International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Tripathi R et al. Int J Reprod Contracept Obstet Gynecol. 2025 Feb;14(2):488-494
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20250182

Original Research Article

Association of physical metabolic markers with perinatal outcomes in low-risk pregnant women: a prospective cohort study

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Received: 03 April 2024
Revised: 19 January 2025
Accepted: 20 January 2025

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ABSTRACT

Background: This prospective study was planned to study the correlation of all physical metabolic markers (BMI, WC, WHR, and WHtR) in the antenatal period with perinatal outcomes.
Methods: All pregnant women who had first antenatal visit before 20 weeks were recruited into the study for period of 1 year. Detailed history was taken followed by a thorough general physical examination (including BMI, WC, WHR, and WHtR as per Indian standards).
Results: In multivariate logistic regression model none of parameters actually predicted the onset of GDM. Incidence of LSCS showed significant association with WC and WHtR. BW>3.5 kgs and NICU admission had a significant statistical association with WHtR.
Conclusions: BMI, WC, WHR and WHtR should be measured in all pregnant women at the first antenatal visit. WC predicts caesarean delivery, BMI predicts large for gestational age baby, and WHtR is a novel marker which predicts both.

Keywords: BMI, GDM, LSCS, Macrosomia, pregnancy, Waist circumference, Waist-to-height ratio, Waist-to-hip ratio

INTRODUCTION

The uterine milieu has a long-lasting effect on the future cardiometabolic health profile of a child. Newborns born to obese mothers are at increased risk of large for gestational age (LGA), macrosomia (>4000 g at birth), or small for gestational age (SGA), as well as having a higher risk of developing obesity and cardiovascular disease in later life. Macrosomia is an independent risk factor for a longer duration of the first and second stage of labor, instrumental delivery, shoulder dystocia, perineal injuries, postpartum hemorrhage, increased frequency of admission to NICU, and lower Apgar scores.[1,2] Proper pre-conceptional counseling and antenatal risk assessment are crucial as mother's health is an important determinant of obstetric and neonatal outcomes. With the ongoing pandemic and the provision of fewer antenatal visits, a special focus should be on evaluating and improving maternal health in the periconceptional/early antenatal period.[3] Physical metabolic markers such as body mass index (BMI), central adiposity measures such as waist circumference (WC), waist hip ratio (WHR), and waist height ratio (WHtR) can be easily measured at the preconceptional/first antenatal visit. WC, WHR, and WHtR, being markers of central adiposity, reflect on visceral fat. These markers have previously been implicated as predictors of diabetes and cardiovascular diseases.[4] They are risk factors for the development of gestational diabetes mellitus (GDM), preeclampsia, the need for caesarean section (CS), the newborn LGA, and macrosomia in antenatal patients in previous studies.[5-7]

However, most previous studies are retrospective, or population registry based where information has been collected using questionnaires. They have measured the correlation of few maternal obesity measures with selected obstetric and neonatal outcomes. Therefore, a prospective study was planned to study the correlation of all physical metabolic markers (BMI, WC, WHR and WHtR) in the antenatal period with obstetric and neonatal outcomes. In this study, the objective was to establish the association between maternal physical metabolic markers and perinatal outcomes along with an attempt to determine which marker is the most useful to predict pregnancy outcomes in low-risk pregnant women.

METHODS

This was prospective cohort study conducted at Maulana Azad Medical College, New Delhi from December 2011-November 2012. All pregnant women who had first antenatal visit prior to 20 weeks were recruited into the study for a period of 1 year.

Selection criteria of the patients

All pregnant women who had first antenatal visit prior to 20 weeks were recruited into the study for a period of 1 year. Women with multiple pregnancy, known cases of diabetes mellitus, hypertension, uncontrolled hypothyroidism, chronic diseases, autoimmune disorders, taking medications known to affect metabolism such as steroids, metformin, etc. and who were unwilling to give their consent were excluded from the study.

Ethical approval

Ethical approval from Institutional Ethics Committee was taken (F.no./11/IEC/MAMC/2011).

Procedure

Written informed consent was obtained from all subjects who met the inclusion criteria and exclusion criteria. A detailed history was taken followed by a thorough general physical examination (including BMI, WC, WHR, and WHtR) and a systemic examination. The weight of the women was measured to the nearest 0.1 kg with a thick digital glass weighing machine. Height was measured to the nearest of 0.1 cm with the stadiometer in erect posture without foot wear. WC was measured around 2.5 cm above umbilicus in standing posture with normal expiration. Hip circumference was measured around the level of the anterior supine iliac spines. These physical markers were measured by 2 trained nursing staff to provide standardised measurements. Routine obstetric examination was performed in all patients.

