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ABSTRACT

***Objectives*: To determine the prevalence of and associated factors for glucose intolerance among antenatal clients at Kenyatta National Hospital at 24-36 weeks of gestation.**
***Design*: Cross-sectional analytical study.**
***Setting*: Kenyatta National Hospital antenatal clinic.**
***Subjects*: One hundred and two (102) antenatal mothers at a gestational age of 24-36 weeks were recruited into the study and underwent a 100g Oral Glucose Tolerance Test (OGTT) after consenting to participate in the study.**
***Results*: From the study 37(36%) had glucose intolerance while 65 (64%) had normal glucose tolerance. Among clients with glucose intolerance, 16.7% met the diagnostic criteria for gestational diabetes, 3.9% had impaired glucose tolerance and 15.7% had impaired fasting glycaemia. Of the clients with normal glucose tolerance 22.5% displayed flat curves. Factors significantly associated with glucose intolerance were: BMI > 25; P-value 0.036: OR 0.37 CI (1.06-6.90), history of and treatment for sub-fertility p-value 0.002: OR 8.69 CI (1.74-43.50) and family history of hypertension; p-value 0.037: OR 2.66 CI (1.04-6.78).**
***Conclusion*: The prevalence of glucose intolerance was 36%. This is much higher than the 5% previously reported. There is need to screen pregnant women for glucose intolerance to prevent the complications usually associated with it.**

INTRODUCTION

Glucose intolerance is defined as a state of impaired glucose homeostasis characterised by hyperglycaemia, abnormalities of lipid and protein metabolism due to the defect in insulin secretion and action (1, 2). There is an increase in trends in the developing nations of cases of diabetes mellitus whose management is expensive whereas in these countries health resources are mostly spent on curative services on communicable diseases. Currently it is only diabetes mellitus which is the only non-communicable disease with a special United Nations Declaration, with 14 November declared as the world's diabetic day (3). Gestational diabetes is estimated to complicate 1-14% of all pregnancies with mild degrees of glucose intolerance being even higher (4-7). It is associated with increased maternal morbidity, foetal/neonatal morbidity and mortality with an increased risk of future micro and macrovascular complications (8-14). These are potentially preventable through early diagnosis and risk modification (15-17). The hormonal changes in pregnancy leads to changes in glucose metabolism which may manifest as various degrees of glucose intolerance in individuals with inherited or acquired defects in glucose regulation.These are caused by insulin deficiency, receptor abnormality or post receptor abnormality resulting in reduced glucose entry into cells with stimulation of lipid and protein metabolism (18, 19). They are classified depending on etiology and clinical presentation. Diabetes Mellitus type 1 and 2 gestational diabetes. Impaired Glucose Tolerance (IGT) is the state of impaired glucose regulation characterised by hyperglycaemia with blood sugar levels below the threshold required to diagnose Diabetes Mellitus Impaired Fasting Glycaemia (19). There is very limited information on the prevalence of glucose intolerance in pregnancy in the Kenyan population; Githaiga in Kenyatta National Hospital in 1991 reported an incidence rate

of 0.15% (20) a previous study gave a prevalence rate estimate of 7%(21).

Prevalence rates for gestational diabetes alone in the world range from 1-14 % depending on the race, ethnic group and screening criteria used (4 - 6, 22). With little information currently available on the prevalence of glucose intolerance in pregnancy in Kenya, this study is aimed at providing this information.

The objective of the study was to determine the prevalence of glucose intolerance among antenatal clinic attendants at 24 to 36 weeks of gestation at Kenyatta National Hospital.

MATERIALS AND METHODS

Study design: This was a cross sectional analytical study, 102 antenatal mothers at 24-36 weeks of gestation were recruited.

Study site: The study was carried out at the antenatal clinic, Kenyatta National Hospital.The clinic handles 300 pregnant mothers weekly.

Study population: This consisted of expectant mothers at 24-36 weeks of gestation who were attending the antenatal clinic during the study period, fulfilled the inclusion criteria and consented to the study.

