ORIGINAL RESEARCH PAPER

Volume-8 | Issue-4 | April-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

TO STUDY THE PREVALENCE OF METABOLIC SYNDROME AND ITS IMPACT ON COMPLICATIONS IN PRE-ECLAMPSIA

Gynecology

Irshad Ahmad Tali Department of Obstetrics and Gynecology, GMC -Srinagar

Hilal Ahmad Tali* Department of Gastroenterology & Hepatology, GMC -Srinagar *Corresponding Author

Rubiya Ryhan Department of Immunohematology and Transfusion Medicine GMC, Srinagar

Samiyah Mufti Department of Obstetrics and Gynecology, GMC -Srinagar

Falak Ara Department of Anaesthesia ,GMC-Srinagar

ABSTRACT

Background: Pre-eclampsia, a syndrome characterized by the new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman, complicates 2–8% of pregnancies and contributes to considerable maternal and neonatal morbidity and mortality. Preeclampsia shares many characteristics of metabolic syndrome (MeS) which has led many investigators to elucidate this relationship. The aim and objective of this study was to assess the prevalence of MS in preeclampsia and its impact on complications in pre-eclampsia.

Methods: The study included 130 cases (41 gestational hypertension (GHTN), 27 mild pre-eclampsia (Mild PET), 47 severe preeclampsia (Severe PET), 13 pre-eclampsia superimposed on chronic hypertension (PSHTN) and 2 eclampsia) based on pre-specified maternal characteristics according to ACOG criteria after 20 th week of gestation. Two hundred normotensive pregnant females served as controls. The frequency of MS was assessed using pregnancy adaptation of MeS definition of the NCEP-ATP III criteria in cases and controls.

Results: Metabolic syndrome was found in 37.7% of preeclampsia group and 12% of control group ($p<0.00$). Among the components of MeS, preeclampsia group was having significantly higher sugars (30% Vs 20%) and body mass index (BMI) (23.8% Vs 7.5%) than controls. The clinical course in preeclampsia with MeS was complicated by IUD (intrauterine death), IUGR (intrauterine growth retardation), preterm delivery, APH and pulmonary edema. Oligohydromnios was less common in preeclampsia with MeS.

Conclusions: The frequency of MeS was higher in preeclampsia group as compared to normotensive group. MeS was more significantly higher in patients with severe preeclampsia. In our study there were no demographic, clinical and laboratory predictors of MeS in preeclampsia. On the other hand, preeclampsia patients with MeS had significant maternofoetal complications.

KEYWORDS

Metabolic syndrome, Preeclampsia, Hypertension

INTRODUCTION

Pre-eclampsia, a syndrome characterized by the new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman, complicates 2–8% of pregnancies and contributes to considerable maternal and neonatal morbidity and mortality.[1–3] The etiology of pre-eclampsia remains unknown despite continued medical research. The pathophysiology of preeclampsia likely involves both maternal and fetal/placental factors. Abnormalities in the development of placental vasculature early in pregnancy may result in relative placental underperfusion/ hypoxia/ ischemia, which then leads to release of antiangiogenic factors into the maternal circulation that alter maternal systemic endothelial function and cause hypertension and other manifestations of the disease.

Medical conditions associated with vascular insufficiency (eg, hypertension, diabetes, systemic lupus erythematosus, renal disease, acquired and inherited thrombophilias) increase the risk of abnormal placentation and preeclampsia.[4,5]

The metabolic syndrome is a clustering of metabolic and CVD risk factor abnormalities with a shared patho-physiology that has demonstrated utility in the non-pregnant population. The metabolic syndrome-an aggregate of risks-confers an increased risk of developing Type 2 diabetes and complex CVD, which appears to be beyond that related to the individual metabolic components.[6-9] The National Cholesterol Education Program (NCEP)-adult treatment panel (ATP III) guidelines, which have gained widespread clinical use, define metabolic syndrome as three or more of five clinically ascertained risk factors: Abdominal obesity, low high density lipoprotein-C (HDL), elevated triglycerides (TG), blood pressure and fasting glucose.[9]The metabolic syndrome concept (aggregate of risk factors) has already demonstrated clinical utility in the non-pregnant population to assess CVD risk. Recently there has been a study which demonstrates that inter-pregnancy metabolic syndrome predisposes to pre-eclampsia[10] which further substantiates the fact that these two disorders share a common pathophysiology.

