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Original Research Article

Occurrence of hypothyroidism and its correlation with reproductive health problems: a cross sectional study

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ABSTRACT

Background: Thyroid dysfunction is 10 times more common in women than in men. Hypothyroidism among women of reproductive age group is linked to menstrual irregularities, polycystic ovarian syndrome (PCOS), miscarriage and infertility. Several studies are available in the literature reporting regarding impact of hypothyroidism on one or the other isolated problems of reproductive health problems.
Methods: This cross-sectional study is conducted including 290 participants having various reproductive health problems attending the gynaecology OPD of a rural based tertiary care hospital of Tamil Nadu during the year 2017-2018.These participants were investigated for thyroid dysfunction and its correlation of hypothyroidism with reproductive health problems viz. menstrual irregularities, Polycystic ovarian diseases (PCOS), infertility and pregnancy loss was studied.
Results: It was observed that 80.6% of the 290 participants were euthyroid and 16.97% were hypothyroid, who presented with menstrual irregularities like menorrhagia (28.6%), oligomenorrhea (20.8%), amenorrhoea (21.3%), PCOS (28.6%), infertility (21.6%) and 23.8% hypothyroid women had pregnancy losses of varying number.
Conclusions: In present study the occurrence of hypothyroidism was found to be 16.89%. Since hypothyroidism has close association with problems like menstrual irregularities, PCOS, miscarriages and infertility, thyroid function test should be routinely recommended for these women. Thyroid dysfunction can be corrected with simple, cost-effective treatment. This will help in improvement in pregnancy outcome and also avoid subjecting women for major surgeries for menorrhagia.

Keywords: Hypothyroidism, Infertility, Menstrual irregularities, Miscarriages, PCOS, Reproductive age

INTRODUCTION

Thyroid diseases are the commonest endocrine disorders worldwide. In India, it has been estimated that about 42 million people suffer from thyroid diseases.[1] Thyroid dysfunction is 10 times more common in women than in men.[2] Prevalence of hypothyroidism in the reproductive age group is 2–4% and has been shown to be the cause of infertility and habitual abortion.[3] Thyroid is the second important endocrine next to pituitary that exerts the effects on the growth, metabolism and all other functions of the body including the reproductive system.

Hypothyroidism women of reproductive age group are more prone for menstrual irregularities, polycystic ovaries, recurrent pregnancy loss and infertility.[4] Various Studies show that women with both overt and subclinical hypothyroidism are at risk of increased incidence of pre-eclampsia, early pregnancy loss, recurrent pregnancy losses, stillbirth, failure of lactation and adverse neonatal

outcome viz Mental retardation and congenital anomalies.[5]

Hypothyroidism affects the reproductive health system directly by causing affecting functioning of hypothalamic-pituitary-ovarian axis and also indirectly through causing disturbance in the functioning of the target organs viz. ovaries. Hypothyroidism, through the altered TSH response, causes hyperprolactinemia. The increased level of prolactin affects the pulsatile release of GnRH leading to delay in LH response thereby resulting into defective luteal phase. This results in increased level of oestrogen leading to anovulation and also menstrual irregularities, infertility, PCOS and recurrent pregnancy loss. Hyperprolactinaemia by decreasing the GnRH release leads to increased levels of FSH with delayed LH response alters the FSH/LH ratio leading to follicular cyst which, in turn, increases the adrenal DHEA leading to arrest in follicle maturation. Increased TSH causes spill over effect on FSH receptors leading to collagen deposition.[6]

Hypothyroidism leads to decrease in level of SHBG. This has two effects 1) On peripheral conversion of androgen to oestrogen through its abnormal feedback at pituitary level leading to increase in the peripheral conversion of androgens to oestrogens and 2) It causes decrease in the levels of plasma testosterone and oestradiol. However, there is increase in unbound fractions of oestrogens.[7] The metabolism of oestrogens is also altered with respect to oestradiol and estrone. The luteal phase defect with its inadequate levels of progesterone leads to excessive and irregular bleeding in presence of unopposed high levels of oestrogen causing menstrual irregularities, ovulatory dysfunction with luteal phase defect leading to infertility, recurrent pregnancy loss(RPL) and PCOS.

