ORIGINAL ARTICLE

GESTATIONAL DIABETES AMONG THE ARSENIC EXPOSED WOMEN FROM ARSENIC CONTAMINATED AREA OF BANGLADESH

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ABSTRACT

Exposure to groundwater arsenic contamination has been demonstrated to be associated with an increased risk of diabetes mellitus in Bangladesh. But, the association between arsenic exposure and Gestational Diabetes Mellitus (GDM) in Bangladesh remains to be reported. This cross-sectional study was carried out to assess the occurrence of GDM amongst pregnant women from the arsenic contaminated area. A total of 200 pregnant women who were aged 20 years and more, having gestational age more than 21 weeks, and had attended a district hospital for antenatal checkup were selected for the study. Of the total 200 participants, 15.5% were found to have GDM and it was significantly high (p=0.029) in women with higher gestational age. Regarding arsenic exposure, 39.5% of the participants were categorized as arsenic exposed and amongst them the proportion of GDM was found high (20.3%). Binary logistic regression analysis showed that the increase in gestational age and BMI, and a higher level of arsenic in urine of the total participants, had significantly ($p<0.05$) ability to predict the likelihood of having GDM (1.2, 1.1 and 9.2 times respectively). While logistic regression analysis among the arsenic exposed participants showed that higher level of BMI was 1.2 times and arsenic in urine was 9.4 times likely to predict the likelihood of having GDM. Thus, it was revealed that the increased concentration of arsenic in urine had the strongest ability to predict the likelihood of developing GDM among the pregnant women. The study concluded that the arsenic exposed pregnant women suffered more from GDM compared to the non-exposed pregnant woman.

Keywords: GDM, Gestational diabetes, Diabetes mellitus, Arsenic, Arsenic toxicity

INTRODUCTION

Diabetes is one of the most common Non-communicable diseases (NCDs) and a major contributor to public health burden. In 2014 an estimated 22 million (8.5%) adults worldwide lived with diabetes which was almost double of the prevalence (4.7%) in 1980[1]. It was also predicted that by 2040, 1 in 10 adult populations would be suffering from diabetes and globally there would be approximately 642 million diabetes patients[2]. The risk factors believed to be associated with this increased prevalence of diabetes are overweight and obese[1].

The diabetes prevalence is rising fast in low and middle-income countries and South East Asian countries top the list, because of its thick population and socio-cultural changes. Bangladesh is one of the top ten countries with regards to diabetes having an estimated 7.1 million diabetics (2015) accounting for 8.3% of the population which is likely to increase to 13.6 million by 2040[3].

According to WHO[4] hyperglycaemia first detected at any time during pregnancy should be classified as either gestational diabetes mellitus (GDM) or diabetes mellitus in pregnancy. GDM is a temporary condition and is a risk factor for developing type II diabetes, as well as risk for diabetes in the offspring. In addition to its inherent complications, GDM may cause adverse pregnancy outcomes, abnormalities in the baby and increased mortality and morbidity of mother and neonates[3-6]. GDM was first documented in 1824 when a mother was found with her foetus having macrosomia and stillbirth; the mother was diagnosed by hyperglycemia symptoms and estimating sugar in dried urine, the symptoms disappeared after birth[7].

In the present day, GDM has become a priority issue of global public health, it has an increasing trend similar to that of Type I and Type II

diabetes[1-3,6,8]. For every 7 birth, one birth is affected by GDM[2]. And among 20.9 million live birth having hyperglycemia, 85.1% (estimated) were born to mothers with GDM[1,3]. Furthermore, globally for every 10 pregnancies, there may be one diabetes and 90% of all this diabetes are GDM[3,6]. Among the top ten Asian countries, the prevalence of GDM in China and India were 12.2% and 14.3% respectively[6]. In Bangladesh, 7-14% women of reproductive age have been reported as diabetic[5] and therefore, a substantial proportion of these women could have had GDM.

