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FREQUENCY OF UNCONTROLLED DIABETES MELLITUS IN LATE 3RD TRIMESTER AND ITS ASSOCIATION WITH MATERNAL OUTCOME

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Abstract

Diabetes mellitus is a metabolic disorder characterized by elevated blood and tissue glucose levels due to absolute or relative insulin deficiency. In addition to several systemic complications, diabetes in pregnant women is associated with poor perinatal outcome. A recent study claimed that not merely the presence of diabetes but also poor glycemic control during pregnancy is associated with adverse maternal outcome. However, the available evidence was limited while there was no such local published material which necessitated the present study. The objectives of this study were to determine the frequency of uncontrolled diabetes mellitus in late 3rd trimester among diabetic pregnant women presenting at a teaching hospital in Punjab and to compare the maternal outcome among pregnant women with controlled versus uncontrolled diabetes mellitus. It was a descriptive case series. Research was conducted at Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital Lahore in a duration of 6 months. This study involved 217 diabetic pregnant women aged between 18-35 years presenting after 34 weeks of gestation. The mean age of the patients was 30.1±3.9 years while the mean gestational age was 39.6±1.6 weeks. Majority (n=190, 87.6%) of the patients were aged between 26-35 years followed by 27 (12.4%) patients aged between 18-25 years. There were 75 (34.6%) primiparas and 142 (65.4%) multiparas. 36 (16.6%) patients had pre-pregnancy diabetes while 181 (83.4%) patients had gestational diabetes. 74 (34.1%) patients were taking oral hypoglycemic while 143 (65.9%) patients were on insulin. HbA1c levels ranged from 5.5% to 7.7% with a mean of 6.5±0.66%. Taking a cut-off value of ≥6.0%, 146 (67.3%) patients had uncontrolled diabetes. 46 (21.2%) patients had polyhydramnios, 146 (67.3%) patients required cesarean delivery and 31 (14.3%) patients acquired post-partum hemorrhage. The frequency of polyhydramnios (27.4% vs. 8.5%; p-value=0.001), cesarean delivery (84.9% vs. 31.0%; p-value<0.001) and postpartum hemorrhage (21.2% vs. 0.0%; p-value<0.001) was significantly higher in patients with uncontrolled diabetes. A substantial proportion of diabetic women in late 3rd trimester had poor glycemic control and had significantly higher frequency of polyhydramnios, cesarean delivery, and postpartum hemorrhage than women with good glycemic control which advocates routine monitoring and strict glycemic control in diabetic pregnant women to improve the maternal outcome in future practice.

Keywords: Gestational diabetes, Pre-pregnancy diabetes, Glycemic control, Maternal outcome

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by elevated blood and tissue glucose levels due to absolute or relative insulin deficiency. In addition to a number of systemic complications, diabetes in pregnant women is associated with poor maternal outcome in the form of polyhydramnios, preterm delivery, increased need for caesarean delivery and postpartum hemorrhage (1, 2). Due to these complications, diabetic screening and good glycemic control are important elements in antenatal care (2). Oral glucose tolerance test (OGTT) has been recommended screening tool with high sensitivity and specificity of 100% (3). The routine practice is to monitor such patients by fasting blood sugar level which however gives information about glycemic control at a specific check point and cannot take into account the peaks in blood sugar level during the past 24 hours particularly those occurring after meal (3, 4). The need for a simpler, more universally acceptable, and accessible test is becoming increasingly apparent. Glycosylated hemoglobin (HbA1c) is currently the most accepted measure of chronic glycaemia outside of

pregnancy. It gives information about the overall glycemic control in the past 3 month's period. It is also more convenient to perform as it doesn't require pre-test fasting and can be performed during routine antenatal visits (5, 6).

Gupta *et al.* used HbA1c level to assess glycemic control and reported that 83% of diabetic pregnant women in their late 3rd trimester had poor glycemic control (HbA1c level >6%). They also observed significantly higher frequency of various maternal complications in women with uncontrolled diabetes; polyhydramnios (21.69 % vs. 11.76%; $p=0.03$), caesarean delivery (89.16% vs. 29.41%; $p=0.01$) and postpartum hemorrhage (22.20% vs. 0%; $p=0.02$) as compared to those with controlled diabetes (HbA1c <6) (7).

