

**Original Article****Association of the Thyroid Function Disorder with Recurrent Pregnancy Loss in Women****Ayesha Naeem<sup>1</sup>, Heema<sup>2</sup>, Sadiq Jan<sup>3</sup>, Bushra Gohar Shah<sup>4</sup>**<sup>1</sup>Assistant Professor of Gynaecology, Khawaja Muhammad Safdar Medical College, Allama Iqbal Memorial Teaching Hospital Sialkot, Pakistan<sup>2</sup>Department of Gynecology, Women and Children Hospital Kohat (KIMS/KMU), Pakistan<sup>3</sup>Department of Gynecology, Islamic International Medical College, Rawalpindi, Pakistan<sup>4</sup>Department of Physiology, Sahara Medical College, Narowal, Pakistan**ARTICLE INFO****Key Words:**

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Received Date: 8<sup>th</sup> July, 2022Acceptance Date: 19<sup>th</sup> July, 2022Published Date: 31<sup>st</sup> July, 2022**ABSTRACT**

Thyroid function disorder is a very common disorder among the general population. Almost 3% of the people around the globe are receiving thyroid replacement therapy around the globe.

**Objectives:** The study aimed to screen the thyroid function disorder among the women with recurrent pregnancy loss. The treatment effects of thyroid disorder on the pregnancy outcomes were also assessed. **Methods:** This longitudinal study was conducted at Allama Iqbal Memorial Teaching Hospital Sialkot and Islamic International Medical College, Rawalpindi for duration of six months from October 2021 to March 2022. The 110 patients were included in the study to screen abnormal thyroid function and its association with recurrent pregnancy loss. All patients were fully aware of the study and informed consent was taken. Different screening test such as free thyroxin ( $FT_4$ ), Thyroid stimulating hormone (TSH), free tri-iodothyronine ( $FT_3$ ) and thyroperoxidase antibodies test were performed and data was collected. The thyroxin was given to the patients with abnormal TSH levels. **Results:** The free thyroxin ( $FT_4$ ), (TSH), free tri-iodothyronine ( $FT_3$ ) and anti thyroperoxidase level were measured. Out of 110 patients that participated there were 36% in which elevated levels of thyroid stimulating hormone was observed. Among these 36%, there were 22% that had the level of TSH more than 10 mU/L and there were 14% patients that had their TSH levels in the range of 7-10 mU/L. These patients were given thyroxin approximately 26-75  $\mu$ g per day and the amount of thyroxin was adjusted according to the level of Thyroid stimulating hormone. Out of these 36% women that had high levels of TSH, there were 21 women that conceived within 1 year of treatment. Among the 33% women with high level of TSH, there were 39 that underwent the anti TPO test. **Conclusion:** Women who face recurrent pregnancy loss should be checked for thyroid abnormality as it was detected that there is significant number of women who face hypothyroidism and recurrent pregnancy loss.

**INTRODUCTION**

The almost 3% of the people around the globe are receiving thyroid replacement therapy. It is very common disorder among the general population. The hypothyroidism affects approximately 4.1 women and 0.6 men per 1000 people. It mostly remains undiagnosed and untreated therefore it can be the cause of repeated pregnancy losses and even infertility [1-2]. Hypothyroidism is the most prevalent thyroid disorder during pregnancy. An estimated 1.5% to 4.4% of pregnant women are reported to be affected by it. Women with hypothyroidism have a lower fertility rate. The

insufficient iodine intake is the main causes of hypothyroidism. Other causes of hypothyroidism include radioactive iodine therapy, autoimmune thyroiditis, and thyroid gland surgery [3-4]. When a woman with hypothyroidism conceives, she may encounter problems including spontaneous and placental abortions, and irreversible harm to the fetus, such as lack of nerve differentiation, poor central nervous system development. Because of the ovulatory dysfunction there is also higher risk of perinatal death. Thyroxin prescriptions and early



diagnosis of these significant problems can improve the outcomes [5]. Thyroid disorders are the second most prevalent endocrine disorder in the pregnant females. Being the hypermetabolic disorder of pregnancy, TD is associated with poor mother and fetal outcomes. Numerous physiological changes that occur during pregnancy might cause hypothyroidism. Because of increased renal loss and iodine transfer to the growing fetus, pregnancy is a condition of relative iodine deficit [6-7]. The increase in oestrogen level during pregnancy rises the levels of thyroxine-binding globulin. The thyroid is stimulated by a weak thyroid stimulating hormone (TSH), and the actions of human chorionic gonadotrophin produce a reduction in serum thyrotropin levels (HCG). It causes a rise in FT4 and a fall in TSH. The fetus receives maternal thyroxin throughout the pregnancy [8]. Before the development of the embryonic thyroid gland, the maternal thyroxin considered as crucial for fetal brain development. Overt hypothyroidism (OH), is characterized by high blood TSH or subnormal FT4 levels. According to the different studies the prevalence of hypothyroidism during pregnancy varies sharply. OH was observed in 2 out of every 1000 pregnancies [9]. Pregnancy-related overt and subclinical maternal hypothyroidism has strong association with poor maternal outcomes. In our research, we are keen to assess the value of thyroid function testing in women who experience repeated miscarriages as well as the impact of thyroid medication on pregnancy[10].

