Risk factors for gestational diabetes mellitus: A prospective case-control study from coastal Karnataka[☆]

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ABSTRACT

Background: Identification of gestational diabetes mellitus (GDM) risk factors is pertinent, for it can be an effective intervention for its prevention. As previous information regarding GDM risk factors from India were mostly descriptive and scarce from coastal Karnataka, a current prospective case-control study was designed to identify GDM risk factors among pregnant women seeking antenatal care.

Methods: A hospital-based prospective matched case-control study was carried among antenatal subjects seeking routine antenatal care at two secondary-level care private hospitals, affiliated to a University Medical College in coastal Karnataka. It comprised of 100 incident GDM cases and 273 frequency-matched controls. Data was collected by personal interviews using a pretested questionnaire. Data was entered and analyzed using Statistical Package for Social Sciences (SPSS), version 15.0.

Results: Risk factors using Carpenter and Coustan criteria and DIPSI criteria were found similar. Pooled data identified following significant GDM risk factors: marital age (25–29 years) (adjusted OR:18.2; 95% CI:1.9–177.6; $p = 0.012$), delayed menarche (adjusted OR:11.4; 95% CI:1.1–124.6; $p = 0.045$), multiparity (adjusted OR:14.1; 95% CI:1.8–109.8; $p = 0.011$), family history of DM (adjusted OR:66.6; 95% CI:6.9–645.2; $p < 0.001$), high maternal perceived stress (adjusted OR:21.6; 95% CI:1.9–248.8; $p = 0.014$), less physical activity (adjusted OR:21.0; 95% CI: 2.8–158.8; $p = 0.003$), and low intake of green leafy vegetables (GLV) (adjusted OR:41.7; 95% CI:3.7–472.4; $p = 0.003$). Positive current polyhydramnios and recurrent vaginal infections were also identified as significant risk factors ($p < 0.05$).

Conclusions: Modifiable risk factors identified were low physical activity, high antenatal perceived stress, multiparity, marital age ≥ 25 years, and low pre-pregnancy intake of GLV, which were also comparable using two criteria in vogue for GDM diagnosis. Pre-conception advice on healthy lifestyle may prove beneficial.

1. Introduction

Gestational diabetes mellitus (GDM), defined as carbohydrate intolerance of variable degree with onset or recognition during pregnancy, has been recently identified as a potential risk factor for Type II Diabetes Mellitus (T2DM).¹ As per International Diabetes Federation (IDF) 2017, one in seven births is affected by GDM. 16.2% (21.3 million) of live births is to women with hyperglycemia in pregnancy

(HIP).² India, being home to 69.2 million diabetic subjects, has also become the “diabetes capital of the world” harboring around four million women with GDM alone.³ Though number of live births affected by HIP has been showing slight increment since 2015, reports of adverse perinatal outcomes due to GDM have been recognized among 86.4% of cases.²

Various risk factors have been identified as predictors of GDM. In general, they predict the occurrence of T2DM as well. They are

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advanced maternal age, positive family history of T2DM, obesity, and glycosuria. In addition, certain maternal and neonatal outcomes in previous pregnancies have also been found associated with greater likelihood of developing GDM in the present pregnancy. They include positive history of spontaneous abortions, GDM, pregnancy induced hypertension (PIH), polyhydramnios, pre-term labor, caesarian deliveries, unexplained still births, macrosomia, congenital malformations, neonatal complications like respiratory distress syndrome (RDS) and hypoglycemia.⁴ Therefore, to avoid the influence of modifiable factors, their early identification plays an important role.

