Determining the links between gestational diabetes mellitus (gdm) and obesity and unfavorable pregnancy outcomes

[1]Ali Siftain, [2]Dr. Saliha Ijaz, [3]Sahrish jabeen, [4]Muhammad Tahmas, [5]Dr Fadiha Attia, [6]Attiqa Khalid, [7]Khurram Shahzad

[1]Lecturer, Department of Public Health, Government College University Faisalabad, aligee005@gmail.com
[2]Al-Khidmat Raazi Hospital Rawalpindi, Saliha_ijaz_khan@yahoo.com
[3]Our Ladys Hospital Navan Republic of Ireland, sahrish.jabeen@yahoo.com
[4]Nishter Institute Of Dentistry, tahmaskhan2008@gmail.com
[5]FMO Haveli DHQ, fahdiaatta96@gmail.com
[6]Tehsil Khuiretta, District Kotli AJK, forpmc123@gmail.com
[7]HIESS, Hamdard University, Karachi, Pakistan, khurramsatti2000@gmail.com, https://orcid.org/0000-0002-5390-1078

ABSTRACT:
Aim: Determining links between gestational diabetes mellitus and obesity and unfavorable pregnancy results.
Methods: The participants in the study took a test called the oral glucose tolerance test among 28 and 36 weeks of pregnancy. The doctors diagnosed gestational diabetes mellitus (GDM) afterwards using specific criteria from the International Association of Diabetes and Pregnancy Study Sets. They measured certain characteristics of the newborns, such as their birth weight, body fat percentage, and the level of a substance called C-peptide in their umbilical cord blood. They also looked at other outcomes, like the likelihood of having a cesarean delivery, preeclampsia (a condition characterized by high blood pressure during pregnancy), in addition shoulder dystocia or birth injury. The participants' BMI remained considered during OGTT. The researchers used a statistical method called multiple logistic regression to see if there were any connections between GDM, obesity, and these outcomes.
Results: On average, the mothers in the study had a body mass index (BMI) of 25.8. About 12.9% of them were considered obese, with a BMI higher than 35.1 kg/m2, and 17.2% were diagnosed with gestational diabetes mellitus (GDM). Compared to women who did not have GDM or obesity, the likelihood of having a newborn through a birth weight above the 95th percentile was 4.18 times higher for those with GDM alone, 1.75 times higher for those with obesity alone, and 4.63 times higher for those with both GDM and obesity. The results were similar for other outcomes like the likelihood of having a primary cesarean delivery, preeclampsia (high blood pressure during pregnancy), and having high levels of cord C-peptide and newborn percent body fat above the 95th percentile. The chances of having a newborn with the birth weight above the 95th percentile increased with higher levels of glucose throughout oral glucose tolerance test (OGTT) and higher maternal BMI. Babies of obese women with GDM weighed, on average, 339 grams more than babies of normal or underweight women (who made up 61.3% of overall females) having normal glucose levels grounded on the OGTT test (which accounted for 62.9% of all women).
CONCLUSION: Both gestational diabetes mellitus and obesity in mothers are linked to negative effects during pregnancy. They can independently increase the chances of experiencing complications. However, when GDM and obesity occur together, their combined impact is even greater than when either condition is present on its own.
Keywords: Gestational Diabetes Mellitus (GDM), Obesity, Pregnancy.
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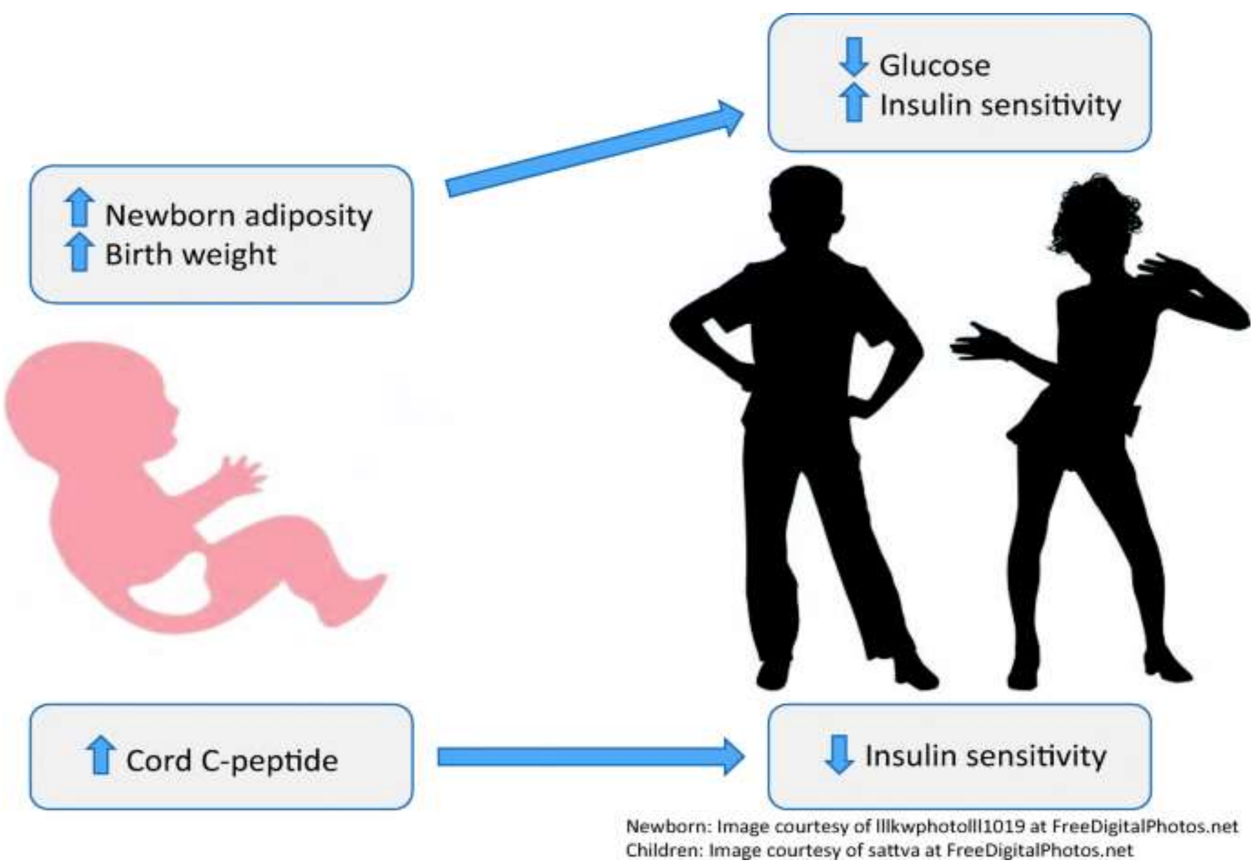
INTRODUCTION:

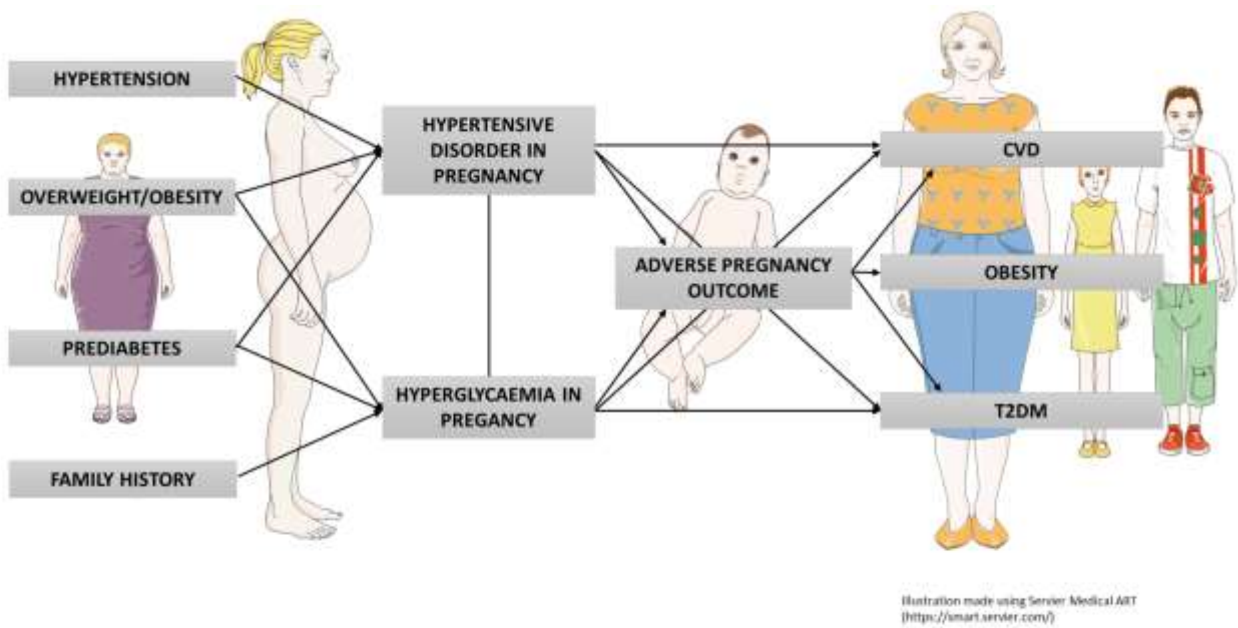
Gestational diabetes mellitus and maternal obesity have separate connections with negative effects on mothers and newborns. They both have similar metabolic features, including higher insulin resistance, high blood sugar levels (hyperglycemia), and increased insulin levels [1]. GDM can have specific effects on clinical outcomes that are not solely attributed to obesity. Maternal obesity, on the other hand, may have metabolic differences, especially among certain ethnic groups [2]. Therefore, it is essential to investigate how these shared metabolic issues, when combined, influence the outcomes of pregnancy. The HAPOS provides the special chance to investigate how gestational diabetes mellitus and obesity, both separately and together, are connected to negative pregnancy outcomes [3]. What makes this study unique is that it was purely observational, meaning that participants and healthcare providers were unaware of the mothers' glucose levels, and no specific recommendations were given regarding the therapy of glucose intolerance or obesity, including dietary guidelines [4]. The main findings of the HAPO Study revealed a consistent and encouraging connection among glucose levels restrained throughout a 2-hour 75-gram oral glucose tolerance test and several important results [5]. These outcomes include having a newborn with a birth weight above the 95th percentile, needing a primary cesarean section, experiencing neonatal hypoglycemia (low blood sugar in newborns), and having high levels of C-peptide in the umbilical cord blood above the 90th percentile [6].

