Prevalence of Gestational Diabetes Mellitus and its association with pregnancy outcomes in three referral hospitals in Bhutan

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ABSTRACT

Introduction: Gestational Diabetes Mellitus (GDM) has been defined as any degree of glucose intolerance with onset or first recognition during pregnancy. There is no national data on the prevalence of gestational diabetes mellitus, and there is no routine screening system for diabetes in pregnancy in Bhutan. This study was carried out to determine the prevalence of GDM and its association with pregnancy outcomes in three referral hospitals in Bhutan. **Methods:** This was a prospective study done between March and December 2016 in three referral hospitals in Bhutan, with 726 participants recruited between 24 to 28 weeks of pregnancy. Two blood samples were taken, one in a fasting state to test fasting blood sugar and another to test blood sugar level 2 hours after drinking 75g glucose in 300ml water. They were analyzed in the Clinical Biochemistry laboratories in the respective hospitals. Cut-off levels of 5.6mmol/L (101mg/dL) for fasting blood sugar and 8.5-mmol/L (153-mg/dL) for 2 hours blood sugar report were used. Women diagnosed with GDM were closely followed up throughout the pregnancy up till delivery. At delivery, information on mother and the baby were collected. **Results:** The prevalence of GDM in the three referral hospitals in Bhutan was 15%. The prevalence of GDM cases in the three hospitals was similar and statistically was not significant. **Conclusions:** Universal screening of pregnant women is recommended to detect hyperglycemia and to achieve euglycemia in order to prevent complications in both mothers and babies.

Keywords: Gestational Diabetes Mellitus; Glycemic control; Hyperglycemia; Insulin; Plasma glucose.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) has been defined as any degree of glucose intolerance with onset or first recognition during pregnancy[1]. Prevalence of GDM varies between 1.4 -14% globally[2] and in India it ranges from 3.8 to 21%[3]. The prevalence of diabetes is increasing globally and Bhutan is no exception. The report on 2007 STEPS survey shows the prevalence of diabetes in Bhutan is 2.5% and this is increasing every year[4]. GDM is considered to be an alerting sign for public health programs sensing increasing loads of diabetes in the population, especially in developing countries[4]. GDM carries risks for both the mother and the neonate. GDM is associated with an increased incidence of maternal hypertension, pre-eclampsia, obstetric intervention and risk of developing Diabetes Mellitus (DM) in later life[5]. The major morbidities associated with infants of gestational diabetic mothers include large for dates, growth restrictions, polycythemia, hypoglycemia, hypocalcemia, respiratory distress and hypomagnesemia[6]. This study was carried out to determine the prevalence of GDM and its association with pregnancy outcomes in three referral hospitals in Bhutan.

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METHODS

This was a prospective study done between March and December 2016 in three existing referral hospitals of Bhutan. The referral hospitals were the Eastern Regional Referral Hospital (ERRH) in Mongar, serving the eastern part of Bhutan, Central Regional Referral Hospital (CRRH) in Gelephu catering to the southern and central part of Bhutan and the Jigme Dorji Wangchuck National Referral Hospital (JDWNRH) in Thimphu, which is the referral hospital for the western part of Bhutan and also functions as the National Referral Hospital.

All the study staff were identified and trained at the beginning of the study in all three centers. Pregnant women within the age range of 18 to 44 years, at 24 to 28 weeks of period of gestation visiting the Antenatal Clinic in these three referral hospitals, were invited to participate in the study on voluntary basis. Patients were recruited starting in March 2016 and the last patient recruitment was done on 15th October 2016. There were 459 patients from JDWNRH, 142 patients from Central Regional Referral Hospital (CRRH), Gelephu and 135 from Eastern Regional Referral Hospital (ERRH), Mongar. All recruited patients were followed up until after their deliveries, which were completed by the end of December 2016. An informed consent was taken either in English or Dzongkha from all the participants. Women with known diagnosis of diabetes (diabetes diagnosed

before 24 weeks of gestation), women with intra-uterine fetal death, known cases of congestive cardiac failure, renal failure and carcinoma were excluded from the study.

An in-house-designed data collection questionnaire was used to collect the data. Information on socio-demographic characteristics, family and medical history, past obstetric history, BMI, delivery outcome, complications and the duration of hospital stay were collected by the trained set of qualified study nurses in all three centers.

All participants who agreed to participate in the study were sent home with instructions to come back the following morning in at least 8 hours of overnight fasting state to do Oral Glucose Tolerance Test (OGTT). On the next morning, two blood samples were taken, one in fasting state and another 2 hours after drinking 75g glucose in 300ml water and analyzed in the Clinical Biochemistry laboratories in the respective hospitals.

