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# ASSOCIATION BETWEEN TSH AND SERUM CREATININE IN EUTHYROID AND HYPOTHYROID DURING PREGNANCY

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**Abstract**

**Introduction:** One of the most common endocrine disorders identified during pregnancy is thyroid illness. Poor results for both the mother and the foetus have been associated with it. Abortion, preeclampsia, abruptio placenta, early labour, and foetal problems like prematurity, low birth weight, stillbirth, and perinatal mortality are the most frequent obstetric outcomes linked to thyroid disorders. A clinical syndrome known as hypothyroidism is brought on by a thyroid hormone shortage, which causes metabolic processes to generally slow down. In the general population, it is a frequent metabolic condition. After diabetes during pregnancy, thyroid illness is the second most prevalent endocrine condition. Pregnant women's physiology is significantly challenged by thyroid dysfunction, which also has important ramifications for both the mother and the foetus.

**Aim and Objectives:** To study the Serum Creatinine level in Euthyroid and Hypothyroid cases in pregnant women and to assess the correlation of serum creatinine with TSH.

**Material and methods:** This was a 12-month comparative cross-sectional study carried out from December 2023 to December 2024 at a tertiary medical centre, Department of Obstetrics and Gynaecology .Out of the 72 participants in the trial, 60 were enrolled; the remaining 10 patients were receiving haemodialysis and were not included in the study. Two individuals were excluded because they were not followed up with. comprising 30 newly diagnosed hypothyroid patients (cases) between the ages of 20 and 40, 30 sex-matched euthyroid people, and 30 healthy controls free of any illnesses. The Cobas e411 electro-chemiluminescence method was used to measure TSH. The Modified Jaffe's method was used to measure the levels of serum creatinine.

**Results:** Thirty hypothyroid patients and thirty controls were among the 60 participants in the current investigation. The age group of 25–29 years old had the highest number of cases and controls (n = 26), followed by the 30–40 year old age group and the age group of 35–40 years old (n = 3).When compared to controls, it was shown that subclinical and hypothyroidism cases had significantly higher serum levels of creatinine and TSH. There was higher mean serum TSH in controls as compared to cases, and the difference among both the groups was significant and mean serum creatinine of cases was 0.82 ± 0.45, and in controls it was 0.53 ± 0.18, there being less mean serum creatinine in controls as compared to cases and the difference between both the groups being significant. There was a significant positive correlation with TSH and serum creatinine in hypothyroid cases.

**Conclusion:** The evaluation of the biochemical parameters (creatinine, TSH) in the current study showed that they were significant markers and that the development, monitoring, and treatment of pregnant women with hypothyroidism depended heavily on their aberrant values.

**Key words:** serum, euthyroid, hypothyroidism, thyroid, creatinine, and TSH

## INTRODUCTION

A normal pregnancy entails physiological alterations to ensure maternal and fetal health. The adaptations are profound and affect nearly every organ system including maternal thyroid and renal function. Thyroid abnormalities are among the most prevalent endocrine conditions found during pregnancy. It is linked to poor results for both the mother and the foetus. Hypothyroidism, hyperthyroidism, and thyroiditis are among the conditions that fall under the umbrella of thyroid dysfunction [1].

Common obstetric issues linked to thyroid abnormalities include abortion, preeclampsia, abruptio placenta, preterm labour, and foetal complications, including low birth weight, preterm birth, stillbirth, and perinatal mortality [2]. A clinical syndrome known as hypothyroidism is brought on by a thyroid hormone deficit, which causes metabolic processes to generally slow down [1].

It is a common metabolic disorder in general population. Thyroid disease is the second most common endocrine disorder after diabetes in pregnancy. Thyroid disease poses a substantial challenge on the physiology of pregnant women and has significant maternal and fetal implications [2].

With numerous anatomical, physiological, and biochemical changes that begin at conception, continue until the baby is born, and then stop after delivery, pregnancy is a normal physiological event. Numerous biochemical markers, including glucose, lipids, electrolytes, urea, creatinine, uric acids, proteins, as well as various trace elements and vitamins, can be measured to see these changes. Pregnancy-related biochemical test results could therefore deviate from the typical reference ranges, leading to an incorrect interpretation of abnormal. This might occasionally result in harmful and needless therapeutic intervention [3,4].