Image 1:



Similarly, very higher maternal BMI was found to be linked to the higher occurrence of certain birth weight results, just like exceeding the 95th percentile, a higher percentage of body fat exceeding the 90th percentile, an increased likelihood of a primary cesarean section, and a higher concentration of cord peptide exceeding the 95th percentile [7-10]. Additionally, elevated maternal glucose levels and BMI remained related through secondary results, with preeclampsia. These issues during pregnancy have both short-term and longstanding metabolic implications for both mother and baby [11]. Therefore, main aim of our research remained to explore individual helps of gestational diabetes mellitus affording to novel standards established by the IADPSG, as well as obesity defined as a BMI of over 34.1 kg/m² between the 28th and 36th weeks of gestation, to contrary maternal and neonatal results [12]. Our hypothesis is that both maternal hyperglycemia and obesity, either autonomously or in mixture, are related through negative obstetric results, with the combined presence of both factors posing a higher danger than either GDM or obesity only [13].

Image 2:



METHODOLOGY:

The Institutional Review Board approved the protocol across all 18 field centers. Every participant gave written well-versed agreement. An outside information monitoring committee was responsible for overseeing the study. The methods used in the study have been previously published, in addition only the brief summary is given now. Overall pregnant females at every field center remained entitled to take part, if they met one or more exclusion criteria specified in previous publication.

Following removing outerwear and shoes, the maternal height and weight measurements were taken to calculate the Body Mass Index (BMI) during the Oral Glucose Tolerance Test (OGTT). Weight was split by height squared (kg/m2) to determine BMI. Height was measured once with a stadiometer or wall-mounted measuring tape with each participant's head pointing forward in the horizontal plane. If the two measurements differed by more than 2.1 cm, the measuring process were repeated. Weight was calculated on a calibrated scale regularly to the nearest 0.2 kg, and if the first two measurements differed considerably more than 0.6 kg, an extra computation was performed. The mean of the two nearest readings was utilized if another measurement was made. Maternal pre-pregnancy weight was collected, however it did not constitute the primary focus of research since their subjective character and the absence of information for 1,975 individuals (9.5%). None of the centers offered individuals tailored therapies depending on their weight or BMI.

In order to consider weight gain during pregnancy, the researchers obtained category limits for BMI and OGTT that could be compared to the BMI categories of nonpregnant individuals established by the World Health Organization (WHO). This was done through a regression analysis of the BMI at the OGTT, taking into account the pre-pregnancy BMI and the gestational age at the time of the OGTT. The results showed that at 32 weeks of pregnancy, a BMI of 33.1 kg/m2 or higher defined obesity, a BMI between 29.6 and 34.8 defined overweight, and a BMI below 29.6 defined normal weight or underweight. As previously mentioned, these cut-off points obtained from the regression analysis correspond to WHO categories of nonpregnant individuals, where class 1 obesity is defined as the BMI of 33.1 kg/m2 or higher, overweight falls between 26.1 and 27.8, and normal or underweight is below 26.1.