Inclusion criteria: Clients attending the antenatal clinic during the study period at 24-36 weeks of gestational without pre-gestational or gestational diabetes and provided informed consent.

Exclusion criteria: Clients who had pre-gestational diabetes mellitus, those already diagnosed with glucose intolerance in the current pregnancy or in previous pregnancy, clients who did not consent and clients on medications for chronic treatment.

Sampling frame: This consisted of antenatal mothers attending the antenatal clinic between November 15th 2008 and 15th April 2009.
The sample size was calculated using the formula for prevalence rates: the prevalence used was 7% being the average of the estimated total prevalence of GDM of 1-14 %(4-7) giving a sample size of 100.

Sampling method: Systematic sampling of every 4thclient reporting to the observation room of the antenatal clinic and met the study criteria was done. Only five clients were recruited per day due to the limitation by the laboratory capacity.

Research personnel: Three research assistants were recruited consisting of a trained nursing officer working in the antenatal clinic and two laboratory technicians working within the biochemistry laboratory who administered OGTT.

Laboratory method: A fasting capillary blood sample was taken 30 minutes after arrival in the laboratory (finger puncture after swabbing the finger with methylated spirit) and tested for sugars. A 300 millilitre solution containing 100g of glucose was then administered orally over five minutes and capillary blood drawn and tested for sugars hourly for three hours. During this period the vital signs of the clients were taken every 15 minutes. Clients were advised to minimise physical activity during the test period. The blood drop obtained after a needle prick was analysed using reflectance meters with accompanying strips. The clients were then provided with snacks at the completion of the study.

Quality control: The Hemocue Glucometer used was run through a control strip whenever any set of glucose strips was opened and then subjected to weekly calibration. The glucose testing was periodically supervised by a qualified pathologist. Standards were maintained in accordance with preset standards. Interpretation of the test results was done according to the Carpenter Couston criterion which is recommended by the ADA (29, 37 - 39).

Normal values: Fasting blood sugar < 5.3mmol/dl, one hour post prandial <10.0mmol/dl, two hour post prandial <8.6mmol/dl, three hour post prandial < 7.8 mmol/dl.

Abnormal values: Any two or more values equal to or greater than the above or a fasting blood glucose ≥ 7.0mmol/dl were classified as GDM. Presence of one abnormal one, two or three hour value was classified as impaired glucose tolerance. A fasting blood sugar more than 5.3mmol/dl but less than, 7.0 mmol/dl was classified as Impaired Fasting Glycaemia (29). A test result where the peak glucose level was less than 7.0 mmo/dl without the normal peak at 30-60 minutes was classified as flat glucose tolerance curve. For analysis, normal glucose tolerance(all three values within normal limits)and Flat curves with fasting glucose below 5.3 mmol/dl were analysed as normal glucose tolerance while GDM, impaired fasting glycaemia and impaired glucose tolerance as `Glucose intolerance'.

Ethical issues: The study was approved by the Kenyatta National Hospital/University of Nairobi Ethics and Research committee (KNH/UON ERC). There was no coercion or financial inducements to the participants. The clients found to be have gestational diabetes(GD) were informed and were then managed by both the Diabetologist and the Obstetricians. Those who had no GD were informed and continued on the routine

antenatal care in the antenatal clinic.

Data management: Data were collected using pre-tested questionnaires and the laboratory test results were recorded on the standard hospital forms. These were checked for completeness before data entry. The analysis was done using SPSS version 15.

RESULTS

The study period was six months, 102 clients were recruited into the study who underwent a three hour 100g OGTT as the methodology above. The results are presented below.