The aim of our study was to evaluate the association between metabolic syndrome (using both clinical and laboratory criteria) and pre-eclampsia and to study the impact of metabolic syndrome on complications in pre-eclampsia.

METHODS

This case-control study was performed in the department of Obstetrics and Gynecology in collaboration with General Medicine, at GMC Srinagar from June 2018 to February 2019 after obtaining approval from institutional Ethical Clearance Committee. Written informed consent was taken from all women recruited. Antenatal women were enrolled in the study after 20th week of gestation.

CASES

Cases included were all patients with gestational hypertension, pre-eclampsia, pre-eclampsia superimposed on hypertension and eclampsia admitted to labor and delivery.Cases (gestational hypertension, pre-eclampsia, pre-eclampsia superimposed on chronic hypertension and eclampsia) were identified based on pre-specified maternal characteristics according to ACOG criteria.5,8

Gestational hypertension

Gestational hypertension was defined as elevated blood pressure (≥140/90 mmHg on two measurements ≥6 h apart) without proteinuria after 20th week of gestation.

Pre-eclampsia

Pre-eclampsia was defined as elevated blood pressure (≥140/90 mmHg on two measurements ≥6 h apart) with proteinuria >300 mg/24 hours or ≥1 +proteinuria on spot urine examination after 20th week of pregnancy.

Pre-eclampsia superimposed on chronic hypertension

Pre-eclampsia superimposed on chronic hypertension was defined as new onset proteinuria > 300 mg/24 hours or ≥1 + proteinuria on spot urine examination in a patient of chronic hypertension after 20 th week of pregnancy.

Eclampsia

Eclampsia was defined as occurrence of seizure in a patient of pre-eclampsia without any personal history of seizures prior to pregnancy or family history of seizures.

Severity of pre-eclampsia

The severity of pre-eclampsia was determined by the involvement of following six sites prior to delivery CNS, renal, liver, hematogic, vascular and fetoplacental unit.

Assessment for metabolic syndrome

Metabolic syndrome was diagnosed by utilizing the pregnancy adaptation of MeS criteria of NCEP ATP III 13 laboratory and clinical criteria and it included (1) Blood pressure, (2) fasting glucose (as a measure of insulin resistance and/or glucose intolerance), (3) obesity (measured as hip to waist ratio or pre-pregnancy body mass index (BMI ≥ 30Kg/ m2), (4) HDL and (5) TG.

The changes made were due to the metabolic abnormalities that occur during pregnancy, and it included.

Blood Pressure

As the study group involves pregnant patients with the diagnosis of hypertension (≥140/90 mmHg), and WHO utilizes 140/90 mmHg instead of 130/85 mm Hg therefore we took BP of 140/90 as criteria for diagnosis of HTN.

Blood sugar

The presence of gestational diabetes was defined by fasting plasma glucose ≥92 mg/dL or a single step OGTT using 75 grams in the fasting state with any single abnormal value of plasma sugar fasting >92 mg/dl, 1 hour >180 mg/dl and 2 hour >153 mg/dl utilizing International association of Diabetes and pregnancy study groups (IADPSG) criteria was used as a measure for insulin resistance.21 Any woman who tested positive for gestational diabetes was considered positive for this factor.

