

Past Medical, Gynecological and Pregnancy-Related History and Independent Metabolic Syndrome Components among Menopausal Women: A Hospital-Based Study

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Abstract

Objectives: Some pathological situations of female reproductive life predispose mother and offspring to higher risk of development of metabolic syndrome. Therefore, we aimed to assess relationships between all significant medical and gynecologic/pregnancy-related antecedents and metabolic syndrome components in menopausal women.

Study design: During a cross-sectional study carried out from August 2014 to January 2015, medical, gynecological and pregnancy-related history was obtained from menopausal women followed for metabolic syndrome at the University of Kinshasa Hospital. Metabolic syndrome was defined as the presence of at least 3 out of 5 criteria according to harmonized definition. Using logistic regression analysis we evaluated the association between history characteristics and metabolic syndrome components ($p < 0.05$ as significant).

Results: 42 menopausal women were consecutively enrolled. Dominating characteristics were family history of hypertension (FH-HT) and diabetes mellitus (FH-DM), personal antecedents of spaniomenorrhea, pregnancy-associated urinary tract infection (UTI), premature delivery, pregnancy-induced hypertension (PIHT), gestational diabetes mellitus (GDM), macrosomia, stillbirth and congenital malformations.

Significant associations (OR; p) were FH-HT with abdominal obesity (6.2; 0.008) and hypertriglyceridemia (4.9; 0.018); FH-DM with abdominal obesity (55.2; 0.000), hypertriglyceridemia (12.2; 0.001) and low HDL (1.8; 0.02); spaniomenorrhea with obesity (14.8; 0.004), HBP (9.8; 0.018) and hypertriglyceridemia (12.9; 0.006). For obstetrical history the picture was: PIHT with abdominal obesity (24; 0.000) and hypertriglyceridemia (8.2; 0.008); GDM with hypertriglyceridemia (11; 0.012); premature delivery with obesity (4.3; 0.04) and HBP (13; 0.006); stillbirth with HBP (7.2; 0.048) and low HDL (12.1; 0.009); macrosomia with obesity (15.9; 0.000) and hypertriglyceridemia (6.9; 0.008).

Conclusion: Apart from known medical risk factors, past spaniomenorrhea emerged as the main gynecological factor whereas premature delivery, gestational diabetes, PIHT, infant's macrosomia, stillbirth and congenital malformations were obstetrical ones associated with components of MS. They are likely to permit early detection and management of MS.

Keywords: Past medical history of women; Gynecological and pregnancy related history; Components of metabolic syndrome; Menopause; Kinshasa

Introduction

Metabolic syndrome (MS) is characterized by a co-occurrence of three out of five following pathological conditions: abdominal obesity, high blood pressure (HBP), elevated fasting plasma glucose (FPG), high serum triglycerides (TG), and low high-density cholesterol (HDL) levels [1]. It increases the risk of developing cardiovascular disease, particularly heart failure and diabetes [1-6]. The underlying causal factor is insulin resistance resulting from the interplay of genetic predisposition with various other factors such as aging, obesity, low physical activity, stress and nutritional behavior (mostly alcohol abuse and carbohydrates-rich foods) [5].

Some pathological situations of female reproductive life such as polycystic ovary syndrome (PCOs), pregnancy induced hypertension (PIHT) and hyperglycemia are now known to expose to a high risk of future MS on both mother and offspring [2-6]. The prevalence of MS has been reported to increase 3-5 folds in women with a history of previous pregnancy-induced hypertension, mostly during their first pregnancy [2-6]. Pregnancy-associated hyperglycemia has been linked not only to adverse short-term outcomes in fetus as well as increased cardiometabolic morbidity in the adulthood life [2-6], but also to the late development of the MS in mother [2-6]. Apart from pregnancy-induced metabolic disturbances, components of prior MS, mainly

abdominal obesity could also induce obstetrical complications such as gestational diabetes, preeclampsia, preterm delivery, fetal growth retardation, macrosomia, stillbirth and perinatal death [7-11].

Very few of numerous publications dealing with these issues come from Sub-Saharan Africa. This is probably owed to unawareness of care providers to diagnose MS and ignorance of concerned patients who do not seek care. Furthermore, the most explored antecedents have been obesity, hypertension, PCOs and gestational diabetes mellitus (GDM). Less if not nothing has been reported on other past medical and obstetrical/gynecological history of female MS patients. The aim of the present study was thus to assess the relationship, if any, between all significant past medical and gynecological/obstetrical history and

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individual components of MS in menopausal women diagnosed MS at the University of Kinshasa Hospital.

