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Prevalence of Subclinical & Overt Hypothyroidism in Infertile Women & Evaluation of Outcome Following Treatment of Hypothyroidism

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Abstract: ***Introduction: The thyroid gland plays a key role in the growth & development, also controls the rate of metabolic processes throughout the body. Thyroid dysfunction is an important contributing factor in female infertility, affecting 2-4% of the population in the reproductive age group. Hypothyroidism affects fertility as it causes hormonal imbalance, anovulation &luteal phase defect. Also, it is often associated with increased prolactin levels. Estimation of thyroid levels is simple & cost effective. It is recommended that estimation of thyroid hormones & serum prolactin levels should be a part of initial workup in an infertility case. Also, hypothyroidism should be managed initially before evaluating other causes of raised prolactin levels. Aim: 1. To estimate the prevalence of hypothyroidism in infertility. 2) To find a correlation between hypothyroidism & raised S. prolactin in infertility. 3) To assess the outcome of infertility after treatment of hypothyroidism. Methodology: A prospective study was conducted on 360 women in the age group of 18-45 years, with primary & secondary infertility, in the Department of Obstetrics & Gynaecology, MGM MCH, a tertiary care hospital. The cases were divided into two groups comprising of 180 subjects each on the basis of type of infertility. Group I consisted of cases of primary infertility, while group II consisted of cases of secondary infertility. Both the groups were further subdivided into three groups respectively. Subgroup A comprised of euthyroid cases, subgroup B comprised of cases of subclinical hypothyroidism, subgroup C comprised of cases of overt hypothyroidism. The study was carried out over a period of one year from May 2017. Cases with hypothyroidism & raised S. prolactin were treated with thyroxine (25-150ug/day) & the response to treatment as well as effect on infertility was evaluated. The results were statistically analysed. Results: The prevalence of hypothyroidism in infertile women is 15%. Prevalence of hyperprolactinemia in infertility is 22.7%, & associated with hypothyroidism is 89.1%. Menstrual dysfunction was seen in 85% of total cases. Altered lipid profile was observed in 25.5% of total cases. Out of 360 cases, 258 cases conceived (71.6%) in a period of one year. Conclusion: Thyroid hormones not only regulate metabolism but also influence the hypothalamo-pituitary-ovarian axis & is an important etiology of female factor infertility. It may remain asymptomatic in many cases & even euthyroid cases may screen positive for thyroid autoantibodies. Hence early screening improves the prospects of conception.***

Keywords: Hypothyroidism, Infertility, Anovulation, Luteal Phase Defect, Thyroxine

1. Introduction

Hypothyroidism is one of the significant treatable cause of female factor infertility. The prevalence of hypothyroidism is 2-4% in the reproductive age group, with overt hypothyroidism affecting 0.5% of women. Thyroid hormones affect estrogen metabolism & menstrual function.

Thyroid dysfunction cause infertility due to anovulatory cycles, as it affects the pulsatile release of gonadotrophin-releasing hormone (GnRH) which is required for cyclical release of follicle- stimulating hormone (FSH) & luteinising hormone (LH) , luteal phase defect, hormone imbalance &hyperprolactinemia. It is also a cause of habitual abortions. Thus normal functioning of thyroid gland is essential for conception & sustenance of a healthy pregnancy.

A slight rise in serum thyroid stimulating hormone (TSH) levels with normal triiodothyronine (T3) &thyroxine (T4) levels, indicate subclinical hypothyroidism (SCH), while high TSH levels & low T3 & T4 levels indicate overt hypothyroidism (OH).

Hyperthyroidism is also associated with increased S. prolactin levels. Prolactin is secreted by anterior pituitary & is regulated by prolactin inhibitory factor (PIF), which is secreted from hypothalamus. Other factors including vasoactive inhibitory peptide (VIP) & thyroid releasing hormone (TRH) increase prolactin secretion.

It is recommended that thyroid dysfunction should be corrected first even in the presence of raised serum prolactin, before evaluating other causes of hyperprolactinemia. S. TSH levels must be maintained below 2.5mU/l in subfertile cases according to American Thyroid Association guidelines for first trimester serum TSH.

2. Aims and Objectives

1) To estimate the prevalence of hypothyroidism in infertility.
2) To find a correlation between hypothyroidism & raised S. prolactin in infertility.
3) To assess the outcome of infertility after treatment of hypothyroidism.

3. Materials and Methods

A cohort of 360 women, with primary & secondary infertility, in the age group of 18- 45 years were evaluated & followed up in the Out Patient Department of Obstetrics & Gynaecology, MGM MCH, a tertiary care hospital in Jamshedpur, East Singhbhum, Jharkhand.

