

Incidence of Menstrual Irregularities Associated With Hypothyroidism in Balochistan, Pakistan

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ABSTRACT

Menstrual disorders are a common problem during adolescence. These disorders may cause significant anxiety for patients and their families. Menorrhagia is frequent debilitating symptoms in gynecological practice resulting in need for repeated curettage and hysterectomy with its attendant morbidity and mortality the etiology of menorrhagia is very diverse, it may be due to systemic conditions like endocrine disorders (thyroid dysfunction), or local lesions of the genital tract (endometrial hyperplasia, pelvic inflammatory disease, endometriosis, benign and malignant tumors) thyroid dysfunction is one of the common cause of menstrual irregularities. There are various menstrual disorders occurring in women, which may be a result of a cause specific to anatomy or it may be due to clotting abnormalities or hormonal causes. There are established linkages between hypothyroidism and menstrual irregularities. The objective of the study was to determine the frequency & type of menstrual irregularities associated with hypothyroidism. Fifty patients were selected for the clinical study, complete history, physical examination and investigations of all patients has carried out. Of which thirty nine patients showed irregular menstrual cycles whereas 11 had regular menstrual cycles. Investigational test performed included Blood test such as (T3, T4, TSH & blood hormones profile), Ultrasound (pelvis), Thyroid scans, endometrial biopsy, Pap smear, high vaginal swab and test for confirmation of ovulation were carried out at CENAR Hospital Quetta. The Examination and tests revealed that menorrhagia in (n=21) cases, oligomenorrhea in (n=19), metrorrhagia in (n=7), polymenorrhea in (n=2), Amenorrhea in (n=2), Early Menarche in (n=6) and primary-infertility in (n=3) patients. The common problem was observed in age group was 25-45 years. Menorrhagia and oligomenorrhea were most regular irregularities found in this study where frequent cause was Hashimoto's Thyroiditis. It is concluded that menstrual irregularities increase with severity of hypothyroidism

Key words: Menstrual disorders, Menorrhagia, oligomenorrhea, hypothyroidism, polymenorrhea,

INTRODUCTION

Menstrual period is a part of ovarian cycle in which series of changes occur in the ovary, uterus, vagina and breast every 28 days on average (Mohan et al., 2007). Some women get through their monthly period easily with few or no symptoms their periods come like clock wise starting and stopping at nearly same time every month. While other women experience physical or emotional symptoms just before or during menstruation, from heavy bleeding and missed periods to unmanageable mood swings these symptoms disturb a woman's life in many ways, (NWHRC, 2008).

The hypothalamus, pituitary, and ovaries form an endocrine axis (known as the HPO axis) that functions via hormonal regulation and feedback loops. This system governs the regulation of

menstruation, which is the cyclic, orderly sloughing of the uterine lining. Any disruption in this axis may result in amenorrhea or menstrual cycle disturbances, (Ann, 2008). Changes in the length of the menstrual cycle generally are due to disturbance as HPO axis (Braunstein, 2007). Thyroid hormone receptors and their messenger RNA have been detected in human granulosa cells and direct effects of iodine and thyroid hormone on ovarian function are purposed recently (Daufas, 2000). Effects of hypothyroidism on reproduction cause decrease fertility from anovulatory cycle, (Alzubaidi, et al., 2002). Menstrual disturbances (especially in menorrhagia), luteal phase defect and hyperprolactinemia are reported by Nelson et al., 2005; Utiger, 1995 and Daufas et al., 2000, respectively. Effect of hypothyroidism on menstrual cycle causes anovulation. It is a common problem caused by thyroid dysfunction. Hypothyroidism can halt ovulation by upsetting balance of the reproductive hormones. If ovulation takes place the

