



OUTCOME OF DIABETES MELLITUS IN PREGNANCY IN A TERTIARY REFERRAL CENTRE

Dr. Umadevi M

Junior Resident, Department of Obstetrics and Gynaecology, Mysore Medical College And Research Institute, Mysore

Sudha R*

Professor, Department of Obstetrics and Gynaecology, Mysore Medical College And Research Institute, Mysore *Corresponding Author

ABSTRACT **BACKGROUND AND OBJECTIVES:** Gestational Diabetes Mellitus is defined as Impaired Glucose Tolerance with onset or first recognition during pregnancy. Undiagnosed or inadequately treated GDM can lead to significant maternal and foetal complications. The increasing prevalence of type 2 diabetes in general, and in younger people in particular, has led to an increasing number of affected pregnancies. Thus, the number of pregnant women with diabetes that was undiagnosed before pregnancy is increasing. The objective of the study is to determine the effects of diabetes mellitus on mother and foetus.

METHODS: A prospective-cum-descriptive study was conducted among 100 cases of pregnant women with Diabetes Mellitus at Cheluvamba Hospital, MMC&RI, during a period of 18 months starting from November 2016 till April 2018 who fulfilled the inclusion criteria. Their socio-demographic characters, maternal and foetal outcomes were recorded and results were concluded using appropriate statistical analysis.

RESULTS: The mean age (\pm SD) of 60 cases of GDM was 27.30 ± 4.99 years and 40 cases of overt diabetes mellitus was 27.83 ± 5.03 years. 63 percent of the cases were diagnosed at first visit and 13 percent of cases were unmasked in the third trimester. Among the maternal effects, incidences of UTIs and gestational hypertensive disorders were 17% and 35% respectively. The predominant mode of delivery the study subjects underwent was LSCS (56%). Among the foetal outcomes, 24 babies had Macrosomia. The number of still-births were higher in cases with overt DM compared to gestational DM ($p=0.045$). Shoulder dystocias and polyhydramnios were also observed in few cases (5 and 7 cases respectively).

INTERPRETATION AND CONCLUSION: Our study has thus provided a useful insight into the maternal and foetal effects of diabetes mellitus during pregnancy. Appropriate diagnosis and management of GDM can improve maternal and perinatal outcome. DIPSI guidelines for screening the subjects are both economical and feasible for evaluation of diabetes mellitus in pregnancy.

KEYWORDS : Gestational Diabetes Mellitus; Pre-Gestational Diabetes; Overt Diabetes Mellitus.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance with recognition or onset during pregnancy, irrespective of the treatment with diet and insulin. The importance of GDM is that two generations are at risk of developing diabetes in the future. Women with the history of GDM are at increased risk of future diabetes, predominantly type 2 diabetes, as are their children. Besides, any abnormal glucose intolerance in pregnant women without GDM is associated with a graded increase in the maternal and foetal outcomes. Thus GDM offers an opportunity for development, testing and implementation of clinical strategies for diabetes prevention. Timely action taken now in screening all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition may prevent in all probability, the vicious cycle of transmitting glucose intolerance from one generation to another¹.

However for the detection and diagnosis of GDM, controversy concerning optimal strategy still continues. Compared to selective screening, universal screening for GDM detects more cases and improves maternal and offspring prognosis. In the Indian context, screening is essential in all pregnant women as the Indian women have an eleven fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women. The recent data shows 16.55% prevalence of GDM in our country. Hence universal screening has become important in our country. For this we need a simple procedure which is economical and feasible. Hence an experimental comparative study is being conducted to find out a one step procedure which can serve both as a screening and a diagnostic tool and is acceptable, feasible to perform in the Indian context².

GDM based on 75gm OGTT defined by WHO predicts adverse pregnancy outcome and warrants treatment. The Diabetes In Pregnancy Study group India (DIPSI) is reporting practice guidelines for GDM in the Indian environment. Due to high prevalence, screening is essential for all Indian pregnant women. The recent concept is to screen for glucose intolerance in the first trimester itself as the fetal beta cell recognizes and responds to maternal glycemic level as early as 16th week of gestation. The screening test is to be performed again around 24th – 28th week and finally around 32nd – 34th week³. It is recommended that universal screening in all pregnant women for diabetes be carried out, and many state governments have now made it

part of routine antenatal care³.