A prospective study was carried out over a period of one year from May 2017. The cases were divided into two groups comprising of 180 subjects each on the basis of type of infertility. Group I consisted of cases of primary infertility, while group II consisted of cases of secondary infertility.

Both the groups were further subdivided into three groups respectively. Subgroup A comprised of euthyroid cases, subgroup B comprised of cases of subclinical hypothyroidism, subgroup C comprised of cases of overt hypothyroidism. Cases with hypothyroidism & raised S. prolactin were treated with thyroxine (25-150ug/day) & the response to treatment as well as effect on infertility was evaluated. The groups & sub groups were comparable in demographic features.

Criteria of Diagnosis

1) **Euthyroidism**: Normal TSH level (0.39- 4.6 mIU/ml)
2) **Subclinical hypothyroidism (SCH):** TSH level ranging from 4.6- 20mIU/ml
3) **Overt hypothyroidism (OH):** TSH level >20 mIU/ml

In reference to S. prolactin-
Hyperprolactinemia: S. prolactin level >25ug/l

Criteria of inclusion: Women with primary & secondary infertility

Criteria of exclusion:

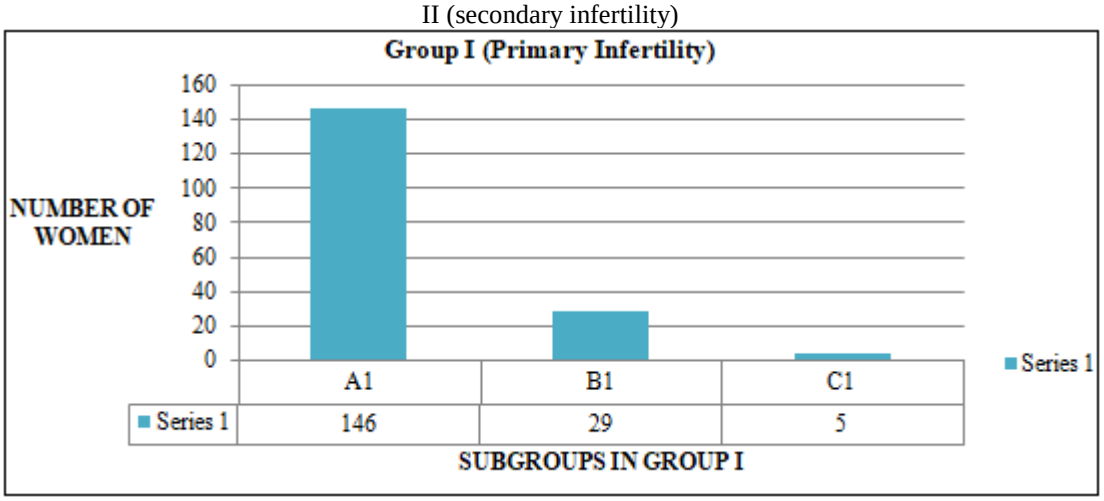
1) Women who were already taking L- thyroxine supplementation or treatment for hyperprolactinemia.
2) Women with an obvious cause of infertility such as tubal blockage, anatomical or cervical factor of infertility, pelvic inflammatory disease, endometriosis.
3) Male factor infertility
4) Women unwilling to participate

Study Design: Prospective study

Methodology: 360 cases, who fulfilled the inclusion criteria, after giving written informed consent, were selected for the study. Detailed history taking, complete general & pelvic examination was done. Investigations & imaging studies as routine infertility workup was done. Serum T3, T4, TSH & S. prolactin levels were measured by chemiluminesence method. All haematological tests including estimation of S.T3, T4, TSH& S. prolactin were carried out in the Department of Clinical Pathology, MGM MCH in collaboration with MEDALL Pathology Lab.

4. Results and Distribution

Table 1: Distribution of women into subgroups A1, B1, C1 in group I (primary infertility), & subgroups A2, B2, C2 in group II (secondary infertility)



