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Research Article

ASSESSMENT OF CPK, SERUM CREATININE AND eGFR IN PATIENTS WITH HYPOTHYROIDISM ON PRE AND POST TREATMENT IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone or, more rarely, from their impaired activity at tissue level. This study was designed to estimate the creatine phosphokinase(CPK), serum creatinine level and estimated glomerular filtration rate(eGFR) in hypothyroidism cases and to assess the correlation with T4 and TSH. This Study included 62 patients of hypothyroidism. There is a significant alteration in creatine kinase, creatinine, and estimated GFR(eGFR) in hypothyroid patients which may be due to renal and muscular damage resulting in renal failure and myopathies. Our study adds to the existing knowledge, the importance of periodic assessment of renal parameters and creatine kinase in hypothyroid patients and effect of hypothyroid treatment on these biochemical parameters.

Keywords: *Creatine phosphokinase,Serum creatinine, Estimated glomerular filtration rate,Thyroid stimulating hormone ,Tetraidothyronine, Hypothyroidism*

INTRODUCTION

Hypothyroidism is a clinical condition characterized by abnormally low thyroid hormone production. Primary hypothyroidism results when thyroid gland fails to produce adequate hormones. In secondary hypothyroidism the hypothalamic-pituitary–thyroid axis works inadequately.

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. Subclinical hypothyroidism is characterized by increased TSH and normal fT3, fT4 serum levels. Subclinical hypothyroidism affects virtually every tissue in the body. This includes slowing of physical and mental activity. Long standing hypothyroidism can cause reversible changes in the metabolic parameters such as increase in serum creatinine.

Thyroid dysfunction causes remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis. Hypothyroidism is accompanied by a decrease in glomerular filtration, elevation of serum creatinine and alteration of the ability for water excretion.

In recent years studies have been conducted to establish a relationship of creatine phosphokinase (CPK) levels in thyroid diseases A majority of patients with hypothyroidism have been shown to have an increased serum CPK. Serum CK was first used as a diagnostic aid in progressive muscular dystrophy. It has since then become important clinical marker for muscle damage. The serum CK levels in healthy individuals depend on age, race, and lean body mass and physical activity. Musculoskeletal disorders often accompany thyroid dysfunction. In addition to well-known observation that musculoskeletal disorders are common in patients with hypothyroidism, they are also observed in thyrotoxicosis and level of CK is altered in both these conditions. Skeletal muscle is affected by hypothyroidism more profoundly in cases of overt hypothyroidism and less so when subclinical hypothyroidism is present. The aim of this study is to

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estimate and compare serum creatinine level, estimated GFR and CPK in hypothyroid patients on pre and post treatment and to correlate with TSH, fT4. The primary objective of this study is to estimate the level of CPK, Serum creatinine and eGFR in newly diagnosed hypothyroid patients and also study the changes of Serum creatinine ,CPK and eGFR levels after control/treatment of hypothyroidism.The secondary objective include study the correlation between CPK, serum creatinine and eGFR with TSH and T4.Medication adherence of hypothyroid patients were also studied.

METHODS

This prospective experimental study was conducted in Endocrinology OP, Department of General medicine at Pushpagiri Medical College Hospital Thiruvalla, Kerala. It was a 6 months study in which patients are recruited based on the inclusion and exclusion criteria. The study was designed as a 6 weeks follow up study in 62 patients. All patients were given a brief introduction of regarding the study and the confidentiality of data. A written informed consent was obtained from the patient or care giver. The level of TSH and T4 was obtained from medical records. For the determination of CPK and serum Creatinine residual blood is collected from laboratory and test were carried out by using semi automatic analyzer of Pushpagiri College of Pharmacy. The eGFR can be calculated by using MDRD(Modification of diet in renal disese) formula. After 6 weeks, the blood sample is collected again and measure CPK,serum creatinine and eGFR.TSH and T4 level is also recorded.

GFR (mL/min/1.73 m^2) = 175 × $(S_{cr})^{-1.154}$ × $(Age)^{-0.203}$ × (0.742 if female) × (1.212 if African American)

Medication adherence can be evaluated by using MMAS-8 scale.

Inclusion criteria:

1. OP patients
2. Both male and female patients whose TSH level is ≥10 µIU/L
3. Patients on age group above 18 years
4. Patients who are willing to sign the informed consent form.

Exclusion criteria:

1. Pregnancy
2. Paediatric patients
3. Patients with TSH level<10 µIU/L
4. Those who are unable to give informed consent form.

