Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2024, 14, 1873-1895
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Analysing the Diagnostic Potency of Oral Glucose Tolerance Test at 20 Weeks of Gestation in High-Risk Pregnancies

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How to cite this paper: Madugalle, M.E.M.Y.D.B., Rathnayake, R.M.C., Rajayohan, T., Kotigala, D.S. and Ruwanpathirana, S.A. (2024) Analysing the Diagnostic Potency of Oral Glucose Tolerance Test at 20 Weeks of Gestation in High-Risk Pregnancies. *Open Journal of Obstetrics and Gynecology*, **14**, 1873-1895.
https://doi.org/10.4236/ojog.2024.1412156

Received: November 15, 2024
Accepted: December 23, 2024
Published: December 25, 2024

Abstract

Background: Gestational Diabetes Mellitus (GDM) poses significant risks to both mothers and fetuses, with an escalating global prevalence. This study addresses the critical need for timely GDM detection in high-risk pregnancies. By comparing the efficacy of the standard 28-week oral glucose tolerance test with an early 20-week screening, the research aims to enhance preventive interventions and minimise complications, contributing valuable insights for optimal GDM management in high-risk populations. **Methodology**: Conducted at Teaching Hospital Peradeniya, Sri Lanka, this prospective cohort study investigated early GDM diagnosis using a 20-week OGTT in high-risk pregnancies with negative booking screens. The research involved 385 singleton pregnancies, assessing risk factors like GDM history, family history of diabetes, macrosomia, BMI > 30 kg/m^2, polycystic ovary syndrome, and advanced maternal age. The study included evaluating GDM incidence at 20 and 28 weeks, analysing risk factor associations, and determining the efficacy of early OGTT compared to routine testing. The data analysis aimed to establish the significance of a 20-week OGTT, identify the main contributory risk factors, and propose an optimal timing for GDM screening in high-risk pregnancies. **Results**: In the study involving 385 high-risk pregnant women, the incidence of gestational diabetes mellitus (GDM) was 7.27% at 20 weeks, 10.91% at 28 weeks, and 81.82% without GDM. Significant associations were found between GDM at 20 weeks, a history of GDM (78.57%), and a family history of diabetes (28.57%) ($p = 0.011$, 0.010 respectively). Notably, the McNemar test revealed no significant association between GDM cases at 20 and 28 weeks. **Discussion and Conclusion**: This study emphasises early diagnosis of GDM

and evaluates outcomes of screening at 20 weeks in high-risk pregnancies. Effective GDM management mitigates short-term complications but raises concern about long-term impacts on offspring. Limited evidence prompts a call for further research to determine the optimal intervention window. Risk factors for early GDM include family history and prior GDM. Recommendations include refining screening protocols and conducting additional randomised trials. The study's strengths lie in its comprehensive analysis, but limitations include its single-cohort nature. Future research should focus on personalised screening approaches and improve gestational age assessments. Overall, this study contributes to the ongoing discourse on early GDM management, highlighting the need for tailored prenatal care.

Keywords

Gestational Diabetes Mellitus (GDM), High-Risk Pregnancies, Early Diagnosis of GDM, GDM at 20 Weeks, Oral Glucose Tolerance Test (OGTT)

1. Introduction

1.1. Background Information and Justification

1.1.1. Gestational Diabetes Mellitus

"Glucose intolerance of any degree with onset or first recognise during pregnancy, and irrespective of whether or not insulin is required or the condition persists after pregnancy" is defined as Gestational Diabetes Mellitus [1]. It is becoming more prevalent in recent years.

Approximately 700,000 mothers deliver in England each year, and up to 5% of these mothers have either pre-existing (chronic) diabetes or gestational diabetes mellitus. Out of these diabetes-complicating pregnancies, the estimated number of gestational diabetes mellitus is approximately 87.5%; 7.5% have type 1 diabetes, and the remaining 5% have type 2 diabetes [2]. Statistics from Europe in 2012 elicited that GDM prevalence is 2% - 6%.

When we look into health statistics, an exponential rise in the prevalence of diabetes is seen worldwide, and South Asia tops the ranking, where its incidence has risen by 111% in the past 10 - 15 years when compared with other parts of the world where the rise is less than 50% [3].

So, being Sri Lankans, our mothers have an inborn risk of developing GDM. Currently, GDM is known to affect 7% of all pregnancies and 14% of high-risk pregnancies [4]. The incidence of gestational diabetes in South India is approximately 16.55%, while our local incidence is about 10.3% [5] [6]. The early diagnosis of GDM is crucial as it gives rise to major maternal and fetal complications.

According to NICE guidelines, GDM is diagnosed using a standard three-point oral glucose tolerance test performed at 24 to 28 weeks of gestation, which belongs to the high-risk category. They also recommend an OGTT at 16 weeks gestation for mothers with a history of GDM, which needs to be repeated at routine 24 - 28

weeks if the initial test is normal. However, NICE screening is known to miss 25% of GDM cases, which might be accountable for omitting maternal age and PCOS from their high-risk factors. Based on the HAPO study, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed a higher fasting and lower 2-hour value without a 1-hour value in diagnosing GDM. When these two screening values are compared, 38% of pregnancies that have missed NICE values resulted in a sizeable gestational age. Being South Asians, Sri Lankan women are already at risk, and according to national guidelines, they are offered a screening test for diabetes at booking visits using an oral glucose challenge test (OGCT).

In the Sri Lankan ante-natal clinic setup, we encounter a significant number of high-risk pregnancies whose booking visit diabetic screening is negative, present with very high OGTT values at routine 28 weeks test. So, the fetus may be exposed to hyperglycemia before 24 - 28 weeks of testing. Healthcare professionals currently have no clear idea of the exact timing of OGTT to be performed, and none of the studies elicit strong evidence for the reason behind the current testing time frame (Liu, Xu *et al.* 2016) [7] [8]. According to the definition, gestational diabetes can occur at any time during pregnancy, although a majority of them are detected after 28 weeks. So ideally, screening should be conducted between 13 and 24 gestational ages. A study conducted in China elicited that pregnant women with gestational diabetes had similar fasting plasma glucose values between 16 - 20 and 20 - 24 gestational weeks [7]. Also, before 16 weeks of gestation, only one-third of mothers with GDM could be diagnosed by OGTT [8]. Two RCTs have been done in Australia and Canada, and evidence suggests that pregnancy outcomes improved with early diagnosis and treatment.

