Original Article

The relationship between metabolic syndrome criteria and preeclampsia in primigravid women

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Abstract

Background: Pregnancy is associated with many physiological changes, which in some cases may cause serious risks such as preeclampsia, and fetal and maternal health threats. Recent research has focused on the relationship between metabolic syndrome and preeclampsia. By identifying appropriate indicators for early diagnosis, maternal–fetal complications can be prevented. The present study aimed to investigate the association between metabolic syndrome indicators and the occurrence of preeclampsia in nulliparous pregnant women.

Materials and Methods: This was a prospective cohort study conducted on 220 nulliparous pregnant women (normal metabolic syndrome) from Isfahan health centers, Iran, selected by random quota sampling method. With physical examination and laboratory results, metabolic syndrome and preeclampsia in the second half of pregnancy were identified. Data analysis was performed using SPSS software. Descriptive statistical tests were used for demographic characteristics, and Chi-square test, Student's independent *t*-test, and Fisher's exact test were used to determine and compare the prevalence of metabolic syndrome indicators and preeclampsia.

Results: The relative frequencies of preeclampsia in the group of pregnant women with metabolic syndrome and the healthy group before week 30 ($P < 0.001$) and after 30 weeks of pregnancy ($P < 0.001$) were significantly different. The results showed a significant difference in the mean triglycerides and fasting plasma glucose between preeclampsia and control groups; however, the mean high density lipoprotein (HDL) in both groups had no significant differences.

Conclusions: Based on the results of this study, it was found that in subjects with the metabolic syndrome during pregnancy, the risk for preeclampsia in the second half of pregnancy was higher than in the general population. In this respect, with the design of preventive programs, such as weight management and lowering harmful blood lipids, this complication in pregnancy can be prevented to some extent, or its serious complications can be decreased by early diagnosis. Controlling these indicators before pregnancy as preconception care for individuals at high risk of preeclampsia is recommended.

Key words: Body mass index, Iran, metabolic syndrome, preeclampsia, prenatal care

Introduction

Pregnancy is a beautiful phenomenon and experience for every woman, and is associated with many physiological changes. During normal pregnancy, almost all organs undergo anatomical and functional changes. These changes can dramatically alter the criteria for diagnosis and treatment of diseases. Some of these changes begin soon after conception and continue throughout pregnancy. Most of the changes occur in response to physiological stimuli provided by the embryo. Some of these changes include the following. Maternal weight gain is about 27.5 pounds or 12.5 kg. Fasting blood sugar level is slightly lower in pregnant women than in non-pregnant women, and after food intake, it gradually increases and the insulin levels also increase. During pregnancy, lipid concentrations, lipoproteins, and apoprotein in plasma increase dramatically.[1] In many mothers, changes are observed which seem to be in accordance with physiological changes. Nonetheless, these changes could be the background for the occurrence of certain disorders during pregnancy.

In several recent studies, the relationship between metabolic syndrome in mother and the incidence of common disorders such as preeclampsia has been studied and, in some cases, proven.[2] Metabolic syndrome is defined as a simple way to identify populations at risk of cardiovascular disease. This syndrome is a risk factor for cardiovascular disease and diabetes. It is also referred to by the names

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cardiometabolic syndrome, insulin resistance syndrome, or Reavan's syndrome. The exact mechanism of metabolic syndrome is not fully understood and it has a very complex pathophysiology. The predisposing factors of metabolic syndrome include stress, obesity, sedentary lifestyle, age, history of cardiovascular disease, diabetes, schizophrenia, and other mental illnesses, rheumatic diseases, psoriasis, and psoriatic arthritis.[3]