A study in Dhaka city[5] revealed that 7.5% of the pregnant women were found to suffer from diabetes. It is evident from different studies[5,9] that the prevalence of GDM in Bangladesh ranges from 6% to 14 %. GDM causes complications both in mother and babies. As reported in Bangladeshi population maternal complications in GDM includes hydramnios, pre-eclampsia, urinary tract infection, puerperal sepsis; on the other hand, low birth weight, respiratory distress, large baby and neonatal jaundice were commonly found in the babies of mothers with GDM[3-5].

Arsenic contamination in groundwater is a major public health problem in Bangladesh. About 50 million people consume tube well water containing arsenic at levels higher than 0.05mg/L which has the likelihood to cause chronic toxicity[10-13]. Prolonged exposure to such doses results in arsenicosis which is characterized by characteristics skin manifestations of melanosis and/or keratosis[10-14]. In additions, individuals with arsenic exposure may develop certain NCDs, many of which have already been reported in arsenic exposed population of Bangladesh[10-13,15]. As such the occurrence of diabetes mellitus has also been reported with an increased prevalence among the chronic arsenic exposed population[15-17]. Recently, it has been revealed that the rural young adults in Bangladesh who had arsenic exposure, 5.6% of them had diabetes mellitus; further the prevalence was found more (7.9%) amongst those with arsenicosis[15]. Increased risk of GDM and impaired glucose tolerance among the arsenic exposed women have been reported elsewhere[18,19]. But GDM in chronically arsenic exposed women of Bangladesh remains to be reported. This study was an attempt to find out the occurrence of GDM among the women who had exposure to arsenic.

METHODOLOGY

This cross-sectional study carried out among the pregnant women who came for an antenatal checkup to a district level hospital in an arsenic contaminated area of Bangladesh. The pregnant women aged 20 years or more, having a gestational age of more than 21 weeks, who came to the hospital for a first antenatal checkup, was approached and her consent to participate in the study was sought. Those who agreed to participate in the study were included as the study participants. The participants who had a previous history of diabetes were excluded from the study. Ultimately a total of 200 pregnant women could be included as the participant of this study. Gestational diabetes mellitus (GDM) of the participating women was diagnosed based on results of FBS and ABF blood sugar examination as per WHO criteria[4]. For ascertaining arsenic exposure, urinary arsenic level of all participating women was determined. Twenty ml of urine sample was collected from each of the participating women and transported to the laboratory following the instructed procedure. In the laboratory, the urine samples were digested and the digested samples were measured for total arsenic by HG-AAS methods. Participants had urinary arsenic higher than 100 µg/L was identified as arsenic exposed[20] and others were identified as non-exposed. Necessary information of the participating women was collected by face to face interview and from the physical examination report.

RESULTS

A total of 200 pregnant women were included in the study, among them 15.5% were found to have GDM (table-1). The age of the participants was between 20 and 35 years, they had a mean age of 24.14±3.99 years and two third (67.5%) of them were younger than 25 years of age. The proportion of having GDM was observed to increase with age. Those having GDM were found to have a higher mean age (25.19±4.28 years) compared to that for those without GDM (23.95±3.92 years), but the difference was not statistically significant. About 50% (99) of the participants had SSC level education and one-third (33.5%) had primary level of education. Mean BMI was found to be significantly higher ($p<0.05$) among those found to be having GDM (25.25 ±4.27 kg/m^2) compared to those not having GDM (23.59±3.37 kg/m^2). GDM was more common in those who were obese (31.2%) and overweight (22.2%) compared to those who had normal BMI (11.5%), and the observed difference was statistically significant (x^2= 6.272; p=0.043).

