CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/records/10566218

https://www.iajps.com/volumes/volume10-december-2023/85-issue-12-december-23/

Available online at: http://www.iajps.com *Research Article*

MATERNAL AND FETAL OUTCOMES AMONG WOMEN WHO MISSED GLUCOSE TOLERANCE TEST DURING THEIR PREGNANCY AS A RESULT OF THE COVID-19 CRISIS

[1]Dr.Nehad Hamad Hamed Almajnoni, [2]Dr.Issam Bin Ali

[1]A Senior Registrar Obstetric and Gynecology, At Royal Commission Medical Center Yanbu, KSA

[2]MD OB/GYNE Assistant Professor, Tunisia FSA Certified, France
Consultant and head of Obstetrics and Gynecology Department,
Royal Commission Medical Center, Yanbu

Abstract:

Background: The lockdown imposed during the early phase of the COVID-19 pandemic has impeded access to antenatal care including gestational diabetes mellitus (GDM) screening, notably between 23 March-28 May 2020, period of strict lockdown.

Objectives: To estimate the impact of missed GDM screening during COVID-19 lockdown on short-term maternal and fetal outcomes.

Methods: A retrospective cohort was conducted to identify all pregnant women whose regular screening period, i.e., gestational age 24-28 weeks, coincided with COVID-19 lockdown period (exposed group, N=142), and to compare their maternal and fetal outcomes with an equivalent-size sample of 142 consecutive pregnant woman who benefited from GDM screening during the two months preceding the lockdown (unexposed group).

Results: In unexposed group, GDM screening showed GDM prevalence of 43.0% (95%CI = 34.7–51.5%), and half (50.8%) were adequately treated. No significant differences in maternal or fetal outcomes were observed between exposed and unexposed groups. Postpartum screening, carried out among 60 (42.6%) of exposed women, showed 14 (23.3%) positive cases. Postpartum GDM cases together with prenatally diagnosed but inadequately treated ones were compared with adequately treated GDM cases, and showed significantly higher incidence of neonatal hypoglycemia (15.8% versus 0.0%, p=0.049) and neonatal intensive care admissions (36.8% versus 3.2%, p=0.003), with relatively higher, but not statistically significant, birthweight (3286.95 versus 3034.52, p=0.075) respectively.

Conclusion: The strict lockdown measures imposed in Saudi Arabia during the early phase of the COVID-19 pandemic was associated with inadequate screening and treatment of GBM, which resulted in increased maternal and fetal risks.

Keywords: Gestational diabetes; screening; COVID-19; lockdown; maternal outcome; fetal outcome

Corresponding author:

Dr.Nehad Hamad Hamed Almajnoni,

A Senior Registrar Obstetric and Gynecology,
At Royal Commission Medical Center
Yanbu , KSA

QR code

Please cite this article in press *Nehad Hamad Hamed Almajnoni* ***et al.,*** **Maternal And Fetal Outcomes Among Women Who Missed Glucose Tolerance Test During Their Pregnancy As A Result Of The Covid-19 Crisis.,** ***Indo Am. J. P. Sci, 2023; 10 (12).***

INTRODUCTION:

Gestational diabetes mellitus (GDM) is an insulin-sensitiveness disorder characterized by its occurrence during pregnancy and is associated with increased obstetrical morbidity including preterm delivery, labor induction, and cesarean sections. It also compromises the neonatal outcome as it increases the risk of neonatal hypoglycemia, macrosomia and neonatal intensive care unit admission.[1] Additionally, GDM increases by four-fold the risk of lifetime type II diabetes and reduces its age of onset by eight years approximately.[2]

The prevalence of GDM has raised significantly since the adoption of the new criteria by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), which recommends oral glucose tolerance test (OGTT) for all pregnant women, and considers a single abnormal result as GDM with no more need for confirmatory second result.[3] In fast-developing countries, notably the Gulf countries, GDM prevalence is reported to be as high as 12-16%, with even higher figures in pregnant women with family history of diabetes or increased parity.[4,5]