Participants were subjected to the 2-hour 75-gram oral glucose tolerance test during period of 32 to 36 weeks of pregnancy (as close to 32 weeks as conceivable). Standardized questionnaires remained utilized to collect data on smoking and alcohol consumption, family history of diabetes and hypertension among first-degree relatives, as well as demographic information. Additionally, the model for random plasma glucose remained composed between 36 and 40 weeks of gestation as the protection precaution to recognize individuals through elevated blood sugar levels above the predetermined edge. Aliquots of fasting and 2-hour OGTT plasma glucose, as well as RPG models, remained examined at the laboratories located in the field centers. The values remained revealed if the fasting glucose level surpassed 5.8 mmol/L, if the 2-hour glucose level was above 14.3 mmol/L, if the RPG level was higher than 9.7 mmol/L, or if any plasma glucose value remained below 3.6 mmol/L. Or else, females, caregivers, and HAPO Study staff persisted unaware of the glucose values. To prevent any confusion caused by variations in analytical procedures among different centers, aliquots of all OGTT specimens remained evaluated at the central laboratory of HAPO. Those outcomes remained utilized for statistics study. Only females who remained unaware of their results and had not undergone any additional glucose testing external the HAPO protocol were involved in assessment.

Descriptive statistics involve calculating average and SD for incessant variables, and the count and percentage for categorical variables. In order to analyze the connections between gestational diabetes mellitus and obesity, both separately and in combination, participants from the HAPO study remained separated into four distinct groups: 1) not any GDM, not any obesity; 2) GDM, no obesity; 3) no GDM, obesity; and 4) GDM, obesity. Two logistic regression models remained then applied to every result, using the group having not any GDM in addition not any obesity as position. Model I comprised adjustments for the field center, or variables utilized to estimate 95th centiles for birth weight and percentage of body fat according to gestational age.

RESULTS:

Out of a group of 56,350 women who were eligible, 29,568 (54.7%) agreed to take part in the study between June 2021 and May 2022. 26,552 women completed a test called OGTT. Some women were excluded from the study for various reasons such as knowing their glucose levels, having tests or giving birth outside of study, or missing important data. The data of 24,319 women were analyzed. The average weight of women at the time of test was 28.9 kg/m2. Around 14.6% of the women were obese and 17.2% had gestational diabetes based on new criteria. Among those with gestational diabetes, 26% were obese. The study found that women with gestational diabetes or obesity had higher chances of giving birth to larger babies, having more body fat in newborns, needing a C-section, developing preeclampsia, and experiencing shoulder dystocia/birth injury when compared to a reference group. The risks were even higher when a woman had both gestational diabetes and obesity. Shoulder dystocia/birth injury remained rare general, but the risks were significantly higher when both gestational diabetes and obesity remained existing.

Supplementary Table A, which is grounded on BMI before pregnancy, shows a similar trend. It indicates that there is a higher likelihood of certain outcomes such as birth weight, newborn body fat percentage, cord C-peptide levels in the 95th percentile, primary cesarean delivery, and preeclampsia for women who have either gestational diabetes or obesity associated to a orientation set. This is true for both Models I and II, and odds ratios for those results are significantly higher compared to those for women with only GDM or obesity. Though, ORs for pre-pregnancy obesity remain lower than the ORs for obesity identified through an oral glucose tolerance test (OGTT), especially when it comes to birth weight, cord C-peptide levels, in addition newborn body fat percentage in 95th percentile. It is important to interpret these findings cautiously because the data on pre-pregnancy weight were obtained through participant recall, 9.5% of information remained missing, and the missing data were not consistently dispersed amongst different centers involved in study.

Table 1: ORs for birth weights above the 95th percentile and average variations in birth weight for plasma glucose and BMI groups:

BMI	**Glucose**		
	GDM	**Normal**	**Intermediate**
Obese	5.35	2.07	3.66
Normal, underweight	2.58	1.00	1.77
Overweight	3.09	1.75	4.52
The average distinction in birth weight			
Obese	264	339	174
Normal, underweight	90	164	0
Overweight	214	288	124

Table 2 displays the chances of having a baby through a birth weight in the 95th percentile for different combinations of a mother's BMI and glucose levels measured through an oral glucose tolerance test. When comparing women who have a normal or underweight BMI with normal glucose levels, we found that the likelihood of having a baby with a birth weight in the 95th percentile increases as both glucose levels and maternal BMI increase. The odds are 3.57 times higher for women with gestational diabetes mellitus associated to these with normal glucose levels, and 3.08 times higher for obese women compared to those with standard or underweight BMI. The change in birth weight in grams, shown in the lower part of Table 2, follows a similar pattern. The change in birth weight becomes larger as together OGTT glucose levels also maternal BMI increase, in comparison to the reference group. The largest difference, 339 grams, is associated with a combination of GDM and obesity. Supplementary Table B, which is grounded on pre-pregnancy weight, displays very comparable design. Though, the odds ratios (ORs) and changes for being overweight or obese based on pre-pregnancy BMI are lesser compared to these based on OGTT BMI.

