of non communicable diseases. Underlined by the increasing life expectancy and lifestyle changes resulting from the reduction in infectious diseases and increased fertility.[8] The prevalence of diabetes in Africa was approximately 3 million in 1994; but the region is due to experience a two-to threefold increase by the year 2010. The highest prevalence is found in populations of Indian origin, followed by black populations and Caucaians. Among the population of Indian origin in South Africa and Tanzania, the prevalence is between 12 and 13 percent. The prevalence in blacks follows a Westernization gradient, with that of rural Africa generally below 1 percent but that of urban Africa between 1 and 6 percent.

In general the prevalence of type 2 diabetes is low in both rural and urban communities of West Africa except in urban Ghana, where a high rate of 6.3 percent was recently reported.[12]

Gestational diabetes mellitus:

It is defined as glucose intolerance that begins, or is first recognized, during pregnancy.1Certain hormones increase during pregnancy, transferring valuable nutrients from the mother to the baby so that the fetus develops and grows. Other hormones block the action of insulin, ensuring that the mother herself does not develop low blood sugar. To compensate, the mother's insulin levels rise. If the mother insulin levels cannot increase sufficiently, rising blood sugar levels will eventuallyresult in gestational diabetes. Untreated, gestational diabetes can lead to complications for both the mother and the baby.[1]

A wide range of complications is associated with the disorder. For the mother, gestational diabetes increases the risk of preeclampsia, cesarean delivery, and future type 2 diabetes. In the fetus or neonate, the disorder is associated with higher rates of perinatal mortality, macrosomia, birth trauma, hyperbilirubinemia, and neonatal hypoglycemia. Some studies have found an association between gestational diabetes and increased perinatal mortality rates, but other studies have shown no increased risk. [6]

Gestational diabetes mellitus (GDM), is the most common metabolic disorder of pregnancy. It is evident that GDM defined in this way will include patients with undiagnosed preexisting type 2 diabetes mellitus (type 2 DM) as well as those with diabetes with first onset during pregnancy. Normal pregnancy is associated with insulin resistance similar to that found in type 2 DM. The reduction in whole-body insulin action becomes apparent in the second trimester, and insulin sensitivity declines progressively. After delivery, whole-body insulin action returns rapidly to normal. Hence, if the onset of diabetes is truly in pregnancy, then it is most likely to occur in the second and third trimesters and glucose tolerance may return to normal after delivery. Nonetheless, women with GDM in whom glucose tolerance becomes normal post-partum remain insulin-resistant compared with women with no history of GDM.[2]

Diabetes in the first trimester is more likely to be type 2 DM that was present but undiagnosed before pregnancy. In these circumstances, glycosylated haemoglobin, giving an indication of average blood glucose concentrations over the previous six to eight weeks, is likely to be raised. Occasionally, the diagnosis of GDM will identify women with type 1 diabetes mellitus. Indeed, the incidence of type 1 DM is greater in pregnancy than in the background population.[8]

Screening for a disease is recommended if the disease is common and clinically important and if a simple screening test exists that will identify the majority of diseased individuals without high rates of false positive or false negative results. [8]

In different series, GDM occurs in 1-14% of pregnancies, with an estimated prevalence in the UK of 4%. Its clinical importance is on three levels—first, the adverse consequences of poorly controlled GDM for the fetus and neonate; second, the increased risk of type 2 DM in later life for the infant; third, the adverse consequences for the mother, especially the predisposition to type 2 DM in later life.[8]

Screening for GDM:

There is no consensus as to the timing of screening, the test to be used or who to screen (universal or selected/targeted screening). The most widely employed screening test in the UK is based on maternal risk factors. However, use of such risk factors (family history of diabetes, previous large-for gestational-age baby or stillbirth) caused 38% of gestational diabetes to go unidentified in one study.[1]Several groups have tried other risk factors (previous neonate >9 lb [4 kg], neonatal death, congenital anomaly, prematurity, family history of diabetes) and clinical findings during pregnancy (obesity, excessive weight gain, glycosuria, proteinuria, hypertension). About half the women with GDM were identified by these means.[2,4]