Diabetes mellitus in pregnancy is associated with adverse outcome not only for the mother, but also for the fetus, neonate, child and adult offspring. Maternal consequences include increased rate of operative and caesarean delivery, preeclampsia, and the future risk for type 2 DM. Fetal complications include macrosomia, shoulder dystocia and birth trauma. The neonate is at risk for respiratory distress syndrome, neonatal intensive care admission, hypoglycaemia, hyperbilirubinemia, polycythemia, and electrolyte imbalances, obesity and type 2 DM⁴.

HISTORICAL PERSPECTIVE

The case report of Fredrica Pepe, age 22, who was admitted to the Berlin Infirmary at 7 months into her fifth pregnancy on 13th November 1823, is probably the first description of GDM in literature. This case report was a part of thesis of Heinrich Gottlieb Bennewitz for the degree of Doctor of Medicine, which he publicly defended at the University of Berlin on 24 June, 1824.

The first series of pregnancy in Diabetes was reported by Duncan (1862).

Glycosuria associated with pregnancy and lactation was recognized by Blot (1856).

Different urinary sugars especially Lactose was isolated in pregnancy and puerperium by Hofmeister (1877).

Dubreuil and Anderodias (1920) identified that the islets of Langerhans in still born fetuses born to diabetic mothers, were hypertrophied.

Insulin was first isolated by Fredrick and Banting (1921) and soon after its advent it was administered by Graham in England and Revenoin USA. Skipper (1933) was the first to classify diabetes in pregnancy according to onset, degree of severity and diabetic content.

Priscilla White (1949) mentioned the high risk factor for developing GDM and also classified GDM.

India leads the world with largest number of diabetic subjects earning the dubious distinction of "the diabetes capital of the world." It was

estimated to have had 31.7 million people having diabetes in year 2000 which is projected to be 79.4 million by year 2030. Both the figures are highest in the world. According to the Diabetes Atlas 2009 published by the International Diabetes Federation, the number of people with diabetes in India in year 2010 was reported to be around 50.8 million which is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken. The so-called Asian Indian Phenotype refers to certain unique clinical and biochemical abnormalities in Indians which includes but is not limited to increased insulin resistance, greater abdominal adiposity i.e., higher waist circumference despite lower body mass index. This phenotype makes Indians more prone to diabetes. Although genes are there to be blamed, but the primary driver of the epidemic of diabetes is the rapid epidemiological transition associated with changes in dietary patterns and decreased physical activity as evident from the higher prevalence of diabetes in the urban population.

OBJECTIVES

- To study the effects of diabetes mellitus in pregnancy on mother
- To study the effects of diabetes mellitus in pregnancy on the foetus.

MATERIALS AND METHODS

SOURCE OF DATA:

100 cases of pregnant women with Diabetes Mellitus at Cheluvamba Hospital, Mysore Medical College And Research Institute during a period of 18 months.

INCLUSION CRITERIA:

- All consenting pregnant women who attend antenatal clinic at Cheluvamba hospital.
- Women with Gestational diabetes mellitus & Pregnant Women with Overt diabetes mellitus.
- Pregnant women of any parity.

Exclusion criteria:

- Known cases of hypertension
- Chronic diseases/cardiac/hepatic/respiratory diseases
- Taking drugs that alter glucose metabolism
- Sickle cell anemia.

METHOD OF COLLECTION OF DATA:

- All mothers who have come for antenatal clinic and meet the inclusion criteria will be recruited. The mothers will be interviewed using partially coded questionnaires with both open and close ended questions.
- A detailed clinical assessment of patient will be performed in the outpatient department including history (any family history of diabetes, history of previous pregnancies & socioeconomic status etc), general physical examination & obstetric examination. Routine investigations during antenatal visits will be done. Informed consent to participation is taken during this initial assessment.
- A standard form will be used to record the date of the tests performed, detailed clinical assessment of patient, including history and examination findings, investigations including the test results.
- The pregnant woman is asked to come to antenatal clinic irrespective of the fasting status. The pregnant woman is asked to ingest 75g anhydrous glucose in 150ml water over 5 minutes. Venous blood is drawn after 2 hour and sent immediately for plasma glucose estimation. The plasma glucose will be estimated in automated analyser in central lab of K.R hospital, Mysore. A specific reagent is used for glucose determination in the analyser. The test is done at 1st antenatal visit, 24 to 28 weeks and 32-36 weeks irrespective of the risk status.
- HBA1C levels will be measured to look for uncontrolled or poorly controlled glycemc status of the mother.
- The mothers will be followed up and encouraged to deliver at Cheluvamba Hospital. They will be asked to come back for postnatal clinic where they will be reviewed. The results will be recorded in the form of proforma.
- Social demographic characteristics, pregnancy complications like pre-eclampsia, urinary tract infection, rate of caesarean section and induction of labour, shoulder dystocia, polyhydramnios, intra

uterine foetal death, macrosomia, prematurity and congenital abnormality in the foetus will be recorded. The data collected will be coded and fed into a computer and analysed with the assistance of a statistician.

SAMPLE SIZE ESTIMATION

Assuming that, the overall primary outcomes considered under the study will occur in 50% of the cases of pregnant women with diabetes mellitus, with an absolute precision of 10% and 95% confidence interval, sample size was calculated to be 100.

The sample size was calculated using the formula,

$$N(\text{sample size}) = 4pq/d^2$$

Where p= prevalence

And q=1-p

d= absolute precision

RESULTS

This is a prospective-cum-descriptive study considering a sample size 100 pregnant women with diabetes mellitus, i.e. both gestational diabetes and pre-gestational diabetes mellitus (Overt diabetes mellitus). The study was conducted over a period of 18 months at Cheluvamba hospital, Mysore. The results are as follows

Table 1: Demographic characteristics- Age wise distribution

	GDM (n=60)	Overt DM(n=40)
Age in years(Mean ± SD)	27.30 ± 4.99	27.83 ± 5.03

Independent 't' test: p=0.608

The mean age (±SD) of 60 cases of GDM was 27.30 ± 4.99 years and 40 cases of overt diabetes mellitus was 27.83±5.03 years

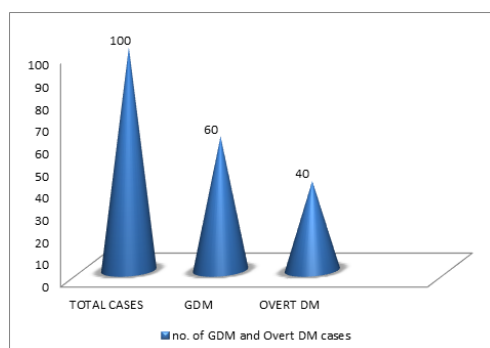
Table 2: Nutritional status of the cases- distribution of cases according to Body Mass Index (Asian criteria)

Nutritional status	Asian BMI criteria (kg/m ²)	Total cases (N=100)
Underweight	<18.5	1
Normal	18.5-22.9	54
Overweight	23-24.9	24
Pre-obese	25-29.9	17
Obese type 1 (obese)	30-40	3
Obese type 2 (morbid obese)	40.1-50	1
Obese type 3(super obese)	>50	0

Out of 100 cases in our study, 24% of the cases were Over-weight and 21% of the cases had BMI ≥25 kg/m² (pre-obese and Obese).

Out of 100 pregnant women with diabetes mellitus considered in our study, 60 cases were diagnosed with Gestational Diabetes Mellitus and 40 cases were diagnosed to have Overt Diabetes Mellitus (pre-gestational diabetes)

Figure 1: Distribution of cases with GDM and Overt DM



Maternal outcome

Table 3: Distribution of cases according to status of gravid

Gravida status	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Primigravida	36	23 (38.3)	13 (32.5)
Multigravida	64	37 (67.7)	27 (67.5)

χ²=0.354, df=1, p=0.552

Out of 100 cases, 36 cases were primigravida and 64 cases were multigravida, among 60 GDM cases 38.3% of the cases were primigravida and 67.7% of the cases were multigravida, where as, out of 40 overt DM cases, 32.5% of the cases were primigravida and 67.5% of the cases were multigravida.