In Saudi Arabia, a recent study using the IADPSG criteria reported 51% of GDM in a total sample of 573 pregnant women, of whom 22.1% had abnormal glucose levels in early screening and 39.4% had abnormal OGTT, and among whom 8.9% developed overt diabetes.[6] These very high local figures, being up to three times higher than the international figures,[7] indicate the outstanding importance of rigorous implementation of the screening protocol among all Saudi pregnant women. This also emphasizes the risk of undiagnosed or lately diagnosed GDM cases and the relative loss of the opportunity for timely and adequate management.[8]
In light of these aspects, and given the ongoing Coronavirus Disease 2019 (COVID-19) pandemic, access to antenatal care for routine pregnancy follow up and GDM screening may have been compromised in several women. Such impact may be particularly significant among women whose regular screening interval, i.e., gestational age 24-28 weeks, coincided with the strict lockdown period that took place between 23 March-28 May 2020. These women were at high-risk of missing the GDM screening due to restricted care offer and prioritization of urgent care, besides reduced care seeking among individuals for non-urgent health problems.[9]

As such, we hypothesized that a number of pregnant women have missed GDM screening during their pregnancy, as an effect of the COVID-19 lockdown, which could have resulted into measurable adverse effects on the pregnancy, mother and fetal outcomes. The present study aimed at exploring one of the dimensions of the COVID-19 pandemic impact on maternal care, namely the screening for gestational diabetes mellitus (GDM). It probed into the following objectives:

- To identify all pregnant women who missed the first-trimester screening for GDM during the COVID-19 lockdown in a single center, and to estimate the percentage of those among them who benefited from post-partum screening.
- To estimate, among women who missed GDM screening, the incidence of GDM as diagnosed in post-partum follow up.
- To estimate the impact of missed GDM screening and appropriate management by comparing maternal and fetal outcomes among these women with unexposed women who were successfully screened before the COVID-19 lockdown.
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METHODS:

Design & Setting

A retrospective cohort study was conducted at the Gynecology & Obstetrics Department of Royal Commission Medical Center , Yanbu , Kingdom of Saudi Arabia.
The Royal Commission Medical Center is a 350-bed public secondary health care center. Its Gynecology & Obstetrics Department has a patient flow of 70 patients/day in outpatient consultations, of whom 85% are pregnant women.
The study was approved by the institutional review board of the Royal Commission Medical Center.

Population & Sampling

The study population comprised two groups of pregnant women, who were categorized according to their exposure to COVID-19 lockdown coinciding with their gestational age 24-28 weeks, representing the regular interval for first-trimester GDM screening.

Exposed group

The exposure group included all pregnant women following at the participating center and who missed the first-trimester GDM screening that was initially or would have been scheduled between 23 March and 28 May 2020, the period of COVID-19 lockdown in Saudi Arabia. A retrospective review of the pregnancy registry was carried out to identify all women who have reached 24-week GA after 22 March 2020 and exceeded 28-week GA before 28 May 2020. Consequently, women who reached 28-week GA

before 23 March 2020 or were below 24 week-GA on 28 May 2020 were excluded, and an eventual missing of GDM screening among these women was assumed to be due to other cause than the COVID-19 lockdown. Additionally, women who were missed for follow up, moved to another city or were transferred to another hospital for follow up were not included. A total 142 eligible women were identified and included in the exposed group.

Unexposed group

The unexposed group included a comparable sample of historical cases of women who benefitted from GDM screening before the COVID-19 lockdown, over a comparable period of two months. Women who were missed for follow up after the GDM screening, moved to another city or were transferred to another hospital before delivery were sorted out. Thus, a total 142 consecutive pregnant women who underwent first-trimester GDM screening between 20 January and 20 March 2020 were included in the unexposed group.

Data collection

A structured data collection sheet was designed on Microsoft Excel to collect the study data, which was divided into five categories: 1) baseline sociodemographic and clinical data such as age, nationality, educational level, residency area, comorbidities, family history of DM, body mass index, etc.; 2) obstetrical history such as gravida, parity, history of GDM or other gestational complication in previous pregnancies, etc.; 3) screening for GDM data among unexposed group, including GA at screening, OGTT results and findings (GDM vs normal), and treatment plan and adherence in case that GDM was diagnosed; 4) delivery and maternal outcome, and eventually post-partum screening for GDM and the respective results; and 5) fetal outcomes including Apgar score, gender, birthweight, macrosomia, hyperglycemia, NICU admission and any other neonatal complications.