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level of LH will be increased. LH stimulates the ovaries to release the ovum. The surge in LH indicates the ovulation. If there is too much or too little thyroid hormone ovulation may not occur, even though the menstrual cycle is regular (Shan and Afia, 2007). Menorrhagia is an anovulatory cycles, the follicular growth occurs with the stimulation from FSH, however due to lack of LH surge, ovulation fails to occur. Consequently no corpus luteum is formed and no progesterone is secreted. The endometrium continues its proliferative phase excessively. When the follicles involute, estrogen level drops and estrogen withdrawal bleeding occurs. Most anovulatory cycles are regular with normal bleeding; however, the unstable proliferative endometrium can shed irregularly, resulting in prolonged heavy bleeding, (Diaz, 2006). In hypothyroidism women has short luteal phase. The luteal phase is the period between ovulation and onset of menstruation. The luteal phase needs to be of sufficient duration. A normal luteal phase is approximately of 13 to 15 days to mature a fertilized egg. A shortened luteal phase can cause failure to sustain a fertilized egg, with loss of very early pregnancy at around the same time as menstruation occurs. Luteal phase defect is a hormonal imbalance affecting ovulatory function and uterine endometrial lining, which can increase a woman risk of both conception difficulties and miscarriage. Hypothyroidism can cause an increase in prolactin secretion called hyperprolactinemia. The hormone produced by the pituitary gland under the influence of thyrotropin releasing hormone from the hypothalamus. TRH stimulate the pituitary gland to secrete both TSH and prolactin, (Daufas, 2000). Fertility is reduced in hypothyroidism due to anovulatory cycle. It was found that absolute epithelial cell volume is decreased in hypothyroidism. The volume of the nucleus had decreased though its relative volume in the cell had increased. The height of the luminal epithelium in hypothyroidism also decreased. Basement membrane thickness significantly increased. These findings suggest that thyroid hormone importantly concerned in maintenance of normal structure of uterine epithelial cell (Alzubaidi, 2002). Singh et al. (1998) reported that Abnormal uterine bleeding pattern in different ways Oligomenorrhea, Polymenorrhea, Menorrhagia, Amenorrhea, Dysfunctional uterine bleeding. Thyroid disorder has been implicated in a broad spectrum of reproductive problems ranging from abnormal sexual development to menstrual irregularities and infertility (Braunstein, 2007).

Taking in view these aspects, a study has been designed to detect incidence of menstrual irregularities in hypothyroid women of Balochistan. The incidence of menstrual irregularities associated with hypothyroidism has been worked out in detail

first time in the history of Balochistan. In addition to estimate the reproductive failure due to menstrual disorder associated with hypothyroidism in pre menopausal women, to determine the association of menstrual disorder with severity of hypothyroidism and to determine the incidence of menstrual disorder in hypothyroidism.

MATERIAL and METHODS

A retro-prospective clinical study was conducted in CENAR (Center for Nuclear and Radiotherapy) Hospital Quetta from May, 2008 to November, 2008. Fifty female patients were selected for study. Patients were selected after complete clinical history general/physical examination and investigations. Patients were not included in the study were pregnant women, nursing mothers, patients not willing, above 45 years, below 15 years, menstrual irregularities due to other gynecological problems. Study was focused on hypothyroid females having menstrual irregularities of age 25 to 45 years. A prescribed performa was designed to collect the relevant information. Complete clinical history of the patients was recorded in performa that was collected during thorough interrogation with the patients.

Patients were gone through a complete examination and findings were noted on individual report. Blood pressure, pulse rate, temperature, colour of the skin, eyebrows weight gain/loss record and thyroid gland examination was recorded. Blood sample of the patients were collected for laboratory tests. Blood test such as (T₃, T₄, TSH & blood hormones profile), Ultrasound (pelvis), Thyroid scans, endometrial biopsy, Pap smear, high vaginal swab and test for confirmation of ovulation were carried out at CENAR Hospital Quetta.

Radio immune Assay (RIA) procedure for determination of Tri-iodothyronine (T₃) was conducted and result was taken in the numerical form (Surks, et al., 1990). RIA procedure for determination Tetra-iodothyroxine (T₄) was performed. RIA procedure for determination of Thyroid Stimulating Hormone (TSH) (Eggertsen, et al., 1988) was used.

Ultrasound of abdomen and pelvis has done to look for the presence of ovaries and a uterus and to rule out any masses or large cysts. Doing a Pap smear of the cervix (the entrance to the uterus) can show whether there is estrogen present. If more than 10% of the cells collected from a Pap smear are of a certain type, then estrogen is present. This can help confirm the function of the ovaries. Ferning of the cervical mucus: Examining the mucus from the cervix (the entrance to the uterus) can show whether estrogen is present. If the mucus dries in such a way that it creates a pattern shaped like a fern, then there

is adequate estrogen. Test for presence of β -HCG in urine was performed.

RESULTS

Research was conducted (May 2008 to Dec 2009) on patients (n=200) and out of that patients (n=50) observed menstrual irregularities are associated with Hypothyroidism at CENAR Hospital Quetta. These patients (n=50) were further examined for clinical study, complete history, physical examination and investigations of all patients has carried out. Of which thirty nine patients (n=39) showed irregular menstrual cycles whereas (n=11) had regular menstrual cycles. Investigational test performed included; Blood test such as (T3, T4, TSH & Blood hormones), Ultrasound (pelvis), Thyroid scans. Certain other techniques like endometrial biopsy, Pap smear, high vaginal swab & test for confirmation of ovulation were carried out. . The Examination and tests revealed that menstrual irregularities was observed; menorrhagia in (n=21) 42%, oligomenorrhea in (n=9) 18%, metrorrhagia in (n=7) 14%, early menarche in (n=6) 12% polymenorrhea in (n=2) 4%, amenorrhea in (n=2) 4%, and primary-infertility in (n=3) 6% patients. The general problem was observed in age group 25-45 years. Menorrhagia and oligimenorrhea were found usual irregularities in this study where well-known cause was Hashimoto's Thyroiditis. According to present results more or less all 50 women had complain of painful menstruation. Hypothyroidism is found due to autoimmune thyroiditis is 33%. The results of the present study have shown that 100% of patient improved after treatment with thyroxin.

