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The Relationship between Maternal Metabolic Variables and Gestational Diabetes in Bangladesh: A Systemic Review and Meta-Analysis

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Abstract **Original Research Article**

Background: Gestational diabetes mellitus (GDM) causes hyperglycemia throughout pregnancy. Overweight/obesity, westernized food, nutritional inadequacies, advanced maternal age, and family history of insulin resistance and/or diabetes are risk factors. GDM normally resolves after birth, but it may have long-term health implications, including an increased risk for T2DM and CVD in the mother and obesity, CVD, T2DM, and/or GDM in the child. This creates a vicious cycle of obesity and diabetes that harms the community's health. Pregnancy serves as a natural "stress test" for the body, hence it's frequently called a "window" into future health. In Bangladesh, GDM studies focus on awareness, risk factors, etc., but not maternal metabolic characteristics. ***Methods:*** This meta-analysis was done. Online database searches on Cumulative Index to NCBI, PubMed, Google scholar, and Bangladesh Journals Online, as well as manual searches of potentially relevant references in review articles, were utilized to locate acceptable research. 3,824 citations were found. 3,252 abstracts/titles were discarded, leaving 176 for full- text analysis. Another 127 were deleted, leaving 49 electronic studies. No unpublished conference papers met our inclusion criteria. Final Systematic review includes 12 publications. ***Results:*** Significant association was found between BMI, HbA1c, Hormone level, CRP. However, no association was found among lipid profile. But association was found betwen TG and LDL-C with GDM. ***Conclusion:*** The meta-analysis suggests that early pregnancy screening of a cluster of metabolic variables may help detect and treat individual risk factors for gestational diabetes. Given the number and quality of included studies, further, better and larger research is needed to corroborate these conclusions.

Keywords: Gestational Diabetes Mellitus, Maternal metabolism, CRP, Lipid profile, metabolic parameter.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a frequent complication of pregnancy characterized by the development of spontaneous hyperglycemia throughout pregnancy [1]. According to the most current report by the International Diabetes Federation (2019), an estimated 223 million women aged 20 to 79 have diabetes. By 2045, this number is expected to reach 343 million. Twenty million or sixteen percent of live births were affected by hyperglycemia during pregnancy. 84% were attributed to gestational diabetes [2]. Overweight/obesity, a westernized diet, nutritional deficiencies, advanced maternal age, and a family history of insulin resistance and/or diabetes are risk factors. GDM often resolves after delivery, but it may have long-term health effects, including as an increased risk for type 2 diabetes (T2DM) and cardiovascular disease (CVD) in the mother and future obesity, CVD, T2DM, and/or GDM in the kid. This adds to a vicious intergenerational cycle of obesity and diabetes that has detrimental effects on the health of the whole community. Unfortunately, there is no generally approved treatment or preventative method for GDM other than lifestyle management (diet and exercise) and sometimes insulin medication, which has limited efficacy because to the frequent insulin resistance. Emerging oral anti-diabetes, such as glyburide and metformin, are promising, but their long-term safety for the mother and kid remains a worry [3, 4].

Improving maternal health and lowering child mortality are two of the eight Millennium Development Goals of the United Nations (MDGs). They provide a unique and formidable challenge for healthcare practitioners across the globe [5, 6]. The MDGs are supported by organizations such as the International Federation of Gynecology and Obstetrics (FIGO), which focuses on reducing non-communicable maternal diseases (NCMDs) and exposures during pregnancy in order to promote the future health of mothers and their kids. FIGO is focusing on hyperglycemia, obesity, hypertension, and poor nutrition during pregnancy to prevent the development of disorders such as obesity and type 2 diabetes mellitus later in life (T2D). This is significant, since the objectives of early intervention are not just to enhance future mother health but also to minimize illness prevalence in future generations [6].

The physiologic changes that occur during pregnancy serve as a natural "stress test" for the body, hence pregnancy is sometimes referred to as a "window" into future health [7]. Pregnancy is a period when many women seek medical treatment, making it an ideal time for preventative healthcare advice. In recent years, it has also become more apparent that the intrauterine environment (e.g., the nutritional quality of the mother) effects the lifetime health of kids [8, 9]. Developmental origins of health and disease (DOHAD) proposes that intrauterine and early infant surroundings have a persistent conditioning or programming influence on the body's metabolism and health later in life.