It has been observed that usual lifestyle modifications or medical interventions offered late in life are of little help as they target only post-primary prevention of overt DM. Today, the need of the hour is to timely identify GDM risk factors so as to prevent subsequent development of overt DM and other long-term complications.⁵ Although Government of India (GoI)⁶ recent initiative to universally screen all Indian pregnant women for GDM has helped in targeting prevention of GDM-related complications, it does not prevent occurrence of GDM. Prevention of glucose intolerance requires rather a comprehensive approach wherein strategies to prevent GDM risk factors during pre-pregnancy phase are also addressed.⁷

Amidst differences in diagnosing GDM due to various existing national and international guidelines without any standard protocols for Indian population, Carpenter and Coustan criteria (1982)⁸ was earlier employed as diagnostic criterion by some treating obstetricians. But it was long debated for being a costly procedure associated with poor patient compliance.⁹ It was only after the GoI launch of local national guidelines in 2014, Diabetes in Pregnancy Study Group India (DIPSI) guidelines was adopted nation-wide.⁶ DIPSI guidelines are at an advantage for being not only simple, but also cost-effective and patient-friendly in contrast to previous guidelines.⁶ Diagnosis and management of conditions like GDM in primary care, largely relies on availability of standard guidelines. In this regard, adoption of GoI guidelines for GDM diagnosis and management is largely beneficial for ensuring uniformity and minimizing diagnostic errors.

As information regarding risk factors for GDM was scarce from coastal Karnataka, the current study was designed to identify GDM risk factors among pregnant women seeking antenatal care at secondary care hospitals in coastal district of Karnataka (South India). Existing literature has been mostly descriptive in nature; hence the study additionally employed an analytical design – *prospective case control study* – with a unique advantage of prospective enrolment of incident cases. Prospective enrolment largely circumvents the risk of recall bias. In addition, it was also postulated to assess similarity in GDM risk factors when either Carpenter and Coustan, or DIPSI criteria was used for diagnosis of GDM.

2. Methods

2.1. Study design and participants

The present study was carried out at two private hospitals of a coastal district. It is situated along the coastline in the southern part of India, covering a population of 1.18 million and is spread over an area of 3575 km². As per District Level Household and Facility Survey (DLHS)-4 (2012–13) of the district, 53.4% of its pregnant women received full antenatal care.¹⁰ The district has good health indicators including 98.8% institutional deliveries, of which 68.1% are delivered in private institutions.¹⁰

The study population included all pregnant women coming for routine antenatal care to secondary care hospitals. Data was collected over the period of 24 months (2014–2016). Cases included incident GDM subjects coming to antenatal out-patient department (OPD). A pregnant woman newly diagnosed with GDM in her present pregnancy by 3-h, 100 g oral glucose tolerance test (OGTT) after 20 weeks of gestation using Carpenter and Coustan Criteria at the health care setting

was recruited as 'case'. *OGTT was done following a positive 1-h 50 g glucose challenge test (GCT) exceeding ≥ 140 mg/dL.* The next pregnant woman, frequency-matched with period-of-gestation (POG) (± 2 weeks), identified as non-GDM by 1-h 50 g GCT value < 140 mg/dL, was included as 'control'. All those pregnant women who had already been diagnosed with diabetes mellitus prior to current pregnancy were excluded from the study. Age as a risk factor for GDM was considered for sample size estimation. Expecting 23.7% of the cases to be > 25 years of age,¹¹ and anticipating a difference of at least 15% in the risk factor profile between the cases and controls to be clinically significant for a power of 80%, at 5% level of significance and 10% non-response rate, a minimum of 73 cases and 219 controls, frequency-matched with POG, were required to be recruited, with a case-to-control ratio of 1:3.

GDM was diagnosed using Carpenter and Coustan criteria during the initiation of the study.⁸ Subsequently, DIPSI criteria was adopted as a new diagnostic criterion from November 2015 onwards.⁶ It was uniformly adopted by the treating obstetricians at both the study settings by consensus following a departmental review. The data collection was continued to interview the predetermined number of cases and controls as per sample size calculation. But in order to ascertain the similarity between risk factors among cases and controls, an additional 27 cases and 54 POG frequency-matched controls (1:2) were recruited according to the new criteria. The additional number was decided based on the time available for data collection.

Accordingly, the operational definition of both cases and controls was changed as per new DIPSI guidelines.⁶ A pregnant woman newly diagnosed with GDM in her present pregnancy by 2-h 75 g single venous plasma glucose after 20 weeks of gestation exceeding ≥ 140 mg/dL (*irrespective of the last meal timings*) at a health care setting was considered as a 'new case'. The next pregnant women, frequency-matched with POG (± 2 weeks), whose 2-h 75 g single venous plasma glucose value was < 140 mg/dL was included as a 'new control' in 1:2 ratio.

