

PREVALENCE AND OUTCOME OF PREGESTATIONAL DIABETES MELLITUS AMONG PREGNANT MOTHERS ATTENDING ANTENATAL CARE AT THREE TEACHING HOSPITALS IN ADDIS ABABA, PROSPECTIVE FOLLOW UP STUDY

Talema Aytnew, MD¹, Delayehu Bekele, MD, MPH¹

ABSTRACT

BACKGROUND: Diabetes mellitus is one of the most common medical conditions complicating pregnancy with a significant impact on maternal and perinatal outcome.

OBJECTIVE: To assess the prevalence of pregestational diabetes mellitus and its pregnancy outcome at three teaching hospitals in Addis Ababa

METHODS: Prospective cohort study was conducted at three teaching government hospitals in Addis Ababa, Ethiopia.

RESULT: There were a total of 19,797 deliveries, among which 80 were women with pregestational diabetes mellitus were identified making a prevalence of 0.4%. Out of these 39(48.8%) had type 1 and 41(51.2%) had type 2 diabetes mellitus. The glycemic control was poor in each trimester with higher fasting, 2-hour post prandial and HgA1C level than the standard. Majority of pregnancies (67.1%) ended up with induction of labor for fetal and maternal indications and 61.8% were delivered by cesarean section. Hypertensive disorders of pregnancy were commonest maternal complication seen in 28.5% of the women. The rate of premature delivery and neonatal intensive care referral was high (53.4%). There was statistically significant association between adverse pregnancy outcome and having preconception care.

CONCLUSION: The Prevalence of pregestational diabetes mellitus was found to be comparable to most setups. The glycemic control was poor in each trimester with higher fasting, 2-hour post prandial and HgA1C level from the standard. These hospitals should have management protocol advocating preconceptional care and tighter glucose control which may help in reducing the adverse maternal and perinatal outcome.

KEY WORDS: Pregestational diabetes mellitus; Pregnancy outcome, prevalence

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BACKGROUND

Diabetes mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. It is caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced¹.

Diabetes is one of the most common medical conditions complicating pregnancy. It is estimated that by the year 2030 more than 360 million people will have diabetes mellitus and as the burden of the disease increases the management of pregnancies complicated by diabetes mellitus will be part of the daily obstetric practice in many regions of the world².

Abnormalities in glucose regulation occur in 3-5% pregnancies. This prevalence may increase with new screening guidelines and increasing prevalence of obesity. Pregestational diabetes accounts about 10% of diabetes in pregnancy and the rest are gestational. Due to the more severe fetal and maternal complications resulting from such diabetes mellitus antedating pregnancy, in 2013, the WHO has divided hyperglycemia in pregnancy as follows: (i) Diabetes in pregnancy: Pregestational diabetes or pregnancy occurring in a women with known diabetes, and Overt diabetes - diabetes first detected during pregnancy; and (ii) Gestational diabetes mellitus³.

Pregestational or overt—diabetes have a more significant impact on pregnancy outcome. The embryo, the fetus, and the mother commonly experience serious complications directly attributable to diabetes. The likelihood of successful outcomes with overt diabetes is related to the degree of glycemic control and the degree of underlying cardiovascular or renal complications⁴.

In a retrospective cohort study done on Omani women, women with pregestational diabetes mellitus had a significantly higher incidence of pre-eclampsia ($p < 0.022$), preterm deliveries ($p < 0.0001$) and cesarean section ($p < 0.001$). Neonatal complications such as RDS, neonatal hypoglycemia, neonatal jaundice and subsequent admission to NICU were significantly

higher for neonates born to mothers with pregestational diabetes mellitus compared to those born to mothers with gestational diabetes mellitus ($p < 0.001$)⁵.

Pre-pregnancy care for women with pre-gestational type 1 or type 2 diabetes mellitus is effective in improving rates of congenital malformations, perinatal mortality and in reducing maternal HbA1C in the first trimester of pregnancy. Pre-pregnancy care might cause maternal hypoglycemia in the first trimester of pregnancy⁶.

Exact incidence of diabetes is not known in Ethiopia. Many mothers are becoming pregnant in the presence of diabetes and are prone to have recurrent pregnancy loss, stillborn, babies with multiple congenital anomalies. This study will help to have baseline data on pregestational diabetes mellitus in this set-up and can be used as a reference for studies in this area.

