

ORIGINAL ARTICLE

Outcome of pregnancy complicated by diabetes at Tikur Anbessa Hospital, Addis Ababa Ethiopia - A five year review¹Getu Admassu, ²Asheber Gaym**Abstract**

Background: Studies on pregnancy outcomes of Ethiopian mothers with diabetes mellitus is limited. This study was undertaken in order to fill this information gap.

Objective: To determine the prevalence of antepartum and intrapartum maternal and perinatal complications of diabetic pregnancy and pregnancy outcomes among Ethiopian pregnant diabetics.

Methods: This is retrospective review of case records of 100 pregnant diabetics and 200 non-diabetic controls attending Tikur Anbessa Hospital from August 1996 to August 2001. Thirty-six women with gestational diabetes and sixty-four with pre-gestational diabetes were included in the study. Prevalence of complications among the diabetics and non-diabetics was computed. Comparison was made among the two groups regarding important pregnancy outcome variables.

Results: The prevalence of gestational and pre-gestational diabetes mellitus during the study period was 0.38 % and 0.37 %, respectively. The obstetric complication included higher rates of Caesarean section, preeclampsia, polyhydramnios and perineal lacerations among the diabetics compared to non-diabetic mothers. In addition, higher rates of preterm delivery, macrosomia and neonatal intensive care unit admissions were noted among diabetic mothers. Maternal and perinatal outcomes were comparable in gestational diabetes mellitus (GDM) and pre-GDM mothers. Poor glycemic control was significantly associated with poor maternal and perinatal outcome.

Conclusion: Higher rates of maternal and perinatal morbidity and mortality are noted among Ethiopian pregnant diabetics compared to international reported rates. However, the rate of complications among the GDM and pre-GDM groups appear to be similar indicating that both should be managed with the same level of intensity. There is a need to revise the diagnostic criteria and management guidelines of pregnant diabetics to reduce the rate of complications to acceptable levels.

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Introduction

Diabetes is a derangement of glucose tolerance accentuated by the pregnancy state because of the increased production of pregnancy related anti-insulin hormones that make the peripheral action of insulin less efficient with advancing gestation (1). Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy (2). Pre-gestational diabetes (pre-GDM)- diabetes predating pregnancy- is recognized as an important cause of maternal morbidity, birth defects, intrauterine fetal death and perinatal mortality. Risk assessment for GDM should be undertaken at the first prenatal visit. Women with clinical characteristics consistent with a high risk of GDM should undergo blood glucose testing at initial antenatal booking (3).

Women who are deemed to be at low risk for diabetes should have blood glucose testing at 24-28 weeks of gestation. A fasting plasma glucose level of greater than 126mg/dl, or a casual plasma glucose level of >200 mg/dl meets the threshold for the diagnosis of diabetes and precludes the need for any glucose challenge. In the absence of such overt hyperglycemia, a two step approach to diagnosis is implemented including an initial screening test by measuring the plasma glucose concentration after a 50 gram oral glucose load. A glucose threshold value >140 mg/dl of the screening test identifies approximately 80% of women with GDM, and the yield is increased to 90% by reducing the cut off to >130 mg/dl. The definitive diagnosis of GDM is made by the 100 gram oral glucose tolerance test (OGTT) conducted on those with an abnormal screening test result. Two abnormal results of the four totals warrant the diagnosis of GDM (3).

The prevalence of GDM ranges from 1-14% of all pregnancies, depending on the population studied and the diagnostic test employed. The prevalence of diabetes in most of Africa is unknown, although WHO estimates that 1-2% of the population of eight countries and 5-10% of two others had the disease (4).

