



## Frequency of subclinical hypothyroidism in chronic kidney disease patients.

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**ABSTRACT... Objective:** To determine the frequency of sub clinical hypothyroidism among chronic kidney disease patients in our population. **Study Design:** Descriptive Cross sectional study. **Settings:** Department of Nephrology, Khyber Teaching Hospital Peshawar. **Period:** February 2018 to September 2018. **Material & Methods:** A total of 145 chronic kidney disease patients were included in this study. Thyroid function tests (TFT, s) were performed in all patients along with history and clinical examination. Sub clinical hypothyroidism was defined as high TSH (normal value 0.27-4.0  $\mu$ IU/ml) and normal Free T47. (0.93 – 1.70 ng/dl). **Results:** Our study shows that Mean age was 55 years with standard deviation  $\pm$  2.83. Eighty seven (60%) patients were male and 58(40%) patients were female. Moreover, 25% patients had subclinical hypothyroidism. **Conclusion:** Our study concludes that the incidence of subclinical hypothyroidism in chronic kidney disease was found to be 25% in our population.

**Key words:** Chronic Kidney Disease, Subclinical Hypothyroidism.

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### INTRODUCTION

Chronic kidney disease is a major health problem worldwide.<sup>1</sup> Globally millions of patients are affected by it and is major cause of mortality and morbidity.<sup>2</sup> It is divided into five stages.<sup>3</sup> With higher stage of disease, the rate of mortality increase.<sup>4</sup> There are many complication of chronic kidney disease as well. Some of which are anemia, cardiovascular disease, metabolic disorders, mineral bone disease.<sup>5</sup>

Among complications, there is an association of thyroid dysfunction with chronic kidney disease. Thyroid gland is one of important gland in the body and play pivotal role in regulating different body functions which include metabolism, proteinsynthesis, body development and also influence other hormone function. It secretes two important hormones namely triiodothyronine (T3) and thyroxine (T4).<sup>6</sup> These hormones nearly affect every organ including kidney. In chronic kidney disease as the patient progresses to higher stage of disease, the prevalence of thyroid dysfunction

increases. Thyroid hormone has protective role on renal functions and its replacement can reverse the change in the renal functions.<sup>7</sup> Thyroid hormones have some important effect on renal physiology by which it increases renal blood flow and glomerular filtration rate. Hypothyroidism can reduce renal blood flow and glomerular filtration rate and vice versa.<sup>8</sup>

Recent data suggests a close relationship of thyroid dysfunction and chronic kidney disease. Different studies are published in different part of the world showing high prevalence of hypothyroidism in chronic kidney disease. Internationally, a study conducted shows a prevalence of 24.4% with subclinical hypothyroidism in chronic kidney disease.<sup>7</sup> Another show a prevalence of 56% with hypothyroidism in chronic kidney disease.<sup>7,9</sup> Nationally, a study by Asif et al shows a prevalence of 53.8% with subclinical hypothyroidism.<sup>10</sup>

Studies conducted in different parts of the world show different frequencies of subclinical

hypothyroidism in chronic kidney disease patients. so the aim of our study is to find out the frequency of subclinical hypothyroidism in chronic kidney disease patients in Khyber Pukhtoonkhuwa (KPK) and to correlate it with the frequencies in other studies and to identify the problem early in the course of disease and give adequate treatment to prevent progression and also if found significant, can be addressed to the health authorities to plan future strategy for the problem.

## MATERIAL & METHODS

This study was descriptive cross-sectional study conducted in Nephrology department of Khyber teaching Hospital, Peshawar from February 2018 to September 2018. Non-probability consecutive sampling technique was used. Sample size was 145 using 24.4% prevalence of subclinical hypothyroidism in chronic kidney disease<sup>7</sup>, 95% confidence interval with more than 7% of error with help of WHO software for sample size determination. Our inclusion criteria included all patients with chronic kidney disease of age above 20 years and below 70 years both male and female. Exclusion criteria included all patients with established hypothyroidism before diagnosed as CKD, all critical patients, and those patients using anti thyroid drugs. These mentioned conditions act as confounders and if included in the study, could introduce bias in the study results. After getting approval from the hospital ethical and research committee all patients meeting the inclusion criteria were included in the study and data was collected. An informed written consent was taken from the patients for inclusion in the study.