In the USA, the glucose challenge test (GCT), first proposed by O'Sullivan, is the most widely used screening test and is recommended by the ADA.[2]This is performed without regard to time or nature of the last meal, at 24-28 weeks' gestation. Women are given 50 g of glucose by mouth and plasma glucose is measured at 1 hour. A positive test is a plasma venous glucose concentration ≥ 7.8 mmol/L. In O'Sullivan's original studies of 752 women, all had a 50 g GCT and a 100 g 3-hour OGTT.[2] The challenge test (with a screen cut-off of 7.8 mmol/L) had a

sensitivity of 88% and a specificity of 82% in those ≥ 25 years. Since then, researchers have not agreed on the threshold values for the GCT, the range of suggested values being 7.2-8.3 mmol/L.[3]The Toronto Tri-Hospital study showed pronounced differences of plasma glucose in the two states. Adjustment of the thresholds to 8.2 mmol, 7.9 mmol, and 8.3 mmol/L for elapsed post-prandial times of < 2, 2-3 and > 3 hours, respectively, increased the positive predictive value of the test from 14.4% to 18.7%.[3]The ADA has subsequently recommended that screening of a pregnant woman is unnecessary if she fulfils all the following criteria: <25 years old; normal body weight; no family history (i.e. first degree relatives) of diabetes; and not a member of an ethnic/racial group with a high prevalence of diabetes (Hispanic, Native American, Asian-American, African-American, or Pacific Islander). The Fourth International Workshop-Conference on GDM, under the sponsorship of the ADA, further recommended that women should be screened if they have a history of GDM or poor obstetric outcome.[3]

The WHO recommends screening by means of maternal risk factor selection. Formal systematic testing with a 75 g 2-hour OGTT for GDM between 24 and 28 weeks of gestation is recommended for older women, those with a previous history of glucose intolerance, those with a history of large-for-gestational-age babies, women from certain high-risk ethnic groups, and any pregnant woman who has a raised fasting or casual blood glucose. Also there may be a case for screening pregnant women from high-risk populations during the first trimester to detect previously undiagnosed diabetes mellitus.[3]

Diagnosis of GDM:

The tests are usually performed between 24 and 28 weeks' gestation. Early criteria for abnormal glucose tolerance in pregnancy, proposed by O'Sullivan and Mahan in 1964, were based on data obtained from the 100 g 3-hour OGTT performed on 752 pregnant women.[14] Abnormal glucose tolerance was defined as ≥ 2 blood glucose values, out of 4, that were greater than or equal to 2 standard deviations above the mean. The requirement for two values to be abnormal was based on a desire to 'avoid misclassification due to laboratory error or occasional single high peaks resulting from unusually rapid absorption of glucose'.[14]These criteria for abnormal glucose tolerance were validated by their prediction of later non-pregnancy glucose intolerance when applied to a second group of 1013 women who had been tested during

pregnancy and followed for 5-10 years post-partum. In 1979 the National Diabetes Data Group (NDDG) revised the O'Sullivan and Mahan criteria, converting the whole-blood glucose values to plasma glucose values by upward adjustment of 15% and the ADA later adopted this.[13] Carpenter and Coustan suggested that the NDDG conversion factor was too high and proposed alternative cut-off values [15] (table 2).