For the diagnosis of Gestational Diabetes Mellitus (GDM), we used the National Institute for Health and Care Excellence (NICE) guideline 2015 recommendation to use the fasting blood glucose level of 5.6mmol/L (101mg/dL) cut-off to diagnose GDM[7]. For the 2 hours blood glucose level, we used the International Association of Diabetes in Pregnancy Study Group (IADPSG) 2010 recommendation cut-off level of 8.5-mmol/L (153-mg/dL).

In our study, 736 patients were recruited, of which 10 were either lost to follow up or found to have frank diabetes, with fasting sugar above 125 mg/dL or random sugar and 2 hours postprandial sugar level above 200 mg/dL. A total of 726 were available for analysis. Women diagnosed with GDM were either put on life style modification with diet and exercise or on medication with Metformin or insulin, depending on blood glucose levels. Women diagnosed with GDM were closely followed up throughout the pregnancy up till delivery. At delivery, information on the mother and baby was collected. Information on complications at delivery, admission of neonates to neonatal intensive care unit (NICU) and number of days spent in hospital were collected.

Ethical clearance (REBH/Approval/2016/010) was obtained from the Research Ethics Board for Health (REBH), Ministry of Health before the start of the study.

Statistical analysis was done using SPSS version 16. To test the significance of differences of proportions of categorical variables between two or more groups, both Fischer's exact test and $\chi 2$ test were used. Student's t-test (two tailed) was used to determine the significance between two continuous variables. A *p*-value of ≤ 0.05 was considered statistically significant.

RESULTS

The prevalence of GDM for the three Regional Referral Hospitals was 15.0%. Table 1 shows the socio-demographic characteristics of GDM and non-GDM cases. The prevalence of GDM cases in the three hospitals was similar and statistically not significant. The mean age of participants, their occupation and monthly income between the GDM group and non-GDM group were similar. Age distribution below and above 25 years is similar in both groups. Table 2 shows the prevalence of GDM stratified by family history, parity, BMI, miscarriage and mode of delivery. This study showed that 15.6% of GDM cases and 9.6% of non- GDM cases had a family history of Diabetes Mellitus, which was prominent but just not statically significant at *p*-value 0.057. The percentage of women who had delivered at least two babies before (Parity of 2 or more) was 26.6% in the GDM group and 16.4% in the non-GDM group, which was statistically significant at *p*-value 0.014.

Table 1. Prevalence of GDM* and socio-demographic characteristics of women attending ANC† in referral hospitals of Bhutan at 24-28 weeks, 2016 (*n*=726)

Variables	GDM n(%)	Non-GDM n(%)	*P value*‡
Total	109(15.0)	617(85.0)	-
Referral Hospitals			
JDWNRH§	70(64.2)	393(63.7)	
CRRH**	18(16.5)	109(17.7)	0.954
ERRH††	21(19.3)	115(18.6)	
Mean age (SD)	25.8(3.4)	26.5(4.5)	0.561^
Age group			
Less than 25 years	39(35.8)	202(32.7)	0.534
25 and above years	70(64.2)	415(67.3)	
Occupation			
Housewife/farmer	58(53.2)	349(56.6)	0.085
Office/Business	51(46.8)	268(43.4)	
Monthly income (In Ngultrum)			
Less than Nu.10,000	30(27.5)	196(31.8)	
Nu.10,000–Nu.20,000	48(44.0)	244(39.5)	0.496
Above Nu. 20,000	31(28.5)	177(28.7)	

**Gestational Diabetes Mellitus*
†Antenatal Clinic
‡Based on χ2 test. ^Based on t-test
§Jigme Dorji Wangchuk National Referral Hosptial
***Eastern Regional Referral Hospital*
††Central Regional Referral Hospital

