VOLUME - 10, ISSUE - 01, JANUARY - 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Biochemistry

EVALUATION OF SERUM CREATININE LEVEL IN SUBCLINICAL HYPOTHYROIDISM

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ABSTRACT

Background: Hypothyroidism is a common endocrinal disorder caused by insufficient production of thyroid hormones. Subclinical hypothyroidism (SCH) can be defined as a state of high serum thyroid stimulating hormone (TSH) levels (less than 10μIU/ml) with normal serum free thyroxine (fT_4) and triiodothyronine (fT_3) levels in the presence or absence of symptoms. Creatinine is a chemical waste product that is produced by muscle metabolism. Creatinine is produced from creatine, a molecule of major importance for energy production in muscles. Thyroid dysfunction can affect renal physiology and development, and on the other hand, kidney disorders can influence thyroid function**.** This study was aimed to find out the status of serum fT_3, fT_4,TSH and serum creatinine levels in subclinical hypothyroid cases and healthy controls. **Materials and Methods:** The present study is descriptive case control study, was conducted in the Department of Biochemistry, J.L.N. Medical College and Associated group of Hospitals, Ajmer (Raj.). 130 cases of subclinical hypothyroidism attending Medical OPD of J.L.N. Hospitals were included and 50 age-sex matched euthyroid controls were selected. **Results:** The mean serum creatinine levels were found to be significantly high in subclinical hypothyroid cases(0.99 $\pm$ 0.19 mg%) as compared to healthy controls (0.75 $\pm$ 0.15 mg%), ($p<0.0001$). **Conclusion:** Serum creatinine can be used as a biomarker for early detection of subclinical hypothyroidism in general population to prevent the morbidity and mortality which are associated with hypothyroidism. Early diagnosis and intervention of subclinical hypothyroid and their cluster of risk factor can prevent the renal dysfunction.

KEYWORDS : Triiodothyronine(T_3), Thyroxine(T_4), Thyroid stimulating hormone(TSH), Chemiluminescence Immunoassay(CLIA) , Subclinical hypothyroidism(SCH), Overt hypothyroidism (OHT), Glomerular filtration rate (GFR)

INTRODUCTION

The hormones produced by thyroid gland are thyroxine (T_4) and triiodothyronine (T_3) , which act through α and β receptors. These hormones play a crucial role in general development and metabolism, normal growth, tissue differentiation, physiology of the kidney, maintain thermogenic and metabolic homeostasis in the adults. [1] Deficiency of thyroid hormones cause hypothyroidism, which is one of the most common endocrine disorder nowadays. The disease causes generalized slowing of metabolic processes.[5,6] Hypothyroidism presents with low production of thyroid hormones, affecting 2-15% of population worldwide. Incidence is higher in women compared to men.[6,7] Subclinical hypothyroidism is a common disorder, particularly in middle aged and elderly individuals. [13]

Subclinical hypothyroidism (SCH) can be defined as a state of high serum thyroid stimulating hormone (TSH) levels (less than 10 μ IU/ml) with normal serum free thyroxine (fT_4) and triiodothyronine (fT_3) levels in the presence or absence of symptoms.[2,3,4] The prevalence of SCH is between 3% and 18% in the general population and higher in women than in men.[15] It is the mildest form of hypothyroidism and the patients usually lack classical signs and symptoms of overt hypothyroidism.[13] SCH patients are at risk for progression to overt hypothyroidism with an average yearly progression rate of 2% to 6% with an increased risk in females.[15] Subclinical hypothyroidism carries the risk of developing overt hypothyroidism with subsequent cardiovascular health risks and renal dysfunction.[16]

Creatinine is a chemical waste product that is produced by muscle metabolism. Creatinine is produced from creatine, a molecule of major importance for energy production in muscles. Thyroid dysfunction can affect renal physiology and development, and on the other hand, kidney disorders can influence thyroid function**.** Serum creatinine is elevated and glomerular filtration rate (GFR) values are reversibly reduced in overt hypothyroid patients than in euthyroid subjects.[17] Hypothyroidism affects every tissue in the body resulting in declination of mental and physical activities. The increased serum creatinine concentration is due to reduction of glomerular filtration rate because of hemodynamic changes in case of hypothyroidism. Serum creatinine may also be increased due to hypothyroid myopathy.[21]