Ethical consideration:

The Institutional ethics committee clearance was obtained, after that study is started. Informed consent was obtained from all patients who met the inclusion criteria were enrolled for the study.

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Statistical analysis:

Analysis of data was done using SPSS VERSION 20.00 statistical software and Mean ± standard deviation of different parameters were compared to determine the difference between two groups by paired 't' test. The significant level were determined by p value. P value less than < 0.05 was considered as significant.

RESULTS

Table 1: Distribution of patients based on age group

Age	Frequency	Percent	Mean±SD	Min	Max
Below 30	16	25.8	39.31±13.91	18	74
30 - 40	23	37.1			
41 - 50	12	19.4			
51 - 60	4	6.5			
Above 60	7	11.3			
Total	**62**	**100.0**			

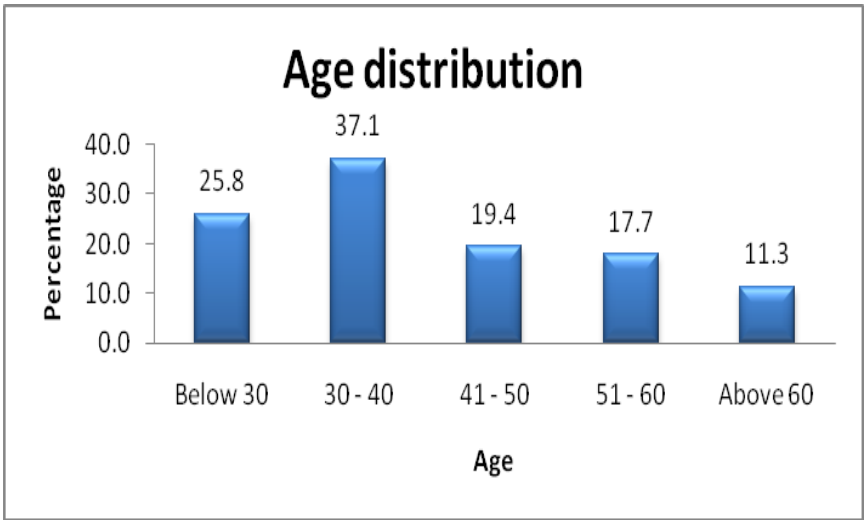

Figure 1: Distribution of patients based on age group

Figure (1) showed the distribution of study samples according to age group, In this study most of the population falls under age group of 30-40.

Table 2: Distribution of patient based on gender

Sex	Frequency	Percent
Male	18	29.0
Female	44	71.0
Total	**62**	**100.0**

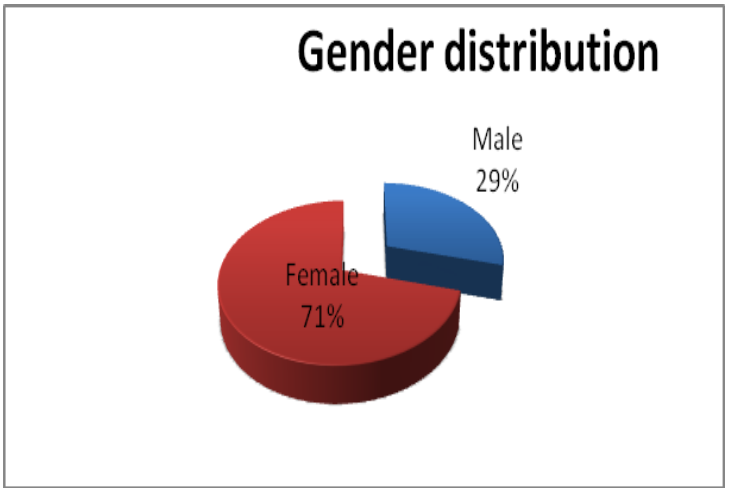

Figure 2: Distribution of patient based on gender

Figure (2) showed the distribution of study samples according to genders. The study had 62 patients, were 44 females which represents (71%) and 18 were males which represents (29%).