Anthropometric assessment

Anthropometric measurement was done measuring height to the nearest centimeter without shoes with a wall mounted ruler and weight to the nearest to 0.1 Kg in light clothing. For the variable of obesity, we utilized pre-pregnancy BMI (calculated using reported height and weight before pregnancy-kg/m2) given the impracticality of waist circumference in gravid women. BMI ≥30Kg/m2 has been utilized in the World Health Organization (1999) diagnosis of metabolic syndrome.15,15

Lipid profile

Clinical endpoints for HDL was based on non-pregnant definition of <50 mg/dL but then TG levels were taken >250 mg/dl as modified by reports of lipid levels in pregnancy.16

Thus, our definition of metabolic syndrome included three out of five of the following components:

- Hypertension (BP≥140/90 mm Hg),
- Diabetes (gestational or pre-gestational) Fasting blood sugar ≥92 mg/ dl or a single step OGTT using 75 grams in the fasting state with any single abnormal value of plasma sugar fasting >92 mg/dl, 1 hour >180 mg/dl and 2 hour >153 mg/dl.
- Pre pregnancy BMI ≥30 Kg/m2,
- HDL ≤50 and
- TG ≥250.

Controls

Controls were enrolled from all normotensive women presenting for delivery at term (≥37 weeks) for spontaneous rupture of membranes, term labor, and induction of labor or caesarean section.

Exclusion criteria

- Multiple gestation pregnancies.
- Untreated hypothyroidism at the time of diagnosis of pre-eclampsia.
- Chronic hypertension without proteinuria.

Statistical analysis

Statistical data analysis was done utilizing SPSS 23. Normality of test was done by Shapiro-Wilk test. Median with Interquartile range (IQR) was calculated for age, body mass index, gestational age at delivery, systolic and diastolic BP, hemoglobin, platelet count, sugar fasting, triglycerides, high density lipoproteins, uric acid, lactate dehydrogenase (LDH), SGOT and SGPT as they were not normally distributed. Nonparametric data was analysed utilizing Mann-Whitney U test. Nominal categorical data between the groups were compared using Chi-square test or Fisher's exact test as appropriate. Continuous categorical data between the groups were compared using sample t-test. $p<0.05$ was considered statistically significant.

RESULTS

A total of one hundred and thirty hypertensive pregnant females were included in this study. The cases included gestational hypertension, mild pre eclamptic toxaemia (PET), severe PET, eclampsia and pre-eclampsia superimposed on chronic hypertension.

Table 1: Baseline characteristic of hypertensive (cases) pregnant females and normotensive (controls) pregnant females.

	Hypertensive pregnant females	Normotensive pregnant females	p value
Age [years] (median (IQR)	31(6)	30 (5)	0.219
BMI [Kg/m^2] (Median (IQR))	31.26 (4)	30.65 (3)	0.065
SBP [mm Hg] (median (IQR))	160 (20)	110 (10)	0.00
DBP [mm Hg] (median (IQR))	106 (21)	70 (20)	0.00
Platelet [10 ^{9} cells/L] (median(IQR))	150 (108)	190 (86)	0.00
SGOT [Units/L] (median (IQR))	37 (73)	24 (13)	0.00
SGPT [Units/L] (median (IQR))	42.5 (75)	19 (13)	0.00
BSF [mg/dL] (median (IQR))	86 (19)	82 (17)	0.003
HDL [mg/dL] (median (IQR))	60.5 (24)	61 (18)	0.78
TG [mg/dL] (median (IQR))	270 (120)	261.5 (62)	0.00
Uric acid [mg/dL] (median (IQR))	9 (5)	6.15 (2)	0.00
LDH [mg/dL] (median (IQR))	405 (515)	264 (74)	0.00
Gestational age at delivery [weeks] (median) IQR))	38 (2)	39 (2)	0.00

Table 2: Contingency table showing distribution (percent) of metabolic syndrome among hypertensive pregnant females and normotensive pregnant females.

	Met Syndrome Absent		Met Syndrome Present		P value
	Count	%	Count	%	
Normotensive group (200)	158	79	42	21	p<0.000
Hypertensive group (130)	70	53.8	60	46.2	

Table 3: Components of metabolic syndrome in hypertensive and normotensive pregnant females.