## METHODS

This longitudinal study was conducted for duration of six months from October 2021 to March 2022. A total of 110 patients who attended the Gynecology department of our institute teaching hospitals were included in the study to evaluate the abnormal thyroid function and its association with recurrent pregnancy loss, all patients were fully aware of the study and written consent was taken from them. Blood samples for TSH, FT3, FT4, and anti TPO were taken. Blood samples were taken for the oral glucose tolerance test, anti-ds DNA, ANA, and TORCH. Different test such as free thyroxin(FT4), Thyroid stimulating hormone(TSH)and free tri-iodothyronin (FT3) were performed and data was collected. The thyroxin was given to the patients with abnormal TSH levels. According to the inclusion criteria woman of age (20 to 40 years old) who had experienced more than three miscarriages were included in the study. The analyzer (Abbott reagent) was used in the Chemiluminiscent Microparticle Immunoassaymethod for assessment of TSH, free tri-iodothyronin, free thyroxine (FT4), and auto-antibody against thyroperoxidase. For FT3 and TSH, laboratory reference values were taken as 0.4-7mU/L.

## RESULTS

A total of 110 patients were taken to study the abnormal thyroid function and its link to recurrent pregnancy loss, all patients were fully aware of the study and written consent was taken from them. Out of 110 patients that participated there were 36% that reported elevated levels of thyroid stimulating hormone. Among these 36%, there were 22% that had these level of TSH more than 10 mU/L, and there were 14% patients that had their TSH levels in the range of 7-10 mU/L. These patients were given thyroxine approximately 26-75 µg per day and the amount of thyroxine was adjusted according to the level of Thyroid stimulating hormone. The response and the adequacy range was analyzed after every six weeks. Out of these 36% women that had high levels of TSH, there were 21 women that conceived within 1 year of treatment. However, the other patients were still on treatment and did not conceive. Their TSH levels were analyzed and carefully monitored including those patients that had anti TPO. Characteristics of the sample were analyzed and it was found that there was no significant difference in the obstetrical features of patients that had subclinical hypothyroidism, euthyroid and thyroid autoimmunity, except for gestational age which was showing variation in these groups.(Table no.1)

| Features                          | Euthyroid  | Thyroid autoimmunity | Subclinical hypothyroidism | p-Value |
|-----------------------------------|------------|----------------------|----------------------------|---------|
| Maternal age (years)              | 35.4 ± 5.4 | 34.3 ± 4.9           | 34.3 ± 4.9                 | 0.21    |
| Nulliparous (%)                   | 41.9       | 35.2                 | 35.2                       | 0.4     |
| Earlier miscarriage (%)           | 24.0       | 32.3                 | 32.3                       | 0.17    |
| Gestational age at abortion(week) | 7.2 ± 1.6  | 9.2 ± 2.1            | 9.2 ± 2.1                  | 0.01    |

**Table 1:** Features of the Sample

Logistic regression analysis showed link between early pregnancy loss and the multiple variables. The early pregnancy loss was seen to be associated with the elevated levels of TSH. Similar trend was seen in case of thyroid autoimmunity and early pregnancy loss. Analysis revealed that both of these factors played role in causing early pregnancy loss. The other two factors had no significant link with pregnancy loss.(table no.3).

| Value of TSH   | No. of women (%) |
|----------------|------------------|
| 0.4-7          | 36 (33%)         |
| 7-10           | 15 (14%)         |
| >10            | 24 (22%)         |
| High FT levels | 12 (11%)         |

**Table 2:** Results showing thyroid function test

Among the 33% women with high level of TSH, there were 39 that underwent the anti TPO test. And it was reported that 5 of them had autoimmune thyroiditis. It was reported by these two women that they also had enlarged nodularity in the thyroid gland as seen in ultrasound. Among 5 of these

patients, three refused to carry out the further testing.

| Variables                   | OR (95% Confidence Interval) | p-Value |
|-----------------------------|------------------------------|---------|
| Maternal age                | 1.06 (0.45-2.22)             | 0.87    |
| Nulliparity                 | 0.91(0.41-2.17)              | 0.91    |
| Earlier miscarriage         | 1.02 (0.45-2.38)             | 1       |
| Thyroid autoimmunity        | 3.3 (1.26-8.52)              | 0.012   |
| Subclinical Hyperthyroidism | 6.24 (1.35-23.4)             | 0.011   |

**Table 3:** Link between early pregnancy loss and multiple variables

One patient reported abnormal sugar profile as per her history in the previous pregnancy and the remaining had hypothyroidism but didn't take any medicine. There were 11% patients that had high FT levels.