Table 3: Comparison of subjects with respect to TSH on consultation and after 6 week

TSH	Mean	SD	Mean difference	95% Confidence Interval of the Difference	Paired t value	P value
On consultation	38.92	36.53	36.95	27.82 – 46.07	8.100	P<0.001
After 6 weeks	1.88	1.84				

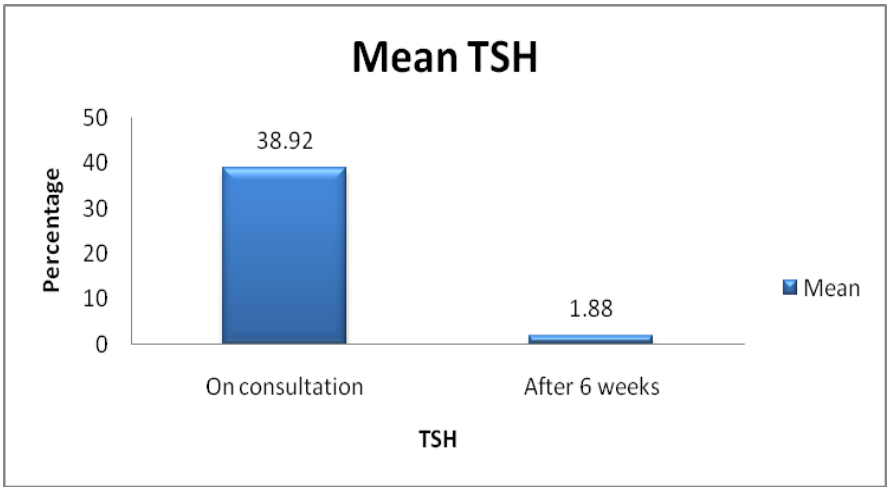

Figure 3: Comparison of subjects with respect to TSH on consultation and after 6 week

Figure (3) showed that on consultation the TSH value of patients were 38.92 µIU/L,which is significantly reduced into 1.88µIU/L after 6 week of treatment. Since P value less than 0.001, the TSH value was significantly decreased after 6 weeks.

Table 4: Comparison of subjects with respect to T4 on consultation and after 6 week

T4	Mean	SD	Mean difference	95% Confidence Interval of the Difference	Paired t value	P value
On consultation	8.32	4.14	8.01	6.63 – 9.4	11.57	P<0.001
After 6 weeks	16.34	3.66				

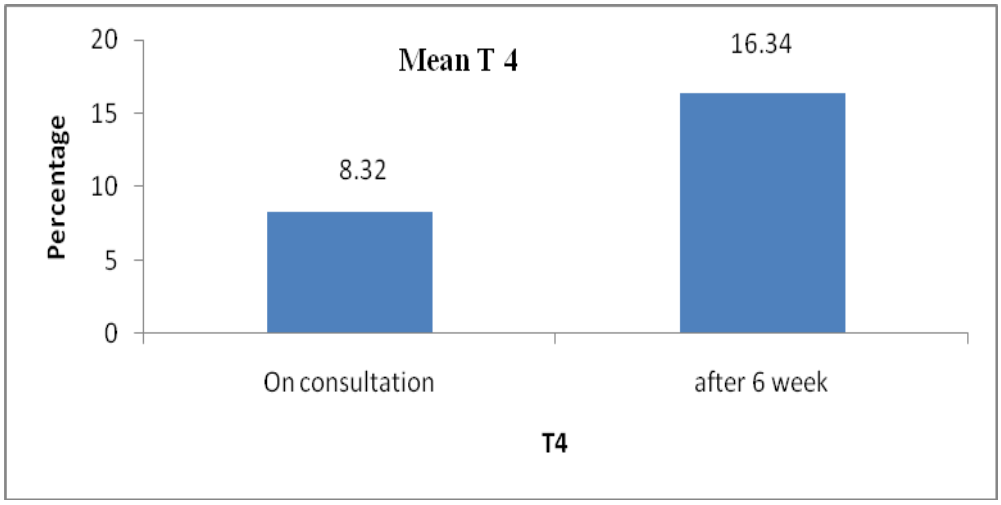

Figure 4: Comparison of subjects with respect to T4 on consultation and after 6 week

Figure (4) showed that, on consultation mean T4 is 8.32 and after 6 week it is 16.34. Since P value less than 0.05, the T4 value was significantly increased after 6 weeks

Table 5: Comparison of CPK on consultation and after 6 week with respect to age.