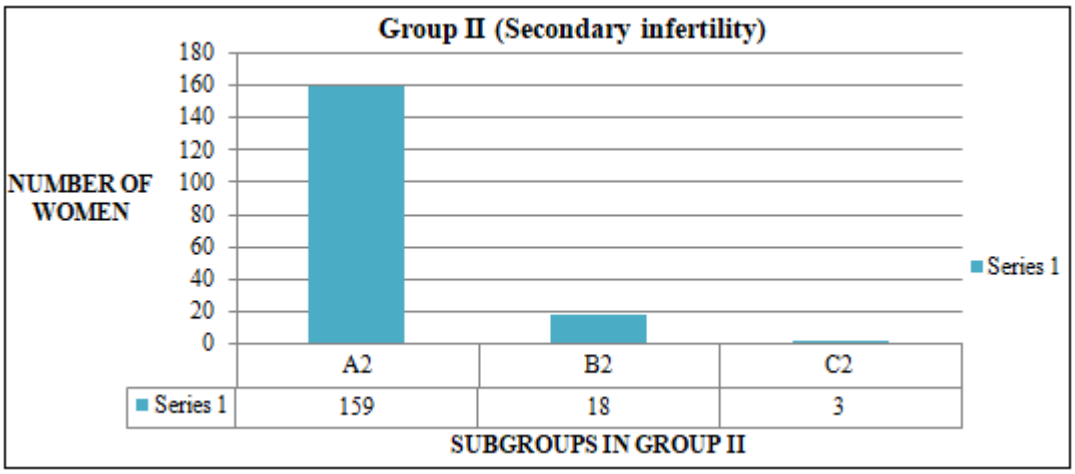
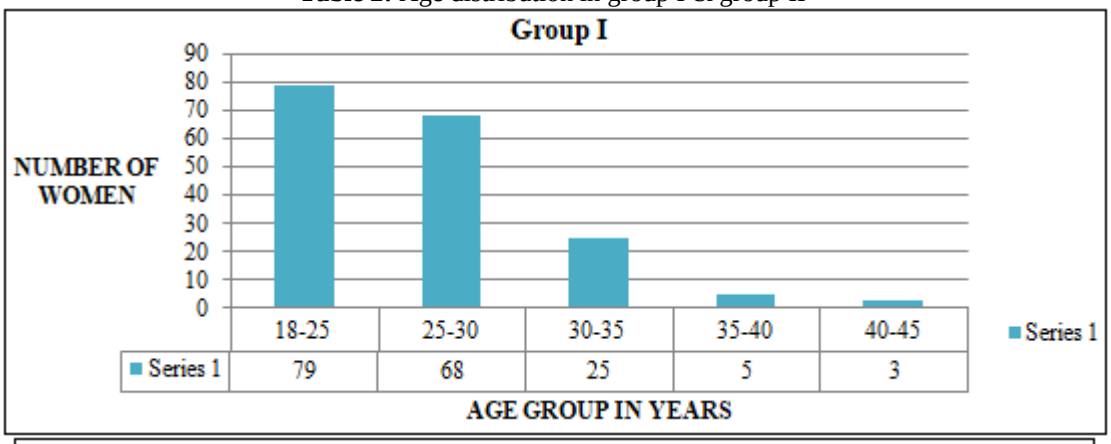


Table 2: Age distribution in group I & group II



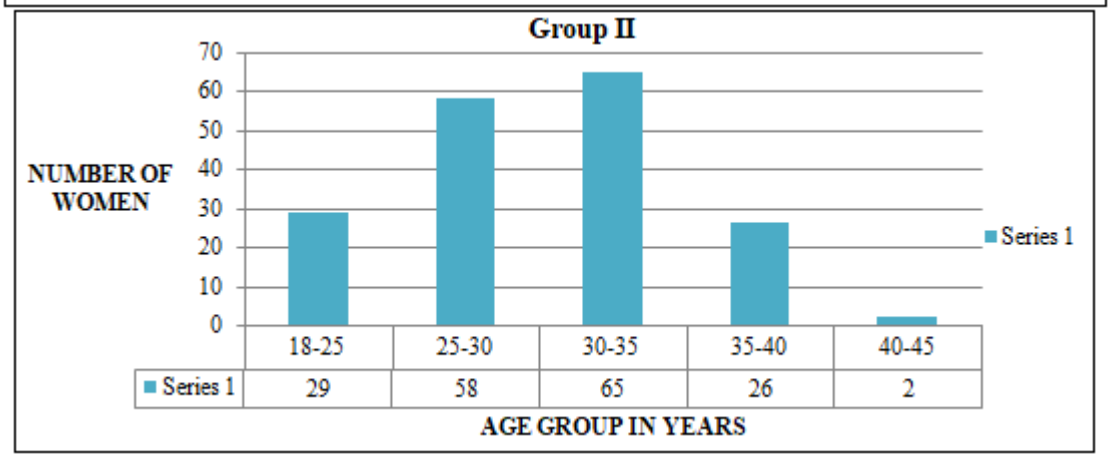
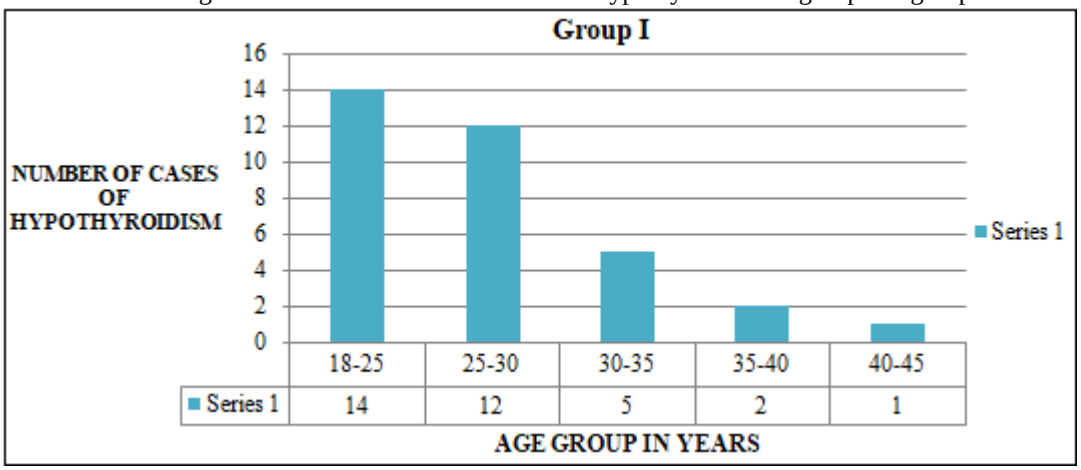


