



ORIGINAL ARTICLE

Dyslipidemia and atherogenic index of plasma in gestational diabetes mellitus with vitamin B12 deficiency.

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ABSTRACT... Objective: To determine frequency of vitamin B12 deficiency and dyslipidemia and calculate atherogenic index of plasma (AIP) in Gestational Diabetes mellitus (GDM). **Study Design:** Observational study. **Setting:** Department of Biochemistry, Liaquat University Jamshoro. **Period:** January 2018 to December 2019. **Material & Methods:** 216 cases of GDM were selected by inclusion criteria. Venous blood sampling collected blood sample that were centrifuged to get sera. Glucose, vitamin B12, and blood lipids were estimated by standard methods. Atherogenic Index of Plasma (AIP) was calculated as log TAG/HDLc ratio. Data was analysed by SPSS 21.0 ver. at 95% CI ($P \leq 0.05$). **Results:** Vitamin B12 deficiency and Dyslipidemia were noted in 151 (69.9%) and 165 (23.61%) of GDM cases respectively ($P=0.0001$). Vitamin B12 was found low as 156.62 ± 82.9 ng/mL. TC (244.07 ± 49.11), TAGs (699.4 ± 249.5), and LDLc (137.9 ± 40.84) were found high and HDLc (33.13 ± 5.71) was low. High and medium risk AIP was noted in 17 (7.87%) and 29 (13.4%) of GDM cases ($P=0.0001$). Vitamin B12 proved negative TC ($r = -0.25$, $P=0.02$), TAG ($r = -0.23$, $P=0.02$), LDLc ($r = -0.79$, $P=0.0001$) and positive correlation with HDLc ($r = 0.76$, $P=0.0001$). **Conclusion:** Vitamin B12 deficiency and Dyslipidemia were noted in 151 (69.9%) and 165 (23.61%) of GDM cases respectively. High and medium risk AIP was noted in 17 (7.87%) and 29 (13.4%) of GDM cases.

Key words: Atherogenic Index, Dyslipidemia, Vitamin B12 Deficiency.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a metabolic disorder of blood glucose homeostasis characterized by hyperglycemia of variable severity and glucosuria noted first time during pregnancy.^{1,2} 80 – 90% of pregnant women are diagnosed as GDM for the first time in pregnancy. Predisposing factors include high body mass index ($>25\text{kg}/\text{m}^2$), family history, macrosomia, previous GDM, polyhydramnios, and women of South East Asia, Black Caribbean, and Middle East, etc. Other risk factors are the polycystic ovarian syndrome (PCOS), pregnancy induced glucosuria, and pregnancy induced hypertension, congenital anomalies, still births, miscarriage, unexplained fetal deaths, etc.^{1,2} IDF shows 16% GDM cases with an incidence of $>200,000$ cases annually. However, incidence varies according to the ethnicity, screening programs, and GDM

criteria of diagnosis used. Its prevalence is inclining in the low and middle income countries. Insulin resistance is common feature of GDM diagnosed at the end of 2nd trimester. GDM appears when pancreatic β -cell function is not sufficient to overcome the anti – insulin hormones and insulin resistance.^{1,2} Metabolic derangement of GDM is aggravated by concomitant malnutrition and vitamin deficiencies. As the B –complex vitamins are essential for glucose metabolism³, this results in altered levels of blood lipids called the dyslipidemia. Dyslipidemia is defined as elevated blood cholesterol and triglycerides in presence of low HDLc.⁴ Deficiency of vitamin B12 has been associated with dyslipidemia in diabetics. Vitamin B12 is an essential vitamin of B- complex family and its deficiency is well noted in general and diabetic populations. Vitamin B12 is needed for DNA methylation,

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lipid metabolisms, cell proliferation, and nuclear division. Its deficiency is linked with dyslipidemia and endothelial dysfunctioning.⁵ Vitamin B12 deficiency is linked with coronary artery disease (CAD), myocardial ischemia, cerebral ischemia, diabetic microvascular complications such as neuropathy.^{5,6} Vitamin B12 deficiency is associated with birth defects, brain malformations, defective myelination, polyhydramnios, respiratory distress syndrome, fetal malformations and still births.^{6,7}

However, scarcity of research is lagging on the epigenetic effects of vitamin B12 deficiency during pregnancy.⁸⁻¹⁰ The present study was conducted to determine frequency of dyslipidemia and atherogenic index of plasma in Gestational Diabetes mellitus with vitamin B₁₂ deficiency.

