A Quantitative Analysis To Evaluate The Association Of Exposure To Organochlorine Pesticides In Gestational Diabetes Mellitus As Compared To Pregnant Women With Normal Glucose Tolerance Test

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KEYWORDS

Gestational Diabetes Mellitus; Organochlorine; Endocrine-Disrupting Chemicals; Insulin Resistance; Pesticides

ABSTRACT

Introduction: Gestational Diabetes Mellitus (GDM) is characterized by glucose intolerance during pregnancy, often asymptomatic but occasionally presenting with severe hyperglycemia. GDM affects 5% to 7% of pregnancies in high-income countries, while in India, it impacts up to 5 million women annually, leading to increased obstetrical complications and long-term health risks. In our study we estimate the levels of organochlorine pesticides in pregnant females, and determine the association of exposure to organochlorine pesticides in Gestational Diabetes Mellitus and in Pregnant women with Normal Glucose tolerance test.

Methods: The study was conducted as an observational cross-sectional study at Sarojini Naidu Medical College, Agra, over 1.5 years (November 2022 to April 2024). Pregnant women (n=100) aged over 18 years, including those with normal glucose tolerance and GDM, were included, while non-pregnant women and those with known diabetes mellitus were excluded. Data analysis involved descriptive statistics and inferential tests, with a significance level set at $p < 0.05$.

Results: GDM patients had a significantly higher mean age and BMI compared to non-GDM patients. Low HDL and high LDL levels were also significantly associated with GDM. Furthermore, levels of P, P'DDD and P, P'DDE were significantly elevated in GDM patients, suggesting a possible link between organochlorine exposure and GDM.

Conclusion: The study indicates a significant association between high BMI and GDM, as well as a positive correlation between organochlorine exposure and GDM. These findings underscore the need for lifestyle modifications and reduced use of organochlorine pesticides to lower GDM prevalence. However, further large-scale studies are necessary to validate these results.

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INTRODUCTION:

Gestational Diabetes Mellitus (GDM) is carbohydrates intolerance of variable severity first time diagnosed during pregnancy. Usually occurs in the second half of pregnancy. The pathogenesis of GDM involves pregnancy-induced insulin resistance exacerbated by inadequate pancreatic β-cell response. Genetic predisposition, evidenced by familial clustering and identified risk genes, suggests a multifaceted etiology. Non-genetic factors such as maternal age, obesity, diet, and lifestyle also contribute significantly.[1]

In high-income countries, GDM complicates 5% to 7% of pregnancies, while in India, it affects up 11%-14%women annually.[2] Recent trends indicate rising incidence, particularly among certain ethnic groups. GDM correlates with increased obstetrical complications like preeclampsia, cesarean delivery, and adverse fetal outcomes such as macrosomia and neonatal hypoglycemia. Moreover, prior GDM increases the risk of recurrence in subsequent pregnancies and predisposes to Type 2 diabetes and cardiovascular disease. [3,4]

In India, GDM prevalence ranges widely, influenced by variable screening program implementation despite governmental mandates.[5] Current research, predominantly urban and hospital-based, underscores gaps in rural and national data. Concerns over rising diabetes rates and associated GDM risk highlight the need for comprehensive epidemiological studies and improved screening strategies.

Endocrine-disrupting chemicals (EDCs), such as organochlorines like DDT and PCBs, are environmental contaminants linked to disrupted glucose metabolism and increased T2DM risk.[6,7] Their presence in everyday products poses developmental risks to fetuses, potentially

leading to intrauterine growth restriction and long-term health issues. This study seeks to clarify the connection between organochlorine exposure and GDM, addressing inconsistent evidence and advocating for safer pest control alternatives to reduce related health risks.

This study aims to evaluate the association between exposure to organochlorine pesticides in Gestational Diabetes Mellitus as compared to pregnant women with normal glucose tolerance test by estimating the organochlorine pesticide levels in pregnant women.

