IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 12 Ver. IX (December. 2016), PP 17-20
www.iosrjournals.org

Association of Metabolic Syndrome with Dysfunctional Uterine Bleeding -A Hospital Based Study

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Abstract:
Introduction: *Metabolic Syndrome is a complex of various conditions which indicates future risk of various non-communicable diseases. Dysfunctional Uterine Bleeding (DUB) is defined as abnormal, irregular bleeding i.e., excessive, prolonged or frequent intervals of bleeding in the absence of demonstrable pelvic disease, complications of pregnancy or systemic disease. Most of the risk factors of DUB were risk factors of Metabolic Syndrome also. Based on this background the current study was conducted with an aim to assess the association of DUB with Metabolic Syndrome.*
Methodology*: The current study was hospital based case control study conducted among women attending the gynaecological clinic at Government General Hospital in Guntur city. Fifty women with DUB and 50 women without DUB were selected. Metabolic Syndrome was identified using NHLBI and AHA criteria. Systolic and diastolic blood Pressures and Waist Circumference were measured. Fasting Plasma glucose, Total Triglycerides, Total Cholesterol and HDL Cholesterol were also estimated. Averages of variables were compared and Odds ratio for each risk factor was calculated to estimate the association between risk factor and DUB.*
Results*: Averages of all the risk factors were high in DUB women when compared to Non-DUB women. All the five risk factors had the odds ratio more than two and showed the association with DUB. Fifty four percent of women with DUB had Metabolic Syndrome whereas no women without DUB had Metabolic Syndrome.*
Conclusion*: DUB was associated with the high prevalence of Metabolic Syndrome.*
Keywords: *Diabetes, Dysfunctional Uterine Bleeding, Lifestyle diseases, Metabolic Syndrome, Non-communicable diseases*

I. Introduction

Globalization brought several changes in social and economic profile of the world. In spite of giving financial benefits to the individuals it also changed the lifestyle of population. Because of these lifestyle changes prevalence of several risk factors for non-communicable diseases increased and they in turn caused the rise of burden of non-communicable diseases throughout the world such as in India. Metabolic Syndrome is a complex of various conditions which indicates future risk of development of various non-communicable diseases such as Diabetes, Hypertension, Hypercholesterolemia, Obesity etc. It can be described as a cluster of abnormalities that confers an increased risk of developing atherosclerotic cardiovascular diseases and also type 2 diabetes mellitus. Urbanization, economic growth, irregular meal times, and lifestyle changes and adoption of western diet are believed to be potential etiological factors for the development of Metabolic Syndrome [1].

The future prediction of the burden of Type-2 Diabetes and cardiovascular disease can be done by estimating the prevalence of metabolic syndrome. The Expert Panel of National Cholesterol Education program Adult Treatment Panel III highlighted importance of identifying and treating patients with Metabolic Syndrome [2]. There were two criteria for identification of Metabolic Syndrome. International Diabetes federation criteria and National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA) criteria. According to NHLBI and AHA revised guidelines -2005, if the individual had at least 3 out of the following 5 conditions, then the individual will be considered as having metabolic syndrome [3]

1. Fasting plasma glucose level ≥100 mg/dl or receiving drug therapy for hyperglycaemia
2. Blood pressure ≥130/85 mm Hg or receiving drug therapy for hypertension
3. Triglycerides ≥150 mg/dl or receiving drug therapy for hypertriglyceridemia
4. HDL cholesterol (HDL-C) < 40 mg/dl in men or < 50 mg/dl in women or receiving drug therapy for reduced HDL-C
5. Waist circumference ≥102 cm (40 inch) in men or ≥88cm (35inch) in women For south Asian, ≥90 cm (35 inch) in men or≥80 cm (32 inch) in women

Currently about 20-30% of the adult population worldwide are affected with Metabolic Syndrome and hence it is now considered as a global epidemic [4, 5]. In India, the prevalence of metabolic syndrome is varying

between 10 to 50% depending on age and sex. The prevalence of Diabetes, Obesity and Dyslipidaemia has significantly increased among the women populations in recent times [6]. The risk of metabolic syndrome is found to increase steeply after 30 years of age [7]. In middle aged populations, higher morbidity among females from the Metabolic Syndrome has been reported than in men [8].

Dysfunctional Uterine Bleeding (DUB) is defined as abnormal, irregular bleeding i.e., excessive, prolonged or frequent intervals of bleeding in the absence of demonstrable pelvic disease, complications of pregnancy or systemic disease [9-12]. It is a common debilitating problem amongst women in all age groups and it accounts for 20% of gynaecology office visits [13]. DUB occurs most commonly at the beginning or at the end of the reproductive years: About 20% of cases occur in adolescent girls and more than 50% of cases were in between the ages of 40 to 50 years [14].

