

Prevalence and Risk Factors for Metabolic Syndrome in Past Child Bearing and Perimenopausal Women with Abnormal Uterine Bleeding

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ABSTRACT

Metabolic syndrome is a disorder of combined lipid and glucose metabolism in a genetically susceptible individual with sufficient visceral adiposity to provoke adipose tissue dysfunction. The major features of metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia and hypertension. It is a major predictor of morbidity and mortality. **Aim and Objectives:** To study the prevalence and risk factors of metabolic syndrome among past childbearing and perimenopausal women with abnormal uterine bleeding. **Methodology:** Cross sectional study in women between 30 to 50 years of age with abnormal uterine bleeding who attended Gynaecology OP in SATH, sample size was 186 patients. Observations and **Results:** Among 186 women studied, 100 of them were found to have metabolic syndrome, the prevalence was 53.76% {95% CI, = [39.6-67.52]}. Significant association was found between metabolic syndrome and age, history of gestational diabetes and gestational hypertension, postpartum weight gain, personal history of excess calorie intake and lack of exercise, history of diabetes, hypothyroidism, hypertension and family history of diabetes and cardiac disease.

Keywords: Abnormal uterine bleeding, Metabolic syndrome, IDF criteria, Diabetes, Hypertension, Weight gain

INTRODUCTION

The metabolic syndrome [MS] is a complex web of metabolic factors that are associated with a twofold risk of cardiovascular disease [CVD] and a fivefold risk of diabetes [if not already present] within five years, with an even higher long-term risk [1]. Persons with metabolic syndrome have a 30% to 40% probability of developing diabetes and /or CVD within 20 years, depending on the number of components present [2]. Presence of metabolic syndrome also predicts unstable lipid-rich plaques and death from premature coronary artery disease [CAD] [3-6]. Among men 45 years and older and women 55 years and older, the metabolic syndrome confers moderately high risk of CAD [10-year risk of 10%-20%]. Because 70% of the overall South Asians have high rates of diabetes and the highest rates of premature coronary artery disease in the world, both occurring about 10 years earlier than in other populations. The metabolic syndrome [MS], which appears to be the antecedent or “common soil” for both of these conditions, is also common among South Asians. Central obesity a risk factor for carcinoma endometrium, ovary, breast and abnormal uterine bleeding, in women with a relatively androgenic hormonal state, as well as coronary artery disease, hypertension and disorders of lipid and carbohydrate metabolism. In our institution we are finding an alarming increase in abnormal uterine bleeding, carcinoma endometrium and ovary, with early

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Receiving Date: August 01, 2020

Acceptance Date: August 26, 2020

Publication Date: September 01, 2020

onset and higher grade, in perimenopausal women attending OPD. Obesity which is found to be increasing with age and physical inactivity, induces a change in hormonal milieu which itself leads to risk of premalignant and malignant changes, coronary heart disease and stroke, along with hypertension, abnormal lipid profile and diabetes. Hence this study is designed to find out the

prevalence of metabolic syndrome in women in the past child bearing and perimenopausal age group, presenting with abnormal uterine bleeding and to identify the risk factors of this syndrome, since, to what extent the metabolic syndrome is contributing to gynaecological morbidity is not studied so far. Hence such a study is designed, so that timely action may be taken for a healthy womanhood.

AIM AND OBJECTIVES

Primary objective

To study the prevalence of metabolic syndrome among past child bearing and perimenopausal women with abnormal uterine bleeding attending Gynaecology OP in SAT Hospital, Thiruvananthapuram.

Secondary objective

To study the risk factors of metabolic syndrome among past childbearing and perimenopausal women with abnormal uterine bleeding attending Gynaecology OP in SAT Hospital, Thiruvananthapuram.

MATERIALS AND METHODS

Methodology

Cross sectional study.

Study Population and Size

186 women between 30 to 50 years of age with abnormal uterine bleeding who attended Gynaecology OP in SATH.