Routine antenatal investigations were done. All prenatal women were tested for GDM by oral glucose tolerance test using a 75 gramme glucose load according to the IADPSG cutoff. All pregnant women recruited were followed up until delivery. The following cut-offs (reference) were taken as per Indian standards.

BMI: Normal: <22.9kg/m^2, Overweight: 23-24.9kg/m^2, Obese: >25kg/m^2.[8]

Waist circumference: <80 cm: Optimum, >80 cm: High.[9]

WHR: <0.81: Optimum, >0.81: High.[9]

WHtR: <0.53: Optimum, >0.53: High.[10]

The overall recruitment and follow up pattern is delineated in Figure 1. The maternal outcomes assessed were mode of delivery(LSCS), occurrence of GDM, and HTN. Among neonatal outcomes, birth weight (BW) >3.5 kg, admission to NICU, and hypoglycemia were evaluated.

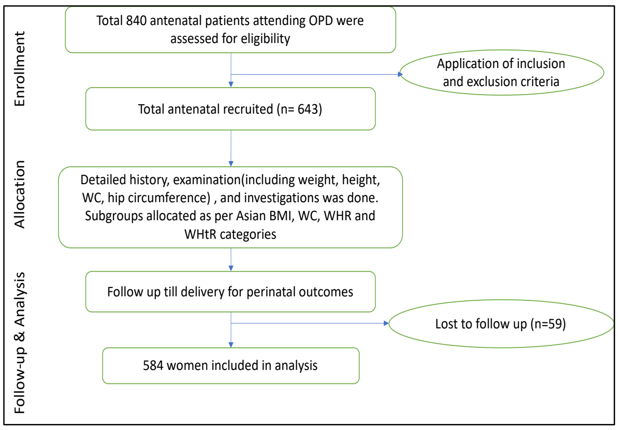

Figure 1: Depicting methodology.

Statistical analysis

The statistical package for social sciences, version 23 (SPSS-23, IBM, Chicago, USA) was used for data analysis. Descriptive statistics were presented in mean ± SD (for quantitative data) and frequency with percentages (for categorical data). The association between categorical variables was tested using the Chi-square test; if the expected frequency was found to be less than 5 in any particular cell, the Fischer exact test was used. A minimum 95% confidence interval or p-value<0.05 was considered statistically significant. Binary logistic regression analysis was used to identify the factors for the outcome variables. Factors found to be statistically significant in univariate logistic regression analysis were subjected to multivariate logistic regression to adjust and control the effect of confounder variables. The results are presented in terms of the odds ratio and the adjusted odds ratio in a univariate and multivariate analysis.

RESULTS

Baseline characteristics

A total of 584 study participants for whom all data were available were included in the final analysis. All the participants recruited were low-risk antenatal cases having no previous obstetrical and medical risk factors with mean POG of 16.35±3.07 weeks. A significant difference was observed between mean age and BMI, WC, WHR and WHtR among participants. Participants with the higher mean age tend to have higher BMI, WC, WHR, and WHtR, respectively. There was no significant relationship between socioeconomic status and BMI, WC, WHR, and WHtR of the participants but distribution of educational status was significant in BMI, WHR, and WHtR groups (Table 1).

Table 1: Sociodemographic details of the study participants according to the various maternal metabolic markers.