The exact mechanism for occurrence of DUB is uncertain but is thought to be caused by dysfunction of hypothalamic-pituitary-ovarian axis [15]. There are two types of DUB [16]. One type, which could be called "ovulatory DUB," presents with the symptom of menorrhagia, but occurs unrelated to systemic coagulopathy, pharmaceutical agents, or any structural anomaly of the uterus. The other type of DUB occurs secondary to anovulation or oligoovulation.The risk factors for Dysfunctional Uterine Bleeding were [14] stress, obesity, poly cystic ovary syndrome, crash diets, irregular sleep patterns, overwork, vigorous exercise and Alcohol abuse. Most of these risk factors were risk factors of metabolic syndrome also. Thus it can be assumed that, prevalence of metabolic syndrome is higher in women with dysfunctional uterine bleeding should be high. Based on this background the current study was conducted with an aim to estimate the prevalence of metabolic syndrome in women with Dysfunctional uterine bleeding and to assess the association of dysfunctional uterine bleeding with metabolic syndrome.

II. Methodology

The current study was hospital based case control study. It was conducted among women attending the gynaecological clinic at Government General Hospital in Guntur city in Guntur district of Andhra Pradesh state. All the women attending to gynaecology department in GGH Guntur during the period from 1-5-2012 to 30-4-2013 were considered as study population. Women aged between 40-49 years were included in the study. Among them 50 women with dysfunctional uterine bleeding were selected as a test group and 50 women without dysfunctional uterine bleeding were selected as a control group. Women population with DUB attributed to the usual causes such as structural gynaecologic abnormalities, cancer, inflammation, systemic disorders, pregnancy, and complications of pregnancy, use of oral contraceptives or certain drugs were excluded from study. Matching was done between the two groups in terms of age. Metabolic syndrome was diagnosed among the study participants using the diagnostic criteria provided by the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA).A prior consent was taken from the selected women. Physical Parameters such as systolic and diastolic blood Pressures (SBP& DBP) and Waist Circumference (WC) were measured for both control and test groups. Biochemical parameters such as Fasting Plasma glucose (FPG), Total Triglycerides (TTG), Total Cholesterol (TCH) and HDL Cholesterol (HDL-C) were also estimated and recorded.

Blood samples were collected in 10-12 hours of fasting state from both control and test groups for the analysis of biochemical parameters. Fasting Plasma glucose was estimated by TRINDER'S METHOD, END POINT technique. Plasma glucose levels 70-110 mg/dl were considered as normal reference value. Triglycerides were estimated by GPO- TRINDER'S METHOD, END POINT technique. Triglyceride levels 50 -150 mg/dl was considered as normal reference interval. Cholesterol levels were estimated by CHOD-PAP METHOD, END POINT technique. Cholesterol levels <200 mg/dl were considered as desirable, 200-239 mg/dl as Borderline high and > 240 mg/dl as high. HDL Cholesterol levels were estimated BY PHOSPHO TUNGSTIC ACID METHOD, END POINT technique. HDL cholesterol level <40mg/dl in males and < 50mg/dl in females were considered as low levels.

Data was recorded in MS-Excel spread sheets and analysed with help of SPSS-21 trial version. Averages of both physical and biochemical parameters were in both groups were compared and tested with standard error of difference between two means. Odds ratio for each risk factor was calculated and estimated the association between risk factor and dysfunctional uterine bleeding.

III. Results

The mean age of study women in test group was 44.04 years whereas in control group the average age was 44.14 years. Table no.1 depicted the distribution of risk factors among the study participants. The mean Fasting Plasma Glucose in test group was 98.44 ±.23.17 mg/dl and 84.64 ±7.79 mg/dl in control group. The Systolic Blood Pressure average in test group women average was 123 ± 11.20 mm of Hg whereas in control group women average SBP was 113.6 ± 8.75 mm of Hg. The mean Diastolic Blood Pressure in test group was 80.4 ± 7.55 mm of Hg and in control group it was 75 ± 5.44 mm of Hg. The average of Total Triglycerides in

test group and control group were 157.62 ± 32.08 mg/dl and 132.84 ±23.02 mg/dl respectively. The mean HDL cholesterol in test group was 43.56 ± 3.24 mg/dl whereas in control group the mean HDL-C was 51.8±4.60 mg/dl. The mean Waist Circumferences in test and control group were87.12 ± 7.54 cm. and 76.28 ± 2.45 cm respectively. Averages of all the risk factors were high in DUB women when compared to Non-DUB women. The differences in the averages of risk factors between test group and control group were tested with standard error of difference between two mean and Z values were calculated and found that the differences were statistically significant at 95% confidence interval (P< 0.05).