The prevalence of diabetes mellitus in the general Ethiopian population is unknown. Seyoum and colleagues conducted a community based survey of gestational diabetes in 18 rural villages of Tigray with a total of 890 pregnant women at gestational age of 24 weeks and above and found a prevalence of 3.7% (5). Lester found a perinatal mortality of 32% among her series of pregnant diabetics from Yekatit 12 hospital during 1976-1984 (6). Jemal and colleagues studied 121 patients over the eight years including 1989-1997 and found live deliveries in 73.7% of insulin dependent diabetics, 100% of non-insulin dependent diabetics and 100% of the gestational diabetics (7). Increasing maternal age carries an increasing risk of abnormal glucose tolerance. Pederson found that more than 85% of women with diabetes in pregnancy were above 25 years of age compared to 40% of those screened below 25 years of age (8,9). Pregnancy induced hypertension (PIH) is reportedly increased two to three times in pregnant diabetics compared to non-diabetics. In the Ethiopian study, Jemal et al found a 14% prevalence of PIH. Keyle reported a much higher rate of 25%(10). Urinary tract infection and acute pyelonephritis are reported in 16% and 6% of pregnant diabetics (11). From Jemal's study, infection of all type was 5.8%, Caesarean section (CS) rate was 38.6% (whereas the total CS rate of the study hospital was 10.3%) and a total labor induction rate of 22.8%. Whereas, Gabbe from the US reported a CS rate of 9.6% (12). Another common complication encountered among diabetic pregnancies is polyhydramnios. Jemal found a 3.3% rate, while the rate was 25% in Pederson's series (7,8). Conservative management of pregnancy in a well-controlled diabetic woman results in a high vaginal delivery rate with some increase in morbidity and mortality(13,14). Gabbe et al reported a 22% rate of macrosomia among his case series of 260 diabetic mothers. For mothers with insulin dependent diabetes (IDM), macrosomia is significantly associated with poor metabolic control (15).The association of maternal diabetes with neonatal respiratory distress is well established (16,17).

A common problem among infants of diabetic mothers (IDM) is early neonatal hypoglycemia which is secondary to excessive insulin secretion after the maternal glucose supply is interrupted (18). With optimal blood glucose control, Jemal and colleagues found a 21.6% neonatal hypoglycemia rate (7). Poor outcomes in pregnancies among women with diabetes are in most cases preventable by optimizing glycemic control. Among the poorly controlled diabetics, the rate was more than nine times the hospital perinatal mortality rate (19).

There are very few studies done in Ethiopia on the association of diabetes mellitus with pregnancy. The objectives of the study were to describe the maternal, perinatal complications and obstetric characteristics of Ethiopian pregnant diabetics in comparison with non-diabetic controls.

Methods and Materials

The study was conducted at Tikur Anbessa Hospital, Addis Ababa, Ethiopia from August 1996 to August 2001. Tikur Anbessa Hospital is a teaching, central referral hospital with a maternity unit having 72 beds. The Endocrinology Unit of the Department of Internal Medicine provided care related to diabetic metabolic control. The study was a cross sectional comparative study. Pregnant diabetics were followed at the antenatal clinics; visiting the Endocrinology clinics at the same time for their metabolic control. The criteria for the diagnosis of gestational diabetes after a 100 gram glucose load were two or more of the following plasma glucose concentrations met or exceeded; fasting blood glucose (105mg%); 1hour (190 mg%); 2 hour (165mg%) and 3 hour value of more than 145mg%. Dietary management was based on the habitual diet of the client, with modifications consisting of avoidance of excess carbohydrates and reduction of fat intake in obese clients. Insulin dosage was adjusted on the basis of twice weekly pre-prandial and once weekly two hours post prandial blood glucose values.

Patients were seen at least every two weeks during the first and second trimester and every week during the third trimester. Good diabetic control was taken as a mean pre-prandial glucose of less than 100 mg/dl or postprandial less than 140 mg/dl. Routine screening for GDM was not performed at the units during the study period with only selective screening performed on the basis of the presence of risk factors for GDM. All mothers with GDM/pre-GDM with poor metabolic control were offered admission to the obstetric ward for metabolic control and evaluation of obstetric complications. Fetal well being was monitored by clinical assessment and biophysical profile and ultrasound scan for fetal weight, polyhydramnios and congenital anomalies. Elective induced delivery was often performed at 38-40 weeks. If there was associated macrosomia and a previous CS, a planned elective CS was performed.

