



Prevalence of Microalbuminuria in Patients with Thyroid Dysfunction

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Abstract

Background: In India, 42 million people suffer from various kinds of thyroid disorders. Thyroid dysfunction and microalbuminuria are associated with endothelial dysfunction. Thus establishing a relationship between the two can play a significant role in prevention of endothelial dysfunction and hence modify diseases like obesity hypertension, diabetes, chronic kidney disease, cardiovascular disease which also have endothelial dysfunction as their basic pathology.

Aim: To study the prevalence of microalbuminuria in patients with thyroid dysfunction.

Materials & Methods: A cross-sectional study done among 100 newly diagnosed thyroid dysfunction patients who are screened for the presence of microalbuminuria along with lipid profile, fasting and post prandial blood sugar along with clinical history. The data collected is analyzed with SPSS version 23.

Results: The prevalence of microalbuminuria in patients with thyroid dysfunction is found to be 43%. In univariate analysis, subjects with subclinical hypothyroidism had 1.08 to 5.63 times higher odds of having microalbuminuria compared to other study subjects and subjects with overt hypothyroidism had 5.03 to 40.9 times higher odds of having microalbuminuria compared to other study subjects both with a significant *p* value of 0.01.

Conclusion: Overt Hypothyroidism is a strong and significant predictor of microalbuminuria compared to subclinical hypothyroidism. Also an inverse relationship between the FT3 and FT4 levels with microalbuminuria is noted.

Keywords: Overt Hypothyroidism, Subclinical Hypothyroidism, endothelial dysfunction and Microalbuminuria.

Introduction

Diseases of the thyroid gland are common across the world. According to various studies it is estimated that around 42 million people in India

suffer from thyroid diseases with goiter, hypothyroidism, hyperthyroidism, hashimoto's disease and carcinoma of the thyroid being the most common entities^[1]. Microalbuminuria, defined as urine albumin to creatinine ratio of 30

to 300mg/g is a valuable marker that predicts endothelial dysfunction^[2]. Hence microalbuminuria has been linked to Diabetes Mellitus, Chronic Kidney Disease and Cardiovascular disease (CVD) where there is generalized endothelial dysfunction.^[3,4] Also previous studies confirming the association of microalbuminuria to cardiovascular disease and mortality has been well established^[5,6]. There is however insufficient data relating thyroid disorders with microalbuminuria. The terms overt and subclinical hypothyroidism can be made only in the absence of severe ongoing illness, when the TSH values have been stable for weeks and when the hypothalamo-pituitary axis is not altered. Subclinical hypothyroidism is a disorder where there is elevated serum Thyroid Stimulating Hormone (TSH) with Free T3, Free T4 (FT3, FT4) in the normal range^[7,8]. Studies done on subclinical hypothyroidism show that there is higher prevalence among women as compared to men with a peak of 21% in women and 16% in men over 74 years of age^[1]. Subclinical hypothyroidism is also associated with coronary artery disease and independent of serum cholesterol levels have been proved to be linked to aortic atherosclerosis and myocardial infarction in elderly women^[9,12]. In the presence of concomitant thyroiditis, due to inflammation and autoimmunity endothelial dysfunction occurs^[11]. The prevalence of subclinical and overt hyperthyroidism based on an epidemiological study conducted at Cochin was found to be 1.6% and 1.3% respectively. More than one-third of the patients of the community detected hyperthyroidism had anti-TPO antibody positive^[1]. Albuminuria is closely associated with metabolic syndrome comprising of syndrome of insulin resistance, hypertension, obesity and dyslipidemia^[12,13]. Also thyroid disorders are known to alter the metabolism of lipids and tend to have an adverse effect on the lipid profile^[14,10]. Added to this hyperthyroidism maybe attributed as an underlying cause for acquired hypercholesterolemia. From the above statements it is likely

that there may be a relationship between microalbuminuria and thyroid disorders. Thus microalbuminuria as an indicator of vascular damage secondary to endothelial dysfunction is well known^[9,15]. So our study relating thyroid hormones to microalbuminuria may throw some light in the preventive aspects of the entire spectrum of diseases associated with endothelial damage.

Aim of the study

To study the prevalence of microalbuminuria in patients with thyroid dysfunction in a tertiary care centre.

Materials and Methods

100 Patients in the age group of 18-85 years with thyroid dysfunction attending our outpatient department are selected after obtaining due consent, a cross sectional study for a period of 6 months is conducted. *Inclusion criteria:* Newly detected thyroid disorder patients by thyroid function test with the following values taken to diagnose the derangement. Serum Free T3: 2.4-4.2pg/ml Serum Free T4:0.7-1.24ng/dl TSH:0.34-4.25µIU/ml. *Exclusion Criteria:* Patients on treatment for hypo or hyperthyroidism, or with history of thyroidectomy, or on drugs that alter thyroid function such as amiodarone, lithium, anti-epileptics etc, or overt proteinuria, known cases of diabetes mellitus, systemic hypertension, coronary artery disease and chronic kidney disease or pregnancy were excluded from the study.

Method of Study: Patients attending the general medicine outpatient department were randomly selected and evaluated for thyroid dysfunction using a thyroid profile test. Investigations included lipid profile, blood urea nitrogen, fasting and post prandial blood sugar along with detailed history. All participants were advised to refrain from heavy exercise the day before. A single void first morning urine sample is obtained for urinary albumin-creatinine ratio measurement. Statistical Analysis was done by SPSS version 23 (demo

version). Continuous variables were expressed as Mean with Standard deviation. Categorical variables were expressed in numbers and percentages. Chi square test with or without Yates correction and Fischers test was used for univariate analysis. Factors significant by univariate analysis were taken for multivariate analysis. P value of less than 0.05 is considered statistically significant for rejecting null hypothesis.