Maternal Metabolic Variables

Lipid Profile

During pregnancy, the glucose and lipid metabolism of women is known to shift. Due to the increased release of hormones, such as placental growth hormone, which stimulate the transplacental transfer of glyconutrients to the baby, insulin resistance rises during pregnancy [10]. In light of the fact that pregnant women use lipids as an energy source, their plasma levels of cholesterol and triglyceride are rather high [11]. In contrast, previous research has revealed that the timing of blood collection throughout the various stages of pregnancy is a crucial consideration. Due to the changes in lipid profile throughout the second and third trimesters of pregnancy, additional variables, such as pregnancy-related problems and/or placental malfunction, may hamper interpretation of cause or effect [12].

It has been shown that the maternal metabolic environment changes during the first trimester as a result of an increase in blood levels of estrogen and progesterone, followed by pancreatic beta-cell hyperplasia and an increase in insulin production [13]. Hyperinsulinemia causes a decrease in blood glucose concentration by increasing peripheral glucose use followed by glycogen storage in tissues. In addition, it decreases lipolysis while increasing fat accumulation [14].

During the second and third trimesters, fuel modifications in the mother lead to a reduction in glucose (for the fetus) and an increase in the concentration of fatty acids in plasma, resulting in gestational diabetes and hypertension, respectively. Freinkel referred to these alterations as "accelerated hunger" and "facilitated anabolism" [15]. GDM and HTN may increase the risk of maternal and fetal problems during and after delivery. Dyslipidemia, the third component of the metabolic syndrome linked to insulin resistance, is a well-known cardiovascular risk factor [16, 17].

Hormone

Reportedly, elevated levels of estrogen, progesterone, human placental lactogen (hPL), human placental growth hormone (hPGH), cortisol, TNF, ILs, etc. cause the decline in maternal insulin sensitivity [18]. Due to insulin resistance, pregnant women use more fats than carbs for energy, and carbohydrates are saved for the developing baby. Thus, it functions as a physiological adaptation of the mother to guarantee that the fast-developing fetus receives an appropriate quantity of carbohydrates [19]. Pregnancy is known to cause significant bodily changes. It not only raises the need for metabolic fuel for fetal growth and development of its related structures, but also produces hormonal changes in the body that may lead to alterations in lipid profile during the several trimesters of pregnancy [20]. It has been shown that the maternal metabolic environment changes during the first trimester as a result of an increase in blood levels of estrogens and progesterone, followed by pancreatic beta-cell hyperplasia and an increase in insulin production [21].

Obesity

Overweight and obesity have become a worldwide pandemic [22]. Obesity is a threat to maternal health in women of reproductive age, with implications ranging from gestational diabetes (GDM) [23] and unfavorable pregnancy outcomes to type-2 diabetes (T2D) and cardiovascular illnesses [24]. Women with GDM are unable to promote glucose elimination and reduce glucose synthesis and fatty acid (FA) levels [25]. Each and when combined, maternal obesity and GDM are associated with unfavorable short- and long-term baby outcomes [26-28]. Women with a history of GDM continue to have an elevated risk of getting type 2 diabetes in the future [29]. GDM and type 2 diabetes share several risk factors, including obesity and overweight, and many consider GDM a precursor to type 2 diabetes [30]. Kim *et al.,* (2010) discovered that a higher BMI is related with an increased risk of GDM [31].

C-Reactive Protein

Pregnancy is an anti-inflammatory state; nonetheless, there is an increase in inflammation during the early stages of pregnancy, such as during implantation, which leads to an increase in numerous inflammatory mediators [32]. A high maternal CRP is linked to miscarriage, early labor and membrane rupture, toxemia of pregnancy, fetal development limitation, and chorioamnionitis [33, 34]. According to research, high levels of C-reactive protein are associated with type 2 diabetes [35]. Increased blood levels of CRP can cause hyperglycemia through increasing insulin resistance [36]. Increased blood sugar and levels of glycosylated hemoglobin (HbA1c), which cause the generation of CRP, may be the mechanism by which inflammation causes diabetes [37].