Table 1: GDM status of the pregnant women by age, education and BMI

Characteristics		GDM		Total	Test of significance
		Yes (%)	No (%)	n=200	
GDM		31 (15.5)	169 (84.5)	200 (100)	
Age (years)	20-24	18 (13.3)	117 (86.7)	135 (67.5)	
	25-29	08 (19.5)	33 (80.5	41 (20.5)	$x^{2\spadesuit}$=1.509; p=0.470
	30 and Above	05 (20.8)	19 (79.2)	24 (12.0)	
	Mean±SD	25.19±4.28	23.95±3.92	24.14±3.99	t^{*}=-1.599; p=0.111
Education	Upto Primary	14 (20.9)	53 (79.1)	67 (33.5)	
	SSC	11 (11.1)	88 (88.9)	99 (49.5)	$x^{2\spadesuit}$=3.065; p=0.216
	HSC & Above	06 (17.6)	28 (82.4)	34 (17.0)	
BMI (Mean±SD)		25.25±4.28	23.59±3.37	23.85±3.57	t^{*}=-2.408; p=0.017
BMI category	Normal	16 (11.5)	123 (88.5)	139 (69.5)	
	Over weight	10 (22.2)	35 (77.8)	45 (22.5)	$x^{2\spadesuit}$= 6.272; p=0.043
	Obese	05 (31.2)	11 (68.8)	16 (08.0%)	

** Independent sample t test, ♠ Chi squared test*

None of the participants having less than 25 weeks of pregnancy was found to have GDM, GDM was detected in those whose gestation had completed 25.04 weeks or more. Among women who had crossed the 28th week of gestation, a higher proportion (17.9%) was found to have GDM. However, those with GDM had significantly higher (p<0.05) average gestational age (30.59±2.31 weeks) compared to that for those without GDM (29.23±3.30 weeks). GDM was more common in participants with second pregnancy (17.1%) than in participants with first pregnancy (15.9%) or higher order pregnancy (11.9%) but the difference was not statistically significant (table-2).

Table-2: Obstetrical history and GDM status of the pregnant women

Obstetrical History		GDM		Total	Test of significance
		Yes (%)	No (%)		
Gestational age (weeks)	Upto 24	0 (0)	12 (100)	12 (6.0)	
	>24-28	07 (13.0)	47 (87.0)	54 (27.0)	$x^{2\spadesuit}$= 3.061; p=0.216
	>28	24 (17.9)	110 (82.1)	134 (67)	
	Mean ±SD	30.59±2.31	29.23±3.30	29.44 ±3.20	t^{*}=2.196; p=0.029
Parity	Parity 0	14 (15.9)	74 (84.1)	88 (44.0)	
	Parity 1	12 (17.1)	58 (82.9)	70 (35.0)	$x^{2\spadesuit}$= 0.570; p=0.752
	Parity≥2	05 (11.9)	37 (88.1)	42 (21.0)	

** Independent sample t test, ♠ Chi squared test*

Table-3 shows arsenic levels in urine of the participants. Those having GDM had a significantly (p= 0.026) higher mean concentration of arsenic in urine (0.123± 0.0044 mg/L) than those not having GDM (0.072±0.0028 mg/L). Amongst those considered to be having arsenic exposure (urinary arsenic >0.100 mg/L), urine arsenic level was significantly higher (t=-2.260; p= 0.027) in those having GDM (0.395 mg/L) compared to those not having GDM (0.258 mg/L). On the other hand, urine arsenic level was not found to be significantly higher (p=0.824) in non-exposed participants with GDM (0.035±0.0018 mg/L) compared to that for non-exposed non-GDM (0.034±0.0019 mg/L) participants. Though not significantly high, GDM was found to be more common amongst those considered as having arsenic exposure (20.3%) compared to that in participants consider as not having arsenic exposure (12.4%).

Table-3: Arsenic exposure and GDM status of the pregnant women

Arsenic in urine		GDM		Total	Test of Significance
		Yes (%)	No (%)		
Urine arsenic level(mg/L)	Non-exposed	0.035±0.0018	0.034±0.0019	0.034±0.0018	t^{*}=-0.222; p= 0.824
	Log transformed	1.550±0.2516	1.532±0.2769	1.534±0.2730	
	Exposed	0.395±0.0029	0.258±0.0017	0.281±0.002	t*=-2.260; p= 0.027
	Log transformed	2.606±0.4627	2.411±0.2329	2.449±0.2998	
	Over all	0.123±0.0044	0.072±0.0028	0.080±0.0034	t^{*}=-2.239; p= 0.026
	Log transformed	2.068±0.6479	1.860±0.4999	1.896±0.5303	
Arsenic exposure status	Non-exposed (≤0.100 mg/L)	15 (12.4)	106 (87.6)	121 (60.5)	$x^{2\spadesuit}$=2.252; p=0.133
	Exposed (>0.100 mg/L)	16 (20.3)	63 (79.7)	79 (39.5)	