Results

The characteristics with all the variables in the study population in Table 1. In our study of the 100 subjects taken, 88 are females and 12 are males (Table 2). Maximum 33% are in the age group of 46-55 years (Table 2, Figure1). 40% are healthy and 37% are overweight (Table 3). 88% of the study subjects have a normal glycemic status. The rest of 12% has impaired glucose tolerance (Table 4, Figure 2). It is found that 47% of the patients has microalbuminuria (Table 13) as shown with abnormal urine albumin creatinine ratio. 94% of the study subjects has normal triglyceride levels. Only 6% of the total has elevated triglyceride levels (Table 5, Figure 3). 45 patients has normal Total cholesterol levels and the rest 55 patients has borderline to high total cholesterol levels (Table 6, Figure 4). Table 7 shows that 97% patient has normal serum albumin and 3% with hypoproteinemia. Among the 100 subjects in the study 78% are hypothyroid with 33% of the subjects having overt hypothyroidism and the rest, 45% having subclinical hypothyroidism. Remaining 22% had hyperthyroidism of which 19 patients are having overt hyperthyroidism and 3 are having subclinical hyperthyroidism (Table 8, Figure 5). Among the various age groups, analysis revealed that majority(27%) of the patients with hypothyroidism fall in the age group between 46 to 55 years and the lowest prevalence of hypothyroidism of 4% was in the age group between 16 to 25 years(Table 9, Figure 6). The highest prevalence of hyperthyroidism(6%) is also

in the same range of 16 to 25 yrs as with hypothyroidism. 15 patients with overt hypothyroidism and 22 patients with subclinical hypothyroidism were overweight. 4 with overt and 8 with subclinical hypothyroidism has class 1 obesity. None of the patients with hyperthyroidism were overweight or obese(Table 10, Figure 7). 14 females with dyslipidemia has overt hypothyroidism while 15 has subclinical hypothyroidism. A total of 7 females with dyslipidemia has hyperthyroidism(Table 11, Figure 8). A total of 11 females with hypothyroidism has impaired glucose tolerance and only one with hyperthyroidism shows impaired glucose tolerance(Table 12, Figure 9).

Of the 100 subjects in the study 57 are in normal range of albuminuria and 43 has microalbuminuria out of which 36 were females and 7 were males. Of the 78 subjects with hypothyroidism 37 fell into the normal albuminuria range. The rest 41 has microalbuminuria. Among them 27 patients with overt hypothyroidism has microalbuminuria and 14 with subclinical hypothyroidism has microalbuminuria. 20 subjects with hyperthyroidism has normal protein excretion with one each with subclinical and overt hyperthyroidism having microalbuminuria(Table 13, Figure 10). On analyzing the FT3 levels in 43 patients with microalbuminuria it was found that 30 has FT3 between the range of 0.5 to 2.5 pg/ml and the rest 13 has FT3 in the range of 2.51 to 4.50pg/ml. There is a negative correlation of FT3 with microalbuminuria with a p value of 0.01(Table 14, Figure 11). On comparing the FT4 ranges in the 43 subjects with microalbuminuria it is found that 28 has levels less than 0.7ng/dl, 14 in between the range 0.7 to 1.24ng/dl and 1 above 1.24ng/dl. Again there is a negative correlation of FT4 with microalbuminuria with a p value of 0.01(Table 15, Figure 12). 41 patients with microalbuminuria has TSH levels above 4.25mIU/ml and 2 patients with less than 0.34mIU/ml. Here we infer that there is a positive correlation of TSH with microalbuminuria with a

p value of 0.01 (Table 16, Figure 13). In univariate analysis of risk factors for microalbuminuria, only subclinical and overt hypothyroidism has significant association. Presence of dyslipidemia, impaired glucose tolerance, BMI, Age and Sex had no significant association with microalbuminuria. The factors significant by univariate analysis are then taken

for multivariate analysis and the results are as shown below. Overt Hypothyroidism is a strong and significant predictor of microalbuminuria compared to subclinical hypothyroidism in both univariate and multivariate analysis.

Table 1: Characteristics of the study population

S.no.	Variables	Mean \pm standard deviation	95% confidence interval of the mean
1.	Age of the Subject in years	47.67 \pm 13.77	44.94 to 50.4
2.	Body Mass Index	25.15 \pm 4.81	24.2 to 26.11
3.	Fasting Blood Sugar (FBS)	80.42 \pm 17.03	77.04 to 83.8
4.	Post Prandial Blood Sugar (PPBS)	126.09 \pm 12.86	123.54 to 128.64
5.	Blood Urea Nitrogen (BUN)	15.31 \pm 3.27	14.66 to 15.96
6.	Total Protein	7.24 \pm 0.63	7.12 to 7.37
7.	Serum Albumin	4.19 \pm 0.51	4.09 to 4.29
8.	Serum Creatinine	0.892 \pm 0.282	0.836 to 0.948
9.	Free T ₃	3.07 \pm 1.43	2.79 to 3.36
10.	Free T ₄	1.27 \pm 1.09	1.05 to 1.49
11.	Thyroid Stimulating Hormone (TSH)	6.61 \pm 4.20	5.77 to 7.44
12.	Total Cholesterol	206.99 \pm 52.36	196.6 to 217.38
13.	Triglycerides	110.96 \pm 36.83	103.65 to 118.27
14.	Urine Albumin Creatinine Ratio	64.07 \pm 76.02	48.99 to 79.15

Table 2: Age and Sex distribution

Age	Male	Female	Total
18-25	0	6 (100%)	6
26-35	2 (16.7%)	10 (83.3%)	12
36-45	3 (13%)	20 (87%)	23
46-55	3 (9.1%)	30 (90.9%)	33
56-65	3 (20%)	12 (80%)	15
66-75	1 (12.5%)	7 (87.5%)	8
76-85	0	3 (100%)	3
Total	12 (12%)	88 (88%)	100