All parts of the questionnaire applied for either group, except part three which applied only for unexposed group, and post-partum screening for GDM that applied only for exposed group.

Statistical methods

Statistical analysis was performed with the Statistical Package for Social Sciences version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables are presented as frequency and percentage, while continuous variables are presented as mean ± standard deviation (SD) and or median 75th centile (P75), as applicable. Comparisons between the exposed and unexposed groups used, as applicable, chi square or Fisher's exact test for categorical variables and independent t-test or Mann-Whitney U test for numerical variables. Where maternal and fetal outcomes showed statistical significance, analysis was completed by the calculation the risk ratio (RR) for developing the concerned outcome in the exposed group, by reference to the unexposed group. A *p* value of <0.05 was considered to reject the null hypothesis.

RESULTS:

Comparing baseline demographic and clinical parameters in the study groups

Out of the 142 initially included women in the exposed group, one was excluded because of substantial data missing. The mean age of women from the exposed group was three years greater than their counterparts, but this difference was not statistically significant (p=0.233). On the other hand, a statistically significant difference was observed regarding educational level and residency area, where exposed women had higher education (p=0.001) and were less likely originating from rural areas (p<0.001). Otherwise, no significant difference in baseline clinical parameters was noted between the two cohort groups (**Table 1**).

Comparing obstetrical history in the study groups

Women who missed GDM screening were comparable to controls in terms of gravida (p=0.520), parity (p=0.449) and complications in previous gestations, except for the frequency of cesarean which was higher among unexposed group (p=0.032). Additionally, exposed group were likely to be more adherent to follow up in their previous pregnancies (p<0.001). Further, retrospective assessment of the GDM risk among exposed group showed that 17.7% were at high-risk (**Table 2**).

Screening for GDM in unexposed group

In unexposed group, GDM screening including OGTT was carried out at the between GA 27-28 in half patients, showing a GDM prevalence of 43.0% (95%CI = 34.7 – 51.5%). Majority of diagnosed cases were treated with diet and exercise (91.8%) and only 8.2% were prescribed insulin. Assessment of treatment adherence showed that only 50.8% of the diagnosed women had adequate adherence to treatment (**Table 3**).

Assessment of the impact of missed screening on maternal and fetal outcome

Comparison of delivery and maternal outcomes in the two groups showed less frequent cesarean section among exposed group (32.6% vs 47.9%, p=0.009) and comparable GA at delivery (mean=38.33 vs 38.13

weeks, p=0.183) and incidence of preeclampsia (4.3% vs 3.5%, p=0.770), by reference to unexposed group respectively. Further, post-partum OGTT was carried among 60 out of the 141 (42.6%) exposed women and was abnormal among 14 of them, indicating a prevalence of postnatally diagnosed GDM of 23.3% (95%CI = 13.4 – 36.0%).

Fetal outcomes showed no difference in Apgar score at 1 (p=0.184) or five minutes (p=0.057), birthweight (p=0.738), or microsomia (p=0.066). However, although not statistically significant, hypoglycemia was relatively more frequent in exposed (4.3%) versus unexposed (0.7%) group (p=0.066). No further differences in neonatal outcomes were observed (**Table 4**).

We compared the outcomes of women who were diagnosed GDM postnatally (N=14) with those who had normal post-partum OGTT (N=46) from the exposed group. Results showed significant increase in cesarean sections (50.0% versus 21.7%, p=0.040) and noticeable and near-significant increase in neonatal hypoglycemia (14.3% versus 0.0%, p=0.051), in addition to relative increase in NICU admissions (35.7% vs 13.0%, p=0.107) among women with post-partum GDM versus without, respectively (**Table 5**).

