Original Article

Metabolic Profile of Offspring of Mothers with Gestational Diabetes Mellitus

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is defined as diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes before gestation. Unrecognized and untreated GDM confers significantly greater maternal and fetal risk, which is largely related to the degree of hyperglycemia. The specific risks of diabetes in pregnancy include but are not limited to, spontaneous abortion, pre-eclampsia, fetal anomalies, macrosomia, neonatal hypoglycemia, hyperbilirubinemia, and respiratory distress syndrome. Additionally, GDM is also implicated in long-term metabolic derangements in the offspring in the form of obesity/overweight, hypertension, dysglycemia, insulin resistance, and dyslipidemias later in life. To determine the prevalence of anthropometric and metabolic derangements in children between 1 and 5 years of age, born to women with GDM. **Methods:** This hospital-based cross-sectional study was conducted between November 2019 and November 2021 at our Pediatric Endocrine Clinic. Women were diagnosed as having GDM based on the American Diabetes Association Criteria (2019). History regarding the treatment of the GDM (diet only/diet and medical treatment) and detailed physical examination, including anthropometry and blood pressure, were recorded. Blood samples were collected from children for the estimation of their metabolic profile. **Results:** Overweight, obesity, and severe obesity were present in 18 (11.3%), 2 (1.3%), and 2 (1.3%) children, respectively. Hypertension was found in 21 (19.4%) children. Elevated LDL, triglyceride, and total cholesterol were seen in 3 (1.9%), 84 (52.5%), and 1 (0.6%) children, respectively. Impaired fasting glucose (IFG) was found in 6 (3.8%) children, while 27 (16.9%) subjects were found to be having impaired glucose tolerance after OGTT. Insulin resistance was found in 30 (18.8%) children. GDM mothers with a higher BMI tended to have children with a higher BMI (correlation coefficient, r = .414, $P < .001$). Higher serum triglyceride levels (r = −0.034, $P = 0.672$) were recorded in children, irrespective of the BMI of their mothers. There was no significant correlation of maternal BMI with blood pressure (r = −0.134, $P = 0.091$) or with HOMA-IR (r = 0.00, $P = 0.996$) in children. However, mothers with a higher BMI had children with statistically higher fasting blood glucose (r = +0.339, $P = <0.001$) as well as blood glucose 2 hours after OGTT (r = +0.297, $P = <0.001$). This positive correlation of maternal BMI with the glucose metabolism of their offspring was observed for both male and female genders. **Conclusion:** Children of women with GDM had a higher BMI, and the mode of treatment for GDM did not lead to differences in childhood BMI. The higher BMI of a GDM mother is associated with altered glucose metabolism in their offspring. Deranged levels of triglyceride across the gender were not found to be statistically significant. This has implications for future metabolic and cardiovascular risks in targeting this group for intervention studies to prevent obesity and disorders of glucose metabolism as one potential strategy to prevent adverse metabolic health outcomes.

Keywords: BMI, cardiovascular risk, gestational diabetes, metabolic profile, offspring

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. World Health Organization estimated that approximately 420 million people are affected by diabetes worldwide.[1] Gestational diabetes mellitus is defined as diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes before gestation. It is the most common medical complication of pregnancy. The prevalence of GDM in India ranges from 6 to 9% in rural

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and 12 to 21% in urban areas.[2] It is estimated that about 4 million women are affected by GDM in India, at any given point of time.[3] The prevalence of GDM is 11% higher among women from the Indian subcontinent than those from Europe.[4] The high rate implies that the Indian population has a higher incidence of DM and impaired glucose tolerance and is at a greater risk of developing GDM.

GDM is also implicated in long-term metabolic derangements in the offspring in the form of obesity/overweight, hypertension, dysglycemia, insulin resistance, and dyslipidemia. According to the International Diabetes Federation (IDF), approximately 16% of total births are complicated by hyperglycemia during pregnancy.[5] There is, however, insufficient evidence regarding whether treatment confers long-term metabolic benefits on offspring. This study is planned to identify metabolic derangements in children born to mothers with GDM at an early age and to initiate appropriate intervention.

Materials and Methods

This hospital-based cross-sectional study was conducted between November 2020 and November 2022 in the Pediatric Endocrine clinic.