METHODS AND MATERIALS

A prospective follow up study was conducted at the three teaching hospitals in Addis Ababa Ethiopia from 1 January 2016 to 30 December 2016. The three teaching hospitals were Saint Paul's, Black lion and Yekatit 12 hospital. These hospitals run residency program under Addis Ababa University and Saint Paul's hospital millennium medical college in Addis Ababa, the capital city of Ethiopia.

A structured questionnaire was used to interview study participants. For administering the structured questionnaire, nurses who were working at ANC clinics at the three hospitals filled the initial socio-demographic data, attached the second part of the questionnaire on the clients' card and gave a code and reported to the principal investigator. The remaining data was filled by the person who attended the delivery. Medical record review at each hospital was conducted by the principal investigator to complete any missing information.

Adverse pregnancy outcome was the dependent variable. The independent variables were maternal age, type of diabetes mellitus, and duration of diabetes, treatment of diabetes before pregnancy, preconceptional care, maternal blood glucose level, gestational age, birth weight and mode of delivery.

Data was entered and analyzed using SPSS version 20. Results are presented as percentages and comparison of the results was performed by the chi-squared test. All tests are two-sided and the level of significance will be set at $P < 0.05$. Bivariate analysis was done to see relationship between dependent and independent variables. Multivariate analysis was done to control the confounding variables and variables which had a p value of ≤ 0.2 in bivariate analysis were included.

OPERATIONAL DEFINITIONS

Pregestational Diabetes mellitus:- Patients who were diagnosed to have diabetes prior to the current pregnancy.

Macrosomia:- Birth weight of 4000 grams or greater was taken to classify macrosomic babies.

Adverse pregnancy outcome definitions:- The WHO guidelines define APO as an event of low birth weight, preterm birth, stillbirth, or abortion. So in our study APOs means the above definition on WHO guideline plus maternal complications like hypertensive disorders of pregnancy. Presence of any of the following, low birth weight, preterm birth, stillbirth, or abortion, congenital anomaly,

RESULTS OF THE STUDY

1. Socio demographic characteristics and reproductive performance (Table I)

Over the study period there were a total of 19,797 deliveries at the three teaching hospitals and 80 were women with pregestational diabetes mellitus making prevalence of 0.4%.

Twenty five (31.2%) of them had follow up and delivered at SPHMMC, 38 (47.5%) at Black Lion hospital and the remaining 17(21.2%) at Yekatit 12 hospital. Majority, 71(88.8%) were from urban area, 78(97.5%) were married and 79(98.8%) were educated. Majority of the women, 62(77.5%) were between the age group of 20-35 years, 3(3.8%) were below 20 years of age and 15(18.8%) were above age 35 years. About 57(71.2%) have parity of one to four, 19(23.8%) were primigravids and

the rest (5%) were grand multipara. The other sociodemographic characteristics are shown in table 1.

2. The profile of diabetes and glycemic control during pregnancy (Table-II & III)

The distribution of type one and two diabetes is almost equivalent. Nearly half, 39(48.8%) were type 1 and 41(51.2%) were type 2 with duration of illness being less than 10 years in 67(83.8%). Fifty five (68.8%) of them were on insulin, 20(25%) on oral hypoglycemic agents and 6(6.2%) on dietary management before the current pregnancy.

Forty-one (51.2%) of the study populations had glucometer at home for monitoring of their blood glucose level. Forty two (52.5%) of the women were not on any form of contraceptive and half of them had preconceptional care.

Table I- Sociodemographic characteristics of pregnant mothers with pregestational diabetes who had followed and delivery at three teaching hospitals in Addis Ababa from 1 January 2016 – 30 December 2016

Name of hospital	St.Paul's	25	31.2
	Black lion	38	47.5
	Yekatit 12	17	21.2
AGE (Years)	<20	3	3.8
	20-35	62	77.5
	>35	15	18.8
Residency	Urban	71	88.8
	Rural	9	11.2
Marital status	Married	78	97.6
	Single	1	1.2
	Divorced	1	1.2
Religion	Orthodox	51	63.8
	Muslim	19	23.8
	Protestant	10	12.4
Occupation	House wife	37	46.2
	Employed	36	45
	Unemployed	7	8.8
Educational Status	Uneducated	1	1.2
	Primary school	24	30
	Secondary school	42	52.6
	University	13	16.2
Reproductive performance	Primigravida	19	23.8
	1-4	57	71.2
	Grandmultipara	4	5
Type of pregestational diabetes	Type 1	39	48.8
	Type 2	41	51.2
Duration of diabetes(In years)	<10	67	83.8
	10-20	12	15
	>20	1	1.2
Type of therapy	Insulin	55	68.8
	Oral hypoglycemic agent	20	25
	Dietary	5	6.2
Use of contraceptive	Yes	38	47.5
	No	42	52.5
Preconceptional Care	Yes	40	50
	No	40	50
Presence of glucometer at home	Yes	39	48.8
	No	41	51.2