Estimation of the impact of untreated GDM on maternal and fetal outcome

To estimate the impact of missed treatment, we analyzed the outcomes in undiagnosed or inadequately treated GDM cases (N=19), including postnatally diagnosed ones from the exposed group (N=14) and nonadherent ones from the unexposed group (N=5), by comparison to those who were timely diagnosed and adequately treated from the unexposed group (N=31). Results showed significantly higher incidence of neonatal hypoglycemia (15.8% versus 0.0%, p=0.049) and NICU admissions (36.8% versus 3.2%, p=0.003) in addition to relatively larger, but not statistically significant, birthweight (mean=3286.95 versus 3034.52, p=0.075) among inadequately treated versus adequately treated GDM respectively (**Table 6**).

DISCUSSION:

Summary of findings

The present retrospective cohort study probed into the impact of complete COVID-19 lockdown on the preventive and therapeutic management of GDM in a high-flow maternity in Western Saudi Arabia. The main hypothesis consisted of confirming or rejecting the cascade causation relationship between 1) undergoing complete lockdown and reduced access to care, 2) missing the regular screening for GDM, 3) being undiagnosed and untreated, and 4) experiencing maternal and fetal adverse impact. Findings showed an estimated GDM prevalence of 43% in antenatal screening, and 23.3% in postpartum screening and the latter was associated with a significant increase in cesareans and an increase trend of neonatal hypoglycemia incidence and NICU admissions. However, no differences in maternal and fetal outcomes were found between screened (unexposed) and non-screened (exposed) women. At the next level, the effect of treatment failure was demonstrated by a significant increase in neonatal hypoglycemia incidence and NICU admission among undiagnosed or inadequately treated GDM cases, besides an increase trend in birthweight. These effects are summarized in a flowchart, in **Figure 1**.

Impact of missing the first-trimester screening

The present study design failed to demonstrate a direct impact of missed GDM screening on maternal and fetal outcomes, as the comparisons between exposed and unexposed groups were inconclusive, although the two groups were well adjusted regarding baseline demographic, clinical and obstetrical parameters. However, findings showing that GDM was timely diagnosed among 43.0% of unexposed women, while only a minority (14, i.e., 9.9%) was postnatally diagnosed among exposed group, suggest that COVID-19 lockdown may have resulted in 34% of the concerned pregnant women being undiagnosed and consequently nontreated for GDM.

The absence of significant direct impact of missed screening on maternal and fetal outcomes does not downplay the effectiveness or cost-effectiveness of the universal screening for GDM. International evidence of effectiveness and cost-effectiveness of GDM screening is consistent. A study by Mission et al. demonstrated that the implementation of IADPSG-based GDM screening is effective, and its cost-effectiveness is upheld for every 2.0% patients diagnosed and treated for GDM.[10] Another binational study demonstrated a high cost-effectiveness of GDM screening accounting for up to $72 420 net savings per disability-adjusted life year DALY averted.[11] Conversely, findings were inconclusive from a systematic review including six studies that analyzed the cost-effectiveness of both the screening and treatment of GDM in high-income countries. Authors explained the lack of cost-effectiveness of the “screen-and-treat” strategy in high-income countries by the high detection rate of GDM in routine practice, reducing the proportion of screening-based detection.[12]

In the present study, several confounders and biases may explain the inconclusive findings regarding the impact of missed screening. Among these plausible explanations is the small sample size that may have weakened the statistical power of the comparative analyses. Another possible confounder is the level of treatment implementation in the unexposed group, which may have been significantly impacted as an effect of the restrictive measures coinciding with the treatment period, notably adherence with diet and exercise that represented more than 90% of therapeutic indications in patients who screened positive. This hypothesis is in line with international data showing significant deterioration in diet and exercise practice during the COVID-19 lockdown period, which resulted in important weight gain and metabolic disorders among both diabetic patients and the general population.[13] Pregnant women were probably among the most vulnerable categories to be affected with lockdown restrictive measures. Nevertheless, the COVID-19 crisis has enabled to gain valorous clinical experiences in the remote management of patients, including pregnant women.[14]

