Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE

DOI: 10.53555/jptcp.v30i18.3172

A COMPARATIVE STUDY OF C-PEPTIDE AND OTHER SURROGATE MARKERS OF INSULIN RESISTANCE IN GESTATIONAL DIABETES MELLITUS

Dr. M. Lenin[1], Dr. J. Sivakumar[2], Dr. Kuzhandi velu[3] Dr. S. SelvaKumar[4], Dr. Ramesh Ramasammy[5]

[1]Assistant Professor, Sri Lakshmi Narayana Institute of Medical science Puducherry, Leninaug1989@gmail.com

[2]Professor, Department of Biochemistry, Dhanalakshmi Srinivasan Medical college and Hospital, Perambalur, Tamil Nadu, drselvaphysiology@gmail.com

[3]Assistant Professor, Department of Biochemistry, Mahatma Gandhi Medical college and Research Institute, Pondicherry

[4]Assistant professor, Department of Physiology, Dhanalakshmi Srinivasan Medical college and

[5]*Professor, JIPMER, Puducherry Rameshrdr30@gamil.com

***Corresponding Author:** Dr. R. Ramesh Ramasammy

*Professor, JIPMER, Puducherry Rameshrdr30@gamil.com

AIM: The current study aimed to investigate the relationship between C-peptide and other surrogate markers in patients with gestational diabetes mellitus in the Puducherry population.

Methodology: Five milliliters of venous blood (without anticoagulant) were drawn from pregnant women with and without GDM. The fasting glucose level was determined using the glucose oxidase method (GOD-POD), and the fasting lipid profile (total cholesterol, TAG-C, HDL-C, and LDL-C) was measured using an auto analyzer and the IFCC Approved method. Insulin resistance markers

such as c-peptide and HOMA-IR were calculated. Insulin levels were calculated. Insulin was measured using chemiluminescence technology in a Roche auto analyzer (cobas e411).

Result: C-peptide had a strong relationship with insulin and HOMA-IR. In GDM, C-peptide has a higher sensitivity (88%) and specificity (89%). Conclusion: This study found a link between C-peptide levels and insulin levels in GDM patients in Puducherry, and C-peptide levels are predictive of GDM.

Conclusion: C-peptide can also be used to determine glycemic control status. C-peptide levels are used to predict gestational diabetes mellitus**.**

Keywords; Gestational diabetes mellitus, C-peptide, Insulin Resistance, HOMA-IR,

Introduction

GDM (gestational diabetes mellitus) is defined as carbohydrate intolerance that occurs or is first recognised during pregnancy after 20 weeks of gestation (1). According to recent data, our country has a 16.55 percent prevalence of GDM. Pregnant women with GDM account for 90-95 percent of pregnancy-complicating diabetes. Women who have GDM are more likely to develop GDM in subsequent pregnancies. (2). GDM has been linked to a number of biochemical events, including oxidative stress, insulin resistance, preeclampsia, hyperglycemia, macrosomia, and maternal hormonal changes (3). The presence of GDM in a pregnancy increased the risk of perinatal morbidity and mortality (4). Some pregnant women with limited beta cell capacity for pregnancy compensation will have induced insulin resistance due to genetic variations that are responsible for insulin secretion and carbohydrate utilisation are more susceptible to GDM. (6).

C-peptide has been identified as a surrogate marker for diabetes mellitus. C-peptide is the connective peptide between insulin chains A and B. This is essential for insulin biosynthesis and processing. Preproinsulin is first translocated into the endoplasmic reticulum of pancreatic beta cells with an A-chain, C peptide, a B-chain, and a signal sequence in the insulin synthesis pathway. A signal peptidase cleaves the signal sequence from the N-terminus of the peptide, resulting in proinsulin. The C-peptide is removed after proinsulin is packaged into vesicles in the Golgi apparatus (Beta granules), leaving the A-chain and B-chain bound together by disulphide bonds to form the insulin molecule. C-peptide is an endogenous marker of pancreatic beta cell function that is secreted in response to enteral and blood glucose levels (7). Ahren and Larsson 2002 et al. discovered that decreased C-peptide secretion can result in glucose intolerance. (8). As a result, the current study was designed to investigate the relationship of C-peptide and other surrogate markers in pregnant women with gestational diabetes mellitus in the Puducherry population (9), which will aid us in determining the functional utility of beta cells in the pancreas.