Methods

Our study was a cross sectional one carried out from August 2014 till January 2015 at the Department of Internal Medicine of University of Kinshasa Hospital, DR Congo. It consisted of collecting data on past medical history, and gynecologic and pregnancy-related characteristics of consecutive menopausal women with established diagnosis of MS. Data were collected using a sheet with specified items to be fulfilled by a resident in the Department of Internal Medicine and to be validated by a specialist of the Department of Obstetrics and Gynecology. A personal contact with patients was scheduled only if important data were missing in patients' files. Metabolic syndrome was diagnosed according to harmonized definition [1] based on at least 3 out of 5 criteria: abdominal obesity (waist circumference \geq 80 cm), high blood pressure (systolic pressure \geq 130 mmHg, or diastolic pressure \geq 85 mmHg), hyperglycemia (\geq 5.6 mmol/l), high serum triglycerides (\geq 1.69 mmol/l) and low HDL cholesterol (\leq 2.8 mmol/l).

Statistical analyses were performed with SPSS Version for 18.0. Comparisons of categorical parameters between groups were performed using chi-square or Fisher exact test as appropriate. Associations between medical and obstetrical/gynecological characteristics and components of MS were assessed using logistic regression analysis with Odds ratio (OR) calculations (95% confidence interval, CI). A p value $<$ 0.05 was considered statistically significant.

For Ethical considerations, the research protocol was approved by the Faculty Committee for Research Ethics in Medicine in keeping with the requirements of the Helsinki Declaration. Patients contacted for completion of files gave their written informed consent for enrollment in the study.

Results

A total of 42 menopausal patients were consecutively enrolled, with mean age 58.5 ± 9.1 (SD) years, gravidity 6.3 ± 3.3 , parity 5.2 ± 2.9 , BMI 29.6 ± 5.6 kg/m² and waist circumference 100.1 ± 7.4 cm (Table 1). Their mean systolic (SBP) and diastolic (DBP) blood pressure were 159 mm Hg \pm 22 mm Hg and 92 ± 14 mm Hg, respectively (Table 1).

Main past medical history characteristics were family history of diabetes mellitus (FH-DM) (66.7%) and hypertension (FH-HT) (57.1%). Most frequent gynecological and pregnancy-related-history features were spaniomenorrhea 28.6%), urinary tract infection (UTI) during pregnancy (52.4), premature delivery (35.7%), pregnancy induced hypertension (PIHT) (22.7%), gestational diabetes mellitus (GDM) (28.6), infant's macrosomia (26.2%), stillbirth (26.2) and congenital malformations (23.8) (Table 1).

Table 2 summarizes the frequency of individual MS components among the study population. Frequencies observed for HBP, hyperglycemia, high serum TG, central obesity, and low HDL were 39 (92.9%), 34 (81.0%), 26 (61.9%), 25 (59.5%) and 24 (57.1%) of patients, respectively.

Statistically significant associations between past medical, gynecological/pregnancy-related history and individual MS components are also depicted in Table 2. FH-DM emerged as the main past medical history characteristic strongly associated with individual MS components (Abdominal obesity, OR 55.2; hypertriglyceridemia, OR 12). Spaniomenorrhea was the past gynecological history feature most strongly linked to individual MS components (Central obesity,

OR 14.8; hypertriglyceridemia, OR 12.9; HBP, OR 9.8). Among past pregnancy-related characteristics, premature delivery (with HBP, OR 13), PHIT (with abdominal obesity, OR 24), macrosomia (with abdominal obesity, OR 15.9) and stillbirth (with low HDL, OR 12) were strongly associated with individual MS components. Although hyperglycemia was one of individual MS components most frequently encountered (81%) in the present case series, it was associated with neither past medical nor gynecological and pregnancy-related history characteristics.