Criteria for Diagnosing Metabolic Syndrome

IDF criteria were used for diagnosing metabolic syndrome in these women. According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have,

- Central obesity [waist circumference ≥ 80 cm for Indian women], plus any two of the following four factors,
- Raised triglyceride level: ≥ 150 mg/dl [1.7 mmol/L], or specific treatment for this lipid abnormality.
- Reduced HDL cholesterol: < 40 mg/dl [1.03 mmol/L] in males and < 50 mg/dl [1.29 mmol/L] in females, or specific treatment for this lipid abnormality.
- Raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mm of Hg, or treatment of previously diagnosed hypertension.
- Raised fasting plasma glucose: ≥ 100 mg/dl [5.6 mmol/L], or previously diagnosed type 2 diabetes.

Exclusion Criteria

Smoking, acute illness or any treatment of inflammatory or chronic infectious disease during the previous 3 months, patients taking antipsychotics, steroids, subjects with evidence of severe hepatic or renal disease.

Data Collection

1. FBS, PPBS by glucose oxidase kit
2. Fasting serum lipid profile done in semi autoanalyser
3. Following anthropometric measurements are taken as-

- Weight: is measured on a standard beam balance scale, with patient wearing light clothes, no foot wears.
- Height: measured with patient standing barefooted against wall with feet together, with patient looking forward, with body as straight as possible. The head level position was marked with pencil, and the height measured from the ground keeping the tape straight.
- Waist circumference: was measured at the midpoint between the inferior margin of ribs and superior border of iliac crest.
- Hip circumference: was measured at the level of the greater trochanters.
- Blood pressure: recorded using sphygmomanometer in sitting position on right upper limb.
- Body Mass Index: is an index of body fat and is used for diagnosis of obesity. It is calculated from the following formulae,

$$\text{BMI} = \text{Body weight [kg]} / \text{Height}^2 \text{ [m}^2\text{]}$$

Waist Hip ratio [WHR]: calculated by dividing waist circumference by hip circumference. It gives an indication about distribution of fat, thus defining central or visceral obesity.

The measurement was taken thrice and means value was taken in all cases.

Study Period- Six months.

Observations and Analysis

The study conducted was a cross - sectional study among 186 women who attended Gynaecology OP with abnormal uterine bleeding. Among 186 women studied, 100 of them were found to have metabolic syndrome, the prevalence was 53.76% {95% CI, = [39.6-67.52]}. In the following section I would like to analyse the determinants and associative factors by a case control approach.

Table 1: Age group

Age group[yr]	MS present	MS absent	Total
30 - 34	1[1%]	7[8.1%]	8[4.3%]
35 - 39	10[10%]	16[18.6%]	26[13.9%]
40 - 44	39[39%]	41[47.7%]	80[43.1%]
45 - 49	40[40%]	20[23.3%]	60[32.3%]
≥ 50	10[10%]	2[2.3%]	12[6.4%]
Total	100 [100%]	86[100%]	186 [100%]

Chi square value - 16.97, with degrees of freedom - 4, p-value - 0.002

As shown in Table 1, age and metabolic syndrome was found to have a significant association. While 1% had MS in 30-34-year age group, it increased to 40% in 45-49-year age group compared to 23.3% in 45-49-year age group with metabolic syndrome absent.

Table 2: History of gestational diabetes and gestational hypertension

Disease	MS present	MS absent	Total
Absent	76[76%]	83[96.5%]	159[85.5%]
GDM	13[13%]	0	13[7%]
GHTN	11[11%]	3[3.5%]	14[7.5%]
Total	100[100%]	86[100%]	186[100%]

Chi square - 16.92, degrees of freedom- 2, p-value- 0.0001

A highly significant association was found between history of gestational diabetes and hypertension with metabolic syndrome as shown in Table 2. Among 100 patients with metabolic syndrome, 13% had history of GDM and 11% had GHTN compared to other group with no metabolic syndrome, where none had history of GDM and only 3.5% had history of GHTN.