Table 1
The study population by socio-demographic characteristics (N=102)

Socio-demographic Characteristic	Frequency n=102	Percentage (%)
Age		
< 25 years	21	20.6
≥ 25 years	81	79.4
Marital status		
Single	11	89
Married	89	11
Residence in the past 10 years		
Rural	13	12.7
Urban/rural then urban	89	87.3
Level of education		
Primary and below	13	13.0
Secondary and above	87	87.0
Employment status		
Currently employed	58	56.9
Self	30	51.7
Salaried	28	48.3
Unemployed	44	43.1
Income per month (ksh)		
< 15,000	36	62.1
15,000-30,000	22	37.9
Pre-pregnancy BMI		
≥ 25	36	35.3
< 25	41	40.2
Unknown	25	24.2

Seventy nine percent of the participants were aged 25 years and above with a mean age of 29.3 years.Eleven percent were single while eighty nine were married. Most had resided in urban centre within the past ten years. Eighty seven had received at least secondary education.

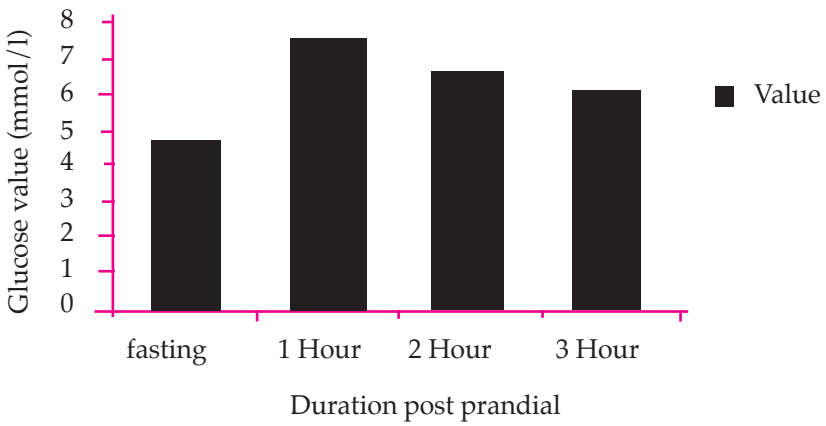
Table 2
Obstetrics and familial characteristics

1. Obstetric characteristic	Frequency	(%)
Gravidity (102)		
Primigravid	36	35.3
Multigravid	66	64.7
Glycosuria in current pregnancy	4	3.9
Polyhydramnous in current/past pregnancy	1	1
Pregnancy larger than dates	15	14.7
Previous neonatal weight ≥ 4000g	8	7.9
Previous pregnancy wastage	16	15.6
Hypertension in previous pregnancy	11	10.8
History of Gestational diabetes	1	1
History of infertility	10	9.8
Medical treatment for sub-fertility	6	5.9
2. Familial characteristics	Frequency	(%)
Family Hx of diabetes	20	19.6
Family Hx of hypertension	24	23.5
Family Hx of sudden death	6	5.9
Family Hx of CVA	9	8.8
Family member with obesity	4	3.9

Only one client had been diagnosed with glucose intolerance in previous pregnancy which subsided after delivery. Fifteen point six percent of the participants reported an adverse pregnancy outcome; an abortion, stillbirth or preterm delivery. Seven point eight percent had had a previous delivery to a neonate ≥4000g, nine reported having sub-fertility, out of which six had received treatment. The mean birth weights for previous deliveries were 3.19 kg (SD 0.69) for first; 3.22 kg (SD 0.73) for second and 3.86 kg (SD 0.30) for third deliveries. Nineteen percent of participants gave a positive family history of diabetes while 23% had a family history of hypertension. Few reported family history of other vascular disease.

Mean blood glucose values: The mean blood glucose values were 4.82mmol/dl fasting (1.00), one hour post prandial of 7.59mmol/dl (1.55), two hour post prandial of 6.68 mmol/dl (1.35) and three hour post prandial of 6.15 mmol/dl (1.29) with the ranges of 3.1-12.1mmol/l, 3.4-11.9 mmol/l, 4.0-9.8 mmol/l and 3.8-12.2 mmol/dl for fasting, one, two and three hour post prandial respectively.

Figure 1
Mean blood glucose values of the participants



Glucose tolerance patterns: Out of the 102 participants, 42 (41.2%) had normal glucose tolerance, 23 (22.5%) met the diagnostic criteria of flat curves, while 19.6 had mild degrees of glucose intolerance (one abnormal value). Sixteen point seven met the diagnostic criteria of gestational diabetes mellitus (Table 3).