3. Methodology

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Institutional ethical committee (*IEC:623/2014*) approval was obtained prior to initiation of the study and subsequent modification, due to change in the diagnostic criteria and sample size, was duly notified to the ethics committee. Subject information sheet was distributed to all study subjects and written informed consent was obtained from all individual participants included in the study. Newly diagnosed GDM cases were identified from the antenatal OPD. On the same day, POG frequency-matched controls were also identified. Cases and controls fulfilling the inclusion criteria were then interviewed. Data was collected by personal interviews using a pretested questionnaire.

3.1. Assessment of pre-pregnancy diet

The pre-pregnancy diet of recruited participants was assessed using the food frequency questionnaire. Intake of food items per week with respect to broad nutrient groups was elicited through dietary recall method.

3.2. Assessment of socio-economic status

Socio-economic status (SES) was assessed using modified Udai-Pareek Scale.¹² A score of < 40 was identified as belonging to low, 40–70 middle, and ≥ 70 high SES.¹²

3.3. Assessment of stress

Assessment of stress was done using a standard questionnaire – the Cohen 10-item Perceived Stress Scale (PSS).^{13,14} Participants were asked to respond to each question on a 5-point Likert scale ranging from zero (never) to four (very often), that indicates how often they have felt or thought a certain way within the past month. Positively-worded items were reverse scored and ratings were summed across all 10 items. Scores so obtained ranged between zero and 40; higher composite scores indicating greater perceived stress, and vice versa. In the present study, the PSS score of < 20 was graded as low whereas ≥ 20 was considered as high stress.^{13,14}

3.4. Assessment of physical activity

Data regarding physical activity was obtained by administering a standardized questionnaire – the long form of International Physical Activity Questionnaire-long form (IPAQ).¹⁵ This version of IPAQ assesses physical activity across a comprehensive set of four domains, viz., work, transport, domestic and garden (yard), and leisure time-related physical activities in the last seven days of interview.¹⁵ Domain-specific sub-scores were then assigned pertaining to each physical activity type. Total score was computed as the summation of duration (in minutes) and frequency (days) for all activities types across all domains. Data so collected were reported in metabolic equivalent-minutes per week (MET-minutes/week), which can be computed by weighing each type of activity by its energy requirements defined in METs. These METs are multiples of resting metabolic rates. MET-minute/week was then computed for each activity as follows:¹⁵

MET-minutes/week = MET level $\times$ minutes of activity/day $\times$ days/week.

Total score was calculated for each domain, and then, the overall grand total was estimated. The overall grand total scores so computed were sub-categorized into three levels of physical activity:¹⁵

- 1 High: Total physical activity ≥ 3000 MET-minutes/week
- 2 Moderate: Total physical activity 600 to < 3000 MET-minutes/week
- 3 Low: Total physical activity < 600 MET-minutes/week.

Both Cohen-10 item PSS and IPAQ scales were translated from original English version into local Kannada language by two native Kannada speaking medico-social workers independently. Translations and back translations were matched and finalized, pilot tested and validated.

3.5. Anthropometric measurements

Anthropometric measurements were taken for all the subjects. Weight was measured using a standard weighing scale (in kgs) kept on a firm horizontal surface, recorded to the nearest 500 g. Height was measured using a measuring tape or stadiometer (in cms) to the nearest one cm. Subjects were requested to stand upright barefoot with their back against wall, heels together and looking forward.¹⁶ Pre-pregnancy body mass index (BMI) was calculated as the ratio of pre-pregnancy weight (kgs) to square of height (metres).¹⁶ Weight at first antenatal registration in first trimester was considered as pre-pregnancy weight. Weight gain for the current pregnancy was computed by subtracting 'pre-pregnancy weight' from 'current weight'.