The Canadian study showed that active involvement and treatment had reduced mean birth weight, neonatal fat mass, LGA, birth weights > 4 kg, shoulder dystocia, cesarean section rate, pre-eclampsia, and gestational hypertension.

Therefore, the testing period for early OGTT would be 16 - 20 gestational weeks. So, we chose 20 weeks of gestation as the ideal period for early OGTT since it may provide 4 to 10 additional weeks for managing gestational diabetes, which may result in a significant positive outcome. So, by performing an early OGTT at 20 weeks of gestation, GDM could be detected, which might be late to be diagnosed by screening at 28 weeks.

Following the diagnosis, proper management with nutritional input, regular exercises, and insulin use, if appropriate, will be beneficial in terms of minimising short-term maternal and neonatal complications [9]. But still, the offspring of GDM mothers are at risk of long-term complications such as diabetes, obesity, and metabolic disorders. One hypothesis might be undue exposure of the fetus to maternal hyperglycemia before diagnosis. However, evidence is yet to be found in terms of the benefits of diagnosing and treating gestational diabetes before 28 weeks gestation [7].

So, it is worth determining whether it is possible to detect GDM around 20 weeks to prevent or minimise the complications mentioned above, which will be

potentially advantageous. So, the results of this study would provide scientific evidence about the most appropriate time for OGTT in high-risk pregnancies whose booking screening is negative.

1.1.2. Pathophysiology of Gestational Diabetes Mellitus

Pregnancy is an insulin-resistant state, where diabetogenic hormones that are secreted by the placenta, such as progesterone, cortisol, HPL, GH, and prolactin levels, are very high. It is said that insulin resistance is known to develop by the second trimester, persist throughout pregnancy, and resolve with the delivery of the placenta [10].

Maternal hyperglycemia affects the whole duration of pregnancy, from fertilisation until delivery. It is known to cause changes in gene expression through fetal programming, which ultimately increases the fetus's future risk of obesity, diabetes, and other health hazards. So, the principal aim of managing diabetes is to achieve euglycemia throughout pregnancy. By this, Congenital anomalies, miscarriages, LGA, stillbirths, birth trauma, and neonatal hypoglycemia can be reduced.

Maternal blood glucose crosses the placenta, while insulin doesn't. So, maternal hyperglycemia causes stimulation of fetal insulin production. Also, it stimulates placental hormone secretion like hPL, IGF, and TNF, which results in fetal macrosomia and organomegaly.

Congenital malformations secondary to maternal hyperglycemia are as follows.

Cardiac disorders such as TGA, VSD, and Dextrocardia.

CNS disorders like spina bifida, anencephaly, hydrocephaly, and holoprosencephaly.

Rare manifestations like caudal regression.

Women who are usually diagnosed with GDM have normal glucose tolerance following delivery. But during the next 20 years of life, the majority of them will develop chronic diabetes, making GDM one of the most predictive factors for the development of chronic diabetes later in life. So, this group of women should be screened for diabetes six weeks postpartum and annually afterwards using the FPG or HBA1C test.

1.1.3. Oral Glucose Tolerance Test (OGTT)

If we look into the history of OGTT, it was first recommended that GDM be diagnosed in pregnant mothers at 24 - 28 weeks by the French College of Gynecologists and Obstetricians in 1996 [11]. In the year 2000, the American Diabetes Association recommended OGTT at 24 - 28 weeks for screening of GDM [4] because a significant number of mothers demonstrated insulin resistance at this time; however, insulin resistance is known to begin during the second trimester [12]. However, the impact of hyperglycemia may start before 24 - 28 weeks.

Standard three-point oral glucose tolerance test (OGTT)

OGTT is the most widely accepted diagnostic test.

Women attending this test should have an unrestricted carbohydrate meal and fast for more than eight hours.

Blood is first taken to estimate fasting plasma glucose level.

Then 75 g of glucose is dissolved in 300 ml of water, and she is offered this solution to drink within ten minutes. The solution is made palatable by adding some lime.

Blood is then drawn to estimate plasma glucose levels in 60 and 120 minutes (Table 1).

Table 1. Recommended cut-off values in different guidelines.

Recommended cut-off values in different guidelines				
Guideline		Fasting	1 hour	2 hours
Sri Lankan national guideline	mg/dl	92	180	140
	mmol/l	5.1	10	7.8
NICE guideline	mg/dl	100	N/A	140
	mmol/l	5.6	N/A	7.8
IADPSG criteria	mg/dl	92	180	153
	mmol/l	5.1	10	8.5

N/A-Not available.

2. Objectives of the Study

2.1. General Objectives

To see whether there is a significant difference in detecting gestational diabetes mellitus at 20 weeks compared to routine 28 weeks gestation using a standard three-point oral glucose tolerance test in high-risk pregnancies whose booking visit screen is normal.

2.2. Specific Objectives

1) Assess the incidence of GDM at 20 weeks gestation.

2) Assess the incidence of GDM at 28 weeks gestation.

3) Assess the prevalence of selected risk factors for GDM at 20 weeks gestation.

4) Assess the association of the evaluated risk factors with GDM at 20 and 28 weeks gestation.

3. Literature Review

Even though worldwide practice and most of the guidelines suggest performing OGTT at 24 - 28 weeks of gestation, management usually starts in the third trimester, which might be late given preventing complications.

There is insufficient evidence for why this test was performed in this period. However, very few studies have been done in this regard to find out the possibility of early diagnosis of gestational diabetes mellitus at 20 weeks of gestation.

Bin Liu *et al.* performed a prospective, longitudinal cohort study in China in 2016 called early diagnosis of gestational diabetes mellitus [7]. They conducted

this study for low-risk pregnant mothers in the First Affiliated Hospital of Sun Yat-sen University, recruiting 570 pregnant women. Their inclusion criteria were Singleton expectant mothers between 18 and 40 who presented to their antenatal clinic before 18 weeks of gestational age. Their exclusion criteria were high-risk, as motioned below.

1) Past medical history of gestational diabetes or pre-existing diabetes mellitus.

2) Family history of DM (first-degree relative with diabetes) .

3) Previous history of macrosomia (baby with birth weight > 4000 g) or a history of stillbirth.

4) Body mass index (BMI) of >30 kg/m^2.

5) Medications: corticosteroids, antipsychotics.

6) Polycystic ovary syndrome (PCOS).

