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# Is intermittent fasting really beneficial for women with GDM? A mini-review

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**ABSTRACT**

**Objective.** Intermittent fasting (IF) is a diet regime that has been widely explored for its effect on weight loss, heart health and oxidative stress, especially in Type 2 Diabetes. The number of women suffering from Gestational Diabetes Mellitus (GDM) is increasing globally. Hence, the following review aims to explore the importance of IF in women suffering from GDM concerning maternal and neonatal outcomes and dietary quality and compliance.
**Materials and Methods**. A systematic literature search was done using PubMed, Scopus, Google Scholar and Web of Science to review the interrelationship between intermittent fasting and GDM.
**Results.** Evidence from studies support that intermittent fasting or other types of energy restriction along with exercise helps to improve mother and foetus-related outcomes in women with GDM. Evidence suggests that IF can help reduce blood sugar levels and weight of women suffering from GDM. A mother performing IF during pregnancy, especially with GDM, poses a risk to the ideal development and growth of the child, resulting in infants with low birth weight or excessive birth weight along with other complications.
**Conclusions.** Various dietary regimes are prescribed for women with GDM. Our review illustrates how the role of IF in women with GDM is controversial. On one side, IF has shown beneficial effects on maternal health in women suffering from GDM. On the other side, IF shows questionable results on neonatal outcomes.

## INTRODUCTION

Gestational Diabetes Mellitus (GDM), according to World Health Organisation, is defined as intolerance to glucose that happens in pregnant women and is marked by onset or diagnosis during pregnancy [1]. The American Diabetic Association defines GDM as diabetes detected in the second or third trimester of pregnancy that was not overt diabetes before gestation [2].
Globally, GDM impacts the lives of 18.4 million women, accounting for 86.4% of during-pregnancy hyperglycaemia, defined as any high glucose range. According to a study, the risk of developing GDM is higher among Asian Indians, and the prevalence was 25 (**Figure 1**). The existing literature shows that the number of women suffering from GDM in India varies from 4% to 14%. The prevalence of GDM in western parts of India is 9.4% [3]. Therefore, it is imperative to detect and prevent GDM to improve neonatal and maternal outcomes [4].
There are several factors responsible for the development of GDM. GDM is thought to arise due to insulin resistance caused by pregnancy hormones, obesity, sedentary lifestyle, faulty dietary habits, stress or metabolic syndrome, which is not suffi-