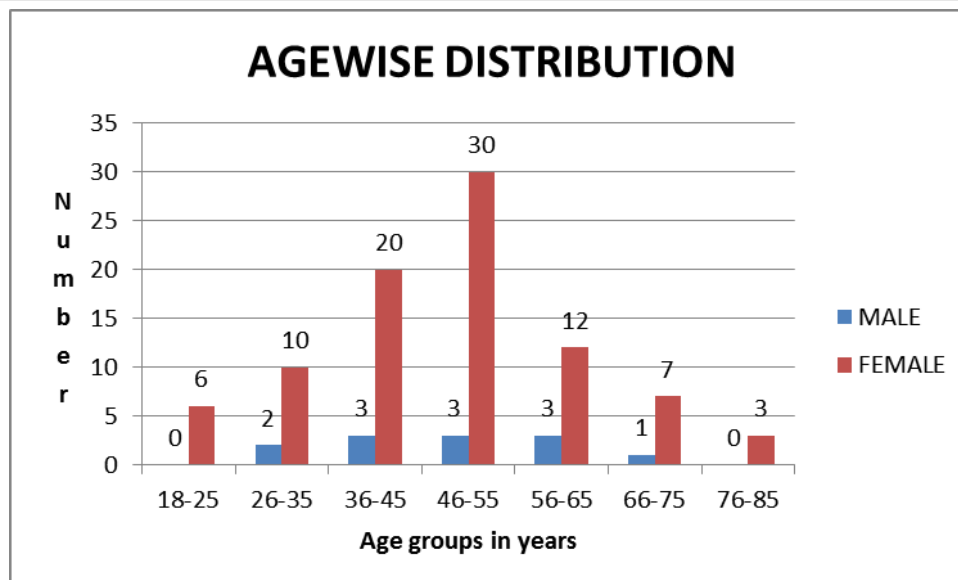


Figure 1: Age Distribution

Table 3: BMI and Age wise distribution

Age in years	Body mass index of the study population					
	<18.5	18.5-24.9	25-29.9	30-34.9	35-39.9	>=40
18-25	1 (11.1%)	1 (2.5%)	2 (5.4%)	2 (16.7%)	0	0
26-35	0	5 (12.5%)	7 (18.9%)	0	0	0
36-45	1 (11.1%)	10 (25%)	8 (21.6%)	4 (33.3%)	0	0
46-55	3 (33.3%)	12 (30%)	11 (29.7%)	5 (41.7%)	1 (100%)	1 (100%)
56-65	1 (11.1%)	6 (15%)	7 (18.9%)	1 (8.3%)	0	0
66-75	1 (11%)	5 (12.5%)	2 (5.4%)	0	0	0
76-85	2 (22.2%)	1 (2.5%)	0	0	0	0
Total	9	40	37	12	1	1

Table 4: Sex wise distribution of glycemc status in study subjects

Glycemc status of the subjects	Sexwise distribution		Total
	Male	Female	
Normal	11 (12.5%)	77 (87.5%)	88
IGT	1 (8.3%)	11 (91.7%)	12
DM	0	0	0

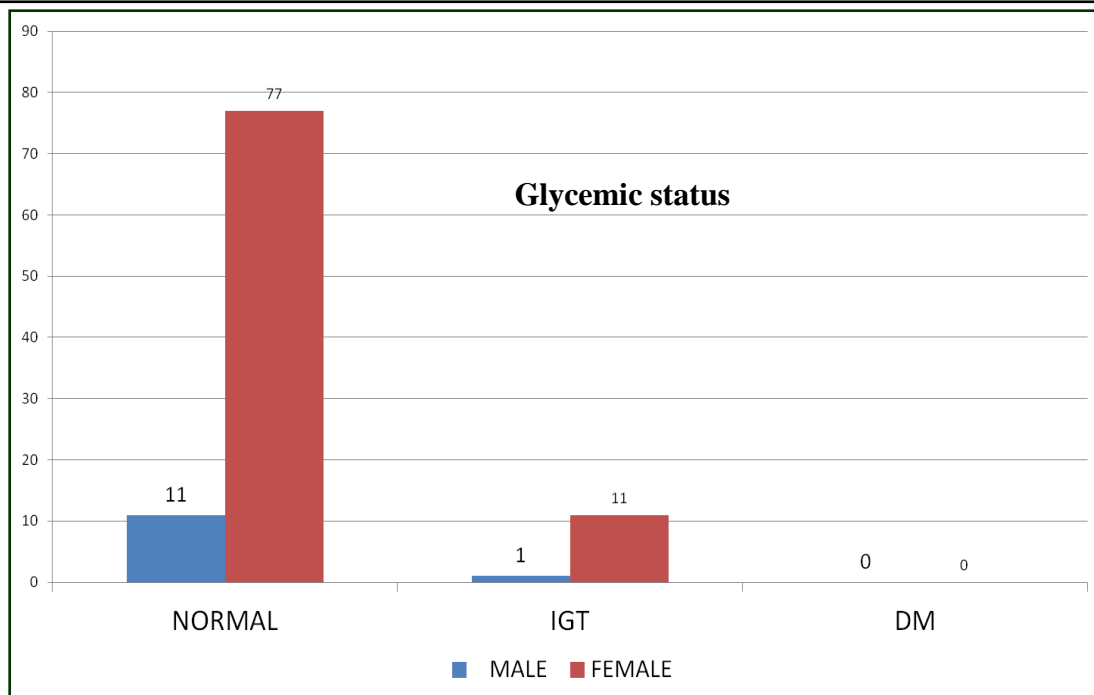


Figure 2: Glycemic Status of the study subjects.

Table 5: Serum Cholesterol levels of the study population

Serum cholesterol	Sexwise distribution		Total
	Male	Female	
Normal <200	7 (15.6%)	38 (84.4%)	45
Borderline 201 – 240	2 (11.8%)	15 (88.2%)	17
High >300	3 (7.9%)	35 (92.1%)	38

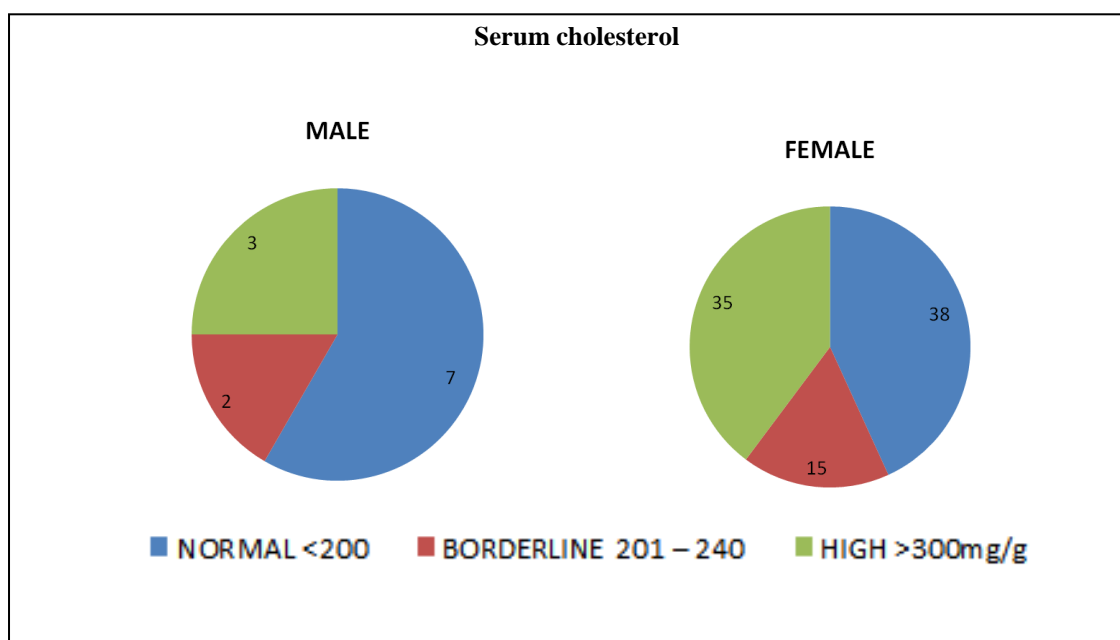


Figure 3: serum cholesterol of the study subjects.