Maternal diabetes is associated with poor maternal outcome is already established (1, 2). But the results of Gupta *et al.* (7) show that not merely diabetes, but its poor control is attributable to these maternal complications and that HbA1c can be effectively used to identify those who are particularly at higher risk. The evidence is however limited to a single international research paper and to the best of candidate's knowledge there is no such local published material. The purpose of the current study is to determine the frequency of poor glycemic control (HbA1c >6%) in local pregnant women which will give an insight into the magnitude of problem.

The results of the present study may also enable selection of HbA1c level as a more suitable screening tool for poor glycemic control during antenatal visits and identification of high-risk women so that appropriate and timely intervention can decrease the morbidity associated with maternal diabetes.

METHODOLOGY

STUDY DESIGN & SETTINGS

It's a descriptive case series. Research was conducted at Department of Obstetrics and Gynecology Unit-IV, Sir Ganga Ram Hospital, Lahore. Duration of study was 6 months. Sample size of 217 cases was calculated with 95% confidence level and 5% margin of error while taking expected frequency of uncontrolled diabetes mellitus among diabetic pregnant women in late 3rd trimester to be 83% (7).

SAMPLING TECHNIQUE AND SAMPLE SELECTION

Patients were selected by Non-Probability, Consecutive Sampling.

INCLUSION CRITERIA

1. Pregnant women in late 3rd trimester (≥ 34 weeks as per dating scan) aged between 18-35 years having diabetes mellitus as per operational definition.
2. Patients who signed written informed consent to participate in the study.

EXCLUSION CRITERIA (RISK FACTORS FOR POOR MATERNAL OUTCOME)

1. Multiple Pregnancies and those with congenital defects and abnormal presentation (as per dating scan).
2. Placenta previa (as per dating scan)
3. Multiparas ≥ 5 , known hypertensive (Blood Pressures $\geq 140/90$ mmHg on at least two occasions 4 hours apart) and obese (BMI ≥ 30 kg/m²).

STATISTICAL ANALYSIS

All the collected data was entered and analyzed through SPSS version 21.0. Mean $\pm$ SD, post-stratification chi-square test has been applied taking $p \leq 0.05$ as statistically significant.

RESULTS

The age of the patients ranged from 18 years to 35 years with a mean of 30.1 ± 3.9 years. Majority ($n=190$, 87.6%) of the patients were aged between 26-35 years followed by ($n=27$, 12.4%) patients aged

between 18-25 years. The gestational age of the patients ranged from 37 weeks to 42 weeks with a mean of 39.6 ± 1.6 weeks. There were (n=75, 34.6%) primiparas and (n=142, 65.4%) multiparas. (n= 36, 16.6%) patients had pre-pregnancy diabetes while (181, 83.4%) patients had gestational diabetes. (n=74, 34.1%) patients were taking oral hypoglycemic while (n=143, 65.9%) patients were on insulin as shown in Table I.

Table I. Baseline characteristics of study participants

Characteristics	Participants n=217
Age (years)	30.1 $\pm$ 3.9
• 18-25 years	27 (12.4%)
• 26-35 years	190 (87.6%)
Gestational Age (weeks)	39.6 + 1.6
• 37-39 weeks	93 (42.9%)
• 40-42 weeks	124 (57.1%)
Parity	
• Primiparas	75 (34.6%)
• Multiparas	142 (65.4%)
Type of Diabetes	
• Pre-pregnancy Diabetes	36 (16.6%)
• Gestational Diabetes	181 (83.4%)
Treatment	
• Oral Hypoglycemic	74 (34.1%)
• Insulin	143 (65.9%)

HbA1c levels ranged from 5.5% to 7.7% with a mean of $6.5 \pm 0.66\%$. Taking a cut-off value of $\geq 6.0\%$, (n=146, 67.3%) patients had uncontrolled diabetes as shown in Table II. There was no statistically significant difference in the frequency of uncontrolled diabetes across various subgroups of patients based on patient's age (p-value=0.942), gestational age (p-value=0.900), parity (p value=0.870), type (p-value=0.931) and treatment (p-value=0.810) of diabetes as shown in Table III.

