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Evaluation of Thyroid Function Test in Infertile Women

Anuja Joshi, Sumitra Thapa, Samriddhi Basnet, Kapil Dev Joshi

Department of Obstetrics and Gynaecology, Nepal APF Hospital, Balambu, Kathmandu, Nepal.

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CORRESPONDENCE
Anuja Joshi
Department of Obstetrics and Gynaecology
Nepal APF Hospital, Balambu, Kathmandu, Nepal
Email: anuja179@hotmail.com

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ABSTRACT

Introduction: In women of reproductive age group thyroid dysfunction can lead to a variety of gynecological disorders ranging from menstrual irregularities to subfertility. There is a known association of hyperthyroidism and hypothyroidism with menstrual disturbances and decreased fecundity. The aim of this study is to determine the thyroid function status of infertile women presenting to subfertility clinic of Paropakar Maternity and Women's Hospital (PMWH)

Methods: This was a descriptive cross-sectional quantitative study conducted at Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu from 1st August to 1st November 2018. Women that were diagnosed with primary and secondary subfertility in OPD were sequentially enrolled after obtaining informed written consent. Infertile women (n=70) attending subfertility clinic were investigated for hypothyroidism, hyperthyroidism and other causes of subfertility and enrolled for study. Women with known thyroid disorders, congenital anomaly of genital tract and other obvious organic anomaly were excluded from the study.

Results: 66% of study population had primary subfertility. Most of the infertile women (70%) were euthyroid. Subclinical Hypothyroidism was most common (20 %) type of thyroid disorder. 66% cases had regular menstrual cycle. Oligomenorrhoea was most common type of irregular menstrual cycle. 73% of infertile women had normal BMI.

Conclusions: After ruling out the male factor of subfertility and structural abnormalities of the infertile women, performing TFT can be recommended in all cases of subfertility.

INTRODUCTION

Subfertility is a complex disorder with significant medical, psychosocial and economic aspects recognized as a public health issue by the World Health Organization (WHO). Subfertility is the inability of a couple to conceive after one year of regular unprotected intercourse[1,4,9]. About 18- 20% of couples in the reproductive age are infertile[37,38]

It can be divided into two broad categories - primary and secondary subfertility[9,41,42]. Primary subfertility refers to when a couple has never conceived despite cohabitation and adequately timed intercourse. Secondary subfertility refers to those cases where people had achieved pregnancy previously but regular unprotected sexual intercourse has not resulted in a second pregnancy.

In women of reproductive age group thyroid dysfunction can lead to a variety of gynecological disorders ranging from menstrual irregularities to subfertility[2,3,12,17]. There is a known association of hyperthyroidism and hypothyroidism with menstrual disturbances and decreased fecundity[5,7,11]. The menstrual pattern is influenced by thyroid hormones directly through

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impact on the ovaries and indirectly through impact on Sex Hormone Binding Globulin (SHBG), Prolactin, Gonadotrophin Releasing Hormone (GnRH) secretion and coagulation factors[10,13,18]. Treating thyroid dysfunction can reverse menstrual abnormalities and thus improve fertility[19].

Abnormalities of thyroid function, hypothyroidism as well as hyperthyroidism are associated with variety of changes in reproductive system including delayed onset of puberty, menstrual irregularities and recurrent fetal wastages[6,15,20]. Anovulation is more commonly noted in association with hyperthyroidism[21,32]. Significant interrelations have been found between thyroid disorders and gonadal functions by various laboratory & clinical studies.

Subfertility can be due to female causes as well as male causes[11]. Female causes are more common than male causes which accounts for 40% and 35% respectively followed by combination of both male and female cause in 10-20% and idiopathic in 10-20%[11]. Infertilities, either primary or secondary will occur for almost 15% of all women worldwide[4,37]. Female subfertility occurs in about 37% of all infertile couples[4]. Its rate has been reported to range from 0.6% to 3.4% for primary subfertility and 8.7% to 32.6% for secondary subfertility.[4]

METHODS

Ethics: Procedure followed were in accordance with ethical standard of institutional review board of National Academy of Medical Sciences (NAMS), who gave approval for this study. Written consent was taken each participant.