MATERIAL & METHODS

An observational study was conducted at the Department of Biochemistry, Liaquat University of Medical and Health Sciences, Jamshoro. Study was conducted from January 2018 to December 2019. Patients were collected from the Department of Gynecology and Obstetrics, Liaquat University Hospital Jamshoro/Hyderabad. A sample of 216 diagnosed cases of Gestational Diabetes mellitus (GDM) were collected through non-probability purposive technique. GDM was defined according to the American Diabetes Association.⁸ Inclusion criteria were; diagnosed GDM cases, age 20 – 40 years, 2 – 3 trimester of pregnancy, and single fetus. Already diagnosed cases of DM, metformin therapy, insulin resistance, polycystic ovarian syndrome (PCOS) and those suffering major systemic illness were excluded from study protocol. Volunteers GDM cases were interviewed about purpose of study. They were informed that study will cause no harm to them and their babies. Only those pregnant ladies were included who gave a volunteer consent.

Patients were examined by a senior consultant gynecologist before entry into the study protocol. Patient's data and findings of physical examination were saved in a proforma. Patient's personal data was kept confidential in lockers. Only principal investigator had access to the Biodata and physical examination findings. Study

was taken permission from institutional ethics committee (LUMHS/REC/634). Patients handling was according to the "Helsinki's Declaration" for conducting human research. Volunteer GDM cases were asked for venous blood sample collection from a prominent peripheral vein preferably of upper arm. 5 ml venous sample was taken in a sodium fluoride containing glass tubes. Sera were got by centrifuging blood at x3000 rpm for fifteen minutes. Sera were preserved at – 20 °C temperature in refrigerators. Sera was used for glucose estimation by hexokinase method and vitamin B12 by ELISA method⁹ using commercial kit (Abcam, USA). Blood total cholesterol (TC), triglycerides (TAGs), LDLc and HDLc were detected using Cobas chemistry analyzer. Atherogenic Index of Plasma (AIP) was calculated as log TAG/HDLc ratio.¹⁰ AIP grading was done as; low risk (- 0.3 – 0.1), medium risk (0.1 – 0.24) and high risk (>0.24).¹⁰ Results were analysed on SPSS 21.0 ver. Categorical variables were calculated by CHI-square test and continuous variable were calculated by Student's t-test. Output of categorical results was presented as frequency and % while, continuous output was tabulated as mean+/- SD. Data analysis level of significance was 95% CI (P≤0.05).

RESULTS

Mean (±SD) age, fasting and random blood glucose, vitamin B₁₂, total cholesterol (TC), triglycerides (TAGs), low (LDLc) and high density (HDLc) lipoproteins cholesterol of GDM cases is shown in Table-I. Vitamin B₁₂ was found low as 156.62±82.9 ng/mL. TC (244.07±49.11), TAGs (699.4±249.5), and LDLc (137.9±40.84) were found high and HDLc (33.13±5.71) was low. Vitamin B₁₂ deficiency and Dyslipidemia were noted in 151 (69.9%) and 165 (23.61%) of GDM cases respectively (P=0.0001). High and medium risk AIP was noted in 17 (7.87%) and 29 (13.4%) of GDM cases (P=0.0001). Vitamin B₁₂ proved negative TC (r= -0.25, P=0.02), TAG (r= -0.23, P=0.02), LDLc (r= -0.79, P=0.0001) and positive correlation with HDLc (r= 0.76, P=0.0001) (Figure-1 to 4).