Table 3: Age distribution & number of cases of hypothyroidism in group I & group II



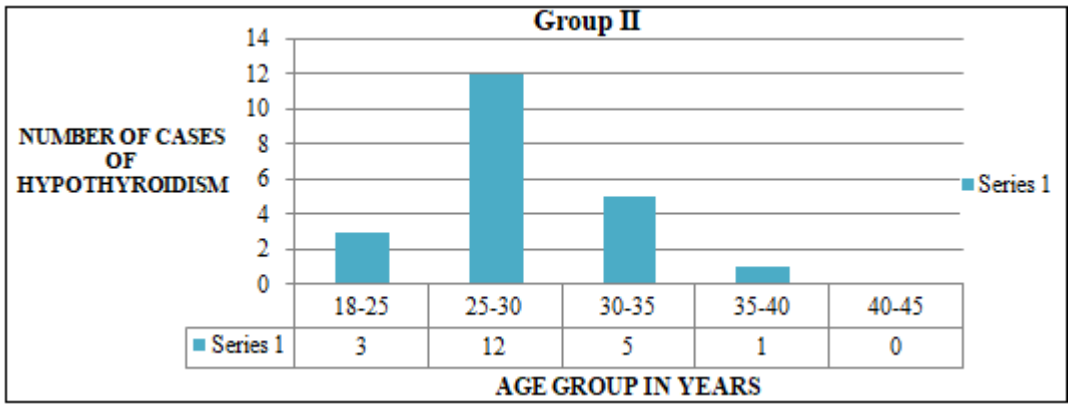
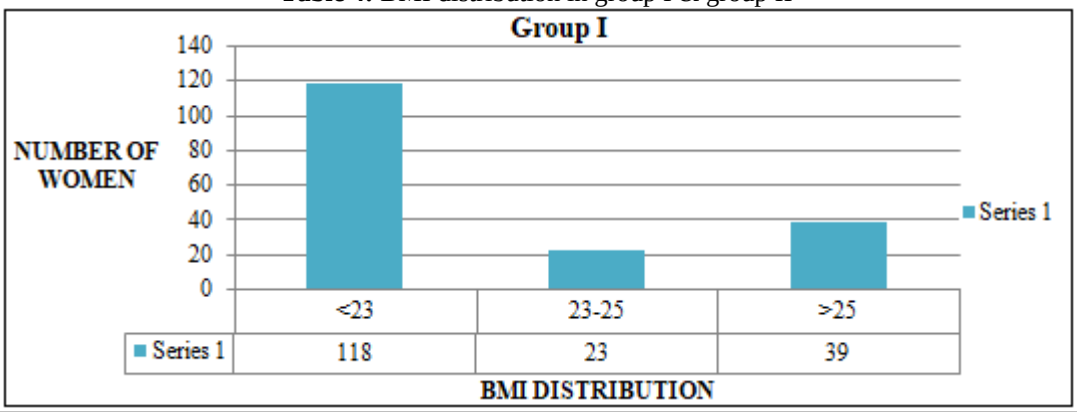