According to International Diabetes Federation (IDF), in 2019, 8.4 million adults in Bangladesh had diabetes, and this number is expected to nearly quadruple by 2045 to 15.0 million [38]. GDM is more common in urban Bangladesh than in rural Bangladesh, with a prevalence of 12.9% [39, 40]. More than two million people in Bangladesh have diabetes but have not yet received a diagnosis [41]. In Bangladesh, undiagnosed occurrences of diabetes in pregnant women are a major problem in terms of healthcare access and nutrition [42]. Frequently, women either do not seek treatment for their illnesses or do so from untrained practitioners [43]. In Bangladesh, a national maternal and newborn health guideline has been proposed for the care of GDM patients, although there is no standard screening of all pregnant women for GDM [44]. Only 55% of pregnant women receive antenatal care (ANC), and 45% of pregnant women with GDM would remain undiscovered. Pregnant women do not typically attend the ANC between 24 and 28 weeks of gestation [45]. GDM screening is performed infrequently, especially in rural regions and at lower levels of health care facilities [46]. Optimizing glycemic control and improving pregnancy outcomes are the fundamental for gestational diabetic mellitus (GDM) therapy [47, 48].

HbA1

Glycated hemoglobin A1c (HbA1c) is generated when glucose attaches non-enzymatically to the N-terminal valine of the β-chain of hemoglobin. Erythrocytes have a lifespan of 120 days; therefore, HbA1c indicates long-term glycemic exposure, expressing the average glucose concentration over the previous 8–12 weeks [49]. HbA1c is frequently used to assess glycemic control and direct treatment. Some organizations promote its usage for the screening and diagnosis of diabetes mellitus [50]. The HbA1c test does not need fasting, making it more comfortable for pregnant women than the 100g OGTT. Compared to glucose tests, HbA1c may be determined at any time of day, has less biological variance, greater reproducibility, and more analytical stability [49]. However, its application in diagnosing GDM has not yet been suggested. There have been studies comparing the efficacy of the HbA1c test as a GDM diagnosis tool to the 75g OGTT [51] and 100g OGTT [52].

Various study is conducted in Bangladesh related to GDM predominantly on awareness level, risk factors, etc., however there is no study related to the maternal metabolic variables associated with GDM. Therefore, a systemic review and meta-analysis on metabolic variables and GDM is conducted in Bangladesh.

METHODS

This systematic review adhered to the Cochrane methodology and the meta-analysis of observational studies in epidemiology (MOOSE) group's reporting guidelines.

Selection Criteria for the Study

Cohort, case-control, and cross-sectional observational studies were taken into consideration for this systematic review if they included the following details: Metabolic variable as an exposure variable (for cohort studies) or one of the risk factors, and GDM as an outcome variable (for cohort studies) or to identify cases (in case-control studies) (in case– control studies).

Women who had undergone an examination for gestational diabetes during their index pregnancy and who had information on metabolic variables such C-reactive proteins in the first trimester (either self-reported or tested), gestational hypertension produced during the late trimester, HbA1 and hormones levels were eligible for inclusion. Participants of any age, gender, educational level, socioeconomic class, race or ethnicity who met the aforementioned requirements were accepted. Patient's BMI taken at the beginning of the study were also included. Patients who had chronic hypertension, diabetes (type 1 and 2) that had been previously diagnosed, thyroid disorders, chronic kidney disease, cardiovascular disease, autoimmune and chronic inflammatory diseases, active infections, who had taken antibiotics within two weeks of the sample collection, seasonal allergies, and who were taking corticosteroids or non-steroidal anti-inflammatory drugs were also excluded from the study.

Search Strategy for Identification of Studies:

The following phrases were used in the search strategy, which was created with the help of a librarian with expertise in systematic reviews based at the World Health Organization (WHO), and were customized for each database searched: 'body mass index' or 'BMI AND GDM' or 'body mass index AND GDM or 'C-reactive protein AND GDM' or 'CRP AND GDM '' or 'Lipid profile' or Lipid profile AND GDM' or 'Hormones and GDM' or 'HbA1c' or HbA1c AND GDM' or 'Gestational Diabetes' or Pregnancy induced Diabetes'.

Electronic database searches on Cumulative Index to NCBI, PubMed, Google scholar and the Bangladesh Journals Online, as well as manual searches of possibly eligible references in review articles, were used to identify suitable studies. The searched articles were published between 2010 to 2022 and language taken of only English articles. There were no limitations by country. In addition to reviewing classic review articles, textbooks, and published letters for possibly qualified works, we evaluated the references for every article selected for a comprehensive manuscript evaluation. In addition to evaluating the abstract books of worldwide congresses of obstetrics and gynecology, endocrinology, and obesity, the search for unpublished research from year (2010–2022).