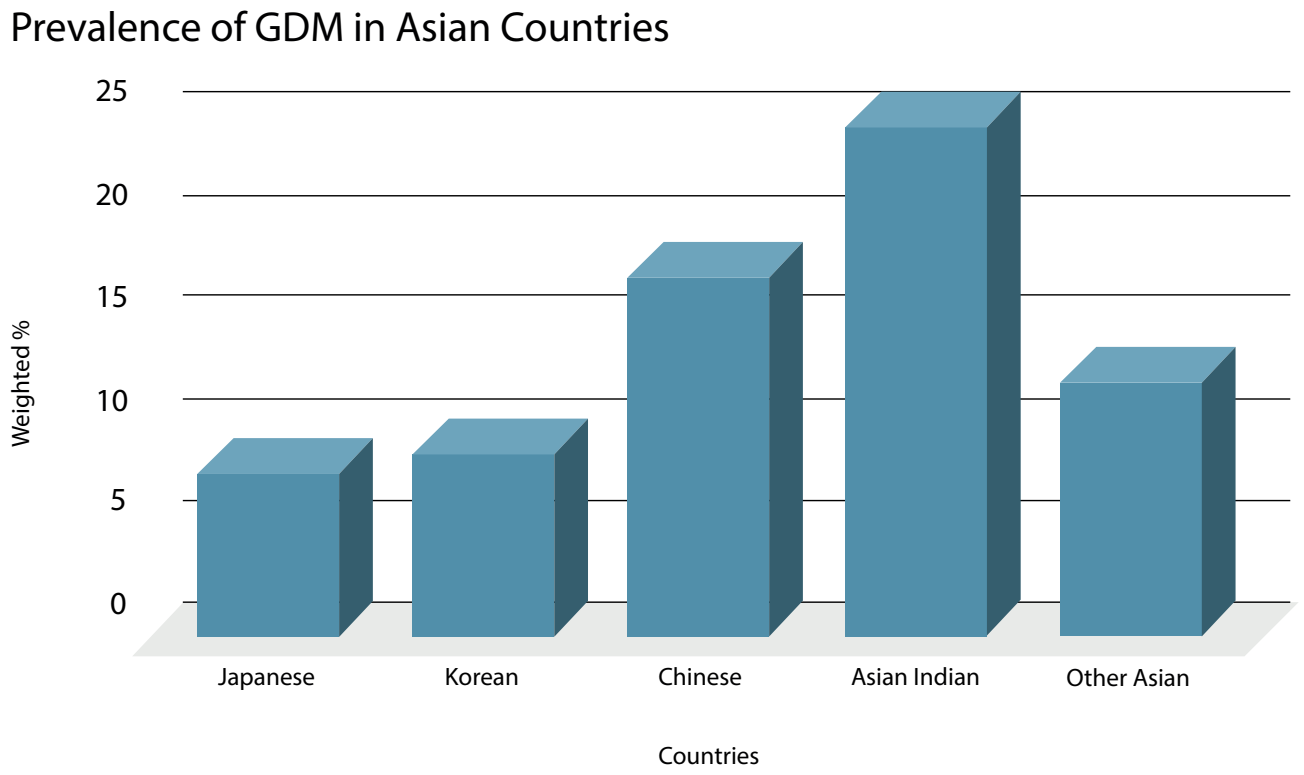


**Figure 1.** *Prevalence of GDM in Asian women.*

ciently justified by the pancreatic β-cells via higher proliferation and insulin production [5]. A cross-sectional study conducted in Brazil concluded that main determinants of GDM are obesity, especially central obesity, excessive gestational weight with BMI > 35 kg/m$^2$, physical inactivity, late pregnancy, multiple pregnancies, and a familial record of diabetes [6]. Pons *et al*., also suggest that an adequate pre-pregnancy nutritional status lowers the risk of developing GDM [7]. By making the appropriate lifestyle changes and managing the modifiable risk factors, the risk of developing GDM can be reduced. Diet is one of the modifiable predictors of non-optimal glucose tolerance during the gestational period. Previous studies say that diets high in total fat, saturated fat, red and processed meats and a high glycaemic index raise the chances of developing GDM, while polyunsaturated fats, carbohydrates and fibre are protective. According to a study by Zhang *et al*., a diet with low fibre and a high glycaemic index was related to more chances of developing GDM [8]. It also stated that a diet high in fibre and a low glycaemic load was associated with reduced blood sugar levels in the women diagnosed with GDM. The patient's diet is of significant concern and importance in the pathogenesis, progression, and treatment of GDM. Both diet quality and quantity are equally vital. Since there is increased inflammation in the body during diabetes and fat mass increases, intermittent fasting comes to the rescue in reducing weight and improving insulin sensitivity [9].

Various studies have been done to assess the impact of women's advanced age as well as pre pregnancy obesity, and it concluded that both these factors resulted in higher maternal and neonatal complications. Better outcomes can be expected with a timely and adequate approach [10]. It has also been found out that different types of diabetes don't impact the maternal and neonatal outcomes differently. Regardless of the type of diabetes, if proper treatment is given, pregnancy outcomes can be improved [11]. Time and mode of delivery is very important to judge pregnancy outcomes. There is not enough evidence to conclude anything concrete and more studies are required for stating anything substantial in this regard [12].