Research shows during pregnancy, the size of the thyroid gland increases by 10% in countries with adequate iodine stores and by approximately 20% to 40% in countries with iodine deficiency[3]. During pregnancy, thyroid hormone production increases by around 50% along with a similar increase in total daily iodine requirements.

A normal pregnancy entails physiological alterations to ensure maternal and fetal health. The adaptations are profound and affect nearly every organ system including maternal thyroid and renal function [5]. The high levels of human chorionic gonadotropin (hCG) in early pregnancy mimic the role of thyroid-stimulating hormone (TSH). Thereby, the production of thyroid hormones increases with a concomitant decrease in TSH [6,7]. This physiological effect is pronounced, and TSH shows considerable dynamics within the first trimester of a pregnancy which necessitates the use of pregnancy-specific reference intervals in the assessment of maternal thyroid function [5,8].

Mostly the period of pregnancy is divided into two halves based on the metabolic state and development during pregnancy as first half as an anabolic phase whereby pregnant women accumulates most of the nutrients in regard to future increased demand for the supply to the fetus and health of self. In the second phase known as catalytic phase there is increased catalytic activity aimed at to fulfil the increased demands of the fetus [9]. There are so many anatomical and physiological changes occur due to increase in vascular and interstitial space in kidney which lead to enlargement of kidney. The most marked structural changes are the dilatation of the calyces, renal pelvis and ureters resulting in hydronephrosis [10]. Which is most commonly founded with variable frequency and peak incidence found at late pregnancy.

As the pregnancy progresses, these changes occur due to the compressive impact of the uterus' weight and the influence of progesterone on the ureter's tone and power of contraction [11]. The most significant indicator of thyroid hormone function is thyroid stimulating hormone (TSH), which is released by the anterior pituitary's thyrotrope cells and is crucial for the regulation of the thyroid

axis.TSH is a very sensitive and specific parameter for determining thyroid function and is important in early detection or exclusion of thyroid disorders. Hypothyroidism is an endocrine disease, which presents with decreased synthesis of thyroid hormones and their diminished action resulting in decreased metabolic processes and is associated with biochemical dysfunction which includes raised serum creatinine and uric acid levels [12.13].

An chemical substance, urea is essential to the nitrogen-containing molecule. The kidney filters it into urine and it is a waste product from dietary protein [7, 8]. In addition to causing mental retardation and cretinism, maternal hypothyroidism during the first trimester can be detrimental to the development of the foetal brain. It includes stunting of physical and mental development [14].

Urea and creatinine are important parameters in diagnosis, the prognosis of follow up of chronic kidney disease [9]. Uric acid is the end product of purine metabolism is excreted by the kidney and its level is important in the reduced glomerular filtrate rate [10].Kidney plays an important role in the metabolism of thyroid hormone, chronic kidney disease cause uremia and affects the hypothalamus-pituitary thyroid axis which impairs synthesis and secretion of triiodothyronine (T3) and tetraiodothyronine (T4).

Increases in thyroxine binding proteins, thyroid hormone production, renal iodine excretion, and the thyroid stimulatory effects of human chorionic gonadotrophin (hCG) are all linked to normal pregnancy. During pregnancy, the physiology and function of the thyroid undergo substantial changes. Since the foetus depends on the mother's circulating thyroxine (T4) throughout the first trimester, these are especially crucial. Depression is primarily caused by changes in the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-adrenal (HPA) axis.

Because creatinine and TSH are crucial for the diagnosis, prognosis, and medical treatment of euthyroid and hypothyroid in pregnant women at a tertiary care facility, the current study was conducted with this goal in mind.

