Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL 16, ISSUE 2, 2025

A COMPARATIVE EVALUATION OF TSH AND SERUM CREATININE IN EUTHYROID AND HYPOTHYROID PREGNANT WOMEN ATTENDING A TERTIARY CARE CENTRE

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Abstract

Introduction: Thyroid disease is one of the most prevalent endocrine abnormalities discovered during pregnancy. It has been linked to poor maternal and fetal outcomes. The most common obstetric consequences related with thyroid abnormalities are abortion, preeclampsia, abruptio placenta, premature labor, and fetal issues such as prematurity, low birth weight, still birth, and perinatal mortality. Hypothyroidism is a clinical syndrome resulting from a deficiency of thyroid hormones, which in turn results in a generalized slowing down of metabolic processes. 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.

Aim and Objectives: Estimation of 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 Comparative cross-sectional study conducted in the Department of Obstetrics and Gynaecology for a period of 12 months at a tertiary care centre.The study involved 72 participants out of which 60 were included in the study because 2 were excludeddue to loss to followup,the remaining 10 patients were undergoing hemodialysis and were excluded from the study. Including 30 recently diagnosed hypothyroid patients with the age ranging 20-40 age (cases) and sex matched euthyroid individuals and 30 healthy controls without any diseases were included. TSH were quantified using the Cobas

e411 electro-chemiluminescence technique. Serum creatinine levels were measured using the Modified Jaffe's method.

Results: In the present study out of 60 participants, including 30 hypothyroid patients and 30 controls, were studied. The maximum numbers of cases and controls were observed 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).It was observed that there was a significant elevation in serum levels of creatinine and TSH in subclinical and hypothyroidism cases when compared to controls.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 current study's assessment of biochemical parameters (creatinine, TSH) revealed that they were important indicators, and that their abnormal values were crucial for the development, observation, and treatment of pregnant women with hypothyroidism.
Key words: TSH, Thyroid, Creatinine, Hypothyroidism, Euthyroid, Serum

INTRODUCTION

One of the most common endocrine disorders identified in pregnancy is thyroid disorder. It is associated with adverse maternal and fetal outcomes. Thyroid dysfunction encompasses a range of disorders affecting the thyroid gland, including hypothyroidism, hyperthyroidism, and thyroiditis [1].

Abortion, preeclampsia, abruptio placenta, preterm labor, and fetal complications are prematurity, low birth weight; still birth and perinatal death are the common obstetric complications associated with thyroid disorders [2]. Hypothyroidism is a clinical syndrome resulting from a deficiency of thyroid hormones, which in turn results in a generalized slowing down of metabolic processes[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].

Pregnancy is a normal physiological phenomenon with many anatomical, physiological and biochemical changes which occurs starting from the conception and extends up to the birth of

newborn and subsides after delivery. These changes can be observed by measuring various biochemical parameters like glucose, lipids, electrolytes,urea, creatinine, uric acids, proteins, including different trace elements and vitamins. The result of biochemical tests during pregnancy may therefore differ from the normal reference ranges, so they may be mistakenly interpreted as abnormal. Which may sometime falsely lead to unnecessary and dangerous therapeutic action [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. This changes happen from the effect of progesterone on the tone and force of contraction of the ureter to the compression effect exerted by the weight of the uterus as the pregnancy advances [11]. Thyroid stimulating hormone (TSH) secreted by thyrotrope cells of anterior pituitary, plays a very important role in the control of thyroid axis and serves as the most important marker of thyroid hormone action. 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].

Urea is an organic compound and plays a vital role in the nitrogen-containing compound. It is a waste product from dietary protein and is also filtered into urine by the kidney [7,8]. Maternal hypothyroidism during the first trimester can be harmful for fetal brain development and can also lead to mental retardation and cretinism. It includes impairment of mental, physical growth and 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).

Normal pregnancy is associated with an increase in renal iodine excretion, an increase in thyroxine binding proteins, an increase in thyroid hormone production, and thyroid stimulatory effects of human chorionic gonadotrophin (hCG). There are significant changes in thyroid physiology and function during pregnancy. These are particularly important in the first trimester when the fetus relies on circulating maternal thyroxine (T4). Alteration in the hypothalamic–pituitary–thyroid (HPT) axis and the hypothalamic–pituitary–adrenal (HPA) axis is a main cause of depressive disorder.