In hypothyroidism, there is increased sensitivity of ovary to GnRH that leads to marked hypertrophy of ovaries and forms multiple follicular cysts leading to PCOS. It also decreases the coagulation factors vii, vii, ix, xi causing heavy menstrual blood loss. Heavy menstrual blood loss is the earliest clinical feature in subclinical hypothyroidism and it also causes RPL.[8] Recent studies conducted in 2015-2016, at Tamil Nadu and Maharashtra, concluded that the prevalence of hypothyroidism is as high as 27% among the women suffering from Abnormal uterine bleeding (AUB) and 19% are hypothyroid among infertility. [9-11]

This present study is conducted with the objective of determining the occurrence of hypothyroidism in rural women and the correlation of hypothyroidism and reproductive health problems.

METHODS

Study Design: Hospital based Cross sectional study.

Sample Size: 290 participants

Sample Size Calculated by using formula: N=4pq/L2

p= prevalence is 27.5%[9]
q is 100-P=72.5%
L is 20% error of Prevalence
N = (4 x 27.5 x 72.5) / (5.5)2 = 7975/30.25 = 263.64
264 + 10% nonresponse = 264+26=290

Study setting: (Place of study): Gynaecology OPD of a rural based tertiary care hospital attached to medical college institutions.

Study Population: All Women of age groups 15-45 years with reproductive health problem namely menstrual irregularities, infertility, PCOS, early pregnancy loss and recurrent pregnancy loss who were attending gynaecology OPD in tertiary care rural hospital, Ammapettai, Kancheepuram District.

Inclusion criteria

All women of age between 15-45 years with reproductive health problems attending gynaecology OPD, namely menstrual irregularities, infertility, PCOS, early pregnancy loss and recurrent pregnancy loss. Women having newly diagnosed hypothyroid women who are not on treatment who attended OPD with reproductive health problems were also included in the study

Exclusion criteria

All Pregnant women, women who are already on treatment for hypothyroidism and women diagnosed as having gynaecological malignancies were excluded. Study period: December 2017–October 2018. Ethical issues: Ethical clearance obtained from IEC (IEC No 2017/356).

Women attending Gynaecology OPD between 15-45 years for reproductive health problems viz menstrual irregularities, infertility, PCOS, early pregnancy loss, recurrent pregnancy loss were enrolled. After counselling and obtaining informed written consent from all the participants, the demographic data, age, education status, detailed clinical history, menstrual history was elicited as per proforma. After calculating BMI, general physical examination, gynaecological examination, thyroid gland examination was carried out. The data was entered in a pre-structured proforma. Participants were subjected to routine and relevant investigations in addition to thyroid Function Tests. The participants were asked to come after overnight fasting. In the morning and 5 ml of venous blood was collected from all patients by vene puncture and the blood was allowed to clot at room temperature and after separation of serum, it was centrifuged for 10 mins.

The Thyroid analysis was conducted by Electrochemiluminescence (ECL technology) using

immune assay analyser Roche Cobas e411 by using a standard kit.

Operational definition:

Following reference values were used[12]

Normal values:

- Free T3 - 2.4-4.2pg/ml
- Free T4 - 0.7-1.24 ng/ml
- TSH - 0.5-4.5mIU/ml

Euthyroid:

- Normal FT4: 0.7-1.24ng/ml
- normal TSH: 0.5-4.5 m IU/ml

Hypothyroidism (Overt):

- FT4 <0.7ng/ml,
- TSH->4.5 m IU/ml

Subclinical hypothyroidism:

- Normal FT4: 0.7 to 1.24ng/ml
- TSH >4.5mIU/ml L

Statistical analysis

The data collected was entered in MS-Excel sheet and subjected for statistical analysis. Descriptive statistics (by using SPSS version 23.0) such as frequency and percentage were calculated. The correlation of hypothyroidism and reproductive health problems was done by chi-square test. A p-value of 0.05 or less was taken to indicate a significant difference.