7) Mothers did not consent to undergo OGTT twice or were unwilling to follow up and deliver in their centre.

The study's primary objective was to compare the results of early OGTT and regular OGTT (at 24 - 28 gestational weeks) on diagnosis of gestational diabetes mellitus.

Also, the results of early and regular OGTTs were compared, and the sensitivity, specificity, positive predictive value, and negative predictive value of early OGTT on diagnosis of GDM were studied; also, the importance of early diagnosis of GDM was analysed.

Another study was performed in De Soysa Maternity Hospital Colombo, Sri Lanka, titled "Diabetes in pregnancy among Sri Lankan women: gestational or pre-gestational," in 2010 using a sample size of 140 mothers [13]. There, it was mentioned that the ideal timing of OGTT in South Asian women is unknown.

So, one of their objectives was to assess the optimal timing of OGTT in diagnosing GDM. First, PPBS was offered to all mothers who have not been diagnosed with diabetes, and if it is >120 mg/dl, OGTT was provided as early as possible.

They analysed that out of 140 mothers, 82% had GDM, 18% had pre-gestational diabetes, and out of GDM mothers, 64% had been diagnosed before 24 weeks, and 36% had been diagnosed between 24 - 28 weeks. So, one of their recommendations is the current pregnancy screening time for OGTT in Sri Lanka, which requires review.

4. Research Plan

4.1. Method

The early diagnosis of GDM in high-risk pregnancies whose booking screen is normal was a cohort follow-up study. It was carried out in the Teaching Hospital Peradeniya, Sri Lanka.

4.2. Study Population

4.2.1. Inclusion Criteria

Singleton pregnancies were asked to participate in this study who were registered in

our ante-natal clinic before 20 weeks gestation and were screened for diabetes at booking clinic visits, which were negative and had one or more following risk factors.

1) History of GDM.

2) Family history of diabetes mellitus. (first-degree relative).

3) Previous macrosomia (baby with a birth weight of >3500 g) (According to the local setup, macrosomia is >3.5 kg rather than 4.5 kg).

4) Body mass index (BMI) of >30 kg/m^2.

5) Polycystic ovary syndrome.

6) Advanced maternal age.

4.2.2. Exclusion Criteria

1) Multiple pregnancies.

2) Mothers with chronic diabetes.

The inclusion of participants with risk factors like a history of GDM, family history of diabetes, macrosomia, BMI >30 kg/m^2, PCOS, and advanced maternal age focuses on a population at elevated risk for GDM, making it relevant for studying the efficacy of early screening methods (OGTT at 20 weeks). Exclusion of multiple pregnancies simplifies the analysis by reducing variables introduced by multiple pregnancies, ensuring the focus remains on the study's primary objectives. Multiple Pregnancies have unique metabolic challenges and outcomes, which could confound the results of the study. Excluding pre-existing cases of diabetes ensures the study evaluates the onset and early diagnosis of GDM rather than pre-existing conditions.

4.3. Sample Size

The primary purpose of this study was to evaluate the value of an OGTT at 20 weeks of gestation as a potential earlier diagnostic tool for screening GDM in high-risk pregnant women. For this purpose, the sample size estimation method for the follow-up study was applied.

Relative precision 0.1

Confidence level 95%

Required sample size 385

(ref: sample size determination in health studies - A practical manual, S. K. Lwanga S. Lemeshow World Health Organization Geneva 191). The primary purpose of this study was to evaluate the value of an OGTT at 20 weeks of gestation as a potential earlier diagnostic tool for screening GDM in high-risk pregnant women. For this purpose, the sample size estimation method for the follow-up study was applied [14].

4.4. Participant Selection and Recruitment

First, mothers who fulfilled the mentioned inclusions were selected by research personnel, and the study's objectives, procedure and benefits were explained. Secondly, interested participants were evaluated for exclusion criteria. Finally, informed written consent was obtained from selected participants before the

initiation of the study.

Once the selection process was completed, each participant was provided with an identification number linked with other information specific to each participant, including name, age, parity, and clinic NO. Two contact numbers of the participants were recorded to minimise the loss of follow-up.

Following recruitment, basic history was recorded, and special attention was given to the risk factor profile mentioned in the inclusion criteria. The number of risk factors was noted under each individual's datasheet.

Gestational age was assessed according to ISUOG guidelines. A dating ultrasound scan was provided for every pregnant woman as early as 10 + 0 to 13 + 6 weeks gestation to establish accurate gestational age. The following assumptions were used in dating ultrasonography.

- Post-conception age + 14 days is considered as gestational age.
- The parameters of the fetus correspond to post-conception age.
- Measuring structures should be normal.
- Measurements are reliable.
- The ultrasound machine is calibrated correctly.

From 11 to 13 + 6 weeks of gestation, CRL and BPD are the most reliable parameters for dating of pregnancy. Measurements were made transabdominal and trans-vaginally. Unless above 84mm, CRL measurement was recommended to determine the gestational age, and HC can be used after this stage as it is more precise than BPD.

Early OGTT was performed at 20 weeks gestation, and reports were reviewed at 22 weeks after they underwent a mid-trimester growth/anomaly scan.

After an overnight fast, standard three-point OGTT was performed using 75 g glucose. Samples were analysed at the respective hospital laboratory where the study was conducted.

If the test value came as >92 mg/dl for FPG, >180 mg/dl for the first hour, and >153 mg/dl for the second hour, gestational diabetes was diagnosed, and our centre continued the specific management of the patients with proper nutritional referral and medical management accordingly.

First, each pregnant woman with gestational diabetes was monitored for glycaemic control using blood sugar series (BSS). As the second step, proper dietary advice was provided after referring them to our nutrition clinic, and advice on appropriate exercises, essential for lifestyle modification, was given.

Thirdly, according to BSS values, if plasma glucose values are continuously high or become uncontrollable following lifestyle modification and nutritional inputs, oral hypoglycemic agents or therapy with insulin were provided following endocrinology referral. Finally, the decision of mode of delivery and time was advised by a consultant obstetrician when the patient presented to 36 weeks clinic follow-up based on the glycemic control.

Mothers with negative results for early OGTT were followed up per routine setup. Regular OGTT was offered at 28 weeks of gestation, and information was collected as before.