Age	CPK				Paired t value	P value
	On consultation		After 6 weeks			
	Mean	SD	Mean	SD		
Below 30	273.41	279.24	106.93	42	2.496	0.025
30 - 40	255.19	232.39	91.72	41.04	3.472	0.002
41 - 50	168.51	72.28	80.7	38.4	4.272	0.001
51 - 60	251.6	41.16	56.12	20.72	6.717	0.007
Above 60	262.86	312.37	83.96	43.25	1.616	0.157

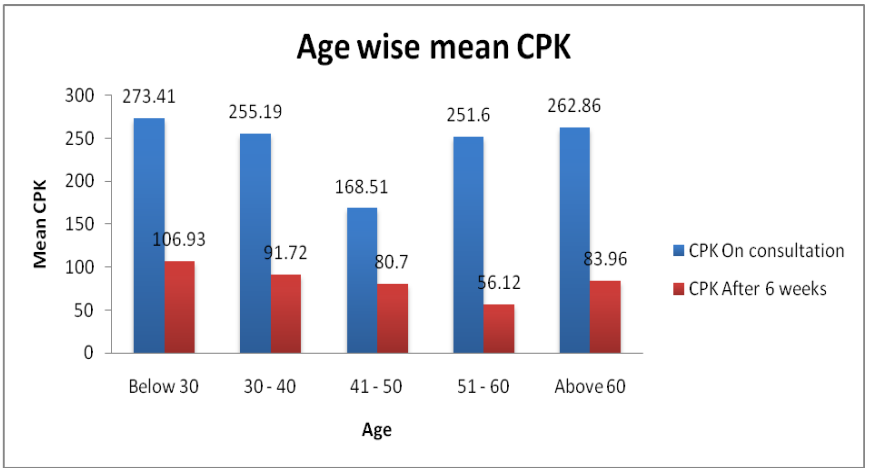

Figure 5: Comparison of CPK on consultation and after 6 week with respect to age.

Figure (5) ,showed that age group of below 30 years shows more prone to rise in CPK than other groups. Age group of 41-50 shows no abnormal rise in CPK. All age groups of CPK values are normalized after 6 weeks of hypothyroidism treatment.

Table 6: Comparison of serum creatinine on consultation and after 6 week with respect to age

Age	SERUM CREATININE				Paired t value	P value
	On consultation		After 6 weeks			
	Mean	SD	Mean	SD		
Below 30	1.44	0.91	0.71	0.17	3.358	0.004
30 - 40	1.6	0.82	0.76	0.24	5.172	P<0.001
41 - 50	1.69	0.54	0.74	0.19	5.112	P<0.001
51 - 60	2.02	1.32	0.68	0.18	1.893	0.155
Above 60	1.69	1.36	0.6	0.12	2.084	0.082

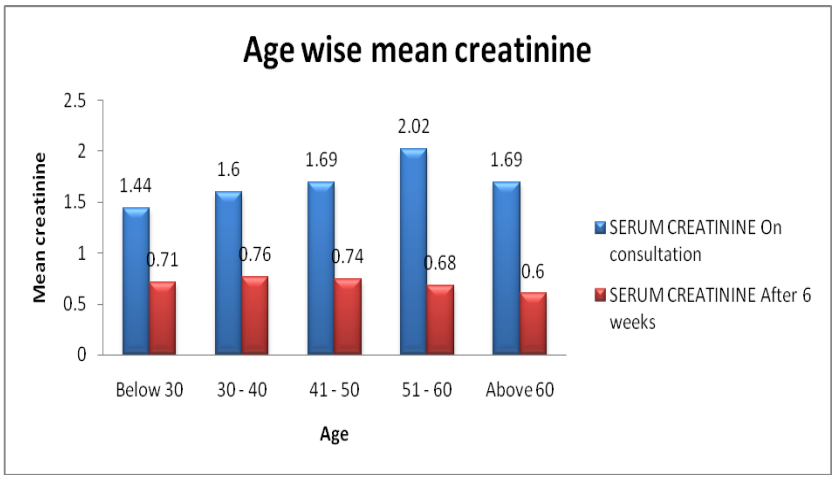

Figure 6: Comparison of serum creatinine on consultation and after 6 week with respect to age

Figure (6) showed that mean serum creatinine of all age groups were increased on consultation and decreased after 6 weeks treatment of hypothyroidism.