Materials and Methods:

The current case-control study was conducted at a tertiary health care facility in Puducherry, with approval from the Institute's human ethics committee and written informed consent from study subjects. The pregnant women were selected from Tamil Nadu and Puducherry and ranged in age from 20 to 38 years. DIPSI (Diabetes in Pregnancy Study Groups India) criteria were used to screen both primi and multigravida women for GDM at 24-28 weeks of gestation. Following screening, 100 pregnant women with GDM and 100 pregnant women without GDM were included in this study. Exclusion criteria include those suffering from chronic diseases such as T2DM, autoimmunity, and inflammatory disease..

Blood sample collection:

A venous blood sample of five millilitres (without anticoagulant) was collected from pregnant women with and without GDM. After allowing the blood samples to clot at room temperature, they were separated and stored at -20oC. The fasting glucose level was determined using the glucose oxidase method (GOD-POD), and the fasting lipid profile (total cholesterol, TAG-C, HDl-C, and LDL-C) was measured using an auto analyzer and an IFCC-approved method. Insulin resistance markers such as c-peptide and HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) were calculated. Insulin was measured using chemiluminescence technology in a Roche auto analyzer (cobas e411). A formula was used to calculate insulin resistance and sensitivity using the HOMA-IR and QUCKI (The quantitative insulin-sensitivity check index) indices.

Insulin Resistance calculations:

HOMA-IR = Fasting glucose (mg/dL) ×Fasting Insulin (mIU/mL)/405

QUICKI = (1/log (fasting Insulin (mIU/mL) + log (fasting glucose (mg/dL))

Statistical Analysis:

In the current study, descriptive and inferential statistical analysis were performed in MS EXCEL. All continuous measurement results were presented as mean SD, and categorical measurement results were presented as number and percentage. For data analysis, the statistical software SPSS17, Medcal online version, and Epidata were used. To determine the significance of the study subjects, an independent student test was used. Pearson correlation and odds ratio analysis were used to investigate the relationships between C-peptide and biochemical markers in the study subjects.

RESULTS:

Based on the inclusion and exclusion criteria, the study subjects were divided into two groups: 100 pregnant women with GDM (case group) and 100 pregnant women without GDM (control group). Table.1 depicts the comparison of biochemical markers between case and control groups. A statistical analysis revealed a significant difference in DIPSI (p=0.00), HbA1c (P=0.03*), and Insulin (P=0.00) levels between pregnant women with GDM and non-GDM. There was no statistically significant difference in fasting glucose levels between pregnant women with GDM and those who did not have GDM