In this study 54(67.5%) of the mothers didn't have any determination of HgA1C during their pregnancy. HgA1C was determined for only 11(13.75%) women in the first trimester and the mean HgA1C value was 8.6%. The mean FBS and 2 hour postprandial RBS in the first trimester of pregnancy was 98.3 and 154.9 respectively. HgA1C was determined for only 6(7.5%) women in

the second trimester with a mean value of 9.03%. The mean FBS and 2 hour postprandial RBS in the second trimester of pregnancy was 100 and 144.3 respectively. HgA1C was determined for only 13 (16.3%) women in the third trimester and the mean was 7.2%. The mean FBS and 2 hour postprandial RBS in the third trimester of pregnancy was 98 and 142 respectively.

Table II: - The Average maternal Glycemic control of pregnant mothers with pregestational diabetes who had follow and delivery at three teaching hospitals in Addis Ababa from 1 January 2016 – 30 December 2016

Trimesters	FBS	2-Hour postprandial	Glycosylated hemoglobin
First	98.3	154.9	8.6%
Second	100	144.3	9.03%
Third	98	142	7.2%

3. Maternal, Fetal and Neonatal Complications (Table-III and IV)

Out of the 80 women 55(68.8%) didn't have any maternal complication. Ten women (12.5%) has preeclampsia, 11.2% chronic hypertension out of which two experience superimposed preeclampsia. Four (5%) women had gestational hypertension. Totally hypertensive disorder of pregnancy is the commonest (28.5%) maternal complication seen in our study. Two women have diabetic ketoacidosis (2.5%) and one end up with spontaneous abortion and the other with preterm labor. There were two women with diabetic nephropathy and one has intrauterine growth restriction and one woman with non-proliferative diabetic retinopathy.

Out of the 80 deliveries 10 (12.5%) had fetal complications 3 stillborn (3.75%), 3 (3.75%) congenital anomaly and 4 (5%) spontaneous abortion.

Majority of pregnancies (67.1%) ended up with induction of labor for fetal and maternal indications and 61.8% delivered by cesarean section. From the cesarean section

38.3% were elective and 61.7% emergency. There were 6(7.9%) instrumental deliveries and one birth injury (elbow dislocation) after forceps delivery. Nearly one-third (30.3%) of the deliveries were preterm and majority in the normal birth weight range (73.7%), with 7(9.2%) of babies born macrocosmic and low birth weight babies account for 17.1%.

More than half of neonates (53.4%) were referred to neonatal intensive care unit because of prematurity. Hypoglycemia, Jaundice, RDS and birth injury were seen in 6.8%, 4.1%, 10.9% and 1.4% respectively. The one neonate admitted for birth injury had elbow dislocation after forceps delivery.

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Table III: - Maternal, Fetal and Neonatal Complications of mothers who had pregestational diabetes mellitus and had follow up and deliver at three teaching hospitals in Addis Ababa, January 1- December 30 2016

Outcome measures	Frequency	Percent
Maternal Comorbidities		
No comorbidity	55	68.8
Preeclampsia	10	12.5
Chronic Hypertension	9	11.2
Gestational hypertension	4	5
Diabetic ketoacidosis	2	2.5
Fetal complications		
Abortion	4	5
Congenital anomaly	3	3.75
Stillborn	3	3.75
No complication	70	87.5
Onset of labor		
Spontaneous	25	32.9
Induced	51	67.1
Mode of delivery		
SVD	23	30.3
Cesarean section	47	61.8
Instrumental	6	7.9
Gestational age at time of birth		
<37	23	30.3
≥37	53	69.7
Birth-weight		
<2500	13	17.1
2500-3999	56	73.7
≥4000	7	9.2

Table IV: - Multivariate analysis of adverse pregnancy outcome in mothers with pregestational diabetes who had follow up and delivery at three teaching hospitals in Addis Ababa from 1 January 2016 – 30 December 2016