Subclinical primary hypothyroidism is suspected to be mostly due to chronic autoimmune thyroiditis, characterized by a mild asymptomatic goiter and high titer of serum thyroid autoantibodies.[23,24] Other less common causes include drug-induced hypothyroidism, subacute thyroiditis, radiation thyroiditis, and postpartum thyroiditis.[23,25]

MATERIALS AND METHODS

The present study is descriptive case control study, was conducted in the Department of Biochemistry, J.L.N. Medical College and Associated group of Hospitals, Ajmer (Raj.). 130 cases of subclinical hypothyroidism attending Medical OPD of J.L.N. Hospitals were included and 50 age-sex matched euthyroid controls were selected. Venous blood sample were collected from all the participants under aseptic precaution and serum was separated and biochemical parameters of this study were measured by following methods-Thyroid Profile (fT_3, fT_4, TSH) by- Chemiluminescence Immunoassay method and serum creatinine by –Jaffe's colorimetric kinetic method. The present study was approved by institutional ethical committee.

For control group

Age and sex matched healthy individuals.

Inclusion Criteria for study group

Age group between 20-50 year of both sex diagnosed as SCH individuals.

Exclusion Criteria for study group

- Persons with hypothyroidism.
- Persons with coronary artery disease
- Persons with diabetes or those with stroke
- Persons with a history of arthritis
- Smokers/alcohol users
- On diuretics
- Thyroid supplementation and antithyroid agents.
- Persons using drugs that affect serum creatinine
- Pregnant women

Statistical analysis

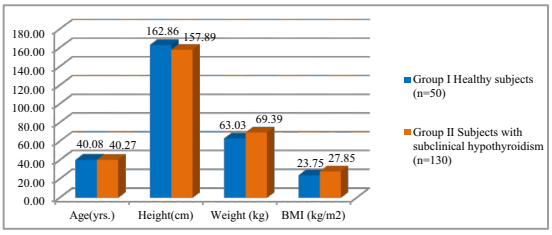
All data were analysed by SPSS-13 version. P< 0.01 were considered as significant.

RESULTS

A total of 180 subjects were studied. The results are summarized in Tables and Figures. The Table-1, Figure-1 shows that the Mean±SD of weight and BMI were more in subjects with subclinical hypothyroidism than healthy subjects and the difference was significant (P<0.001). The Mean±SD of height was less in subjects with subclinical hypothyroidism than healthy subjects (controls) and the difference was significant (P<0.001) while the mean age was not significant (P>0.005).

Table– 1 Anthropometric Parameters of Healthy subjects v/s Subjects with subclinical hypothyroidism

Parameters	GROUP-I Healthy subjects Mean ± SD (n=50)	GROUP-II Subjects with subclinical hypothyroidism Mean ± SD (n=130)	P-Value
Age(yrs.)	40.08 ± 8.83	40.27 ± 7.89	>0.005
Height(cm)	162.86 ± 7.54	157.89 ± 7.22	<0.001
Weight (kg)	63.03 ± 5.16	69.39 ± 5.34	<0.001
BMI (kg/m^2)	23.75 ±0.82	27.85 ± 1.52	<0.001



Fig– 1 Comparison of Anthropometric Parameters of Healthy subjects v/s Subjects with Subclinical hypothyroidism.

Table-2, Figure-2 shows distribution of subclinical hypothyroidism among female and male subjects. Among the total number of 130 subjects with subclinical hypothyroidism in our study were 102 (78%) females and male patients were 28 (22%) in the ratio of 3.6:1.