A total of 160 apparently healthy children (1–5 years) born to GDM mothers attending Pediatric OPD were enrolled in the study after due consideration of inclusion and exclusion criteria. An informed written consent was obtained from the parents of children who were eligible for participation in the study. They were informed about the study protocol in detail before the commencement of the study. History regarding the treatment of the GDM (diet only/diet + metformin + insulin), detailed physical examination, including anthropometry and blood pressure, were recorded on the predesigned proforma. A blood sample was collected from children for the estimation of their metabolic profile. Fasting glucose, glucose after OGTT, and fasting lipid estimation were performed on the same day, while the sample for fasting insulin level estimation was stored at − 20°C until the time of analysis.

Data Management and Analysis: Statistical analysis was done using the Statistical Package for Social Science (IBM SPSS version. 20.0) Software for Windows. For categorical data, frequencies, and percentages with 95% CI were used. For normally distributed continuous data, description was done using the mean and standard deviation (SD), while Student's *t*-test and One-way ANOVA were used to compare the mean between two groups and more than two groups, respectively. For continuous data that were not normally distributed, the Mann–Whitney test or Kruskal–Wallis test was used as applicable.

Ethical Aspect

The Study Protocol was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College and Hospital, Faculty of Medicine (IEC/JNMC/551, dated 02/12/21). Written Informed consent for participation in the study as well as consent for blood sampling was obtained from parents/legal guardian of the children. They were informed about the study protocol in detail before the commencement of the study.

Results

The mean age of participants was 2.86 (±1.28) years with a male-to-female ratio of 0.92:1. Around three-quarters (71.9%) of children had their BMI within normal limits, while 14.4% of children had a BMI below the normal for age and sex. A total of 136 (85%) children had normal stature, and 24 (15%) children had short stature. Blood pressure was normal in 103 (64.4%) children, elevated in 26 (16.3%), stage 1 in 22 (13.8%), and stage 2 in 7 (5.6%) children [Table 1].

Table 2 shows the prevalence of an altered lipid profile in children of GDM mothers. LDL was within an acceptable range

Table 1: Prevalence of obesity and hypertension in offspring of GDM mother

Children attributes	Frequency (%)
BMI	
Underweight	23 (14.4)
Normal weight	115 (71.9)
Overweight	18 (11.3)
Obese	2 (1.2)
Severe obese	2 (1.2)
Blood pressure	
Normal	103 (64.4)
Elevated	26 (16.3)
Stage1	22 (13.8)
Stage2	9 (5.6)
Height	
Normal stature	136 (85)
Short stature	24 (15)

Table 2: Prevalence of altered lipid metabolism in children of GDM mother

Lipid profile	Frequency (%)
LDL	
Acceptable	153 (95.6)
Borderline	4 (2.5)
High	3 (1.9)
HDL	
Acceptable	18 (11.2)
Borderline	14 (8.8)
High	128 (80.0)
Triglyceride	
Acceptable	40 (25.0)
Borderline	36 (22.5)
High	84 (52.5)
Total cholesterol	
Acceptable	145 (90.6)
Borderline	14 (8.8)
High	1 (0.6)

for most study participants 153 (95.6%). HDL was observed to be high in 80% of the participants. Serum triglyceride levels were high in 84 (52.5%) and borderline in 36 (22.5%), while only 36 (22.5%) had normal triglyceride levels. Total cholesterol was acceptable in the majority of study participants 145 (90.6%).

Table 3 shows the insulin resistance indices of children and their association with gender. Overall, 133 (83.1%) children were found to have normal OGTT, and the remaining 27 (16.9%) had impaired OGTT. A total of 157 (98.1%) had normal fasting insulin, only 3 (1.9%) had high fasting insulin, and the difference between the two genders was not statistically significant ($P = 0.092$). With regard to HOMA-IR, 130 (81.3%) fell into the normal category, and 30 (18.8%) were insulin resistant. The difference with regard to the gender of the children was not significant ($P = 0.560$).

Correlation between insulin resistance and methods of treatment for GDM.

In the diet-only group, 19.40% of children were found to have insulin resistance compared to 15.40% in the diet + insulin group [$P = 0.787$, Figure 1].

Correlation between maternal BMI and BMI of children.