Data Analysis

Using Review Manager, all analyses were performed (V5.4.1). For the major meta-analyses, studies giving odds ratios (OR) or relative risks (RR) with 95% confidence intervals (CIs) were analyzed, since these data are most suited to answer issues regarding prognosis. Using restricted maximum likelihood random-effects models, data were pooled to account for heterogeneity between studies and outcome measures [53]. Adjusted analyses with a core set of prognostic variables were provided after unadjusted analyses (maternal age, maternal BMI, ethnicity). Due to the fact that many of the included studies did not account for all four variables, we chose to include at least one core covariate in each model.

Using the I2 statistic, heterogeneity was determined. The significance threshold for heterogeneity was established at $p< 0.10$, with an $I2 > 50\%$ indicating rather significant levels of heterogeneity [54]. Sources of heterogeneity were investigated by removing outlier studies from the meta-analysis in a series of sensitivity analyses and recalculating the effect size to identify the impact of those studies [55]. We examined studies with a different direction of impact, a large effect size, or a significant risk of bias that were outliers [54]. If 10≥ studies were available, publication bias was determined by visually inspecting funnel plots [56].

RESULTS

The online database search revealed 3,824 citations (Fig. 1). In the initial screening (abstracts/titles), 3,252 citations were eliminated, leaving 176 for full-text analysis. At this stage, another 9127 were removed, leaving 49 studies from the electronic search included. From the conference proceedings, no unpublished papers that satisfied our inclusion criteria were discovered. 12 papers are included in the final systematic review.

In table 1, out of 4 study, 3 of the study (Mahmudul Hossain, *et al.*, 2020 [58], Yasmin Akhter *et al.*, 2017[65], Nusrat sultana *et al.*, 2016 [67]) in my research showed significant association between BMI and GDM; 27.17 ± 3.3 kg/m2, 26.88±4.16 kg/m2 and 26.7±4.4 kg/m2, respectively.