Table 4: Distribution of cases according to previous history of abortions

History of abortion	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
No	66	41 (68.3)	25 (62.5)
Yes	34	19 (31.7)	15 (37.5)

$\chi^2=0.364$, df=1, p=0.546

Total number of cases with previous history of abortion were 34, out of which, 19 cases were in the GDM category and 15 cases were in Overt DM.

Table 5: Distribution of cases according to the gestational age at which they were diagnosed to have diabetes in pregnancy

Diagnosis by OGTT	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
1st Visit	63	40 (66.7)	23 (57.5)
24 – 28 week	24	12 (20.0)	12 (30.0)
32 – 36 week	13	08 (13.3)	05 (12.5)

$\chi^2=1.333$, df=2, p=0.514

Out of the 100 cases, maximum number of cases were diagnosed at the 1st visit (63). Out of these cases diagnosed at 1st visit, 66.7% of cases were GDM and 57.5% of the cases were overt DM.

Table 6: Distribution of cases with UTI (urinary tract infection)

UTI	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Present	17	10 (16.7)	07 (17.5)
Absent	83	50 (83.3)	33 (82.5)

$\chi^2=0.012$, df=1, p=0.913

Out of 100 cases, 17 cases had urinary tract infection, 10 (16.7%) of these 17 cases were having GDM and 07 (17.5%) were having overt DM.

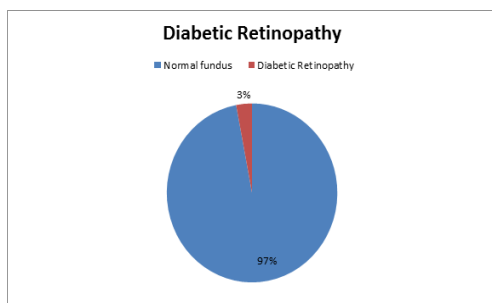
Table 7: Distribution of cases with pre-eclampsia and gestational hypertension

Status of hypertensive disorders	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Severe preeclampsia	09	01(1.7)	08(20.0)
Non severe preeclampsia	20	15(25.0)	05(12.5)
Gestational hypertension	06	05(8.3)	01(2.5)
Normal	65	39(65.0)	26(65.0)

$\chi^2=12.200$, df=3, p=0.007

The outcome of severe pre-eclampsia was found to be more in Overt DM group (20%) than GDM group (1.7%)

Figure 2: Distribution of cases with diabetic retinopathy



Three cases among 100 cases were diagnosed to have proliferative Diabetic retinopathy during fundoscopic examination. Two cases were found to be among overt diabetics and 1 was found to be in GDM category.

Table 8: Distribution of the cases according to mode of delivery

Mode of delivery	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Spontaneous Abortion	10	04 (6.7)	06 (15.0)
LSCS	56	37 (61.7)	19 (47.5)
Induced vaginal delivery	08	03 (5.0)	05 (12.5)
Spontaneous vaginal delivery	26	16 (26.6)	10 (25.0)

$\chi^2=4.240$, df=3, p=0.237

Out of 100 cases, 56 cases underwent LSCS. 23 Cases were operated as Emergency Caesarean and 33 cases were operated by Elective LSCS. The rate of LSCS and spontaneous delivery were more in GDM category and the rate of abortion was found to be more among Overt diabetics.

Table 9: Distribution of cases according to the treatment for diabetes

Mode of Treatment	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Insulin	56	24 (40.0)	32 (80.0)
MNT	37	35 (58.3)	02 (5.0)
No treatment	07	01 (1.7)	06 (15.0)

$\chi^2=31.403$, df=2, p<0.001

Among 100 cases included in the present study, 56 cases were on insulin therapy out of which 32 cases belonged to Overt DM, 37 cases were on Medical Nutrition Therapy (MNT) of which 35 cases were in GDM group.