Impact of inadequate treatment of GDM

Although not initially in the scope of this study, subgroup analysis showed that inadequate treatment of GDM, irrespective of the timeliness of the diagnosis, was associated with significant increase in adverse outcomes, notably the fetal and neonatal risk. Findings showed frequent fetal hypoglycemia and NICU admissions among women who were missed for screening and those who were timely diagnosed but had inadequate adherence to treatment. Additionally, although not statistically significant, birthweight of babies born to inadequately treated GDM mothers were ~250g larger, on average, compared to their counterparts. Untreated GDM has several maternal and fetal adverse effects, both in the short and the long term, and these were thoroughly explored with strongly evidenced relationships. Maternal adverse outcomes such as pregnancy-induced hypertension and preeclampsia, in addition to delivery complications such as premature rupture of membranes, preterm labor and cesareans delivery were all reported to be increased in GDM patients.[15–17] In the present study, analysis of postnatally diagnosed GDM found significant increase in the percentage of cesareans and relatively shortening of GA at delivery, by reference to women who had normal postpartum OGTT. Regarding fetal outcome, macrosomia and metabolic complications including neonatal hypoglycemia are frequently reported in the short-term.[18,19] Beside these short-term complications, inadequately treated GDM entails several long-term complications, notably metabolic and cardiovascular risk in mothers and metabolic and neurodevelopmental complications in offspring; all add to the health and economic burden of GDM.[20] Furthermore, the benefit of treating GDM on short-term outcomes was also demonstrated, and substantial evidence supports that aggressive treatment can dramatically reduce the GDM adverse outcomes.[8] Depending on the indication, both non-pharmacological interventions, such as dietary modifications and physical exercise, and pharmacological treatment such as insulin and oral hypoglycemic agents were observed to improve the short-term outcomes such as fetal macrosomia and the neonatal metabolic complications, and hypertensive disorders in the mother.[18,21–23]

Altogether, these observations highlight the importance of both timely diagnosis and effective initiation and monitoring of the treatment to enable successful GDM screening strategy and maximize its effectiveness and cost-effectiveness. Local studies on the impact of COVID-19 lockdown on treatment adherence may be interesting to support the conclusions of this study and to explore the weak link of the screening-treatment-goal approach.

Limitations

The present study is limited by the retrospective design, small sample size and overlap of the GDM treatment period with the lockdown period, which relatively weakened the comparative analysis of the primary outcome.

CONCLUSION:

The strict lockdown measures imposed in Saudi Arabia during the early phase of the COVID-19 pandemic was associated with an estimated 43 cases of undiagnosed and untreated GDM out of each 100 women whose screening interval coincided with the lockdown period. Absence of screening with inadequate treatment are associated with increased maternal and fetal risks notably cesareans, high birthweight, fetal hypoglycemia and NICU admissions. On the other hand, the lockdown measures have probably impacted the effective implementation of the treatment by impeding access to care for monitoring and reducing adherence of the patients notably to dietary modifications and physical exercise with the closure of the gym clubs. Both timely diagnosis and effective initiation and monitoring of the treatment are important to enable successful GDM screening strategy and maximize its effectiveness and cost-effectiveness.

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Tables & Figures

Table 1: Baseline demographic and clinical data in exposed and unexposed groups

Parameter	Category	Exposed (N=141)		Unexposed (N=142)		p-value
Sociodemographic data						
Age	Mean, SD	36.63	5.56	33.46	5.92	.223
Nationality	Saudi	129	91.5	127	89.4	
	Non-Saudi	12	8.5	15	10.6	.686
Education	Up to middle school	10	7.1	3	2.1	
	Secondary	40	28.4	71	50.0	
	University +	90	63.8	68	47.9	.001*
Professional status	Housewife	73	51.8	87	61.3	
	Employed	51	36.2	45	31.7	
	Student	17	12.1	10	7.0	.182
Residency area	Urban	127	90.1	105	73.9	
	Rural	14	9.9	37	26.1	<.001*
Clinical data						
Comorbidities	Hypertension	1	0.7	2	1.4	1.000[F]
	Obesity	13	9.2	14	9.9	.855
	Polycystic ovarian S	4	2.8	5	3.5	1.000 [F]
Smoking	Yes	1	0.7	1	0.7	1.000 [F]
Family history of DM	First-degree relative	63	44.7	70	49.3	.437
	Other	34	24.1	42	29.6	.300
BMI	Mean, SD	28.67	6.23	28.54	5.36	.853
BMI category	Underweight	1	0.7	1	0.7	
	Normal	39	27.7	38	26.8	
	Overweight	52	36.9	56	39.4	
	Obesity I	27	19.1	26	18.3	
	Obesity II	15	10.6	18	12.7	
	Obesity III	7	5.0	3	2.1	.842