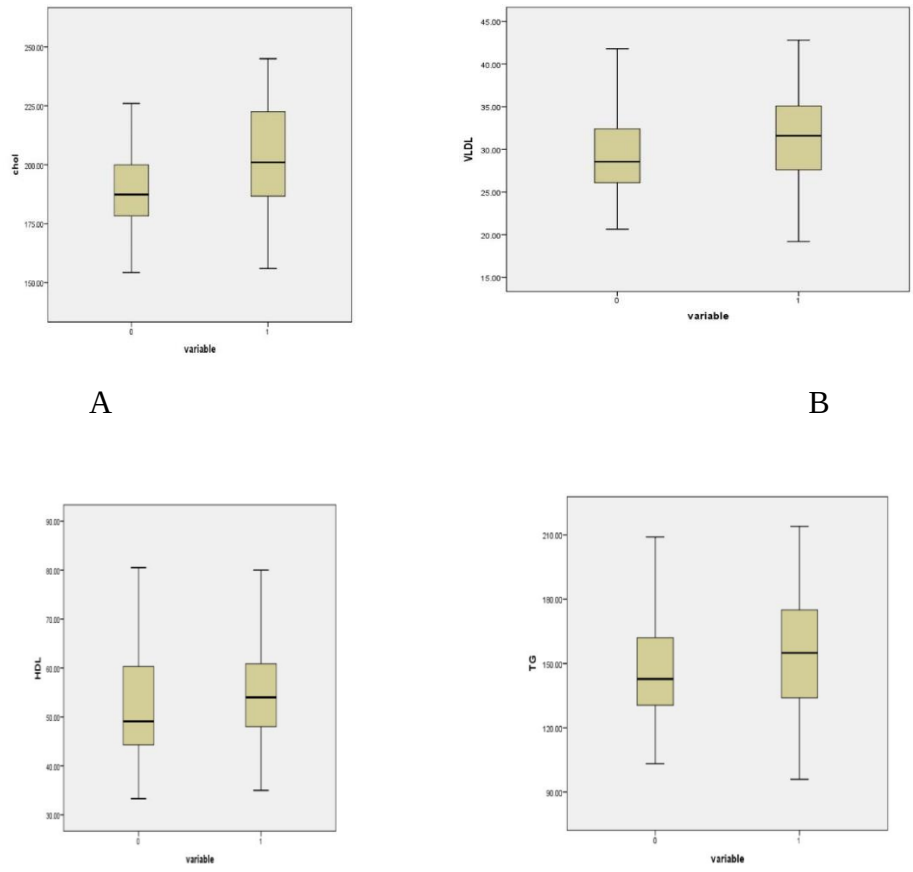

Image 1: Box plot of lipid profile, A- cholesterol, B-Very low density lipoprotein, C-High Density lipoprotein

Image 1 depicted The line within the box represents the median for each plot of lipid profile levels. The box's lower and upper lines represent the 25th and 75th percentiles, respectively. Cholesterol, HDL-C, and LDL-C levels were found to be significantly higher in the GDM and non-GDM groups. TGL-C and VLDL-C showed no significant differences between GDM and non-GDM groups.

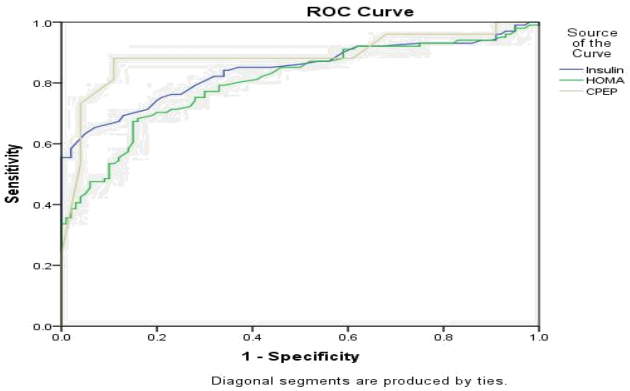

Image 2: ROC curve of Insulin Resistance

Sensitivity and specificity of Insulin resistance

Markers	**Sensitivity**	**Specificity**	**AUC**	**Upper**	**Lower**
C-peptide mg/dL	88%	89%	0.88	0.93	0.83
Insulin mg/dL	89%	72%	0.84	0.89	0.78
HOMA-IR	75%	72%	0.80	0.86	0.74

Image 2: The ROC (Receiver operating curve) showed that C-peptide had an optimum cut off at 0.88 (AUC =0.88) with 88 percent sensitivity and 89 percent specificity and a significant under curve. Insulin had the best cut off at 0.84 (AUC =0.84), with 89 percent sensitivity and 72 percent specificity. In Gestational diabetes mellitus groups, HOMA-IR had an optimum cut off of 0.80 (AUC = 0.80), with 75% sensitivity and 72% specificity.

Table 2: Mean and standard deviation of biochemical parameters in GDM

Parameters	**Non-GDM**	**GDM**	**P value**
Weeks	25 ± 1.32	26.26 ± 3.40	0.34
Fasting glucose (mg/dL)	60.0 ±13.5	61.8 ± 14.02	0.18
DIPSI (mg/dL)	119.1 ± 10.6	161.6 ±11.02	0.00**
HbA1c%	5.2±0.60	5.4 ± 0.86	0.03*
Insulin mg/dL	9.1±1.1	13.3±2.38	0.00**
HOMA-IR	1.6±0.29	2.5±0.52	0.00**
C-peptide mg/dL	0.94±0.37	1.3±1.2	0.02**

QUCKI	0.35±0.01	0.34±0.01	0.00**

Table 2 shows that DIPSI (*P=0.00***), HbA1C (*P=0.00***), Insulin (P=0.00**), C-peptide (*P=0.02*),* QUICK (*P=0.00***) are significant with GDM group and non GDM group.