Table 2. Percentage of key characteristics in GDM vs Non-GDM patients

Variables	GDM (*n*=109)	Non-GDM (*n*=617)	*p*-value
	n(%)	*n*(%)	
Family history of diabetes			
Yes	17(15.6)	59(9.6)	0.057
No	92(84.4)	558(90.4)	
Parity number			
less than 2	80(73.4)	516(83.6)	
2 and above	29(26.6)	101(16.4)	0.014
Body mass index			
<18.5	4(3.7)	31(5.0)	
18.5-24.9	38(34.9)	248(40.2)	
25.0-29.9	24(22.0)	126(20.4)	0.27
≥ 30	43(39.4)	212(34.4)	
BMI above 25			
Yes	67(61.5)	338(54.8)	
No	42(38.5)	279(45.2)	
Miscarriage			0.058
Yes	11(10.1)	33(5.3)	
No	98(89.9)	584(94.7)	
Mode of delivery			0.050
C-section	33(30.3)	146(20.1)	
Normal/vacuum delivery	76(69.7)	471(79.9)	0.367
Durations of hospital stay			
Up to 3 days	77(70.6)	497(80.6)	0.022
≥ 4 days	32(29.4)	120(19.4)	
Birth Weight			
Low birth weight(<2500gm)	13(11.9)	42(6.8)	
Normal weight(2500-4000gm)	92(84.4)	547(88.7)	0.169
Macrosomia (>4000gm)	4(3.7)	28(4.5)	
Period of Gestation			
Less than 37 weeks	4(3.7)	24(3.9)	0.586
37-42 weeks	105(96.3)	593(96.1)	

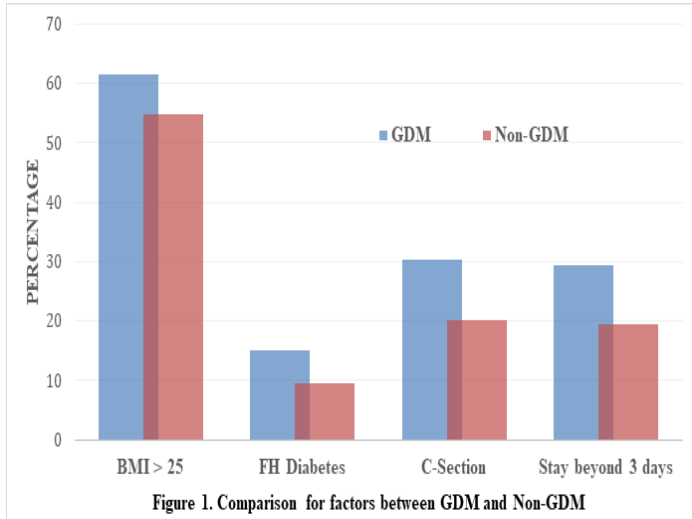

Figure 1. Comparison for factors between GDM and Non-GDM

Figure 1. Comparison for factors between GDM and Non-GDM

There was significant difference when women were compared between the groups with BMI above 25 and below 25 (*p*-0.001). History of past miscarriage was noted in 10.1% of cases of GDM and 5.3% of non-GDM cases. 30.3% of GDM cases had caesarean section delivery, as compared to only 20.1% in non-GDM group. Among the GDM cases, 29.4% stayed beyond 3 days in the hospitals as compared to 19.4% of non-GDM cases. The difference with parity and duration of stay in hospital in the two groups was statistically significant with p-value ≤ 0.05.

Figure 1 compares the factors affecting GDM and non-GDM. 39.4% of women with GDM had BMI over 30 and 34.4% of women without GDM had BMI over 30. Positive family history of Diabetes was found in 15.6% of GDM cases as compared to 9.6% of non-GDM group. Caesarean section delivery differed in the two groups with 30.3% in GDM cases and 20.1% in non-GDM cases. Staying 4 days or more in hospital was noted in 29.4% of GDM cases and 19.4% of non-GDM cases.

The maternal complications such as pre-eclampsia, polyhydramnios, shoulder dystocia and perineal tear were not different in the two groups. The low APGAR scores, preterm deliveries, rate of NICU admissions and newborns large for gestational age were not different from the non-GDM group. The main reason may be attributed due to good management of the diagnosed cases of GDM and delivery at 38 weeks.

DISCUSSION

This is the first study done in Bhutan to find out the prevalence of GDM, the associated factors and association of GDM with maternal and fetal outcomes in women attending antenatal clinics in Bhutan. GDM is one of the emerging common medical complications in pregnancy8. The prevalence of GDM found in this study for the three referral hospitals in Bhutan was 15%.

This is slightly higher than the reported global prevalence of 1.4 to 14% 2. Our findings are within the range of

GDM prevalence found in India of 3.8 to 21%[3], but lower than in Qatar with prevalence of 16.3%7 and United Arab Emirates prevalence of 20.6%[9]. The prevalence of GDM which was found to be high in these three regions could be because of various reasons such as environmental diversity with varied cultural practices of food habits and psychosocial factors, increasing habits of rice consumption, socio-behavior factors, and relative lack of physical exercise.

