Rate of Preeclampsia Influenced by Severity of Gestational Diabetes

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ABSTRACT

Introduction

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. GDM has well known adverse effects on pregnancy and its outcome, especially on the fetus. GDM has been found to be more prevalent in urban areas than in rural areas. Diabetic pregnancies complicated by preeclampsia are of concern because of poor maternal and perinatal outcome. The purpose of the study was if the rate of preeclampsia is influenced by severity of gestational Diabetes**.**

Material and methods: 100 pregnant women who are diagnosed as having gestational diabetes, followed up till the delivery for the development of preeclampsia**.** All pregnant women with gestational diabetes who gave the informed consent and detailed history.

Results: Incidence of preeclampsia in pregnant women with Gestational Diabetes is 30%**.** Rate of preeclampsia was increased with increasing the fasting blood sugar levels of OGTT. GDM Patients who developed preeclampsia had significant higher HbA1C levels (7.47) compared to GDM patients who did not (6.42). Mean birth weight of GDM with PE group is lower (2.94 +/- 0.65) than that of GDM without PE group (3.26 +/- 0.67). Significant difference in NICU admissions among two groups. Among GDM patients who developed preeclampsia, most of the cases (53.3%) GDM was diagnosed in third trimister.

Conclusion: Early detection of Gestational diabetes with good antenatal care and strict glycemic control may decrease the incidence of preeclampsia. Regular and more frequent Blood Pressure monitoring is required in Gestational Diabetes pregnant women, so there by we can decrease the maternal morbidity and mortality.

Keywords: Preeclampsia, Gestational Diabetes

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[1] Pregnancy induces progressive changes in maternal carbohydrate metabolism. As pregnancy advances insulin resistance and diabetogenic stress due to placental hormones necessitate compensatory increase in insulin secretion. When this compensation is inadequate gestational diabetes develops. GDM has well known adverse effects on pregnancy and its outcome, especially on the fetus. Hence the only way to diagnose this disorder remains the screening method. Clinical recognition of GDM is important because therapy including medical nutrition therapy, insulin when necessary and antepartum fetal surveillance can reduce the well described GDM associated perinatal morbidity and mortality. The prevalence of GDM in India varies from 3.8 to 21% in different parts of the country, depending on the geographical locations. GDM has been found to be more prevalent in urban areas than in rural areas.[2] For a given population and ethnicity, the prevalence of GDM corresponds to the prevalence of Impaired Glucose Tolerance (IGT) in non-pregnant adult within that given population. Although the prevalence of GDM is usually reported as 2 to 5% in pregnant women, it can be as high as 14% depending on the population described and the criteria used for diagnosis.

The prevalence of GDM is increasing globally but there is lack of uniformity in screening policy to be used i.e., universal or selective, as well as the diagnostic criteria to be used. Diabetic pregnancies complicated by preeclampsia are of concern because of poor maternal and perinatal outcome. Although hypertensive disorders are more frequent in women with pregestational diabetics. The question of whether they take place more frequently in gestational diabetes remains controversial. Several studies have reported increased risk for gestational hypertension and preeclampsia in pregnancies complicated by diabetes. Other studies however, have not.[3] Both these conditions affect mother and fetus, resulting in high maternal, fetal, and perinatal morbidity and mortality. A better understanding of the association between these two conditions may lead to more effective strategies for prenatal care so there by we can improve maternal and perinatal outcome. The purpose of the study was if the rate of preeclampsia is influenced by severity of gestational Diabetes, we can decrease the maternal and perinatal morbidity and mortality.

MATERIAL AND METHODS

Hundred pregnant women who are diagnosed as having gestational diabetes, followed up till the delivery for the development of preeclampsia during the period of November 2015 to October 2017 at modern government maternity hospital, petlaburz. These patients were randomly selected according to the following inclusion and exclusion criteria.

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Inclusion Criteria

all pregnant women with gestational diabetes who gave the informed consent and detailed history.