Table 1: Patients examined in CENAR (O.P.D) (n=200)

Age group	Hypothyroidism	Hyperthyroidism	Euthyroid
25 - 45years	50	35	115

Table 2: Thyroid Status

Age group	=n	Hyperthyroidism
25 - 45years	23	23
35 - 45 years	27	27

Table 3: Menstrual Irregularities (n=50)

Irregular Menstrual cycle	Regular Menstrual Cycle	Irregular menstrual cycle
39	11	78%

Thyroid Profile: The Thyroid profile was also performed in those ten subjects in whom the LH surge was negative. Results show decreased T₃, T₄ and increased TSH levels in three subjects showing hypo-thyroidism. While the remaining 7 subjects showed normal thyroid hormone levels. (Normal

ranges for T₃: 2.5 – 5.8 n mol/L; T: 11– 23 pm; TSH: 0.17 – 4. 0 m IU/L).

It was observed that menstrual irregularities tent to be more frequent in sewer hypothyroidism which represented in the results as present study as the menstrual irregularities are directly proportional to the level of TSH. Test for presence of β -HCG in urine (pregnancy test) to check for pregnancy, was carried out and observed negative in all patients. Ultra sound report of pelvic scan was observed in normal limit.

Table 4: Frequency of the clinical features observed in hypothyroid patients.

Symptoms	=n
Appearance	
Normal	66
Fatty	14
Thin	20
Weight Changes	
Gain	12
Loss	30
Stable	58
Increased Sensation	
Cold	26
Heat	20
Normal	54
Appetite Changes	
Normal	63
Increase	15
Decrease	22
Bowel Habits	
Normal	68
Constipation	22
Loose Motion	10
Nervous System	
Nervousness/ Anxiety	2
Depression	6
Delayed relaxation of deep tendon reflexes	2
Edema	
Edema of face	16
Peripheral edema	2
Per orbital edema	4
Menstrual Irregularities	42

Table. 5 Thyroid Scan Shows types of Goiter

Cause	n=
Cold Nodules	14
Hot Nodules	17
Diffuse Goiter	6
Multi Nodular	7
Nodular Goiter	4
Total	50

DISCUSSION

This research focuses on women coming to Cenar Hospital Quetta with Hypothyroidism and menstrual irregularities associated with it. The aim of this study was to recapitulate knowledge of physiology, pathology and clinical aspects of both thyroidal and

gonadal axis interactions (Casey, 2006). Some studies have reported that as many as three out of four woman with thyroid conditions have some form of menstrual problems at a rate that is two to three times higher in woman without thyroid problems (Kris et al., 2008). Thyroid disease is frequently the reason behind problems with a woman's menstrual cycles.

During present research it was observed that 78% women were affected. Girls who have either very early or late menstruation should be evaluated for a potential thyroid problem, as thyroid problem can frequently be a cause of early or delayed puberty and menstruation. Hypothyroidism in girls may trigger very early menstruation i.e. before the age of 10 years. This early puberty is known as "Precocious Puberty" (Mary, 2008). According to present results 12% girls came with early menarche. Hypothyroidism was more prevalent in infertile group (Singh et al, 1998).

Normal ovarian function requires normal levels of thyroid hormone. Deficiency of thyroid hormone causes direct suppression of ovaries resulting in menstrual irregularities which can lead to infertility (Shika, 2007). In another study thyroid hormone receptors have been describe in human oocytes, where they synergize with the LH/HCG receptors mediated by FSH to exert direct stimulatory effect on granulosa cell function and on trophoblastic differentiation (Wakim et al, 1993). Trokoudes (2006) reported that serum TSH levels were a significant predictor of invitro fertilization failure in women with infertility. TSH concentration significantly increased among women who produced oocytes that failed to achieve fertilization (Kris et al, 2008). Above studies reflects that hypothyroidism is the cause of infertility which is observed 6% in present study.

Hypothyroidism is also associated with menorrhagia because as altered production as coagulation factors, such as decreased levels of factors VII, VIII, IX, and XI (Petta, 2001). Menorrhagia in adolescent is usually caused as anovulatory, anovulatory bleeding is common in some endocrine disorders such as hypothyroidism and polycystic ovary syndrome (Gray, 2007). According to Kris et al (2008) menorrhagia and oligomenorrhea are the common irregularities in hypothyroidism which is same as found in the present study that is 42% and 18% respectively? The researcher also observed that menstrual irregularities tend to be more frequent in sewer hypothyroidism which represented in the results as present study as the menstrual irregularities are directly proportional to the level of TSH.