Table 6: Serum Triglycerides levels of the study population

Serum Triglycerides	Sexwise distribution		Total
	Male	Female	
Low	0	0	0
Normal	11 (11.7%)	83 (88.3%)	94
High	1 (16.7%)	5 (83.3%)	6

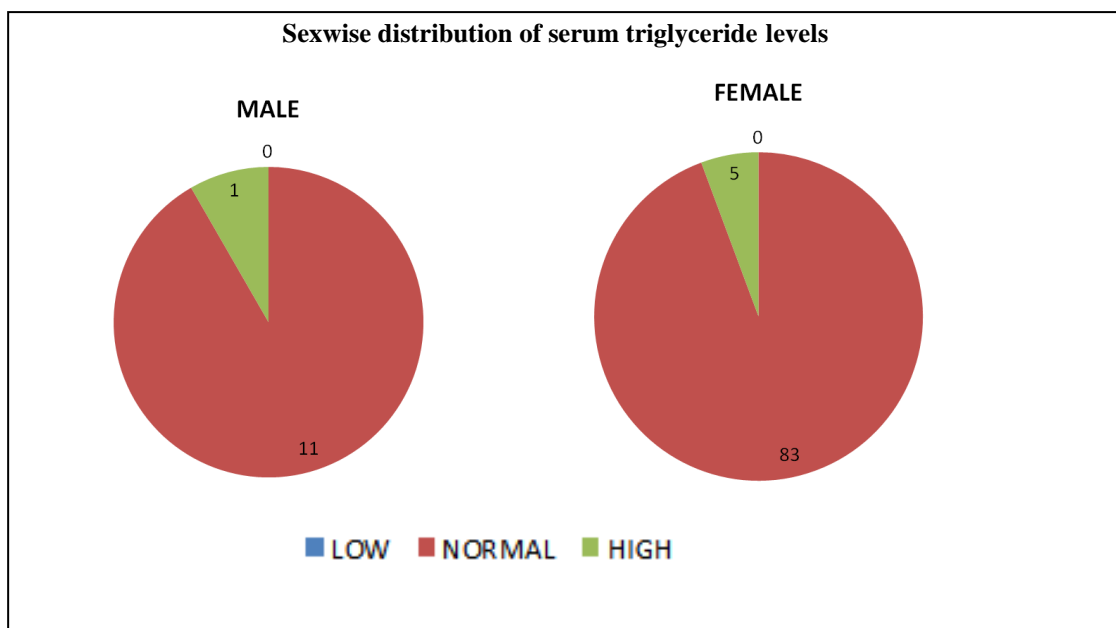


Figure 4: serum triglyceride levels of the study subjects.

Table 7: Sexwise distribution of Serum Albumin in study subjects

Serum albumin	Sexwise distribution		Total
	Male	Female	
Low	0	3 (100%)	3
Normal	12 (12.4%)	85 (87.6%)	97
High	0	0	0

Table 8: Sexwise distribution of thyroid dysfunction in study subjects

Sex	Thyroid dysfunction status			
	Overt hypothyroid	Subclinical hypothyroid	Overt hyperthyroid	Subclinical Hyperthyroid
Male	8	3	1	0
Female	25	42	18	3
Total	33	45	19	3

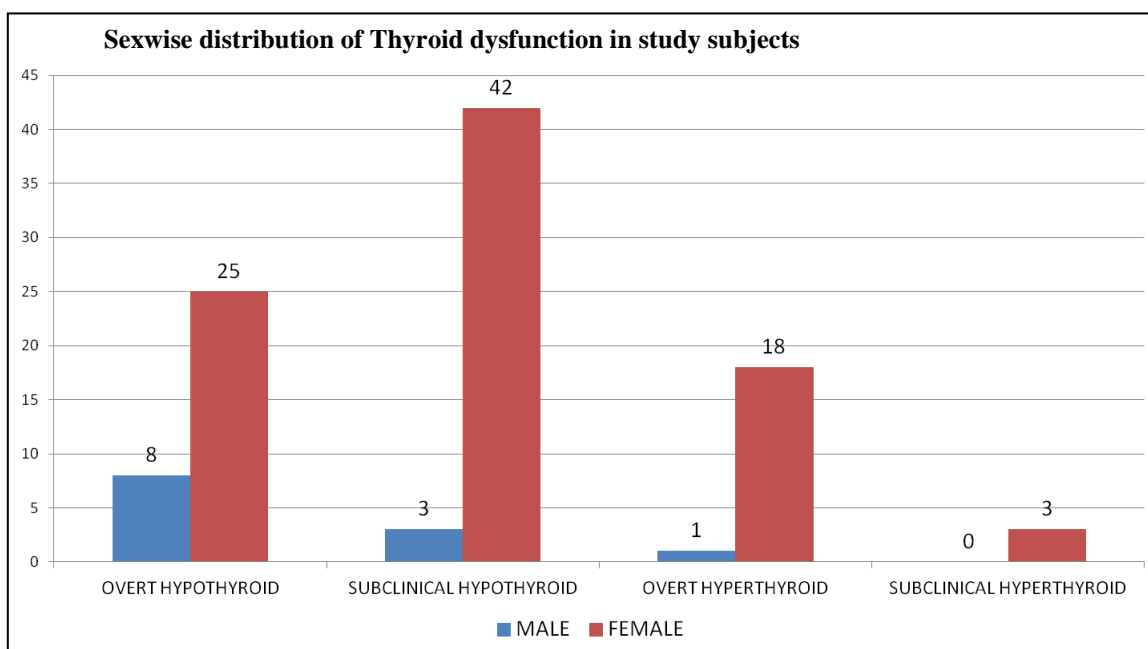


Figure 5: Sex Distribution of thyroid dysfunction in study subjects.

