International Journal of Community Medicine and Public Health
Iqbal M et al. Int J Community Med Public Health. 2021 Jun;8(6):3116-3119
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040
DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20212023

Short Communication

Diabetic dyslipidemia and type 2 diabetes mellitus as early as six weeks post-partum: a nested case control study

Meesha Iqbal[1], Paramjit Gill[2], Iqbal Azam[3], Romaina Iqbal[3]*

[1]Department of Community and Public Health, Idaho State University, Idaho, USA
[2]Warwick Medical School-Health Sciences, University of Warwick, UK
[3]Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan

Received: 29 March 2021
Accepted: 24 April 2021

***Correspondence:**
Romaina Iqbal,
E-mail: romaina.iqbal@aku.edu

ABSTRACT

Women who develop diabetes during pregnancy (Gestational diabetes mellitus-GDM) increase their risk of developing type 2 diabetes mellitus (T2DM) post-partum by 70%. The average time to develop T2DM varies and is not widely studied. T2DM is associated with increased risk of developing dyslipidemia leading to cardiovascular diseases. We intended to study the association of dyslipidemia and T2DM as early as 6 weeks post-partum. A matched case control study was designed, and conditional logistic regression analysis applied to get adjusted matched odds with 95% confidence intervals. Our study revealed increased serum LDL levels in the cases compared to the controls (p=0.03). However, no association was seen with other lipid parameters.

Keywords: Dyslipidemia, Diabetes mellitus, Gestational diabetes mellitus

INTRODUCTION

The burden of type 2 diabetes mellitus (T2DM) is on a rise.[1] Globally, 425 million people suffer from T2DM (one in eleven) and this is projected to increase to 629 million by 2045.Three quarters of people with type 2 diabetes mellitus live in low and middle income countries. One in every six pregnant women develops gestational diabetes mellitus (GDM).[2] These women are globally seven times more likely to develop type 2 diabetes mellitus later in life as compared to other women.[3] In Pakistan, 26.3% of the population has T2DM and 14.4% are pre-diabetics, contributing 3% of the proportionate mortality rate.[1,4] In Pakistan, one in every seven women develops GDM.[5]

T2DM is associated with myriad complications including dyslipidemia, which is a risk factor for cardiovascular diseases.[6] The cardiovascular diseases including the ischemic heart diseases and stroke have remained the leading cause of mortality for the past 15 years.[7] It is estimated that 72-85% of the diabetics suffer from dyslipidemia including low HDL, high LDL, VLDL and IDL.[8] A positive correlation has been noted between serum HbA1C levels and the severity of dyslipidemia.[9] However, little is known on how early dyslipidemia develops after the onset of T2DM.The aim of our study was to determine the differences in the blood lipid levels in women who developed T2DM after GDM and those who reverted back to the euglycemic levels 6 weeks post-partum.

METHODS

Our study was a nested matched case-control design in the parent study; Pakistan prevention program-gestational diabetes mellitus (PPP-GDM). PPP-GDM was a randomized control trial with behavioral intervention. The

baseline and end-line measurements included administration of questionnaires for socio-demographic and reproductive history, anthropometric measurements and laboratory investigations including lipid profile of the participants. The participants were enrolled from Aga Khan hospital (AKU) and Jinnah post-graduate medical college (JPMC), Karachi. The study continued from September 2015 to December 2017. Ethical clearance was taken from the ethical review committee of Aga Khan hospital (AKU) prior to the commencement of the study.

For the purpose of our study, women who did not revert back to euglycemic status 6 weeks postpartum were considered cases and women who reverted were taken as controls. Each case was matched with a maximum of five controls based on age (+2 years), enrollment site and the time of recruitment (within 3 months). The total sample size achieved was 131, including 42 cases and 89 controls. A total of 41 participants were from AKU (7 cases, 34 controls) and 90 from JPMC (35 cases, 55 controls).