Diabetic women (GDM and pre-GDM) who delivered after 28 weeks of gestation during the study period at the hospital were included in the study. The controls were non-diabetics who delivered after 28 weeks gestation at the same hospital and taken by simple random sampling technique from the general obstetric population during the same period. During the study period, there were 150 deliveries from diabetic women, of which 100 charts were retrieved and included in the study. Thirty six of these were GDM cases while 64 pre-GDM. For each diabetic, two controls were taken from the total non-diabetic population who delivered during the study period. The source population for the study was all women who delivered at the hospital during the study period. A sample size of 43 cases of diabetes was calculated using the formula for two population proportions with the assumption of Caesarean delivery rate of 38.6% and 10.3% among diabetic and non-diabetic pregnancies respectively; a standard normal delivery rate of 1.96 and a power of 0.8. Thus the number of cases studied (100) was much higher than the calculated sample size.

Data was collected from patient's charts using a structured data collection format. Cases of diabetes were identified from delivery registration book and the Endocrinology Clinic registry and two non-diabetics were taken by simple random sampling from mothers who delivered on the same day as the diabetic mother. Information on neonates referred to the neonatal intensive care units (NICU) were collected from their respective charts. The variables of interest collected were maternal age, maternal weight, and gestational age, mode of delivery, type of diabetes, level of metabolic control, maternal/perinatal complications and outcome. Data was analyzed using EPI-INFO version 6 statistical package. Results were organized as frequencies, ratios and tables. A p-value of <0.05 was considered significant. Ethical clearance for the study was obtained from the Department of Obstetrics and Gynecology and permission for identification of cases and chart retrieval was obtained from the Tikur Anbessa Hospital Administration and the Endocrinology Unit of the Department of Internal Medicine, Addis Ababa University.

Results

Sociodemographic and obstetric characteristics

There were a total of 19,820 deliveries attended and registered during the study period. One hundred fifty (0.76%) were delivered from diabetic women. One hundred charts were retrieved and included in the study. The remaining 50 (40 GDM and 10 pre-GDM) charts could not be retrieved. The youngest patient was 20 years and the oldest 45 years (16 and 42 among the controls, respectively). The mean maternal age was 30.5 years (25.7 among the controls). Fifty seven percent of the diabetic mothers were older than 30 years.

An increasing rate of diabetes was noted with advancing age. Age greater than 25 had a much higher risk compared to those below 25 (OR3.85; 95% CI 1.97-7.63). Ninety Seven percent were married and housewives and 96% came from Addis Ababa. Maternal weight ranged from 42 -111 kgs (48-91 kgs in the control group). The mean maternal weight was comparable among the cases and controls (69.6 and 67.6 kgs respectively). Increase in body weight had no statistically significant association with diabetes. The mean parity was 3 for the cases and 2 among the controls (Table 1).

Table I: Sociodemographic and obstetric characteristics of diabetic mothers and controls, Tikur Anbessa Hospital, Addis Ababa, Ethiopia, 1996-2001

Characteristics	GDM		Pre-GDM		Non-diabetics	
	No.	%	No.	%	No.	%
Age(years)						
<25	4	11.2	10	15.6	77	38.5
25-35	23	63.8	42	65.6	111	55.5
>35	9	25	12	18.8	12	6
Total	36	100	64	100	200	100
Parity						
1	11	30.6	17	26.6	11.7	58.5
2-4	21	58.3	41	64	68	34
5-9	4	11.1	6	9.4	15	7.5
Total	36	100	64	100	200	100
Maternal weight at delivery (kg)						
<60	4	11.1	23	36	47	23.5
61-70	11	30.6	17	26	82	41
71-80	11	30.6	17	26	52	26
81-90	6	16.6	6	9.2	15	7.5
>90	4	11.1	1	1.6	4	2
Total	36	100	64	100	200	100
Gestational age (weeks)						
<37	10	27.7	15	23.4	13	6.5
≥37	26	72.3	48	76.6	187	93.5
Total	36	100	64	100	200	100

Preterm delivery among the diabetics was 25% while term delivery was 71% with only 4% delivering post term (6.5%, 84% and 9.5% among the controls, respectively). The mean gestational age was 37 weeks and five days for the cases and 40 weeks for the controls. Labor was spontaneous in 34 (34%) of the cases while 27(27%) were induced. Fifty four cases delivered spontaneously while 4(4%) had assisted vaginal delivery and 42 (42%) had a Caesarean delivery. The corresponding figures were 123 (61.5%) spontaneous labor and only seven(3.5%) had induced labor. Caesarean delivery among the controls was 31(15.5%) and 39(19.5%) having an assisted vaginal delivery.