Table 3: Weight Gain after Delivery

Weight gain	MS present	MS absent	Total
Nil	8[8%]	64[74.4%]	72[38.7%]
≤ 5kg	7[7%]	11[12.8%]	18[9.7%]
6 - 10kg	36[36%]	7[8.1%]	43[23.1%]
11 - 15kg	31[31%]	2[2.3%]	33[17.7%]
16 - 20kg	18[18%]	2[2.3%]	20[10.8%]
Total	100[100%]	86[100%]	186[100%]

Chi- square - 101.80, degrees of freedom - 4, p-value - 0.0001

As shown in Table 3, a highly significant association was found between postpartum weight gain and metabolic syndrome. While in <5kg weight gain only 7% had metabolic syndrome, 18% had metabolic syndrome in 16-20kg weight gain group compared to 2.3% in women with no metabolic syndrome with same weight gain.

Table 4: Hypertension

Hypertension	MS present	MS absent	Total
Present	44[44%]	5[5.8%]	49[26.3%]
Absent	56[56%]	81[94.2%]	137[73.7%]
Total	100 [100%]	86[100%]	186[100%]

Chi - square-34.74, degrees of freedom- 1, p-value- 0.0001

There was a highly significant association between hypertension and metabolic syndrome, as shown in Table 4. Among 100 patients with metabolic syndrome 44% had hypertension while only 5.8% had hypertension in non-metabolic syndrome.

Table 5: Diabetes Mellitus

DM	MS present	MS absent	Total
Present	64[64%]	8[9.3%]	72[38.7%]
Absent	36[36%]	78[90.7%]	114[61.3%]
Total	100[100%]	86[100%]	186[100%]

Chi - square - 58.30, degrees of freedom - 1, p-value - 0.0001

As shown in Table 5, a highly significant association was found between diabetes mellitus and metabolic syndrome. Among 100 women with metabolic syndrome, 64% had diabetes compared to 9.3% in non-metabolic syndrome group.

Table 6: Hypothyroidism

Hypothyroidism	MS present	MS absent	Total
Present	30[30%]	13[15.1%]	43[23.1%]
Absent	70[70%]	73[84.9%]	143[76.9%]
Total	100[100%]	86[100%]	186[100%]

Chi - square - 5.76, degrees of freedom- 1, p- value - 0.01

A significant association was found between hypothyroidism and metabolic syndrome. as shown in Table 6. Among 100 women with metabolic syndrome, 30% had hypothyroidism while only 13% had hypothyroidism in non-metabolic syndrome group.

Table 7: Hypercholesterolemia

Hypercholesterolemia	MS present	MS absent	Total
Present	15[15%]	1[1.2%]	16[8.6%]
Absent	85[85%]	85[98.8%]	170[91.4%]
Total	100[100%]	86[100%]	186[100%]

Chi - square- 11.26, degrees of freedom - 1, p-value- 0.001

As shown in Table 7, a highly significant association was found with hypercholesterolemia and metabolic syndrome. Among 100 women with metabolic syndrome, 15% had hypercholesterolemia, while only 1.2% had hypercholesterolemia in non-metabolic syndrome group.

Table 8: PCOS

PCOS	MS present	MS absent	Total
Present	6[6%]	0	6[3.2%]
Absent	94[94%]	86[100%]	180[96.8%]
Total	100[100%]	86[100%]	186[100%]

Women with PCOS have significantly more chance to have metabolic syndrome, as seen in Table 8.

Table 9: Family H/O of Hypertension

HTN	MS present	MS absent	Total
Present	27[27%]	21[24.4%]	48[25.8%]
Absent	73[73%]	65[75.6%]	138[74.2%]
Total	100[100%]	86[100%]	186[100%]

Chi-square - 0.16, degrees of freedom-1, p-value- 0.68

No significant association was found between family history of hypertension and metabolic syndrome, as shown in Table 9.

Table 10: Family H/O of DM

DM	MS present	MS absent	Total
Present	41[41%]	10[11.6%]	51[27.4%]
Absent	59[59%]	76[88.4%]	135[72.6%]
Total	100[100%]	86[100%]	186[100%]

Chi square- 20.04, degrees of freedom- 1, p-value- .0000076

As shown in Table 10, a highly significant association was found between family history of diabetes mellitus and metabolic syndrome. Among 100 women with metabolic syndrome, 41% had family history of diabetes mellitus compared to 11.6% in non-metabolic syndrome group.