Baseline Characteristics	Adverse pregnancy outcome		COR Yes	AOR No	95% confidence interval	P-Value
Hospital						
SPHMMC and Yekatit 12	23	19	0.432	-	-	0.082
Black lion	28	10	-	-	-	-
Type of PGDM						
Type 1	23	16	1.498	-	-	0.387
Type 2	28	13	-	-	-	-
Duration of PGDM						
≤10 Years	41	26	0.473	-	-	0.288
>10 years	10	3	-	-	-	-
Treatment before conception						
Insulin	32	23	0.439	-	-	0.129
OHG and dietary	19	6	-	-	-	-
Preconceptional care						
Yes	28	10	-	-	-	-
No	21	19	0.24	0.033	0.065,0.892	0.033
Presence of Glucometer						
Yes	21	19	0.24	0.033	0.065,0.892	0.033
No	30	10	-	-	-	-
3rd trimester 2-hour postprandial blood glucose level						
≤120	10	4	1.488	-	-	0.616
>120	31	25	-	-	-	-
Maternal Age						
≤35 years	38	27	0.217	-	-	0.056
>35 years	13	2	-	-	-	-

DISCUSSION

Pregestational diabetes mellitus is an important problem which has a significant impact on the maternal and perinatal outcome. It is now accepted that the best form of care in these pregnancies can be provided through specialized multidisciplinary clinics⁷.

The prevalence of pregestational diabetes mellitus in this study was 0.4% which is close to other studies where preexisting diabetes complicates pregnancies at a rate of 1-3 per 1,000 births. Prevalence of type 1 and 2 DM were reported as ranging from 0.20 to 0.70% in a systemic review entitled burden of diabetes mellitus during pregnancy in low- and middle-income countries⁸. In a study designed similar to ours done at district hospital in Australia prevalence of PGDM was 0.63%⁹. The prevalence of pregestational diabetes increased from 3.1 per 1000 births in 1996-98 to 4.7 per 1000 in 2002-04 driven mainly by a sharp increase in type II diabetes¹⁰.

The mean age of the women was 30.6 years which is comparable to other studies 31.5 years and 28.5yrs + 2.2years^{11, 12}. These shows that type 2 diabetes mellitus is being diagnosed in younger age which may be because of a change in life style and obesity. The mean age of mothers in our study was higher in type 2 mothers 32.7 years than those of type 1 (27.4 years). In both cases it is lower than other studies. In the study done by Hayfaa A Wahabi et al the mean age was 35.3 ± 5 and 34.4 ± 6 years and in another study done by A.A Sobande et al it was 36.0 ± 3.2 and 30.5 ± 7 for type 2 and 1 diabetes respectively^{11, 13}. Among patients with age ≥ 35 years 4(20%) are mothers with type 1 DM and the rest 16 (80%) are women with type 2 DM.

Forty two (52.5%) of the women were not on any form of contraceptive. This means it is difficult to institute preconceptional care like supplementation of folic acid, achieving glycemic control and assess end organ damage before conception unless we improve use of contraceptive among these clients.

The Confidential Enquiry in Maternal and Child Health reported that only 34% of women with diabetes had preconception counseling, 28% in Atlantic seaboard 2006-2007 study and in our study 50% of the clients had preconceptional care, which was determined as any checkup and consultation to a physician before getting pregnant. This may be explained because most of them are from urban area and has access to health care^{9, 14}. The importance of having preconceptional care should be emphasized since it showed significant association with adverse pregnancy outcomes [OR (0.033), 95% CI (0.065, 0.892)].

In our study the glycemic control of the clients was poor in each trimester especially the 2-hour postprandial is >130 and it should have been ≤120. The average HgA1C in our study at each trimester is higher than the target of 7%. Though we didn't show significant association between glycemic control and adverse pregnancy outcome due to small sample of study population, all hospital should have standard protocol to achieve good glycemic control. In the antepartum period one of the indicators of poor glycemic control is polyhydraminous which was seen in 2.5% of the cases lower than other studies 11.3 %¹³.

In this study adverse pregnancy outcomes are more commonly seen in type 2 diabetic mellitus than type 1, though not significant [OR (1.498), 95% CI (0.599, 3.746), P=0.387] like the study done in King Khalid University Hospital.⁽¹¹⁾ The rate of spontaneous abortion is 5% which is closer to the study done in Sweden in which they used 532 pregnancies complicated by pregestational IDDM, spontaneous abortion rate in these pregnancies was 7.7%¹⁵.

