

Metabolic syndrome and reproduction: Current perspectives in Nigeria



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Olulope Ajayi,^{1*} and Mabel Charles-Davies²

ABSTRACT

Metabolic syndrome (MS) is a clustering of cardiovascular disease risk factors. It is a major health challenge globally, with an increased prevalence in the developing world. Studies on its role on reproduction in Nigeria are currently sparse. This article therefore, examines current knowledge on metabolic syndrome and reproduction in

Nigerians. Academic databases including PubMed as well as Google search engine were searched between 2012 and 2019 for metabolic syndrome in reproduction in Nigerian males and females. Current observations suggest that metabolic syndrome adversely affects reproduction.

Key words: metabolic syndrome, infertility, menopause, preeclampsia

*Correspondence to:
Olulope Ajayi Department of
Biochemistry, College of Medical
Sciences, Edo University Iyamho,
Edo State
olufema01@yahoo.co.uk or olulope.olufemi@edouniversity.edu.ng

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INTRODUCTION

Metabolic syndrome (MS) is a multi-factorial endocrinopathy framed by classical cardiovascular risk factors such as insulin resistance, hyperglycaemia, abdominal obesity, pro-inflammatory state, essential hypertension and dyslipidaemia.¹ The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) defined MS as the presence of at least three of the following clinical criteria: waist circumference (>88 cm in women, > 94 cm in men), high density lipoprotein-cholesterol (HDL-C) <50 mg/dl, blood pressure \geq 130/85 mmHg, fasting plasma glucose \geq 110 mg/dl, triglyceride >150 mg/dl.² The presence of a component of MS increases the risk of future development of MS, therefore early detection of MS components could lead to targeted interventions.³

The International Diabetes Federation (IDF) estimates that approximately 25% of the world's population has MS.⁴ This estimate however varies due to age, gender and ethnicity.⁵ In Nigeria, MS affects about 33.1% of the population, thus predisposing them to cardiovascular disease (CVD).⁶ This increased prevalence has been attributed to the adoption of western lifestyle which is marked by reduced physical activity and substitution of the traditional African diet rich in fruits and vegetables for the energy-laden foods.⁷ Elevated waist circumference, reduced HDL-C and high blood pressure are prevalent MS components in Nigerians, however, with gender differences.⁸ In a Nigerian study, elevated waist circumference was more frequent in females while reduced HDL-C was more frequent in males.⁸

MS is more common in Nigerian females with type-2 diabetes mellitus (DM 2) compared with males.⁹ This is a sharp contrast to reports from the United States that showed a higher prevalence in white males than females.¹⁰ MS is known to increase with age.⁸ A Nigerian study observed 72.5% of the study participants aged 50 years and above compared with 27.5% that were aged less than 50 years.⁹ This has been attributed to the involvement of aging in different pathologies. Aging is associated with insulin resistance and increased visceral adiposity which are important in the pathogenesis of MS.⁹

The role of metabolic syndrome in reproduction has not been adequately studied in Nigerians. This review is therefore aimed at discussing the relationship of MS with reproduction in Nigerian males and females. This may lead to improvement in the management of these conditions thus, improving quality of life.

METHODOLOGY

Academic databases particularly PubMed and Google search engines were searched between 2012 and 2019 for studies on MS and reproduction in Nigeria using expressions such as 'MS and male infertility in Nigeria', 'MS and female infertility in Nigeria',

MS, Male Sexual Function and Infertility

MS is characterized with male and female infertility with male factor infertility present in 20-50% of couples either independently of or in conjunction with female factor.¹¹ In Nigeria, male factor infertility has a prevalence of about 40%.¹²

¹ Department of Biochemistry, College of Medical Sciences, Edo University Iyamho, Edo State

² Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan

The male sexual function is an intricate, multi-component biologic process that involves mechanisms for the regulation of libido, arousability, penile tumescence, rigidity, orgasm, ejaculation and sexual satisfaction. Testosterone plays an important role in these mechanisms.^{13,14} Androgen-deficient men have decreased overall sexual activity.¹⁵ Low levels of total and free testosterone as well as sex hormone-binding globulin (SHBG) are peculiar to males with MS and DM 2. Hypogonadism characterized by diminished libido, erectile dysfunction and poor nocturnal and early morning erection was found in 20-38% and 46-55% of men with MS and DM 2 respectively in a Nigerian study.¹⁶ This indicates a higher prevalence of hypogonadism in Nigeria than previously thought. Moreover, risk factors of CVD; obesity (general and central) as well as dyslipidaemia showed a strong correlation with hypogonadism in another Nigerian study.¹⁷

Obesity interferes with the hypothalamic-pituitary-gonadal axis which could result in hypogonadism.¹⁸ Hypogonadotropic hypogonadism results from testicular deficit, hence, impaired spermatogenesis and low testosterone level. Hypergonadotropic hypogonadism emanates from the insufficiency at the hypothalamus and/or pituitary gland. This results in low secretion of luteinizing hormone (LH) and FSH as well as reduced stimulation of the leydig cells to secrete testosterone.¹⁸

Dysglycaemia, dyslipidaemia and obesity are capable of inducing oxidative stress in the testicular microenvironment. This could result in sperm plasma membrane damage with nuclear/mitochondrial DNA fragmentation occurring in response to reactive oxygen species (ROS) generation. Decreased ATP synthesis and systemic inflammation can also contribute to increased sperm nuclear DNA (nDNA) fragmentation in MS. This contributes to decreased fertility in males with MS.^{1,19} Furthermore, high scrotal temperature, sleep apnea, increased adipokines and adipose-derived hormones are consequences of obesity that adversely affect male fertility by interrupting spermatogenesis.¹⁹