In 2004, the American Heart Association established the criteria for diagnosis of metabolic syndrome, including: Increase in waist circumference of more than 102 cm or 40 inches in men and more than 88 cm or 35 inches in women; increase in triglycerides of greater than or equal to 150 mg/dl or 1.7 mmol; reduction in high density lipoprotein (HDL) of less than 40 mg dl (3.1 mmol) in men and less than 50 mg/ dl (29.1 mmol) in women; blood pressure greater than or equal to 130.85 mm Hg; and increase in blood glucose of more than or equal to 100 mg dl (6.5 mmol).[4] Recent studies report on the relationships between the indicators of this syndrome and increased preeclampsia (particularly in its extreme forms).[3] In fact, many of the risk factors for preeclampsia are considered as risk factors for metabolic syndrome.[4] Prevalence of metabolic syndrome is reported to be 35% in pregnancy-induced hypertension and 30% in preeclampsia.[5] Clinical symptoms of preeclampsia include blood pressure greater than or equal to 149.90, with proteinuria greater than or equal to 300 mg in 24-h urine, and strip test greater than or equal to +1 after 20 weeks of pregnancy.[1] High blood pressure is very common during pregnancy and causes bleeding and severe infection, which in turn are the major causes of morbidity and mortality associated with pregnancy.[1] However, the number of patients with serious complications caused by preeclampsia is much greater than the death rate.[3]

The reported incidence of this complication, based on the diagnostic criteria and the study population, ranges from 2 to 35%.[5] According to the World Health Organization, in 2014, the incidence of preeclampsia in developing countries is 19%, and it is 28% in Africa, 23% in South America, 33% in Delhi, India, 87% in Tripura, 35% in Pakistan, and 42% in Afghanistan.[6]

The results of a study showed that the risk of premature cardiovascular disease, cerebrovascular disease, peripheral artery disease, and mortality from cardiovascular disease in women with a history of preeclampsia was twice that of healthy women. The results indicate that there is a significant relationship between the severity of preeclampsia and the risk of cardiovascular disease in pregnant women with metabolic syndrome ($P < 0.001$)in the preeclampsia group and 6.78 in the healthy group.[7]

The relationship between increase in blood pressure during pregnancy and insulin resistance or hyperinsulinemia has been confirmed in several studies.[2] In the study by Mazar, indicators of metabolic syndrome associated with preeclampsia were approved.[8] One of the indicators of metabolic syndrome is increased triglyceride. The study by Ray *et al*. reported a positive association between increased maternal triglycerides and preeclampsia.[9] In a study conducted by Downs *et al*., the relationship between metabolic syndrome indicators and preeclampsia was assessed in 169 women after 32 weeks of pregnancy. The results of this study showed that in women with preeclampsia, systolic and diastolic blood pressure, serum glucose, and triglyceride levels were higher than in the control group. In the case group, the mean systolic blood pressure was 135 mmHg and the diastolic pressure was 90 mmHg, but in the control group it was 100.65; mean fasting blood glucose level was 160 in the case group and 89.5 in the control group; and triglyceride level was 245 in the case group and 135 in the control group. This indicated a significant relationship between indicators of metabolic syndrome and preeclampsia ($P < 0.001$).[10]

Another study showed that 27% of pregnant women under study had metabolic syndrome and the long-term complication observed in this group was heart disease. The indices of blood pressure, triglycerides, fasting blood glucose, and HDL were examined, and the relationship between obesity during pregnancy and preeclampsia was confirmed.[11] In the study by Dorbeny, the relationship between pre-pregnancy weight gain, obesity during pregnancy, and preeclampsia was approved; it was observed that in women with pre-pregnancy weight gain, there was a higher prevalence of preeclampsia. In this study, 4.4% of those with metabolic syndrome had preeclampsia symptoms. In the case of existence of another indicator of metabolic syndrome, the percentage was 3.8%.[12]

Given these results, it seems that the prevalence of metabolic syndrome is also higher in women with a history of preeclampsia; therefore, these mothers are in need of review. Counseling on lifestyle may help prevent future complications of the metabolic syndrome.[11] In this respect, mothers should be under care during pregnancy. In addition, given the importance of early detection of preeclampsia in prevention of maternal and neonatal complications after 20 weeks of pregnancy, which is the time of preeclampsia incidence, the improvement in prenatal care leads to early detection and early appropriate treatment of the disease, and it significantly decreases the mortality rate for the mother, fetus, and neonates.