RESULTS

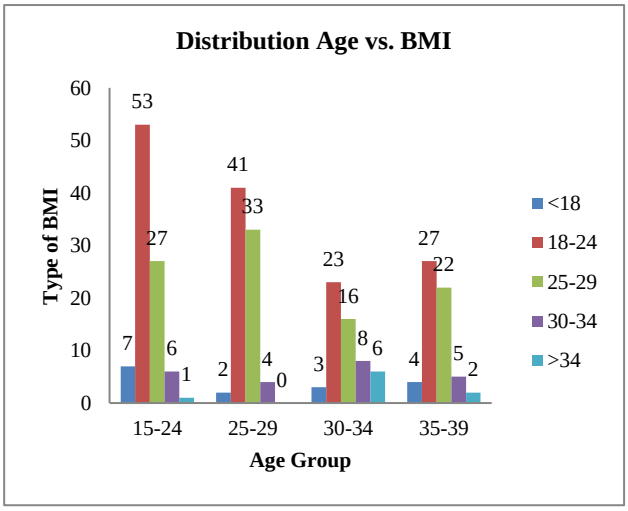

Figure 1: Distribution of Age vs. BMI.

Figure 1 show that the majority (60%) in the study were belonging to the 15-31. Age group with mean age being 30.31 and median age 29 years. The study shows that majority of participants having normal BMI fall between 18-24years of age group.

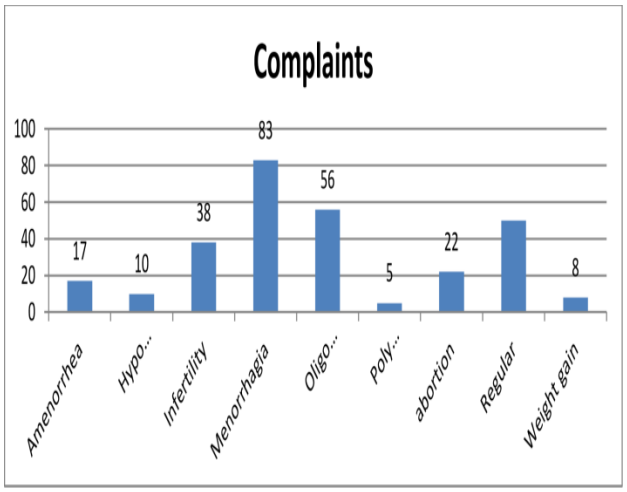

Figure 2: Distribution of participants according to reproductive health problems.

In Figure 2 shows the distribution of participants according to reproductive health problems (with presenting complaints). The present study shows that out of the 290 Study population,83(28.6%) of participants had menorrhagia and 56 (19%) had oligomenorrhoea. Thrity eight with infertility, whereas 22 participants presented with pregnancy loss. Only 17 participants had amenorrhea and 10 had hypomenorrhea.

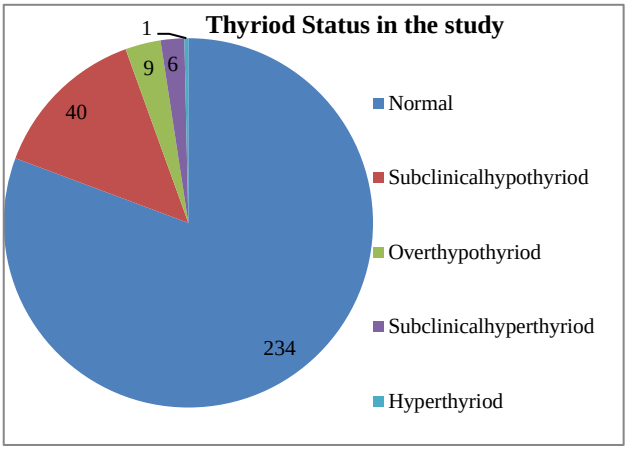

Figure 3: Study of thyroid status.