Intermittent Fasting (IF), as proposed in various research papers, is defined as a diet protocol wherein there are intervals of fasting – either no food is consumed, or there is a drastic reduction in calorie intake – followed by intervals of unrestricted consumption [13]. Anton *et al*. have explored the term

metabolic switch, meaning when the body shifts from using glucose as its primary fuel for energy to fatty acids and its derived ketones [14]. This switch happens preferentially by the body, and this best describes how IF works in the human body to alter the metabolism. During the fasting phase, ketones are favoured as an energy source for both the body and the brain because the glycogen stores in the liver get depleted due to prolonged fasting, which is generally post 12 hours after taking in food and then starving. This, in turn, causes increased lipolysis and hence more fatty acids and glycerol, making the body use these as fuel. Hence IF changes the body's metabolism for carbohydrates, fats, proteins and other nutrients [15].

IF is beneficial for reducing weight and improving insulin sensitivity by altering the metabolism, as explained previously [16]. Decreased energy intake (achieved through IF) results in sustained lower insulin secretion and more AMP-activated protein kinase levels, which regulates hunger and satiety, subsequently improving insulin sensitivity and glucose homeostasis [17].

There is a lack of reviews on studies that relate GDM and IF, hence this review aims to elaborate on the relationship between GDM and IF and its related benefits and disadvantages. We checked the databases PubMed, Scopus, Google Scholar and Web of Science with the keywords – gestational diabetes mellitus, intermittent fasting, maternal health, neonatal outcomes, diet quality, dietary compliance, and weight loss barriers. We used the papers collected to study the effects of IF on maternal outcomes in women suffering from GDM, evaluate the effect of IF on foetal outcomes in women with GDM and assess the dietary quality, compliance, and weight loss barriers in women with GDM following IF.

## EFFECTS OF IF ON MATERNAL OUTCOMES IN WOMEN WITH GDM

GDM results in short- and long-term problems in the pregnant woman and her child. It puts women at risk of hypertension and preeclampsia. Also, there are chances of caesarean sections and developing future T2DM. Obesity, in the case of GDM, may necessitate insulin therapy during gestation and exponentially increase a woman's chances of being prone to Type 2 Diabetes Mellitus (T2DM) after childbirth [18]. It is well-documented that a woman with a history of GDM is at risk of developing T2DM, heart disease, and dyslipidaemia in later life [19, 20]. The chances of T2DM after GDM is up to 7.5 times more than after a regular pregnancy [21]. A Danish study concludes that metabolic syndrome is three-fold more likely to develop in women with GDM compared to women without GDM [22]. In India, there is less awareness about GDM and its risk to foetal and maternal health [23]. This can be overcome by setting standard screening and diagnostic criteria for pregnant women.

Existing evidence indicates that restrictive diet and exercise interventions help improve obstetrical, mother and child outcomes in women suffering from GDM and reduce the risk for intergenerational obesity [24]. A study was conducted to see the result of a very low-energy diet (1,600 kcal/day) and a low-energy diet (1,800 kcal/day), with or without personalized exercise sessions, among women with GDM in normal pregnancy. The study showed that very low-energy and low-energy diet therapies do not appear to induce differences in the obstetrical, mother and child outcomes in women suffering from GDM. The author also suggests that, in this case, IF would help the participants reduce weight and improve their blood sugar levels in women with GDM during pregnancy [25].

One randomized control trial concluded that the IF diet was more beneficial than continuous energy-restricted diets in reducing weight in obese women with a prior history of GDM. This study intended to investigate whether a 2-day very low-calorie diet followed in an intermittent pattern was equal to moderate daily caloric control over 12 months in obese women with GDM. The results showed that a 2-day 500 kcal (2,100 kJ) Intermittent Energy Restriction diet resulted in good weight reduction compared to a regular 1,500 kcal (6,000 kJ) Continuous Energy Restriction diet in the sample. The mean ± SD of weight reduction was remarkable over time ($p < 0.001$), but not by diet group (Intermittent Energy Restriction -4.8 ± 5.0 kg; Continuous Energy Restriction -3.2 ± 5.0; $p = 0.2$). The mean between-group difference was 1.6 kg (95%CI -4.2 to 1.0 kg; $p = 0.2$). There were no remarkable group differences in change in Glycosylated Haemoglobin (HbA1c), fasting plasma glucose, fasting serum insulin, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) or 2-h oral glucose tolerance seen at 12 months ($p > 0.05$) [26].