Table :2 -Distribution of subclinical hypothyroidism among female and male subjects

Female with subclinical hypothyroidism	Male with subclinical hypothyroidism	Total
102(78%)	28(22%)	130

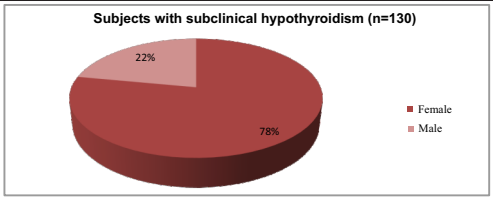


Fig -2 Distribution of subclinical hypothyroidism among female and male subjects

Table -3, Figure -3 shows age wise distribution among subclinical hypothyroid subjects. There is increase in distribution of number of subjects with subclinical hypothyroidism as the age advances from 20 years to 50 years. The distribution of number of subclinical hypothyroid cases with age wise distribution is age between 20-25 n=11, 26-30 n=15, 31- 35 n=17, 36-40 n=24, 41-45 n=28 and 46-50 n=35.

Table-3 Age wise distribution among total number of subclinical hypothyroidism subjects

Age Groups (in years)	Subjects with Subclinical Hypothyroidism (n=130)
20-25	11
26-30	15
31-35	17
36-40	24
41-45	28
46-50	35
Total	**130**

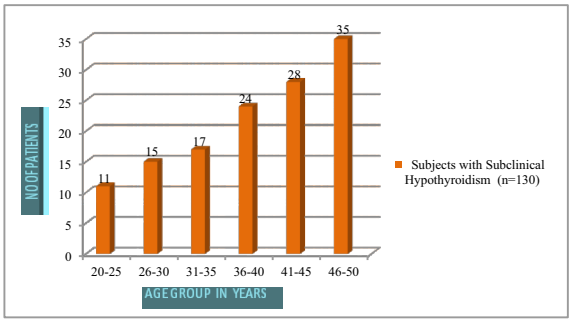


Fig- 3 Age wise distribution among total number of subclinical hypothyroidism subjects

Table-4, Figure-4 shows the Mean ± SD of serum fT_3 (3.06 ± 0.20 v/s 3.25 ± 0.22) pg/ml , fT_4 (0.75 ± 0.07 v/s 0.81 ± 0.0.07) ng/dl in subjects with subclinical hypothyroidism compared to healthy subjects (controls) was significantly (P<0.0001) decreased. The Table-2, Figure-2 also shows that the level of serum TSH (7.52 ± 1.18 v/s 2.52 ± 1.13) μIU/ml, serum creatinine (0.99±0.19 v/s 0.75 ± 0.15) mg% in subjects with subclinical hypothyroidism compared to healthy subjects (controls) were significantly (P<0.0001) raised .

Table–4 Comparison of Biochemical Parameters of Healthy subjects v/s Subjects with subclinical hypothyroidism

Biochemical Parameters	Group-I Healthy Subjects Mean± SD (n=50)	Group-II Subjects with subclinical hypothyroidism Mean± SD (n=130)	P value
fT_3 (tri - iodothyronine) (pg/ml)	3.25 ± 0.22	3.06 ± 0.20	<0.0001
fT_4 (thyroxine) (ng/dl)	0.81 ± 0.07	0.75 ± 0.07	<0.0001
TSH (thyroid stimulating hormone) (μIU/ml)	2.52 ± 1.13	7.52 ± 1.18	<0.0001
serum creatinine (mg%)	0.75 ± 0.15	0.99 ± 0.19	<0.0001

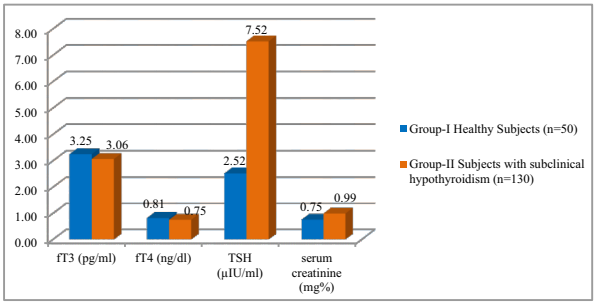


Fig-4 Comparison of Biochemical Parameters of Healthy subjects v/s Subjects with Subclinical hypothyroidism