## MATERIAL AND METHODS

This was a 12-month cross-sectional study carried out in the Hind Medical Institute of Medical Sciences' Obstetrics and Gynaecology Department from December 2023 to December 2024 in Uttar Pradesh, India. Out of the 72 participants in the trial, 60 were enrolled; the remaining 10 patients were receiving haemodialysis and were not included in the study. Two individuals were excluded because they were not followed up with. There were 60 participants in the trial, including 30 newly diagnosed hypothyroid patients between the ages of 20 and 40, 30 sex-matched euthyroid people, and 30 healthy controls who were disease-free.

### Inclusion Criteria

1. Subjects with detailed history including history of cardiovascular disease, diabetes mellitus, hypertension, and surgery or any drug intake and family history of renal, muscular, liver disorders with no other associated disease such as cancer, tuberculosis
2. Female group of different age group (20-40 years)

### Exclusion Criteria

1. Any systemic disease such as psychiatric disease, and connective disease
2. Subjects on medication such as anticancer, antithyroid drug and steroid drug
3. Males were excluded
4. Females below 20 years and above 40 years were excluded from the study.
5. Patients who were undergoing hemodialysis

### Data collection procedure-

The Selection of subjects for the study was made based on a detailed history and proper clinical examination such as name, sex, age, address. For the diagnosis of chronic kidney disease, clinical history, and physical findings with supportive biochemical evidence were taken as criteria.

**Study procedure:**
**Blood parameters assessed:** TSH levels using Cobas e411 (electro-chemiluminescence technique). Serum creatinine levels using Modified Jaffe's method.

**Test principles:**
**TSH estimation (Cobas e411-electro-chemiluminescence):** TSH levels were measured using the Cobas e411 system, which uses electro-chemiluminescence technology. This method makes use of certain antibodies that have a ruthenium molecule attached to them. TSH is measured using monoclonal antibodies that are labelled with a ruthenium compound and are directed against human TSH. There are various stages to the procedure. First, a sandwich combination is formed by the sample, biotinylated monoclonal TSH-specific antibody, and a monoclonal TSH-specific antibody labelled with a ruthenium complex. After streptavidin-coated microparticles are added, the complex forms a bond with the solid phase via the biotin-streptavidin interaction. Finally, the chemiluminescent emission generated by applying a voltage is measured to determine TSH levels. This method ensures high sensitivity and specificity for assessing thyroid function [12].

**Serum creatinine estimation (Modified Jaffe's method):** The Modified Jaffe's method, an enzymatic colorimetric assay in which creatinine forms a yellow-orange complex with picrate under alkaline conditions, was used to measure the levels of serum creatinine. The content of creatinine in the sample directly correlates with the rate at which dye is formed. Because creatinine is freely filtered by the glomeruli and not substantially reabsorbed or secreted by the renal tubules, this approach enables the evaluation of renal function. Accurate measurement of creatinine levels is ensured by correcting the data for nonspecific reactions brought on by serum/plasma pseudo-creatinine chromogens [13]. The precision and dependability of the study's data are enhanced by these test concepts, which clarify the biochemical mechanisms underpinning the assessment of thyroid hormones and creatinine levels.

| Biochemical parameters | Range |
|---|---|
| **Creatinine** | 0.6-1.5 mg/dl |
| **TSH** | 0.4- 4.5 micro-IU/ml |

**Table 1: Normal level of biochemical parameters.**

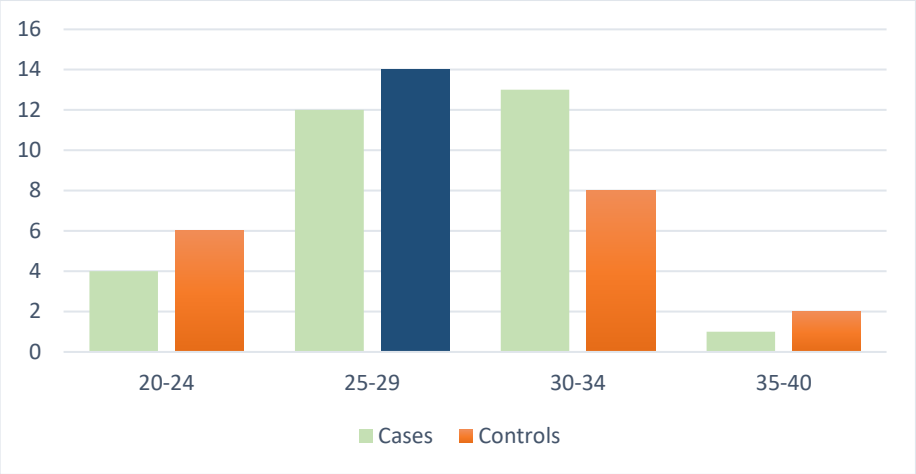
All the above parameters were performed by the commercial available kit methods.
**Statistical analysis-** Microsoft Excel worksheets were used and data were analyzed using SPSS version 20.00.