Table 3: Prevalence of altered glucose metabolism and insulin resistance in children of GDM mother

Variables	Frequency (%)
Fasting blood glucose	
Normal	154 (96.3)
Impaired	6 (3.8)
Blood glucose after OGTT	
Normal	133 (83.1)
Impaired	27 (16.9)
Fasting insulin	
Normal	157 (98.1)
High	3 (1.9)
HOMA-IR	
Normal	130 (81.3)
Insulin resistance	30 (18.8)

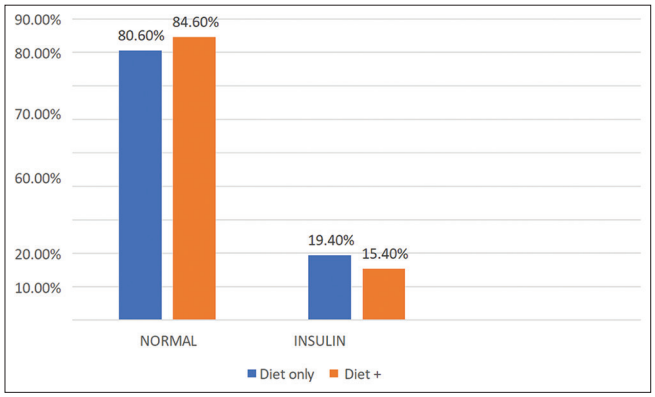

Figure 1: Association of HOMA-IR status of children with mode of treatment in mother

A statistically significant positive correlation was obtained between the BMI of mothers and their children, suggesting that mothers with a higher BMI tend to have children with a higher BMI as well [Pearson correlation, r = 0.414, $P < .001$, Figure 2].

Discussion

In our study, the prevalence of underweight was 14.4%, overweight was 11.3%, obesity was 2%, and severe obesity was 2% of the study population. The rest of the study population had their BMI within the normal limit. In the latest National Family Health Survey (NFHS 5), for under 5 years, the prevalence of underweight children at the National level was reported to be 32.1%, and the prevalence of obesity was 3.4%.[6] Hannah Nijs and Benhalima (2020)[7] in their narrative review found a higher prevalence of overweight and obesity in offspring exposed to GDM compared to unexposed offspring. In a prospective cohort study in Canada, Nicole Coles *et al*. (2020)[8] followed the children of GDM mothers. They reported a higher BMI z score in the offspring of GDM mothers at 3 years of age. While in another study, Mark B Landon *et al*. (2015),[9] found that the frequencies of BMI ≥95th (20.8% and 22.9%) and 85th (32.6% and 38.6%) percentiles were not significantly different in those who were treated as compared to untreated offspring ($P = 0.69$ and $P = 0.26$).

In our study population, blood pressure was within normotensive range in the majority of children—103 (64.4%), elevated in 26 (16.3%), stage 1 in 22 (13.8%), and stage 2 in 7 (5.6%) children. Other studies have explored the association of GDM with offspring blood pressure with conflicting findings. The initial Pima Indian studies (including 7–11 year age group) reported elevated systolic blood pressure in the offspring exposed to maternal diabetes (T2DM or GDM), independent of adiposity, compared to offspring born to mothers with a normal glucose tolerance during pregnancy who subsequently developed T2DM after pregnancy but before 40 years of age.[10] Landon MB *et al.* (2017)[11] found that maternal hyperglycemia in pregnancy is independently associated with the risk of abnormal glucose tolerance, obesity, and higher BP at 7 years of age. Aceti *et al*. (2012)[12]