Glucose tolerance pattern of the study subjects: Overall, the total number of clients with normal glucose tolerance was 65(63.7%) that is normal plus flat curves while 37 (36.3%) had glucose intolerance (impaired fasting glycaemia, impaired glucose tolerance and Gestational Diabetes Mellitus) as depicted in figure 2. Of the clients with glucose intolerance, 48 % were at a gestational age of 28 weeks and below while 52 % were more than 28 weeks gestational age (figure 2).

Figure 2
Glucose tolerance patterns of study subjects

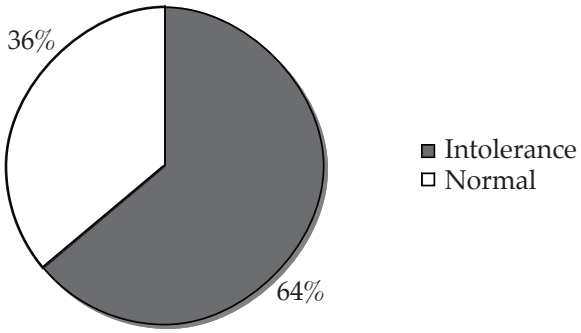


Table 3
Obstetric characteristics and glucose intolerance.

	Glucose intolerance		O.R(95% CI)	P-Value
	Yes (%)	No (%)		
Gravidity				
Primigravid	14(39.0)	22(61.0)	1.19(0.51-2.76)	0.69
Multigravid	23(34.8)	43(65.2)		
Glucosuria in current pregnancy	3(75.0)	1(25.0)	5.65(0.57-56.39)	0.10
Excess liquor in this pregnancy	1(100.0)	0(0)	-	0.18
Current pregnancy larger than dates	6(40.0)	9(60.0)	1.21(0.39-3.71)	0.75
Neonatal weight ≥ 4000g	5(62.5)	3(37.5)	3.2(0.73-14.38)	0.11
Neonatal NBU admission	2(22.2)	7(77.8)	0.47(0.09-2.41)	0.36
Previous pregnancy loss	6(37.5)	10(62.5)	0.58(0.23-1.48)	0.25
Hypertension in pregnancy	4(36.4)	7(63.6)	1.00(0.27-3.69	1.0
Hx of gestational D.M	1(100.0)	0(0)	-	0.18
Difficulty in conception	8(80.0)	2(20.0)	8.69(1.74-43.50)	0.002
Treatment for sub-fertility	5(83.3)	1(16.7)	10(1.12-89.22)	0.013

No association was demonstrated between parity, larger for gestational age pregnancy, prior pregnancy loss, hypertension, polyhydramnous, Glycosuria and neonatal NBU admission and glucose intolerance. Positive history of difficulty in conception and treatment for infertility were associated with statistically significant risk of abnormal glucose tolerance test (Table 3).

DISCUSSION

The study comprised of 102 participants with a mean age of 29.3 years and a median age of 28.0 years (SD 5.40). Seventy nine percent of clients in the study were above 25 years. Githaiga in 1991 demonstrated that 75 % of mothers with diabetes mellitus were above 25 years (20) while in this study 41% of mothers with glucose intolerance were above 25 years. Thirty five percent of these had glucose intolerance were multiparous a figure different from Githaiga *et al* where 91 % with abnormal glucose intolerance were multiparous. Other similar studies have associated glucose intolerance to high parity (23,24). In the study, the mean birth weights for clients with glucose intolerance was similar to the study population with regard to the first delivery but high for the second and third deliveries thus; 3.1, 3.4 and 3.9 kg for first, second and third deliveries respectively

Glucose intolerance is associated with higher birth weight due to glucose deposition and increased adiposity (10, 20). Foetal macrosomia is estimated to complicate one in every word pregnant mothers with glucose intolerance (11). Previous findings in KNH have found a prevalence of foetal macrosomia in diabetic mothers to be 24.1 % (21). In the study only

7.8 % of mothers gave a history of previous infant birth weight ≥ 4000g. Sixty three percent of them had glucose intolerance though the association was not statistically significant. This is higher than the findings of the Nairobi birth survey IV which showed an incidence rate of foetal macrosomia of 4.2 % in the general population and 1.3 % in teenagers (25).