## RESULT

Demographic information was documented for each of the 60 participants in the current study, which included 30 hypothyroid patients and 30 controls.Women were split into age groups ranging from 20 to 40 years old. The age group of 25 to 29 years old had the highest number of cases and controls (n = 26), followed by the 30 to 40 year old age group and the age group of 35 to 40 year old (n = 3). This demonstrates unequivocally that young women are more frequently impacted. (Graph 1 and Table 2).

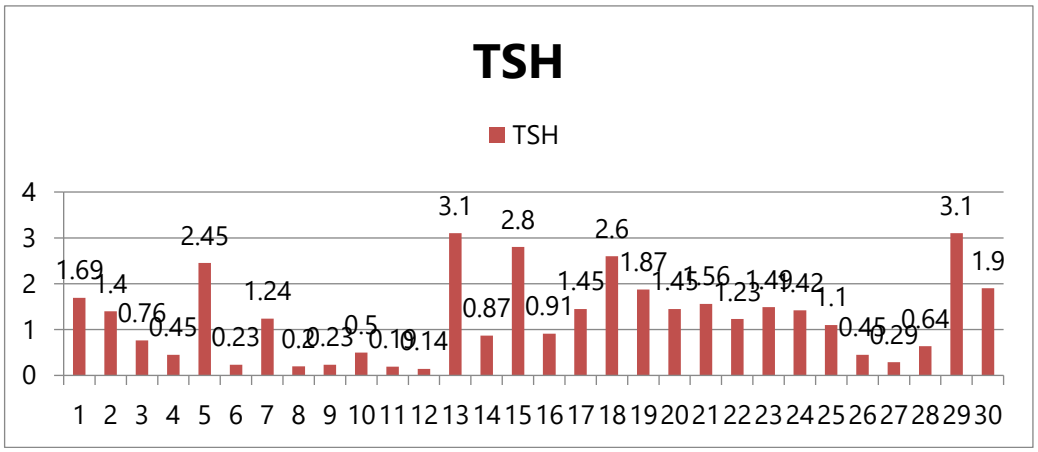
| Age (years) | Case (n=30) | Control(n=30) | Total |
|---|---|---|---|
| **20-24** | 4 | 6 | 10 |
| **25-29** | 12 | 14 | 26 |
| **30-34** | 13 | 8 | 21 |
| **35-40** | 1 | 2 | 3 |
| **Total** | 30 | 30 | 60 |