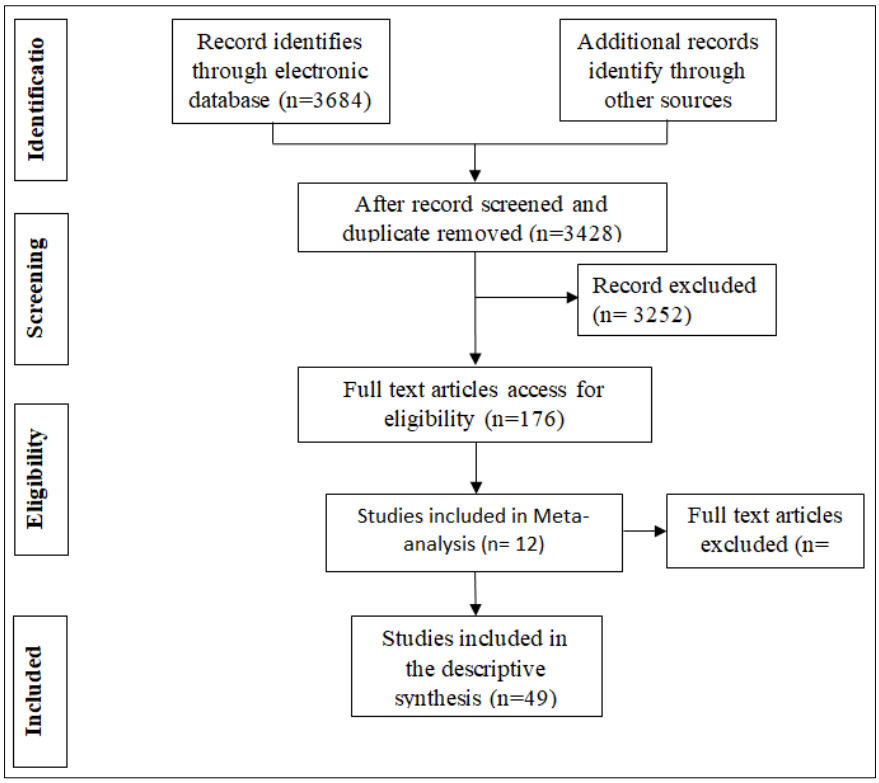

Fig 1: PRISMA Flow chart

Table1: Metabolic variables and GDM

Author name	Type of study	Population size	Year	Main exposure	Result
Bishwajit Bhowmik *et al.*, 2019 [57]	prospective multi-center study	498	April 2011 and June 2012	BMI in early pregnancy	154 (30.9%) were underweight, 241 (48.4%) had normal weight and 103 (20.7%) were overweight found in the early pregnancy.
Mahmudul Hossain, *et al.*, 2020 [58]	Cross-sectional study	62	January 2017 to December 2017	serum lipid profile and BMI, among women with gestational diabetes mellitus (GDM)	50% were GDM (age: 27.52 ± 4.8 years, body mass index (BMI: 27.17 ± 3.3 kg/m2).Women with GDM showed relatively higher BMI. Fasting lipid profiles among GDM women, total cholesterol: 194.21 ±42.18mg/dl, p = 0.187; HDL-C: 47.50 ± 16.17 mg/dl, p = 0.928; LDL-C: 109.25 ± 28.80 mg/dl, p = 0.220 and triglyceride 204.78 ± 58.50mg/dl, p = 0.891) were not significantly association.
Md.Mim Obaidullah *et al.*, 2021 [59]	Observational study	232	2021	Role of lipid profiles andTG/HDL cholesterol ratio associated with fasting glucose in GDM subjects.	TG and LDL-cholesterol were significantly higher ($p < 0.001$) in GDM individuals (220.95 ± 67.4 and 149.54 ± 32.4, respectively)
Fahmida Rashid *et al.*, 2017 [60]	Case-control study	60	January 2009 to December 2009	Lipid profile in GDM patients	GDM was discovered to have a different lipid profile than healthy individuals. There was no statistically significant difference between both groups' serum TC and LDL-C levels. Serum TG levels were statistically greater and HDL-C levels were statistically lower in gestational diabetes ($p<0.05$) compared to healthy pregnant women.
Fatema N *et al.*, 2016 [61]	Case-control study	297	August 2005 to November 2007	Assesselevatedserum CRP in GDM patients	CRP could predict development of GDM in 59% with sensitivity 61% and specificity 83%. C-peptide in the 50th percentile could predict development of GDM in 58% with sensitivity 72% and specificity 93%. The present data indicates that CRP and C-peptide both is sensitive markers in predicting GDM.
Shahid M.M *et al.*, 2021 [62]	Cross sectional study	628	January 1 2019 to December 31 2019	association between gestational diabetes mellitus (GDM) and thyroid status (TS) throughout pregnancy in Bangladesh	Mean F.T4 of the GDM group was lower in all three trimesters. The mean TSH of the GDM group was more deficient in the early stage of pregnancy but higher in the later stage (3rd trimester). Euthyroid cases were significantly higher (83.8%; $p<.001$) while subclinical hypothyroidism (9.5%; $p<.001$) and transient hyperthyroidism (2.4%; $p<.001$) cases were significantly lower in GDM group.
Sharmin A *et al.*, 2021 [63]	Case-control study	80	August 2017 to July 2018	SHBG level in pregnancy and to analyze the association of SHBG with GDM	Women with GDM were found to have significantly lower levels of Sex hormone-binding globulin (SHBG) compared to the controls ($p<0.05$)
Ahmed F *et al.*, 2013 [64]	Cross-sectional comparative study	110	January 2010 to December 2010	relationship between HbA1c & Gestational Diabetes Mellitus	HbA1c(6%) were more increased in GDM patients than that of the normal pregnancy((6.95±1.38% Vs 5.05 ±0.27 %, $p<0.001$).Pearson,s correlation coefficient (r) showed that there are