Table 4: BMI distribution in group I & group II



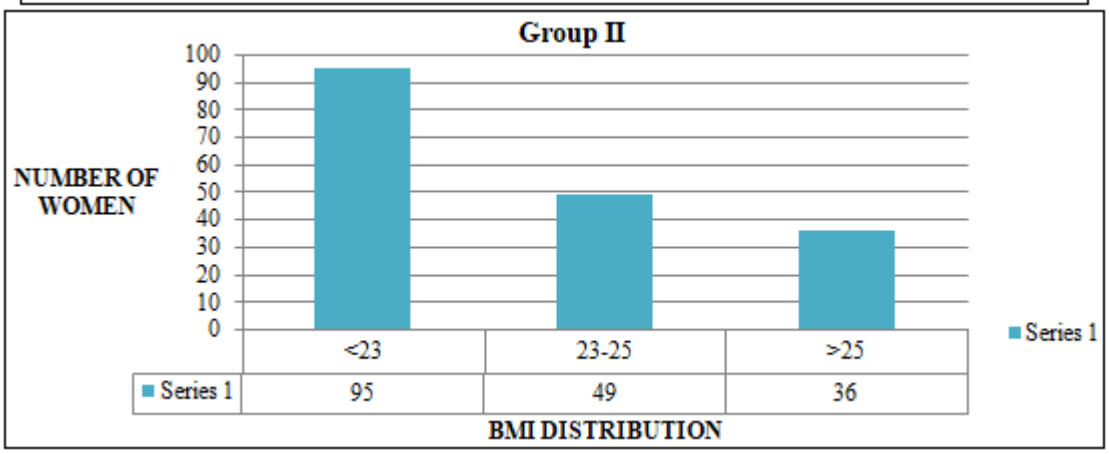
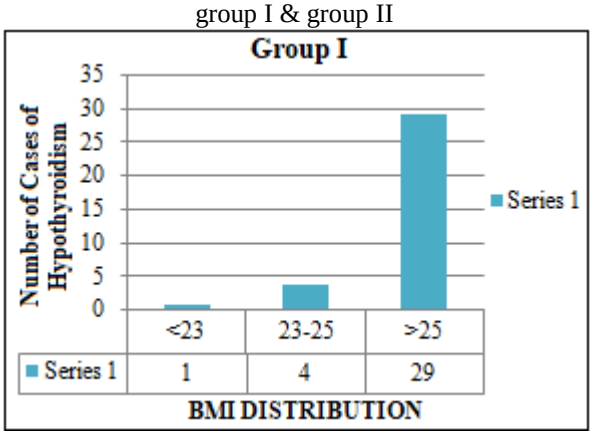


Table 5: Association between BMI & hypothyroidism in group I & group II



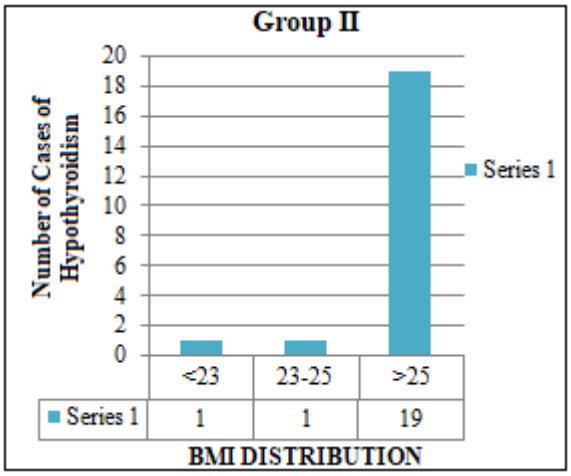


Table 6: Positive family history of hypothyroidism in group I & group II

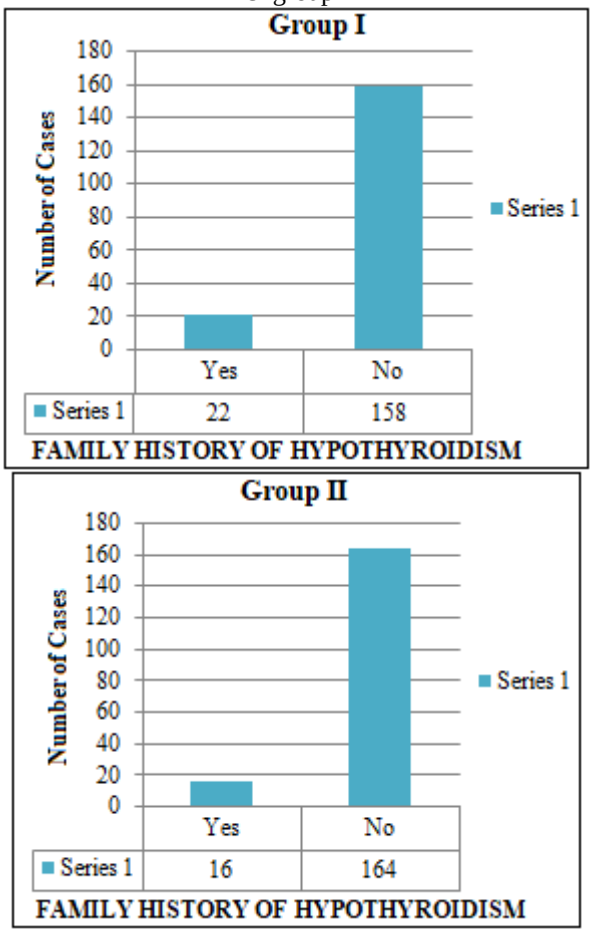


Table 7: Association between positive family history & hypothyroidism in group I & group II