With regards to thyroid status of participants (figure 3) majority of them have normal thyroid status (80.6%), whereas the prevalence of sub-clinical hypothyroidism is 13.79% and overt hypothyroidism 3.1%. We have excluded 7 patients of Hyperthyroidism from the study to get meaningful statistics and P - value. Only 283 patients are included in the study with reproductive health problems.

It is observed that in study participants increased BMI is closely related to the increased occurrence of hypothyroidism (Figure 4). This difference was found to be statistically significant with Test Statistic and P- Value 13.80 and 0.01 respectively. (Fisher's Exact - Chi-square test used).

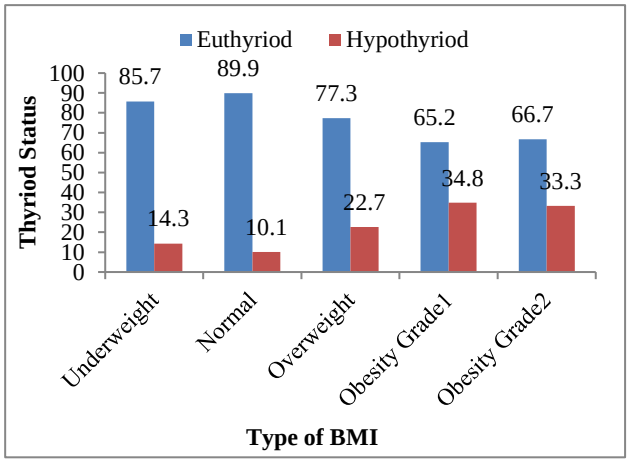

Figure 4: Thyroid status with BMI (%).

Thyroid status with duration of bleeding

Table 1: Cross-tabulation of status of thyroid vs. duration of bleeding.

Type of bleeding	Euthyroid	Hypothyroid	P - value
Normal	84.8% (169)	15.2% (30)	8.360 0.031 (Fisher Exact Chi-Square Test used)
Hypomenorrhea	95.2% (20)	4.8% (1)	
Menorrhagia	71.4% (45)	28.6% (18)	
Oligomenorrhea	79.2% (61)	20.8% (16)	

Table 1 shows that out of the 283 normal and hypothyroid patients, the duration of bleeding was significantly associated with thyroid status with Test Statistic and P- Value 8.36 and 0.031 respectively. (Chi-Square Test Used). Hypothyroidism with Menorrghia was associated in 28.6% and oligomenorrhea in 20.8% which was most common menstrual abnormality in this study.

Table 2: Cross-tabulation of status of thyroid vs. PCOS.

Thyroid status	PCOS absent	PCOS present	Test statistics and P - value
Euthyroid	85% (199)	15% (35)	6.80 0.33 (Chi-Square 2 Test Used)
Hypothyroid	71.14% (35)	28.6% (14)	

Table 2 shows that out of 49 participants having PCOS, in 14 (28.6%) women were diagnosed to have hypothyroidism and 35 (15%) had normal thyroid status. This difference was found to be statistically significant with Test Statistic and P- Value 6.80 and 0.33 respectively. (Chi-Square Test used).

Table 3: Cross-tabulation of status of thyroid vs. infertility.

Fertility status	Euthyroid	Hypothyroid	Test statistics and P - value
No infertility	83.1% (204)	16.9% (41)	1.315 0.711 (Fisher Exact Chi-Square Test Used)
Infertility	78.4% (30)	21.6% (8)	

Table 3 shows that Hypothyroidism with infertility was associated in 21.6% cases, but Test Statistic and P- Value which is found to be1.315 and 0.711 respectively, are not statistically significant. (Fisher Exact Chi-Square Test Used). However, there was an observed clinical difference with the increased presence of infertility among hypothyroid patients.