METHODS:

This hospital-based observational cross-sectional study was conducted at the tertiary centre of North India on 100 pregnant females who attended the outpatient department for routine antenatal check-ups over a span of 1.5 years, from November 2022 to April 2024., after obtaining consent from the patients.

Inclusion Criteria:

1) Pregnant females of age more than 18 years.
2) Pregnant females with normal glucose tolerance test
3) Pregnant females with Gestational diabetes mellitus

Exclusion Criteria:

1) Any non-pregnant female.
2) Pregnant female with a known case of diabetes mellitus.

Participants were divided into two distinct groups based on their glucose tolerance status:

Group 1 (Control Group): 50 pregnant females who exhibited a normal glucose tolerance test (GTT).

Group 2 (Study Group): 50 pregnant females diagnosed with Gestational Diabetes Mellitus (GDM) according to the criteria set by DIPSI.

Laboratory Investigations

Fasting Blood Glucose Levels, 2-Hour Post-Prandial Glucose Levels, Oral Glucose Tolerance Test (OGTT), Lipid Profile, Serum Organochlorine levels, Organochlorine Pesticide (OCP) Analysis

The following organochlorines pesticides were analyzed due to their known persistence and potential endocrine-disrupting effects:

- Beta-hexachlorocyclohexane (Beta-HCH)
- Dieldrin
- Endosulfan
- P,P’-dichlorodiphenyl-dichloroethylene (P,P’DDE)
- O,P’-dichlorodiphenyl-dichloroethylene (O,P’DDE)
- P,P’-dichlorodiphenyl-dichloroethane (P,P’DDD)

The data collected from the patients were compiled in a Microsoft Office Excel sheet and were analysed using SPSS software version 25.0. A p-value of < 0.05 was considered statistically significant. The results were displayed in tabular and graphical format.

OBSERVATIONS AND RESULTS:

Table 1: Association of Age between GDM and non-GDM

Variable		Mean ± SD	p-value
Age	GDM	28.28 ± 4.445	0.027
	Non-GDM	26.38 ± 4.035	

Table 2:ASSOCIATION OF BMI WITH GDM

Variable		Mean ± SD	p-value
BMI	GDM	25.34	<0.001
	Non-GDM	20.99	

Table 3: Association of HDL between GDM and non-GDM patients

Variable	Level (mg/dL)	GDM (%)	Non-GDM (%)	p-value
HDL	Acceptable 40-60	27.0%	36.0%	0.02
	Desirable > 60	8.0%	2.0%	
	Low < 40	15.0%	12.0%	

Table 4: Association of LDL between GDM and non-GDM patients

Variable	Level (mg/dL)	GDM (%)	Non-GDM (%)	p-value
LDL	Acceptable 100-129	2.0%	6.0%	0.04
	Borderline 130-159	1.0%	3.0%	
	Desirable <100	20.0%	25.0%	
	High 160-189	27.0%	16.0%	

Table 5: Association of P,P'DDD between GDM and non-GDM

Variable		Mean ± SD	p-value
P,P'DDD	GDM	0.53 ± 1.687	0.002
	Non-GDM	0.22± 0.09	

Table 6: Association of P,P'DDE between GDM and non-GDM

Variable		Mean ± SD	p-value
P,P'DDE	GDM	3.10 + 2.26	0.002
	Non-GDM	1.76 + 1.86	

RESULTS :

The study analyzed various parameters to compare Gestational Diabetes Mellitus (GDM) and non-GDM patients. The mean age of GDM patients was significantly higher than that of non-GDM patients (p=0.027)(Table 1). The mean period of gestation (POG) was slightly higher in GDM patients, but this difference was not statistically significant (p=0.858). GDM patients had a significantly higher mean BMI compared to non-GDM patients (p<0.001)(Table 2).

Total cholesterol levels were higher in GDM patients, though notstatistically significant (p=0.114). Low HDL levels were more common in GDM patients and were statistically significant (p=0.02),high LDL levels more common in GDM patients as compare to non GDM patients and were statistically significant (p=0.04)(Table 3,4). Triglyceride levels were elevated in GDM patients but without statistical significance (p=0.512).