**Table 2: Age wise distribution of the cases**

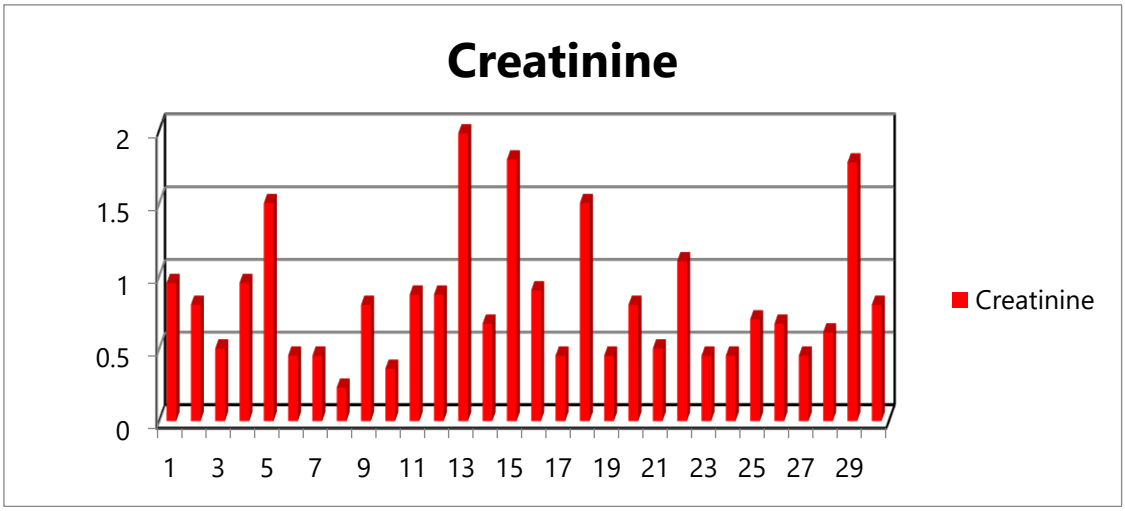



**Graph 1: Graphical Representation ofAge wise distribution of case and controls.**

Graph 2 and Graph 3 shows TSH and serum creatinine levels distribution in different groups of 30 cases.




**Graph 2: Graphical Representation of frequency distribution of Serum TSH levels among Cases**



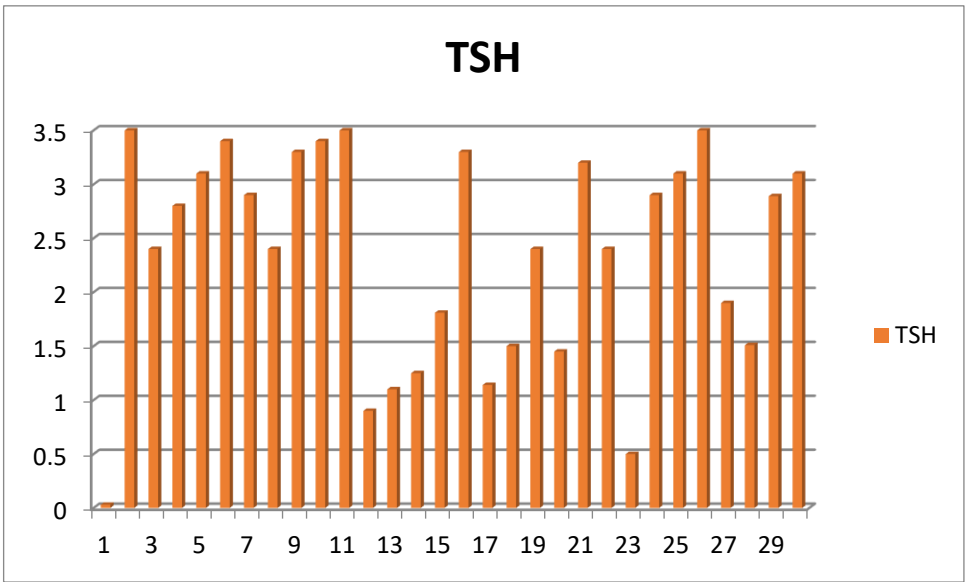

**Graph 3: Showing frequency distribution of Serum Creatinine levels among cases**

Mean serum creatinine of cases was 0.83 ± 0.45, and in controls it was 0.54 ± 0.18, there being less mean serum creatinine in controls as compared to cases and the difference between both the groups being significant. Mean serum TSH in cases was 1. 25 ± 0.87, and in controls it was observed to be