All patients were worked up with detailed history, clinical examination. Blood samples taken were analyzed for thyroid function tests. Data was analyzed using Statistical Package for Social Sciences (SPSS) version 17 or higher version. Mean  $\pm$  standard deviation was calculated for continuous Variables like age, T4 and TSH level of patients. Frequency and percentages were calculated for qualitative variables like gender and subclinical hypothyroidism. Subclinical hypothyroidism was stratified among age and

gender to see effect modifier. Post stratification chi-square test was applied keeping p-value less  $\leq 0.05$  as significant. All these results were presented in the form of tables and charts.

## RESULTS

This study was conducted at Nephrology department of Khyber teaching Hospital, Peshawar in which a total of 145 patients were observed to determine the frequency of subclinical hypothyroidism in chronic kidney disease patients in our population. Subclinical hypothyroidism was defined as high TSH (normal value 0.27-4.0  $\mu$ IU/ml) and normal Free T4. (0.93 – 1.70 ng/dl). The results were analyzed as:

Age distribution among 145 patients was analyzed as 22(15%) patients were in age range 31-40 years, 32(22%) patients were in age range 41-50 years, 43(30%) patients were in age range 51-60 years, 48 (33%) patients were in age range 51-60 years. Mean age was 55 years with standard deviation  $\pm 2.83$ .

Gender distribution among 145 patients was analyzed as 87(60%) patients were male and 58(40%) patients were female.

Status of thyroid function among 145 patients was analyzed as all the patients had T4 range 0.93-1.70 ng /dl. Whereas 109(75%) patients had TSH range  $\leq 0.27 - 4.0 \mu$ IU/ml and 36(25%) patients had TSH  $>4.0 \mu$ IU/ml. Mean TSH was 4  $\mu$ IU/ml with standard deviation  $\pm 2.37$ . (Table-I)

Subclinical hypothyroidism among 145 patients was analyzed as 36(25%) patients had subclinical hypothyroidism in CKD while 109(75%) patients didn't had subclinical hypothyroidism in CKD. (Table-II)

Stratification of subclinical hypothyroidism with age and gender is given in Table-III and Figure-1. respectively.

T4	Frequency	Percentage
0.93-1.70 ng /dl	145	100%
> 0.93-1.70 ng /dl	0	0%
Total	145	100%
TSH	Frequency	Percentage
≤ 0.27 - 4.0μIU/ml	109	75%
> 4.0μIU/ml	36	25%
Total	145	100%

**Table-I. Status of thyroid function test (T4 and TSH). (n=145).**

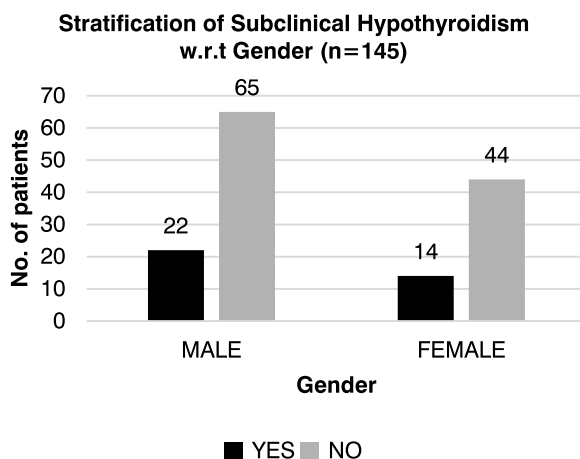
Mean T4 was 1.1 ng/dl with standard deviation ± 1.12, while Mean TSH was 4μIU/ml with standard deviation ± 2.37