Beta HCH,Endosulfan, and Dieldrin levels were higher in GDM patients, but none showed statistical significance. Conversely, P,P'DDD and P,P'DDE levels were significantly higher in GDM patients as compare to non GDM patients (p=0.002), while O,P'DDE levels were higher in non-GDM patients, though not statistically significant (p=0.972)(Table 5&6).

DISCUSSION :

Endocrine disrupting chemicals (EDCs) can interfere with the endocrine system, increasing the risk of Type 2 Diabetes Mellitus (T2DM). Pregnant women are particularly vulnerable to EDC exposure, with over 50 chemical combinations. A study aimed to study the clinical profile and pattern of exposure of various organochlorines and their association with GDM in 100 pregnant females.

In our study, mean age of studied case was 27.33 ± 4.33 years (28.28 ± 4.445 for GDM cases and 26.38 ± 4.035 for non-GDM cases) and the participant's age ranged from 20 to 36 years which was comparable to findings of **Shapiro GD et al [8]**In this study, the mean period of gestation (POG) averages 26.26 weeks, with a standard deviation of 2.21 weeks. The range is from 20 to 32 weeks, indicating that the sample includes participants at various stages of their pregnancies, predominantly in the mid to late second trimester. The mean POG of GDM patients was slightly higher than non-GDM patients and but not found statistically significant, (p-0.858) (26.30 ± 2.50 for GDM cases and 26.22 ± 1.909 for non-GDM cases). Findings were consistent with **Robledo C et al [9].**

In present study, mean BMI of GDM patients was 25.34 while that of non-GDM was 20.99 with a p value of <0.001 making association significant. Over weight is a risk factor for insulin resistance and metabolic syndrome. Close findings were seen in systemic review by **Fatemeh et al .**

We study the levels of Total cholesterols (TC), Triglycerides (TG),LDLs (low density lipoproteins) and HDL(high density lipoprotein) in GDM and non-GDM cases. In our research there was no remarkably significant difference in TG and TC levels in GDM and non-GDM group, whereas there was remarkably significant difference found in LDL and HDL level in GDM cases as compare to non-GDM cases. **Wabg J et al[10]**reported that throughout the course of pregnancy, there was a gradual increase in TGs, TCs, LDL level, and the TG/HDL-C ratio; in contrast, HDL-C levels increased throughout the first and second trimesters, with a minor drop in third. They draw a conclusion that a higher risk of glucose intolerance was linked to mother age, pre-pregnancy BMI, and TG/HDL ratio in the first trimester.

In our study we measured 6 Organochlorine compound (Endosulfan, Beta HCH, Dieldrin, O, p´DDE, P, p´DDD and P, p´ DDE) in both GDM cases and non-GDM cases.The mean Endosulfan level was 174.82pg/ml, with a substantial standard deviation of 66.416, reflecting high variability. The levels of Endosulfan were in GDM group (mean = 179.32) as compared to non-GDM group (mean = 170.32), indicating no statistically remarkably difference (p= 0.50).The mean Beta- HCH (beta-hexachlorocyclohexane) level was 2.35pg/ml, with a high standard deviation of 6.76, indicating significant variability. Beta- HCH levels in non-GDM (mean = 1.10) and GDM (mean = 4.70), did not show statistically significant difference (p = 0.55).

Dieldrin levels average 1.32pg/ml, with a standard deviation of 6.27, suggesting variability among participants. However, Dieldrin levels, although more in the GDM cases (mean = 2.17) as compared to cases of non-GDM (mean = 0.47), but not show a statistically remarkable difference (p > 0.05).The average O, p´DDE(O,p´- dichlorophenyl-dichloroethylene) level is 3.64 pg/ml, with a high standard deviation of 3.97, indicating substantial variability. In contrast, O, p´DDE levels were slightly more in the non - GDM cases (mean = 3.65) compared to the GDM cases(mean = 3.63), but not show a statistically significant difference (p= 0.972). The average P, p´DDD(P,p´- dichlorophenyl - dichloroethane) 0.26 µg/L with a high deviation

of 1.216,suggesting variability among participants. Similarly P, p´ DDD concentration were in GDM cases (mean 0.53) compared to non-GDM cases (mean 0.22) indicating statistically significant(p value 0.002).The average P, p´ DDE(P, p´- dichlorophenyl-dichloroethylene) level was 2.43µg/L, with a standard deviation of 2.170. P, p´ DDE levels revealed a significant difference between non-GDM (mean = 1.76) and GDM (mean = 3.10) groups ($p < 0.05$).