Table 9: Age wise distribution of thyroid dysfunction in study subjects

Age	Thyroid dysfunction status				Total
	Overt hypothyroid	Subclinical hypothyroid	Overt hyperthyroid	Subclinical Hyperthyroid	
18-25	0	4	2	0	6
26-35	5	6	0	1	12
36-45	12	6	5	0	23
46-55	11	16	5	1	33
56-65	4	8	2	1	15
66-75	1	4	3	0	8
76-85	0	1	2	0	3
Total	33	45	19	3	100

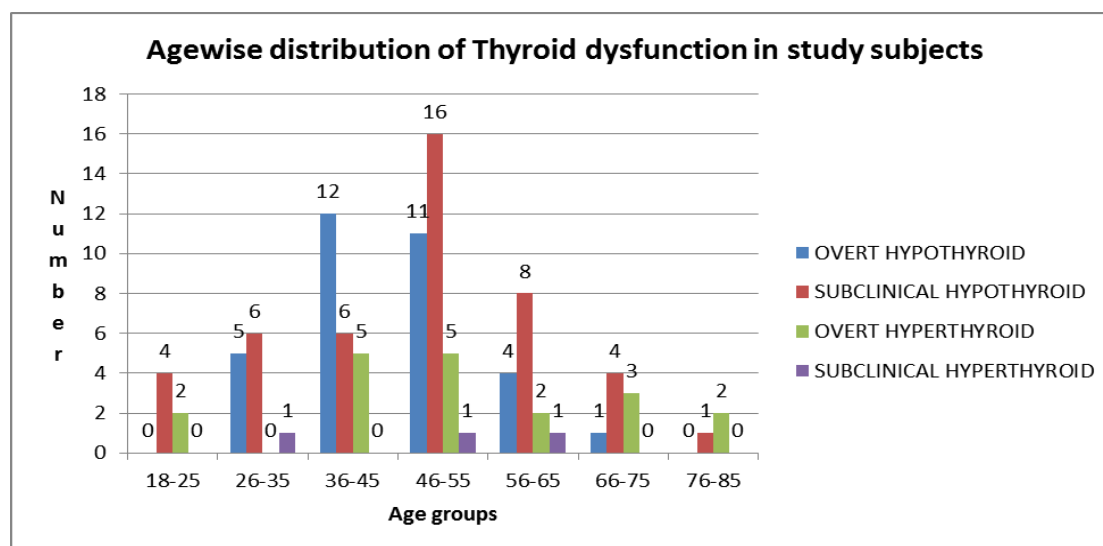


Figure 6: Sex distribution of thyroid dysfunction in study subjects

Table 10: BMI distribution of thyroid dysfunction in study subjects

BMI	Thyroid dysfunction status				Sex		Total
	Overt hypothyroid	Subclinical hypothyroid	Overt hyperthyroid	Subclinical Hyperthyroid	Male	Female	
Underweight	1	1	7	0	1 (11.1%)	8 (88.9%)	9
Healthy	13	12	12	3	6 (15%)	34 (85%)	40
Overweight	15	22	0	0	3 (8.1%)	34 (99.9%)	37
obesity class 1	4	8	0	0	2 (16.7%)	10 (83.3%)	12
Obesity class 2	0	1	0	0	0	1 (100%)	1
Obesity class 3	0	1	0	0	0	1 (100%)	1
Total	33	45	19	3	12	88	100

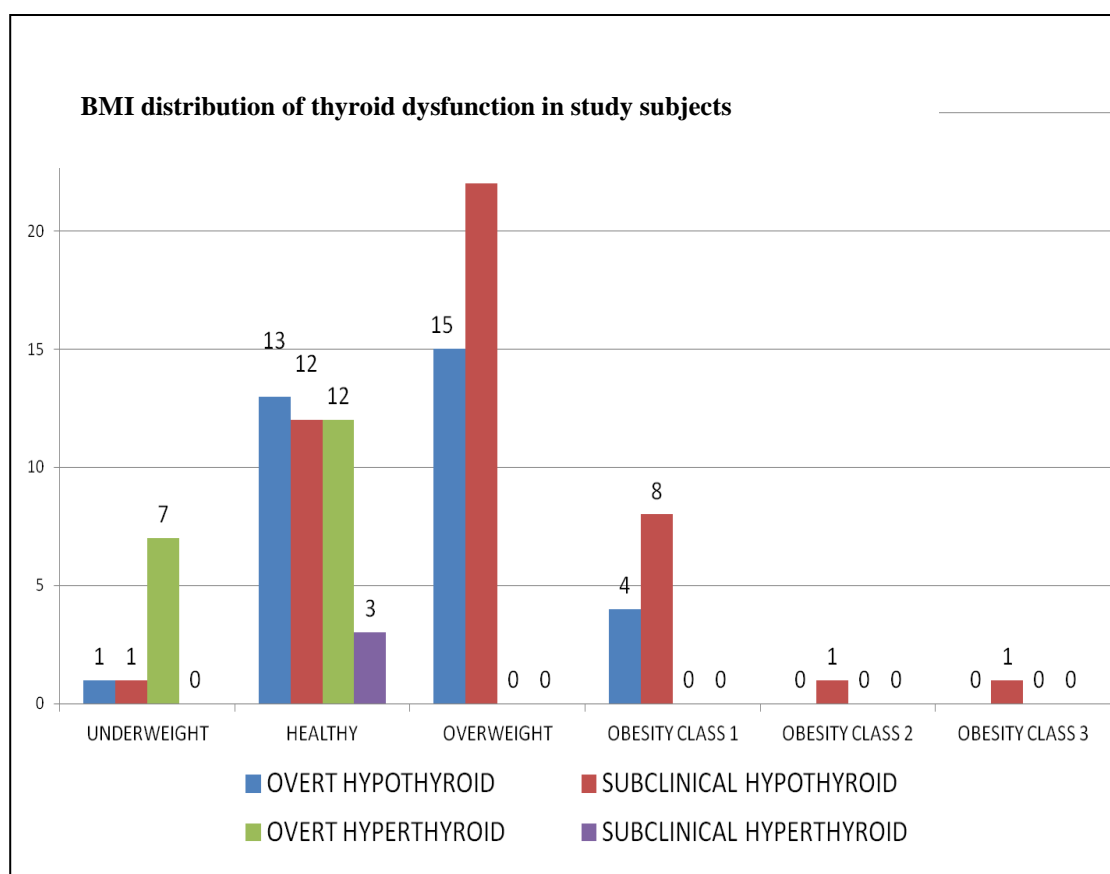


Figure 7: BMI distribution of thyroid dysfunction in study subjects.