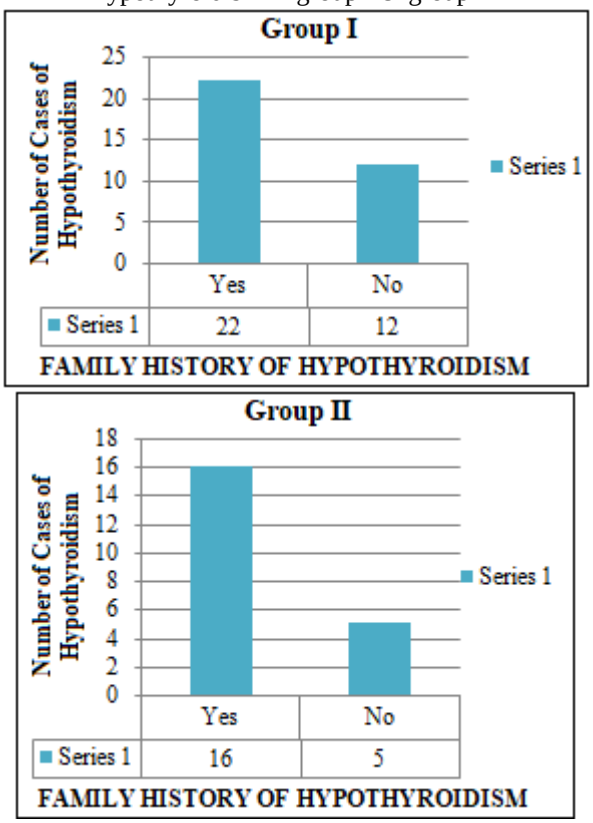


Table 8: Number of cases with menstrual dysfunction in group I & group II

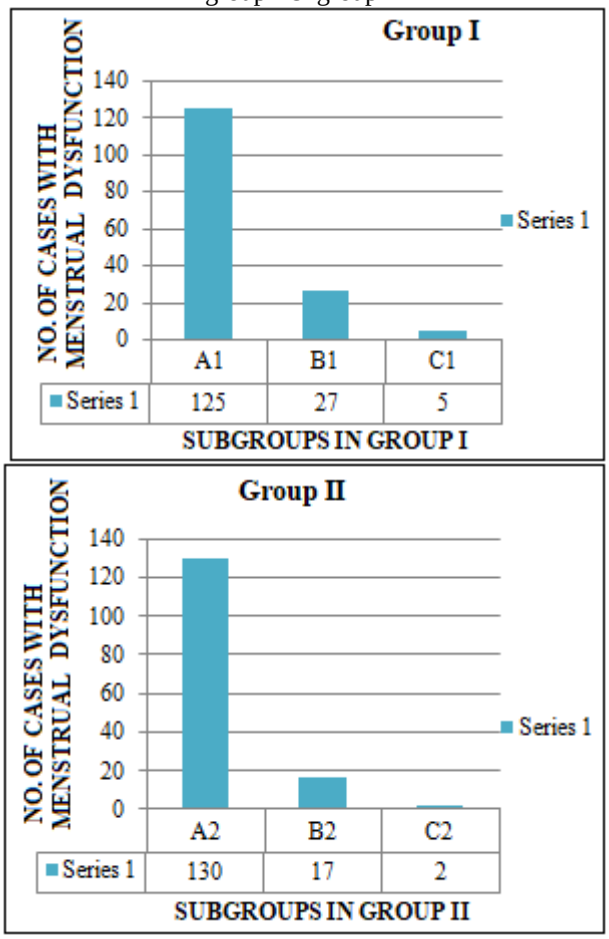


Table 9: Pattern of menstrual dysfunction in group I & group II

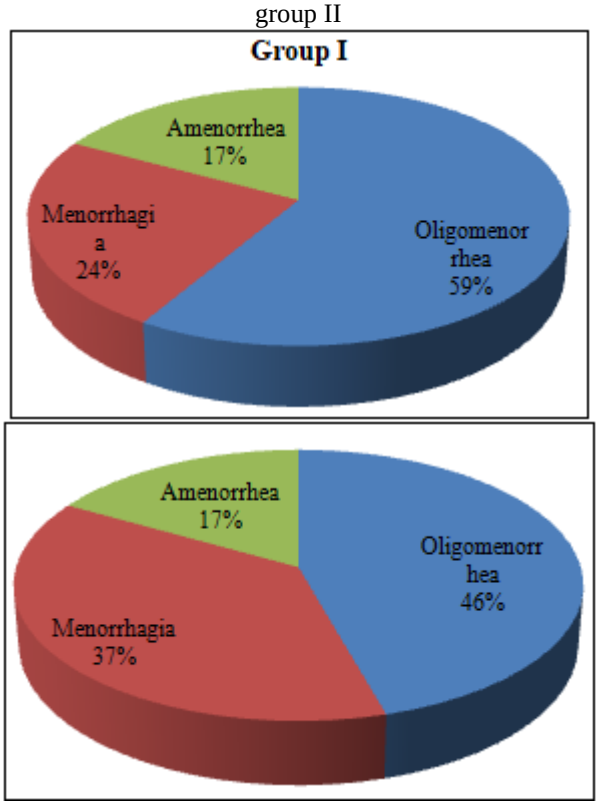


Table 10: Number of cases ofhyperprolactinemia in group I & group II

Total number of cases	Cases of hyperprolactinemia
Group I (180)	36 (20%)
Group II (180)	46 (25.5%)

Table 11: Association between hyperprolactinemia& hypothyroidism in group I & group II

No. of cases of hypothyroidism	No. of cases of hyperprolactinemia
Group I (34)	30 (88.2%)
Group II (21)	19 (90.4%)

Table 12: Number of cases of hyperlipidemia in group I & group II

Total no. of cases	Cases of hyperlipidemia