The WHO recommends a standard OGTT, performed after overnight fasting (8-14 hours); 75 g anhydrous glucose is given in 250-300 mL water, and plasma glucose is measured fasting and after 2 hours. Pregnant women who meet criteria for diabetes mellitus or impaired glucose tolerance in the non-pregnant state are classified as having GDM. Unlike the O'Sullivan and Mahan thresholds, the WHO criteria were not developed specifically for use in pregnant women, nor were they validated by their ability to identify pregnancies at increased risk for adverse outcome. A major advantage of the WHO criteria is that the 75 g 2-hour OGTT is used as for non-pregnant individuals.[15]

The WHO and ADA criteria for GDM have been compared; 127 Pima Indian women with no previous history of type 2 DM were studied with both protocols. It was found that 11 women who met the WHO diagnosis of GDM also included 2 women with GDM by the ADA criteria. The other 9 patients with GDM by WHO criteria had an excess of macrosomic babies and caesarean sections: 16 of the 127 women had infants > 4 kg, of whom 6 were correctly identified as abnormal by the WHO criteria compared with 1 out of the 16 by the ADA criteria. Of the 7 delivering by caesarean section, 4 had abnormal glucose tolerance by WHO criteria, none of them by ADA criteria. Although the numbers in this study were small, there is now a move towards using the diagnostic 75 g 2-hour OGTT in pregnancy and the results from the HAPO study are awaited for definitive evidence.[12]

The initial screening for gestational diabetes is accomplished by performing a 50-g, one-hour glucose challenge test at 24 to 28 weeks of gestation. Patients do not have to fast for this test. To be considered normal, serum or plasma glucose values should be less than 130 mg per dL (7.2 mmol per L) or less than 140 mg per dL (7.8 mmol per L). Using a value of 130 mg per dL or higher will increase the sensitivity of the test from 80 to 90 percent and decrease its specificity, compared with using a value of 140 mg per dL or higher. Thus, the lower screening level of 130

mg per dL identifies more patients with gestational diabetes at the cost of more false positive results. Current recommendations from the American Diabetes Association (ADA) and the American College of Obstetricians and Gynecologists (ACOG) accept either value for defining an abnormal initial screening result. [6]

An abnormal one-hour screening test should be followed by a 100-g, three-hour venous serum or plasma glucose tolerance test. After the patient has been on an unrestricted diet for three days, venous blood samples are obtained following an overnight fast, and then one, two, and three hours after an oral 100-g glucose load. During the test period, patients should remain seated and should not smoke. Two or more abnormal values are diagnostic for gestational diabetes.[6]

The diagnostic criteria from the National Diabetes Data Group (NDDG) have been used most often, but some centers rely on the Carpenter and Coustan criteria, which set the cutoff for normal at lower values (Table 1). Compared with the NDDG criteria, the Carpenter and Coustan criteria lead to a diagnosis of gestational diabetes in 54 percent more pregnant women, with an increased cost and no compelling evidence of improved perinatal outcomes. While the ADA supports use of the stricter criteria, the most recent ACOG practice bulletin supports the use of either criteria set. Whole blood glucose values are approximately 10 to 15 percent lower than serum or plasma values.[6]

(Table1): Criteria for Abnormal Result on 100-g, Three-Hour Oral Glucose Tolerance Tests in Pregnant Women

Blood sample	National Diabetes Data Group	Carpenter and Coustan
Fasting	105 mg per dL (5.8 mmol per L)	95 mg per dL (5.3 mmol per L)
1-hour	190 mg per dL (10.5 mmol per L)	180 mg per dL (10.0 mmol per L)
2-hour	165 mg per dL (9.2 mmol per L)	155 mg per dL (8.6 mmol per L)
3-hour	145 mg per dL (8.0 mmol per L)	140 mg per dL (7.8 mmol per L)
Gestational diabetes mellitus is diagnosed if two or more of the values (venous serum or plasma glucose levels) are met or exceeded.		

(Table 2): Diagnosis of gestational diabetes mellitus, WHO criteria.