Table 11: Sexwise distribution of dyslipidemia in patients with thyroid dysfunction

Sex	Thyroid dysfunction status			
	Overt hypothyroid	Subclinical hypothyroid	Overt hyperthyroid	Subclinical Hyperthyroid
Males With dyslipidemia	1	1	1	0
Females with dyslipidemia	14	15	5	1
Total	15	16	6	1

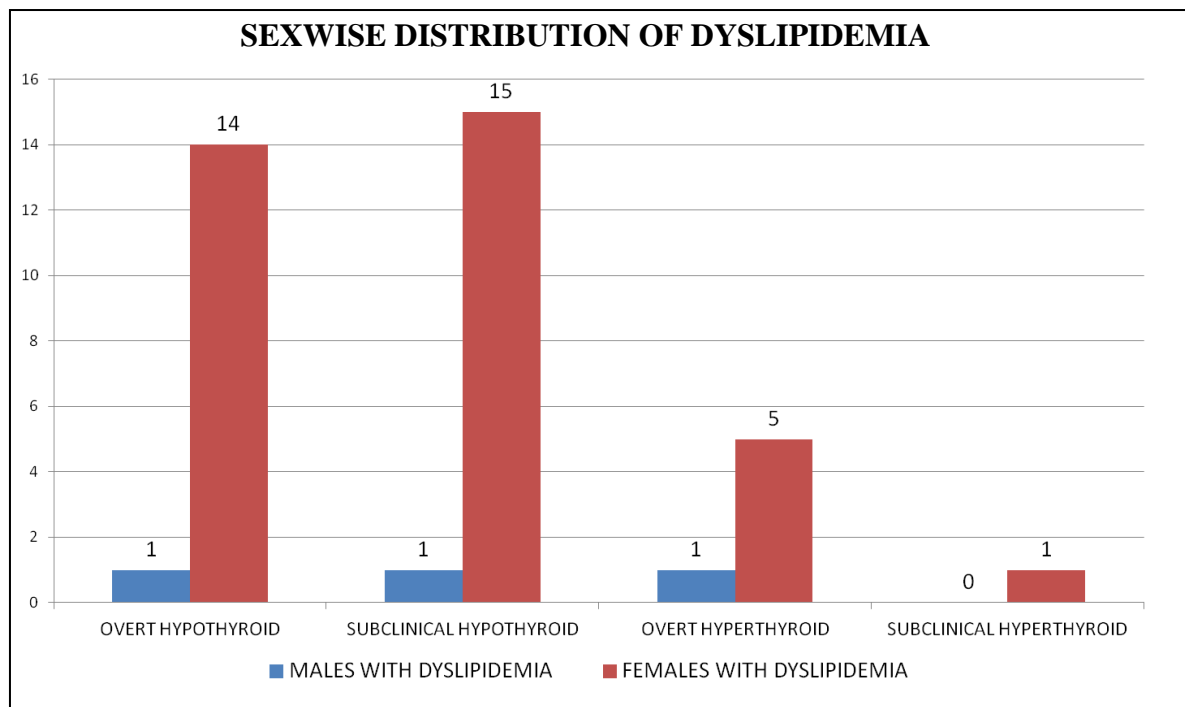


Figure 8: Sex distribution of thyroid dysfunction in study subjects.

Table 12: Sexwise distribution of IGT in patients with thyroid dysfunction

Sex	Thyroid dysfunction status			
	Overt hypothyroid	Subclinical hypothyroid	Overt hyperthyroid	Subclinical Hyperthyroid
Males with IGT	1	0	0	0
Females with IGT	2	8	0	1
Total	3	8	0	1

Sexwise distribution of IGT

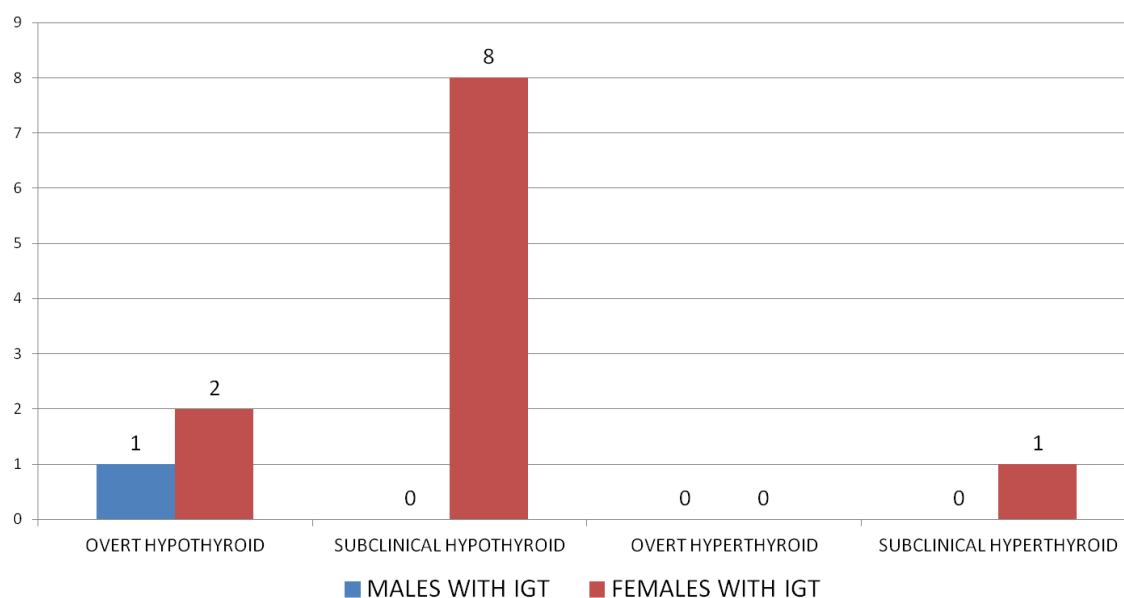


Figure 9: Sex distribution of IGT in thyroid dysfunction subjects.