Exclusion Criteria

1. Pregnant women with certain risk to develop preeclampsia, chronic HTN, overt DM, renal or collagen vascular disorders, thyroid disorders, heart disease and anaemia
2. 2. pregnant women with multiple gestation
3. 3.H/O preeclampsia in previous pregnancy

Procedure

According to International Association of Diabetes and Pregnancy study groups [IADPSG]-2011 and American Diabetes Association [ADA] Recommendations:75gr OGTT
It is single step procedure
The test is used for both diagnostic and screening purpose.
This test is performed at first antenataI visit.
Patient should be in fasting state [overnight fasting of between 8and 14 hours]. There must be an unrestricted diet during the previous 3 days [with at least 150gr carbohydrate per day] and unlimited physical activity.
Initially fasting blood sample is taken. Patient must be seated throughout the test and not smoke. Test is performed by preparing a glucose solution with 75gr glucose mixed with 200ml of water. patient is made to drink the solution over a period of 5 to 10 minutes. After 1 hour and 2 hours the blood sugar values are evaluated by drawing 2ml of blood in disposable syringe from anticubital vein. Blood samples are taken into the bottles containing anticoagulant sodium fluoride and potassium oxalate in 1:3 ratio. Blood sugar values are evaluated by using glucose oxidase - peroxidase (GOD-POD) method.

Gestational diabetes is diagnosed if any one of the three values is met or exceeded.

fasting blood glucose >= 92 mgldl
post 1hour >= 180 mgldl
post 2 hours >= 153 mgldl.

Once the patient is diagnosed as having GDM, informed consent is taken. patient details and history noted. general physical and local examination done. patient is put on treatment according to the blood sugar levels either medical Nutrional therapy (or) combined (Insulin along with MNT)
Routine investigations are done. Blood pressure recordings and weight gain during each visit noted. All the patients are followed till 6 weeks post natal or postoperative period.

STATISTICAL ANALYSIS

Statistical testing was conducted with the statistical packages for the social sciences system spss version.1.7. continuous variables are presented as mean standard deviation and categorical variables are presented as absolute numbers and percentages. The comparison of continuous variables in GDM alone and GDM with preeclampsia cases was performed by student -t test.

RESULTS

The Mean Gestational age of GDM detection in GDM alone group was 26.2 weeks compared to GDM with preeclampsia (27.45 weeks). No significant difference was found between these two groups (table-1).
The mean 1st hour OGTT value in GDM with PE group was 192.10 mg/dl when compared to GDM alone group(174.46 mg/dl). There was a significant difference found between these two groups.
The mean 2nd hour OGTT value was 172.10 mg/dl in GDM

	Sample	N	Mean	SD	Mean difference	P value
1ST Hour OGTT values (mg/dl)	GDM with PE	30	192.10	43.10	17.64	0.035
	GDM alone	70	174.46	35.83		
2ndhour OGTT values(mg/dl)	GDM with PE	30	172.10	31.75	19.04	0.307 Non significant
	GDM alone	70	153.06	100.83		
HbA1C levels	GDM with PE	30	7.47	1.01	1.05	0.000 Significant
	GDM alone	70	6.42	0.64		
Weight gain	GDM with PE	30	16.58	3.86	3.86	0.000 (significance)
	GDM without PE	70	11.54	2.55		

Table-1: Comparison at the time of GDM detection among two groups

		Preeclampsia		p- value
		GDM with PET (n=30)	GDM without PET (n=70)	
Gestational Age(WK)		27.45± 5.93	26.20± 6.46	0.360
Birth Weight (Kg)		2.94± 0.67	3.26± 0.65	0.001
Delivery type	ELLSCS	7 (23.33%)	22 (31.4%)	NS
	EMLSCS	17 (56.66%)	36 (51.4%)	NS
	ND	6 (20%)	12 (17.1%)	NS
NICU admission	Yes	19 (63.33%)	20 (28.6%)	0.02
	No	11 (36.67%)	46 (65.7%)	0.03
	IUD	0 (0.0%)	4 (5.7%)	NS
NS: Non Significant				