Formal testing usually at 24-28 weeks' gestation. Standard 75 g oral glucose tolerance test performed after overnight fast (8-14h). Glucose concentrations (mmol/L):				
	Whole blood venous	Whole blood capillary	Plasma venous	Plasma capillary
Fasting	≥ 6 . 1	≥ 6 . 1	≥ 7 . 0	≥ 7 . 0
2 h	≥ 6 . 7	≥ 7 . 8	≥ 7 . 8	≥ 8 . 9

Methods:

This is a prospective cross sectional study conducted in Omdurman maternity hospital and Baghdadi medical centre in khartoum state. 200 pregnant ladies aged 18-45 years were included. A 50 gram glucose challenge test was performed by giving an oral 50 gram load of glucose to each lady, with a plasma glucose level estimated one hour later using glucose oxidase spectrophotometric method. All women with plasma glucose value ≥ 130 mg/dl were further subjected to a 3-hr, 100-gram glucose tolerance test (OGTT) to diagnose gestational diabetes mellitus. Data analysis was done using (SPSS) version 11.

Results:

The study performed 100-g GTT to confirm the prevalences and then to calculate the specificity and sensitivity of 50-g GCT in diagnosis of gestational diabetes mellitus. The study compared between the prevalences of gestational diabetes mellitus when applying ≥ 130mg/dl and ≥ 140mg/dl as cut off limits after 50-g GCT, which was found 9% and 8% respectively , with an insignificant probability (P. Value =0.09) as shown in table 3.

The study performed 100-g GTT to confirm the prevalences and then to calculate the specificity and sensitivity of 50-g GCT in diagnosis of gestational diabetes mellitus.

The specificity of 50 gm glucose challenge test was more or less the same for both cut off limits (100%), while the sensitivity of ≥130mg/dl as cut off limit (100%) was greater than that of 140mg/dl cut off limit (89%).

(Table 3):Results of plasma glucose levels of 1 hour fifty gram glucose challenge test applying cut off limit ≥ 130mg/dl:

	N	%	Min	Max	Mean
≥ 130mg/dl	18	9 %	135	243	182
< 130mg/dl	182	91 %	61	127	103
Number examined	200	100%			

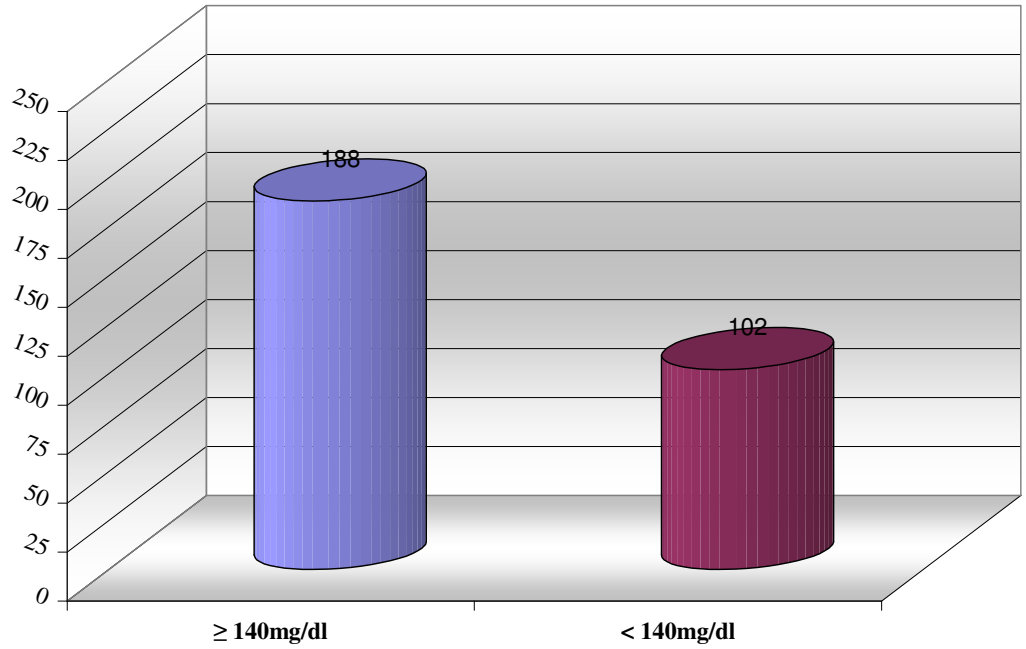
(Table 4):Results of glucose levels applying 100g GTT for samples ≥ 130mg/dl:

	N	Min	Max	Mean
Fasting	18	79	189	137
One hour	18	215	396	281
Two hours	18	185	314	230
Three hours	18	138	281	196
Specificity value = 100 %				
Sensitivity value = 100 %				

(Table5) :Results of plasma glucose levels of 1 hour fifty gram glucose challenge test applying cut off limit ≥ 140mg/dl:

	N	%	Min	Max	Mean
≥ 140mg/dl	16	8 %	145	243	188
< 140mg/dl	184	92 %	61	138	102

Number examined	200	100 %	

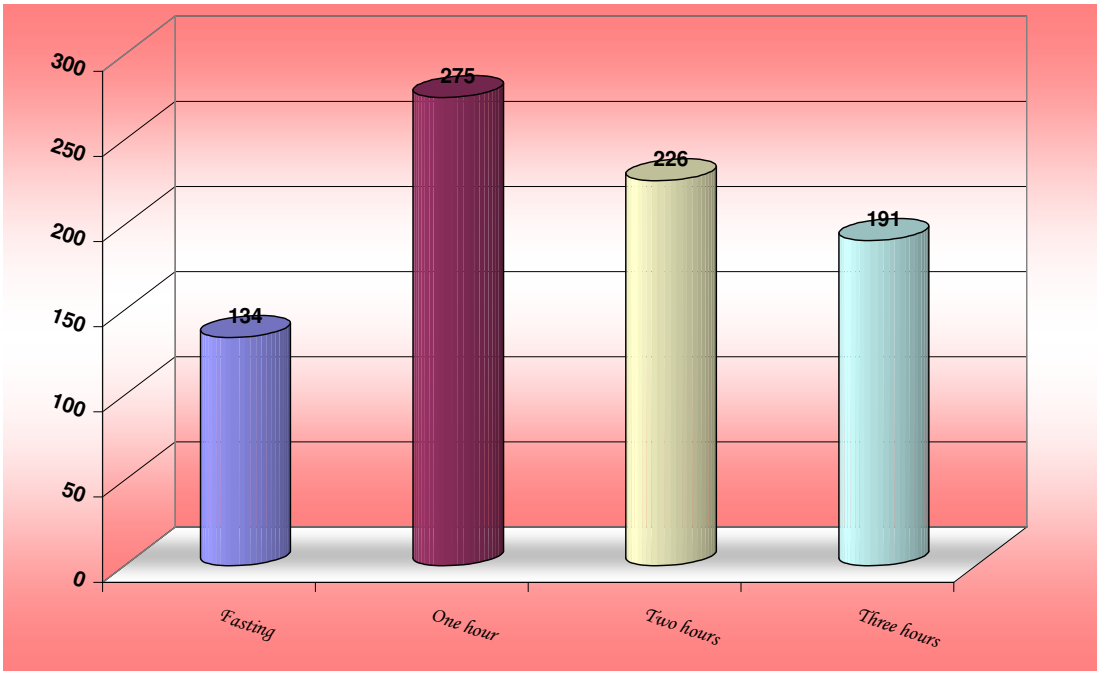


(Fig 1): Results of mean plasma glucose levels of 1 hour fifty gram glucose challenge test applying cut off limit ≥ 140mg/dl

(Table6)Results of 100g GTT for samples ≥ 140mg/dl:

	N	Min	Max	Mean
Fasting	16	79	182	134
One hour	16	215	396	275
Two hours	16	185	314	226
Three hours	16	138	281	191
Specificity value = 100 %				