Study site and design: This was a cross-sectional quantitative study conducted at Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu from 1st August to 1st November 2018. Cases were enrolled six days in a week and except Saturdays and public holidays. Women that were diagnosed with primary and secondary subfertility in OPD were sequentially enrolled after obtaining informed written consent.

Sample size was determined based on an average prevalence rate of subfertility among Nepali women of 25% and was estimated at 70[12]. After obtaining informed written consent from each participant, an interview administered questionnaire was used to collect data which included personnel biodata, medical history, surgical history, family history, drug history, features suggestive of thyroid disorders like fatigue, heat and cold intolerance, muscle cramps, palpitation, hoarseness of voice, diarrhea and constipation, gain or loss of weight, dryness of skin, coarse hair, hair loss and exophthalmos were taken. Anthropometric measurements including height, weight, body mass index (BMI), as well as detail clinical examination including per abdominal, per speculum and per vaginal examination were done in all cases. Women with known thyroid disorders, congenital anomaly of genital tract and other obvious organic anomaly were excluded from the study.

Sample Collection and laboratory analysis: Under all aseptic condition approximately 5 ml of venous blood was collected from cubital fossa. The test of TFT was done via automated quantitative "Enzyme Linked Fluorescent Assay" technique using VIDAS machine, then the participants was told to follow at subfertility Centre with TFT reports. The report value was compared with the standard reference lab value of PMWH. FSH, LH, prolactin, progesterone and estrogen were also analyzed using ELISA technique. Ultrasonography (USG) of abdomen and pelvis, Hysterosalpingography was done in every patient., Semen analysis of male partner was also carried out. Endometrial biopsy was done in selected cases as required according to hospital protocol.

The assay-specific reference ranges were 0.25–4.0 mIU/L for TSH, 0.8–1.7 ng/dL for FT4, 2.2–4.2 pg/mL for FT3. Subclinical hypothyroidism (SCH) was defined as TSH >4 mIU/ml with a normal FT3 and/or FT4 concentration. Clinical Hypothyroidism was defined as TSH level greater than 4 mIU/ml with a FT4 and/or FT3 concentration below the reference range. Clinical hyperthyroidism was defined as TSH level less than 0.25 mIU/L with a FT4 and/or FT3 concentration above the reference range and subclinical hyperthyroidism was defined as TSH

<0.25 mIU/L with a normal FT4 and/or FT3 concentration. No extra burden was imposed to the patient as this research was conducted on the basis of regularly performed tests in cases of subfertility for the diagnosis of specific cause and making a specific management plan.

Statistical Analysis: Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 25.0. Frequencies and percentages were obtained for categorical variables. P-values ≤ 0.05were considered significant in all analysis.

RESULTS

Seventy infertile patients were studied in the subfertility OPD of PMWH. Fifty-eight cases (82.8%) were from age group of 26-30 years with mean age of 27.77 years. Age distribution according to types of subfertility is shown in fig(1).

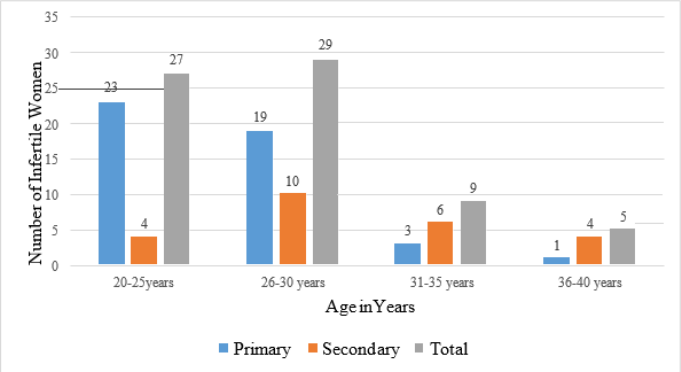

Figure 1: Age distribution according to types of subfertility

Fifty one infertile women(73%) had normal BMI. Two patient were underweight and twelve patients(17%) were overweight. Fourty two patients (60%) visiting subfertility clinic were from outside Kathmandu valley. Subfertility was found common among literate women(86%). Primary subfertility was present among fourty six (66%) cases and secondary subfertility was present among twenty four (34%) cases. Fifty five cases (78.57%) had duration of subfertility of less than five years; twelve cases (17.14%) of infertile women had duration of subfertility of 5-10 years and three cases (4.2%) of infertile women had duration of subfertility of more than 10 years. Minimum duration of subfertility was two years and maximum duration was nineteen years. Regular menstrual cycle was present among forty six (66%) cases and twenty four (34%) infertile women had irregular menstrual cycle. Types of irregular menstrual pattern of infertile women is shown in fig (2).