4.5. Data Analysis

The data analysis for this study employed the Statistical Package for the Social Sciences (SPSS) software. Descriptive statistics were used to outline the incidence of GDM at 20 weeks, 28 weeks, and the absence of GDM within the study cohort. Descriptive statistics were also employed to elucidate sociodemographic characteristics and the prevalence of specific risk factors associated with GDM. The risk factors were a history of GDM, family history of diabetes, polycystic ovary syndrome, advanced maternal age, and BMI > 30 $kg \cdot m^{-2}$. The McNemar test was employed to investigate the association between GDM at 20 weeks, GDM at 28 weeks, and the absence of GDM. Chi-square tests were applied to delineate the association between each specific risk factor and the categories of GDM. For the comparison of age, Ultrasound Dating Scan (USS), and Period of Amenorrhea (POA) under each category of GDM, the One-Way Analysis of Variance (ANOVA) test was employed. This test explored mean differences among multiple groups, providing insights into how age, USS dating, and POA vary among women with GDM at 20 weeks, GDM at 28 weeks, and those without GDM.

4.6. Outcome Measures

Following the analysis of data, we were able to fulfil the main objective.

The effectiveness of performing an OGTT at 20 weeks for high-risk pregnancies compared to 28 weeks was determined.

Main contributory risk factors were identified, and the optimal timing of OGTT for high-risk pregnancies was revised.

4.7. Ethical Considerations

This study had little or no added risk to participants. All participants were provided with an informed written consent. Also, routine antenatal care was provided to every individual who participated in this study, and mothers diagnosed with GDM were followed up according to guidelines and unit protocols.

5. Results

5.1. Descriptive Statistics

Three hundred eighty-five participants fulfilled the inclusion criteria. In the study's comprehensive analysis of 385 women, the mean age was 29.63 years, with a standard deviation of 6.528. Among them, 28 women developed gestational diabetes at 20 weeks, characterised by a younger average age of 24.75 years. In contrast, the 42 women who developed gestational diabetes at 28 weeks had an average age of 31.83 years. Meanwhile, the 315 women without gestational diabetes had an average age of 29.83 years (**Figure 1**).

The assessment of parity revealed that among the 67 nulliparous women, 5 developed gestational diabetes at 20 weeks, 11 at 28 weeks, and 51 remained without gestational diabetes. Among the 318 multiparous women, 23 developed gestational diabetes at 20 weeks, 31 at 28 weeks, and 264 did not develop gestational diabetes.

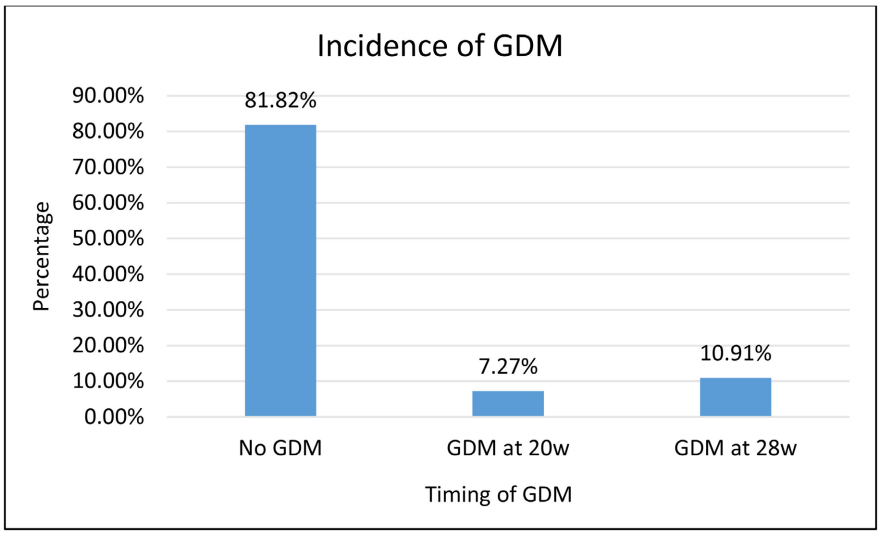


Figure 1. The graphical illustration of the incidence of GDM at 20 w, GDM at 28 w and no GDM.

Examining specific risk factors (labelled A to F), it was observed that 78.57% of women with gestational diabetes at 20 weeks had a history of gestational diabetes (A), while 50% of those developing it at 28 weeks had a similar history. Family history of diabetes mellitus (B) was present in 28.57% of women with gestational diabetes at 20 weeks and 50% at 28 weeks. Previous macrosomia (C) was observed in 28.57% of women with gestational diabetes at 20 weeks and 16.67% at 28 weeks. A body mass index (BMI) of >30 kg/m^2 (D) was found in 28.57% of women with gestational diabetes at 20 weeks and 33.33% at 28 weeks. Polycystic ovary syndrome (E) was present in 25% of women with gestational diabetes at 20 weeks and 16.67% at 28 weeks. Lastly, advanced maternal age (F) was observed in 25% of women with gestational diabetes at 20 weeks and 33.33% at 28 weeks.

Regarding the mean dating ultrasound scan (USS) and period of amenorrhea (POA), women with gestational diabetes at 20 weeks had a mean USS of 7.5 weeks and a mean POA of 7.25 weeks. For those with gestational diabetes at 28 weeks, the mean USS was 8.83 weeks, and the mean POA was 8.50 weeks. In contrast, women without gestational diabetes had a mean USS of 8.52 weeks and a mean POA of 8.44 weeks.

Examining the number of risk factors, 25% of women with gestational diabetes at 20 weeks had one risk factor, 50% had two, and 21.43% had three. Among those with gestational diabetes at 28 weeks, 16.67% had one risk factor, 66.67% had two, and 16.67% had three. In the group without gestational diabetes, 34.92% had one risk factor, 30.16% had two, and 29.84% had three. Additionally, 3.57% of women with gestational diabetes at 20 weeks had four risk factors, while 5.08% of those without gestational diabetes had four risk factors. Table 2 summarises the key study findings.