Parameters	Overall	BMI				WC			WHR			WHtR		
		≤22.9	23-24.9	≥25	P value	<80 cm	>80 cm	P value	<0.81	>0.81	P value	<0.53	>0.53	P value
Total subjects	584	306 (52.4)	130 (22.3)	148 (25.3)	-	428 (73.3)	156 (26.7)	-	252 (43.2)	332 (56.8)	-	450 (77.1)	134 (22.9)	-
Age (years) (mean± SD)	24.9±3.5	24.2±3.2	25.0±3.7	26.21±3.7	<0.001	24.4±3.3	26.3±3.8	<0.001	24.4±3.3	25.3±3.7	0.021	24.5±3.4	26.3±3.8	<0.001
Education														
Illiterate N (%)	36 (6.2)	16 (5.3)	11 (8.3)	9 (6.0)		25 (5.8)	11 (7.1)		24 (7.2)	12 (4.8)		12 (9.0)	24 (5.3)	
Primary N (%)	59 (10.1)	26 (8.6)	13 (9.9)	20 (13.4)		39 (9.1)	20 (12.9)		42 (12.7)	17 (6.8)		21 (15.8)	38 (8.4)	
Middle to senior secondary N (%)	381 (65.2)	217 (71.6)	84 (63.6)	80 (53.7)	0.010	292 (68.1)	89 (57.4)	0.121	202 (60.8)	179 (71.0)	0.031	75 (56.4)	306 (67.9)	0.020
Graduate and above N (%)	108 (18.5)	44 (14.5)	24 (18.2)	40 (26.9)		73 (17.0)	35 (22.6)		64 (19.3)	44 (17.5)		25 (18.8)	83 (18.4)	
Socio-economic status														
Upper N (%)	12 (2.0)	5 (41.7)	2 (16.7)	5 (41.7)		6 (50.0)	6 (50.0)		4 (33.3)	8 (66.7)		9 (75.0)	3 (25.0)	
Upper middle N (%)	75 (12.8)	38 (50.7)	18 (24.0)	19 (25.3)		54 (72.0)	21 (28.0)		30 (40.0)	45 (60.0)		61 (81.3)	14 (18.7)	
Lower middle N (%)	304 (52.0)	161 (53)	61 (20.1)	82 (27)	0.558	217 (71.4)	87 (28.6)	0.134	135 (44.4)	169 (55.6)	0.895	230 (75.7)	74 (24.3)	0.672
Upper lower N (%)	176 (30.1)	89 (50.6)	46 (26.1)	41 (23.3)		138 (78.4)	38 (21.6)		75 (42.6)	101 (57.4)		136 (77.3)	40 (22.7)	
Lower N (%)	17 (2.9)	10 (58.8)	5 (29.4)	2 (11.8)		14 (82.3)	3 (17.6)		8 (47.1)	9 (52.9)		15 (88.2)	2 (11.8)	

BMI: Body mass index; WC: Waist circumference; WHR: Waist-hip ratio; WHtR: Waist-Height Ratio

Table 2: Association of maternal and neonatal pregnancy outcomes with various maternal metabolic markers (n=584).

Parameter	Total	Body mass index				WC			WHR			WHtR		
		<22.9	23-24.9	>25	P value	<80 cm	>80 cm	P value	<0.81	>0.81	P value	<0.53	>0.53	P value
GDM (n=584)														
Yes N (%)	39 (6.5)	8 (2.6)	4 (3.0)	27 (18.1)	<0.001	11 (2.6)	28 (18.1)	<0.001	7 (2.8)	32 (9.6)	0.001	16 (3.6)	23 (17.3)	<0.001

Continued.

Parameter	Total	Body mass index				WC			WHR			WHtR		
		<22.9	23-24.9	>25	P value	<80 cm	>80 cm	P value	<0.81	>0.81	P value	<0.53	>0.53	P value
No N (%)	545 (93.3)	295 (97.3)	128 (97.0)	122 (81.9)		418 (97.4)	127 (81.9)		245 (97.2)	300 (90.4)		435 (96.5)	110 (82.7)	
LSCS (n=582)														
Yes N (%)	91 (15.6)	42 (12.6)	20 (15.2)	29 (19.6)	0.441	57 (13.3)	34 (22.1)	0.008	40 (15.9)	51 (15.4)	0.677	56 (12.4)	35 (26.5)	<0.001
No N (%)	491 (84.4)	261 (87.5)	112 (84.9)	118 (79.8)		372 (86.7)	119 (77.3)		212 (84.1)	279 (84.3)		394 (87.4)	97 (73.5)	
Hypertension (n=584)														
Yes N (%)	20 (3.4)	4 (1.4)	3 (2.2)	13 (8.7)	<0.001	7 (1.6)	13 (8.4)	<0.001	2 (0.8)	18 (5.4)	0.002	10 (2.2)	10 (7.5)	0.006
No N (%)	564 (96.6)	299 (98.6)	129 (97.7)	136 (91.3)		422 (98.4)	142 (91.6)		250 (99.2)	314 (94.6)		441 (97.8)	123 (92.5)	
Birth weight > 3.5 Kg (n=584)														
Yes N (%)	10 (1.7)	3 (1.1)	2 (1.5)	5 (3.4)	0.307	6 (1.4)	4 (2.6)	0.331	2 (0.8)	8 (2.4)	0.136	5 (1.1)	5 (3.8)	0.038
No N (%)	574 (98.3)	300 (99.4)	130 (98.5)	144 (96.6)		423 (98.6)	151 (97.4)		250 (99.2)	324 (97.6)		446 (98.9)	128 (96.2)	
NICU admission (n=582)														
Yes N (%)	16 (2.7)	7 (2.5)	1 (0.8)	8 (5.4)	0.103	9 (2.1)	7 (4.6)	0.108	5 (2.0)	11 (3.3)	0.324	9 (2.0)	7 (5.3)	0.041
No N (%)	566 (97.2)	296 (97.5)	131 (99.2)	139 (94.6)		420 (97.9)	146 (95.4)		247 (98.0)	319 (96.7)		441 (98.0)	125 (94.7)	
Hypoglycemia (n=582)														
Yes N (%)	3 (0.5)	0	2 (1.5)	1 (0.7)	0.239	1 (0.2)	2 (1.3)	0.111	0	3 (0.9)	0.129	2 (0.4)	1 (0.8)	0.659
No N (%)	579 (99.4)	303 (100.0)	130 (98.5)	146 (99.3)		428 (99.8)	151 (98.7)		252 (100.0)	327 (99.1)		448 (99.6)	131 (99.2)	

