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COMPARATIVE STUDY OF THYROID DYSFUNCTION IN PATIENTS WITH DYSFUNCTIONAL UTERINE BLEEDING

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ABSTRACT DYSFUNCTIONAL UTERINE BLEEDING (DUB) AND ITS CLASSIFICATION Dysfunctional uterine bleeding is defined by various authors in many waysleading to confusion as to, which are the exact entities, which come under thisheading. NOVAK defines it as "bleeding without a causative uterine lesion such as tumor infection or complications of pregnancy, although frequently there may be associated cysts of the ovary". SUTHERLAND defines DUB as "Abnormal uterine bleeding which is not explained by any palpable lesions of the reproductive organs".43 CROSSEN defines it as "irregular, excessive, scanty or prolonged bleeding of endometrial origin, occuring without neoplasia, infection, pregnancy, blood dyscrasias, trauma or hormone administration".44 TAYLOR restricts the term DUB to be applied only when all possible causes for irregular, excessive or prolonged bleeding have been excluded. Such as exclusive approach would tend to eliminate from consideration any uterine bleeding for which an etiology has been uncovered.45 TELINDE defines DUB as a symptom complex that in absence of pregnancy, neoplasm, infection or intrauterine lesions.46 SPEROFF describes DUB variety of bleeding manifestations of anovulatory cycles (in absence of pathology or medical illness).47 39 JEFFCOATES defines it as "excessive, prolonged, unpatterned bleeding from the endometrium unrelated to structural or systemic disease and thus other diagnosis must be excluded.48 DEWHURST defines DUB as "abnormal bleeding from the uterus in the absence of organic disease of the genital tract".49 DAWN refers it as a excessive uterine bleeding where no organic, systemic, haematologic or pelvic cause can be detected.50 Two areas of general agreement can be obtained from these sources – first, the necessity to exclude bleeding arising from organic disorders of the reproductive tract in order that an entity may qualify as DUB. Secondly, the presupposition that endocrinologic abnormalities have a significant relationship to DUB. Adequate clinical examinations of abdomen and pelvis, uterine curettage, hysteroscopy or atleast an endometrial biopsy are essential to exclude organic disease of the uterus. In recurrent severe abnormal uterine bleeding repeat curettage should be done to avoid previously missed organic disease.1 Hence, a provisional diagnosis of DUB is made clinically.

KEYWORDS : Dysfunctional Uterine Bleeding (DUB), Thyroid Dysfunction, Abnormal Menstrual Bleeding, Reproductive Age Group

INTRODUCTION

Menstruation is the cyclical uterine bleeding occurring during reproductive age between menarche and menopause. Normal menstruation represents the cyclical shedding of secretory endometrium and is essentially a progesterone withdrawal bleeding caused by degeneration of corpus luteum if the ovum is not fertilized.49 The endometrium is composed of glands and stroma, and has the following layers, a superficial functional layer 'decidua functionalis' (which is further divided into stratum compartum & stratum spongiosum) responding to hormones. The basal layer 'decidua basalis' is responsible for the regeneration of the endometrium. 43 Under the influence of monthly cyclic production of estrogen and progesterone by ovaries, endometrium undergoes cyclic changes through the following phases2:- Proliferative phase - Secretory phase - Menstrual phase Proliferative phase It Corresponds to the follicular phase of the ovarian cycle. It follows the menstrual phase and concludes at ovulation. During this phase estrogen from the growing follicle causes regeneration of the endometrium from the basalis layer. VEGF is a highly potent endothelial nitrogen produced by the endometrium in response to the rising estrogen and associated hypoxia.3 Short, narrow and straight glands become longer and tortuous due to estrogen influence and stroma becomes dense and compact. Secretory phase This is the progestrational phase of endometrial cycle which begins after ovulation. It corresponds to the luteal phase of the ovarian cycle, it extends from ovulation till onset of next menses. The progesterone dominated secretory phase bring about secretory changes in the estrogen 44 primed endometrium with the primary aim to produce appropriate environment for implantation. The histopathological examination of the endometrium during secretory phase gives typical 'saw toothed' and 'cork screw' appearance in the cross section.29 At the peak of secretory phase one week after ovulation the endometrial thickness is about 5 to 6 mm. If the ovum is not fertilized, the corpus luteum degenerates and menstruation starts around 14th day after ovulation. Menstrual phase Shedding of endometrium takes place during this phase and it lasts for about 3 to 5 days. Regulation of menstrual cycle (endocrine control) The hypothalamo-pitutary axis The hypothalamus secretes the gonadotrophin releasing hormone (GnRH), with varying frequency and amplitude leading to the release of follicle stimulating hormone(FSH) and luteinising hormone(LH) from the anterior pituitary gland. • The follicular phase shows high amplitude more frequent pulses withfrequency increasing before LH surge with dominance of FSH • The luteal phase has low amplitude, less frequent pulses leading to thepredominance of LH • One pulse every hour is typical of follicular phase and one pulse every 2 to 3 hours is typical of luteal phase51 45 Criteria for normal menstrual cycle Menstrual cycle is judged by three clinical parameters Cycle length: It is the interval between the first day of one period and the first day of the next.51 During the active reproductive years, menstruation occurs at approximately 28 +/- 7 days. Each woman has her own rhythm which