Table: 3 shows the Pearson's correlation between C peptide versus DIPSI, Hb1c, Insulin and Insulin resistance

Markers	C-peptide	
	R Square	***P value***
DIPSI (mg/dL)	**0.32**	**0.00**
HbA1C	**0.03**	**0.72**
Insulin mg/dL	**0.40**	**0.00**
HOMA-IR	**0.32**	**0.00**
QUICKI	**0.47**	**0.25**

Table 3 shows that c-peptide has a positive correlation with insulin (P=0.00), DIPSI (P=00), and HOMA-IR (P=0.00), but no correlation with HbA1C (P=0.72) or QUICKI (P=0.25).

Table: 4 Association of C-peptide and other surrogate markers of Insulin resistance

Biochemical Markers	**Yes**	**No**	**Odds**	**95%CI**	**P value**
C-peptide mg/dL	67	33	1	-	-
Insulin mg/dL	81	19	2.0	1.0-4.0	0.02
HOMA-IR	77	21	1.8	0.9-3.4	0.06

Table 4 shows that c-peptide levels are related to insulin levels (ORs = 2.0 95 percent CI 1.0 4.0). There was no correlation between c-peptide levels and HOMA-IR (ORs =1.8, 95% CI 0.9-3.4).

Discussion

In GDM, C-peptide is one of the best indicators of endogenous insulin secretion. (11, 10) Several studies have linked the marker to C-peptide levels, glycemic control, hypoglycemic agents, and the risk of future diabetes complications (12–14). In this study, we looked at c-peptide levels as well as other surrogate markers of insulin resistance in women with gestational diabetes mellitus.

The primary goal of the study was to determine the efficacy of c-peptide levels in GDM and their relationship with other surrogate markers of insulin resistance (15–17). Our findings show that HOMA-IR (P=0.00**), 2-hour glucose levels (P=0.00**), HbA1c (P=0.03*), C-peptide levels (P=0.02*), and QUCKI (P=0.00**) are statistically significant in pregnant women without GDM compared to pregnant women with GDM. In this study, we discovered a positive correlation between C peptide and HOMA-IR (r = 0.32), Insulin (r = 0.40), and DIPSI (r = 0.32) in pregnant women with GDM, but no correlation with other surrogate markers such as QUCKI and HbA1c in the study subject group. C-peptide has a higher sensitivity (88%) and specificity (89%) and is also a better maker of gestational diabetes mellitus (21–23). M. Landin-olsson, Eun Young et al., and Atsushi GOTO et al. discovered that c-peptide had greater sensitivity and specificity for diabetes mellitus. Our research clearly demonstrated that C-peptide and HOMA-IR are strongly associated with insulin markers (ORs = 2.0, P =0.02*).

Conclusion

This study found a link between C-peptide levels and insulin levels in pregnant women with GDM in the Puducherry population. According to our findings, C-peptide levels are a useful marker of insulin resistance in gestational diabetes mellitus. C-peptide can also be used to determine glycemic control status. C-peptide levels are used to predict gestational diabetes mellitus.

Conflicts of interest: Indian council of Medical Research

Reference

1. Virjee S, Robinson S, Johnston DG. Screening for diabetes in pregnancy. J R Soc Med. 2001 Oct;94(10):502–9.
2. Gupta K, Parmar M, Dubey S. Incidence of Gestational Diabetes Mellitus in Pregnant women from Rural Background Attending Antenatal Care Clinic. Int J Med Res Rev [Internet].2015Mar31[cited2017Oct10];3(02).Availablefrom:http://medresearch.in/index.php/IJMRR/article/view/229
3. Vani K. Alterations in lipid profile in gestational diabetes mellitus (GDM) and type 2 DM women during pregnancy. Int J Med Res Rev [Internet]. 2015 Sep 30 [cited 2017 May26];3(08). Available from: http://medresearch.in/index.php/IJMRR/article/view/351
4. Buchanan TA, Xiang AH. Gestational diabetes mellitus. J Clin Invest. 2005 Mar 1;115(3):485–91.
5. Gutch M, Kumar S, Razi SM, Gupta KK, Gupta A. Assessment of insulin sensitivity/resistance. Indian J Endocrinol Metab. 2015;19(1):160–4.