Table 7: Comparison of e GFR on consultation and after 6 week with respect to age

Age	e GFR				Paired t value	P value
	On consultation		After 6 weeks			
	Mean	SD	Mean	SD		
Below 30	85.4	68.42	131.59	59.98	2.767	0.014
30 - 40	67.4	65.89	111.23	45	3.127	0.005
41 - 50	46.98	18.49	117.77	44.14	4.988	P<0.001
51 - 60	45.35	41.7	127.88	29.83	2.663	0.076
Above 60	60.47	37.72	125.23	64.24	1.975	0.096

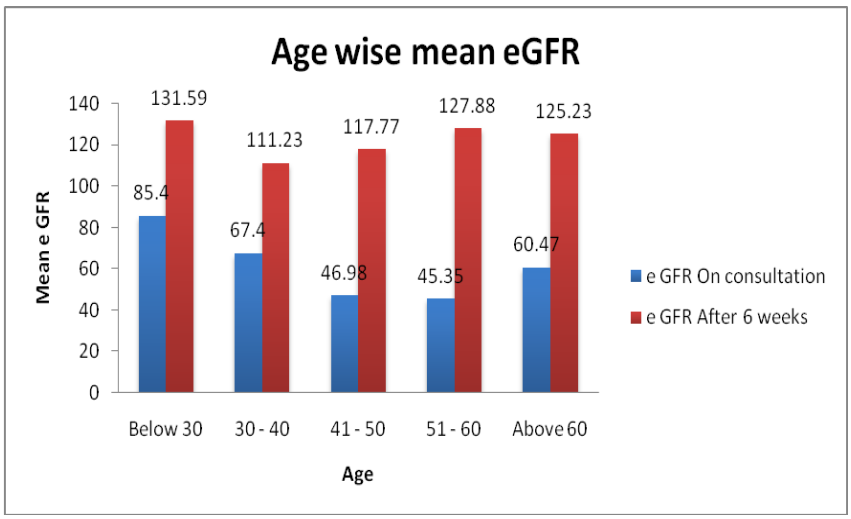

Figure 7: Comparison of e GFR on consultation and after 6 week with respect to age

Figure (7) showed that, significant mean differences in, on consultation and after 6 weeks of eGFR values. This shows a significant increase in e GFR after control of hypothyroidism.

Table 8: Correlation between CPK, serum creatinine and e GFR with TSH and T4

Pair of Variables	Pearson Correlation	P value
TSH - T4	-0.609	P<0.001
TSH – CPK	0.673	P<0.001
TSH - SERUM CREATININE	0.673	P<0.001
TSH - e GFR	-0.326	0.01
T4 – CPK	-0.511	P<0.001
T4 - SERUM CREATININE	-0.517	P<0.001
T4 - e GFR	0.356	0.005
CPK - SERUM CREATININE	0.705	P<0.001
CPK - e GFR	-0.338	0.007
e GFR - SERUM CREATININE	-0.716	P<0.001

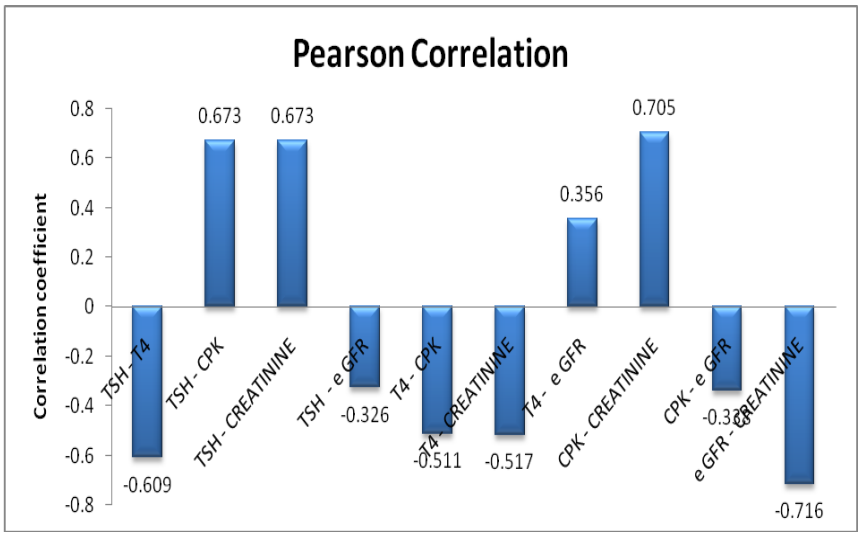

Figure 8: Correlation between CPK, serum creatinine and e GFR with TSH and T4

Figure (8) showed that TSH shows positive correlation with CPK, serum creatinine and negative correlation with e GFR and T4.And T4 shows positive correlation with e GFR and negative correlation with CPK and serum creatinine.