BMI: Body mass index; WC: Waist circumference; WHR: Waist-hip ratio; WHtR: Waist-Height Ratio

The prevalence of GDM was 6.7% in the present study. GDM and HTN showed a highly significant association with BMI, WC, WHR, and WHtR. The caesarean section rate was 15.6 % in the present study. The incidence of LSCS showed a significant association with WC and WHtR while no significant association with BMI and WHR was observed. BW >3.5 kgs and admission to the NICU had a significant statistical association with WHtR. Neonatal hypoglycaemia was not significantly associated with any of the maternal markers (Table 2).

Table 3: Multivariate logistic regression for association with metabolic parameters with GDM and LSCS.

Variable	Crude's odds ratio	Adjusted odds ratio	95% confidence interval	P value
BMI				0.1
≤22.9	Reference	Reference		
23-24.9	0.97	0.71	0.08-6.13	
≥25	1.13	2.14	0.22-20.12	
WC				0.05
<80 cms	Reference	Reference		
>80 cms	8.38	2.98	0.97-9.14	
WHR				0.2
<0.81	Reference	Reference		
>0.81	3.73	1.84	0.72-4.72	
WHtR				0.7
<0.53	Reference	Reference		
>0.53	5.684	0.832	0.281-2.464	
BMI				0.5
≤22.9	Reference	Reference		
23-24.9	1.11	1.36	0.45-4.09	
≥25	0.80	1.11	0.34-1.59	
WC				0.010
<80 cms	Reference	Reference		
>80 cms	1.21	1.86	1.16-2.99	
WHR				0.07
<0.81	Reference	Reference		

Continued.

Variable	Crude's odds ratio	Adjusted odds ratio	95% confidence interval	P value
>0.81	0.62	1.60	0.95-2.70	
WHtR				
<0.53	Reference	Reference		<0.001
>0.53	3.70	2.54	1.58-4.09	

*For GDM, adjusted for Age, education, socioeconomic status, LSCS, BW, NICU admission, Neonatal hypoglycaemia; For LSCS, adjusted for Age, education, socioeconomic status, GDM, BW, NICU admission, Neonatal hypoglycaemia

In univariate logistic regression analysis for GDM metabolic predictors, all physical metabolic markers (BMI, WC, WHR, and WHtR) were found to have a significant statistical association. Putting all the variables in the multivariate logistic regression model, none of the above parameters actually predicted the onset of GDM (Table 3).

After the multivariate logistic regression model, WC and WHtR (as in univariate analysis), were found to actually predict the occurrence of LSCS. Pregnant ladies with a WC greater than 80 cm were found to have 1.8 times more chances (AOR-1.86) of having a LSCS delivery than those with a WC less than 80 cm. Pregnant women with a WHtR of more than 0.53 were found to have 2.5 times more odds (AOR-2.54) of having a LSCS delivery than those with a WHtR of less than 0.53 (Table 3).

We analyzed relative association of all physical metabolic markers with BW >3.5 kg through receiver operating characteristic curve (ROC). ROC curves for the risk of having a baby with more than 3.5 kg of birth weight depicted that WHtR >0.53 (AUC 0.7) was the best predictor followed by BMI> 25 kg/m^2 (AUC 0.66), WHR >0.81 (AUC 0.63), and WC > 80 cm (AUC 0.57) (Figure 2).