Table 4: Cross-tabulation of status of thyroid vs. history of pregnancy loss.

	Euthyroid	Hypothyroid	Test statistics and P - value
No pregnancy loss	83% (217)	17% (44)	0.866 0.626 (Fisher Exact Chi-Square Test Used)
Pregnancy loss	72% (16)	28% (6)	

Table 4 shows that out of the 283 normal and hypothyroid patients, the history of previous abortion was not significantly associated with thyroid status with Test Statistic P- Value 0.866 and 0.626 respectively. (Fisher Exact Chi-Square Test Used). However, there was an observed clinical difference with increased abortions among hypothyroid patients.

DISCUSSION

As stated earlier hypothyroidism is 10 times more common in females as compared to male. Hypothyroidism has adverse effect on the female reproductive system and cause various problems like menstrual irregularities, PCOS, infertility etc and may cause adverse pregnancy outcome. The present study was planned with the objective of determine the occurrence of hypothyroidism in women having these various health

problems and also to find out their association with hypothyroidism.

In the present study having 290 women participants attending gynaecology OPD, it was noticed that (80.6%) were euthyroid and 40 (13.79%) subjects were having sub-clinical hypothyroid whereas only 9 (3%) subjects were diagnosed to have overt hypothyroidism. Hyperthyroidism was noticed in only in 7 women. Six (2%) cases were diagnosed to have subclinical hyperthyroidism and 1(0.3%) woman having clinical hyperthyroidism. The overall occurrence of hypothyroidism accounts to 16.79%, in these rural women.

The occurrence of hypothyroidism noticed in present study is low as compared to various study conducted in other parts of India. In the study conducted at Nellore (2015) at tertiary care hospital the prevalence was 21.8%, a study conducted at sea food consuming area of Kerala (2015) it was 26.75%,study conducted in Navi Mumbai tertiary care hospital (2015) was 27%, prospective observational study at secundrabad (2016) was 19% and observational study conducted at Gujarat medical college (2017) was 29% As mentioned earlier this area is coastal, as it is a seafood consuming population the chance of iodine deficiency causing hypothyroid is not very common and so the prevalence of hypothyroidism in the present study must be less when compared to other studies. [8,13,15,16] It may be also due to intake of iodised salt for last more than 3 decades that had improved iodine status overall in general population.

Correlation of hypothyroidism with BMI

As the BMI increases, the prevalence of hypothyroid status also increases shown in Figure 4. As hypothyroidism is associated with insulin resistance, hyperglycaemia and hyperestrogenism as BMI increases hypothyroidism also increases.

Correlation of hypothyroidism with menstrual disorders

On comparing the present study with the studies conducted by various researchers one can safely state that amongst all menstrual problems menorrhagia can be ranked as the top most disorder for which women consult the Gynaecologists. A study conducted at Navi Mumbai medical college hospital shows association with menorrhagia was 27% and oligomenorrhea in 20.8%.[14] A prospective observational study (2016) conducted in OBG Department, in women between 15 and 45 years shows association of hypothyroidism with menorrhagia in 57.89% and oligomenorrhea in 5.26% patients.[15] Another study at Gujarat tertiary care hospital had association with hypothyroidism and menorrghia in32.5% and oligomenorrhea in15.3%.[16] Similar study was conducted in Pondicherry, Medical College Hospital, where the association of hypothyroidism with menstrual disorders was found to be as high as 72.5% with menorrhagia and also shown that 22.7% of cases had oligomenorrhea.[17]

In present study only 28.6% of total participants (who were having various reproductive health problems) were diagnosed to have hypothyroidism with menorrghia. As compared to other studies the present study reports less number of women with hypothyroidism and menorrhagia since in the present study the inclusion criteria were broader as compared to other studies. All cases attending the Gynaecology OPD were screened for thyroid function test unlike other studies (for example, only AUB cases or women in the age group was 15-45 years).