Hypothyroidism	Frequency	Percentage
Yes	36	25%
No	109	75%
Total	145	100%

**Table-II. Subclinical Hypothyroidism. (n=145).**

Hypo-thyroidism	31-40 years	41-50 years	51-60 years	61-70 years	Total
Yes	5	8	11	12	36
No	17	24	32	36	109
Total	22	32	43	48	145

**Table-III. Stratification of subclinical hypothyroidism W.R.T age. (n=145)**



**Figure-1**

Chi Square test was applied in which P value was 0.8752

## DISCUSSION

Chronic kidney disease is a silent global epidemic. The exact prevalence of CKD in Pakistan is not known, but given the fact that diabetes mellitus, which is the most common cause of CKD, is very common in Pakistan; therefore it is not surprising that CKD will be highly prevalent in Pakistan.<sup>11</sup>

We included 145 patients in our study of which 87 were males while 58 were females. Mean+SD of age was 55+2.83. Twenty five percent patients had subclinical hypothyroidism in CKD.

Internationally, a study conducted shows a prevalence of 24.4% with subclinical hypothyroidism in chronic kidney disease.<sup>7</sup> Another show a prevalence of 56% with hypothyroidism in chronic kidney disease.<sup>9</sup> Nationally, a study by Asif et al shows a prevalence of 53.8% with subclinical hypothyroidism.<sup>10</sup>

Literature has reported that 4% to 10% of general population suffers from subclinical hypothyroidism<sup>11</sup> and the prevalence is estimated to be higher in the elderly i.e up to 26%.<sup>12</sup> Similarly, numerous studies in the past showed that thyroid disorders were even more common in patients with CKD.<sup>7,13</sup> In addition, some of these studies reported thyroid abnormalities in CKD patients have higher mortality and morbidity compared to those who have normal thyroid profile.<sup>4,14</sup> A number of factors are believed to cause this higher mortality; some of these include the presence of autoimmunity, deranged iodine metabolism and increased peripheral resistance.

Currently, more research is going on to determine the prevalence of hypothyroidism with regards to the stage of chronic kidney disease. In this regard Lo *et al.* recently reported that subclinical and clinical hypothyroidism was more common in patients with higher stage of kidney disease compared to others. They noted that the frequency of hypothyroidism was more than 20% in patients with eGFR <60 ml/min per 1.73 m.<sup>15,16</sup> In our study the prevalence was found to be 25%. The differences in our results may be due to that in Lo et al, the study population was much younger and total T4 levels assessment

was done as opposed to FT4 levels.

Subclinical hypothyroidism has a number of etiological causes with autoimmune thyroid disease being the most common. Other less common causes include drugs, subacute thyroiditis, radiation thyroiditis, and postpartum thyroiditis.<sup>17-19</sup> Subclinical hypothyroidism has been demonstrated to adversely affect the cardiac functioning. In addition, it is now reported that it may deteriorate the risk factors for ischemic heart disease especially hypertension and dyslipidemia.<sup>20,21</sup>

Our study was not without limitations. Firstly, our sample size was small and larger sample size is required to establish any relationship between hypothyroidism and chronic kidney disease. Secondly, we relied on eGFR which does not accurately measures the renal function and are thus subjected to errors. Thirdly, we could not identify and separate patients with sick euthyroidism and finally, we did not stratify our patients into different classes of CKD based on eGFR and thus did not correlate the frequency of hypothyroidism with the severity of CKD.

## CONCLUSION

Our study concludes that the incidence of subclinical hypothyroidism in chronic kidney disease was found to be reasonably high in our population. We therefore recommend that there should be high level of suspicion in considering the diagnosis of subclinical hypothyroidism in patients with CKD.





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### AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Tahir Rashid	Substantial contributions to the conception or design of the work.	
2	Irfan Mirza	The acquisition, Analysis or interpretation of data for the work.	
3	Abdul Rauf	Drafting the work or revising it critically for important intellectual content.	
4	Syed Hassan Mustafa	Drafting the work or revising it critically for important intellectual content.	
5	Talha Durrani	Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.	
6	Zarmeena Aftab	Drafting the work or revising it critically for important intellectual content.	