Group I (180)	42 (23.3%)
Group II (180)	50 (27.7%)

Table 13: Association between hyperlipidemia& hypothyroidism in group I & group II

No. of cases of hypothyroidism	No. of cases of hyperlipidemia
Group I (34)	29 (85.2%)
Group II (21)	17 (80.9%)

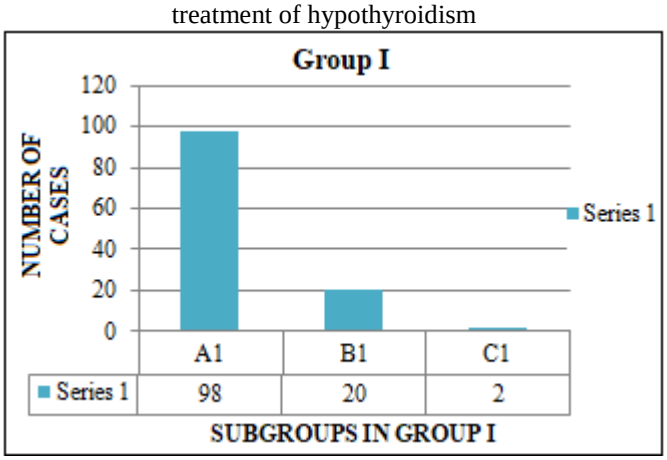
Table 14: Mean TSH levels in group I

Group I	Mean TSH level
A1	2.57 ± 1.24
B1	6.79 ± 2.03
C1	12.48 ± 1.16

Table 15: Mean TSH levels in group II

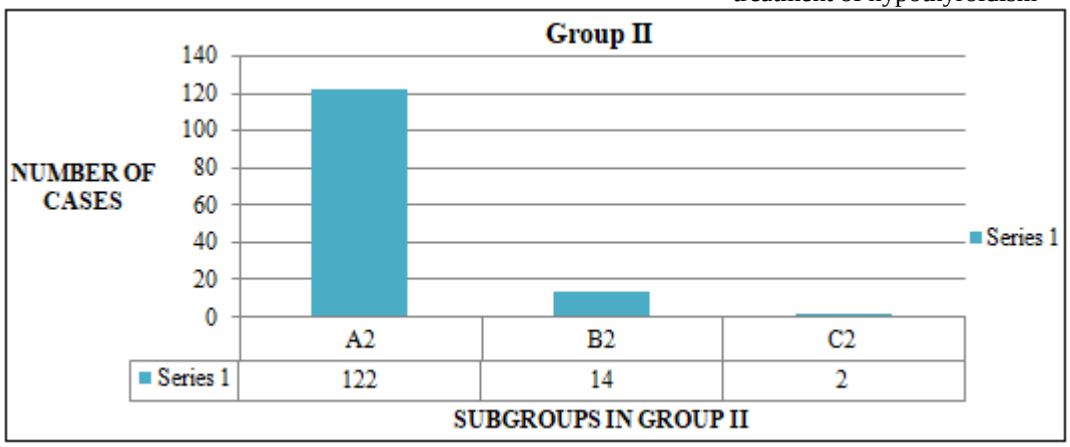
Group II	Mean TSH level
A2	3.05 ± 1.53
B2	5.82 ± 0.95
C2	15.32 ± 1.87

Table 16: Number of cases of conception in group I after treatment of hypothyroidism



Group I	No. of cases	No. of cases who conceived
A1	146	98 (67.1%)
B1	29	20 (68.9%)
C1	5	2 (40%)
Total	180	120 (66.6%)