Table 13: UACR distribution in patients with thyroid dysfunction

UACR	Thyroid dysfunction status				Sex		Total
	Overt hypothyroid	Subclinical hypothyroid	Overt hyperthyroid	Subclinical Hyperthyroid	Male	Female	
Normal	6	31	18	2	5	50	57
Microalbuminuria	27	14	1	1	7	36	43
Overt proteinuria	0	0	0	0	0	0	0

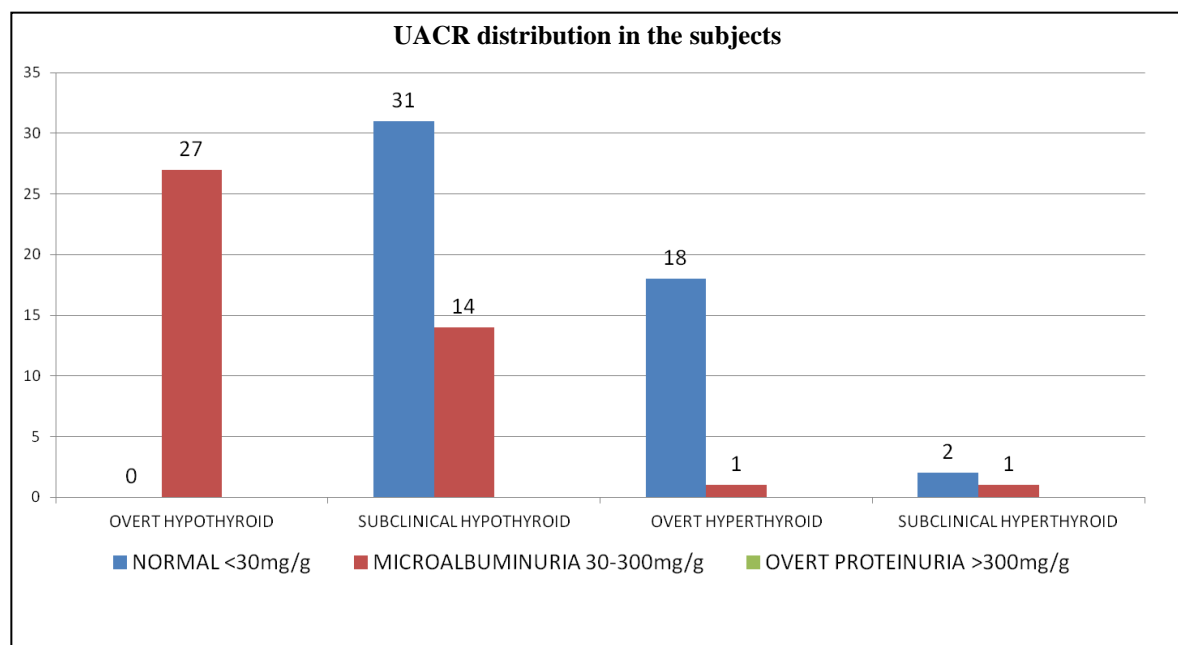


Figure 10: UACR distribution in study subjects.

Table 14: FT3 range in subjects with microalbuminuria

Free T3 range	Number of subjects with microalbuminuria
0.5-2.50pg/ml	30
2.51-4.50pg/ml	13
4.51-6.50pg/ml	0
6.51-8.50pg/ml	0

Figure 11: Correlation of FT3 with urine albumin creatinine ratio

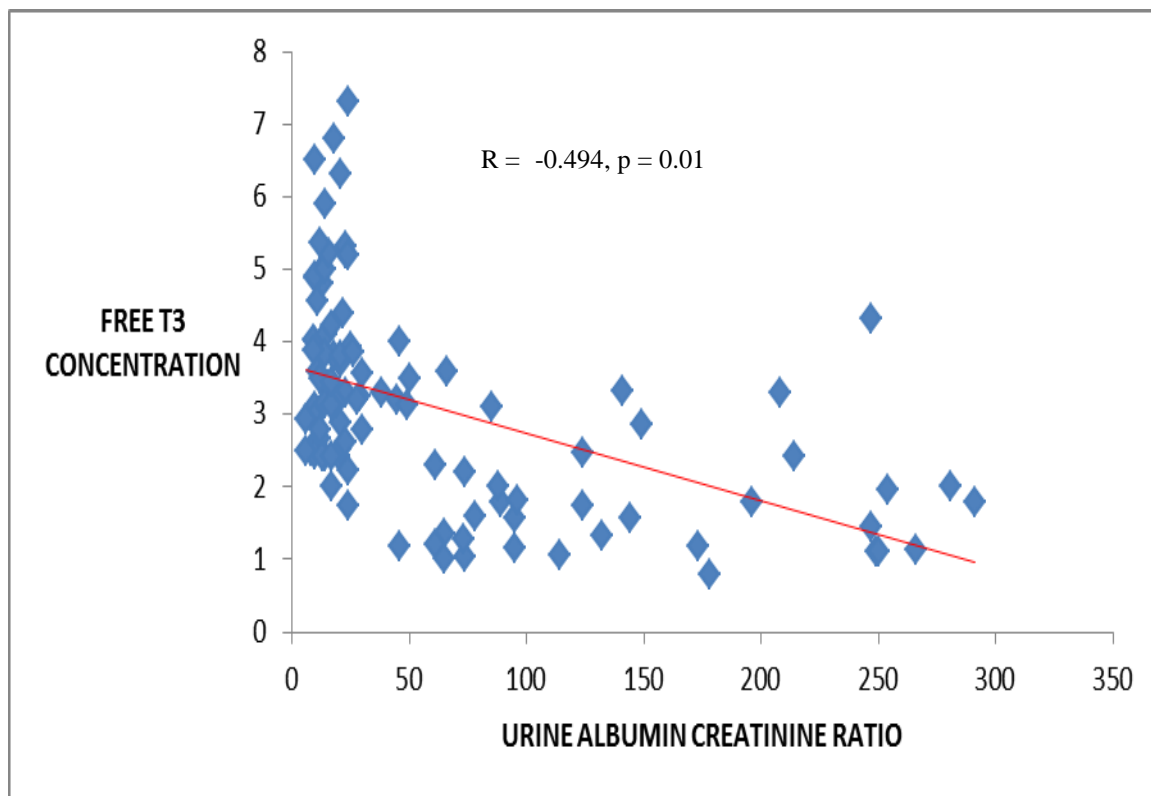


Table 15: FT4 range in subjects with microalbuminuria

Free T4 range	Number of subjects with microalbuminuria
< 0.7 ng/dl	28
0.7-1.24 ng/dl	14
>1.24 ng/dl	1