3.6. Statistical analysis

Data was entered and analyzed using Statistical Package for Social Sciences (SPSS), version 15. The results are expressed as percentages and proportions for categorical variables. Comparison of the risk factors among cases and controls was done using univariate logistic regression,

Fig. 1. Recruitment of study subjects.

and odds ratio (OR) with 95% confidence interval (CI) was calculated to study the association between the different variables. Variables found to have $p < 0.20$ were used for multiple logistic regression to identify the independent risk factors for GDM and adjusted odds ratio with 95% CI was computed. A $p < 0.05$ was considered to be statistically significant.

4. Results

In the present study, total 100 GDM cases and 273 POG frequency-matched controls were recruited at an overall case-to-control ratio of 1:2.7 (Fig. 1). Among the total, 52 cases and 156 controls were recruited based on Carpenter and Coustan criteria (case-to-control ratio of 1:3). Following change in the diagnostic criteria, remaining 48 cases and 117 controls were enrolled based on DIPSI guidelines (case-to-control ratio of 1:2.4). The mean ($\pm$ SD) POG of diagnosis for cases was 27 weeks 2 days ($\pm$ 5 weeks 2 days) while for controls, POG was 26 weeks 2 days ($\pm$ 4 weeks 2 days).

The baseline socio-demographic characteristics of the study subjects (Table 1) showed higher odds of GDM among those aged ≥ 30 years (Crude OR 17.3, $p < 0.001$). Age at menarche was earlier among controls as against cases ($p < 0.001$). Majority of the Christians were older than Hindus, thus the odds of GDM was higher among Christians compared to Hindus (Crude OR 4.7, $p = 0.002$). Odds of GDM cases being overweight (≥ 60 kgs) in their pre-pregnancy period was higher than controls (Crude OR 2.6, $p = 0.001$). Odds for high stress (Crude OR 12.9), and low-to-moderate physical activity (Crude OR 5.9) among GDM cases was also higher than controls ($p < 0.001$). Pertaining to obstetric details of current pregnancy (Table 2), 85.3% of the controls were primigravida while 66% of cases were multigravida ($p < 0.001$). Odds of GDM was higher for multiparity compared to nulliparous women (Crude OR 11.5, $p < 0.001$). 58.8% of the cases had higher weight gain (≥ 7 kgs) compared to 23.7% of the controls (Crude OR 4.5, $p < 0.001$). Polyhydramnios was present among 61% of the cases in contrast to only five controls ($p < 0.001$).

In past obstetric history, among the multigravid subjects, 34.8% of the cases ($n = 23$) had past history of GDM compared to 2.5% of controls ($p = 0.004$). Among multigravida, 18.2% ($n = 12$) had recurrent vaginal infections, 31.8% ($n = 21$) polyhydramnios, and 13.6% ($n = 9$) had pre-term deliveries in the past whereas none of the multigravid controls reported these events. Total 86 births were reported in the past. Information regarding birth weight was available only for 81 babies. Odds of GDM was higher among those who gave birth to macrosomic babies (≥ 3.5 kgs) more than once (36.5%) than controls (3.4%) ($p = 0.009$).

Table 1
Baseline characteristics of study subjects.