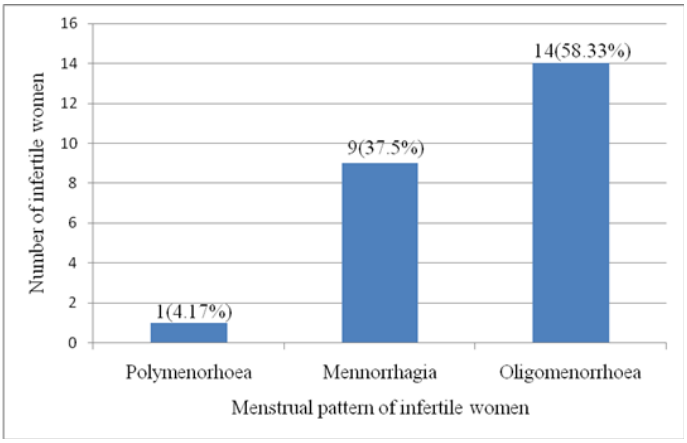

Figure 2: Types of irregular menstrual pattern in infertile women

Thyroid disorder was seen only among twenty-one (30%) infertile women. Forty-nine (70%) cases of subfertility were euthyroid. Subclinical hypothyroidism was most common (20%) thyroid disorder found among them. Clinical hyperthyroidism was found in five cases (7.1%) and clinical hypothyroidism was found in two cases (2.9%) of infertile women. Distribution of thyroid disorder in primary and secondary subfertility is shown in fig (3).

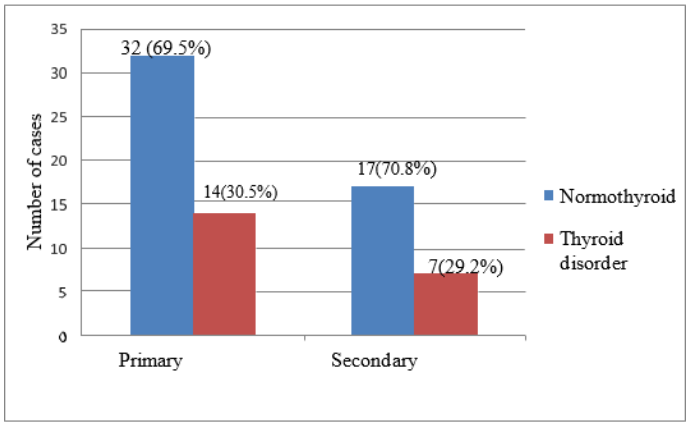

Figure 3: Thyroid disorder in primary and secondary subfertility.

DISCUSSION

41.42% of infertile women in this study was in the age group of 26- 30 years, The finding was similar to study done by Akhter et al.[38] where 78% of infertile women were from age group 21-30 years. Also, in a different study by Biradar et al[44] and shanthakumari et al.[42] subfertility was found most common among early age group.

In our study, mean age of infertile women was 27.7(+4.81) years. This result was similar to study conducted by Rijal et al.[12] in Nepal who reported the mean age of infertile women as 26.3 years. In a Study conducted by Allow et al.[40] in Yemen, the mean age of infertile women was 27.41±4.93 years. However, in a study conducted by Arjoki et al.[23] in Finland and Abalovich et al.[14] in Argentina, the mean age was 30 years. Similarly in a study conducted by Raber et al.[45] showed the mean age of infertile women was 32 years. The cause of less mean age of infertile women in our study might be due to early marriage in our society.