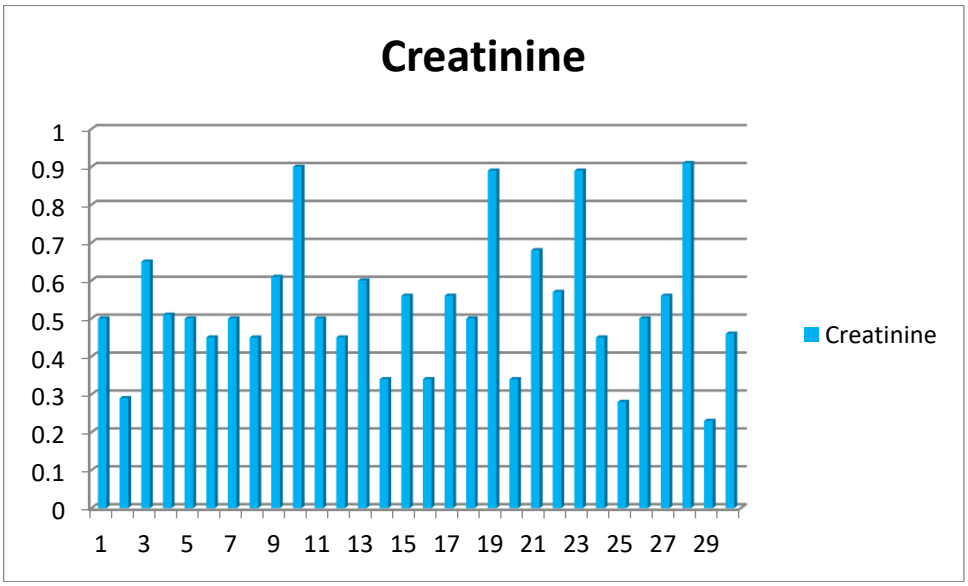
2.35 ± 0.98. There was higher mean serum TSH in controls as compared to cases, and the difference among both the groups wasstatiscally significant. (Table no. 3)

| Parameters | Case (n=30) | Control(n=30) | P value |
|---|---|---|---|
| **TSH (micro-IU/ml)** | 1.25 ± 0.87 | 2.35 ± 0.98 | 0.006 |
| **Serum creatinine (mg/dl)** | 0.82 ± 0.45 | 0.53 ± 0.18 | |

**Table 3: Comparison of level of TSH and creatinine**




**Graph 4: Graphical Representation of Bar Chart showing frequency distribution of Serum TSH levels among Control group**




**Graph 4: Graphical Representation of Bar Chart showing frequency distribution of Serum Creatinine levels among Control group**

In the present study the statistically significant was observed with Chi $^2$ : 3.33, P-value: 0.006.

## DISCUSSION

Because it is linked to notable changes in creatinine levels, thyroid dysfunction—whether it manifests as subclinical or overt thyroid disease—is acknowledged as a risk factor for chronic renal disease [3].

A clinical condition known as hypothyroidism is brought on by a deficiency of thyroid hormones, which causes all metabolic processes to slow down generally. Hypothyroidism is more common in women and varies by region. Significant changes in kidney function are caused by thyroid dysfunction; the most prevalent kidney abnormalities linked to hypothyroidism are decreased renal plasma flow, decreased glomerular filtration rate, and higher blood creatinine levels. In both adults and children, a reversible increase in serum creatinine is linked to primary subclinical hypothyroidism [15].

Hypothyroidism is one of the most common endocrine disorders in India. It affects 2-15% of population worldwide and women are more commonly affected compared to men. Most common cause is iodine deficiency and another cause is autoimmune thyroid disease characterized by elevated anti-Thyroid Peroxidase antibody.

Western studies showed the prevalence of hypothyroidism in pregnancy as 2.5%, whereas for hyperthyroidism between 0.1 to 0.4% Hyperthyroidism seen in 0.2%–0.4% of pregnant women and is commonly related with Grave's disease. The incidence of hypothyroidism in pregnancy is between 0.5%–3.5% [16].

In the present study, it was noted that there were 72screened out of which 60 were participants, including 30 casesand 30 controls subjects were enrolled. It was found that the maximum numbers of cases and controls were recorded in the age group of 25-29 years of age (n= 26) followed by the age group of 30-40 years of age and least for 35-40 years of age (n=3).

This study was in support to the study by Arora P where a higher prevalence of hypothyroidism among individuals aged 21-30 (33.53%) was observed [15]. There were other findings which were similar to the studies performed by the other research investigator by Mahantesh BB et al(2015) [17] , Swati Srivastava et al (2018) [18] and Lise Husted et al (2023) [19], in which the maximum age group was observed between 25-35 years of age .