* Statistically significant result ($p<0.05$); [F] Fisher's exact test

Table 2: Obstetrical history in exposed and unexposed groups

Parameter	Category	Exposed (N=141)		Unexposed (N=142)		p-value
Gravida	Mean, SD	3.9	2.3	3.7	2.3	.520
	Median, P75	4	5	3	5	.430 [M]
	Range	1	10	1	9	
Parity	Mean, SD	2.1	1.8	2.1	1.8	.449
	Median, P75	2	3.5	2	3	.466[M]
	Range	0	8	0	7	
Previous pregnancy complications	GDM	17	12.1	27	19.0	.106
	Hyperglycemia	1	0.7	7	4.9	.066[F]
	PIHTN	19	13.5	18	12.7	.842
	Preterm delivery	6	4.3	7	4.9	.786
	Cesarean	35	24.8	53	36.6	.032*
	Abortion	57	40.4	52	36.6	.511
	Stillbirth	3	2.1	3	2.1	1.000[F]
	Macrosomia	0	0.0	2	1.4	.498 [F]
	Congenital anomaly	1	0.7	1	0.7	1.000 [F]
Previous pregnancy follow up	Adherent	30	21.3	82	57.7	
	Moderately adherent	64	45.4	47	33.1	
	Non-adherent	47	33.3	13	9.2	<.001*
GDM risk level [§]	Low	116	82.3			
	High	25	17.7	-	-	-

GDM: Gestational diabetes; PIHTN: pregnancy-induced hypertension

[§] The risk level was assessed retrospectively on the exposed group only

[M] Mann-Whitney U test; [F] Fisher's exact test; * statistically significant difference ($p<0.05$)

Table 3: Screening for gestational diabetes and management in unexposed group (N=142)

Parameter	Category	Statistics	
Gestational age at screening	24	27	19.0
	25	21	14.8
	26	24	16.9
	27	25	17.6
	28	45	31.7
Fasting blood glucose	Mean, SD	4.94	0.66
1H OGTT	Mean, SD	8.77	1.99
2H OGTT	Mean, SD	7.10	1.88
OGTT result	Normal	81	57.0
	Abnormal (GDM)	61	43.0
Treatment[§]	*Diet and exercise*	*56*	*91.8*
	Insulin	*5*	*8.2*
Adherence to treatment[§]	*Adherent*	*31*	*50.8*
	Moderately adherent	*25*	*41.0*
	Non-adherent	*5*	*8.2*

OGTT: Oral glucose tolerance test
Values are frequency, percentage; except if otherwise specified
[§] Percentages calculated out of abnormal OGTT result (N=61)

Table 4: Delivery and post-partum outcomes in exposed and unexposed groups

Parameter	Category	Exposed (N=141)		Unexposed (N=142)		p-value
Delivery and maternal outcome						
GA at delivery	Mean, SD	38.33	1.21	38.13	1.38	.183
	Median, P75	38	39	38	39	.266
Preterm	Yes	8	5.7	11	7.7	.486
Delivery mode	Vaginal	95	67.4	74	52.1	
	Cesarean	46	32.6	68	47.9	.009*
Preeclampsia	Yes	6	4.3	5	3.5	.770[F]
Post-partum OGTT	Not done	81	57.4	NA	NA	
	Done	60	42.6	NA	NA	-
Result [§]	*Abnormal (GDM)*	*14*	*23.3*	NA	NA	
	Normal	*46*	*76.7*	NA	NA	
Fetal outcome						
Apgar 1min	Median, P75	8	8	8	8	.184 [M]
Apgar 5min	Median, P75	9	9	9	9	.057 [M]
Gender	Male	56	39.7	77	54.2	
	Female	85	60.3	65	45.8	.014*
Birthweight	Mean, SD	3090.15	407.18	3073.08	449.22	.738
Macrosomia	Yes	2	1.4	3	2.1	1.000[F]
Hypoglycemia	Yes	6	4.3	1	0.7	.066
NICU admission	Yes	27	19.1	29	20.4	.788
Other neonatal complications	Need for phototherapy	3	2.1	1	0.7	.371
	Respiratory distress	0	0.0	1	0.7	1.000[F]
	Birth trauma	0	0.0	0	0.0	-
	Shoulder dystocia	0	0.0	0	0.0	-