Variable	GDM Cases	
	Mean	SD
Age (years)	36.29	9.434
FBS (mg/dl)	136.27	35.35
RBS (mg/dl)	254.25	65.92
Vitamin B ₁₂ (ng/mL)	156.62	82.95
TC (mg/dl)	244.07	49.11
TAGs (mg/dl)	699.46	249.53
LDLc (mg/dl)	137.97	40.84
HDLc (mg/dl)	33.13	5.71

TC- total cholesterol
GDM – gestational diabetes mellitus

Table-I. Biochemical findings in GDM cases. (n=216)

	GDM Cases		X ² -Value	P-Value
	Frequency	%		
Yes	151	69.9	107.00	0.0001
No	65	30.09		
Total	216	100		

GDM – gestational diabetes mellitus

Table-II. Vitamin B₁₂ deficiency in GDM cases (n=216)

	GDM Cases		X ² -Value	P-Value
	Frequency	%		
Yes	51	23.61	353.00	0.0001
No	165	76.38		
Total	216	100		

GDM – gestational diabetes mellitus

Table-III. Dyslipidemia in GDM cases. (n=216)

Categories	Aip Risk Score		X ² -Value	P-Value
	Frequency	%		
Low risk (-0.3–0.1)	170	78.7	678.0	0.0001
Medium risk (0.1–0.24)	29	13.41		
High risk (>0.24)	17	7.87		
Total	216	100		

Table-IV. Atherogenic index of plasma.

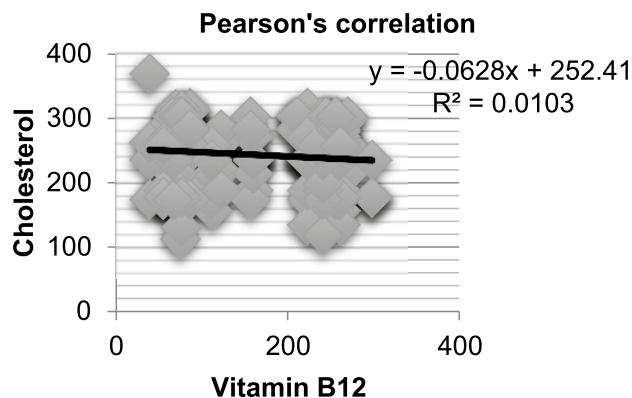


Figure-1. Curve show negative correlation of cholesterol and vitamin B₁₂ (r= - 0.25, P=0.02)

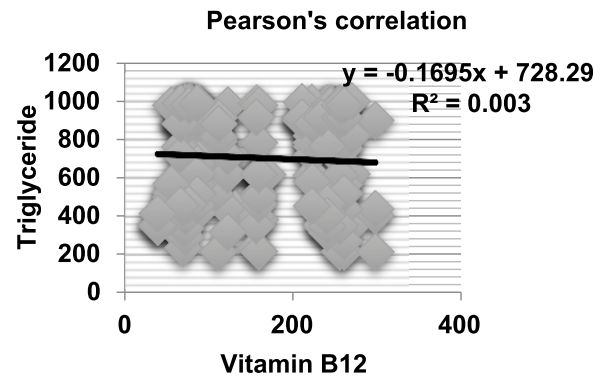


Figure-2. Curve shows negative correlation of triglycerides and vitamin B₁₂ (r= - 0.23, P=0.02)

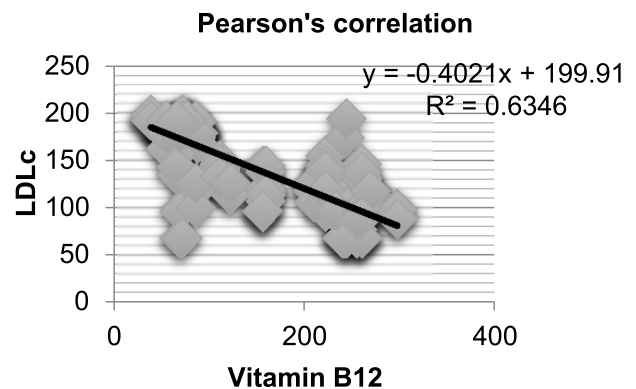


Figure-3. Curve shows negative correlation of LDLc and vitamin B₁₂ (r= - 0.79, P=0.0001)