The prevalence of familial risk factors for microvascular disease ranged from 19% for diabetes which is five times higher than our estimated national prevalence of type 2 diabetes in the general population, which is estimated at 3.3 %. This was not statistically significant, P-value 0.05: OR 2.66(1.4-6.78), perhaps due to the small sample size. Twenty four percent reported a family history of hypertension which was statistically significant, P-value 0.037; OR 2.66 (1.04-6.78); an alarming figure considering that this was a non-selected low risk population.Only a small proportion reported a family history of obesity (3.9%) which is unreliable since it is a subjective assessment though it was not a statistically significant association.

The results showed a prevalence of glucose intolerance of 36% with gestational diabetes comprising 16.7%, mild degrees of glucose intolerance was 19.6% while flat curves comprised 22.5%. This depicts high rates of glucose intolerance as compared to previous estimations of less than 1% incidence of gestational diabetes by Githaiga in 1986 (23). Rates of 7 % for East Africa have been estimated in the year 2002 though this was based on fasting blood glucose (26). This is in line with the current observations that have demonstrated similar increase especially in third world Nations (1,2). However, most studies have restricted screening to a gestation of 24-28 weeks hence this could lend support to the benefit of extending the screening time to beyond 28 weeks to increase detection rates (27) as 52 % of mothers with glucose intolerance in this study were between 29 to 36 weeks. The prevalence of flat curves which is thought to be due to intestinal stasis with reduced absorption is slightly more (22 %) than that observed in previous studies by Thuo in 1980 which showed figures of 18 % (28).

The ADA recommends a two stage screening approach starting with a one hour 50g glucose challenge followed by a three hour OGTT in populations with low prevalence rates. In populations with rates more than 2%, a one step screening approach using an OGTT is recommended (13). Our antenatal clients meet the criteria for routine three hour OGTT beginning at 24 weeks gestation.

Wagaarachchi and others have demonstrated lower maternal age to be associated with a 50% lower incidence of GDM as compared to mothers of advanced age (29). Among our antenatal population, mothers aged less than 25 years had a three fold lower risk of glucose intolerance compared to mothers aged over 25 years, 19% versus 41% respectively. Only 28% of clients who earned less than Ksh15,000 had glucose intolerance as compared to 50 % with income more than Ksh 15,000; an indicator of the effect of socio-economic status though the difference was not statistically significant. There was no difference in residence in the past ten years and employment status with glucose intolerance contrary to expectation as urban residence or migration from rural to urban centre has consistently been associated with a higher risk of glucose intolerance (2,29). A pre-pregnancy BMI ≥ 25 was positively associated with glucose intolerance; a similar finding to other studies (17). This could be a risk factor per se but could also be influenced by maternal age, parity and socio-economic status. Of note is that 35% of the study population had a pre-pregnancy BMI of ≥25, a figure far above the estimation given by the 2003 Kenya Demographic and Health Survey of 23% (24). Only one mother with glucose intolerance had a history of glucose intolerance in prior pregnancy which had subsided post delivery. This low prevalence could be due to lack of routine screening among our antenatal population hence most asymptomatic mothers are not diagnosed.

History of infertility was associated with glucose intolerance, P-value 0.002; OR 8.69 (1.74-43.50).The causes and treatment modalities for the infertility were not documented. Glucose intolerance is a preventable illness that is associated with high morbidity and mortality due to associated macrovascular and microvascular complications including blindness, coronary artery disease, diabetic feet and neuropathy. From this study, it is obvious that we are at a high risk like most other third world nations (1,2). The cost of screening is only about three dollars per person. This should be a wakeup call to screen mothers to avoid complications from diabetes in pregnancy.

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