Discussion

The aim of the present cross-sectional study was to assess the relationship, if any, between past medical, gynecological and pregnancy-related history and individual MS components in menopausal women. The main findings are as follows: first, FH-DM emerged as the past medical history feature most strongly associated with individual MS components; second spaniomenorrhea was the main past gynecological history characteristic most strongly linked to individual MS characteristics; third, premature delivery, PHIT, infant's

| General Characteristics | Mean | SD |
|--------------------------|-----------|------|
| Age (yr) | 58.5 | 9.1 |
| Gravidity | 6.3 | 3.3 |
| Parity | 5.2 | 2.9 |
| BMI (kg/m ²) | 29.6 | 5.6 |
| Waist Circumference (cm) | 100.1 | 7.4 |
| Systolic BP (mm Hg) | 159 | 22 |
| Diastolic BP (mm Hg) | 92 | 14 |
| Antecedents | Frequency | % |
| FH-HT | 24 | 57.1 |
| FH-DM | 28 | 66.7 |
| Spaniomenorrhea | 12 | 28.6 |
| UTI during pregnancy | 22 | 52.4 |
| Premature delivery | 15 | 35.7 |
| PIHT | 5 | 22.7 |
| Congenital malformations | 10 | 23.8 |
| Macrosomia | 11 | 26.2 |
| Stillbirth | 11 | 26.2 |
| GDM | 12 | 28.6 |

Table 1: General characteristics and main antecedents of the study group.

| MS components | Past history characteristics | p | Adjusted OR | CI |
|------------------------------|------------------------------|-------|-------------|-----------|
| HBP (92.9%) | Spaniomenorrhea | 0.018 | 9.8 | 1.1 85.2 |
| | Premature delivery | 0.006 | 13 | 1.5 113.3 |
| | Stillbirth | 0.048 | 7.2 | 1.8 63.6 |
| Hypertriglyceridemia (61.9%) | Spaniomenorrhea | 0.006 | 12.9 | 1.5 112.2 |
| | FH-HT | 0.018 | 4.9 | 1.3 19.0 |
| | FH-DM | 0.001 | 12.2 | 2.5 59.2 |
| | PIHT | 0.008 | 8.2 | 1.5 43.4 |
| | GDM | 0.012 | 11 | 1.3 96.2 |
| Abdominal obesity (57.1%) | Macrosomia | 0.008 | 6.9 | 1.6 30.6 |
| | Spaniomenorrhea | 0.004 | 14.8 | 1.7 129.0 |
| | FH-HT | 0.008 | 6.2 | 1.6 24.1 |
| | FH-DM | 0.000 | 55.2 | 5.8 527.7 |
| | Premature delivery | 0.044 | 4.3 | 2.0 18.8 |
| Low HDL (57.1%) | PIHT | 0.000 | 24 | 2.7 210.8 |
| | Infant's macrosomia | 0.000 | 15.9 | 2.9 87.1 |
| | FH-HT | 0.022 | 1.8 | 1.2 2.9 |
| | Stillbirth | 0.009 | 12.1 | 1.4 106.8 |

Table 2: Associations between medical, gynecological/pregnancy-related history and individual MS components.

macrosomia and stillbirth were characteristics of pregnancy-related history most strongly associated with individual MS components.

The finding of a relationship between FH-DM and MS and/or its individual components is well established and agrees with previous reports. Indeed, Nelson et al. [12] reported that FH-DM, as a proxy of genetic predisposition, was associated with MS and its components. They found that FH-DM was most strongly associated with individual traits of hyperglycemia and low HDL-C and conferred significant increased odds of MS. Furthermore, Park et al. [13] noted that ORs for MS among women with a FH-HT/Stroke was higher than that in those without FH-HT. The results of aforementioned studies do suggest a common etiology for at least some components of MS, the basis of which likely to be genetic [12,13].