Table 11: Family H/O of Cardiac Disease

Cardiac Disease	MS present	MS absent	Total
Present	24[24%]	9[10.5%]	33[17.7%]
Absent	76[76%]	77[89.5%]	153[82.3%]
Total	100[100%]	86[100%]	186[100%]

Chi-square - 5.80, degrees of freedom - 1, p-value - 0.016

A significant association was found between family history of cardiac disease and metabolic syndrome, as shown in Table 11, 24% in metabolic syndrome group compared to 10.5% in non-metabolic syndrome group.

Table 12: Calories Intake

Calories	MS present	MS absent	Total
Deficient	1[1%]	44[51.2%]	45[24.2%]
Excess	93[93%]	16[18.6%]	109[58.6%]
Appropriate	6 [6%]	26[30.2%]	32[17.2%]
Total	100[100%]	86[100%]	186 [100%]

Chi - square - 107.54, degrees of freedom - 2, p-value- 0.0001

As shown in Table 12, a highly significant association was found between dietary calories intake and metabolic syndrome. Among 100 patients with metabolic syndrome, 93% had excess calorie intake while only 18.6% had excess calorie intake in non-metabolic syndrome group.

Table 13: Exercise

Exercise	MS present	MS absent	Total
Sedentary	31[31%]	5[5.8%]	36[19.4%]
Moderate	69[69%]	80[93%]	149[80.1%]
Heavy	0	1[1.2%]	1[0.5%]
Total	100[100%]	86[100%]	186[100%]

Chi- square- 19.47, degrees of freedom - 2, p- value- 0.0001

A highly significant association was found between exercise and metabolic syndrome, as shown in Table 13. Among women with metabolic syndrome 31% did sedentary work, while only 5.8% in non-metabolic syndrome did sedentary work.

DISCUSSION

The prevalence of metabolic syndrome was 53.76% in this study. While in study conducted by National Health and Nutritional Examination Survey [NHANES] 2003 -2006, the prevalence was 34%. In a study conducted by American Diabetes Association among the prevalence of metabolic syndrome in 2005, based on the NCEP definition, the unadjusted prevalence of the metabolic syndrome was $34.5 \pm 0.9\%$ [percent \pm SE] among all participants, $33.7 \pm 1.6\%$ among men, and $35.4 \pm 1.2\%$ among women. Based on the IDF definition, the unadjusted prevalence of the metabolic syndrome was $39.0 \pm 1.1\%$ among all participants, $39.9 \pm 1.7\%$ among men, and $38.1 \pm 1.2\%$ among women. The IDF definition led to higher estimates of prevalence in all of the demographic groups, especially among Mexican-American men. In study conducted by Deepa et al., in 2007, the prevalence of metabolic syndrome in Thiruvananthapuram was 32% in males and 47% in females, in Chennai 37% in males and 35% in females, in Delhi 19% in males and 32% in females, in Bangalore

25% in males and 46% in females, compared to Indian population 29% in males and 46% in females and US population 43% in males and 38% in females. The prevalence in Thiruvananthapuram was higher than in western and metropolitan population.

In my study, age and metabolic syndrome [MS] was found to have a significant association. Many studies have shown a 50% to 75% higher prevalence of MS among South Asian women than men. In India, the overall prevalence of MS was 29% in men and 46% in women. In the United Kingdom, the age adjusted prevalence was 41% higher among South Asian men and 140% higher among South Asian women compared with whites. Furthermore, compared with whites, MS develops 10 years earlier among South Asian men and 20 years earlier among South Asian women. The prevalence of MS increases from 10% at age 20 to 29 years to 53% by 60 years. In study conducted by NHANES, 20% of males and 16% of females under age 20 years had metabolic syndrome, it increased to 41% in males and 37% in females in 41 - 59 years group and 52% of males and 54% of females more than 60 years had metabolic syndrome.

In study conducted by Saikant Kanjilal et al., the prevalence of metabolic syndrome in females was highest in 50-59-year age group. A highly significant association was found between history of gestational diabetes and hypertension with metabolic syndrome in my study.

In Danish study, by Jaennat et al., the prevalence of the metabolic syndrome was three times as high in women with prior diet-treated GDM, compared with age-matched control subjects. It is hypothesized that women with gestational dysglycemia may have an underlying latent metabolic syndrome at an early stage in its natural history [7].