Variables	Cases(N = 100); n(%)	Controls(N = 273); n(%)	Crude Odds Ratio(95% CI)	p-value
Age (years)				
≤ 25	16(16.0)	117(42.9)	1.0	
26–29	25(25.0)	131(48.0)	1.4(0.7–2.7)	0.333
≥ 30	59(59.0)	25(9.1)	17.3(8.6–34.8)	< 0.001
Age at marriage (years)				
< 25	30(30.0)	166(60.8)	1.0	
25–29	48(48.0)	98(35.9)	2.7(1.6–4.6)	< 0.001
≥ 30	22(22.0)	9(3.3)	13.5(5.7–32.2)	< 0.001
Duration of marriage (months)				
< 12	20(20.0)	130(47.6)	1.0	
12–35	22(22.0)	86(31.5)	1.7(0.9–3.2)	0.133
36–59	31(31.0)	36(13.2)	5.6(2.9–11.0)	< 0.001
≥ 60	27(27.0)	21(7.7)	8.4 (4.0–17.5)	< 0.001
Age at menarche (years) [§]				
11	14(14.0)	91(33.3)	1.0	
12	23(23.0)	140(51.3)	1.1(0.5–2.2)	0.857
13	39(39.0)	28(10.3)	9.1(4.3–19.0)	< 0.001
≥ 14	24(24.0)	14(5.1)	11.1(4.7–26.5)	< 0.001
Religion				
Hindu	82(82.0)	245(89.7)	1.0	
Muslim	7(7.7)	21(7.7)	1.0(0.4–2.4)	0.993
Christian	11(11.0)	7(2.6)	4.7(1.8–12.5)	0.002
Education				
< Class 7 [†]	8(8.0)	18(6.6)	1.0	
Class 8th–12th	67(67.0)	221(81.0)	0.7(0.3–1.6)	0.4
Graduation & above	25(25.0)	34(12.4)	1.7(0.6–4.4)	0.392
Occupation				
Homemakers	89(89.0)	259(94.9)	1.0	
Working	11(11.0)	14(5.1)	2.3(1.0–5.2)	0.05
SES Class				
Low	8(8.0)	49(17.9)	1.0	
Middle & High	92(92.0)	224(82.1)	2.5(1.1–5.5)	0.021
Stature (cms)				
< 150	8(8.0)	38(13.9)	1.0	
150–159.9	69(69.0)	183(67.0)	1.8(0.8–4.0)	0.159
≥ 160	23(23.0)	52(19.1)	2.1(0.8–5.2)	0.109
Pre-pregnancy weight (kgs) [‡]				
< 50	29(29.0)	106(44.0)	1.0	
50–60	31(31.0)	79(32.8)	1.4(0.8–2.6)	0.226
≥ 60	40(40.0)	56(23.2)	2.6(1.5–4.7)	0.001
Pre-pregnancy BMI (kg/m ²) [‡]				
< 25	67(67.0)	200(83.0)	1.0	
≥ 25	33(33.0)	41(17.0)	2.4(1.4–4.1)	0.001
Cohen Perceived Stress Scale Score				
Low Stress	47(47.0)	251(91.9)	1.0	
High Stress	53(53.0)	22(8.1)	12.9(7.2–23.1)	< 0.001
IPAQ Score (MET-minutes/week)				
High	43(43.0)	223(81.7)	1.0	
Low-to-moderate	57(57.0)	50(18.3)	5.9(3.6–9.8)	< 0.001

§None of the subject had attained menarche < 11 years of age.

†One subject in the control was illiterate.

‡BMI could not be computed for 32 subjects as they did not remember their pre-pregnancy weight.

Abbreviations: BMI: Body Mass Index; IPAQ: International Physical Activity Questionnaire.

Pertaining to family history, exposure rates for both maternal and paternal history of DM was significantly more among cases ($p < 0.001$). Information regarding pre-pregnancy diet showed higher odds of GDM for consumption of cereals ≥ 20 times per week ($p < 0.001$). Controls proportionately consumed higher amounts of protective foods (green leafy vegetables, vegetables, fruits, and milk) compared to cases ($p < 0.001$). Odds of GDM cases consuming non-vegetarian food ≥ 4 times a week (56%) was 1.7 times higher than controls ($p = 0.025$). Intake of sweets was similar among cases and controls ($p = 0.509$).

Due to switch of diagnostic criteria from Carpenter and Coustan to DIPSI guidelines during the study period, the risk factor profile was compared between the two diagnostic criteria (Table 3). The association of risk factors for GDM using either criteria was found to be similar. Following risk factors were identified in common; age ≥ 30 years, age at marriage ≥ 30 years, age at menarche ≥ 13 years, multiparity, family

history of DM, high perceived stress levels, less physical activity, less protective foods in pre-pregnancy diet.

As risk factors were similar between two criteria, multivariate analysis was done for pooled data (Table 4). Modifiable risk factors identified were age at marriage (25–29 years), multiparity, high stress, less physical activity, and low intake of green leafy vegetables. The key non-modifiable risk factors identified were maternal and paternal history of DM, and age at menarche ≥ 14 years.