may change after marriage or child birth.49 Treloar et al reported at university of Minnesota in his prospective study over 30 years in Caucasian women that the cycle length usually varies by 1 to 2 days each month and only 50 % women have cycles within 26-30 days range. Median cycle length declines from 28.87 (+/-2.75) days at age of 20 years to median of 26.8(+/-2) days by 40 years of age.52 In reference to this study, in general cycles with length less than 24 days are considered polymenorrhoea and those with more than 35 days are considered oligomenorrhoea. Regularity of cycle length depends upon HPO axis. The immediate post menarche cycles are irregular and long due to immaturity of hypothalamus and pituitary, as a result of which regular 46 ovulation is yet to be established. Again in perimenopausal period cycles become irregular and mostly longer due to diminished number of follicles with increased resistance to gonadotrophin stimulation.1 Duration of menstrual blood loss: As per Gullibaud and Bonner (1978), normal range of duration of bleeding is 2 to 7 days with an average of 5 days. Shorter (hypomenorrhea) or longer (hypermenorrhea) than this is considered abnormal.53 Menstrual blood loss: Average blood loss per cycle is considered to be 35-40 cc. This is equivalent to daily loss of 0.6 mg to 0.7 mg of iron throughout each month.49 According to Rybo et al (1985) parity has a small effect on MBL, multiparas have a slightly higher average loss than nulliparas.54 WHO report mentions that in western European populations, the average blood loss during menstruation varies from 31-39 ml while Chinese and Japanese populations it is 47 54 ml and 52-56 ml respectively.55 In Swedish population, Hallberg et al observed significant increase in the incidence of iron deficiency anaemia when the MBL was 80 ml or more.56 Following are the terminologies used for describing abnormal bleeding pattern.51 Menorrhagia: is prolonged (> 7 days) and /or excessive (>80ml) uterine bleeding that occurs at regular intervals. 47 Polymenorrhoea: is uterine bleeding that occurs at regular intervals less than 21 days apart. Oligomenorrhoea: is infrequent uterine bleeding that occurs at intervals more than 35 days apart. Metrorrhagia: is uterine bleeding that occurs at irregular but frequent intervals, the amount of uterine bleeding is variable and the duration of flow is often prolonged. Menometrorrhagia: prolonged uterine bleeding that occurs at irregular intervals.

PATHOPHYSIOLOGY OF DUB There are three reasons for the self-limited character of estrogenprogesterone withdrawal bleeding. • It is a universal endometrial event: menstrual changes occur simultaneously in all segments of the endometrium. • The estrogen primed endometrial tissue which has responded to appropriate levels of progesterone is structurally stable, and random breakdown of tissue due to fragility is avoided. • Inherent in the events that preclude the onset of menstruation are factors involved in stopping menstrual flow. Platelets and fibrin play a direct role in the homeostasis achieved in a bleeding menstrual 48 endometrium. Intravascular thrombi are seen in the functionalis layer and are localised to the shedding surface of the tissue. Fibrinolysis occurs in the endometrial tissue limiting fibrin deposition in the proximal, still unshed layer. After early dependence on thrombin plugs to restrain blood loss, later generalised vasoconstrictive homeostasis without thrombin plugs occur. In the past decade, studies have shown increased endometrial fibrinolysis and an alteration in prostaglandin balance as local uterine abnormalities present in dysfunctional uterine bleeding. • Increase PGE2 and F2alpha. • Increase endometrial fibrinolysis • Structural changes in the spiral arterioles and venous sinuses of endometrium such as perivascular fibrosis, subendothelial hyaline degeneration, hyperplasia and hypertrophy of smooth muscle and elastosis(salvator, 1958) • Abnormal vascularity of the endometrium. • Delayed regeneration of the endometrium • Excessive endometrial tissue necrosis by hydrolytic enzymes from Golgilysosomal complex. • Deficient formation and release of endometrial vasoconstrictor substance. 49