DISCUSSION

In recent years, subclinical hypothyroidism is unknowingly emerging as a major public health problem in India and it produces an enormous burden on the economy of the country due to high prevalence, risk of progression to overt hypothyroidism and it can lead to adverse cardiovascular consequences. Subclinical hypothyroidism (SCH) and Overt hypothyroidism (OH) are common in the elderly people especially in the women. Subclinical hypothyroidism carries the risk of developing overt hypothyroidism, subsequent cardiovascular health risks and renal dysfunction. Hypothyroidism causes generalized slowing of metabolic processes.[5,6] Subclinical hypothyroidism is a common disorder, particularly in middle aged and elderly individuals.[13]

Presence of thyroid antibody raises the risk of developing subclinical and then progressing to overt hypothyroidism. Role of iodine is somewhat controversial and iodine sufficient area have higher incidence of developing SCH than the iodine insufficient.[22] A community based longitudinal study of 11 years has also reported an association of weight change and SCH. [26]

In the present study weight and BMI were more in subjects with subclinical hypothyroidism than healthy subjects (controls) and difference was statistically significant ($p<0.001$) while the mean age and sex matched were not significant ($p>0.005$), it also shows that the mean height was less than controls and the difference was significant.

Our findings are in concordance with Kumar P. et al. (2018) which also showed that body mass index (BMI) was higher in SCH group (26.44±2.19 kg/m2) compared to control group ($21.98 \pm 1.40\ kg/m^2$) .[41]

Present study shows that the prevalence of sub clinical hypothyroidism is more in females when compare to males. Our findings are in concordance with study done by Manisha Panchal et al.(2019) which showed that female and male subjects with subclinical hypothyroidism were 68% and 32% respectively[40] A similar previous study done by Bashir H et al.(2013) also shows that prevalence of subclinical hypothyroidism was more in female subjects as compare to males.[29]

It is evident that there is increase in number of cases of subclinical hypothyroidism as the age advances from 20 years to 50 years. Our studies are in agreement with S. Senthilkumaran et al. (2015) which also show increase in number of cases of subclinical hypothyroidism as the age advances.[30]

Our study shows that serum fT_3, serum fT_4 level were less and serum TSH was more in subjects with subclinical hypothyroidism than healthy controls and difference was statistically highly significant ($P<0.0001$). A similar trend was reported in a study done by Bhutal MB et al. (2020) which also suggest that serum ft_3, serum fT_4 levels were significantly lower and serum TSH was significantly higher in subjects with subclinical hypothyroidism as compared to normal healthy controls.[18]

Previous studies show that in hypothyroidism there is decreased myocardial contractility and stroke volume with increased peripheral vascular resistance, which reduces the effective renal plasma flow and GFR, causing decreased clearance of creatinine which leads to elevation of serum creatinine levels. [19,20] The increased serum creatinine concentration is due to reduction of glomerular filtration rate because of hemodynamic changes in case of hypothyroidism. Serum creatinine may also be increased due to hypothyroid myopathy.[21]

The present case-control study evaluated the biochemical marker of renal function such as creatinine in subjects with subclinical hypothyroidism and compared the results with those of healthy euthyroid controls. The present study concludes that there is significant increase in serum creatinine levels in subclinical hypothyroid subjects as compared to healthy controls. Similar changes in serum creatinine with hypothyroidism have been evaluated in support of the present study.[18,19,31-39]

CONCLUSION

Serum creatinine was found to be elevated in subjects with subclinical hypothyroidism . There is a probable scope of reversing the decline in renal function in subjects with subclinical hypothyroidism. Serum creatinine can be used as a biomarker for early detection of subclinical hypothyroidism in general population to prevent the morbidity and mortality which are associated with hypothyroidism. Early diagnosis and intervention of subclinical hypothyroidism and their cluster of risk factor can prevent the renal dysfunction and progression of subclinical hypothyroidism to overt hypothyroidism(OHT). Based on the laboratory investigations and symptoms, subjects of SCH need to be monitored and treated individually.

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