Among all patients with pregestational diabetes, the risk of congenital anomalies is reported at 6 - 7%. There is a dose-response curve to these risks, with the highest risk observed among women who are poorly controlled in the periconceptional period and throughout pregnancy. Atlantic seaboard 2006-2007 study congenital anomaly was 2.4% and in our study it's was 3.75%⁹. The stillbirth rate in women with PGDM from Australia was 2.8%,

2.5% in Atlantic seaboard study, 3.4% in King Khalid University Hospital and in our case 3.75%^{7, 9, 11}. The higher incidence of congenital anomaly and stillbirth rate in our study may be as a result of the poor glycemic control.

The prevalence of cesarean deliveries has consistently been reported to be higher in pregestational diabetic pregnancies than in nondiabetic pregnancies. Cesarean rates have been in the range of 24-66% in diabetic patients, rates that were three to five times the rates in nondiabetic women^{12,16}. Also in a prospective evaluation of pregnancy outcomes in pregestational diabetes along the Atlantic seaboard 2006-2007 the caesarean section rates were greater (43%), in Omani study 60.3%, in our study it was 61.8% which was high. The rate of emergency c-section was also higher (61.7%) than other reports (25%)⁹.

According to Confidential Enquiry into Maternal and Child Health (CEMACH), 67% of women with DM had a higher incidence of caesarean section, which was mainly iatrogenic as a result of early induction of labour¹⁴. Induction of labour was done in 14 (60.8%) at district hospital in Australia which is close to our result which is 67.1%.

Recent population-based data from Sweden revealed a 25% rate of preterm delivery (<37 weeks gestation) in women with IDDM, in an Omani study it was also 25.9% and in our study it was 30.0%⁵. The higher percentage of preterm delivery in our study may be accounted to the poor glycemic control and iatrogenic intervention for fetal or maternal indications.

Eleven percent of the infants delivered to the diabetic mothers were macrosomic in a study at King Khalid University, 7.9% in Indian study, 10.3% in Omani study. But in our case it is 9.2%^{5, 11, 17}. Women with type 2 DM had a slightly higher frequency of large babies compared to type 1. There were two cases of intrauterine growth restriction one from each type of DM and the duration of DM was between 10-20 years in both cases. The NICU referral rate was 48% in the Atlantic seaboard study, 56% in a study done at a district general

hospital in Australia and 49% in a retrospective study in Nigeria which was comparable to our study (53.4%)^{7,9,18}. Pregnancy-induced hypertension/ preeclampsia was three times more common in women with PGDM (14%), (11%) in Indian study, 10.8% in study at tertiary hospital in Saudi Arabia, in Omani cohort study 17.2% which are comparable to our study (12.5%)^{5,9,13,17}. As it seen in other studies type 1 diabetes is more often associated with preeclampsia and type 2 diabetes with chronic hypertension 60% and 66.7% respectively. Incidence of diabetic ketoacidosis is low 1% to 2% mostly in type 1 DM. Though rate of maternal mortality secondary to DKA is not well known, but fetal mortality has been reported to be as high as 10%. In our study DKA diagnosed in 2 (2.5%) both were women with Type 1 DM pregnancy and these two pregnancies ended up with abortion and preterm delivery.

STRENGTH AND LIMITATIONS OF THE STUDY

The strength of this study was that it was a prospective follow up study, selection of those hospitals where most of the diabetic clients in the study area would be managed and the fact that it was conducted in a multicenter setting. The limitations of the study are lack of data on important factors such as maternal body mass index and the small sample size of the diabetic patients.

CONCLUSIONS

The Prevalence of pregestational diabetes mellitus was found to be 0.4% comparable to most setups. The glycemic control was poor in each trimester with higher fasting, 2-hour post prandial and HgA1C level than the standard. Hypertensive disorders of pregnancy were commonest maternal complication and cesarean section is high accounting 61.8% of deliveries. The rate of premature delivery and NICU referral was high. There is significant association between preconceptional care and adverse pregnancy outcome. These hospitals should have management protocol advocating preconceptional care and tighter glucose control.

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CORRESPONDING AUTHOR:

Talema Ayteneu

Department of Obstetrics and Gynecology, St. Paul's
Hospital Millennium Medical College, Addis

Email: talemaa@yahoo.com

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