Correlation of hypothyroidism with polycystic ovarian syndrome

In the present study it was observed that 28.6% hypothyroid with PCOS. The incidence of PCOS ranges from 21.6%-32% in hypothyroid women. A case control study conducted at a tertiary care hospital in West Bengal, in which high association of goitre with PCOS was seen in 27.5% and 7.5% in controls.[18] In a study conducted in Pondicherry the association of hypothyroidism with PCOS was seen in 24.8% of cases.[19] In one of the other studies which was conducted at China shown to be association of hypothyroidism with PCOS with 32% and other studies shown association 24% to 21%.[20-22] The incidence reported in present study is comparable to all these studies. In the various studies conducted, has almost same incidence as that of present study since the age group of study are matching. All above mentioned three studies have similar results as that of present study since the participants age group were matching.

Correlation of hypothyroidism with infertility

The present study has comparable findings of hypothyroidism in infertility women. A study conducted in a tertiary care hospital showed correlation of hypothyroidism with infertility in 32.3% infertile women which is little high compared to other studies and this study was conducted in coastal area of Pondicherry where sea-food rich in iodine is consumed.[19] In another hospital based descriptive study conducted in Sholapur shows association of hypothyroidism with infertility in 23%.[11] Other similar study conducted for infertile women with hypothyroidism, where the response of treatment was followed up, which has shown the association of increased TSH more than 4.2 mU seen in 23.9% of cases. Out of which 76.6% conceived after treatment with thyroid hormones.[23] Other studies which were conducted at Bangladesh and Mumbai, on evaluating the thyroid status in infertile women which was shown to be associated with hypothyroidism in 22%.[20,21] Excessive iodine consumption stimulates autoimmune antibodies. In their study autoimmune antibodies are not estimated. Probably these women may have increased autoimmune antibodies.

Correlation of hypothyroidism with early/recurrent pregnancy loss

In the study, conducted in Osmania Hospital, Hyderabad for prevalence of hypothyroidism with miscarriages in first trimester the incidence was less compared to other studies as it is only 4.2%, as it was case -control study compared between cases and controls with or without recurrent pregnancy loss.[23] In the study conducted by in department of obstetrics and gynaecology in Nepal out of 103 patients 47 patients had high TSH and 17 of them conceived with treatment with thyroxine which shows strong association of hypothyroidism with recurrent miscarriages.[24] Another prospective observational study carried out in 100 pregnant women between 6 and 12 weeks of gestation in Rohtak found to have spontaneous abortion in 13% of cases.[25] But in the present study association of hypothyroidism with recurrent loss was 23.8% because both recurrent miscarriages and early single spontaneous abortion was included in the present study

Although all participants of the present study were treated for hypothyroidism with thyroxine, long term follow up of the patients is required to study the effect of the treatment of hypothyroidism. Tests to diagnose thyroid autoimmunity were could not be done which could have explained the association of this type of hypothyroidism with PCOS, infertility and recurrent pregnancy loss.

CONCLUSION

The present study shows occurrence of hypothyroidism in reproductive age group women having various problems related to reproductive health is high (16.89%). On Correlating hypothyroidism with reproductive health problems like menstrual abnormalities, association of hypothyroidism and menorrhagia is more common as compared to other menstrual irregularities. Association of hypothyroidism with PCOS, infertility is significantly high as compared to euthyroid women. Hypothyroidism is frequently found in women having problems like early pregnancy and recurrent pregnancy loss (23.8%). Taking into consideration the frequent association of hypothyroidism observed in the present study, thyroid function test should be considered during routine evaluation, especially in this reproductive age group of women between 15-45 yrs. It should be included in basic infertility workup.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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