Metabolic syndrome as grounds for preeclampsia and, in the long term, cardiovascular diseases is of great

importance. Moreover, there are currently challenges in the early detection of preeclampsia, reduction of maternal and infant morbidity, and improvement of quality of care. Thus, this study aimed to determine the relationship between preeclampsia and metabolic syndrome in pregnant women from selected clinics of Isfahan.

Materials and Methods

In this prospective cohort study conducted in 2013, 221 nulliparous women, who referred to obstetric units of health centers 1 and 2 of Isfahan, Iran, for making files and routine prenatal care, were enrolled in this study. The intended centers 1 and 2 were selected according to the number of centers and the population of mothers through random stratified sampling method using voting. Then, based on the accepted standards of the study, using convenient sampling method, sampling was performed in each center until achieving the specified sample size.

Inclusion criteria for this study included: Being primiparous, having file in their first visit for the first pregnancy (6–10 weeks of pregnancy), having an active record of pregnancy, no history of hypertension, no history of nephrotic syndrome, not suffering from hypothyroidism, no hypertension or a history of hyperlipidemia, lack of hypertension or diabetes mellitus, not using anti-cholesterol drugs and blood sugar drugs during their current pregnancy, and having an Iranian nationality.

Exclusion criteria for this study included: Any medical or obstetric problems during the study (bleeding, miscarriage, and abruption), absence of active parental care, and using non-complementary medicines during pregnancy.

The data collection tools in this study were items such as standard tape, analog pressure gauge device, and standard Bascule scales (all weights were controlled by 1 kg weight control). In each center, the devices were used after standardization with a fixed indicator for all the devices in all clinics. With the approval of the ethics committee of the university, sampling was done in health centers 1 and 2 of Isfahan. After obtaining informed consent from the research unit, and during visits between 6 and 10 weeks of pregnancy, the subjects' waist circumference and blood pressure were recorded. Then, routine pregnancy tests, and measurement of triglycerides, HDL, and fasting blood sugar were performed. For the similarity of results and to avoid distortion of the results, one laboratory was used for the examinations.

During the second visit, at 16–20 weeks, test results were recorded in the same method as in the first stage, routine checkups were performed, and blood pressure was measured. During the third visit, at 26–30 weeks of pregnancy, examinations of the second stage, including triglycerides, fasting blood glucose, and HDL, were done and recorded again. Needless to mention that pregnant women from 20 weeks of pregnancy until the end of pregnancy and the postpartum period, in terms of preeclampsia, were followed according to the study goals, and in case of preeclampsia, they were referred for treatment with a reference letter. Data were recorded in the questionnaire of individual characteristics by interview, and the results of the requested clinical experiments were provided in the checklist. Clinical examinations were performed at each visit by the researcher for all mothers. Coordination of the researcher with mothers before each visit was achieved by telephone. Data analysis was done using SPSS for Windows (version 16; SPSS Inc., Chicago, IL, USA), Chi-square test, Fisher's exact test, and Student's independent *t*-test.

Results

In terms of individuals' characteristics, the mean age of the pregnant women (metabolic syndrome and normal groups) was 22.7 years, minimum age was 16 years, and maximum age was 36 years. Most of them had an education level of diploma and the least of them had master's degree and higher. The most common occupation among the subjects was being housewife.