Table 9: Medication adherence of hypothyroid patients

MEDICATION ADHERENCE	Frequency	Percent
Poor	8	12.9
Medium	19	30.6
High	35	56.5
Total	62	100.0

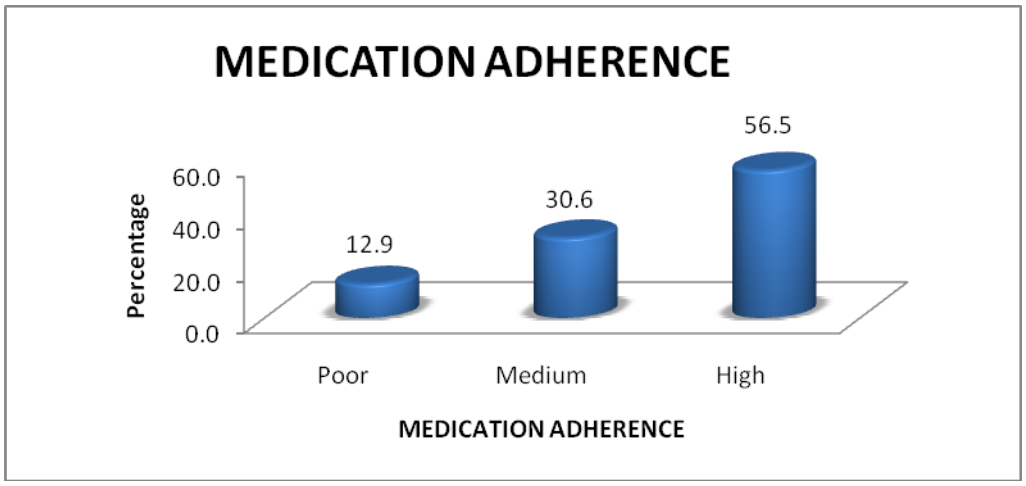

Figure 9: Medication adherence of hypothyroid patients

From the table and figure 17 shows hypothyroid patients have high medication adherence (56.5%).

DISCUSSION

- In this study TSH value is significantly high,and T4 value is decreased than its normal range.
- On consultation mean of TSH value of patients were 38.92%,which is significantly reduced into 1.88% after 6 week of treatment. Since P value less than 0.05,So the TSH value was significantly decreased after 6 weeks.
- The T4 value should be significantly increased after 6 week of treatment.That is on consultation is 8.32 and after 6 week it is 16.34. The percentage of abnormal values on admission was 61.3% and was significantly reduced to 8.1% after 6 weeks. The P value obtained was 0.048 and is less than 0.05, it is concluded that the difference is statistically significant at 5% level of significance.
- Based on age group with respect to abnormal CPK values,age group of below 30 years shows more prone to rise in CPK than other groups. Age group of 41-50 shows no abnormal rise in CPK. All age groups of CPK values are normalized after 6 weeks of treatment.
- Based on age group with respect to abnormal serum creatinine values, on consultation all age groups shows abnormal rise of serum creatinine.The age group of 51-60 shows most prominent rise in serum creatinine(2.02).After 6 week the serum creatinine will be significantly reduced to its normal range(0.68).
- Based on age group with respect to abnormal eGFR values, shows a significant mean differences in, on consultation and after control (6 week) of hypothyroidism.It shows that there was a significant increase in eGFR after control of hypothyroidism($p < 0.05$).
- The study shows, positive correlation between TSH with CPK and TSH with serum creatinine, also shows positive correlation on T4 with eGFR, and CPK with serum creatinine. Negative correlation shows TSH with T4 and,TSH with eGFR and T4 with creatinine ,T4 with CPK, CPK-eGFR, eGFR-creatinine.
- Medication adherence was measured out by using morisky medication adherence scale-8.

Among 62 patients 56.5% (35) shows high thyroid medication adherence.30.6% (19) shows medium adherence and only 12.9% (8) patients shows poor adherence.

CONCLUSION

Patients with hypothyroidism can gradually end up with renal dysfunction and myopathies. This can be prevented by monitoring thyroid hormones levels along with periodic assessment of renal parameters (creatinine and eGFR) and creatine kinase in hypothyroid patients. This may beneficial in reducing the morbidity of patients.So this research shows reversible changes of serum creatinine ,creatine phosphokinase and estimated glomerular filtration rate in patients after treatment of hypothyroidism.The primary choice of hypothyroidism treatment include levothyroxine replacement therapy.

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