Generalized estimating equations were used to calculate statistical differences between the cases and the controls. The variable of socio-economic status was constructed by the technique of factor analysis of variables (monthly family income spent on food, health, clothes, education; owning a washing machine, refrigerator, freezer; number of televisions, air-conditioners, computers, mobile phones, motor-cycles and cars present at home). Conditional logistic regression was applied to calculate matched odds (Crude and adjusted) and $p<0.05$ was considered statistically significant. All analyses were carried out on SPSS version 23.

RESULTS

Table 1 demonstrates the characteristics of the cases and the controls of the study. The mean age of the cases and the controls was 31.19 and 30.30 years, respectively. The mean systolic and diastolic pressure too were higher among the cases (Systolic B.P: 115.5 mmHg in cases vs. 109.1mmHg in controls, p=0.011) (Diastolic B.P: 82.8 mmHg in cases vs. 76.9 mmHg in controls, p=0.002). Among the serum lipid parameters, serum LDL cholesterol levels were significantly higher among the cases (129.1 mg/dl in cases vs. 114.4 mg/dl in controls, p=0.033). No statistical difference was observed in the serum cholesterol, triglycerides, VLDL and HDL levels across the cases and the controls.

Table 2 shows crude matched odds followed by adjusted matched odds with 95% confidence interval. Among the serum lipid profile, serum LDL levels were found to be significantly associated with the cases. A ten unit (mg/dl) increase in the serum LDL levels increased the risk of having T2DM by 10% among the cases (AOR: 1.10; p=0.02).

Table 1: Characteristics of women who do not revert to euglycemic levels (cases) and matched control subjects, (n=131).

Variables	Cases, (n=42) Mean (SE)	Controls, (n=89) Mean (SE)	P value
Socio-demographic characteristics			
Age (Years)	31.19 (0.71)	30.30 (0.74)	0.712
Religion, n (%)			
Muslim	39 (92.9)	86 (96.6)	0.358
Non-Muslim	3 (7.1)	3 (3.4)	
Education (Years)	8.71 (0.71)	10.00 (0.66)	0.796
Education of the husband (Years)	9.29 (0.75)	10.64 (0.71)	0.879
Occupation, n (%)			
Housewife	37 (88.1)	81(91.0)	0.282
Working	5 (11.9)	8 (9.0)	
Socio-economic status, n (%)			
Low	17 (40.5)	26 (29.2)	0.713
Middle	14 (33.3)	31 (34.8)	
High	11 (26.2)	32 (36.0)	
Reproductive history			
Total number of pregnancies	4.02 (0.40)	3.54 (0.36)	0.551
Total number of miscarriages, median (IQR)	0.69 (0.15)	0.87 (0.12)	0.338
Total number of live-births	3.00 (0.28)	2.58 (0.26)	0.312
Anthropometric measurements			
Waist circumference (cm)	90.19 (1.80)	85.65 (1.33)	0.038
Hip circumference (cm)	107.08 (2.32)	103.41 (1.07)	0.138
BMI (kg/m^2)	29.61 (0.95)	27.82 (0.57)	0.110
Mean systolic BP (mmHg)	115.54 (2.05)	109.17 (1.68)	0.011
Mean diastolic BP (mmHg)	82.84 (1.57)	76.96 (1.09)	0.002
Body fat (%)	35.60 (1.40)	35.17 (0.85)	0.787
Serum lipid profile			
Serum cholesterol (mg/dl)	180.40 (5.77)	176.40 (2.98)	0.602
Serum triglycerides (mg/dl)	203.26 (31.09)	140.61 (11.77)	0.077
Serum HDL (mg/dl)	48.14 (4.58)	52.67 (4.68)	0.447
Serum LDL (mg/dl)	129.17 (5.82)	114.47 (3.11)	0.033
Serum VLDL (mg/dl)	42.12 (6.24)	29.21 (2.28)	0.074

*P values and SE reported by GEE.

Table 2: Associations between socio demographic characteristics, reproductive history, anthropometric measurements, laboratory investigations and diabetes mellitus at 6 weeks post-partum in a hospital based matched case control study, Pakistan.