Fetal Outcomes:

Table 10: Distribution of the cases according to the birth-weight of the newborn

Birth weight (in Kilograms)	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
<2.50	17	07 (11.7)	10 (25.0)
2.50 – 3.5	76	40 (66.7)	19 (47.5)
≥3.5	24	13 (21.7)	11 (27.5)

$\chi^2=4.344$, df=2, p=0.114

Considering ≥3.5 kgs as Macrosomia, the total number of cases with Macrosomia are 24 out of 100, 13 cases of which are under GDM category.

Table 11: Number of cases with preterm delivery

Pre-term delivery	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Yes	28	16 (26.7)	12 (30.0)
No	72	44 (73.3)	28 (70.0)

$\chi^2=0.132$, df=1, p=0.716

The total number of preterm deliveries were 28, 16 cases were from GDM and 12 were from Overt DM cases

Table 12: Number of cases with foetal congenital anomalies

Congenital anomaly	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Present	03	02 (3.3)	01 (2.5)
Absent	97	58 (96.7)	39 (97.5)

Fisher Exact $\chi^2=0.057$, df=1, p=0.999

Out of 100 cases, only 3 cases were diagnosed with congenital anomaly, which was found to be more in GDM category than Overt DM (3.3 vs 2.5%)

Table 13: Number of cases with Still-Births

Still-birth	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Yes	11	03 (5.0)	08 (20.0)
No	89	57 (95.0)	32 (80.0)

Fisher Exact $\chi^2=5.516$, $df=1$, $p=0.045$

The maximum number of still-births were found among Overt DM cases, i.e., 20% (8 out of 11) in comparison to GDM (5%).

Table 14: Number of cases with polyhydramnios

Polyhydramnios	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Present	07	04 (6.7)	03 (7.5)
Absent	93	56 (93.3)	37 (92.5)

Fisher Exact $\chi^2=0.026$, $df=1$, $p=0.999$

Out of 100 cases, 7 cases had polyhydramnios, 4 out of which were belonging to GDM category.

Table 15: Number of cases with shoulder dystocia

Shoulder Dystocia	Total (N = 100)	GDM (n = 60) n (%)	Overt DM (n = 40) n (%)
Present	05	03 (5.0)	02 (5.0)
Absent	95	57 (95.0)	38 (95.0)

Fisher Exact $\chi^2=0$, $df=1$, $p=1.000$

Out of 100 cases, 5 cases had shoulder dystocia, 3 out of which was in the GDM category.

DISCUSSION

The mean age of the study group in our present study was found to be 27.30 ± 4.99 among GDM group and 27.83 ± 5.03 among Overt Diabetes mellitus group. The mean age of both the study groups were almost found to be same. Comparing the mean ages in our study with the study of Priyanka et al, the mean ages were found to be almost same as that of our study (27.1 ± 2.44 years). The study by Priyanka et al considered even the non-GDM subjects⁷. In her study, GDM patients were found to be older, with the mean ages of the non-GDM and GDM groups being 24.7 ± 3.11 years and 27.1 ± 2.44 years, respectively. Similar study from South India showed age > 25 years as a risk factor for GDM⁸.

Obesity as a significant risk factor for GDM is supported by several studies finding that overweight or obesity at the start of pregnancy predisposes to GDM. In our study, 24% of the cases were Over-weight and 21% of the cases were pre-obese and Obese. Das et al. and Gomez et al. found that 25% and 50% of women with GDM, respectively, had obesity^{7,8}. In the study of Priyanka et al, a significant proportion of subjects with GDM were overweight [22 (66.67%)] and obese [6(18.18%)]⁵. In our study, the percentage of population belonging to Overweight category was 24% which is lesser than the study of Priyanka et al and 21% of the cases were having BMI of obese category which is more than the study of Priyanka et al.

Insulin being a potent growth factor promotes lipogenesis, protein synthesis, and therefore growth of the foetus. The percentage of macrosomia found according to the study of Hong et al was 6.5%. Our study revealed 24% of the cases with macrosomia which was more than the study of Hong et al⁹. 21.7% of these macrosomic babies in our study were distributed under the category of GDM and 27.5% were distributed under Overt diabetes mellitus group. The study of Priyanka et al revealed 18.1% of the group with Macrosomia which is lesser in comparison to our study. Another study by Wahi et al revealed 16.2% of Macrosomia in untreated GDM group and 10% in the treated GDM group which is lesser in comparison to our study¹⁰.