** Independent sample t test, ♠ Chi squared test*

The impact of age, gestational age, parity, BMI, and arsenic concentration in urine on the likelihood of developing GDM, was assessed by binary logistic regression analysis (table-4). It was found that the combined effects of all these predictors can significantly (x^2=27.929; p=0.000) explain the status of GDM of the participants. R-Square analysis revealed that Cox and Snell=0.130 and Nagelkerke=0.225 for both arsenic exposed and non-exposed participants, indicating a well fitted model with the total variability of the dependent variable. However, gestational age (p=0.044), BMI (p=0.038) and arsenic concentration in urine (p=0.001) were individually found to have the ability to predict the likelihood of developing more GDM. Arsenic in urine was the strongest predictor for GDM. And for every additional mg of arsenic per litre of urine pregnant women were 9.2 times more likely to have GDM. Furthermore, for each week increase of gestational age and each unit increase of BMI the pregnant women were 1.2 and 1.1 times more likely to have GDM.

Table-4: Logistic regression predicting likelihood of occurrence of GDM among the participants

Dependent Variables	GDM status among the exposed and non-arsenic exposed women					95% Confidence Interval	
Independent Variables	**B**	**S.E.**	**Wald**	**P**	**Exp (B)**	**Lower**	**Upper**
Constant	-13.603	3.370	16.292	0.000	0.000		
Age	0.104	0.060	3.016	0.082	1.110	0.987	1.249
Gestational age	0.170	0.084	4.071	**0.044**	1.185	1.005	1.399
Parity			2.809	0.246			
Parity (2)	1.217	0.739	2.708	0.100	3..375	0.793	14.373
Parity (>2)	0.886	0.641	1.910	0. 167	2.426	0.690	8.523
BMI	0.119	0.057	4.297	**0.038**	1.126	1.006	1.260
Urine Arsenic	2.221	0.650	11.656	**0.001**	9.202	2.575	32.960

Over all Chi square 27.929 p=0.000

A second logistic regression (table-5) was carried out on arsenic exposed participants only using the same predictors to see the ability of arsenic exposure to predict the development of GDM. Pseudo R-Square analysis revealed that Cox and Snell=0.209 and Nagelkerke=0.330 for arsenic exposed participants, indicating well fitted model with the total variability of the dependent variable. The combined effect of the predictors was found to be able to significantly (p=0.005) explain the GDM status of the participants. In this analysis, only BMI (p=0.040) and arsenic concentration in urine (p=0.007) were found to have significant ability to predict the likelihood of having GDM. BMI could predict 1.2 times more likelihood of developing GDM amongst arsenic exposed women. On the other hand, increased arsenic exposure was the strongest predictor and for every additional mg of arsenic per litre of urine a pregnant woman was 9.4 times more likely to have GDM.

Table-5: Logistic regression predicting likelihood of occurrence of GDM among the arsenic exposed participants

Dependent Variables	GDM status among the arsenic exposed women					95% Confidence Interval	
Independent Variables	**B**	**S.E.**	**Wald**	**P**	**Exp (B)**	**Lower**	**Upper**
Constant	-14.673	5.290	7.693	0.006	0.000		
Age	0.146	0.099	2.202	0.138	1.158	0.954	1.404
Gestational age	0.123	0.118	1.097	0.295	1.131	0.898	1.425
Parity			2.325	0.313			
Parity (1)	1.497	1.136	1.737	0.188	4.466	0.482	41.354
Parity (≥2)	0.168	0.967	0.030	0.862	1.183	0.178	7.865
BMI	0.180	0.087	4.232	**0.040**	1.197	1.009	1.421
Urine Arsenic	2.238	0.835	7.176	**0.007**	9.371	1.823	44.177