In study by Kousta et al., on impact of ethnicity on glucose regulation and metabolic syndrome following gestational diabetes [8], impaired glucose regulation or diabetes by WHO criteria were present in 37% of women with previous GDM [diabetes in 17%], especially in those of African-Caribbean and Asian-Indian origin [50 and 44%, respectively Vs 28% in European, $p=0.009$]. BMI, waist circumference, diastolic blood pressure, fasting triglyceride and insulin levels, and insulin resistance by homeostatic model assessment [HOMA], were increased following GDM [$p<0.001$ for all, Vs control subjects].

In study by Forest JC et al, white women in their mid-30s, the prevalence of the metabolic syndrome is 3 to 5-fold increase in those with a history of PIH in their first pregnancy. This emphasizes the importance of long-term follow-up assessment for cardiovascular risk factors in these women.

In this study, a significant association was found between postpartum weight gain and metabolic syndrome, while in <5kg weight gain only 7% had metabolic syndrome, 18% had metabolic syndrome in 16-20kg weight gain group compared to 2.3% in women with no metabolic syndrome with same weight gain. In study by Cho et al on postpartum changes in body composition [9], fat mass [FM] and visceral fat area, the components that experienced the greatest changes, increased postpartum.

There was a highly significant association between hypertension and metabolic syndrome. Among 100 patients with metabolic syndrome 44% had hypertension while only 5.8% had hypertension in non-metabolic syndrome group. The metabolic syndrome considerably increases the risk of cardiovascular and renal events in hypertension [10]. It has been associated with a wide range of classical and new cardiovascular risk factors as well as with early signs of subclinical cardiovascular and renal damage. Obesity and insulin resistance, beside a constellation of independent factors, which include molecules of hepatic, vascular, and immunologic origin with proinflammatory properties, have been implicated in the pathogenesis.

In a study by Oqubera AO, Kuku. S from Nigeria concluded that metabolic syndrome occurs in 1 in every 4 persons with thyroid disorders, and as such, routine screening for this cardiovascular risk factor may be of benefit in this group of people, especially in those with hypothyroidism. Sub-clinical

hypothyroidism [SCH] and overt hypothyroidism are recognized risk factors for atherosclerotic cardiovascular disease, hyperlipidemia, low grade inflammation and hypercoagulability [11-13]. There is scanty data on the prevalence and the various associations of SCH and overt hypothyroidism in the South Indian general population.

As metabolic syndrome and hypothyroidism are independent risk factors for the same disease process, namely cardiovascular disease, it is possible that patients suffering from both these disease entities may have a compounded risk. In my study an effort was taken to investigate the proposed association between these two disease entities and found a significant association between them. Similar to my observation the study by Uzunlulu et al., [14], had showed that prevalence of hypothyroidism to be 16.4% [n = 36] in the Metabolic Syndrome group [n = 220].

Isomaa and his colleagues [15] showed that individuals with metabolic syndrome were at a three-fold greater risk of coronary heart disease and stroke, and more than a fivefold greater risk of cardiovascular mortality.

Condition commonly detected in a younger age group and associated with a high risk of progression to diabetes is polycystic ovary syndrome [PCOS]. Interestingly, many of the features of the metabolic syndrome, including insulin resistance, obesity, and dyslipidemias, are also present in PCOS. In my study I could find a highly significant association between PCOS and metabolic syndrome. Women with PCOS have a higher prevalence and a greater degree of hyperinsulinemia [16,17] and insulin resistance [18-20] than weight-matched control subjects. In study by Legro et al., women who have PCOS, as many as 30% have impaired glucose tolerance [IGT] and an additional 7.5% have diabetes [21].

However, as carefully reviewed by Legro [22] not all women with PCOS have the metabolic syndrome, and prospective data do not yet support an increased occurrence of CVD in all women with PCOS.

In this study, a significant association was found between family history of cardiac disease and metabolic syndrome, 24% in metabolic syndrome group compared to 10.5% in non-metabolic syndrome group. In study by Jean et al, MS is associated with parental premature CVD independently of classical CV risk factors, suggesting that MS is a contributor to the familial aggregation of premature CVD [23].