Table-2: Pregnancy outcome measurements

	GDM with PE (n=30)	GDM without PE (n=70)	p-value
Maternal age (years)	24.45± 5.54	25.99± 4.46	0.143
Gestational age at OGTT (weeks)	27.45± 5.93	26.20± 6.46	0.360
Fasting OGTT (mg/dl)	112.39± 15.63	98.16± 18.72	0.000*
1st hour OGTT (mg/dl)	192.10± 43.10	174.46± 35.83	0.035*
2nd hour OGTT (mg/dl)	172.10± 31.75	153.06± 100.83	0.307
Hb A1c levels	7.47± 1.01	6.42 ± 0.64	0.000*
Obesity	25 (80.6%)	43 (61.4%)	NS
Weight gain during pregnancy (Kg)	16.58± 3.86	11.54± 2.55	0.000*
Booked Cases	11 (35.5%)	52 (74.3%)	NS
*Statistically significant (p<0.05)			

Table-3: Patient selected characteristic data

Birth Weight	Total no. of cases	GDM with PE (n=30)		GDM without PE (n=70)	
		Count	Column N%	Count	Column N%
<1.5 kg	2	1	3.2%	1	1.4%
1.6- 2.4 kg	15	3	12.9%	12	17.1%
2.5- 3 kg	35	13	41.9%	22	31.4%
>3 kg	48	13	41.9%	35	50.0%
Total	100	30	100.0%	70	100.0%
Mean+SD		2.94 +0.65 kgs		3.26 +0.67 Kgs	
P-Value		0.001 (significant)			

Table-4: Distribution of cases according to birth weight

Fasting Blood Sugar levels	Total no. of cases	GDM with PE (n=30)		GDM without PE (n=70)		Preeclampsia
		Count	Column N%	Count	Column N%	%
90-100mg/dl	53	5	16.1%	48	68.6%	9.4%
101-110mg/dl	28	10	35.5%	18	25.7%	64.2%
111-120mg/dl	9	7	22.6%	2	2.9%	77.7%
>120mg/dl	10	8	25.8%	2	2.9%	80%
Total	100	30	100.0%	70	100.0%	
Mean+SD		112.39+15.63		98.16+18.72		
P-value		0.000				

Table-5: Distribution of cases according to FBS levels of 75 hr OGTT

Gravida	Total no. of cases	GDM with PE (n=30)		GDM without PE (n=70)		% of preeclampsia
		Count	Column N%	Count	Column N%	
Primi	30	14	45.2%	16	22.9%	46.6%
Second gravid	33	8	25.8%	25	35.7%	24.24%
Thirdgravida	21	6	19.4%	15	21.4%	28.57%
Fourth gravida and above	16	2	9.7%	14	20.0%	12.5%
Total	100	30	100.0%	70	100.0%	

Table-6: Distribution of cases according to Gravida and Incidence of Preeclampsia

	GDM with PE (n=30)		GDM without PE (n=69)	
	Count	Column N%	Count	Column N%
Preterm delivery	20	66.66%	25	35.7%
Term delivery	10	33.33%	45	64.3%
Total	30	100.0%	70	100.0%

Table-7: Distribution of cases according to Pre-term and term delivery

with PE, when compared to GDM alone, it was 153.06 mg/dl. No significant difference was found between these two groups.