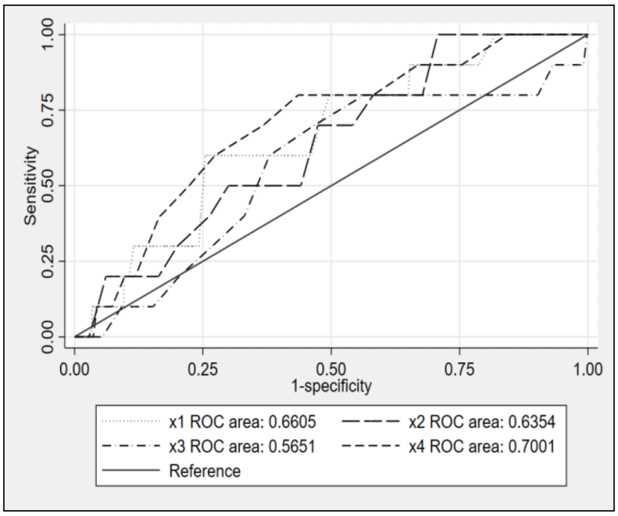

Figure 2: ROC curve of birth weight >3.5 kgs. x1: BMI, x2: WHR, x3: WC, x4: WHtR

DISCUSSION

In this prospective cohort study, we examined the effect of BMI, WC, WHR, and WHtR on pregnancy and neonatal outcomes. We reported 25.0% and 26.2 % of our pregnant women as overweight and obese respectively, which is almost the same as reported in the NFHS-4 data and another study using Indian using Asian cut-off points.[11] The mean age of the participants was higher in the overweight, obese group, WC > 80 cm and WHtR >0.53 groups in our study, as reported by others.[5] It implies that pregnant women conceiving at a higher age are more at risk of being obese and poorer pregnancy outcomes and requires close monitoring. Our study showed that socioeconomic status bears no significant association with the prevalence of obesity in pregnant women which is in contradiction by other studies.[12,13] Educational status showed significant association with BMI, WHR, and WHtR. The study by Anwanyu et al also stated that formal education and health promotion campaigns support the development of healthy lifestyle practices and reduces the prevalence of obesity.[14]

Gao et al. reported that both BMI and WC led to a significantly higher incidence of primary caesarean section. Applying multivariate logistic regression analysis, we found a significant association between WC and WHtR with caesarean delivery. This is partly in contradiction with Gao et al as the current study showed association with WC and not BMI.[5] This could be due to the difference that they have used pre-pregnant BMI and WC in their study. Another study done by Suresh et al quoted the same findings as our study. They also reported that central adiposity markers fare well as compared to generalised obesity marker (BMI) in predicting adverse outcomes in pregnancy.[15] Mcdonnold et al analyzed that data of 2276 low risk nulliparous pregnant women upto 16 weeks of gestation to find out predictive ability of WHR as compared to BMI in predicting LSCS and risk of large for gestational age infant. They reported that BMI is better than WHR in predicting LSCS, however, both are not strong predictors of cesarean delivery in low-risk women BMI (AUC = 0.6) versus WHR (AUC = 0.58).[6] Our study also could not find a significant association of cesarean delivery with BMI and WHR.

Our study demonstrated the advantage of WHtR >0.53 in predicting a 2.21 times higher risk of LSCS. Although we did not find any studies in pregnant women with WHtR, WHtR has been implicated as the better marker compared to BMI, WC, WHR, and WHtR to predict metabolic syndrome in nonpregnant individuals.[16] In a recent study published in 2022, Zang et al. observed that WHtR was the best predictor of cardiovascular diseases in hypertensive adults compared to BMI, WC, and WHR.[17] WHtR is an unexplored marker in pregnant women and its role in predicting perinatal outcomes needs to be evaluated.

BMI, WC, WHR and WHtR didn't predict the risk of developing GDM after regression analysis in our study. This is in contradiction to an Indian study published previously.[18] However, when we dug deeper into the literature, we witnessed very interesting studies. Narayan et al stated that the South Asian population has reduced insulin secreting potential and lower compensatory reservoir of insulin.[19] Wells et al also reported that lower lean body mass and short height are responsible for the development of diabetes.[20] The development of GDM in low-risk pregnant women could be attributed to ethnicity and genetics according to the findings of the present study.

All the physical metabolic markers (BMI, WC, WHR, WHtR) showed significant association with hypertension as found in another study on preelamptic pregnant women.[21] The pregnant women with higher BMI, WC, WHR, and WHtR tend to develop HTN more frequently.