In the current study it was noted that the mean serum TSH in cases was 1.25± 0.87, and in controls it was 2.35 ± 0.98. There was higher mean serum TSH in controls as compared to cases, and the difference among both the groups was significant. This finding was in accordance with other study by Swati Srivastava et al [19]in which mean serum TSH in cases was 1.8120 ± 1.0844, and in controls, it was 2.5233 ± 0.7447. There was other study by Mahantesh BB et al (2015) which was in support to the present study [17].

In the present study**,** mean serum creatinine of cases was recorded to be 0.82 ± 0.45, and in controls it was 0.53 ± 0.18, there being less mean serum creatinine in controls as compared to cases and the difference between both the groups being significant. This finding was found to be parallel with other study performed by Shilpa M et al [20]in which serum creatinine between cases and controls was 1.29 ± 0.65 and 0.81 ±0.32 respectively. Similar study by Mahantesh BB et al [17]was observed in which the levels of serum creatinine in subclinical hypothyroid cases (0.95 ± 0.21) were higher compared to euthyroid subjects (0.66 ± 0.11). and similar finding by Dilipkumar M Kava (2019)[21] was recorded in which the level of creatinine was 0.65 ± 0.13 in pregnant women. There was another study which was in support to the current study where mean creatinine levels was observed to be (1.05 mg/dl) [22].

TSH exerts a direct influence on the thyroid gland and has been found to affect kidney function, particularly concerning the creatinine levels. Studies have established an association between TSH and glycated albumin [23], as well as between TSH and serum creatinine levels [24] particularly among individuals diagnosed with hypothyroidism. In individuals with overt hypothyroidism and TSH levels ≥10.0 μIU/l, there is a marked increase in the serum levels of urea, creatinine and uric acid. Similarly, patients with subclinical hypothyroidism exhibit significantly higher serum levels of urea and creatinine [25]. TSH demonstrates a significant association with serum creatinine levels in both overt and subclinical hypothyroidism cases [26].

Thyroid dysfunction is the most frequent endocrinological condition during pregnancy, second only to diabetes. It has recently become the most popular topic of research in clinical endocrinology. Thyroid function should be assessed throughout pregnancy because it has been shown to influence fetal-maternal outcomes. As soon as pregnancy is confirmed, thyroid physiology changes, which

remain throughout the pregnancy but are reversible postpartum. Thus, thyroid problems during pregnancy increase foetal, maternal, and neonatal morbidity and mortality. This makes it critical to identify women at risk by early screening and prompt treatment.

This was, as far as we know, the first study to examine the connection between creatinine and TSH in pregnant women with hypothyroidism who resided in a northern Indian rural community. Additionally, TSH and creatinine were evaluated simultaneously in this study. However, as the findings of our study are solely based on data gathered from a single institution, there are certain limitations to take into account [27, 28]. Therefore, before extending our findings to a larger sample of pregnant women with hypothyroidism, more research is required to validate our findings. Furthermore, we can only demonstrate a correlation—not a causal relationship—between TSH and creatinine in pregnant women with hypothyroidism because our study was set up as a case-control.

Creatinine levels in patients with hypothyroidism should be closely monitored, and any changes should be discussed with their healthcare provider.

## CONCLUSION

Thyroid disorders can have serious repercussions for both the mother and the unborn child if they are not appropriately identified and treated during pregnancy. When treating thyroid disorders in pregnant women, a multidisciplinary approach is essential. A multidisciplinary team of an endocrinologist, obstetrician, primary care physician, nurse practitioner, and chemist should oversee its management. Subclinical hypothyroid people have significantly higher serum creatinine levels. Therefore, in patients with elevated serum creatinine levels, hypothyroidism should be taken into consideration. A limited sample size and a brief time period are two of the study's shortcomings that could impact how broadly the findings can be applied. It's crucial to regularly check these metrics for hypothyroid patients.

## DECLARATIONS:

**Conflicts of interest: There is no any conflict of interest associated with this study**

**Consent to participate:** There is consent to participate.

**Consent for publication:** There is consent for the publication of this paper.

**Authors' contributions: Author equally contributed the work.**

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