Spaniomenorrhea emerged as the main characteristic of past gynecological history associated with individual MS components suggesting a previous or current underlying polycystic ovarian syndrome (PCOS). Indeed, spaniomenorrhea is one of the main gynecological features of PCOS, a well-known insulin resistant state associated with MS and its individual components [14]. PCOS is now recognized as a common, heterogeneous, heritable disorder affecting women throughout their lifetime. Its clinical presentation varies widely. Women with PCOS often seek care for menstrual disturbances, clinical manifestations of hyperandrogenism, and infertility. Menstrual disturbances commonly observed in PCOS include oligomenorrhea, amenorrhea, and prolonged erratic menstrual bleeding. A meta-analysis performed for studies with BMI-matched controls [14] showed that PCOS is associated with a higher prevalence of metabolic syndrome compared to women without PCOS (odds ratio [OR] 2.20, 95% CI 1.36–3.56). Lean women with PCOS were also more likely to have metabolic syndrome than lean women without PCOS (OR 3.00, 95% CI 1.24–6.78). Spaniomenorrhea was associated with individual MS components obesity, hypertriglyceridemia and HBP. The prevalence of insulin resistance in PCOS ranges from 50%–70% and occurs independently of obesity. The effect of obesity on insulin resistance is additive to that of PCOS [14]. An increased risk of dyslipidemia linked to insulin resistance and subsequent hyperinsulinemia has been demonstrated in PCOS. Lipid abnormalities include reduced high density lipoprotein-cholesterol (HDL-C), increased triglycerides, and increased low density lipoprotein-cholesterol (LDL-C) [14]. Several studies conclude that women with PCOS have an increased prevalence of hypertension. Potential mechanisms of hypertension in PCOS include endothelial dysfunction, as evidenced by increased endothelin-1 levels [8] and increased aldosterone concentrations related to insulin resistance [14].

Pregnancy is now known to host certain pathological situations that favor the development of MS with subsequent deleterious effects on both mother and offspring. Maternal pregnancy-related features associated with individual MS components were GDM (with hypertriglyceridemia) and PIHT (with abdominal obesity) whereas newborn-related characteristics were prematurity (with obesity and HBP), stillbirth (with HBP and hypertriglyceridemia) and macrosomia (with abdominal obesity and hypertriglyceridemia).

Numerous clinical and experimental studies have confirmed that early developmental influences can lead to cardiovascular, pulmonary, metabolic and psychological disorders regardless of birth weight [15]. Low birth weight premature infants demonstrate growth patterns in the early years of their life (catch up growth) that differ from those of large for gestational age (LGA) and preterm peers, who do not experience that steep weight gain. Children small for gestational age

may be predisposed to metabolic abnormalities upon exposure to postnatal environment risk factors such as low physical activity and/or high energy intake. A consistency body of evidence demonstrates now that being overweight or obese in childhood and adolescence has consequence on overall health and premature mortality [16].

All patients in the present case series were postmenopausal women. It is worth wondering if menopause was a triggering factor or just time when an ignored long-lasting phenomenon had come to appear. It is well known that menopause, through aging and estrogen deficiency-induced weight gain and subsequent obesity, confers a high risk of MS and cardiovascular disease [14,17]. Indeed, the prevalence of obesity has been found to increase in women after they reach the age 40 years; the prevalence reaches between 40-59 years and 73.8% in women over 60 years [17]. In a recent prospective study [18], central obesity was a strong predictor of the risk of incident MS in postmenopausal women. Furthermore, estrogen deficiency has been reported to enhance metabolic dysfunction predisposing to type DM and CVD [18]. In the present case series, the mean age of women was 58 years, most of them being obese.

Literature dealing with relationships between past female reproductive life and risk of MS has been abundant and the most concerned antecedents have been obesity, hypertension, PCOs and gestational diabetes. Very few has come from sub-Saharan Africa where MS is expected to be at least as common as elsewhere [19,20]. The present study is among scarce ones from this geographic area. It includes medical antecedents, question all pregnancy outcomes and focuses on all independent components of MS. Although restricted to menopausal women our findings might broaden the characterization of the syndrome and extend the potential of past medical and reproductive history in prediction and prevention of MS among African women. In spite of these strengths the interpretation of our results should consider some limitations. First, its cross-sectional design precludes the establishment of causal relationships. Second, due to gender-based restriction of the recruitment, post menopause-related diagnosis and low disposal of certain ill persons to consult, the study sample was expectedly small. This does lessen power of our statistical tests and probably accounts for in huge confident intervals likely to mitigate the significance of associations. Finally, as a hospital-based study, selection bias might bring some caution in generalization of conclusions.

Conclusion

In menopausal women, apart from known MS risk factors, spaniomenorrhea emerged as the main past gynecological risk factor whereas premature delivery, gestational diabetes, PIHT, infant's macrosomia, stillbirth and congenital malformations were obstetrical ones associated with individual components of MS. Therefore, using them during reproductive life or early after menopause could help identify subjects with a high risk for future MS and subsequent cardiovascular disease who can benefit from cost-effective preventive measures.

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