HbA1C levels are higher (7.47%) among GDM with

Age groups	Total no. of cases	GDM with PE (n=30)		GDM without PE (n=70)		Preeclampsia
		Count	Column N%	Count	Column N%	%
20-25	**49**	**18**	**58.1%**	**31**	**44.3%**	**36.7%**
26-30	41	9	32.3%	32	45.7%	21.9%
>30	10	3	9.7%	7	10.0%	30%
Total	100	30	100.0%	70	100.0%	
Mean +SD			24.45+5.549		25.99+4.464	
P-value			0.143			
Booked or unbooked cases						
Booked	11	36.67%	52	74.3%	17.4%	
Unbooked	19	63.33%	18	25.7%	51%	
Total	30	100.0%	70	100.0%		

Table-8: Distribution of cases according to occurrence of Preeclampsia

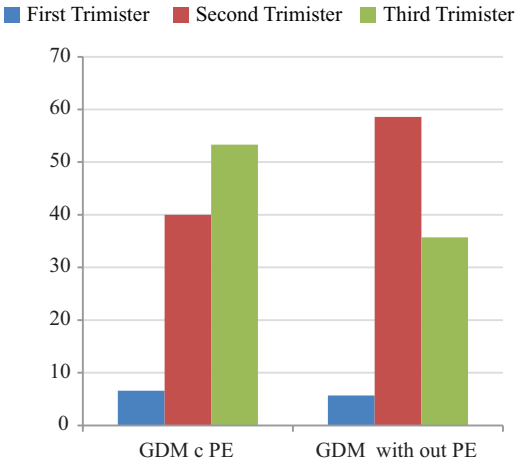

Figure-1: GDM detection according to trimester among two groups

PE compared to GDM without PE (6.42%). Significant difference was found between these two groups

The mean weight gain in GDM with PE group was 16.58 kg, whereas in GDM alone group it was 11.54kg. Significant difference was seen between these two groups (table-2).

Emergency section rate was more than the Elective section rate among both groups. But Emergency section rate was little higher in GDM with PE group (56.66%) compared to GDM alone group (51.4%), which was statistically nonsignificant with p value more than 0.05 (table-3).

NICU Admission rate was 63.33% among GDM with PE group, which was higher than the GDM alone group (28.6%), which was statistically significant with p value 0.02.

Maternal age is statistically similar among two groups with p value 0.143 (non significant).

The Mean Maternal age of GDM with PE group was 24.45 years, compared to GDM alone group, it was 25.99 years. obesity is statistically similar among two groups with p value greater than 0.05 (figure-1).

Among GDM with PE group, In most of the cases (53.3%) GDM was detected in third trimister.

Among GDM without PE group, In most of the cases (58.6%) GDM was detected in second trimester (table-4).

Most of the cases (41.9%) of GDM with PE had their babies birth weight between 2.5-3kg and more than 3 kg. Whereas most of the cases (50%) of GDM alone had their babies birth weight more than 3 kg.

Mean birth weight of GDM with PE group is lower (2.94kg) than that of GDM without PE group (3.26kg). Significant difference was found between these two groups with p value of 0.001.

Mean FBS levels were higher (112.39mg/dl) among GDM with PE compared to GDM without PE (98.36mg/dl). Significant difference was found between these two groups, with p value of 0.000 (table-5).

In GDM with PE group most of the cases were primi's (45.2%), compared to GDM alone most of the cases were second gravida's (35.7%). Most of the patients in the study group were primi (30%) and second gravida (33%) (table-6).

Preterm Deliveries were higher (66.66%) among GDM with PE group, compared to GDM without PE group (35.7%) (table-7).

In GDM with PE group most of the cases (58.1%) were belonging to age group 20-25 years, whereas in GDM alone group most of the cases (45.7%) were belonging to group 26-30 years

In GDM with PE group Mean Age was 24.45 years, compared to GDM alone it was25.99 years.

Most of the cases in the study population were booked cases (63%) (table-8).

Among GDM with PE group most of the cases (90%) were developed preeclampsia in third trimister; 10% developed in second trimester.