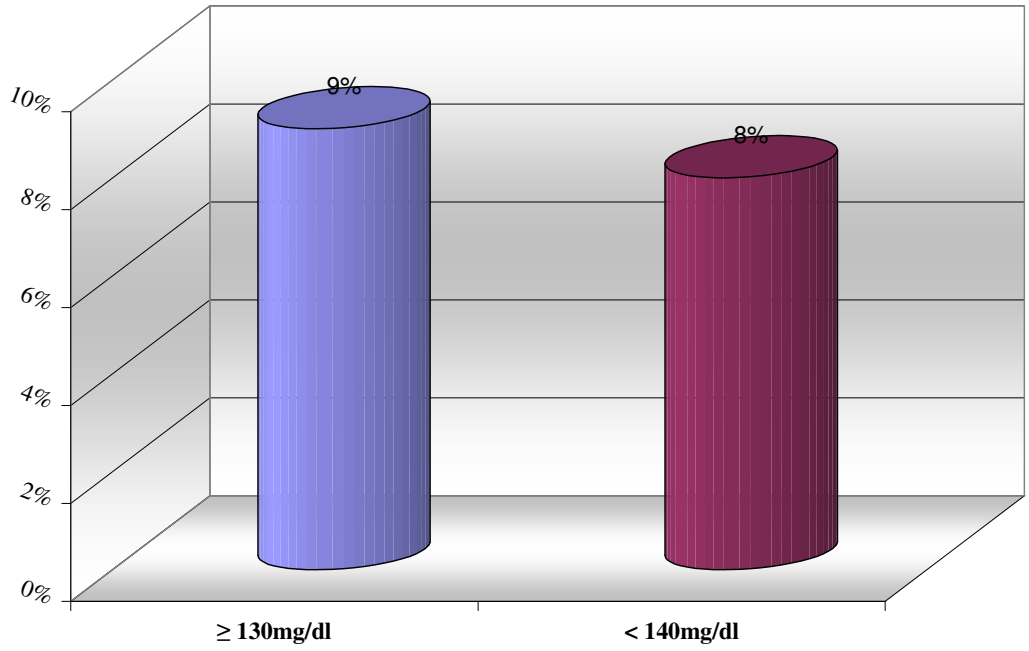
Sensitivity value = 89 %



(Fig 2):Results of mean plasma glucose levels applying 100g GTT for samples ≥ 140mg/dl

(Table 7): Comparison between plasma glucose levels of 1 hour fifty gram glucose challenge test applying WHO or American cut off limits(≥ 140mg/dl and ≥130 mg/dl respectively) :

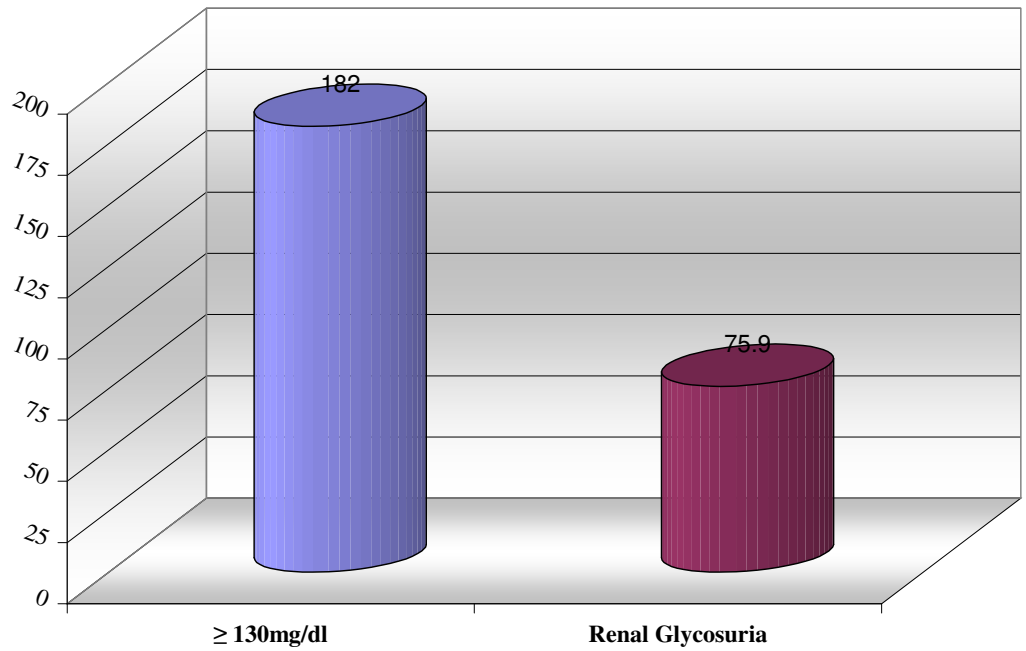
	N	Min	Max	Mean	Std. Dev
≥ 130mg/dl	18	135	243	182	27.7
≥ 140mg/dl	16	145	243	188	23.6