Therefore, the present study was undertaken with the aim to determine the creatinine and TSH as it is important in diagnosis, prognosis, and medical management of euthyroid and hypothyroid in pregnant women at a tertiary care centre.

MATERIAL AND METHODS

This was a Cross-sectional study conducted in the Department of Obstetrics and Gynaecology for a period of 12 months at Hind Medical Institute of Medical Sciences, Uttar Pradesh, India. The study involved 72 participants out of which 60 were included in the study because 2 were excluded due to loss to followup, the remaining 10 patients were undergoing hemodialysis and were excluded from the study. The study involved 60participants, including

30 recently diagnosed hypothyroid patients ranging between 20-40years of age and sex matched euthyroid individuals and 30 healthy controls without any diseases.

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): The Cobas e411 system, which makes use of the electro-chemiluminescence technology, was used to measure TSH levels. This technique uses certain antibodies that have been labelled with a ruthenium compound. Monoclonal antibodies that are directed against human TSH and labelled with a ruthenium

complex are used for TSH measurement. The process involves several phases. Initially, the sample, biotinylated monoclonal TSH-specific antibody, and a monoclonal TSH-specific antibody labelled with a ruthenium complex create a sandwich combination. The complex then bonds to the solid phase through the biotin-streptavidin interaction following the addition of streptavidin-coated microparticles. Lastly, TSH levels are ascertained by measuring the chemiluminescent emission that is produced by applying a voltage. High sensitivity and specificity for evaluating thyroid function are guaranteed by this approach [12].

Serum creatinine estimation (Modified Jaffe's method): Serum creatinine levels were determined using the Modified Jaffe's method, which is an enzymatic colorimetric assay in which creatinine forms a yellow-orange complex with picrate under alkaline conditions. The rate of dye formation is directly proportional to the creatinine concentration in the specimen. This method allows for the assessment of renal function because creatinine is freely filtered by the glomeruli and is not significantly reabsorbed or secreted by the renal tubules. The results are corrected for nonspecific reactions caused by serum/plasma pseudo-creatinine chromogens, ensuring accurate assessment of creatinine levels [13]. These test principles elucidate the biochemical processes underlying the quantification of thyroid hormones and creatinine levels, contributing to the accuracy and reliability of the study's measurements

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.