Table 17: Number of cases of conception in group II after treatment of hypothyroidism



Group II	No. of cases	No. of cases who conceived
A2	159	122 (76.7%)
B2	18	14 (77.7%)
C2	3	2 (66.6%)
Total	180	138 (76.6%)

5. Discussion and Observation

Distribution of cases in group I (A1- 81.1%, B1- 16.1%, C1- 2.8%) & group II (A2- 88.3%, B2- 10%, C2- 1.6%) . 55 out of 360 cases were hypothyroid, hence prevalence of hypothyroidism is 15%. (Table1)

Age: Most of the subjects in group I belonged to the age group of 18-25 years (43.8%), while in 25- 30 years (37.7%), 30-35 years (13.8%), 35-40 years (2.7%), 40-45 years (1.6%).

In group II, 36.1% subjects belonged to the age group of 30-35 years, while in 18-25 years 16.1%, 25-30 years (32.2%), 35-40 years (14.4%), 40-45 years (1.1%).(Table 2)

In group I, 41.1% of cases of hypothyroidism were found in the age group of 18-25 years, 35.2% in 25-30 years, 14.7% in 30-35 years, 5.8% in 35-40 years, 2.9% in 40-45 years. Thus women <25 years of age appear to be at an increased risk of hypothyroidism.

In group II, 57.1% cases were found in the age group of 25-30 years,14.2% in 18-25 years, 23.8% in 30-35 years, 4.7% in 35-40 years & no case in 40-45 years.(Table 3)

However, age is not a statistically significant demographic variable associated with hypothyroidism.

BMI: In group I, 65.5% cases had BMI<23, 12.7% with 23-25, 21.6% with >25. In group II, 52.7% cases had BMI <23, 27.2% with 23-25, 20% cases with >25. (Table 4).

In group I, 0.84% cases with BMI< 23 had hypothyroidism, 17.3% cases with BMI 23-25, & 74.3% cases with BMI> 25 had hypothyroidism. In group II, 1.05% cases with BMI< 23, 2.04% cases with BMI 23-25, 52.7% cases with BMI >25 had hypothyroidism. Hence high BMI & obesity is a significant risk factor associated with hypothyroidism. (Table 5).

Family history: In group I, 12.2% of total cases had a positive family history, while it was negative in 87.7% cases. In group II, 8.8% of total cases had positive family history & 91.1% cases had negative family history. (Table 6)

In group I, 64.7% cases of hypothyroidism had positive family history & 35.2% cases negative. In group II, 76.1% cases of hypothyroidism had positive family history while 23.8% negative. Hence a positive family history is positively associated with hypothyroidism. (Table 7)

Menstrual dysfunction: In group I, 85.6% cases in A1, 93.1% in B1, 100% cases in C1 had menstrual dysfunction. In group II, 81.7% cases in A2, 94.4% in B2, 66.6% in C2 had menstrual dysfunction. (Table 8)

Oligomenorrhea was most common menstrual irregularity observed in 58.5% cases in group I & 45.6% in group II, followed by menorrhagia 24.2% in group I, 37.5% in group II, & amenorrhea 17.1% in group I, 16.7% in group II. (Table 9)

Hyperprolactinemia: In group I, 20% of total cases, while 25.5% of total cases in group II.(Table 10)

Among cases of hypothyroidism, 88.2% in group I, 90.4% in group II had raised S.prolactin. Hence there is a correlation between hypothyroidism &hyperprolactinemia.(Table 11)

Hyperlipidemia: In group I, 23.3% of total cases, while 27.7% of total cases in group II had altered lipid profile. (Table 12)
In cases of hypothyroidism, 85.2% cases in group I & 80.9% cases in group II had hyperlipidemia, thus establishing a positive correlation (Table 13)

Mean TSH levels in group I (Table 14) & group II (Table 15) are estimated.

Conception after treatment of hypothyroidism: In group I, 67.1% cases in A1, 68.9% in B1, 40% in C1 successfully conceived. In group II, 76.7% in A2, 77.7% in B2, 66.6% in C2 conceived. Out of 360 cases, 258 cases conceived (71.6%) in a period of one year.

6. Conclusion

Hypothyroidism is a significant cause of infertility in women in the reproductive age group. Subclinical hypothyroidism is more common than overt hypothyroidism. Also, it is co associated with hyperprolactinemia& results in various menstrual irregularities &dyslipidemia in a significant percentage of cases. Screening for hypothyroidism should be done so that treatment could be started at the earliest to maintain TSH in the lower limit in cases of subfertility & recurrent abortions. Infertility workup should also include prolactin estimation & correction of thyroid abnormality should be done first. Restoration of euthyroid status also effectively improves lipid levels.

7. Conflict of interests

None declared

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