(Fig 3): Comparison of diabetic ladies frequencies between WHO and American cut off limits(≥ 140mg/dl and ≥130) :

(Table8):Comparison between plasma glucose levels ≥ 130mg/dl and < 130mg/dl of ladies have glucosuria:

	N	%	Min	Max	Mean	Std. Dev
Positive glucosuria with plasma glucose ≥ 130mg/dl	18	9 %	135	243	182	27.7
Positive glycosuria with plasma glucose <130mg/dl	35	17.5%	61	96	75.9	9.4
P. value = 0.01						
Specificity value of glucosuria for GDM = 66%						
Sensitivity value of glucosuria for GDM = 100%						



(Fig 4):Comparison between mean plasma glucose levels of < 130mg/dl of ladies have positive or negative glucosuria:

Discussion

As it was mentioned before, the third trimester of pregnancy is the most period to make metabolic changes due to placental load.

The prevalence of maternal and neonatal complications among Sudanese diabetic women and their infants are high. . A Sudanese study confirms that maternal hyperglycaemia emerges as an important factor affecting maternal well-being and neonatal morbidity and mortality.[1]

100g GTT was performed for every lady with ≥ 130mg/dl after 50g GCT. Ladies having two or more abnormal values after GTT were regarded as diabetics. [2]By comparing the mean results of 50 gm glucose challenge test for group I samples (cut off limit ≥ 130mg/dl), and the mean results of 50 gm glucose challenge for group II (<130mg/dl) (table no 1), the result was statistically significant indicating that, the first group that includes 18 samples of 9% prevalence has a higher plasma glucose levels than that of the second group. The specificity of 50 gm glucose challenge test was more or less the same for both cut off limits (100%), while the sensitivity of ≥130mg/dl as cut off limit (100%) was greater than that of 140mg/dl cut off limit (89%). These findings are consistent with the study done by the american academy of family physician, which indicates that ≥130mg/dl is more sensitive than ≥140mg/dl as cut off limits. [2] According to glucosuria and after statistical analysis it was found that the mean concentration of

the first group (positive glucosuria with plasma glucose level of <130mg/dl) was statistically significant lower than those of the second and third group (positive glucosuria with plasma glucose level ≥130mg/dl, and negative glucosuria, respectively), from one hand and from the other hand the prevalence was statistically significant indicating that renal glucosuria is more frequent than diabetes. These finding agrees with the study published by the European Journal of Obstetrics & Gynecology and Reproductive Biology, which stated that the glucosuria during pregnancy is oftentimes not related to diabetes mellitus.[3] Also these findings may explain the number of diabetic ladies in this study (9%) and also may partially indicates that as the frequency of renal glucosuria is increasing, the ability of pregnant ladies to get gestational diabetes mellitus is probably reduced.

Conclusion:

The prevalence of gestational diabetes mellitus was 9% by applying the cut off limit of ≥ 130mg/dl while it was 8% when ≥ 140mg/dl is the cut of limit , among the studied group. This conclude that ≥ 130mg/dl cut of limit for fifty gram glucose challenge test is more sensitive than that of 140mg/dl.

The prevalence of renal glucosuria was significantly higher than the prevalence of diabetes which may be responsible for low frequency of gestational diabetes mellitus and also may be considered as protective phenomena against gestational diabetes mellitus.

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