GA: Gestational age; OGTT: oral glucose tolerance test; GDM: gestational diabetes mellitus; SD: standard deviation; P75: 75th centile; * Statistically significant difference ($p<0.05$); [F] Fisher's exact test; [M] Mann-Whitney U test

[§] Percentages calculated out of the number of patients who underwent post-partum OGTT (N=60). Outcomes in the two subgroups were compared in **Table 5**.

Table 5: Outcomes in women with post-partum diagnosis of GDM versus those with no post-partum GDM (N=60)

Parameter	Category	Post-partum GDM				p-value
		No (N=46)		Yes (N=14)		
Risk category	Low	38	82.6	6	42.9	
	High	8	17.4	8	57.1	.003*
Delivery and maternal outcome						
GA at delivery	Mean, SD	38.61	0.95	37.93	1.21	.032*
Preterm	Yes	0	0.0	1	7.1	.233 [F]
Delivery mode	Vaginal	36	78.3	7	50.0	
	Cesarean	10	21.7	7	50.0	.040*
Preeclampsia	Yes	0	0.0	1	0.7	.233 [F]
Fetal outcome						
Apgar 1min	Median, P75	8	8	8	8	.368 [M]
Apgar 5min	Median, P75	9	9	9	9	.070 [M]
Gender	Male	17	37.0	8	57.1	
	Female	29	63.0	6	42.9	.180
Birthweight	Mean, SD	3077.54	350.28	3133.00	377.25	.612
Macrosomia	Yes	0	0.0	0	0.0	-
Hypoglycemia	Yes	0	0.0	2	14.3	.051 [F]
NICU admission	Yes	6	13.0	5	35.7	.107 [F]
Other neonatal complications	Need for phototherapy	1	2.2	1	7.1	.415 [F]
	Respiratory distress	0	0.0	0	0.0	-

GA: Gestational age; SD: standard deviation; P75: 75th centile; * Statistically significant difference ($p<0.05$); [F] Fisher's exact test; [M] Mann-Whitney U test

Table 6: Outcomes in adequately treated versus undiagnosed or inadequately treated GDM (N=50)

Parameter	Category	Undiagnosed or inadequately treated GDM (N=19)		Timely diagnosed and adequately treated GDM (N=31)		p-value
Delivery and maternal outcome						
GA at delivery	Mean, SD	37.9	1.1	37.9	1.2	.904
Preterm	Yes	1	5.3	1	3.2	1.000[F]
Delivery mode	Vaginal	10	52.6	16	51.6	
	Cesarean	9	47.4	15	48.4	1.000 [F]
Preeclampsia	Yes	1	5.3	0	0.0	.380 [F]
Fetal outcome						
Apgar 1min	Median, P75	8	8	8	8	.387 [M]
Apgar 5min	Median, P75	9	9	9	9	.865 [M]
Gender	Male	11	57.9	18	58.1	
	Female	8	42.1	13	41.9	1.000 [F]
Birthweight	Mean, SD	3286.95	522.17	3034.52	446.75	.075
Macrosomia	Yes	2	10.5	0	0.0	.140 [F]
Hypoglycemia	Yes	3	15.8	0	0.0	.049* [F]
NICU admission	Yes	7	36.8	1	3.2	.003* [F]
Other neonatal complications	Need for phototherapy	1	5.3	0	0.0	.380 [F]
	Respiratory distress	0	0.0	1	3.2	1.000 [F]