The CS rate was significantly higher among the diabetics compared to the control mothers (OR 3.95). The main indications for Caesarean delivery in the diabetic mothers were fetopelvic disproportion (CPD) 16(16%); two or more previous Caesareans 11 (11%); fetal distress 6(6%) and failed induction five (5%). While among the control mothers major indications were fetal distress fourteen(7%), CPD nine (4.5%) and dystocia five (2.5%). The Caesarean section rate due to CPD was significantly higher in the cases as compared to the controls (OR= 4.04). The majority of babies born to diabetics were females (61%) with a female to male ratio of 1.6:1(1:1 in the controls).

Maternal outcome

From the total deliveries during the study period, there were 76 mothers with GDM (0.38%) and 74 with pre-GDM (0.37%).

Among the 100 cases whose charts were obtained for detailed analysis, 36 were having GDM of whom seven(19.4%) were on dietary therapy while 29 (80.6%) were treated with diet plus insulin. All pre-GDMs were treated with insulin.

The mean gestational age at first antenatal visit was 26 weeks and 23 weeks in the GDM and pre-GDM mothers, respectively. Among the diabetic mothers, 60% of the macrosomic babies were born from mothers who started antenatal care in late second or third trimester. The major maternal complications noted among the diabetic mothers in this study were 18(18%) preeclampsia; 10(10%) polyhydramnios; 9(9%) urinary tract infection and 8(8%) preterm labor compared to 6%, 1%, 1% and 1% among control groups, respectively. Preeclampsia occurrence was significantly associated with diabetes compared to non-diabetic mothers (OR=3.44, 95%CI 1.49-2.79). Major intrapartum complications in the diabetics mothers were 7(7%) perineal lacerations and 1 (1%) postpartum hemorrhage compared to 3.5% and 2.5% among the non-diabetics (Table 2). Five deliveries among the diabetic mothers had shoulder dystocia compared to only one among the controls. All five cases were associated with poor glycemic control, perineal lacerations and delivery of a macrosomic infant. Each of the above maternal complications was significantly more among the diabetics compared to the controls. Regarding glycemic control, 55(55%) of the diabetics had good glycemic control while 45(45%) had poor control.

Table 2: Maternal complications among diabetic mothers and non-diabetic controls at Tikur Anbessa Hospital, Addis Ababa, Ethiopia, 1996- 2001

Complications	Case n=100		Control n=200		p-value
	No.	%	No.	%	
Pre-eclampsia/Eclampsia (PE/E)	18	(18)	12	(6)	0.002
Perineal laceration	7	(7)	3	(1.5)	0.01
Polyhydramnios	10	(10)	2	(1)	0.002
Urinary tract infection (UTI)	9	(9)	2	(1)	0.001
Preterm labor	8	(8)	2	(1)	0.002
Postpartum hemorrhage (PPH)	1	(1)	5	(2.5)	
Antepartum hemorrhage	1	(1)	1	(0.5)	

The occurrence of maternal complications was significantly associated with poor glycemic control (Table 3).

However, there was no statistically significant difference in the maternal complication rates between the GDM and pre-GDM mothers.

Table 3: Maternal complications by diabetic status, diabetic type and level of glycemic control, Tikur Anbessa Hospital, Addis Ababa, Ethiopia, 1996-2001

	Maternal Complication				Odds ration	95% CI
	Yes		No			
Diabetic status (n=300)						
Diabetic	59	(59)	41	(41)	8.15	(4.46 14.90)
Non diabetic	30	(15)	170	(85)		
Diabetic type (n=100)						
GDM	20	(58.3)	1	(41.7)	0.96	(0.38 2.40)
Pre-GDM	38	(59.4)	26	(40.1)		
Glycemic control (n=100)						
Good	22	(40)	33	(60)		
Poor	37	(82.2)	8	(17.8)	6.94	(4.48 20.03)

Among pregestational diabetics, 37 cases were insulin dependent diabetes mellitus (IDDM); 27 being non-insulin dependent diabetes mellitus (NIDDM). Mean duration of diabetes was 4.33 years in the combined population. Chronic complications noted in the pregestational diabetics at booking included chronic hypertension in five, nephropathy, neuropathy and retinopathy in two; both of whom had preterm delivery resulting in very low birth weights that ended in early neonatal deaths. One case of NIDDM with neuropathy and one IDDM with cerebral ataxia had live births. There were no maternal deaths in the cases or controls.