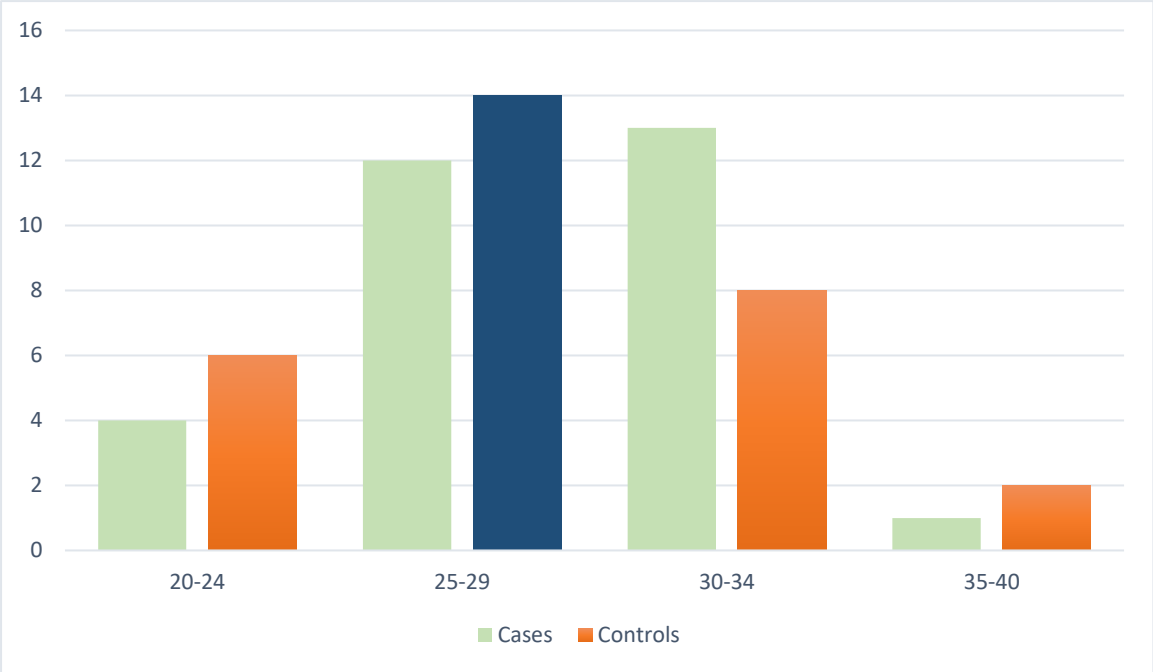
RESULT

In the present study out of 60 participants, including 30 hypothyroid patients and 30 controls, demographic characteristics were recorded.Women were divided in the age group, 20 to 40 years of age group in which maximum numbers of cases and controls were observed in 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 clearly indicate that young women are more commonly affected. (Table 2 and Graph 1).

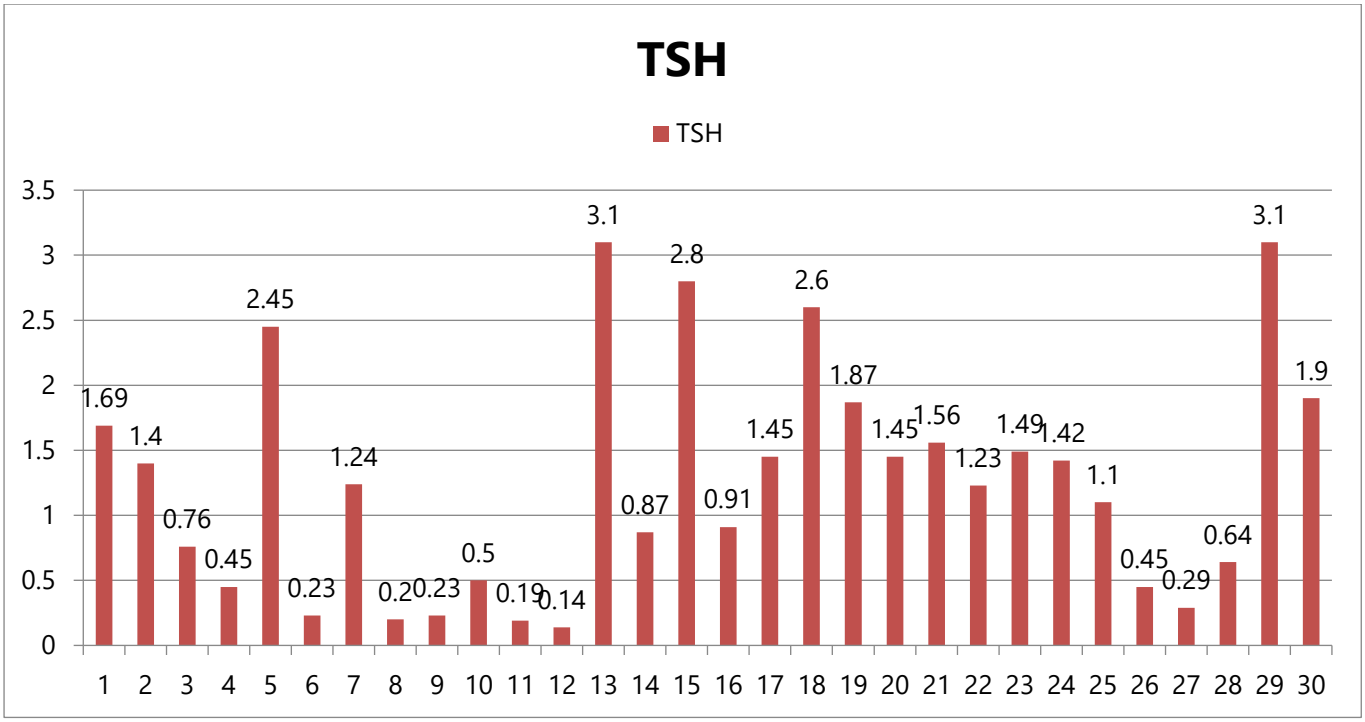
Age (years)	Case (n=30)	Control(n=30)	Total
20-24	4	6	10
25-29	12	14	26
30-34	13	8	21
35-40	1	2	3
Total	30	30	60