Table II. Frequency of controlled/uncontrolled diabetes n=217

Glycemic Control	Frequency (n)	Percentage (%)
Controlled	71	32.7%
Uncontrolled	146	67.3%
Total	217	100.0%

Table III. Stratification of uncontrolled diabetes across various subgroups n=217

Subgroups	n	Uncontrolled DM (n=146)	P-value
Age			
• 18-25 years	27	18 (66.7%)	0.942
• 26-35 years	190	128 (67.4%)	
Gestational Age			
• 37-39 weeks	93	63 (67.7%)	0.900
• 40-42 weeks	124	83 (66.9%)	
Parity			
• Primiparas	75	51 (68.0%)	0.870
• Multiparas	142	95 (66.9%)	
Type of Diabetes			
• Pre-pregnancy Diabetes	36	24 (66.7%)	0.931
• Gestational Diabetes	181	122 (67.4%)	
Treatment			
• Oral Hypoglycemic	74	49 (66.2%)	0.810
• Insulin	143	97 (67.8%)	

Chi-square test, observed difference was statistically insignificant

Patients (n=46, 21.2%) had polyhydramnios, (n=146, 67.3%) patients required cesarean delivery and (n=31, 14.3%) patients acquired post-partum hemorrhage as shown in Table IV. The frequency of polyhydramnios (27.4% vs. 8.5%; p value =0.001), cesarean delivery (84.9% vs. 31.0%; p-value < 0.001) and postpartum hemorrhage (21.2% vs. 0.0%; p-value < 0.001) was significantly higher in patients with uncontrolled diabetes as shown in Table V.

Table IV. Frequency of various maternal outcome measures n=217

Maternal Outcome Measures	Frequency (n)	Percentage (%)
Polyhydramnios	46	21.2
Cesarean Delivery	146	67.3
Postpartum Hemorrhage	31	14.3

Table V. Comparison of various maternal outcome measures between women with controlled and Uncontrolled diabetes mellitus n=217

Maternal Outcome Measures	n	Diabetes Control		P-value
		Controlled (n=71)	Uncontrolled (n=146)	
Polyhydramnios	46	6 (8.5%)	40 (27.4%)	0.001*
Cesarean Delivery	146	22 (31.0%)	124 (84.9%)	<0.001*
Postpartum Hemorrhage	31	0 (0.0%)	31 (21.2%)	<0.001*

Chi-square test,* observed difference was statistically significant

Similar difference was observed across various subgroups based on patient's age, gestational age, parity, type, and treatment of diabetes as shown in Tables VI, VIII, and VIII.

Table VI. Comparison of polyhydramnios between women with controlled and uncontrolled diabetes mellitus across various subgroups n=217

Subgroups	n	Polyhydramnios n (%)		P-value
Age		Controlled DM (n=71)	Uncontrolled DM (n=146)	
• 18-25 years	27	1/9 (11.1%)	5/18 (27.8%)	0.326
• 26-35 years	190	5/62 (8.1%)	35/128 (27.3%)	0.002*
Gestational Age				
• 37-39 weeks	93	2/30 (6.7%)	17/63 (27.0%)	0.023*
• 40-42 weeks	124	4/41 (9.8%)	23/83 (27.7%)	0.023*
Parity				
• Primiparas	75	2/24 (8.3%)	14/51 (27.5%)	0.059
• Multiparas	142	4/47 (8.5%)	26/95 (27.4%)	0.010*
Type of Diabetes				
• Pre-pregnancy Diabetes	36	1/12 (8.3%)	6/24 (25.0%)	0.234
• Gestational Diabetes	181	5/59 (8.5%)	34/122 (27.9%)	0.003*
Treatment				
• Oral Hypoglycemic	74	2/25 (8.0%)	12/49 (24.5%)	0.087
• Insulin	143	4/46 (8.7%)	28/97 (28.9%)	0.007*

Chi-square test,* observed difference was statistically significant

DISCUSSION

In recent years, there has been an increasing focus on diagnostic thresholds that predict the likelihood of adverse outcomes in pregnancy (3). One such marker is HbA1c (glycosylated hemoglobin) which is routinely used for monitoring glycemic control in diabetic patients. Although it is well established

that pregnant women with diabetes have poor feto-maternal outcome, recent research has shown that the risk is even higher in women with poor glycemic control (elevated HbA1c levels) (7). However, the available evidence was limited while there was no such local published material which necessitated the present study.