A highly significant association was found between family history of diabetes mellitus and metabolic syndrome. Among 100 women with metabolic syndrome, 41% had family history of diabetes mellitus compared to 11.6% in non-metabolic syndrome group. In study by Ghosh et al. [24] people with a moderate familial risk of diabetes, and people with a high familial risk of diabetes were between 1.4 and 1.6, and 1.6 and 1.8 times as likely, respectively, to have metabolic syndrome compared to people with average familial risk. Thus, according to this study, family history of diabetes shows a significant, independent association with metabolic syndrome and its traits. This association supports the idea that shared genes and environment contribute to the expression of complex traits such as diabetes and the metabolic syndrome.

No significant association was found between family history of malignancies or hypertension.

A highly significant association was found between dietary calories intake and metabolic syndrome. Among 100 patients with metabolic syndrome, 93% had excess calorie intake while only 18.6% had excess calorie intake in non-metabolic syndrome group. All patients in this study were taking mixed diet. A highly significant association was found between exercise and metabolic syndrome. Among women with metabolic syndrome 31% did sedentary work, while only 5.8% in non-metabolic syndrome did sedentary work. The results of a national US study suggest that women are at greater risk for developing metabolic syndrome than men because they are less likely to do at least 30

minutes of exercise a day. It found that although regular physical activity is linked to better health in both sexes, it is more likely to make a bigger difference for women.

CONCLUSION AND RECOMMENDATIONS

The growing epidemic of metabolic syndrome is a global health issue. The risk for developing metabolic syndrome is determined by the genetic, environmental and physical factors. The genetic risk is estimated from family history of diabetes mellitus, hypertension, and cardiovascular events. Also, if the person was exposed to a hostile intrauterine environment, like, maternal history of gestational diabetes and hypertension, the programming for metabolic syndrome develops in the fetal and neonatal life. Among the associations of metabolic syndrome in this study, post-partum weight gain was the most significant. In our society, the prolonged restricted physical activity after delivery and increased intake of fat and calorie rich food after delivery is the main reason, compared to western population where women return to early normal physical activity. Again, as a part of modernization, there is change in lifestyle of women. Majority have all amenities in their home so that their strain of household job is reduced and the physical activity reduced, but the calorie intake is not compromised and change in eating habits to more refined fatty foods and junk foods.

The increasing trend of diabetes, hypertension and Hypercholesterolemia, leads to damage at molecular and cellular level, which later on progresses to organ damage and reduced life expectancy. Though this study is not a giving a true prevalence of metabolic syndrome among past child bearing and perimenopausal women [as it is not a community-based study], it gives an estimate of prevalence of metabolic syndrome in this age group. The women participated in this study had abnormal bleeding as their complaint, and attended our OPD for its management. Majority had benign pelvic pathology but few had premalignant and malignant changes. The major etiological factor for this was hyperestrogenism, from an ovulation and peripheral aromatization of fat. This study gave us an opportunity to screen them for metabolic syndrome, which apart from their gynaecological problem can lead cardiovascular events and other malignancies.

So metabolic syndrome is definitely having a rising trend in our women, which has to made aware to them, so that life style modification, health checkups and proper control of diabetes, hypertension and Hypercholesterolemia including drug therapy, can help them to lead a better healthy womanhood.

ACKNOWLEDGEMENT

It is as much my pleasant duty, as it is my privilege to express my sincere debt of gratitude to my guide, Prof. Dr. Nirmala.C., Head of the Department of Obstetrics and Gynaecology, SAT Hospital, Medical College, Thiruvananthapuram for her valuable suggestions and inspiring criticism she gave me throughout the course of this study. I owe immense gratitude to Dr. Saboora Beegum, Head of department of Biochemistry, Dr. Jessy. J, Assistant Professor and all the staff of biochemistry laboratory for all the assistance made available to me in conducting this study. I am greatly indebted to Murali Sir for helping me in the statistical analysis of the data. I will be failing in my duty if I do not place on record my sincere thanks to my parents and my husband for their constant encouragement and untiring inspiration, without which this work would not have become a reality. Above all, I humbly thank God Almighty for giving me the strength to complete my study.

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