Perinatal outcome

A total of 100 infants of diabetic mothers (IDMs) were delivered and included in the study (36 GDM and 64 Pre-GDMs). Fourteen (14%) were stillborn and 7(7%) had early neonatal deaths (ENND); the corresponding figures among the controls were 5% and 3.5% respectively (Table 4). Among the stillbirths from the diabetics, 87% of the mothers were noted to have poor glycemic control.

Six early neonatal deaths occurred among the IDMs and all the pregnancies had poor glycemic control. Perinatal mortality rates (PMR) were higher in the diabetic pregnancies (210 per thousand live births) compared to 85 per thousand among the controls.

The risk of perinatal deaths was significantly higher among the diabetics compared to the non-diabetics (OR=2.86). The mean gestational age at delivery was 37.5 weeks (SD 2.7) with a mean birth weight of 3211 grams among the diabetics. There were significantly more infants delivered below 37 weeks of gestation among the diabetics compared to the controls (OR=4.79, 95%CI 2.20-10.59). Macrosomia was significantly associated with diabetes (OR=6.89). The NICU admission rate in the IDMs was 39(39%) compared to 28 (14%) in the controls. Significantly more of IDMs were admitted to the NICU (OR=3.61, 95%CI 3.10-11.78). Apgar scores at 5 minutes, low birth weight and respiratory distress were not statistically different among the cases and controls (Table 4).

Table 4: Perinatal complications encountered among diabetic women and non-diabetic controls at Tikur Anbessa Hospital, Addis Ababa, Ethiopia, 1996-2001

Complications	Cases (n=100)		Controls (n=200)		P-value
	No	%	No	%	
Preterm delivery	25	(25)	13	(6.5)	0.001
LBW	17	(17)	20	(10)	0.12
Macrosomia	20	(20)	7	(3.5)	0.001
Apgar at 5<7	20	(20)	41	(20.5)	0.96
RDS	7	(7)	25	(12.5)	0.21
Hypoglycemia	9	(9)	1	(0.5)	
NICU admission	39	(39)	28	(14)	0.001
ENND	7	(7)	10	(5)	0.48
Stillbirth	14	(14)	7	(3.5)	0.001

Perinatal complications were higher in the IDM group than in the controls (52.1% versus 15.3%; OR=4.20).

Poor glycemic control was significantly associated with poor perinatal outcome (OR= 9.75). There was no difference in perinatal outcome in the GDMs compared to the pre-GDMs (Table 5).

Table 5: Perinatal Complications by diabetic status, diabetic type and glycemic control at Tikur Anbessa Hospital, Addis Ababa, Ethiopia, 1996-2001

	Perinatal Complication		Odds ratio	95%CI
	Yes	No		
Diabetic status (n=300)				
Diabetic	52(53)	48(47)	4.20	(2.42, 7.33)
Non Diabetic	41(17.5)	159(82.5)		
Diabetic type (n=100)				
GDM	16(44)	20(55)	1.61	(0.65, 3.97)
Pre GDM	36(36)	28(44)		
Diabetic control (n=100)				
Good	2(29.1)	38(70.9)	9.75	(3.51, 27.93)
Poor	36(80)	9(20)		

Hydrocephalus was diagnosed in three infants and one infant had ventricular septal defect among the diabetics. These mothers all had poorly controlled pre-GDM, their age ranging from 26-36 years (mean 31.3 years). Hypoglycemia was more common in the IDMs than in the infants of non-diabetic controls. Four IDMs had neonatal hyperbilirubinemia. One IDM from the pregestational diabetics developed polycythemia. Four macrosomic infants of gestational diabetic mothers developed transient brachial plexus palsy.