DISCUSSION

Pregnancy is a diabetogenic state manifested by insulin resistance and hyperglycemia itis implicated to be associated with significant obstetric complications. The incidence of diabetes complicating pregnancy has increased by approximately 40% between 1989 and 2004 (Getahun and colleagues 2008). As incidence of diabetes is rising in epidemic proportion more women of childbearing age are at increased risk of diabetes during pregnancy.[4] Infact, a high prevalence of gestational diabetes around 18% has been reported in India.[5] GDM has been recognized as a clinical entity for 50years.[6] Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance with recognition in or onset during pregnancy irrespective of the treatment with

diet or insulin.[7]

Early studies have strongly indicated untreated carbohydrate intolerance during pregnancy to be associated with higher rates of maternal morbidity and mortality.[8] In the Indian context, screening is essential in all pregnant women as the Indian women have eleven fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women.[9] Hence, universal screening during pregnancy has become important in our country. The screening for glucose tolerance is usually performed around 24-28 weeks of gestation. But a statistically significant number of GDM mothers deliver big babies despite good glycemic control in the third trimester. This is due to influence of maternal hyperglycemia in the early weeks of gestation on the fetal growth. Studies have also shown an increase in betacell mass and insulin secretion in fetus of poorly controlled diabetic women by the 16 th week of gestation. These studies stress the need for screening for GDM during early weeks of gestation. We may not miss any GDM by screening around 24-28 weeks, but a substantial number of pregnant women who develop GDM in the earlier weeks of pregnancy are likely to have a delayed diagnosis and may not receive appropriate medical care. Evidence shows that early screening for glucose intolerance and care could avoid some diabetes related complications in women with gestational diabetes especially preeclampsia.

Mudd LM et al.[8], Schneider S et al, and Freerksen N et al.[10] concluded that GDM and Preeclampsia share many risk factors, including advanced maternal age, nulliparity, multifetal pregnancies, non-white race /ethnicity and prepregnancy obesity. GDM is often listed as a risk factor for the development of Preeclampsia.

Retrospective investigation of 6,47,392 pregnancies in the German Perinatal Quality Registry examined relation between GDM and Preeclampsia while controlling for common risk factors. The authors found that the odds of Preeclampsia were increased among women with GDM, even after controlling for age, nationality, smoking, parity, multifetal pregnancy, pre-pregnancy weight status and gestational weight gain.[11]

In the present study Incidence of preeclampsia is in pregnant women with GDM is 30%. Our findings are comparable with some of the studies like Bartha JL, Romero-Carmona R et al, 2002[14], Van Hoorn J, Dekker G,Jeffries B et al.[12] A study conducted by Jenson DM, Sorensen Bet al,[13] have examined the association between gestational diabetes and preeclampsia, although some have been limited by small sample size or limited descriptive information. We also found that association between gestational diabetes and preeclampsia differed among booked cases and unbooked cases. Percentage of preeclampsia cases among unbooked cases was higher (51%) compared to booked cases (17.4%) While inadequate prenatal care has been described as increasing the risk of preeclampsia by 30 to 35%, according to the studies conducted by Mostello D, Catlin TK, Roman L et al.[7] Studies conducted by Easterling TR, Car DB, Brateng D et al,[8] and Schumucker B et al,[14] have suggested that early detection and aggressive treatment might reduce the risk of preeclampsia.

In our study rate of preeclampsia was assessed in the different severity categories of GDM (by 10 mg/dl increments of fasting value in the OGTT), an ongoing increase in the rate of preeclampsia was identified. GDM patients who developed preeclampsia had significantly higher OGTT values in comparison to GDM patients who did not. According to the present study Mean FBS levels are higher (113.39 mg/dl) among GDM patients who developed preeclampsia, compared to GDM patients who did not (98.36 mg/dl). we found no difference in the age group between GDM patients who developed preeclampsia and patients those who did not. We found Mean Birth Weight of GDM patients who develop preeclampsia is lower (2.94+/-0.65), than that of patients who did not (3.26+/-0.67).