Table 1 shows the mean fasting blood sugar and triglyceride levels and HDL of the participants in weeks 20 and 30 of pregnancy, in terms of exposure and non-exposure groups, or in other words, in pregnant women with metabolic syndrome and healthy women. Fasting blood sugar and triglyceride levels in the two groups were significantly different ($P < 0.001$), but the amount of HDL, with noticeable differences, was not significant. The relative frequency of preeclampsia in pregnant women with metabolic syndrome and healthy subjects before and after 30 weeks of gestation was significantly different ($P < 0.001$). The frequency of preeclampsia before 30 weeks of pregnancy, based on Fisher's exact test, in women with metabolic syndrome was 8.2% (5 people) and in the healthy group was 1.2% (2 people). After 30 weeks of pregnancy, based on Chi-square test, the frequency of preeclampsia in women with metabolic syndrome was 37.7% (23 people) and in the healthy group was 10.6% (17 people). This means that in addition to the 5 people who had preeclampsia before 30 weeks, 18 others were also added to the preeclampsia group, and thus, a total of 23 cases of pregnant women with metabolic syndrome had preeclampsia [Table 2].

Table 1: Comparison of mean TG, FBS, and HDL in normotensive and preeclampsia pregnant women in 20-30 weeks pregnancy

Week of pregnancy	Group	Markers of metabolic syndrome					
		FBS		HDL		TG	
		Mean	SD	Mean	SD	Mean	SD
20 weeks	Preeclampsia pregnant	132.68	165.87	36.97	5.1	188.34	43.49
	Healthy pregnant	85.70	10.55	38	3.92	172	26.60
Results	*t*-test	1.42		0.13		0.72	
	P value	<0.001		0.830		<0.001	
30 weeks	Preeclampsia pregnant	118.11	33.72	47.49	18.42	243.20	17
	Healthy pregnant	103.17	16.97	5.63	7.6S	235.19	69.76
Results	*t*-test	2.52		1.71		2.21	
	P value	<0.001		*P*=0.98		20.001	

HDL: High density lipoprotein, SD: Standard deviation, FBS: Fast blood sugar, TG: Triglycerides

Table 2: Determination and comparison of frequency of preeclampsia in pregnant women with metabolic syndrome and those with out in 20-30 weeks of pregnancy

Week of pregnancy	Group							
	Preeclampsia pregnant			Heal the pregnant women		Results		
	Number		Percent	Number	Percent	Chi-square Number	Fisher	*P* value
20 weeks	Yes	5	8.1	2	1.25		0.02	<0.01
	No	56	91.8	168	98.8			
Total		61	100	160	100			
30 weeks	Yes	23	38.3	17	10.6			<0.001
	No	38	63.3	143	89.6			
Total		60	100	160	100	21.85		

Discussion

In the present study, the relationship between indicators of metabolic syndrome and preeclampsia was studied. Based on the findings, it was observed that relative frequency of preeclampsia in pregnant women with metabolic syndrome and in the healthy group was significantly different ($P < 0.001$). Lorenzo *et al.*, in their study, showed that women with metabolic syndrome, compared to the healthy group, had significantly more blood disorders ($P < 0.001$), 31% increased pregnancy hypertension, and 46% preeclampsia in patients with metabolic syndrome.[13] These results were consistent with the results of the present study.

The results showed a significant difference between the mean triglycerides and fasting plasma glucose in both preeclampsia and healthy groups. Nevertheless, mean HDL had no significant difference in both groups. In the studies of Dane *et al.*, fasting blood glucose, triglyceride levels, and body mass index were significantly different between the two groups of pregnant women with preeclampsia and healthy women ($P < 0.01$). In this study, in the experimental and control groups, fasting blood glucose levels were 187 and 98, triglyceride levels were 321 and 142.5, and body mass index values were 32.87 and 24.21, respectively.[10] In the study by Rabin Aziz *et al.*, the triglyceride levels in women with preeclampsia and in the control group were studied. The results showed that serum triglyceride levels in women with preeclampsia were higher than in the control group, while the mean HDL cholesterol in women with preeclampsia was lower than in the control group. The results showed that serum triglyceride levels in women with preeclampsia (mean 198.36) were higher than in the control group (mean 64.8), while the mean HDL cholesterol in women with preeclampsia (36.2) was lower than in the control group (47.67), with a significant difference ($P < 0.001$).[14] In the study of Kratousku *et al.*, the levels of triglycerides and LDL were examined in the severe preeclampsia and control groups. The results showed significant differences in the mean levels of these markers between the two groups of pregnant women with severe preeclampsia and the control group ($P < 0.001$). Triglyceride level in the experimental group was 198.76 and in the control group was 167, and low density lipoprotein (LDL) level in the experimental group was 309 and in the control group was 217.[15] The results of these studies were consistent with those of the present study. The results indicate a positive