In our study, the correlation analysis highlighted significant positive correlations between OGTT results and several biochemical markers. Specifically, OGTT showed significant correlations with P, p´ DDD (p value 0.02) and P, p´DDE ($p = 0.02$). These correlations suggest that more levels of these markers are correlated with higher OGTT values, indicating their potential role as predictors or contributors to gestational diabetes. The descriptive statistics indicate considerable variability in biochemical markers among the participants. These findings highlight the momentousness of considering individual differences when estimating the influence of these markers on health consequence, particularly in context of gestational diabetes mellitus.

Jiayu Shi et al [11] conclude that of the 6 OCPs explored from their research, p,p'-DDE and βeta-BHC were remarkably associated to T2DM. **Rodrigo et al [12]** study reveal a definite correlation between prevalence of DM and an OCP combination whose main composition arose from p, p'-DDE, o,p'-DDE and HCB,.**Xiangming Y et al [13]**reported There was no discernible relationship between GDM and the other four OCPs.

Tawar N et al [14] found that delta-HCH ($p < 0.01$), hept-achlor ($p < 0.05$), and endrin ($p < 0.05$) were positively correlated with indicators of Endoplasmic reticulum stress and central obesity.**Tyagi S et al [15]** come to the conclusion that when groundwater OCP levels rise, so does the blood OCP level, which tends to raise the possibility of T2DM.**Xu Han et al [16]** concluded OCP exposure is remarkably associated with increased risk of type 2 diabetes in individual of this study.

Sarah I Daniels et al [17] found that that Compared to European whites, immigrants from South Asia had a greater body load of OC pesticides. In this cohort, elevated concentration of βeta-HCH and p,p′-DDE (dicholoro-diphenyl-dichloroethylene) are linked to diabetes mellitus.

Shapiro GD et al [8] reported that there was no proof linking OC insecticides to either GDM or IGT during pregnancy.**Mengling Tang et al [18]**conclude that exposure to organochlorine pollution is related to a higher incidence chance of type 2 diabetes.**Lee DH et al [19]** concluded that among OC insecticides, both trans-nonachlor and p,p´ DDE(dicholoro-diphenyl-dichloroethylene) expressed statistically remarkable associations with prevalent type 2 diabetes.

Turky M et al[20]come to the conclusion that DDE exposure was linked to diabetes incidents.**Rignell et al [21]** reportedthat there was definitive association between subjection to p,p'-DDE in human, increased chance of T2DM..**Saldana TM et al [22]** reported that in women who exposed to OC pesticides during the early phase of pregnancy associated with agricultural exposures had a 2 fold elevated chance of occurring of GDM ($P<0.0001$).

CONCLUSION:

The study highlights that a high Basal Metabolic Index (BMI) is significantly associated with an increased risk of Gestational Diabetes Mellitus (GDM), suggesting that lifestyle modifications to lower BMI could reduce the risk of GDM and its complications. Additionally, the study found a significant positive correlation between exposure to organochlorine compounds (P, p´ DDD and P, p´ DDE) and GDM, indicating that these chemicals may contribute to the rising prevalence of GDM in developing countries. Reducing or restricting the use of organochlorine pesticides could help lower GDM rates. National policies should focus on minimizing the use of these pesticides and promoting alternatives, as seen in developed countries. However, the study's cross-sectional design, small sample size, and

inability to assess long-term exposure effects limit its findings, emphasizing the need for larger, long-term cohort studies to validate these results.

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