In our study GDM patients who developed preeclampsia had higher rates of Nulliparity and gained significantly more weight during pregnancy. These findings are consistent with other studies conducted by Oded Langer et al.[9] GDM patients who developed preeclampsia had significant weight gain (16.58kg), compared to those who did not (11.54kg). In the present study, among GDM with PE group, most of the cases (90%) were developed preeclampsia in the third trimister, whereas 10% of the patients developed in second trimster. In our study Preterm deliveries were higher (66.6%) in patients with GDM who developed preeclampsia, compared to those who did not (35.7%). It is possibly because of the only definitive treatment for the preeclampsia is delivery.

Among 30 cases of preeclampsia one case had eclampsia during intrapartum period. No significant difference was found in mode of delivery among two groups. Probably because of small sample size. The study conducted by Yogev et al, M.J. Xenakis et al, Oded anger et al[9], found higher rates of induction of labour and elective caeserian delivery were observed in GDM patients who developed preeclampsia.

Total IUD'S were 4 out of 100 cases.(4%). Among these two cases were term sudden IUD'S and other two cases were preterm IUD'S at 36 weeks. NO gross congenital abnormalities were found in these four cases. Uncontrolled sugar leveIs were there in sudden IUD cases, these patients were not on reguIar foIIowup NICU admissions were higher (63.33%) among GDM with PE group compared to GDM alone group (28.6%).But according to Yogev, Xenakis, Langer et al,[9] there was no significant difference was found in NICU admissions. Only one case (GDM alone) had a baby with congenital anomaly (1%). That was cleft lip and cleft palate. In the present study HbA1C was done, once the patient was diagnosed as having GDM. The purpose of doing this is to know whether the patient had well controlled sugars in the past 3 months. HbA1C levels were higher among GDM with PE (7.47%), compared to GDM alone group (6.42%). Means GDM with PE patients had uncontrolled sugars in the past 3 months, but these patients goes undetected by the 75 grams OGTT, thereby causing uncontrolled sugars, which is the factor responsible for the development of PreecIampsia.

CONCLUSION

Early detection of Gestational diabetes with good antenatal care and strict glycemic control may decrease the incidence of preeclampsia. We found most of the unbooked cases developed preeclampsia that indicate poor antenatal care, which may be the contributing factor for poor glycemic control and late detection of GDM, thereby increases the incidence of preeclampsia. By doing Universal screening for detection of GDM from the first antenatal visit onwards, we can detect the cases earlier there by achieve strict glycemic control. Whatever the underlying reason for the observed increases in prevalence of GDM, the health care system will require additional resources to provide care during pregnancy and reduce adverse perinatal outcome.

Eventhough Government of India formulating the guidelines for universal screening for GDM, due to economic and health system workload reasons, Universal Screening is not being implemented throughout the India, especially at the level of PHC'S and CHC'S results in about a third of GDM women going undetected thereby causing increased maternal and fetal morbidity and mortality**.** Strengthening the heath system: to meet the increasing demands of delivering diabetes and GDM related care, there is a critical need for incorporating the elements of prevention, surveillance, screening and management into all levels of health care (primary, secondary, tertiary).

Improvement of the public health care system will help provide more equitable delivery of services that is likely to have a large impact on reducing the disease burden and preventing much of the maternal and fetal complications especially preeclampsia. Establishing referral and follow-up systems: given that diabetes and GDM require long term continued care, follow up processes, across different levels of the health care system, are essential to increase operative efficacy, optimize costs, timely treatment and follow up interventions. Providing patient education for enabling self-care and management: public health system constraints, due to shortage of resources, and providers, can be addressed to great extent by empowering community health workers, midwives, women self –help groups and patients and communities with necessary information on GDM and diabetes prevention that they can utilize for self-monitoring and self-care. This can facilitate achievement of improved health outcomes, reduced unnecessary hospital visits, contributing to considerable cost savings for the health system. By doing early detection and giving proper management with strict glycemic control we can decrease the incidence of PreecIampsia. Regular and more frequent Blood Pressure monitoring is required in Gestational Diabetes pregnant women, so there by we can decrease the maternal morbidity and mortality.

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