Author name	Type of study	Population size	Year	Main exposure	Result
					positive correlation between Blood Glucose Level & HbA1c (Fasting Blood Glucose &HbA1c,r=0.869,p=<0.001 and Post Prandial Blood Sugar& HbA1c, r=0.507, p=<.0.001
Yasmin Akhter *et al.*, 2017 [65]	Prospective cohort study	191	January, 2014 to August, 2015	HbA1c, BMI, Gestational Hypertension in GDM patients	HbA1c was significantly higher in GDM (5.42±0.61 p<0.001). gestational hypertension-2.3% (p=0.621), BMI: 26.88±4.16 kg/m2; mean±SD)
MahmudaS *et al.*, 2017 [66]	Descriptive cross sectional study	300	January 2010 to December 2010	glycemic status during different trimester of pregnancy to asses GDM	Out of 300 pregnant women 57% were in 3rd, 32% were in the 2nd and 11 % were in the 1st trimester. The results found 3%, 6.3% and 4.1% pregnant women in the 1st, 2nd and 3rd trimester respectively had significantly raised level of postprandial blood sugar (PPBS) and HbA1c levels with cumulative prevalence of 4.7%. 50% of the pregnant women were treated with GDM in the 1st trimester.
Nusrat sultana *et al.*, 2016 [67]	Cross-sectional study	94	December, 2011 to June, 2013	BMI and OGTT, associated with GDM	BMI (26.7±4.4 kg/m2, p<0.001). OGTT performed before 24 weeks revealed GDM in about 44% (88/202).
Debhnath J *et al.*, 2018 [68]	Case control study	100	June 2006 to December 2007	HbA1c, SBP, DBP among GDM	HbA1c level (%, M±SD) was significantly higher in GDM group (6.09±1.1). SBP (mm of hg) (116±12.2, p=0.005). DBP (mm of hg)(75±7.7, p= 0.002).

No significant association was found between serum lipid and GDM, except by a study by Md. Mim Obaidullah *et al.*, 2021 [59] found TG and LDL-cholesterol were significantly higher ($p < 0.001$) in GDM individuals (220.95 ± 67.4 and 149.54 ± 32.4, respectively). CRP is found to significant associated with GDM as CRP and C-peptide both is sensitive markers in predicting GDM, (Fatema N *et al.*, 2016 [61]).

Hormone such as TSH showed that F.T4 of the GDM group was lower in all three Trimesters, mean TSH of the GDM group was more deficient in the early stage of pregnancy but higher in the later stage (3rd trimester). Euthyroid cases were significantly higher (83.8%; p<.001) while subclinical hypothyroidism (9.5%; p<.001) and transient hyperthyroidism (2.4%; p<.001) cases were significantly lower in GDM group (Shahid M. M *et al.*, 2021 [62]). Another study on hormone, sex hormone-binding globulin (SHBG) by Sharmin A *et al.*, 2021 [63] showed significantly lower levels of Sex hormone-binding globulin (SHBG) among GDM (p<0.05).

HbA1c (6%) were more increased in GDM patients (6.95±1.38% p<0.001) (Ahmed F *et al.*, 2013 [64]). Study by Yasmin Akhter *et al.*, 2017 [65] also showed that HbA1c was significantly higher in GDM (5.42 ± 0.61 p < 0.001). Similarly, Debhnath J *et al.*, 2018 [68] *also showed* HbA1c level was significantly higher in GDM group (6.09±1.1).

One study by Yasmin Akhter *et al.*, 2017 [65] did not found gestational hypertension among GDM patients. However, study Debhnath J *et al.*, 2018 [68] *showed* SBP (mm of hg) (116±12.2, p=0.005) and DBP (mm of hg)(75±7.7, p= 0.002) among GDM patients.

DISCUSSION

This systematic review and meta-goal analysis's was to investigate the relationship between maternal metabolic factors and their constituent parts and GDM, a standalone risk factor for later type 2 diabetes and CVD [69]. Women who were overweight or obese were up to four times more likely to develop GDM, and having the MetS as a cluster of risk factors raised their risk by up to two and a half times. Results persisted in sensitivity analysis to decrease heterogeneity and were consistent in adjusted analyses.

In my research showed significant association between BMI and GDM; 27.17 ± 3.3 kg/m2, 26.88±4.16 kg/m2 and 26.7±4.4 kg/m2, respectively which is an increased risk of overweight among the GDM patietns. Other research revealed that women with overweight or obesity had a two- to fourfold increased risk of developing GDM. A recent meta-

analysis of 33 observational studies revealed a 3.2-fold greater risk of gestational diabetes with rising pre-pregnancy BMI category and a 19% increased risk of gestational diabetes every unit of rise in pre-pregnancy BMI [70]. Overweight or obese pregnant women had greater FPG, insulin, and TG levels than normal-weight pregnant women [71]. However, independent of BMI, a number of the individual studies included in my review demonstrated that metabolic risk factors increased the risk for GDM. Since weight loss is not recommended during pregnancy and it is likely to be difficult to target overweight or obese women prior to conception, my findings reinforce the need to identify additional important modifiable risk factors for GDM [72].