5. Discussion

GDM, defined as carbohydrate intolerance of variable degree with onset or recognition during pregnancy, has been identified as precursor for T2DM. To combat rising T2DM prevalence, timely identification of GDM risk factors during prenatal period will serve as a primordial prevention tool.

Table 2
Determinants of GDM pertaining to present obstetric details.

Variables	Cases(N = 100); n (%)	Controls (N = 273); n (%)	Crude Odds Ratio (95% CI)	p-value
Gravida				
Primigravida	34(34.0)	233(85.3)	1.0	
Multigravida	66(66.0)	40(14.7)	11.3(6.6-19.3)	< 0.001
Parity				
Nulliparous	35(35.0)	235(86.1)	1.0	
Multiparous	65(65.0)	38(13.9)	11.5(6.7-19.6)	< 0.001
Weight gain(kgs) [§]				
< 7	42(42.0)	184(76.3)	1.0	
≥7	58(58.0)	57(23.7)	4.5(2.7-7.3)	< 0.001

[§]32 subjects among controls did not remember their pre-pregnancy weight. Thus, results depicted are provided for 100 cases and 241 controls.

High GDM risk among those aged ≥30 years identified in the present study were supported by other prospective cohort studies carried out by Sharma et al. and Leng et al. using WHO and IADPSG-WHO criteria respectively^{17,18}; although studies carried out in northern India using DIPSI criteria found high risk among ≥25years women.^{19,20}

Table 3
Comparison of significant determinants of GDM with Carpenter and Coustan and DIPSI Criteria.

Variables	Carpenter & Coustan Criteria			DIPSI criteria		
	Cases	Controls	Crude OR (95% CI); p-value	Cases	Controls	Crude OR (95% CI); p-value
	N = 52;	N = 156;		N = 48;	N = 117;	
	n(%)	n(%)		n(%)	n(%)	
Age(years)						
≤25	10(19.2)	70(44.9)	1.0	6(12.5)	47(40.2)	1.0
26-29	12(23.1)	67(42.9)	1.3(0.5–3.1); 0.624	13(27.1)	64(54.7)	1.6(0.6–4.5); 0.0381
≥30	30(57.7)	19(12.2)	11.1(4.6-26.6); < 0.001	29(60.4)	6(5.1)	37.9(11.1-128.6); < 0.001
Age at marriage (years)						
< 25	21(40.4)	104(66.7)	1.0	9(18.7)	62(53.0)	1.0
25-29	16(30.8)	45(28.8)	1.8(0.8–3.7); 0.133	32(66.7)	53(45.3)	4.2(1.8–9.5); 0.001
≥ 30	15(28.8)	7(4.5)	10.6(3.9-29.2); < 0.001	7(14.6)	2(1.7)	24.1(4.3-134.6); < 0.001
Age at menarche (years)						
≤11	9(17.3)	49(31.4)	1.0	5(10.4)	42(35.9)	1.0
12	10(19.2)	86(55.1)	0.6(0.2–1.7); 0.0354	13(27.1)	54(46.1)	2.0 (0.7–6.1); 0.213
13	17(32.7)	12(7.7)	7.7(2.8-21.5); < 0.001	22(45.8)	16(13.7)	11.6(3.7-35.7); < 0.001
≥14	16(30.8)	9(5.8)	9.7(3.3-28.6); < 0.001	8(16.7)	5(4.3)	13.4(3.1-57.4); < 0.001
Parity						
Nulliparous	20(38.4)	124(79.5)	1.0	15(31.3)	111(94.9)	1.0
1	29(55.8)	29(18.6)	6.2(3.1-12.5); 0.001	30(62.5)	6(5.1)	37.0(13.2-103.5); < 0.001
≥2	3(5.8)	3(1.9)	6.2(1.2-32.9); 0.032	3(6.2)	0(0.0)	1.91(< 0.001); 0.999
H/o DM in both parents						
No	12(23.1)	128(82.1)	1.0	17(35.4)	107(91.5)	1.0
Yes	40(76.9)	28(17.9)	15.2(7.1-32.7); < 0.001	31(64.6)	10(8.5)	19.5(8.1-46.9); < 0.001
Cohen Stress Scale						
Low Stress	18(34.6)	136(87.2)	1.0	29(60.4)	115(98.3)	1.0
High Stress	34(65.4)	20(12.8)	12.8(6.1-26.9); < 0.001	19(39.6)	2(1.7)	37.7(8.3-171.0); < 0.001
IPAQ (MET-minutes/week)						
High	24(46.2)	140(89.7)	1.0	19(39.6)	83(70.9)	1.0
Low-to-moderate	28(53.8)	16(10.3)	10.2(4.8-21.6); < 0.001	29(60.4)	34(29.1)	3.7(1.8-7.5); < 0.001
Pulses intake per week						
≥2	16(30.8)	34(21.8)	1.0	22(45.8)	31(26.5)	1.0
< 2	36(69.2)	122(78.2)	0.6(0.3–1.3); 0.192	26(54.2)	86(73.5)	0.4(0.2–0.9); 0.017
GLV intake/week						
≥1	11(21.2)	61(39.1)	1.0	9(18.8)	61(52.1)	1.0
< 1	41(78.8)	95(60.9)	2.4(1.1-5.0); 0.021	39(81.2)	56(47.9)	4.7(2.1-10.6); < 0.001