Table 2: Characteristics:

	N	**Mean**	**SD**
BMI (kg/m2)*	24,321	27.7	5.1
Age (years)*	24,321	29.2	5.8
Height (cm)	24,321	7.1	161.1
Mean arterial pressure (mmHg)*	24,321	8.3	80.9
Plasma glucose			
2-h	24,321	23.5	111.0

Fasting	24,321	6.9	80.9
1-h	24,321	30.9	134.1
OGTT z score sum			
Prepregnant BMI	24,332	5.0	23.9
Gestational age (weeks)*	26,320	1.8	27.8

DISCUSSION:

Gestational diabetes (GDM) and being overweight during pregnancy on their own, as well as when they occur together, are linked to negative outcomes for pregnancy. It may be tempting to compare the effects of these factors in different groups, but we have concerns about doing this [14]. First, when looking at the data in Table 2, here is not any dependable pattern when comparing the risks of GDM without obesity to obesity deprived of GDM. Additionally, once we classified applicants based on their estimated weight before pregnancy, the risks varied more and the relations through obesity deprived of GDM were generally weaker [15]. What stands out the most is that mixture of GDM and obesity is sturdily linked to every negative result [16]. Furthermore, Table 1 obviously shows that being overweight and having moderate levels of maternal glucose are strongly associated through these results. Lastly, GDM and obesity seem to affect results over identical mechanisms [17]. The HAPO Research backs up Pedersen hypothesis, that states that greater levels of maternal glucose are linked to fetal development, similar to the significant connection between the cord C-peptide and fetal fat [18]. Obesity is also connected to fetal hyperinsulinemia, birth weight, and infant fat, as specified in Table 2 and other available research. Additional nutrients which include lipids and amino acids, that are regulated through insulin and insulin confrontation, are also shown to be elevated in both GDM and obesity [19]. The aforementioned factors may have a role in hyperinsulinemia, fetal development, and fat accumulation [20]. However, the specific processes of converting fatty acids into fat in the fetal adipose tissue are not well understood [21].

The association among maternal obesity and negative results during childbirth is significant and independent. Some of the underlying causes of these associations may share similarities with gestational diabetes mellitus (GDM) as mentioned earlier. However, there are other associations that involve different mechanisms. For instance, our study revealed very difficult danger of preeclampsia in obese women without GDM (odds ratio [OR] 4.92, Model II; Table 2) compared to non-obese women with GDM (OR 1.75, Model II) [22]. Obese females tend to have higher insulin confrontation associated to females of normal weight. Therefore, increased insulin resistance may play a role in growth of preeclampsia among obese females and those with GDM [23]. Though, when obesity and GDM coexist, the risk of preeclampsia is even higher (OR 5.95, Model II; Table 2), suggesting the involvement of additional potential mechanisms just like inflammation in expansion of preeclampsia in the high-danger set [24].

In short, both motherly gestational diabetes mellitus in addition obesity have separate associations through negative pregnancy results. However, when the two conditions are combined, their impact is greater than either one alone [25]. While managing GDM involves strict control of glucose levels and leads to a reduced occurrence of adverse outcomes, the ideal approach to managing maternal obesity itself is still uncertain. Until the findings of ongoing research studies become available, it is advisable for obese pregnant women to avoid excessive weight gain during pregnancy, engage in moderate exercise, and follow a sensible diet [26-29].

CONCLUSION:

The previous reports from the HAPO Study have found that higher levels of sugar in blood of pregnant females and being overweight can lead to problems during pregnancy. This new study looks at the effects of gestational diabetes and obesity separately, also together, on pregnancy results. When those aspects are combined, there is a higher risk of problems during pregnancy compared to having GDM or obesity alone.

In Asia, around 8% or 210,500 pregnant women currently have GDM. Using a specific set of criteria called the IADPSG criteria will result in more women being diagnosed with GDM. The increase in GDM cases in the United States and other established nations may be partly attributed to the rise in obesity among females who can have children. About 66% of women in Asia and other developed nations who can have children are overweight or obese. Obesity is also becoming more common in other parts of the world where the HAPO Study was conducted.

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