## DISCUSSION

The primary role of thyroid hormone is the reproductive tissue development and its link with fertility is yet unclear. Studies are going on to find the association between fertility and the thyroid gland functioning [10-11]. However, as per studies the dysfunction of thyroid gland is linked to menstrual irregularity and abnormal sexual development. It is reported that there is link of recurrent pregnancy loss and abnormal functioning of the thyroid gland. The cases like hypothyroid are more known to be linked to such mishaps. As per studies by a group of scientists they found that the overall rate of occurrence of hypothyroidism was 3% whereas the overt thyroid deficiency was reported to be 2 cases in 1000. The occurrence of subclinical hypothyroidism was reported as 5% in women ranging from 18-45 years of age. The risk factor that was shown to be liked to it was heredity however, there must be many other factors that can play role like antimicrosomal antibodies and diabetes [12-13]. The iron deficiency is linked to excessive rates of miscarriage in such patients. Because iron deficiency hinders with the normal functioning of the thyroid gland as the thyroid antibodies are associated with the incidence of abortion even if there is a lack of overt hypothyroidism [14-15]. After a met-analysis and systemic review has helped scientist to report that there is a significant association between thyroid antibodies and the incidence of pregnancy loss. In this study the incidence of pregnancy loss among women suffering from high TSH was 65, whereas it was found that it is not greater occurrence than the normal condition. It was found that there is high chance of co-existence of multiple endocrine abnormality in case of certain women but in this study it was found that only women had recurrent pregnancy loss and diabetes [16]. There is a condition called as subclinical hypothyroidism where women are asymptomatic but if checked through clinical biochemistry the women had high levels of Thyroid stimulating hormone [17]. The studies have shown that up till now there is no case reported where there is link found between subclinical hypothyroidism and

loss of pregnancy. In this study it was found that there were 14% cases found where the patients had subclinical hypothyroidism but here also we found that there was no association between recurrent pregnancy loss and subclinical hypothyroidism [18]. If the woman is suffering from recurrent pregnancy loss, then she should be given treatment and proper care to prevent any mishap during the course of time. According to the studies it was found that there is a link of overt disease and subclinical hypothyroidism. Even in case of patients having hypothyroidism the signs and symptoms like fatigue, decreased vigor, excessive sleep is commonly observed, that's why if such women get pregnant the symptoms of pregnancy are overlooked till they encounter failure in pregnancy or abortion [19]. In 2007, studies were carried out to find the associations between thyroid and the related illness linked to pregnancy loss. In developing countries, it is very difficult to diagnose subclinical hypothyroidism so its link with recurrent pregnancy loss gets undetected every time. So it can be difficult to check such patients and to analyze the data. As per our studies there were also some patients reported that had elevated levels of FT. hyperthyroidism cannot be called as a diagnosis as it is itself a condition and it is depending on so many other causes. It is also linked to many other endocrine disorders [20], there will be further research required in this field to know the exact cause. In case of young children, the main cause comes out to be grave disease or in some cases thyroiditis. In this study there was no evidence found about the thyroid nodularity and hyperthyroidism in these patients. The treatment as prescribed by physician and use of proper iron supplements can help patients recover from any iron deficiency [21]. And it can in turn alter the pregnancy outcomes. So the role of abnormal thyroid function and thyroid antibodies in the recurrent pregnancy loss should be checked so that early treatment can be done to improve the viability of pregnancy [22].

## CONCLUSION

Women who face recurrent pregnancy loss should be checked for thyroid abnormality as it was detected that there is significant number of women who face hypothyroidism and recurrent pregnancy loss. Women that suffer from subclinical hypothyroidism have more ratio of early pregnancy loss. The link of recurrent pregnancy loss was more for hypothyroidism condition as compared to hyperthyroidism. Among all the patients there were one third that got pregnant after treatment with thyroxine which shows that hypothyroidism is treatable and is one of the causes of recurrent pregnancy loss.

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