Abbreviations.

DM: Diabetes Mellitus.

GLV: Green Leafy Vegetables.

H/o: History of

IPAQ: International Physical Activity Questionnaire.

MET: Metabolic Equivalent.

Marital age > 25 years, identified higher odds for GDM in the present study; but this was in contrast to the study done in Oman wherein significant relationship was observed between GDM incidence and marital age < 18 years ($p < 0.010$; likelihood ratio = 43.9).²¹ Another study carried out by Varghese et al. also showed increased GDM prevalence with duration of marriage > 3 years.²² Older age at child bearing increases GDM risk indirectly and this is reflected through delayed age at marriage and longer duration of married life.

GDM risk of with delayed menarche (≥ 14 years) noted in the present study was substantiated by another case-control study carried out in Babol (Mazandaran)²³ where menarche ≥ 12 years was identified as a risk factor. Hormonal, genetic, environmental factors also play a role in menarche onset and subsequent GDM risk.

Obesity has long been associated with high GDM and T2DM risk. This has also been documented by various prospective Indian cohort studies which have reported a high GDM prevalence among subjects with pre-pregnancy BMI ≥ 25 kg/m² irrespective of the diagnostic criteria used.^{17,20} This is in accordance to present study findings; while studies carried out in Odisha found high GDM prevalence among BMI ≥ 30 kg/m².²⁴

Traditional risk factors like stress and physical inactivity incriminated for T2DM have also been proposed as risk factors for GDM.

Table 4

Multivariate logistic regression analysis for association of significant determinants with GDM.

Variables	Crude OR (95% CI); p-value	Adjusted OR (95% CI); p-value
Age (years)		
≤ 25	1.0	1.0
26–29	1.4(0.7–2.7); 0.333	0.09(0.007–1.1); 0.059
≥ 30	17.3(8.6–34.8); < 0.001	1.2(0.07–20.9); 0.913
Age at marriage (years)		
< 25	1.0	1.0
25–29	2.7(1.6–4.6); < 0.001	18.2(1.9–177.6); 0.012
≥ 30	13.5(5.7–32.2); < 0.001	3.5(0.2–69.8); 0.407
Age at menarche (years)		
11	1.0	1.0
12	1.1(0.5–2.2); 0.857	0.1(0.01–0.9); 0.041
13	9.1(4.3–19.0); < 0.001	0.7(0.06–7.8); 0.773
≥ 14	11.1(4.7–26.5); < 0.001	11.4(1.1–124.6); 0.045
Parity		
Nulliparous	1.0	1.0
Multiparous	11.5(6.7–19.6); < 0.001	14.1(1.8–109.8); 0.011
H/o DM in both parents		
No	1.0	1.0
Yes	15.1(8.7–26.3); < 0.001	66.6(6.9–645.2); < 0.001
Cohen Perceived Stress Scale Score		
Low Stress	1.0	1.0
High Stress	12.9(7.2–23.1); < 0.001	21.6(1.9–248.8); 0.014
IPAQ score (MET-minutes/week)		
High	1.0	1.0
Low-to-moderate	5.9(3.6–9.8); < 0.001	21.0(2.8–158.8); 0.003
Frequency of Pulses intake per week		
≥ 2	1.0	1.0
< 2	0.5(0.3–0.8); 0.007	1.04(0.006–0.3); 0.002
Frequency of GLV intake per week		
≥ 1	1.0	1.0
< 1	3.2(1.9–5.6); < 0.001	41.7(3.7–472.4); 0.003