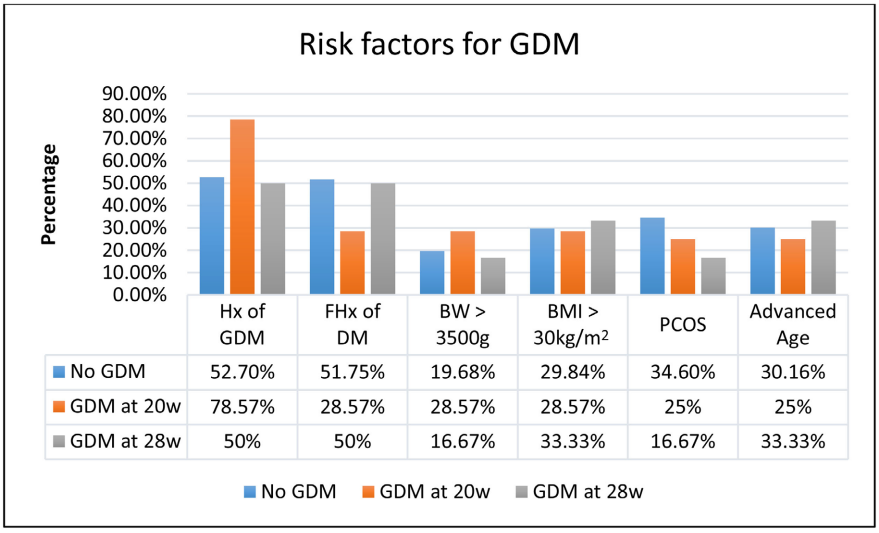
Figure 2 illustrates the percentage of risk factors: History of GDM and family history of diabetes mellitus. (first-degree relative), Previous macrosomia (baby

with birth weight of >3500 g), Body mass index (BMI) of >30 kg/m^2, Polycystic ovary syndrome and Advanced maternal age under each category of GDM. Women diagnosed with GDM at 20 weeks showed the highest prevalence of a history of GDM (78.57%) and significant proportions with a family history of diabetes (28.57%), macrosomia (28.57%), BMI > 30 kg/m^2 (28.57%), PCOS (25%), and advanced maternal age (25%). Women diagnosed at 28 weeks had a higher prevalence of advanced maternal age (33.33%) and family history of diabetes (50%), with lower representation across other factors. Risk factors were comparatively lower in women without GDM. Figure 3 illustrates the total number of risk factors as a percentage under each type of GDM. Women diagnosed with GDM at 20 weeks had 50% with two risk factors and 21.43% with three, highlighting the clustering of multiple risk factors in early diagnosis. At 28 weeks, 66.67% of women had two risk factors, with fewer cases of multiple risk factors compared to early GDM. Among women without GDM, 34.92% had only one risk factor, reflecting a lower risk profile.

Table 2. Key characteristics of the study participants and associated risk factors.

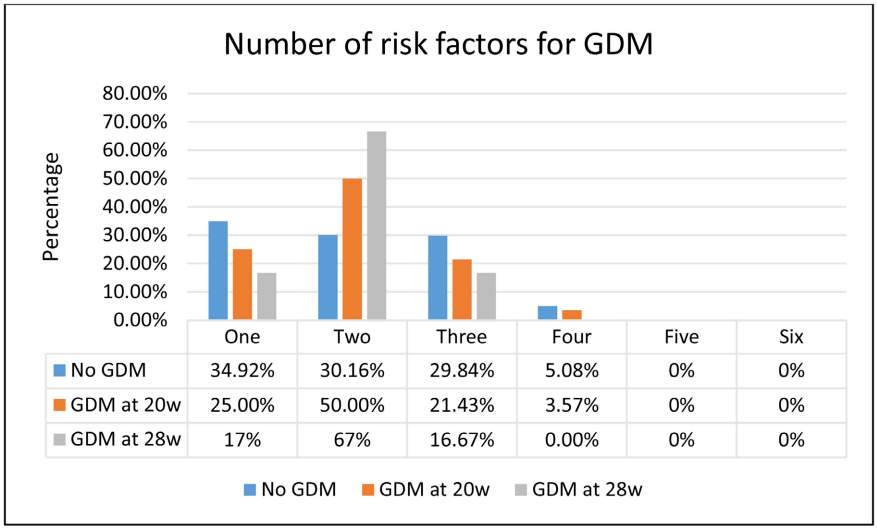
		Total women (n = 385)	Women with onset of GDM at 20 w (n = 28)	Women with onset of GDM at 28 w (n = 42)	Women without GDM (n = 315)
Age(years) Mean ± SD		29.63 ± 6.528	24.75	31.83	29.83
Parity, n (%)	Nulliparous	67	5	11	51
	Multiparous	318	23	31	264
Dating USS (weeks) Mean ± SD		8.45 ± 2.44	7.5	8.83	8.52
POA (weeks) Mean ± SD		8.34 ± 2.584	7.25	8.50	8.44
Risk factors, n (%)	A	209 (54.29%)	22 (78.57%)	21 (50%)	166 (52.70%)
	B	192 (49.87%)	8 (28.57%)	21 (50%)	163 (51.75%)
	C	77 (20%)	8 (28.57%)	7 (16.67%)	62 (19.68%)
	D	116 (30.13%)	8 (28.57%)	14 (33.33%)	94 (29.84%)
	E	123 (31.95%)	7 (25%)	7 (16.67%)	109 (34.60%)
	F	69 (17.92%)	7 (25%)	14 (33.33%)	48 (15.24%)
Number of risk factors, n (%)	1	124 (32.21%)	7 (25%)	7 (16.67%)	110 (34.92%)
	2	137 (35.58%)	14 (50%)	28 (66.67%)	95 (30.16%)
	3	107 (27.79%)	6 (21.43%)	7 (16.67%)	94 (29.84%)
	4	17 (4.42%)	1 (3.57%)	0 (0%)	16 (5.08%)
	5	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	6	0 (0%)	0 (0%)	0 (0%)	0 (0%)

A. History of GDM, B. Family history of diabetes mellitus. (first-degree relative), C. Previous macrosomia (baby with birth weight of >3500 g), D. Body mass index (BMI) of >30 kg/m^2, D. Polycystic ovary syndrome, E. Advanced maternal age.



	Hx of GDM	FHx of DM	BW > 3500g	BMI > 30kg/m²	PCOS	Advanced Age
No GDM	52.70%	51.75%	19.68%	29.84%	34.60%	30.16%
GDM at 20w	78.57%	28.57%	28.57%	28.57%	25%	25%
GDM at 28w	50%	50%	16.67%	33.33%	16.67%	33.33%

Figure 2. Risk factors are a percentage under each category of GDM.



	One	Two	Three	Four	Five	Six
No GDM	34.92%	30.16%	29.84%	5.08%	0%	0%
GDM at 20w	25.00%	50.00%	21.43%	3.57%	0%	0%
GDM at 28w	17%	67%	16.67%	0.00%	0%	0%

Figure 3. Total number of risk factors as a percentage under each category of GDM.

