Hypothyroidism and early pregnancy loss: an overview
Puja Verma*, Dipti Roy

INTRODUCTION
Thyroid disorders are associated with adverse pregnancy outcomes. They can lead to spontaneous miscarriages. Miscarriage or spontaneous abortion is defined as expulsion or extraction of the embryo or foetus weighing <500 g, or before 20–22 weeks of gestation. It is the most common complication of early pregnancy.1 The various causes of early pregnancy loss are genetic, anatomic factors, autoimmune disorders, endocrine dysfunction, thrombophilia, life style factors, maternal infections and may be idiopathic.

Thyroid disorders constitute one of the most common endocrine disorders in pregnancy.2 Pregnancy is associated with profound modifications in the regulation of thyroid function. These changes are the result of various factors like an increase of thyroxine-binding globulin (TBG) due to elevated estrogen and human chorionic gonadotropin (hCG), increased renal losses of iodine due to increased glomerular filtration rate, modifications in the peripheral metabolism of maternal thyroid hormones, and modification in iodine transfer to the placenta.3

Women with thyroid dysfunction both overt and subclinical are at increased risk of pregnancy-related complications such as threatened abortion, preeclampsia, preterm labour, placental abruption, and postpartum haemorrhage. Foetal complications include first-trimester spontaneous abortions, low-birth-weight babies, preterm delivery, intrauterine growth retardation, high rates of still birth and neonatal deaths, neonatal hyperbilirubinemia, higher incidence of neonatal hypothyroidism, and increased perinatal mortality.4

Thyroid disorders can be either hypothyroidism or hyperthyroidism. Euthyroid women are defined as those having normal TSH (0.1–2.5 μIU/l) in first trimester. Subclinical hypothyroidism is defined as high TSH (>3.0 μIU/l) in the presence of normal levels of Free T4 (0.8–2.0...
ng/dl). Overt hypothyroidism is defined as high TSH (>3.0 μIU/l) with low Free T4 (<0.8 ng/dl). Subclinical hyperthyroidism is defined as low serum TSH (<0.2 μIU/l) concentration with normal Free T4 (0.8–2.0 ng/dl) and overt hyperthyroidism is defined as with high Free T4 (>2.0 ng/dl) with decreased TSH (<0.2 μIU/l).

The aim of this study was to determine the prevalence of hypothyroidism in women with early pregnancy loss.

METHODS

The study was a cross sectional study conducted in the department of obstetrics and gynaecology, Nalanda medical college and hospital from December 2017 to June 2018. One hundred and four pregnant women with early pregnancy loss (missed abortion, incomplete and complete abortion) were included in this study.

After proper written consent, 104 women were enrolled. All recruited subjects underwent a detailed history and examination as per standard pre-structured protocol. Detailed history was taken and patient’s age and last menstrual period was noted. The period of gestation was calculated by last menstrual period. The demographic and clinical details were noted. Patient’s menstrual history, obstetric history, past medical and surgical history and family history of thyroid disoders were also elicited in detail. A general physical examination was done. BMI was calculated based on the pre-pregnancy weight and height.

Patients with multifetal gestation, known thyroid and metabolic disorders like diabetes, hypertension, and a history of pregnancy loss were excluded from the study.

Blood samples were taken for estimation of TSH (thyroid stimulating hormone) and free T4 levels. Thyroid status of women was established on the basis of standard cut-off levels. Prevalence of hypothyroidism (both overt and subclinical) was calculated. Euthyroid women are defined as those having normal TSH (0.1–2.5 μIU/l) in first trimester. Subclinical hypothyroidism is defined as high TSH (>3.0 μIU/l) in the presence of normal levels of Free T4 (0.8–2.0 ng/dl). Overt hypothyroidism is defined as high TSH (>3.0 μIU/l) with low Free T4 (<0.8 ng/dl). Subclinical hyperthyroidism is defined as low serum TSH (<0.2 μIU/l) concentration with normal Free T4 (0.8–2.0 ng/dl) and overt hyperthyroidism is defined as with high Free T4 (>2.0 ng/dl) with decreased TSH (<0.2 μIU/l).