Table VII. Comparison of cesarean delivery between women with controlled and uncontrolled diabetes mellitus across various subgroups n=217

Subgroups	n	Cesarean Section n (%)		P-value
Age		Controlled DM (n=71)	Uncontrolled DM (n=146)	
• 18-25 years	27	3/9 (33.3%)	15/18 (83.3%)	0.009*
• 26-35 years	190	19/62 (30.6%)	109/128 (85.2%)	<0.001*
Gestational Age				
• 37-39 weeks	93	9/30 (30.0%)	52/63 (82.5%)	<0.001*
• 40-42 weeks	124	13/41 (31.7%)	72/83 (86.7%)	<0.001*
Parity				
• Primiparas	75	7/24 (29.2%)	43/51 (84.3%)	<0.001*
• Multiparas	142	15/47 (31.9%)	81/95 (85.3%)	<0.001*
Type of Diabetes				
• Pre-pregnancy Diabetes	36	4/12 (33.3%)	23/24 (95.8%)	<0.001*
• Gestational Diabetes	181		101/122 (82.8%)	<0.001*
Treatment				
• Oral Hypoglycemic	74		41/49 (83.7%)	<0.001*
• Insulin	143	15/46 (32.6%)	83/97 (85.6%)	<0.001*

Chi-square test,* observed difference was statistically significant

Table VIII. Comparison of postpartum hemorrhage between women with controlled and uncontrolled diabetes mellitus across various subgroups n=217

Subgroups	n	Postpartum Hemorrhage n (%)		P-value
Age		Controlled DM (n=71)	Uncontrolled DM (n=146)	
• 18-25 years	27	0/9 (0.0%)	4/18 (22.2%)	0.125
• 26-35 years	190	0/62 (0.0%)	27/128 (21.1%)	<0.001*
Gestational Age				
• 37-39 weeks	93	0/30 (0.0%)	13/63 (20.6%)	0.007*
• 40-42 weeks	124	0/41 (0.0%)	18/83 (21.7%)	0.001*
Parity				
• Primiparas	75	0/24 (0.0%)	11/51 (21.6%)	0.014*
• Multiparas	142			
Type of Diabetes		0/47 (0.0%)	20/95 (21.1%)	0.001*
• Pre-pregnancy Diabetes	36			
• Gestational Diabetes	181	0/12 (0.0%)	5/24 (20.8%)	0.088
Treatment		0/59 (0.0%)	26/122 (21.3%)	<0.001*
• Oral Hypoglycemic	74			
• Insulin	143	0/25 (0.0%)	12/49 (24.5%)	0.007*

Chi-square test,* observed difference was statistically significant

In the present study, the mean age of the patients was 30.1±3.9 years. A similar mean age of 30.2±7.9 years has been reported by Bano *et al.* (2015), among diabetic pregnant women presenting at Jinnah Postgraduate Medical Centre, Karachi (8). Zakir *et al.* (2017) reported similar mean age of 31.3±5.3 years among such women at Khyber Teaching Hospital, Peshawar (9) while Waheed *et al.* (2013) reported it to be

29.8±4.6 years at Pakistan Institute of Medical Sciences, Islamabad (10). Zaman *et al.* (2013) reported comparable mean age of 28.1±2.7 years among such women at Bahawal Victoria Hospital Bahawalpur (11).

Our observation is also in line with that of Jayathilaka *et al.* (2011) who reported similar mean age of 32.2±5.3 years among Srilankan diabetic pregnant women (12). Swaroop *et al.* (2015) reported comparable mean age of 29.9±3.2 years in India (13). Qadir *et al.* (2012) reported comparable mean age of 32.3±2.8 years in diabetic pregnant women presenting at Alhada Military Hospital, Taif, KSA (14) while Bashir *et al.* (2018) reported it to be 31.7±5.7 years in Qatar (15). A comparable mean age of 31.4±4.5 years has been reported by Feig *et al.* (2017) in Canadian diabetic pregnant women (16). Sweeting *et al.* (2016) reported similar mean age of 32.9±5.0 years in Australia (17) while Kuo *et al.* (2017) reported it to be 33.3±3.9 years in Taiwan (18).