6. Cerf ME. Beta Cell Dysfunction and Insulin Resistance. Front Endocrinol [Internet]. 2013Mar27;4.Availablefrom: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3608918
7. Chailurkit L, Jongjaroenprasert W, Chanprasertyothin S, Ongphiphadhanakul B. Insulin and C-peptide levels, pancreatic beta cell function, and insulin resistance across glucose tolerance status in Thais. J Clin Lab Anal. 2007;21(2):85–90.
8. Hare KJ, Vilsbøll T, Asmar M, Deacon CF, Knop FK, Holst JJ. The Glucagonostatic and Insulinotropic Effects of Glucagon-Like Peptide 1 Contribute Equally to Its Glucose-Lowering Action. Diabetes. 2010 Jul;59(7):1765–70.
9. Halliday HL, Reid MM, Hadden DR. C-peptide levels in transient neonatal diabetes. Diabet Med J Br Diabet Assoc. 1986 Jan;3(1):80–1
10. Viikari J, Rönnemaa T, Koskinen P. Glucagon-C-peptide test as a measure of insulin requirement in type 2 diabetes: evaluation of stopping insulin therapy in eleven patients. Ann Clin Res. 1987;19(3):178–82
11. Kampmann U, Madsen LR, Skajaa GO, Iversen DS, Moeller N, Ovesen P. Gestational diabetes: A clinical update. World J Diabetes. 2015 Jul 25;6(8):1065–72
12. Leighton E, Sainsbury CA, Jones GC. A Practical Review of C-Peptide Testing in Diabetes. Diabetes Ther. 2017 Jun;8(3):475–87.
13. Jones AG, Hattersley AT. The clinical utility of C-peptide measurement in the care of patients with diabetes. Diabet Med. 2013 Jul;30(7):803–17.
14. Chaudhury A, Duvoor C, Reddy Dendi VS, Kraleti S, Chada A, Ravilla R, et al. Clinical Review of Antidiabetic Drugs: Implications for Type 2 Diabetes Mellitus Management.
15. Front Endocrinol [Internet]. 2017 Jan 24;8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5256065/
16. Singh B, Saxena A. Surrogate markers of insulin resistance: A review. World J Diabetes. 2010 May 15;1(2):36–47.
17. Cersosimo E, Solis-Herrera C, Trautmann ME, Malloy J, Triplitt CL. Assessment of Pancreatic β-Cell Function: Review of Methods and Clinical Applications. Curr Diabetes Rev. 2014 Jan;10(1):2–42.
18. Basit A, Riaz M, Fawwad A. Glimepiride: evidence-based facts, trends, and observations. Vasc Health Risk Manag. 2012;8:463–72.
19. Leibowitz G, Kaiser N, Cerasi E. β- Cell failure in type 2 diabetes. J Diabetes Investig. 2011 Apr 7;2(2):82–91.
20. Cernea S, Dobreanu M. Diabetes and beta cell function: from mechanisms to evaluation and clinical implications. Biochem Medica. 2013 Oct 15;23(3):266–80.

21. Marrif HI, Al-Sunousi SI. Pancreatic β Cell Mass Death. Front Pharmacol [Internet]. 2016Apr6;7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4821858/
22. AMERICAN DIABETES ASSOCIATION. Diagnosis and Classification of Diabetes Mellitus. 31.
23. Bianchi C, Miccoli R, Trombetta M, Giorgino F, Frontoni S, Faloia E, et al. Elevated 1-Hour Postload Plasma Glucose Levels Identify Subjects With Normal Glucose Tolerance but Impaired β-Cell Function, Insulin Resistance, and Worse Cardiovascular Risk Profile: The GENFIEV Study. J Clin Endocrinol Metab. 2013 May 1;98(5):2100
24. Radaelli T, Farrell KA, Huston-Presley L, Amini SB, Kirwan JP, McIntyre HD, et al. Estimates of Insulin Sensitivity Using Glucose and C-Peptide From the Hyperglycemia and Adverse Pregnancy Outcome Glucose Tolerance Test. Diabetes Care. 2010 Mar;33(3):490–4.
25. Shaat N, Ekelund M, Lernmark A, Ivarsson S, Ramelius A, Perfekt R, et al. Genotypic and phenotypic differences between Arabian and Scandinavian women with gestational diabetes mellitus. Diabetologia. 2004 Jun 1;47:878–84.
26. Ohkura T, Shiochi H, Fujioka Y, Sumi K, Yamamoto N, Matsuzawa K, et al. 20/(fasting C-peptide × fasting plasma glucose) is a simple and effective index of insulin resistance in patients with type 2 diabetes mellitus: a preliminary report. Cardiovasc Diabetol. 2013 Jan 22;12:21.