GA: Gestational age; SD: standard deviation; P75: 75th centile; * Statistically significant difference ($p<0.05$); [F] Fisher's exact test; [M] Mann-Whitney U test

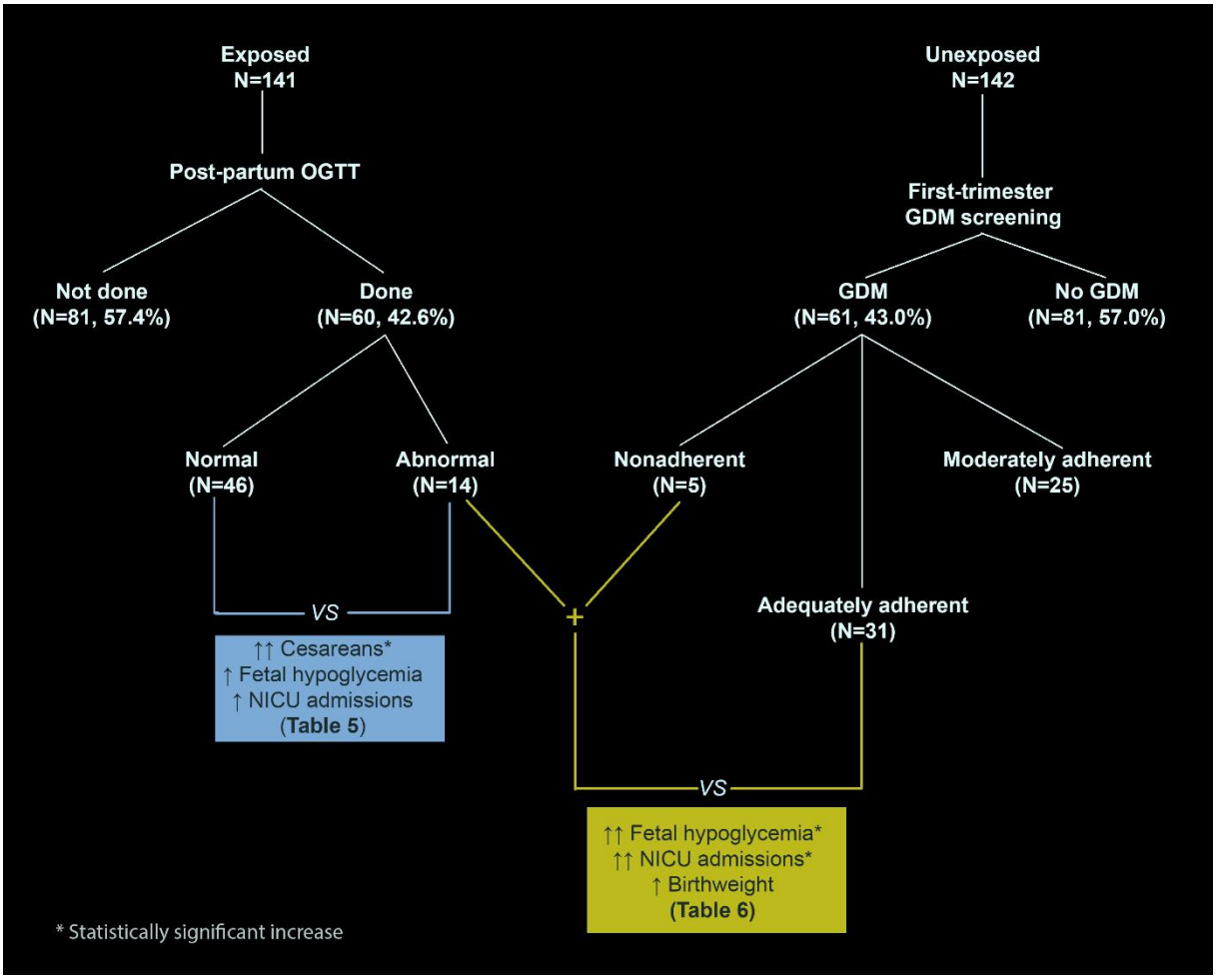

Figure 1: Flowchart of the main subgroup analysis and their respective findings