ANOVULATORY BLEEDING38,39 Anovulation or oligo-ovulation is the commonest cause of abnormal uterine bleedingwhen no organic cause has been found. The characteristic feature is the absence of active corpus luteum tissue in the ovary. A follicle ripens but fails to rupture, the ovum dies and follicle may go onto cyst formation whether it forms a cyst or not, it produces oestrogen for time and this act on the uterus without being opposed by progesterone. The production may be continuous at a moderate level, or intermittently high and low. In either case the uterus responds by hypertrophy of its myometrium and endometrium, and the latter may become polypoidal. On section the endometrium shows the picture of hyperplasia, usually of cystic type (SWISS CHEESE) but occasionally adenomatous. Bleeding is acyclical it is continuous for 2-8 weeks and can be so heavy as to threaten life. In about half the cases it is preceded by a short period of amenorrhoea which coincides with a continuously high production of oestrogen by the follicle and this type of clinical picture was earlier often labelled as metropathia haemorrhagica. When the granulosa cells becomes less active or when the endometrium grows so thick that the supply of oestrogen becomes relatively inadequate, oestrogen withdrawal bleeding takes place. The bleeding is always painless. On examination the uterus feels slightly enlarged and its sometimes possible to palpate cystic ovaries. A definitive diagnosis is only by histological examination of curettings. 50 The underlying cause is unknown personally the failure in ovulation, reflects an abnormal gonadotrophin stimulus. Behind this there is often a hypothalamic and cortical basis, as in the case of other forms of dysfunctional bleeding, being mostly seen in nervously tense and emotional subjects. It recurs most commonly during the few years preceding the menopause, but is occasionally seen in girls aged 12-20 years. In the latter it shows a strong tendency to spontaneous cure.

MATERIAL AND METHODS

Source of data This study will be carried out in the department of Obstetrics and Gynaecology, Index Medical Hospital And Reserch Center Indore, October 2012 to June 2014. 140 women with a provisional diagnosis of dysfunctional uterine bleeding from our hospital will be selected for the study. Study Design Study Period : A prospective study : 18 Months (December 2012 to August 2014) DETAILS OF THE STUDY INCLUSION CRITERIA • All cases provisionally diagnosed to have dysfunctional uterine bleeding from puberty to premenopausal age groups. • All patient having major complaint of menstrual disturbances e.g., menorrhagia, polymenorrhoea, polymenorrhagia, metropathia hemorrhagica, metrorrhagia, Oligo and hypomenorrhoea. 52 EXCLUSION CRITERIA • Patients who are on Antithyroid drug or thyroid hormones, IUCD users, history of bleeding disorder will be excluded. • Patients with organic lesions of genital tract. Procedure of Study • A detailed history was obtained with special relevance to age, bleeding pattern. • Onset, duration, amount of bleeding, complaints related to thyroid dysfunction was noted in detail. • A thorough clinical examination including general physical examination, neck examination, gynaecological, and systemic examination was carried out, with special reference to thyroid dysfunction; in cases with a provisional clinical diagnosis of DUB. • Patients having thyroid disease were excluded. • All these patients were subjected to routine investigations like hemoglobin percentage, blood counts, urine examination for albumin, sugar, microscopy, bleeding time, clotting time, (to rule out coagulation defect) and USG Abdomen & peivis. • Then all patients were subjected for T3, T4, TSH and TPOAb estimation in their sera. Investigations were estimated by Chemiluminescence Immuno Assay (C.L.I.A) method using reagent Monobind I N C; USA;Kit. with the help of fully automatic Alpha lite machine in Bio-chemical lab at Index. Drop of reagent monobind I N C mixed with collected blood and using special programming chart they place it in the fully automatic analyzing machine Alphalite, made in FRANCE. These test will be done in fasting blood samples.seen in girls aged 12-20 years. In the latter it shows a strong tendency to spontaneous cure.

RESULTS

Below the age of 20 years, 18 cases were euythroid, 2 had sub clinical hypothyroidism and 2 had hyperthyroidism. Among the cases belonging to 21-30 years, 13 cases were euthyroid and 1 had hypothyroidism and 2 had subclinical hypothyroidism. Among the age group of 31-40 years, 51 patients were euthyroid, 2 had hypothyroidism and 4 had subclinical hypothyroidism. Above the age of 40 years,2 patients had hypothyroidism, 2 patients had sub clinical hypothyroidism.

Patients who presented with menorrhagia have prevalence of 26% of thyroid dysfunction, this appears to be the most common bleeding pattern according to this study to be associated with thyroid disorders. Patients who presented with oligomenorrhoea had 18% prevalence of thyroid disorder.

Menorrhagia is the most common bleeding pattern 45%(10 cases) in age group less than 20 years, 75%(12 cases) in age group 21 – 30 years, 42%(24 c0ases) in age group 31 – 40 year, 35 %(14 cases) in age group more than 40 years. In the unmarried group which constituted of 25 patients, 5(20%) patients had thyroid disorders. In the nulliparous group consisting of 17 patients, 2(12%) had thyroid dysfunction. Among 19 para 1 patients who took part in the study, 4(21%) patients had thyroid dysfunction. In the patients who were para 2, out of 46

patients 4(9%) patients had thyroid disorders. In patients who were para 3, out of 24 cases,1(4%) case had thyroid disorder . With parity 4 or more 1(12%) out of 9 cases had thyroid dysfunction.

DISCUSSION

Compared to Other Authors study in the present study the percentage of patients with thyroid dysfunction in the age group below 20 years is 22.22 % V/s 11.67 %. In the authors study the percentage of thyroid abnormalities in the age group of 21-30 years is 16.67 % in our study it is 23.07 %. The percentage of patients in 31-40 years of age group in 11.76 % in our study and in the author's study it is 48.33 %.

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