	Hypertensive pregnant group (130)		Control group (200)		P value
	(count)	(percentage)	(count)	(percentage)	
Elevated BMI (Kg/m2)	81	62.3	124	62	0.955
Elevated BP (mm Hg)	130	100	0	0	0.000
Low HDL (mg/dL)	33	25.4	46	23	0.620
Elevated TG (mg/dL)	71	54.6	110	55	0.945
Abnormal sugar (mg/dL)	39	30	40	20	0.038

Table 4: Correlation of demographic and biochemical parameters of hypertensive pregnant females with and without metabolic syndrome.

	PIH without MS	PIH with MS	p Value
Age [years] (median (IQR)	31 (7)	30 (4)	0.909
BMI [Kg/m2] (Median (IQR))	29.79 (3)	32.56 (3)	0.000

SBP [mm Hg] (median (IQR))	158 (20)	164 (30)	0.008
DBP [mm Hg] (median (IQR))	100 (22)	110 (18)	0.028
Platelet [10 9 cells/L] (median (IQR))	161 (104)	138.5 (129)	0.612
OT [Units/L] (median (IQR))	37 (60)	46 (130)	0.362
PT [Units/L] (median (IQR))	40 (58)	50.5 (106)	0.067
BSF [mg/dL] (median (IQR))	83.5 (12)	94.5 (27)	0.000
Uric acid [mg/dL] (mean±SD)	9.45 ± 3.15	9.29 ± 3.31	0.715
HDL [mg/dL] (median (IQR))	63 (20)	55 (26)	0.013
TG [mg/dL] (median (IQR))	241 (85)	320 (119)	0.000
Gestational age at delivery [weeks](median) IQR))	38 (2)	38 (2)	0.006

Table 5. Overall complication rates in hypertensive pregnant females with metabolic syndrome.

	No Complications	Complications	Pvalue
PIH No MS	45 (64.3%)	25 (35.7%)	0.100
PIH & MS	30 (50%)	30 (50%)	

Table 6. Individualized complications in hypertensive pregnant females with metabolic syndrome.

	PIH No MS	PIH with MS
IUD	2 (33.3%)	4 (66.7%)
IUGR	5 (38.5%)	8 (61.5%)
Preterm	2 (28.6%)	5 (71.4%)
DIC	0 (0%)	1 (100%)
CCF	1 (50%)	1 (50%)
PPH	7 (100 %)	0 (0%)
APH	0 (0%)	5 (100%)
Pulmonary edema	0 (0%)	2 (100%)
Oligohydromnios	6 (85.7%)	1 (14.3%)
AFD	2 (66.7%)	1 (33.3%)
PRES	0 (0%)	2 (100%)

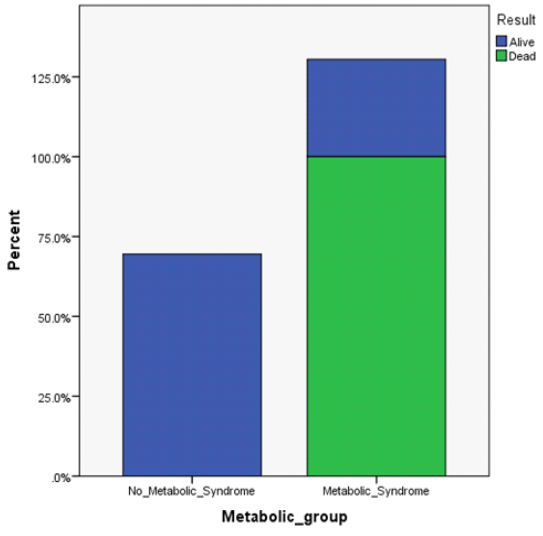
Table 7. Table showing modes of delivery in hypertensive pregnant patients with metabolic syndrome.

	NVD	LSCS	Pvalue
PIH No MS	26 (37.1%)	44 (62.9%)	0.651
PIH & MS	20 (33.3%)	40 (66.7%)	

Table 8. A 2X2 contingency table showing mortality rates in hypertensive patients with metabolic syndrome.