The incidence of primary amenorrhea in United States is less than 1%. The incidence of secondary amenorrhea (due to cause other than pregnancy) is about 4% per year. No evidence indicates that the

prevalence of amenorrhea varies according to national origin or ethnic group. However local environment factors related to nutrition and prevalence of chronic disease undoubtedly have an effect (Ann, 2008). Sewer hypothyroidism also leads to ovulatory dysfunction due to numerous interactions as thyroid hormones with reproductive system (Redmond, 2004). Amenorrhea due to hypothyroidism is 31% (Singh et al., 1998) which is 4% according to the finding of present study.

Hypothyroidism is associated with painful menstrual periods known as dysmenorrhea can include an achy or stabbing low back ach, nausea, leg aches, feeling of fullness, headaches and bowel disturbance (Mary 2008). Pain from menstrual cramps is caused by uterine contractions, triggered by prostaglandins, hormone like substances that circulate in blood. Other associated symptoms like diarrhea or an occasional feeling of faint that is because of prostaglandins. Prostaglandins speed up the contraction of intestinal muscle resulting in diarrhea and lower the blood pressure by relaxing the blood vessels lead to feeling of faintness (NWHRC, 2008). According to present results more or less all 50 women had complain of painful menstruation.

Autoimmune thyroiditis is most common autoimmune disorders, affecting 5-20% of woman as reproductive age (Janssen et al, 2004). The prevalence of hypothyroidism in woman of reproductive age varies between 2% to 4% and is largely due to autoimmune thyroiditis (Petta et al., 2007). Autoimmune thyroid disease is among the most common human autoimmune disorders (Singh, 1998). Studies on the risk of infertility associated with autoimmune thyroid disorders shows strong association between autoimmune thyroid disorders, endometriosis and ovarian failure (Kris, 2008). According to result of present study the cause of hypothyroidism is autoimmune thyroiditis is 33%. During 17 years period more than 1000 patients treated with thyroid hormone, even though their blood test for hypothyroidism were normal. In many of these cases thyroid hormone was the only treatment that helped them. Symptoms and conditions that improved are chronic fatigue, depression, infertility and menstrual irregularities (Alzuaidian et al., 2002). Studies in which the menstrual loss was measured treatment of hypothyroidism with thyroxine decreased menstrual blood loss (Casey and Leveno, 2006). The results of the present result have shown that 100% of patient improved after treatment with thyroxine.

Tissues throughout the body are sensitive to hormone levels that change throughout a woman's menstrual cycle. Studies suggest that rising and falling hormone levels may also influence chemicals in the brain, including a substance called serotonin, which affects mood. However, it is not clear why

some women develop PMS or PMDD and others do not. Levels of estrogen and progesterone are similar in women with and without these conditions. The most likely explanation, based upon several studies, is that women who develop PMDD are exquisitely sensitive to changes in hormone levels. Premenstrual syndrome (PMS) causes symptoms one to two weeks before a woman's menstrual period. Common symptoms include feeling tired, bloated, irritable, and anxious. The cause of PMS and PMDD is not known. Some women may be very sensitive to changes in hormone levels. Hormone levels normally change before and during the menstrual period. Pre-Menstrual Symptoms are 66% in present research

In present study the common presenting feature was menorrhagia that is 42 which is less than 69.65% by (Yusuf et al., 1996). While oligomenorrhagia was same in both studies as it was 18%. Polymenorrhagia was 4% in present as compared to 11.1% by (Yusuf et al., 1996).

Results of present study are in accordance with other reports Singh et al, 1998, Mohan et al., 2007; Petta, 2007 and Kris, 2008. Thus if thyroid dysfunction is detected pharmacotherapy may be a superior alternative to surgical intervention like hysterectomy (Yusuf et al, 1996)

CONCLUSION

Of the 50 hypothyroid patients 39 (78%) had irregular cycles and 11 (22%) had regular periods. Frequent age group is affected by thyroidism at 25-45 years and general cause of disease is Hashimoto's thyroiditis. Menstrual irregularities increase with severity of hypothyroidism. On the basis of result it is concluded that menorrhagia 42% and oligomenorrhea 18% are common irregularities in hypothyroidism among the women of Balochistan. It is recommended that thyroid function should also be monitored in routine investigation as there is increasing evidence in both experimental and clinical studies that hypothyroidism can lead to menstrual irregularities amenorrhea an ovulation and infertility. Thus if thyroid dysfunction is detected pharmacotherapy may be a superior alternative to surgical intervention like hysterectomy.

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