A study by Rasmussen *et al*. shows that a diet with a high carbohydrate content in the first half of the day results in more glycaemic variation, but low fasting

blood glucose levels, compared to a diet with a low carbohydrate content in the first half of the day and a high carbohydrate intake in the second half of the day [27]. Additionally, insulin resistance, shown as HOMA-IR, decreases remarkably during the first diet. The final results of this research show that a carbohydrate variability of 50% in the first half of the day favours low blood glucose and better insulin sensitivity in women with GDM. The objective of a study conducted by Wang *et al*. was to explore the effect of fasting duration, which included the time when the last food or meal was taken, and the time duration when it was consumed (morning, afternoon or night), and to examine their effect on the glucose levels by performing a glucose challenge test on the pregnant women [28]. The authors concluded that both the fasting duration and time influenced blood glucose levels. It was found that a fasting duration of 6.5 hours or more positively affected blood glucose levels by 2.7 times. The relationship between the fasting time, time of the day, and blood glucose levels were also affected by age and maternal obesity. Multivariate analysis revealed that the participants assessed during the afternoon and late evening had lower blood glucose levels, which may be due to a shorter fasting interval. In the screening and diagnosis of GDM, time duration and fasting duration are modifiable factors that need to be addressed for clinical and epidemiological studies [29]. Developing GDM during pregnancy increases the risk of developing non-communicable diseases in the later part of life [11]. While some evidence suggests that IF helps reduce blood sugar levels and body weight, contradictory results indicate that intermittent fasting is not beneficial for women with GDM and has side effects on the child's health. Hence, the effect of IF on women with GDM has to be explored further.

## EFFECT OF IF ON NEONATAL OUTCOMES IN WOMEN WITH GDM

GDM during pregnancy may have severe ill effects on an infant's health. The infant is at risk of developing foetal hyperglycaemia, excessive birth weight, respiratory distress syndrome caused by insufficient lung surfactant, foetal hypoglycaemia, prematurity, low calcium levels, and high bilirubin levels [30, 31]. The Pedersen hypothesis explains the foetal adiposity and macrosomia that occurs in an infant born to a woman with GDM. It suggests that intrinsic foetal pancreatic beta-cell enlargement of the organ "pulls" glucose across the placenta, *i.e*., assists in the glycaemic control of the mother. Foetal adiposity occurs due to increased alpha-glycerophosphate, which synthesises the foetal adipocytes. This alteration happens due to an increase in foetal size due to foetal hyperinsulinemia [32]. A case-control study conducted in Qatar concluded that high birth weight was more prevalent in infants born to women with GDM despite antenatal diabetic care and management [30]. Similarly, a retrospective study conducted in India concluded that an infant born to a woman with GDM is at higher risk of developing obesity, T2DM and dyslipidaemia in later life [31]. High birth weight is proportional to obstetrics complications during delivery and later in life. Postpartum, the neonate is at increased risk of developing neonatal hypoglycaemia, respiratory distress syndrome, diseases of the heart muscle, and hypocalcaemia [23].

Insulin resistance and BMI of the mother during pregnancy are linked with a disbalance of placental metabolites like carbohydrates, BCAA, lipids, folate and choline, which are related to increased foetal size and weight. Placental deoxyribonucleic acid methylation, which adversely affects foetal development, is also seen due to GDM. Increased rates of miscarriage, dystocia, caesarean section, neonatal death, premature birth, congenital anomalies, macrosomia, respiratory distress, neonatal jaundice, hypoglycaemia, hypocalcaemia, and polycythaemia are seen in GDM [18].