Abbreviations.

DM: Diabetes Mellitus.

GLV: Green Leafy Vegetables.

H/o: History of.

IPAQ: International Physical Activity Questionnaire.

MET: Metabolic Equivalent.

A prospective cohort study from Western Massachusetts identified increased stress levels from early-to-mid-pregnancy as a risk factor for GDM, concurring with present study findings.²⁵ Risk associated with physical inactivity prior or during early pregnancy has been reported by Harizopoulou et al. (Greek-version of IPAQ), similar to the present study.²⁶

Multigravid status is a proven risk factor of GDM.¹⁹ Risk of GDM with weight gain of > 7 kgs in the present pregnancy was supported by a study done in Rohtak, Haryana.¹¹ Cohort studies from Northern China also found higher GDM prevalence among subjects with greater weight gain from pre-pregnancy to GCT testing.²⁶ Studies carried out by Dahiya et al.,¹⁹ and Nanda et al.²⁴ have reported polyhydramnios, vaginal infections and pre-term labor to be associated more with GDM subjects, comparable to the present study findings. Positive association between GDM, glycosuria and proteinuria has also been reported in literature.²⁷

Hospital-based prospective studies carried out in different parts of India identified past history of GDM, PIH, abortions, and caesarian sections to be more likely among GDM subjects.²⁷ Positive associations between macrosomia and GDM irrespective of study design and diagnostic criteria has been well established,²⁴ which was in line with the present study findings.

Significant association between GDM and family history of DM have been reported by multiple Indian studies.^{11,20,24} Arora GP et al.,²⁸ have reported high prevalence of GDM among subjects consuming high calorie diet especially non-vegetarian diet similar to the present study. Lesser consumption of protective foods is a known risk factor for T2DM and GDM risk factor profile which was similar, to the findings of the

present study too.

The key objective of the study was to identify risk factors in coastal/seaside area. The unique features of this study population are high literacy rates, availability and ease of access to health facilities, universal utilization of antenatal care services and 100% institutional deliveries. Although it would have been ideal to highlight these variables, the differences are underscored as these characteristics are shared uniformly between cases and controls. Hence, these features have not been identified in the analysis.

Thus to conclude, the key risk factors for GDM were maternal and paternal history of DM, age at menarche ≥ 14 years, age at marriage (25–29 years), multiparity, high perceived stress, less physical activity, and low intake of green leafy vegetables. Prospective enrolment of GDM cases in 1:3 case-to-control ratio, in a hospital setting is the main highlight of the study. Change of diagnostic criteria during the study course, a possible limitation in any prospective design; indirectly helped in paralleling the two criteria with respect to risk factors and confirmed no difference between diagnostic criteria. Non-uniformity in GDM diagnostic criteria, across centres and geographical areas makes comparisons difficult. Eliciting dietary information during a single interview has been another limiting factor. Furthermore, hospital-based data collection limits the generalizability of the study findings. But community-based identification of GDM cases is a difficult task, due to varying time periods of diagnosis and multitude of tests and varying diagnostic criteria in practice. Thus, this hospital based approach was most feasible and pragmatic in a region where institutional antenatal care is universal; and hence the findings reflect the population scenario closely.

Disclaimer

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Declaration of competing interest

Nil.

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