Over all Chi square 18.557; p=0.005

DISCUSSION

Prevalence of GDM is reported to be increasing and has become an important cause for adverse pregnancy outcomes both in rural and urban areas in Bangladesh [3,9,21]. In Canada, GDM has increased from 3.5% to 5.2% in 6 to 7 years[17], and in 9 years had increased from 2% to 7.62% in India[22]. In the present hospital-based study 15.5% of the pregnant women were found to have GDM, this figure was higher than that reported from the previous studies[4.9]. In a previous study carried out in different hospitals of Dhaka city 10 years back, reported that 7.5% of their study participants had GDM[4]. In another hospital based study[23]conducted in Chittagong reported that 13.7% of the pregnant women had GDM. The Chittagong study further reported that GDM was more common among the women who were in the third trimester (56.3%) followed by 31.2% in those who were in the second trimester. Another study[3] conducted in Bangladesh reported a high prevalence of GDM in the first trimester of pregnancy. A much higher prevalence (65.3%) of GDM in the 3rd trimester of pregnancy has been reported from India[24]. The current study revealed that those having GDM had a significantly (p=0.029) a higher gestational age (30.59±2.31 weeks) than those without GDM (29.23±3.30). This study also revealed that GDM was detected as early as 25th gestational week. Furthermore, after removing the effect of possible confounders in regression analysis it was found that with each unit increase in gestational age a pregnant woman was 1.12 times more likely to have gestational diabetes.

Regarding overweight and obesity, studies[19,22,25] conducted in Bangladesh and elsewhere revealed an association of overweight and obesity with GDM. The present study also revealed a statistically significant higher occurrence of GDM among the overweight (22.2%) and obese (31.2%) pregnant women. None the less, BMI was found to be significantly higher (p=0.017) in pregnant women with GDM (25.25±4.27 Kg/m^2) than that in women without GDM (23.59±3.37). Furthermore, logistic regression analysis revealed that after removing the effects of possible confounders it was found that for every unit increase of BMI the pregnant women were 1.1 times more likely to develop GDM. In case of arsenic exposed pregnant women for every unit increase of BMI the likelihood of having GDM was found to increase 1.2 times.

Studies conducted in Bangladesh[3,13,23,26], found a higher occurrence of GDM among the multigravida and older age. In the present study, no such association was found with the occurrence of GDM amongst the pregnant women with multigravida. In this study, 44% of the participants were pregnant for the 1st time, while rest of them were in their second or higher pregnancy. However, this study revealed that the proportion of GDM increased with the age of the pregnant women.

Arsenic is diabetogenic and higher occurrence of diabetes mellitus has been reported amongst the arsenic exposed population in Bangladesh and elsewhere[10,15-17,27-32]. Recently, a significantly higher prevalence of diabetes mellitus has been revealed from Bangladesh[15] amongst the arsenic exposed young adults aged 30 to 39 years compared to those not having such exposure. Further, the study revealed an increased likelihood of finding more GDM among the arsenic exposed young women[15]. The pregnant women in the current study were mostly young adults and a higher proportion of GDM (20.3%) was found amongst the arsenic exposed than that of the non-exposed women (12.4%). After adjustment of possible confounders, in logistic regression analysis, it was found that those with arsenic exposure had the strongest likelihood of developing GDM. Among all participants, each unit increase of arsenic in urine the pregnant women were 9.2 times more likely to have GDM. On the other hand, among the participants who were arsenic exposed for each unit increase of arsenic in urine the pregnant women were 9.4 times more likely to have GDM. Thus, the study indicated that the arsenic exposed women are at a higher risk of developing GDM. Therefore, for the early identification of GDM, the arsenic exposed pregnant women should be encouraged for regular antenatal checkup particularly for monitoring their blood glucose level. And in the arsenic contaminated area of Bangladesh, diabetes screening programme may be integrated with community clinic activities for the early detection and management of diabetes in pregnancy.

CONCLUSION

This hospital-based study concluded that pregnant women with arsenic exposure had a higher likelihood for developing GDM than those without such exposure. Thus, pregnant women from the arsenic contaminated area should be routinely monitored for diabetes.

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