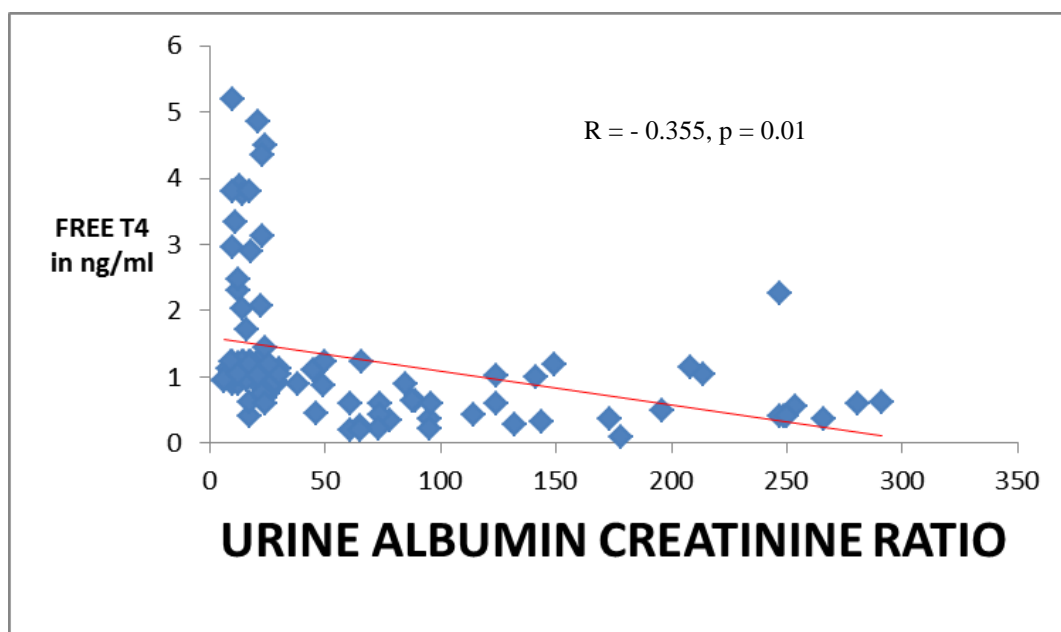
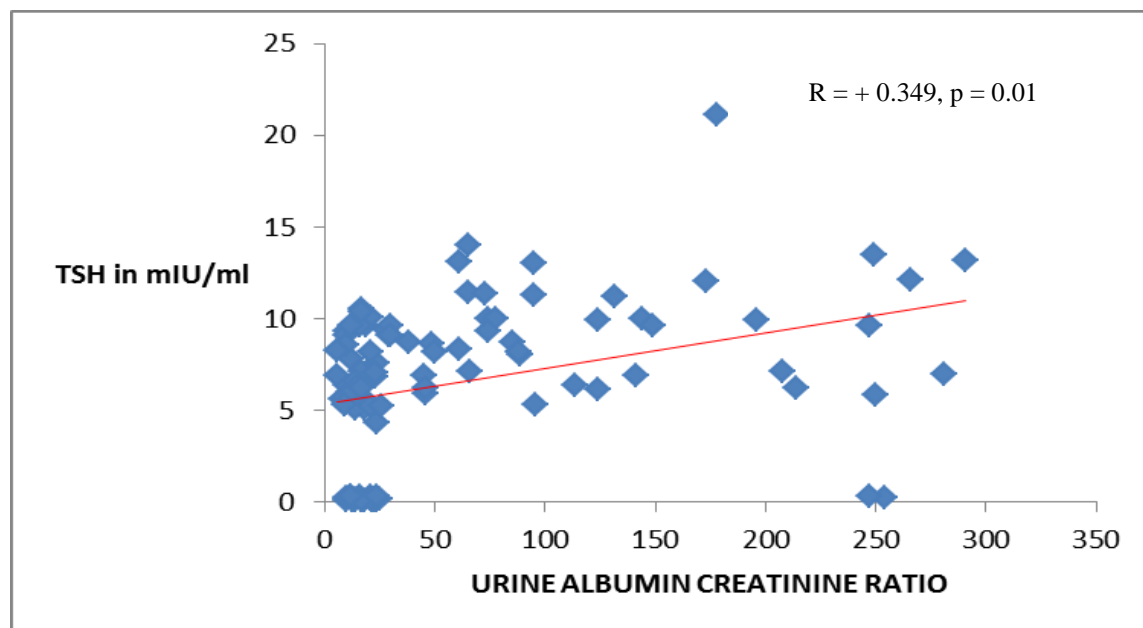


Figure 12: Correlation of FT4 with urine albumin creatinine ratio

Table 16: TSH range in subjects with microalbuminuria

TSH range	Number of subjects with microalbuminuria
< 0.34 miu/ml	2
0.34-4.25 miu/ml	0
>4.25 miu/ml	41

**Figure 13:** Correlation of TSH with urine albumin creatinine ratio

Discussion

Thyroid disorders are also a major contributor to morbidity in our country. Coexistence of other metabolic disorders such as diabetes mellitus, dyslipidemia and metabolic syndrome complicate the scenario. Presence of coronary artery disease, cerebrovascular accidents and chronic kidney diseases in such patients add to the disease burden further. Presence of microalbuminuria in most of the above condition indicates widespread endothelial damage and further helps us to identify patients at risk of development of other conditions. As hypothyroidism coexists with many of the above conditions it necessitates early evaluation of microalbuminuria to identify endothelial dysfunction. In the study published by Shanghai Centre for Endocrine and metabolic diseases, done by Yulin Zhou et al in 2008-2009 analyzing the correlation between FT3 and microalbuminuria in a Chinese population of around 3346 people, it was concluded that there is an inverse correlation between FT3 and

microalbuminuria [7]. Similarly our study too establishes the above conclusion along with an additional inverse relationship of FT4 and positive correlation of TSH with microalbuminuria. The Thyroid peroxidase and Thyroglobulin antibodies are also worked up as part of the Thyroid panel in the first study while our study analyzed only FT3, FT4 and TSH.

The case control study done by Mervat M.El-Eshrawy et al in 2012 on a pre-diabetic Egyptian population concluded that Subclinical Hypothyroidism was independently associated with microalbuminuria [8]. From our study it is noted that, only subclinical and overt hypothyroidism had significant association with microalbuminuria although Overt and subclinical hyperthyroidism are also analyzed. Overt Hypothyroidism was a strong and significant predictor of microalbuminuria compared to subclinical hypothyroidism in both univariate and multivariate analysis.

Conclusion

Our study concluded that there is an increased prevalence of hypothyroidism among females. All forms of thyroid dysfunction both hypothyroidism and hyperthyroidism were more common in the age group of 46 to 55 years. . Also a significant association of subclinical and overt hypothyroidism with microalbuminuria is present in this study. There is no significant association between Age, Sex, BMI, IGT and dyslipidemia with microalbuminuria. A higher prevalence of overweight individuals were also present in the same age group. On analyzing the presence of hypothyroidism, there was a high prevalence of hypothyroidism in the females with both impaired glucose tolerance and dyslipidemia individually. Thus microalbuminuria plays an important role in thyroid dysfunction and thus plays an important role in screening of patients with other co-existent illness such as prediabetes, hypertension, coronary artery disease and metabolic syndrome.

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Conflict of interest

All authors contributed equally in developing the manuscript.

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