According to one of the studies in my review, a rise in fasting TG and LDL was related with an increased probability of developing GDM. Increased TG are connected with insulin resistance, which not only accelerates the process of MetS but is also a key determinant in the development of type 2 diabetes and CVD [73, 74]. In a recent study including 500 Chinese people, TG had a positive link with insulin resistance in those with normal glucose tolerance, but a negative, independent correlation with beta cell activity in those with dyslipidemia [73]. My comprehensive review revealed only three research evaluating the association between Lipid profile and GDM, and only one of these studies demonstrated a correlation between TG and LDL and GDM. Although these data are significant and show a potentially essential link between MetS in early pregnancy and risk for GDM, the existing studies were insufficient, necessitating more research.

In my review only one study was conducted in association of CRP and GDM where they showed a sensitive marker and predictor of GDM. Other research on hs-CRP shown that the highly sensitive indicator is useful and cost- efficient for the diagnosis and screening of gestational diabetes [75-77].

In my study, hormones such as TSH revealed that the GDM group's F.T4 was lower in all three Trimesters, but the GDM group's mean TSH was more deficient in the first trimester but higher in the third (3rd trimester). According to the ATA, it is crucial to monitor thyroid function during pregnancy, especially in women at risk for thyroid disease, such as those with a prior history of thyroid disease, a history of unexplained abortion, autoimmune illnesses, or a familial history of thyroid disease [78]. The American Thyroid Association also recommends that women with TD risk factors get a thyroid function test prior to pregnancy planning and as soon as the pregnancy is confirmed.Yang *et al.*, observed that low thyroid hormone levels in early pregnancy are related with an increased risk of developing GDM; hence, earlier screening of thyroid hormone levels throughout pregnancy was recommended [79]. In all three trimesters, the average levels of serum F.T4 in the GDM group were statistically insignificantly lower than in the non-GDM group. During the 1st and 2nd trimesters, the average levels of TSH were likewise insignificantly lower not the GDM group. Regarding negligible changes in thyroid function testing, my research concurred with earlier research.The median value of the hormone SHBG in this study was 245.0 nmol/L (195.8-278.1 nmol/L), which is statistically significant. Similar observations were made for SHBG levels, with the median in the GDM group being 224.5 nmol/l (166.2-283.8) and in the control group being 295.9 nmol/l (233-370) [80]. In the research by Anderson and Zhiqun, the GDM group had considerably lower SHBG levels than the control group. SHBG concentration was 53.64±31.91 nmol/l in the GDM group and 71.33±30.03 nmol/l in the control group [81].

In my present review, all three study showed HbA1c was significantly higher in GDM patients. Similar results were also found in other studies [82, 83]. Increased levels of glycated hemoglobin, a sign of inadequate blood glucose regulation, have been linked to retinopathy, nephropathy, and cardiovascular disease. The risk of developing and progressing microvascular and nerve problems is substantially correlated with the HbA1c. Microvascular problems increase extremely quickly when HbA1c levels are high (>9.0-9.5%) [84]. Due to the strong relationship between HbA1C levels and GDM blood sugar levels. As a result, it is a trustworthy predictor of overall glycaemic management in individuals with diabetes during pregnancy [82]. The levels of HA1c, which represent the average blood glucose level over the previous 6 to 8 weeks, are unaffected by daily variations in blood glucose levels. Therefore, HbA1c is a helpful marker of recently managed blood sugar and may be used to track how medication therapy affects blood sugar levels [82].

SBP and SBP are linked to GDM in this review. According to Vembergre *et al.*, (2002), the degree of glucose intolerance during pregnancy may be related to pregnancy-induced hypertension [85]. Compared to women with normal blood pressure, women with hypertension had a twofold greater chance of developing GDM. Additionally, Gonsalves *et al.*, (2005) noted that women with GDM and gestational hyperglycemia had an increased risk of hypertension [86].

CONCLUSION

The meta-analysis shows some evidence that early pregnancy evaluation of several metabolic variables, as a cluster of factors, gives a possible chance to identify and treat individual risk factors as an essential strategy for preventing gestational diabetes. Given the total quantity and quality of included studies, further, bigger, and higher- quality research is required to confirm these findings.

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