5.2. Association between Three Groups: GDM at 20 w, GDM at 28 w and No GDM

The test statistics report the results of the McNemar test with continuity correction, examining associations among three groups: GDM 28 & GDM 20, GDM 28 & NO GDM, and GDM 20 & NO GDM, based on a dataset comprising 385 participants. The McNemar test assesses changes or associations in paired nominal data. For the comparison between GDM cases at 28 weeks and those at 20 weeks, the Chi-square value was 2.028 with an asymptotic significance of 0.154, indicating no statistically significant association. In contrast, when comparing GDM cases at 28 weeks with those without GDM and GDM cases at 20 weeks with those without GDM, highly significant Chi-square values of 206.295 and 236.528 were observed, with asymptotic significances of 0.000. These results suggest a robust and statistically significant association between the presence or absence of gestational

diabetes at different gestational weeks, emphasising the importance of gestational age in the manifestation of gestational diabetes. Table 3 compares the statistical significance of the incidence of GDM at 20 w, GDM at 28 w, and no GDM.

Table 3. Statistical significance between incidence of GDM at 20 w, GDM at 28 w and no GDM.

	Test Statistics[a]		
	GDM 28 & GDM 20	GDM 28 & NO GDM	GDM 20 & NO GDM
N	385	385	385
Chi-Square[b]	2.028	206.295	236.528
Asymp. Sig.	0.154	0.000	0.000

a. McNemar Test; b. Continuity Corrected.

5.3. Statistical Association between Each Category of GDM and Risk Factors

In the comparative analysis of three groups of women—those who developed gestational diabetes at 20 weeks (n = 28), those with onset at 28 weeks (n = 42), and women without gestational diabetes (n = 315)—the investigation extended to various parameters, including parity and specific risk factors labelled A to F. The associated p-values were scrutinised for statistical significance.

For parity, the p-values for nulliparous women were 0.463 for those with gestational diabetes at 20 weeks, 0.538 at 28 weeks, and 0.459 for those without gestational diabetes, suggesting no statistically significant differences in this aspect.

The examination of various risk factors among women with gestational diabetes at different gestational ages (20 weeks and 28 weeks) and those without gestational diabetes revealed distinct p-values for each factor. Regarding Risk Factor A (History of GDM), the p-values were 0.011, 0.334, and 0.148 for women with gestational diabetes at 20 weeks, 28 weeks, and those without, respectively. For Risk Factor B (Family History of Diabetes), the corresponding p-values were 0.010, 0.558, and 0.060. Risk Factor C (Previous Macrosomia) displayed p-values of 0.202, 0.367, and 0.453 across the groups. Similarly, Risk Factor D (BMI > 30 kg/m^2) had p-values of 0.470, 0.375, and 0.483. For Risk Factor E (Polycystic Ovary Syndrome), the respective p-values were 0.236, 0.016, and 0.009. Lastly, Risk Factor F (Advanced Maternal Age) demonstrated p-values of 0.248, 0.008, and 0.005, indicating a statistically significant association between advanced maternal age and the onset of gestational diabetes at both 20 and 28 weeks. These findings provide insights into the differential impact of specific risk factors on the development of gestational diabetes at different stages of pregnancy.

Additionally, the examination of the number of risk factors revealed significant differences. The p-values were 0.861 for women with gestational diabetes at 20 weeks, 0.001 at 28 weeks, and 0.001 for those without gestational diabetes. Table 4 summarises the association of parity, individual risk factors and total number of risk factors with each category of GDM.

Table 4. Association of parity, individual risk factors and total number of risk factors with each category of GDM.

		Women with onset of GDM at 20 w (n = 28) P-value	Women with onset of GDM at 28 w (n = 42) P-value	Women without GDM (n = 315) P-value
Parity, n (%)	Nulliparous Multiparous	0.463	0.538	0.459
Risk factors, n (%)	A	0.011	0.334	0.148
	B	0.010	0.558	0.060
	C	0.202	0.367	0.453
	D	0.470	0.375	0.483
	E	0.236	0.016	0.009
	F	0.248	0.008	0.005
Number of risk factors, n (%)	1 2 3 4 5 6	0.861	0.001	0.001

A. History of GDM, B. Family history of diabetes mellitus. (first-degree relative), C. Previous macrosomia (baby with birth weight of >3500 g), D. Body mass index (BMI) of >30 kg/m^2, D. Polycystic ovary syndrome, E. Advanced maternal age.

5.4. One Way ANOVA Test for Comparison of Age, USS Dating and POA under Each Category of GDM

In the analysis of variance (ANOVA), the distribution of age, USS (Ultrasound dating), and POA among groups was examined. For age, the between-groups variation contributed significantly, with a sum of squares of 969.237, degrees of freedom (df) of 3, and a mean square of 323.079. The F-statistic was 7.995, indicating a statistically significant difference (p = 0.001). The within-groups sum of squares was 15396.389. USS and POA showed no significant differences among groups. USS had a between-groups sum of squares of 57.007, df of 3, and a mean square of 19.002, resulting in an F-statistic of 3.249 (p = 0.220). The within-groups sum of squares was 2228.447. Similarly, for POA, the between-groups sum of squares was 59.377, df of 3, and a mean square of 19.792, yielding an F-statistic of 3.011 (p = 0.300). The within-groups sum of squares for POA was 2504.400. These results provide insights into the variance in age, USS, and POA across different groups, with age demonstrating significant differences. **Table 5** compares the mean differences in age, USS dating, and POA among three groups of GDM at 20 w, GDM at 28 w, and no GDM.

Table 5. Comparison of the mean differences of age, USS dating and POA among three groups of GDM at 20 w, GDM at 28 w and no GDM.

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
Age	Between Groups	969.237	3	323.079	7.995	0.001
	Within Groups	15396.389	381	40.410		
	Total	16365.626	384			
USS	Between Groups	57.007	3	19.002	3.249	0.220
	Within Groups	2228.447	381	5.849		
	Total	2285.455	384			
POA	Between Groups	59.377	3	19.792	3.011	0.300
	Within Groups	2504.400	381	6.573		
	Total	2563.777	384			

6. Discussion

6.1. The Rationale for Early GDM Diagnosis

GDM poses a substantial health risk to both mothers and infants, necessitating effective screening strategies for early detection and management. This discussion critically analyses the study's findings, addressing the implications of performing an OGTT at 20 weeks in high-risk pregnancies with negative screening at booking visits.