Variables	Matched COR, (95% CI)	Matched AOR (95% CI)
Religion		
Muslims	1	1
Non-Muslims	2.78 (0.54-14.35)	2.33 (0.23-22.85)
Occupation		
Housewife	1	1
Working	2.42 (0.58-10.04)	5.61 (0.71-44.06)
Total number of miscarriages	0.77 (0.52-1.14)	0.73 (0.43-1.23)
Waist circumference (cm)*	1.10 (0.95-1.33)	0.95 (0.65- 1.40)
Hip circumference (cm)*	1.10 (0.90-1.27)	1.00 (0.59-1.68)
Mean systolic BP (mmHg)**	1.21 (0.90-1.48)	0.81 (0.43-1.62)
Mean diastolic BP (mmHg)**	1.48 (1.00-2.36)	1.62 (0.59-4.41)
Serum triglycerides (mg/dl)**	1.00 (1.00-1.00)	0.94 (0.81-1.00)
Serum LDL (mg/dl)**	1.10 (1.00-1.21)	1.10 (1.00-1.34)
Serum VLDL (mg/dl)**	1.21 (1.00-1.34)	1.10 (0.66-1.96)

*The matched odds ratios are displayed for 5 unit increase in the predictor variable, ** The matched odds ratios are displayed for 10 unit increase in the predictor variable

DISCUSSION

Our study found a positive association between the serum LDL levels and the development of T2DM at six weeks post-partum following gestational diabetes mellitus. Our results are in line with other studies that have found similar results. A recent meta-analysis determining the association of the lipid parameters and the risk of T2DM concluded that they have the ability to reflect the risk of T2DM (n=10). It was shown that the serum LDL levels were minutely but significantly higher among the cases as compared to the controls (SMD: 0.44; 95% CI: 0.11-0.77).[10] Another study in India also demonstrated a positive correlation between fasting blood sugar levels and serum LDL (Pearson correlation coefficient: 0.072).[8] In contrast to our study, most of the other studies have reported a positive association between T2DM and other serum lipid parameters; total cholesterol, serum HDL, serum TG and serum VLDL.[8-10] We assume that the small sample size of our study was unable to detect the other associations.

The biologic plausibility of diabetes and dyslipidemia has been widely studied. Insulin is a key hormone in the regulation of lipid metabolism. It is postulated that insulin promotes the clearance of serum-LDL by increasing LDL receptor expression and activity on the peripheral cells.[11] The lack of insulin or insulin resistance in diabetes thus contributes to an increased level of serum-LDL. However, our study design was not powered to detect the development of dyslipidemia resulting from T2DM.

The major strength of our study was that the association of T2DM and dyslipidemia has not been previously studied in women of GDM as early as six weeks post-partum, to the best of our knowledge. This would be a corner stone in revealing the association in this particular group of women. We also applied vigorous analytical techniques to come up with robust results. Most of the established co-variates of dyslipidemia such as BMI, body fat, blood pressure etc. were adjusted for in the analysis. However, our study does not come without limitations. The sample size of our study was not calculated a-priori as this was a nested study design in the larger project. We are not sure if our sample was adequately powered to detect the associations. Our study also could not establish the temporal association of dyslipidemia and T2DM due to the design of the study. Lastly, the glycemic status of the participants when they entered pregnancy was un-known, it is likely that some of them already had frank diabetes that only got diagnosed once they entered our study.

CONCLUSION

This study has highlighted the association of T2DM and dyslipidemia at a very early stage. This association needs to be further evaluated in this particular group before we look into its etiology and risk factors.

Funding: MRC (MR/M022048/1)
Conflict of interest: Paramjit Gill is a trustee of the South Asian Health Foundation, is part funded by the NIHR Applied Research Collaboration West Midlands and a NIHR Senior Investigator. The views expressed in this publication are those of the authors and not necessarily those of the NIHR or the UK Department of Health and Social Care.
Ethical approval: Not required

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Cite this article as: Iqbal M, Gill P, Azam I, Iqbal R. Diabetic dyslipidemia and type 2 diabetes mellitus as early as six weeks post-partum: a nested case control study. Int J Community Med Public Health 2021;8:3116-9.