The mother's dietary intake in terms of quality, quantity and, therefore, the availability of micro and macronutrients required for transfer through the placenta is crucial for foetal growth and development [33]. The incompetence of the maternal-placental supply to fulfil the foetal nutrition requirements impacts a variety of neonatal adaptations and changes during growth and development [34]. Metabolic changes related to maternal diet restriction, including hypoglycaemia, increased free fatty acid levels, and amino acid levels, affect neonatal outcomes, eventually affecting the baby's quality of life. Lumey *et al*. 1998 stated that when pregnant women did not have enough food, especially during their third trimester, it led to LBW children taking birth. But no such change was seen with food restriction during the first trimester [32].

According to the study by Mirghani *et al*., there was no difference in the APGAR score at 1 and 5 minutes when comparing infants of the fasted and non-fasted group of women with GDM [35]. However, admission to the special care baby unit was

significantly more frequent in the fasted group than in the control group (p = 0.001). Maternal diet restriction is linked with a higher risk of GDM and induction of labour. The number of times patients were admitted to the special care baby unit increased. This paper also concluded that the prevalence of developing complications in pregnancy and the incidence of caesarean section was comparatively more in the fasted group than the non-fasted group. Though the role of a mother's fasting on her child's weight is still to be explored more evidently, Prentice *et al*., in 1983, concluded that a higher rate of low birth weight infants was observed in women practising Ramadan, which is also a type of intermittent fasting. Other studies showed that maternal GDM leads to macrosomia and infants with high birth weight. Mothers who fasted 13 hours or longer, irrespective of GDM status, were at a higher risk of delivering a premature baby [36].

The baby's weight is majorly associated with women's carbohydrate intake [37]. Foetal carbohydrate uptake during the mother's IF depends on the mother's blood glucose level as well as contributions by hormonal, cardiovascular and metabolic adaptations [30]. Hence, IF in women with GDM is linked with an alteration in the frequency and pattern of human foetal breathing movements. The biophysical profile and foetal heart trace assessment were not affected due to GDM [35].

Conclusively, a mother performing IF during pregnancy, especially with GDM, poses a risk to the ideal growth and development of the foetus, the most common abnormalities being macrosomia which is excessive foetal birth weight, respiratory distress and hypoglycaemia. It can lead to premature birth and even foetal death in severe cases.

## DIETARY QUALITY AND COMPLIANCE IN WOMEN WITH GDM FOLLOWING IF

It has been observed that a reduction in body weight after GDM helps to reduce the risk of developing T2DM in the later part of life. The process of weight loss can be challenging for women with GDM. IF is an alternative form of continuous energy restriction. A randomized control trial was conducted to examine whether an intermittent 2-d very low-calorie diet was non-inferior to moderate daily caloric restriction over 12 months in overweight women with previous GDM. The study compared the dietary quality and compliance of women on intermittent energy restriction and continuous energy restriction. The study results demonstrated that a 2-d 500 kcal intermittent energy restriction diet results in comparable weight loss to a daily 1,500 kcal continuous energy restriction diet in the participants. The study also evaluated the participant's dietary quality-fats (monounsaturated fatty acids, polyunsaturated fatty acids, unsaturated fats and cholesterol), carbohydrates, fibre, total sugar, protein, caffeine, and alcohol intake – between 3 and 12 months of the participants. Wholes grains, pulses and fruits are good source of inositol, one of the reviews demonstrated that inositol (myo- inositol and D chiro-inositol) helps in sensitizing the insulin, which in turn helps in reducing the blood sugar levels [38, 39]. The study found a significant difference in the dietary quality of the participants on intermittent fasting compared to participants on continuous energy restriction. The latter had improved diet quality. According to the author, the common barriers faced by the participants were "finding it hard to stay on a diet" (n = 83, 69%). There is a further need to study the dietary quality and compliance of women with GDM on IF to understand the dietary characteristics of IF in GDM [40].