Following the diagnosis of GDM, the subsequent management plays a pivotal role in mitigating short-term complications for both the mother and the neonate. Effective management strategies encompass glycemic monitoring, lifestyle modifications, nutritional counselling, exercise, and insulin administration if deemed appropriate. These interventions aim to control maternal glucose levels and reduce the risk of immediate complications associated with GDM, contributing to improved maternal and neonatal outcomes [15].

Despite the immediate benefits of proper management, a significant concern emerges in the long-term health of offspring born to mothers with a history of GDM. Studies have consistently indicated that these children face an elevated risk of developing diabetes, obesity, and metabolic disorders later in life [16]-[19]. The heightened susceptibility to such conditions in the offspring is attributed, in part, to their exposure to maternal hyperglycemia before the diagnosis of GDM.

Current guidelines advocate for early diagnosis and management of GDM, recognising the potential long-term consequences. The rationale is grounded in the belief that early intervention may not only enhance maternal, fetal, and neonatal outcomes in the short term [20]-[23] but also holds promise in averting or mitigating the risk of chronic health issues in the offspring.

However, a critical gap in the existing body of evidence is the limited data on the specific benefits of diagnosing and treating GDM before the conventional 24

- 28 gestational weeks. While the overarching recommendation emphasises early intervention, the precise timing for optimal outcomes remains uncertain. The lack of conclusive evidence highlights the need for further research to delineate the ideal window for intervention in order to maximise the benefits of GDM management.

Understanding the intricate interplay between early diagnosis, effective management, and long-term implications is crucial. It prompts a reevaluation of existing protocols to refine the timing and intensity of interventions for GDM, given the increasing prevalence of gestational diabetes and the growing recognition of its potential impact on the future health trajectory of both mothers and their offspring.

Lore Raets *et al.* [24], in their narrative review, observed that, in general, studies indicate that women diagnosed with early GDM face a heightened risk of adverse pregnancy outcomes. However, it is noteworthy that the administration of treatment for GDM in early pregnancy, as opposed to later stages, does not consistently result in improved outcomes. Among the reviewed studies, seven reported positive pregnancy outcomes associated with the early treatment of GDM [25]-[31]. Conversely, five studies found no discernible beneficial effects when diagnosing or treating GDM early, particularly in relation to maternal and neonatal outcomes [32]-[36]. Narrative reviews are inherently biased and can't proceed with a meta-analysis or quality assessment of individual studies. Therefore, generalizability review findings are limited and need to be re-explored through well-designed systematic reviews. However, rather than arriving at solid conclusions, the narrative study findings can be used to get some insights for planning future research.

RCTs are essential for evaluating the efficacy of treating early-onset gestational diabetes mellitus GDM in improving pregnancy outcomes compared to the standard treatment initiated at 24 - 28 weeks of pregnancy. **Table 6** provides a comprehensive overview of several well-recognised RCTs in this domain. The "Treatment of Booking Gestational Diabetes Mellitus" (ToBOGM) study, alongside the "Early Gestational Diabetes Screening in the Gravid Obese Woman" (EGGO) study and "Lifestyle in Pregnancy" (LiP) study, primarily concentrated on high-risk populations and obese women. In contrast, the "Effect of Early Screening and Intervention for Gestational Diabetes Mellitus on Pregnancy Outcomes" (TESGO) and "Prediabetes in Pregnancy, Can Early Intervention Improve Outcomes" (PINTO) studies encompassed a broader spectrum, including lower-risk women in their study cohorts.

The results from these RCTs indicate that the benefits of early diagnosis and treatment of GDM remain a topic of debate, warranting further exploration and investigation. The sample sizes of these RCTs showed a considerable heterogeneity ranging from 47 to 2068. EGGO 2020 lacked a blinding approach for both patients and investigators [40]. In PINTO 2018, non-adherence to the allocated treatment protocol was significant. Heterogeneity in sample sizes, high risk of bias, and non-adherence to treatment protocols should be taken into consideration when interpreting the study findings with caution.

Table 6. Randomised controlled trials evaluating the efficacy of treating early-onset gestational diabetes mellitus GDM vs. standard treatment initiated at 24 - 28 weeks of pregnancy.

Study	Subjects (N)	Study Population	Timeframe Testing (Weeks)	GDM Criteria	Comparison	Main Results
PINTO 2018 [37]	47	Women with singleton pregnancy and without ODIP	<14.0 weeks	HbA1c/between 5.9 and 6.4%/two h 75 h OGTT New Zealand criteria	Standard care vs. early intervention in pregnancies complicated by prediabetes	Recruitment rates were lower than expected. Non-adherence to the allocated treatment protocol was more significant in the early intervention group than in the controls.
TOBOGM 2023 [38]	802	High-risk women with singleton pregnancy	<20.0 weeks (4 - 19.6 weeks)	Two h 75 g OGTT/ IADPSG criteria	Women with booking GDM receiving immediate Treatment vs no treatment (Repeat OGTT at 24 w)	Immediate treatment of gestational diabetes before 20 weeks' gestation led to a modestly lower incidence of a composite of adverse neonatal outcomes than no immediate treatment; no material differences were observed for pregnancy-related hypertension or neonatal lean body mass.
TESGO 2023 [39]	2068	Singleton pregnancy without ODIP	18 - 20 weeks	75 g 2 h OGTT/ IADPSG criteria	Early screening group (18 - 20 weeks) vs. standard screening group (24 - 28 weeks)	Early screening and intervention of GDM by the one-step method does not improve pregnancy outcomes as compared to standard practice.
EGGO 2020 [40]	922	Obese women (BMI_30 kg/m^2) without ODIP and history of bariatric surgery	14 - 20 weeks	2-step method: 1 h 50 g GCT followed by a three h 100 g OGTT/C&C criteria	Early GDM screening (14 - 20 weeks) vs. routine screening (24 - 28 weeks)	Early GDM screening in obese women did not reduce the composite perinatal outcomes, such as macrosomia, C section and shoulder dystocia.
LIP 2018 [41]	90	Obese pregnant women with singleton pregnancy	12 - 15 weeks	2 h 75 g OGTT/ IADPSG Criteria	Lifestyle intervention vs standard care	Lifestyle intervention was not effective in improving obstetric or metabolic outcomes.