Our study revealed that the percentage of cases with gestational

hypertension was 6%. The study of Priyanka et al revealed that the most common complications seen in GDM mothers were gestational hypertension (36.4%) which is more in comparison to our study. Gajjar also found that most common maternal complication seen in GDM mothers was gestational hypertension (36.4%)¹¹.

In the study done by Gajjar et al, the Caesarean delivery rate was found to be 19.5% in the GDM patients¹¹. The study done by Priyanka et al revealed a Caesarean delivery rate of 78.8% amongst the GDM patients, with the most common indication being arrest of labour⁵. Our study revealed a Caesarean delivery rate of 56% in the Diabetes in Pregnancy Group with GDM group having 7.7% of the Caesarean delivery rates and Overt GDM having 47.5% of the Caesarean rates. This shows that in our study, the rate of caesarean delivery was found to be more among GDM cases than in Overt Diabetes mellitus cases. The most common indication for caesarean delivery in our study group was found to be previous LSCS in labour (15 cases) followed by Foetal distress (11 cases) and Failed induction (9 cases). Considering the Caesarean deliveries among GDM cases in our study (61.7%), the study done by Gajjar et al showed lesser rates (19.5%)¹¹. This is quite a high probability because in our setup, there is lack of adequate intrapartum fetal monitoring and surveillance techniques due to less infrastructure and greater patient load. Hence, lesser number of high risk patients are given trial of labor and hence more number of patients are delivered by Lower Segment Caesarean Section. But the study done by Priyanka et al showed higher rates (78.8%) in comparison to our study (61.7%) due to similar reasons⁵.

Our study showed that prevalence of stillbirth was 11%. The maximum number of still-births were found among Overt DM cases (20%) in comparison to GDM cases (5%). The study done by Priyanka et al showed a stillbirth rate of 9.09% in GDM deliveries⁵. In a study conducted by Odar et al in Uganda, a stillbirth rate of 16.7% was found¹².

The prevalence of preterm delivery according to our study was found to be 28%, 26.7% of which was under GDM category and 30% of the cases were under Overt diabetes mellitus category. In the study conducted by Wahi et al, the prevalence of preterm delivery was found to be 16.13% in the untreated GDM cases and 4.2% in the treated GDM cases. Hence, the prevalence was found to be more in our study in comparison to the study conducted by Wahi et al¹⁰.

Our study revealed rate of spontaneous abortion of 10%, 6.7% of which was under GDM category and 15% was under Overt Diabetes Mellitus category. The study of Galindo et al revealed a spontaneous abortion rate of 7.9% in GDM group¹³.

The study conducted by Galindo et al revealed 13.4% of congenital anomalies which is higher than our study (3%)¹³. Our study revealed 5% of shoulder dystocia in the GDM category. The study conducted by Wahi et al, revealed 6.45% of shoulder dystocia in the untreated GDM group and 1.2% in the treated GDM group¹⁰.

CONCLUSION

Diabetes mellitus is an important non-communicable disease and a public health concern which affects a broad spectrum of population within the country and worldwide. It is also known to affect maternal and fetal life adversely during pregnancy. Our prospective observational study thus aimed to assess cases diagnosed with overt as well as gestational diabetes and study the impact the disease has on them.

Emphasis was laid not only on the maternal and fetal effects but also on the time of diagnosis of the disease. The study results show that a significant number of cases were diagnosed in the 1st visit, and a chunk of cases were diagnosed following administration of oral glucose tolerance test in the subsequent visits. Thus it may be necessary to conduct this test, at least once, even in subsequent trimesters to identify the disease.

Our study aimed to study the maternal and fetal effects of overt as well as gestational diabetes in pregnant women. As for the maternal effects, our study shows that UTIs and hypertensive disorders in pregnancy are common complications in these cases. Majority of the cases were notably subjected to LSCS and Induction of labour. Among the fetal effects, the most common effect on babies that was demonstrated from

our study was an abnormal birth-weight (Macrosomia). Other significant but less commonly noted effects were still-births, preterm deliveries, shoulder dystocias, polyhydramnios. A small proportion of babies were also noted to have congenital anomalies.

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