The current study reports that WHtR is associated with the incidence of BW >3.5 kg, followed by BMI, WC and WHR, respectively. All the maternal physical markers predicted BW >3.5 kg in newborn with WHtR emerging as superior marker. Although WHR is a commonly used marker, WHtR is a newer marker that shows a promising role in the prediction of perinatal outcomes (LSCS, BW >3.5 kg, NICU admission) in low-risk pregnant women according to the findings of the present study. A general population based study stated WHtR is a superior predictor of diabetes and hypertension as compared to other markers.[22] Future studies exploring role of WHtR as the marker of obesity and its association with pregnancy outcomes should be planned.

In an Indian study done by Kutchi et al using the same cut-off for BMI as present study (New Indian Asian Guidelines), it was demonstrated that BMI >25 kg/m^2 in Indian pregnant women upto 16 weeks gestation is associated with large for gesstational age baby as opposed to women having BMI <25 kg/m^2. Our study reproduced these findings too.[18] A prospective study reported that the waist hip ratio in the third and fourth quartiles (median values were 0.75 and 0.81for the third and fourth quartile, respectively) led to a significantly higher percentage of macrosomia (>4000 grams, 4500 grams) and large for gestational age >95 centile after adjusting for contributing factors.[7] Using the same cut-off point, our study also showed near significant association between WHR and BW. The reproducibility of findings in pregnant women having different ethnicity and geography confirms that maternal physical metabolic markers could serve as cost-effective markers to predict perinatal outcomes in even low risk pregnant women. Routine use of these markers in pregnant women may be a cost-effective method to improve perinatal outcomes. ASHA, ANM, and grass route workers could be easily trained to measure this marker in pregnant women at their first visit and refer women at risk to higher centres. This will result in the timely detection and treatment of pregnant women at risk and therefore in better perinatal outcomes.

Studies have found an association of maternal obesity with admission to the NICU and neonatal hypoglycemia.[2,15,23] However, our study showed an association with only WHtR and not with other markers probably due to the low-risk nature of our cohort, resulting in a smaller number of newborns with the above outcomes.

Strengths: The strengths of the present study are; it is prospective, every metabolic measure is measured by trained designated personnel in the same group of women, ensuring precision and reducing observation and recall biases, comprehensive maternal and neonatal outcomes were evaluated, included pregnant patients up to the second trimester and thus demonstrating the benefit to measure physical metabolic beyond the first trimester, extensive data on baseline characteristics and use of regression analyzes to predict independent association of various metabolic markers to pregnancy outcomes.

Limitations: The limitations of the present study are the nonavailability of prenatal physical metabolic markers and other biochemical and hormonal biomarkers of adiposity. However, many studies have shown the benefit of measuring physical metabolic markers up to 28 weeks.[24] Furthermore, physical metabolic markers can be used as a proxy for biochemical and hormonal markers with excellent reproducibility of results in cost-constrained settings.

CONCLUSION

This study revealed the importance of physical metabolic markers in predicting perinatal outcomes in low-risk pregnant women in the antenatal period. All pregnant women should undergo a detailed physical examination at the first antenatal visit and BMI, WC, WHR and WHtR should be measured. WC predicts caesarean delivery, BMI predicts large for gestational age baby, and WHtR is a novel marker which predicts both. All the four markers are not associated with the onset of GDM in low risk pregnant women. The onset of GDM could be due to ethnicity and genetics; therefore, all women should undergo screening for GDM. Universal screening is the only way to control the epidemic of diabetes in pregnant women in India. Since in developing countries routine prenatal visits are not so common and most pregnant women present with OPD in the first/early second trimester, our study signifies the fact that it is never too late to take preventive measures to improve perinatal outcomes. These easily measured markers could be used by ASHAs and other grass-root level workers to timely detect and refer at risk women. The benefit of measuring WHtR in pregnant women must be explored in future prospective studies. Currently, interventional studies with various perinatal outcomes as the end point are needed to establish the causal association between physical metabolic markers and pregnancy outcomes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee (F.no./11/IEC/MAMC/ 2011)

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Cite this article as: Tripathi R, Verma D, Singh N, Ramji S, Mishra N, Pandey S, et al. Association of physical metabolic markers with perinatal outcomes in low-risk pregnant women: a prospective cohort study. Int J Reprod Contracept Obstet Gynecol 2025;14:488-94.