Table no.2 depicted the association of risk factors with Dysfunctional uterine bleeding among the study women. All the five risk factors had the odds ratio more than two and showed the association with Dysfunctional uterine bleeding. Among them Waist circumference above 80 cm and HDL-C below 50 mg/dl were highly associated with Dysfunctional uterine bleeding followed by DBP above 85 mm of Hg, FPG above 100 mg/dl, SBP above 135 mm of Hg and TGL above 150 mg/dl. Twenty seven women among the fifty DUB women were with the metabolic Syndrome i.e. with 3 or more risk factors. But metabolic syndrome was not observed among the fifty Non-DUB women. From the above results, it can be concluded that he risk of Dysfunctional uterine bleeding among the women having metabolic syndrome was very high when compared to women not having metabolic syndrome.

IV. Figures and Tables

Table no.1 Distribution of Risk factors among the study women

Risk Factor	DUB Women (n=50)	NON-DUB Women (n=50)	Z -Value /P- Value
Fasting Plasma Glucose in mg/dL	98.44±23.17	84.64±7.79	4 / <0.05
Systolic Blood Pressure in mm of Hg	123±11.20	113.6±8.75	4 / <0.05
Diastolic Blood Pressure in mm of Hg	80.4±7.55	75±5.44	4.1 / <0.05
Triglycerides in mg/dL	157.62±32.08	132.84±23.02	4.4 / <0.05
HDL Cholesterol in mg/dL	43.56±3.24	51.8±4.60	10.5 / <0.05
Waist Circumference in cm.	87.12±7.54	76.28±2.45	9.7 / <0.05
Overall Risk Analysis	3.04±1.10	0.74±0.75	16.4 / <0.05

Table no.2 Risk factors comparison between the study groups

Risk Factor	DUB Women (n=50)	NON-DUB women (n=50)	Odds ratio
FPG above 100mg/dl	14	3	8.43
SBP above 135 mm of Hg	20	4	7.66
DBP above 85 mm of Hg	15	1	21
TGL above 150 mg/dl	28	9	5.79
HDL below 50 mg/dl	48	17	46.58
WC above 80 cm	42	0	∞
Metabolic syndrome	27	0	∞

V. Discussion

In our present study we observed that women with dysfunctional uterine bleeding had more than twice increased risk of type 2 diabetes mellitus than women with normal menstrual cycles. This finding is consistent with study by Solomon et al who observed that women with long (40+days) or irregular menstrual cycles were more than twice as likely to develop type 2 diabetes mellitus over the 10 year study period than women with usual cycles. Women with very short cycles (21 days or less) were 1.5 times more likely to develop the condition than those with normal cycles. Another cross sectional study in pima India also showed an increased frequency of type 2 diabetes in those women with a history of very long menstrual cycles[17].

In our present study we observed that women with dysfunctional uterine bleeding had significantly high prevalence of waist circumference, hypertension, diabetes mellitus and hypercholesterolemia. This finding is consistent with study by Solomon et al., they reported that women having irregular cycles tended to have higher body mass index and were more likely to report histories of diabetes mellitus, hypertension, and hypercholesterolemia than women with a history of regular menstrual cycles [17]

In our present study we also observed that women with dysfunctional uterine bleeding had significantly high prevalence of low HDL cholesterol compared to control group. Many population-based

studies of the Middle East as well as the current study, low HDL cholesterol followed by abdominal obesity has been the most common component of the metabolic syndrome. The underlying mechanisms for increase in prevalence of components of metabolic syndrome remain unknown.

Possible mechanism: - PCOS and dysfunctional uterine bleeding both are obesity related comorbidities. Obesity is related to the increased peripheral conversion of androgens to estrogens in the adipose tissue [3, 8]. This becomes a major risk factor for type 2 diabetes, associated with infertility and menstrual abnormalities [7]. Higher estrogen concentrations result in menstrual abnormalities and anovulation by negative feedback at the hypothalamo-pituitary level [18].

Obesity is associated with elevated levels of free androgens through increased peripheral aromatization of testosterone to estradiol in the fat tissues. In addition, obese women have decreased sex hormone-binding globulin (SHBG) levels, which causes increased levels of circulating or free testosterone [19, 20]. Finally, elevated insulin levels stimulate production of androgens in ovarian stromal tissue. These changes in the concentration of gonadal steroid hormones with obesity cause disruption of normal ovulation and irregular menstrual bleeding, which can be described as amenorrhea, oligomenorrhea, menorrhagia, menometrorrhagia, or dysfunctional uterine bleeding.

Limitations: Obesity could be a confounding factor, which could be a limitation for this study. It may influence the dysfunctional uterine bleeding and metabolic syndrome. Selection of premenopausal women (40-49 years) excluding younger age groups is another limiting factor. Prevalence of obesity is less in younger women when compared to premenopausal women. The prevalence of obesity and being overweight was observed to increase according to an increase in age among the population of 20 to 69 years-olds for both men and women.

VI. Conclusion

Dysfunctional Uterine Bleeding (DUB) associated with the high prevalence of Metabolic Syndrome. It can be considered as an example for web of causation of disease theory. Further prospective studies were needed to prove the causation of Metabolic Syndrome because of Dysfunctional Uterine Bleeding

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