	Alive	Death	Pvalue
PIH No MS	70	0	0.124
PIH & MS	58	2	

Figure: Stacked bar chart showing mortality rates in hypertensive pregnant patients with metabolic syndrome.



DISCUSSION

Pregnancy is considered as an acid test for development for metabolic abnormalities, and the spectrum of these metabolic abnormalities include metabolic syndrome, dyslipidaemia and gestational diabetes mellitus. Metabolic syndrome (MeS) is being the cluster of all atherosclerotic risk factors.[17,19] The basic pathogenic mechanism of metabolic syndrome (MeS) is insulin resistance [20] in addition to an unhealthy diet, poor lifestyle, obesity and genetic factors.[17,21-23] The presence of two components of MeS during pregnancy i.e. hypertension and glucose intolerance can lead to poor placental perfusion, endothelial dysfunction and abnormal placental development.[24] Placental hypoperfusion is a critical component in the pathogenesis of preeclampsia because it elaborates a variety of factors into the maternal bloodstream that alter maternal endothelial cell function and lead to the characteristic systemic signs and symptoms of preeclampsia.[25-31]

The prevalence of MeS in PET in our study was 37.7% as compared to 12 % in controls and is in accordance with studies conducted earlier.[35-37] The prevalence of MeS in hypertensive disorders of pregnancy has varied geographically from 7.6% in a Chinese study to 66% in an Iranian study.[38,39]

There was no significant difference in age in the PET patients with MeS as compared to PET patients without MeS. These results are in accordance with observations made by previous investigators.39 Present study indicated that higher BMI, blood pressure, triglycerides, sugar and low HDL were significantly associated with MeS in PET. This is in accordance with the results observed by earlier studies.[39] There was no statistically significant difference in platelets, liver function test, serum uric acid levels among PET with MeS group as compared to the PET without MeS group.

The overall complication rates in current study were higher in the PET with MeS although the difference was statistically insignificant. IUGR, IUD, preterm delivery and APH were significantly higher in PET with MeS, whereas oligohydromnios and PPH were significantly higher in PET without MeS. The reason being the endothelial dysfunction caused by metabolic syndrome leads to complications like IUGR, IUD, APH and preterm delivery whereas oligohydromnios was more common in PET without MeS group as sugars were significantly higher in the PET with MeS group and lastly there were two deaths in our study in the hypertensive pregnant group, one each in PET with MeS and PET without MeS and the difference was statistically insignificant.

CONCLUSIONS: The frequency of MeS was higher in preeclampsia group as compared to normotensive group. MeS was more significantly higher in patients with severe preeclampsia. In our study there were no demographic, clinical and laboratory predictors of MeS in preeclampsia. On the other hand, preeclampsia patients with MeS had significant maternofoetal complications.

REFERENCES

1. Report of the National high blood pressure education program working group on high blood pressure in pregnancy. Am J ObstetGynecol 2000;183:S1–22.
2 Sibai B, Dekker G, Kupferminc M. Pre-eclampsia.Lancet 2005;365: 785–99.
3 Duley L. The global impact of pre-eclampsia and eclampsia. SeminPerinatol 2009;33:130–7.
4. ACOG Committee on Practice Bulletins--Obstetrics. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. ObstetGynecol 2002; 99:159.
5. Dekker GA. Risk factors for preeclampsia. ClinObstetGynecol 1999; 42:422.
6. Funai EF, Friedlander Y, Paltiel O, Tiram E, Xue X, Deutsch L, et al.Long-term mortality after preeclampsia. Epidemiology 2005;16:206-15.
7. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.
8. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientifi c Statement. Circulation 2005;112:2735-52.
9. McLaughlin T, Abbasi F, Kim HS, Lamendola C, Schaaf P, Reaven G.Relationship between insulin resistance, weight loss, and coronary heart disease risk in healthy, obese women. Metabolism 2001;50:795-800.
10. Stekkinger E, Scholten R, van der Vlugt M, Van Dijk A, Janssen M, Spaanderman M. Metabolic syndrome and the risk for recurrent pre-eclampsia: a retrospective cohort study. BJOG 2013;120:979–986.
11. Pereira MA, Kottke TE, Jordan C, O'Connor PJ, Pronk NP, Carreón R. Preventing and managing cardiometabolic risk: the logic for intervention. Int J Environ Res Public Health. 2009;6(10):2568-84.
12. Grundy SM. Metabolic syndrome pandemic. Arteriosclerosis, Thrombosis, Vascular Biol. 2008 Apr 1;28(4):629-36.
13. Lann D, LeRoith D. Insulin resistance as the underlying cause for the metabolic syndrome. Med Clin North Am. 2007 Nov 30;91(6):1063-77.
14. Carnethon MR, Loria CM, Hill JO, Sidney S, Savage PJ, Liu K. Risk factors for metabolic syndrome: the Coronary Artery Risk Development in Young Adults (CARDIA) study, 1985–2001. Diabetes Care. 2004;27(11):2707-15.
15. Alberti KGMM, Eckel RH, Grundyetal SM, Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120(16):1640-5.