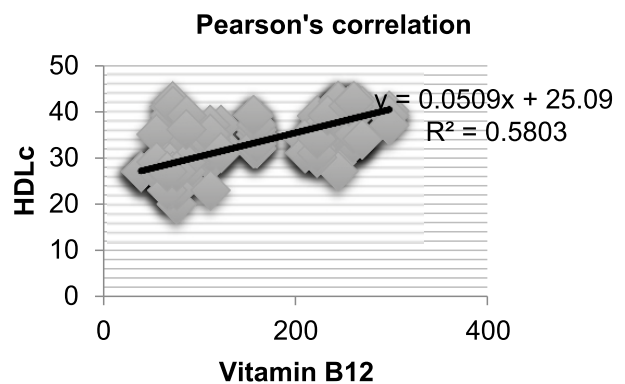


Figure-4. Curve shows positive correlation of HDLc and vitamin B₁₂ (r= 0.76, P=0.0001)

DISCUSSION

Gestational Diabetes mellitus is a grave complication of pregnancy induced hormonal imbalance in peculiar ethnicity and varies in geographical areas. Present observational is the first reporting on the frequency of dyslipidemia

and atherogenic tendency (AIP) in vitamin B12 deficient GDM cases. We found vitamin B₁₂ deficiency and Dyslipidemia were noted in 151 (69.9%) and 165 (23.61%) and high and medium risk AIP was noted in 17 (7.87%) and 29 (13.4%) of GDM cases (P=0.0001). The findings are consistent with previous studies.^{5,7} Nutritional deficiency of vitamin B12 is highly prevalent in the Pakistan^{11,12} and its deficiency in GDM may complicate the health of pregnant mothers and babies equally.^{11,13} The present study highlights the issue of pregnant women suffering GDM and concomitant vitamin B12 deficiency, dyslipidemia and atherogenic tendency. The findings are in agreement with previous studies.^{13,14}

Deficiency of vitamin B12 in pregnant mothers has been reported previously.^{15,16} A previous study reported occurrence of insulin resistance and increased adiposity in vitamin B12 deficient pregnant female.¹⁶ The study concluded the risk of GDM is doubled in vitamin B12 deficient pregnant female. Our findings are supported by both above studies.^{15,16} In present study vitamin B₁₂ deficiency was found in 69.9% of total study sample that is in agreement with a previous study¹⁷ that found 67% vitamin B12 deficiency in pregnant female. Deficiency of vitamin B12 deficiency is already highlighted by previous studies.^{11,12} Nutritional deficiencies are prevalent in the developing countries and similar is scenario of Pakistan.¹¹ However, it is very astonishing the vitamin B12 deficiency has been reported in pregnant women of developed country¹⁸, whose food intake is labeled as balanced diet. In present study we noted dyslipidemia in the 165 (23.61%). High and medium risk AIP was noted in 17 (7.87%) and 29 (13.4%) of GDM cases (P=0.0001) in present study. Finding of AIP is first analyzed in GDM cases from our institute and is incomparable. The present study noted vitamin B₁₂ proved negative TC (r= -0.25, P=0.02), TAG (r= -0.23, P=0.02), LDLc (r= -0.79, P=0.0001) and positive correlation with HDLc (r= 0.76, P=0.0001). The finding is in agreement with a previous report.¹⁸ Vitamin B12 deficiency in GDM cases has been reported by a previous study¹⁹ from UK and further added the risk of GDM is increased 2.59 time in vitamin B12 deficient pregnant female.

We conclude the pregnant female suffering from gestational diabetes mellitus need utmost monitoring of vitamin B12 screening and supplementation to prevent grave complications of dyslipidemia and atherogenicity. The present research is an observational study conducted with small sample size with confounding factor of nutritional deficiency, hence finding is not justified to generalize to other geographical areas.

CONCLUSION

We found increased frequency of cases vitamin B₁₂ deficiency and dyslipidemia in of GDM cases respectively. High and medium risk of atherogenicity (AIP) was increased GDM cases. Vitamin B12 shows negative correlation with total cholesterol, triglycerides, and low density lipoproteins (LDLc). Vitamin B12 screening may be adapted as routing screening test in gestational diabetes mellitus to prevent grave complications in mothers and their babies.






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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Shehmeen Khan	Conception and design, Statistical expertise, Critical revision.	
2	Sabreena Abbas	Critical revision of the article for important intellectual content.	
3	Afsheen Abro	Critical revision of the article for important intellectual content.	
4	Beenish Ghafar Memon	Critical revision of the article for important intellectual content.	
5	Farhat Sultana	Data collection, Drafting of the article.	
6	Hafsa Usman Shaikh	Data collection, Drafting of the article.	