Discussion

This study described the sociodemographic profile and pregnancy outcome of Ethiopian pregnant diabetics. The prevalence noted in this study is lower when compared to other reported rates for GDM from Ethiopia and other developed countries. The implementation of selective screening method based on the presence of risk factors for GDM may be one possible reason for this low rate as over fifty percent of mothers with GDM lack these supposed risk factors. Many patients with GDM might be undetected in our population due to the lack of universal screening.

The finding of a higher association of diabetes with maternal age above 25 years concurs with earlier observations with Pederson (9). The finding of a higher rate of diabetes in the multipara may be explained by the association of multiparity with higher age groups. Increasing body weight had no significant association with diabetes in our study but this could be due to the fact that there were few obese women in our study. The rate of preeclampsia (18%) is similar to Pederson's and Jemal's findings (7,8). The significantly higher rate of perineal laceration among diabetic deliveries noted in our study was most probably due to the higher rate of macrosomic babies in both pregestational and gestational diabetics. Polyhydramnios was ten times more common among the diabetics being much higher than Jemal's previous study from the same hospital but lower than Pederson's series (7,8).

The higher rate of preterm labor found in our study was associated with premature rupture of the membranes and preeclampsia in about 70%. This agrees with the findings of Green et al (19). Close monitoring of blood pressure and fetal well being on each visit with an optimal management of pre-eclampsia may reduce the associated high rate of preterm labor. The very high CS rate found in our study (42%) is comparable to Jemal's study and is within the range reported in most published series of diabetic pregnancy (20-60%) (11, 12). The very high rate of macrosomia may be due to the relatively later initiation of antenatal care in our obstetric population. To reduce the associated morbidity and mortality, risk assessment for GDM and the appropriate management should be initiated early at the first prenatal visit and efforts must be made to encourage mothers to undertake their booking in the first trimester.

Maternal complications were not significantly different in the GDM (58.3%) compared to the pre-GDM mothers (59.4%). This finding supports previous observations that pregnancy morbidity and mortality in GDM are less than that for pregestational diabetics. However in cases of poorly managed GDM cases complication rates might approach those of pre-GDMs.

It is thus necessary to give more emphasis to the diagnosis and management of GDM in a similar way to pre-GDM.

The gross perinatal mortality of 210 noted in this study is much higher than the non-diabetics indicating the significant risk diabetic pregnancy poses in our obstetric population. It was also double the hospital perinatal mortality rate of 102.8 per thousand noted during the same time period. The rate is much lower than Lester's study of some years back from the same city (32%). The high rate of poor glycemic control noted in our study with stillbirths (85%) and early neonatal deaths (71.4%) is the more probable explanation of the high PMR. Macrosomia (>4000 grams) occurred in 20% of our cases which was in the lower range of reported series (20-40%) (14). It is comparable to Jemal's study (22%) and that reported by Gabbe. Within the limitations and challenges, we should aim for tight metabolic control among our pregnant diabetics in order to reduce this high rate of macrosomia. In spite of the significant association of diabetes with preterm delivery, the rate of low birth weight (17%) was not very different from the non-diabetics (10%). The neonatal hypoglycemia rate noted in this study (9%) is lower than Jemal's findings (21.6%) and lies within the reported rates among IDMs (5-15%) (7). This may be due to the smaller sample size of our study. That routine autopsy was not performed on all stillbirths in our hospital may also lead to lower detection rate of anomalies in our series. The higher rate of NICU admission in our series was largely attributed to macrosomia, preterm delivery and hypoglycemia.

The correlation of poor glycemic control with poor pregnancy outcome was corroborated in our study as well. Poor perinatal outcome was significantly associated with poor glycemic control. The use of glycosylated hemoglobin assay and the rule of tight metabolic control with measurement of blood glucose upto seven times per day can improve the perinatal outcome.

Diabetes complicating pregnancy is associated with a higher rate of preeclampsia, polyhydramnios, perineal laceration, preterm delivery, CS, macrosomia and NICU admission rate compared to other series.

Both GDM and pre-GDM should be managed with similar vigor as they have similar complication rates. The high rate of complications appears to be correlated to the poor glycemic control noted in our series.

The management of metabolic control in our unit needs to be revisited. Early initiation of prenatal care should be encouraged in our obstetric population. Large scale prospective studies need to be conducted to clearly describe the prevalence of GDM in our obstetric population.

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