Hence, there is strong evidence that IF helps with weight loss in women with GDM. But the available evidence suggests dietary quality and compliance is affected by IF in women with GDM or with history of GDM. Hence, education is needed for women following IF.

## WEIGHT LOSS BARRIERS FACED BY WOMEN WITH GDM FOLLOWING IF

Ratner *et al*. explained that the reason to study the role of weight loss and its barriers in GDM is that it determines the future risk of T2DM [40]. Family environment (n = 67, 56%) and behavioural regulation (n = 83, 69%; n = 76, 63%) are the two main weight loss barriers faced by women with gestational diabetes following IF. The only way to surpass this hurdle is by using strategies to improve behavioural regulation and consideration of a dietary change in the family home setting. According to this study done by Gray *et al*., at 12 months, there was no significant relationship between weight loss and the barriers to weight loss (p > 0.05) [40]. For a successful intervention, it is important to understand the barriers faced by women to lose weight [41]. According to the author, the common

barriers faced by the participants were "finding it hard to stay on a diet" (n = 83, 69%) (Theoretical Domains Framework domain: behavioural regulation), "finding it hard to deal with hunger while on a diet" (n = 76, 63%) (Theoretical Domains Framework domain: behavioural regulation) and "family responsibilities taking priority over weight loss"(n = 67, 56%) (Theoretical Domains Framework domain: environmental context and resources). There were no significant differences in the barriers to weight loss and weight-loss success between intermittent dieters and continuous dieters.
Therefore, the barriers to weight loss, *i.e.*, family environment and behavioural regulation, can be tackled by appropriate strategies in both intermittent and continuous dieters.

## DISCUSSION AND CONCLUSIONS

The prevalence of GDM worldwide is increasing at an alarming rate, which needs to be addressed, and preventive measures must be researched extensively. GDM causes numerous short-term and long-term complications in the mother and the infant. It predisposes pregnant women to hypertension and preeclampsia. Similarly, the incompetence of the maternal-placental supply to fulfil the foetal nutrition requirements impacts a variety of neonatal adaptations and changes in growth and development. IF can be considered a weight loss option in women with GDM during pregnancy because it helps improve insulin resistance in the body. The choice of IF as a mode to lose weight long-term may benefit from an intervention focusing on improving dietary quality on fasting days. Considerable evidence supports the beneficial effects of IF on women with GDM through a mechanism that improves insulin sensitivity and lowers blood glucose levels. Although IF has shown protective effects on maternal health in women with GDM, it shows questionable results on neonatal outcomes. The infant is at risk of developing foetal hyperglycaemia, excessive birth weight, respiratory distress syndrome, foetal hypoglycaemia, prematurity, low calcium levels, and high bilirubin levels. Family environment and behavioural regulation are the two main weight loss barriers faced by women with GDM following IF. Conclusively, further research is needed to find a stronger interrelationship between IF and GDM and their associated factors.

### *Strengths and limitations of the review*

A strength of the present review is that the literature has been extracted from four different credible databases making it more reliable. A combination of appropriate keywords was used to filter the review, and research gaps have been defined in the review; hence, it can act as a reference for future studies. On the other hand, there are a few limitations in the review. Due to the lack of literature already present, a lesser number of papers were considered for this review, and old studies were included because the results are still relevant. In the absence of EQUATOR guidelines for a mini-review, we have used the narrative review checklist by the Academy of Nutrition and Dietetics.

## COMPLIANCE WITH ETHICAL STANDARDS

### *Authors contribution*

S.A., M.P.: Conceptualization, data curation, methodology, resources, visualization, writing – original draft, writing – review and editing. D.G.: Methodology, project administration, supervision, writing – review and editing.

### *Funding*

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### *Study registration*

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### *Disclosure of interests*

The authors declare that they have no conflict of interests.

### *Ethical approval*

N/A.

### *Informed consent*

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### *Data sharing*

N/A.

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