Table 2: Age wise distribution of the cases

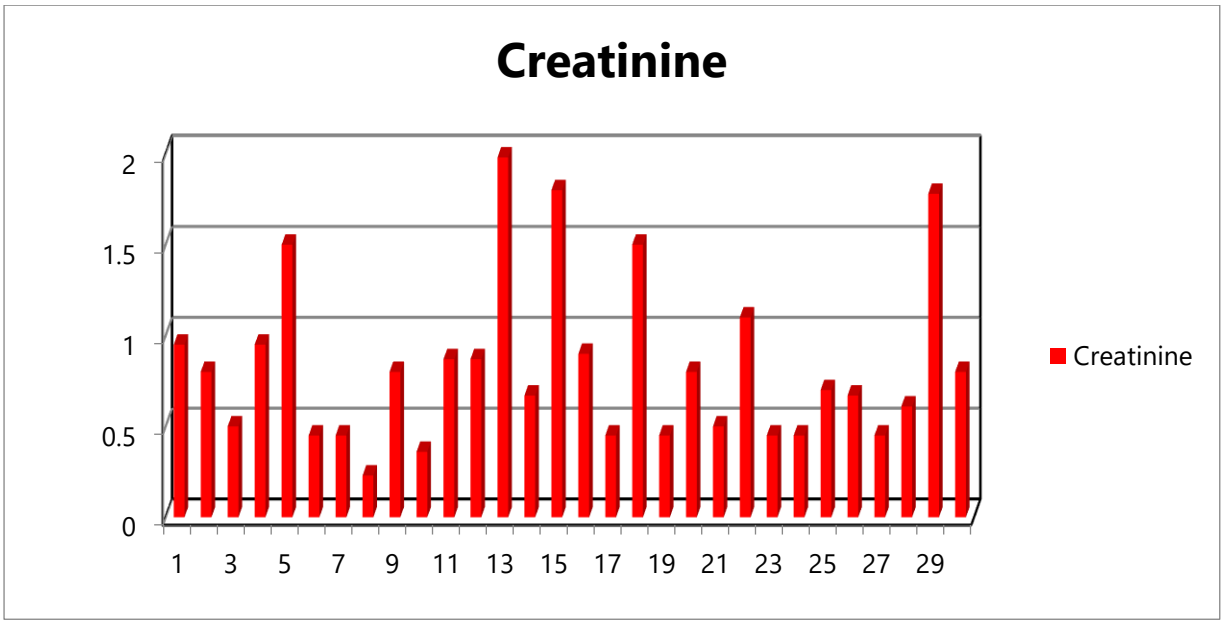


Graph 1: Graphical Representation ofAge wise distribution of case and controls.

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



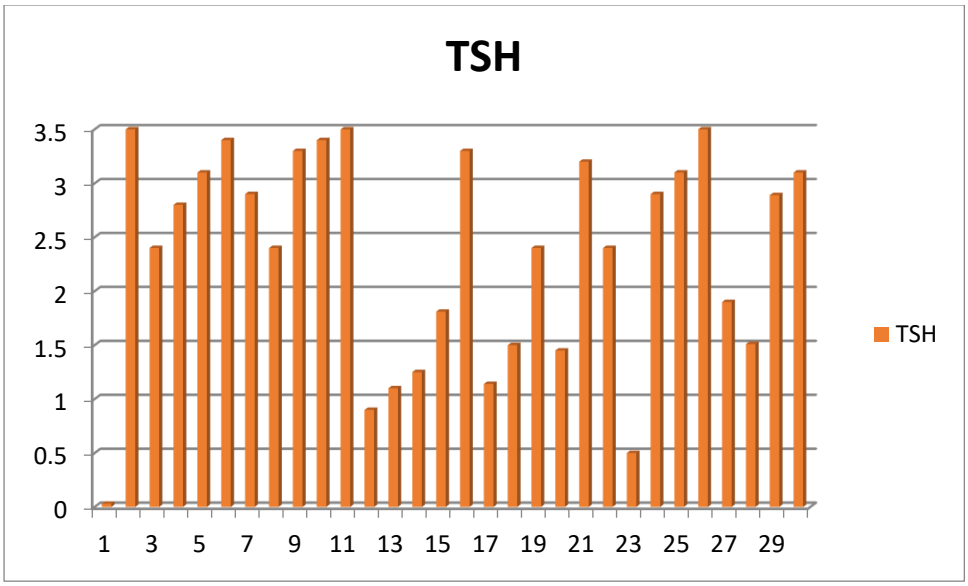
Graph 3: Showing frequency distribution of Serum Creatinine levels among cases