relationship between increased levels of triglycerides and maternal fasting blood glucose, and preeclampsia. After a systematic evaluation of the results of these studies, it can be found whether these indicators are suitable markers for predicting preeclampsia or not.

Sizmansca *et al*. showed the existence of indicators of metabolic syndrome alone or combinations of them during pregnancy as an independent risk factor in the development of severe preeclampsia. In this study, the level of triglycerides in diabetic pregnant women compared to non-diabetic women was reported.[16]

In recent years, a number of evidences in relation to abnormal lipid metabolism as a predisposing factor for preeclampsia in the mothers have been pointed out. They report that LDL cholesterol and triglyceride increase with a decrease in HDL cholesterol several months after delivery in women with a history of preeclampsia.[13] Kratousku believes that dyslipidemia associated with preeclampsia can occur due to endothelial dysfunction. Accumulation of cholesterol and triglycerides in patients can even cause damage to endothelial function. It was observed that the impaired function of lipids and oxidative modification of LDL during pregnancy are particularly followed by hypertriglyceridemia, increased lipid peroxides, and dense LDL.[15] Increased LDL oxidative susceptibility has been reported in a spectrum of severe preeclampsia. Several studies have reported abnormal lipid metabolism as a risk factor for preeclampsia.[13-15]

Although the etiology of preeclampsia is unclear, abnormal placental replacement and endothelial dysfunction result in hypoxia and exacerbation of the inflammatory response, oxidative stress, and damaged endothelium.[13] Placental vasculopathy and impaired endothelial function may be important factors for occurrence of preeclampsia.[7,13,17]

Women who have metabolic disorders and are overweight or obese during early pregnancy may face risk factors such as hyperlipidemia and atherosclerosis, insulin resistance, and impaired endothelial function during pregnancy.[7,18,19]

Conclusion

In a prospective study, it was shown that among women with metabolic syndrome, the risk of hypertension in pregnancy, and preeclampsia and diabetes in late pregnancy were increased.[20] In the study by Neli *et al*., it was observed that women who had gestational diabetes during their pregnancy were at a higher risk for metabolic syndrome than other women in the first year after delivery. There is a relationship among the pathophysiology of preeclampsia, and insulin resistance and metabolic syndrome due to endothelial dysfunction.[21]

In metabolic syndrome disorders, such as insulin resistance, glucose intolerance, hyperinsulinemia, increased triglycerides, reduction of HDL cholesterol, and blood pressure were observed. Other abnormal findings in metabolic syndrome include abnormal weight gain, inflammation and microalbuminuria, hyperuremia, non-natural fibrinolysis, and coagulation.[22] Our findings show that metabolic changes (such as changes in carbohydrate and lipid metabolism) occur in patients. Furthermore, these changes play a key role in the pathogenesis of vascular dysfunction. These findings support the relationship between indicators of metabolic syndrome and preeclampsia. These features are common with pregnancy-induced hypertension. Therefore, based on the results of these studies, programs, such as controlling weight, treatment, and controlling the metabolic disorders before pregnancy, should be designed to prevent these complications if diagnosed during pregnancy. The management of pregnancy in order to reduce the cases of preeclampsia and its complications is recommended.

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