High prevalence of subfertility among literate women can be due to increase in national literacy rate. In our study, 72.85% had normal BMI, 17.15% were overweight, followed by 7.15% of obese and the least 2.85% underweight. This is similar to the study by shantakumari et al.[42] where 55% of infertile women had normal BMI, 26.7% of women had overweight, 10% were underweight and 8.3% were obese. In contrast to it, in a cross-sectional study conducted by Dhandapani et al.[43] subfertility was common among overweight women (42.65%), followed by women with normal BMI (41.67%), 8.33% cases were underweighted and 7.35% cases were obese. Similarly in another cross-sectional study conducted by Sudha et al.[39] in India among 635 infertile women, most of the infertile women were obese-54.25%, 27.8% were overweight, 6.2% were underweight and only 11.8% had normal BMI. Aliyu et al.[30] also found that out of 205

patients 33.2 % (68) of infertile patients were obese. Both overweight and underweight is a preventable risk factor for subfertility and precautionary measures to manage them may be an effective way of reducing the risk of subfertility.

In my study, 78.57% of infertile women had duration of subfertility of less than 5 years, 17.14% had duration of 5-10 years and 4.2% had duration of >10 years. Similar result was found in a cross- sectional study done by Sudha et al.39 in India, who reported that 80% of infertile women had duration of subfertility of less than 5 years. Mean duration of subfertility in present study was 3.7 years. In a study by Allow et al.[40] the mean duration of subfertility was 2.38±1.93 years. Raber et al.[45] conducted a similar study where the mean duration of subfertility was 2.5 years. However, in a study done by Farhi et al.[41] in Israel the mean duration of subfertility was 1.7+-1.8 years only. The minimum duration of subfertility was 2 years and maximum were 19 years. Social factors in a conservative society like ours might hinder the infertile women to seek early treatment for subfertility. Majority of infertile women (66%) were of primary subfertility and 34% were of secondary subfertility. This was similar to study conducted by Farhi et al.[41] who reported 65% of infertile women to have primary subfertility and 35% to have secondary subfertility. Prevalence of primary subfertility was higher than secondary subfertility in the study done by Bharti et al.[31] and Raber et al.[45] where 67.62% and 72% of infertile women had primary subfertility respectively. Women suffering from primary subfertility might be more conscious of not having a child than women of secondary subfertility, thus seeking treatment. This might be the reason of higher prevalence of primary subfertility than secondary.

Irregular menstrual cycle, common manifestation of anovulation is usually resent in infertile women. But 66% of infertile women had regular menstrual cycle and only 34% were found to have irregular menstrual cycle. This is similar to study conducted by Arjoki et al.[23] who reported 34% of infertile women to have irregular menstrual cycle. Irregular menstrual pattern was reported in 23.4%, 53.3% and 70% in a study conducted by Krassas et al.[17], Rahaman et al.[37] Akhter et al.[38] respectively. The most common menstrual pattern was oligomenorrhoea (58.33%) similar to study conducted by Akhter et al.[38] who reported 59%.

This study showed that 30% of infertile women, had thyroid disorder. Prevalence of thyroid disorder of 25.6% was noted in the study conducted by Rijal et al.[12] in Nepal and in a study conducted by Verma et al.[13] prevalence of thyroid disorder in infertile women was 23.8%. Likewise, Rahaman et al.[37] reported a prevalence of 33.3%. However, in a study conducted by Arojoki et al.[23] in Finland comprising 299 infertile women, the prevalence of thyroid disorder was found to be 4%, which was very less than this study. This difference in prevalence of thyroid disorder could be because of difference in iodine status in different countries.

In my study, 22.8% of infertile women had hypothyroidism, compared to hyperthyroidism which was present in 7.1% of cases. Bhrarti et al.[31] reported 24% hypothyroidism in 454 infertile women. Study conducted by Rijal et al.[12] reported that 20.1% of thyroid dysfunction was hypothyroidism and only 5.5 % was hyperthyroidism. Subclinical hypothyroidism was the most common subtype of thyroid disorder. In my study, 20% of infertile women had subclinical hypothyroidism. Subclinical hypothyroidism was found to be 12% by Biradar et al.[44] and 62.7% by Verma et al.[13]

CONCLUSIONS

More than three-fourth of cases had history of subfertility for less than five years and 80% of cases were in between 20-30 years of age. After excluding male factor and structural factor amongst infertile women, 70% were euthyroid and 23 % were hypothyroid. Thus, after ruling out the male factor of subfertility and structural abnormalities of the infertile women, performing TFT can be recommended in all cases of subfertility.

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