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

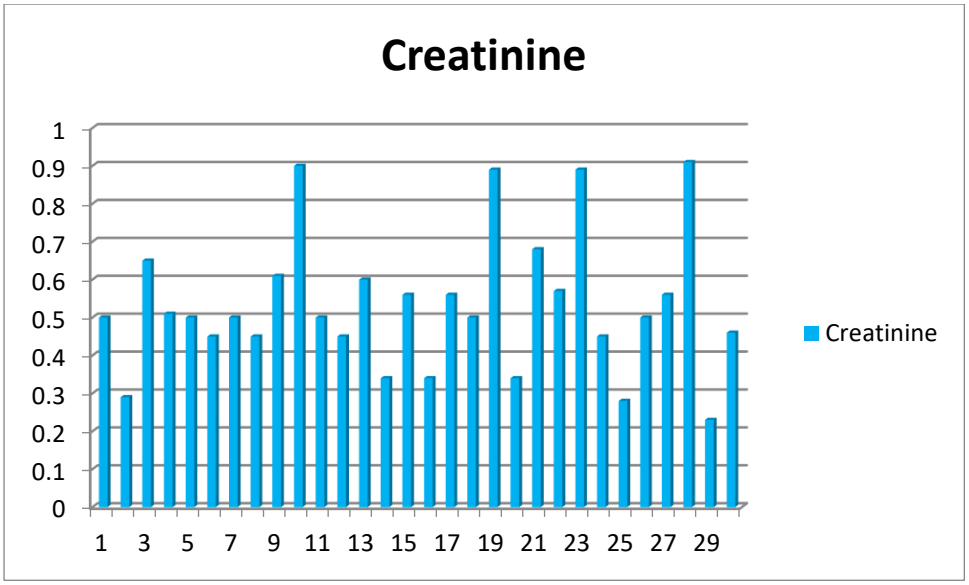
both the groups being significant. Mean serum TSH in cases was 1. 25 ± 0.87, and in controls it was observed to be 2.35 ± 0.98. There was higher mean serum TSH in controls as compared to cases, and the difference among both the groups wasstatiscally significant. (Table no. 3)

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

Thyroid dysfunction, whether in the form of subclinical or overt thyroid disease, is recognized as a risk factor for chronic kidney disease due to its association with significant alterations in creatinine levels [3].

Hypothyroidism is a clinical illness caused by thyroid hormone shortage, which results in a generalised slowdown of all metabolic processes. The prevalence of hypothyroidism varies by area and is higher in women. Thyroid dysfunction produces major alterations in kidney function, and the most common kidney derangements associated with hypothyroidism include elevated blood creatinine levels, reduced glomerular filtration rate, decreased renal plasma flow. Primary subclinical hypothyroidism is associated with a reversible elevation of serum creatinine in both adults and children [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.

To the best of our knowledge, this was the first study to look into the relationship between creatinine and TSH in pregnant women with hypothyroidism who lived in a rural area in northern India. Furthermore, this investigation measured both TSH and creatinine concurrently. However, there are certain limitations to consider, as our study's conclusions are based entirely on data collected from a single institution [27,28]. As a result, further research is needed to confirm our findings before applying them to a larger sample of pregnant women with hypothyroidism. Furthermore, because our study was designed as a case-control, we can only establish a correlation between TSH and creatinine in pregnant women with hypothyroidism, not causality.

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

CONCLUSION

If thyroid disease is not properly recognised and treated during pregnancy, it can have major consequences for both the mother and the baby. It is critical to use an interdisciplinary approach when treating pregnant women with thyroid illness. It should be managed by a

multidisciplinary team that includes an endocrinologist, obstetrician, primary care physician, nurse practitioner, and chemist. Serum creatinine levels are considerably greater in subclinical hypothyroid individuals. Thus, hypothyroidism should be considered in patients with increased serum creatinine levels. The study has some limitations, including a small sample size and a short time frame, which may affect the generalisability of the results. Regular monitoring of these measures is critical for patients with hypothyroidism.

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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