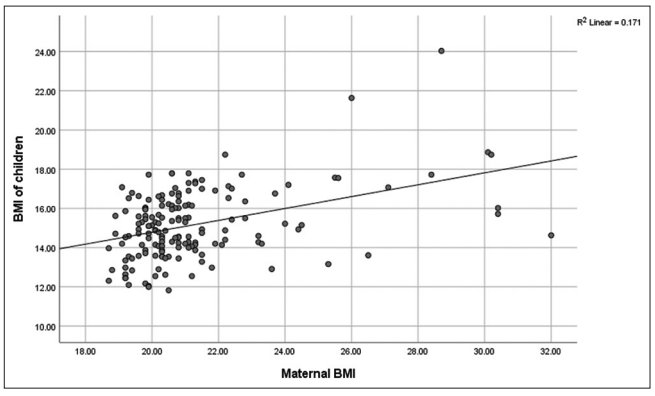

Figure 2: Correlation between maternal BMI and BMI of children

analyzed the relationship between diabetic pregnancy and offspring blood pressure in childhood. This study revealed that systolic BP was higher in the offspring of diabetic mothers (mean difference 1.88 mmHg [95% CI 0.47, 3.28]; $P = 0.009$). Offspring of mothers with gestational diabetes had similar diastolic BP to controls, but systolic BP was higher in offspring of mothers with GDM (1.39 mmHg [95% CI 0.00, 2.77]; $P = 0.05$).

We found high levels of LDL, TAG, and total cholesterol in 1.9%, 52%, and 0.6% of children, respectively. Beyerlein *et al.* (2012)[13] also reported that there was no difference in cholesterol levels in the offspring of GDM mothers at a mean age of 10.3 years compared to those of non-GDM mothers. However, similar to our study Wing Hung Tam *et al*. (2010)[14] in their small Chinese cohort reported lower high-density lipoprotein cholesterol at a median age of 8 years, but at a mean age of 15 years old, there were no significant differences in the lipid profiles of those born to mothers with GDM compared to controls. With the limited data available, it appears that in childhood, we cannot conclude on associations between maternal GDM and offspring lipid metabolism.

In our study, out of 160 children 6 (3.8%) had impaired fasting BG. We also found 133 (83.1%) children had normal OGTT and the remaining 27 (16.9%) had Impaired OGTT after 2 hours. However, Wing Hung Tam *et al*. (2017)[11] in their study in Hong Kong reported significantly higher odds of impaired OGTT (2hr) in children of GDM mothers compared to non-GDM mothers (Adjusted OR 2.00, 95% CI 1.21–3.31). Similarly, Maki Kawasaki *et al*. (2018)[15] in their systematic review also reported a higher 2 hr PG glucose in children of GDM mothers compared to controls. Research conducted by Sonali S. Wagle *et al.* (2021)[16] in Pune, India, found more glucose intolerant than ONDMs. On OGTT, the older ODMs (≥10 years) had a higher prevalence of glucose intolerance compared to ONDM.

With regard to HOMA-IR, 130 (81.3%) fell into the normal category, and 30 (18.8%) were insulin resistant. Like our study, Heike Boerschmann *et al*. (2010)[17] reported that HOMA-IR was increased in the offspring of mothers with gestational diabetes mellitus (OGDM) compared with the offspring of mothers with no gestational diabetes mellitus ($P = 0.01$, adjusted for sex and age). Ghattu V. Krishnaveni *et al*. (2015)[18] also reported higher insulin resistance (as assessed by HOMA-IR) than control children, even after controlling for age, sex, and socioeconomic status in multiple regression analyses. However, contrary results have also been reported in other studies. Carla A. Borgoño *et al.* (2012)[19] did their study and found that HOMA-IR at 1 year did not differ between infants born to mothers with and without GDM ($P = 0.74$).

Conclusions

The majority of children of GDM mothers in our study were of normal weight, and a considerably large proportion were found to have a deranged metabolic profile and high blood pressure levels. This underlines the importance of improving screening strategies, especially in low-income countries. Longer follow-up of the offspring of GDM mothers is necessary to definitively address the impact of maternal GDM on offspring metabolic health.

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Authors' contribution

NM: Drafting of manuscript, analysis of data, and critical review.
AA: Concept, Design, Analysis, Visualization, Interpretation of data, drafting of manuscript and critical review.
HA: Data acquisition and Review draft critically.
SM:
All the authors approved the final version of the manuscript to be published and agreed to be accountable for all aspects of the work.

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Conflicts of interest

There are no conflicts of interest.