MS and Female Infertility

Infertility, defined as failure to conceive after unprotected regular sexual intercourse for two years in the absence of known reproductive pathology, affects about 10% of married couples in Africa, with sub-Saharan Africa having the highest prevalence.^{20,21,22,23} MS is associated with disorders of female reproduction, high incidence of menstrual dysfunction, anovulation and infertility in obese women of reproductive age.²⁴

Delay in spontaneous conception was observed in Nigerian obese women. A 5% reduction in the probability of achieving pregnancy for every unit of BMI exceeding 29 kg/m² was also observed. Oligomenorrhoea and hypomenorrhoea were associated with obesity in the study population.²⁵ This could be due to defective folliculogenesis.²⁶ Hyperinsulinaemia, a typical feature of MS inhibits folliculogenesis thus, decreasing fertility in obese women.²⁷ Another Nigerian study found a significantly elevated LH and prolactin as well as significantly reduced progesterone and oestradiol in infertile women compared to fertile women.²⁸

MS and Preeclampsia

Preeclampsia is diagnosed when a pregnant woman develops hypertension and significant proteinuria after 20 weeks gestation.²⁹ The pathophysiology of preeclampsia is still a subject of much speculation, it is however, thought to involve defective placental development.³⁰ Defective invasion of the maternal spiral arteries in the deciduas and myometrium by foetal cytotrophoblasts results in reduced uterine perfusion and placental ischaemia which induces the release of bioactive factors that mediate the pathology of preeclampsia.³¹ This could result/ culminate in intrauterine growth restriction or death.³²

Preeclampsia is a leading cause of maternal morbidity and mortality. A lot of people are unaware of its danger signs and complications.³³ In Nigeria, its prevalence ranges from 2% and 16.7%.^{34,35} Maternal obesity increases the risk of preeclampsia. BMI at first visit to antenatal clinic ≥ 25 kg/m² and previous history of preeclampsia are its major risk factors in a Nigerian study.³⁶ Furthermore, overweight or obese women at 20 weeks gestation are about 4 fold increased risk when compared with normal weight women.³⁶

In another Nigerian study, C-reactive protein and fibrinogen were associated with preeclampsia.³⁷ Obesity is a subclinical inflammatory state in which there is an increased production of interleukin-6 that stimulates C-reactive protein which promotes insulin resistance and CVD complications.³⁸ Elevated serum triglycerides and total cholesterol as well as lower HDL levels were reported in women with preeclampsia in Nigeria. This could be a sign of compromised vascular function.³⁹

Copeptin, a 39-amino acid peptide was reported as a reliable predictor of preeclampsia in a Nigerian study and may distinguish between severe preeclampsia and mild preeclampsia.⁴⁰ A recent study in Egypt suggested it as a possible marker of obesity-induced insulin resistance.⁴¹

An American study showed that preeclampsia is characterized by increased insulin resistance, hypertriglyceridemia, low high-density lipoprotein cholesterol, high low-density lipoprotein cholesterol, and high maternal and foetal plasma amino acid concentrations.⁴² It is therefore believed that preeclampsia is a case of MS occurring in pregnancy.

MS and Polycystic ovary syndrome

Polycystic ovarian syndrome (PCOS) is a major endocrinopathy among women of reproductive age and constitutes a major health and economic burden.⁴³ It confers a substantially increased risk for DM 2.⁴⁴ Its prevalence of between 12.2 and 27.6% has been reported in Nigeria using different criteria.^{45,46,47} Polycystic ovarian syndrome is characterized by menstrual irregularities, hyperandrogenism and infertility.^{48,49} Issues of MS in women with PCOS have generated tremendous interest.⁵⁰ Features such as insulin resistance and hyperinsulinaemia are common to women with MS and PCOS.⁵¹ Reports showed that PCOS increases the risk of MS.^{52,53}

Dysglycaemia is common in Nigerian women with PCOS, particularly those with higher serum testosterone levels.⁵⁴ Obese women with PCOS were reported to have significantly high plasma glucose, total cholesterol, triglyceride, low density lipoprotein but lower level of high density lipoprotein.⁵⁵ The pathogenicity of elevated BMI (overweight and obesity) in PCOS is attributed to reduction in cholecystokinin secretion, dysregulation of ghrelin, increased level of neuropeptide Y and androgens. These could enhance insulin resistance, a peculiar feature of MS.⁵⁵

Insulin resistance is attributed to a post binding defect in receptor signaling as a result of increased receptor substrate-1 serine phosphorylation that selectively affects metabolic pathways in classic insulin target tissues and the ovary. Insulin functions as a co-gonadotropin by its ability to modulate ovarian steroidogenesis. The genetic disruption of insulin signaling in the brain suggests its importance in ovulation and body weight regulation.⁴⁴ Hyperinsulinaemia amplifies LH action on theca cells, increases androgen levels and reduces SHBG levels.^{56,57,58} Hyperandrogenism and hyperinsulinaemia impair follicle development thus, adversely affecting fecundity.⁵⁹

CONCLUSION

Observations from this study show that metabolic syndrome adversely affect reproduction. Healthy lifestyle and diet should be adopted to reduce the

incidence of metabolic syndrome. This will go a long way in improving human reproduction.

CONFLICT OF INTEREST

Authors declare that no conflict of interest exists.

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