RESULTS

A total of 104 patients admitted in emergency department of obstetrics and gynaecology with early pregnancy loss were recruited in this study. Fifty nine women were primigravida accounting to 56.73%. Forty five women were multigravida (47.26%). The mean age of women was 22±3.4 years (n=104). The mean age of women in hypothyroid group was 24±2.3. The mean BMI in euthyroid women was 22.1±2.0 and in hypothyroid women was 22.8±3.2

**Table 1: Comparison of age and BMI**

| Comparison            | Mean age (years) | Mean BMI (kg/m²) |
|-----------------------|------------------|------------------|
| Normal women          | 22±3.4           | 22.1±2.0         |
| Hypothyroid women     | 24±2.3           | 22.8±3.2         |

The mean TSH level was 2.3±1.3 μIU/l. Twenty two women had increased TSH level (>2.5 μIU/l) accounting to 21.15% of total women and rest 78.84% women were euthyroid.

![Figure 1: Distribution of women according to TSH levels.](image)

According to Figure 1, 15.38% of women presenting with early pregnancy loss were overt hypothyroid and 5.76% of women had subclinical hypothyroidism. The mean TSH level in hypothyroid group was 4.9±2.1. None of the women was hyperthyroid.

DISCUSSION

This study done on 104 women presenting to the emergency department in a tertiary care centre with early pregnancy loss shows that hypothyroidism is a significant cause of abortion. Twenty-two women had hypothyroidism. Abalovich et al showed that untreated hypothyroidism, subclinical or overt at the time of conception is associated with higher miscarriage rate as compared to euthyroid subjects. Ashoor et al demonstrated a significant association between low maternal free thyroxine (FT4) during the first trimester and fetal loss, in pregnancies complicated by subclinical hypothyroidism.

In a retrospective cohort study done on patients with recurrent pregnancy loss the 72.7% were euthyroid (721/992), 19.4% (192/992) were borderline-subclinical hypothyroid, and 5.4% (54/992) were sub-clinically hypothyroid (SCH). They concluded that treatment of hypothyroidism in pregnancy should be initiated based on a TSH >4 mIU/l. Treatment initiation based on thyroid
autoimmunity or a TSH>2.5 mIU/l may result in overtreatment.7

In a study done to determine the frequency of hypothyroidism in women with recurrent pregnancy loss in first trimester in the Indian population hypothyroidism was found in 4.12% women with RPL. The differences in the levels of serum T3, T4 and TSH between euthyroid and hypothyroid women were found significant in women with RPL in first trimester.8

Salek et al found that the prevalence of hypothyroidism for twin pregnancies was no higher than that for singleton pregnancies; 6.42% (7/109) vs. 5.32% (264/4965), respectively. They concluded that each first trimester screening center should establish its TSH and fT4 reference ranges. Their center had higher upper reference limits of TSH than that of the universally fixed limit of 2.5mU/L, which led to a lower measured prevalence of maternal hypothyroidism.9

A study was done by Zhang et al to evaluate the relationship between subclinical hypothyroidism (SCH) and the risk of miscarriage before 20 weeks of pregnancy. They found that SCH is a risk factor for miscarriage in women before 20 weeks of pregnancy, and early treatments can reduce the miscarriage rate. Regardless of the diagnostic criteria used, the miscarriage rate increased as long as a pregnant woman was confirmed to have SCH. In addition, SCH patients with thyroid autoimmunity have a higher prevalence of miscarriage, while isolated SCH patients also have a higher miscarriage rate than euthyroid women which is also seen in our study. They recommended early screening and treatments to avoid adverse pregnancy outcomes and complications.10

CONCLUSION

Hypothyroidism if untreated can lead to first trimester abortions. It is also a cause of recurrent abortion in Indian population. All pregnant women should be screened for thyroid disorders in their first visit and treatment should be started at the earliest.

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