We observed that majority (87.6%) of the patients were aged between 26-35 years followed by (n=27, 12.4%) patients aged between 18-25 years. Our observation is in line with that of Qadir *et al.* who reported similar frequency of 18-25 years (12.0%) and 26-35 years (88.0%) age groups in diabetic pregnant women in KSA (19). Mishra *et al.* (2018) also reported similar distribution of 18-25 years (16.0%) and 26-35 years (84.0%) age groups in Indian diabetic pregnant women (20).

In the present study, there were (n=75, 34.6%) primiparas and (n=142, 65.4%) multiparas. Bano *et al.* reported similar frequency of primiparas (38.0%) and multiparas (62.0%) in diabetic pregnant women in local population (8). A similar frequency of primiparas and multiparas has been observed in local diabetic pregnant women by Shirazi *et al.* (2010) who reported it to be 35.0% and 65.0% respectively at Pakistan Institute of Medical Sciences, Islamabad (21). Swaroop *et al.* in India (13) and Sweeting *et al.* (18) in Australia reported similar distribution of primiparas (34.0%) and multiparas (66.0%) in diabetic pregnant women.

We observed that (n=36, 16.6%) patients had pre-pregnancy diabetes while (n=181, 83.4%) patients had gestational diabetes. Similar results have been published by another local study where the author reported the frequency of pre-pregnancy and gestational diabetes to be 16.5% and 83.5% respectively at Agha Khan University Hospital, Karachi (22). Naz *et al.* (2010) also reported similar frequency of pre-pregnancy (20.0%) and gestational (80.0%) diabetes at University Medical and Dental College, Faisalabad (23). Wahabi *et al.* (2017) reported similar frequency of pre-pregnancy (15.1%) and gestational diabetes (84.9%) in Saudi pregnant women (24). Jayathilaka *et al.* observed similar frequency of pre-pregnancy and gestational diabetes in Srilankan pregnant women and reported it to be 18.0% and 82.0% respectively (12).

In the present study, 34.1% patients were taking oral hypoglycemic while 65.9% patients were on insulin. Qadir *et al.* reported similar frequency of oral hypoglycemic (36.0%) and insulin (64.0%) use by diabetic pregnant women in Saudi Arabia (14). A similar frequency of use of oral hypoglycemic (31.2%) and insulin (68.8%) by diabetic pregnant women has been reported Tabib *et al.* (2013) in Iran (25).

We observed that 67.3% patients had uncontrolled diabetes. The frequency of polyhydramnios (27.4% vs. 8.5%; p-value=0.001), cesarean delivery (84.9% vs. 31.0%; p-value<0.001) and postpartum hemorrhage (21.2% vs. 0.0%; pvalue<0.001) was significantly higher in patients with uncontrolled diabetes. Our observation is in line with the previously published study by Gupta *et al.* who reported the frequency of uncontrolled diabetes to be 83.0% in Indian pregnant women. He also reported similar significantly higher frequency of polyhydramnios (21.69% vs. 11.76%; p=0.03), caesarean delivery (89.16% vs. 29.41%; p=0.01) and postpartum hemorrhage (22.20% vs. 0%; p=0.02) among such women in line with the present study (7).

The present study is first of its kind in local population and adds to the limited international research evidence on the topic. In the present study, a substantial proportion of diabetic women in late 3rd trimester had poor glycemic control and had significantly higher frequency of polyhydramnios, cesarean delivery and postpartum hemorrhage than women with good glycemic control which advocates routine monitoring and strict glycemic control in diabetic pregnant women to improve the maternal outcome in future practice.

A very strong limitation to the present study was that we didn't consider the effect of glycemic control on fetal outcome, nor we considered the effect of good glycemic control in women with poor glycemic control previously in terms of feto-maternal outcome which would have further highlighted the importance of glycemic control and role of monitoring of HbA1c in pregnant women. Such a study is highly recommended in future research.

CONCLUSION

A substantial proportion of diabetic women in late 3rd trimester had poor glycemic control and had significantly higher frequency of polyhydramnios, cesarean delivery and postpartum hemorrhage than women with good glycemic control which advocates routine monitoring and strict glycemic control in diabetic pregnant women to improve the maternal outcome in future practice.

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