6.2. Prevalence of Early GDM

Among the 385 participants included in our study, 28 individuals (7.27%) developed gestational diabetes at 20 weeks, while 42 participants (10.91%) developed gestational diabetes at 28 weeks. The majority of the cohort, comprising 315 women (81.82%), did not develop gestational diabetes. These findings underscore the varying incidence of gestational diabetes at different stages of pregnancy within our study population.

Clarke *et al.* [36], a retrospective study with 769 women, used a risk factor profile comparable to the present study. They reported a substantially higher rate of early GDM at 17.3%, which is lower than the 27.4% recently reported in Australia (n = 4873) [42] and internationally. The smaller sample size of the present study (n = 385) compared to the above studies may misjudge the actual prevalence of

early GDM in high-risk Sri Lankan women. Evaluating the accurate prevalence becomes challenging when considering studies with diverse diagnostic criteria and populations. Nevertheless, the identification of Early GDM comprises a notable portion of GDM diagnoses, underscoring the necessity for robust evidence to support early screening practices.

The results indicate a statistically non-significant association between GDM incidence at 20 and 28 weeks, as evidenced by the McNemar test. Although statistically insignificant, a considerable proportion of women were diagnosed with GDM at 20 w. This finding suggests that the development of GDM is a dynamic process, and the timing of screening plays a critical role.

However, the highly significant associations when comparing GDM cases at 28 weeks with those without GDM and GDM cases at 20 weeks with those without GDM highlight the distinct trajectories of these groups. The dynamic nature of GDM development underscores the need for a nuanced approach to screening timelines. While routine screening at 28 weeks remains essential, the study provides compelling evidence for considering additional screening at 20 weeks, especially in high-risk populations. This approach aligns with the evolving understanding of GDM as a continuum rather than a static condition.

6.3. Factors Predicting Early GDM Diagnosis

Understanding the interplay between identified risk factors and GDM development is crucial for refining screening protocols. Risk factors, including a history of GDM, family history of diabetes mellitus, previous macrosomia, BMI > 30 kg/m^2, polycystic ovary syndrome, and advanced maternal age, were examined during the current study. Notably, 78.57% of women with GDM at 20 weeks had a history of GDM, while 28.57% had a family history of DM. Among the concerned risk factors, only a family history of DM and a history of GDM were significantly associated with GDM diagnosis at 20 w. Family history, PCOS, and advanced maternal age also exhibited notable associations with other categories of GDM, emphasising the multifactorial nature of GDM development.

Maternal age emerged as a significant factor, with younger women more likely to develop GDM at 20 weeks, whereas older women showed a higher incidence at 28 weeks. This age-related divergence raises intriguing questions about the underlying physiological mechanisms contributing to GDM. While advanced maternal age is a known risk factor for GDM, the study's findings suggest a nuanced relationship that merits further exploration.

Contrastingly, ultrasound dating and the period of amenorrhea did not exhibit significant differences among groups. This result suggests that the timing of GDM development may not be directly influenced by the accuracy of gestational age assessments during early pregnancy. However, the absence of statistically significant differences does not diminish the importance of accurate dating for overall prenatal care.

Pinpointing the precise risk factors for diagnosing GDM at 20 weeks is a

complex task with a single cohort of women. The current study identifies a significant association between GDM at 20 weeks and a family history of diabetes mellitus, as well as a history of GDM. However, it is essential to acknowledge the limitations of drawing definitive conclusions from this single study. Further research across diverse populations is imperative to establish a comprehensive understanding and generalizability. Systematic reviews and meta-analyses should be conducted to aggregate findings and address these concerns systematically. This study, while valuable as a catalyst, serves primarily to stimulate more extensive research in this underexplored domain rather than to provide conclusive insight.

While numerous studies, such as the [24] [36] [43], have detailed various risk factors associated with GDM, the majority of these studies have not sufficiently elucidated which risk factors are more effective in predicting the onset of early GDM.

Early identification of these risk factors for predicting GDM at 20 weeks provides a valuable window for intervention, potentially mitigating the impact of GDM on maternal and fetal health. It is crucial to implement precise criteria for conducting the OGTT at 20 weeks to prevent unnecessary maternal hospital visits, enhance the experience for pregnant mothers, and optimise healthcare expenditure. By carefully selecting individuals at high risk or displaying early indicators of gestational diabetes, healthcare providers can customise the testing strategy. This approach not only lessens the burden on pregnant women and healthcare resources but also ensures an efficient screening process. The goal is to strike a balance between timely diagnosis and the overall well-being and convenience of expectant mothers.

6.4. Strengths and Limitations

This study has several notable strengths. Firstly, its comprehensive analysis of participant data involving 385 women adds depth to the understanding of GDM and its implications. The inclusion of a detailed overview of completed randomised controlled trials RCTs enhances the study's contextual relevance. The focus on identifying risk factors and their associations contributes to a multifaceted exploration of early GDM diagnosis.

Despite its strengths, this study has several limitations. Generalizability to broader populations may be constrained by being a single cohort study. In addition, this study has not explicitly explored the potential beneficial effects of early diagnosis of GDM. While it identifies risk factors and associations, it does not delve into the specific interventions and outcomes associated with early versus late GDM diagnoses, making practical applicability less significant.

6.5. Recommendations

In light of the study's findings and limitations, several recommendations can guide future research and clinical practice. First and foremost, the need for more RCTs is underscored to ascertain whether early-onset GDM treatment offers

superior clinical outcomes compared to the conventional treatment initiated at 24 - 28 weeks of pregnancy. These trials should be well designed with minimal risk of bias, adhere to treatment protocols, and include adequate follow-up data on maternal and neonatal outcomes. Following the evidence from well-designed research, refining screening protocols is also recommended, with a specific emphasis on considering additional screening at 20 weeks, particularly in high-risk populations. The association of particular risk factors with GDM at different time points underscores the need for personalised risk assessments. Tailoring screening protocols based on individual risk profiles can enhance the sensitivity and specificity of early GDM detection. Lastly, given the importance of accurate dating for prenatal care, continued efforts to improve the precision of gestational age assessments are warranted.

7. Conclusion

In conclusion, this study contributes significantly to the evolving landscape of GDM screening, underscoring the importance of considering individual risk profiles and the dynamic nature of GDM development during pregnancy. The study contributes to the ongoing debate on the benefits of early GDM management. Further research, including RCTs and comprehensive reviews, is crucial for establishing evidence-based guidelines and optimising maternal and neonatal outcomes in GDM cases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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