16. Edwardson CL, Gorely T, Davies MJ, Gray LJ, Khunti K, Wilmot EG, Yates T, Biddle SJ. Association of sedentary behaviour with metabolic syndrome: a meta-analysis. PloS one. 2012 Apr 13;7(4):e34916.
17. Dekker GA. Risk factors for preeclampsia. Clin Obstet Gynecol. 1999;42:422.
18. Wang X, Athayde N, Trudinger B. A proinflammatory cytokine response is present in the fetal placental vasculature in placental insufficiency. Am J Obstet Gynecol. 2003;189:1445.
19. Redman CW, Sargent IL. Preeclampsia and the systemic inflammatory response. Semin Nephrol. 2004;24:565.
20. Roberts JM, Speer P. Antioxidant therapy to prevent preeclampsia. Semin Nephrol. 2004;24:557.
21. Makris A, Thornton C, Thompson J, Thomson S, Martin R, Ogle R et al. Uteroplacental ischemia results in proteinuric hypertension and elevated sFLT-1. Kidney Int. 2007 May 2;71(10):977-84.
22. Yinon Y, Nevo O, Xu J. Severe intrauterine growth restriction pregnancies have increased placental endoglin levels: hypoxic regulation via transforming growth factor-beta 3. Am J Pathol. 2008;172:77.
23. Rusterholz C, Hahn S, Holzgreve W. Role of placentally produced inflammatory and regulatory cytokines in pregnancy and the etiology of preeclampsia. Semin Immuno Pathol. 2007;29:151.
24. Maynard S, Epstein FH, Karumanchi SA. Preeclampsia and angiogenic imbalance. Annu Rev Med. 2008;59:61.
25. Smith GN, Walker MC, Liu A, Wen SW, Swansburg M, Ramshaw H et al. Pre Eclampsia New Emerging Team (PE-NET). A history of preeclampsia identifies women who have underlying cardiovascular risk factors. Am J Obstet Gynecol., 2008;200(58):e1- 8.
26. Stekkinger E, Zandstra M, Peeters LL, Spaanderman ME. Early-onset preeclampsia and the prevalence of postpartum metabolic syndrome. Obstet Gynecol. 2009 Nov 1;114(5):1076-84.
27. Lu J, Zhao YY, Qiao J, Zhang HJ, Ge L, Wei Y. A follow-up study of women with a history of severe preeclampsia: relationship between metabolic syndrome and preeclampsia. Chinese Med J. 2011 Mar;124(5):775-9.
28. Zhang TM, Zeng P, Han YW, Zhu XF, Zhu W, Feng C. Prevalence of metabolic syndrome in the city of Beijing. Chin J Diab. 2006;14:349-52.
29. Rafeeinia A, Tabandeh A, Khajeniazi S, Marjani A. Metabolic syndrome in preeclampsia women in gorgan. Open Biochemistry J. 2014;8:94.