References

1. Nanditha A, Ma RC, Ramachandran A, Snehalatha C, Chan JC, Chia KS, *et al*. Diabetes in Asia and the pacific: Implications for the global epidemic. Diabetes Care 2016;39:472-85.
2. Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, *et al*. Screening and diagnosing gestational diabetes mellitus. Evid Rep Technol Assess (Full Rep) 2012;1-327.
3. Kayal A, Mohan V, Malanda B, Anjana RM, Bhavadharini B, Mahalakshmi MM, *et al*. Women in India with gestational diabetes mellitus strategy (WINGS): Methodology and development of model of care for gestational diabetes mellitus (WINGS 4). Indian J Endocrinol Metab 2016;20:707-15.
4. Mistry SK, Das Gupta R, Alam S, Kaur K, Shamim AA, Puthussery S. Gestational diabetes mellitus (GDM) and adverse pregnancy outcome in South Asia: A systematic review. Endocrinol Diabetes Metab 2021;4:e00285. doi: 10.1002/edm2.285.
5. IDF Diabetes Atlas 10th Edition. International Diabetes Federation. Published 2021. Available from: https://diabetesatlas.org/data/en/. [Last accessed on 2023 Jan 28].
6. Blondeau B, Joly B, Perret C, Prince S, Bruneval P, Lelievre- Pegorier M, *et al*. Exposure in utero to maternal diabetes leads to glucose intolerance and high blood pressure with no major effects on lipid metabolism. Diabetes Metab 2011;37:245-51.
7. Nijs H, Benhalima K. Gestational diabetes mellitus and the long- term risk for glucose intolerance and overweight in the offspring: A narrative review. J Clin Med 2020;9:599. doi: 10.3390/jcm9020599.
8. Coles N, Patel BP, Birken C, Hanley AJ, Retnakaran R, K Hamilton J. Determinants of insulin resistance in children exposed to gestational diabetes in utero. Pediatr Diabetes 2020;21:1150-8.
9. Landon MB, Rice MM, Varner MW, Casey BM, Reddy UM, Wapner RJ, *et al*. Mild gestational diabetes mellitus and long-term child health. Diabetes Care 2015;38:445-52.
10. Bunt JC, Tataranni PA, Salbe AD. Intrauterine exposure to diabetes is a determinant of hemoglobin a(1)c and systolic blood pressure in pima Indian children. J Clin Endocrinol Metab 2005;90:3225-9.
11. Landon MB, Mele L, Varner MW, Casey BM, Reddy UM,

Wapner RJ, *et al*. The relationship of maternal glycemia to childhood obesity and metabolic dysfunction. J Matern Fetal Neonatal Med 2020;33:33-41.
12. Aceti A, Santhakumaran S, Logan KM, Philipps LH, Prior E, Gale C, *et al*. The diabetic pregnancy and offspring blood pressure in childhood: A systematic review and meta-analysis. Diabetologia 2012;55:3114-27.
13. Beyerlein A, Nehring I, Rosario AS, von Kries R. Gestational diabetes and cardiovascular risk factors in the offspring: Results from a cross-sectional study. Diabet Med 2012;29:378-84.
14. Tam WH, Ma RC, Yang X, Li AM, Ko GT, Kong AP, *et al*. Glucose intolerance and cardiometabolic risk in adolescents exposed to maternal gestational diabetes: A 15-year follow-up study. Diabetes Care 2010;33:1382-4.
15. Kawasaki M, Arata N, Miyazaki C, Mori R, Kikuchi T, Ogawa Y, *et al*. Obesity and abnormal glucose tolerance in offspring of diabetic mothers: A systematic review and meta-analysis. PLoS One 2018;13:e0190676.
16. Wagle SS, Phatak S, Ambardekar S, Dattatrey B, Deshmukh MK, Kamat R, *et al*. Overweight-obesity and glucose intolerance in offspring of Indian diabetic mothers. medRxiv 2021. doi: 10.1101/2021.05.17.21257222.
17. Boerschmann H, Pflüger M, Henneberger L, Ziegler AG, Hummel S. Prevalence and predictors of overweight and insulin resistance in offspring of mothers with gestational diabetes mellitus. Diabetes Care 2010;33:1845-9.
18. Krishnaveni GV, Veena SR, Jones A, Srinivasan K, Osmond C, Karat SC, *et al*. Exposure to maternal gestational diabetes is associated with higher cardiovascular responses to stress in adolescent Indians. J Clin Endocrinol Metab 2015;100:986-93.
19. Borgoño CA, Hamilton JK, Ye C, Hanley AJ, Connelly PW, Sermer M, *et al*. Determinants of insulin resistance in infants at age 1 year: Impact of gestational diabetes mellitus. Diabetes Care 2012;35:1795-7.