This study also provides information about the risks for GDM which could be used for preventive programs or clinical identification. The risk factor observed to be significant in this study in women with GDM was of mothers with higher parity. Family history of Diabetes has been reported to be associated with GDM[10]. In our study, 15.6% of GDM cases had family history for diabetes, as compared to 9.6% in non-GDM case but this was not just statistically significant. Our study found that women with GDM had a higher percentage of parity two and over (26.6%) compared to women without GDM (16.4%). more than two had higher prevalence of GDM (26.6%) compared to parity less than two (16.4%). This is similar to a study done in urban Kashmir in North India[11]. Women with GDM had higher BMI in comparison to women without GDM in our study. Prevalence of GDM increasing with higher BMI has been also seen in other studies[12]. It is important to inform all obese women considering pregnancy about the risks of developing GDM and its complications.

A maternal adverse factor observed for GDM cases in this study was longer duration of hospital stay (29.4% vs 19.4%). All patients undergoing caesarean section are usually discharged on the third postoperative day. It was also observed that there were higher chances of delivering by caesarean section (30.3% vs 20.1%). A study done in Western Rajasthan, India, showed C-Section rate was found to be 78.8% among GDM patients[13].

There was no statistical difference in birth weight of babies in the two groups. This may be due to the management protocol being followed in the hospitals in Bhutan once GDM cases were diagnosed, having close monitoring on diet and control of weight gain during pregnancy. All diagnosed with GDM were initially put on diet control with help of dieticians and moderate exercise with minimum of 30 minutes' walk daily. Their fasting and 2-hour postprandial sugar levels were checked after 2 weeks and those with high levels were put on metformin 500mg twice daily in addition to their diet control and exercise. Again, this group was followed up with sugar levels after 2 weeks and those with high sugar levels were switched to injection insulin. All patients on metformin or insulin were admitted for delivery by 38 completed weeks, and those only on diet control were admitted for delivery at 40 weeks. This is in contrast to a study conducted in India, which observed macrocosmic babies in 18 % of women with GDM compared to 3.64% in non GDM group[13].

The mean age, occupation and monthly income between GDM group and the non-GDM groups of participants were similar. 35.8% of women with GDM and 32.7% of women without GDM were below the age of 25. This is in contrast to a study conducted in Western Rajasthan which found increasing GDM prevalence with increasing age[12]. Considering these factors, it is difficult to exclude a possible genetic susceptibility of the Bhutanese race to develop GDM. Earlier report showed that pregnant women of Asian origin were ethnically more prone to develop glucose intolerance compared to other ethnic groups[14].

Our study is a hospital-based study, and it has limitations to generalizing the finding to rural settings. However, we believe that our study has good representation of information of the referral hospitals. All the institutional deliveries occur in these three regional referral hospitals due to presence of gynecologic services including caesarean facilities. Based on information from the Annual Health Bulletin 2015[15], out of total reported deliveries of around 11000 births, 60% of the total institutional births occurred in these three referral hospitals. There were only about 582 home births in the country in 2015. It is suggestive of high prevalence of GDM at the national level.

Our study has good use for the Reproductive Health and Nutritional Program of the Ministry of Health of Bhutan for being the only prospective study done for GDM. Based on our finding of relatively high prevalence of GDM (15.0%), there needs to be proper strengthening of the GDM screening in antenatal clinics across Bhutan.

CONCLUSIONS

The prevalence of GDM in women attending ANCs in the referral hospitals in Bhutan was 15.0%. GDM is widely prevalent geographically, socio-economically and irrespective of age of participants in three regions. Similar high prevalences of GDM in all three regions suggests that there is an unaddressed health situation that needs proper attention.

We draw the following recommendations for the Nutritional and Reproductive Health Programs; to have health education programs for school health and adolescents to encourage them to have a healthy diet and maintain body weight to reduce the risk of GDM in their later lives. Universal screening of pregnant women during the antenatal period is recommended to detect GDM. A future study of similar nature involving the district hospitals and Basic Health Units is recommended to fill the knowledge gap about the actual prevalence of GDM in the community.

ACKNOWLEDGEMENTS

We are very grateful to the UNFPA Country Office for the funding to do this research through the Department of Midwifery and Nursing of the Faculty of Nursing and Public Health. We also thank all the nurses, physicians and other staff working in the three health centers where this study was conducted. Finally, we would like to thank all the patients who participated in the study.

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AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

PD: Concept, analysis of data, study design, manuscript drafting and critical reviews

SJ: Concept, analysis of data, study design, manuscript drafting and revisions

NG: Concept, analysis of data, study design, manuscript drafting and revisions

KC: Concept, analysis of data, study design, manuscript drafting and revisions

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Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

GRANT SUPPORT AND FINANCIAL DISCLOSURE

None