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Originalinvestigations/commentaries

Association of thyroid function abnormalities and neck ultrasound Findings in patients with ulcerative colitis (UC): single center study

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Abstract. Most previous reports of the association between thyroid disease and ulcerative colitis (UC), have been on individual case reports or case series. It is important to determine the true nature of this observed association to justify regular screening for thyroid disease in patients with UC. Objective: to assess the prevalence of different thyroid disorders in patients already diagnosed with UC. Methods: This is a cross-sectional study, conducted in the IBD clinic at Alrajhy Liver-Gastroenterology Hospital, Assiut University. A total of 95 participants (75 UC patients and 20 healthy volunteers) were investigated and with the group of control were compared. The recruitment started in November 2020. The study ended in August 2022. Patients with UC, and willing to participate, along with 20 healthy volunteers, were assessed at the baseline and every 6 months, with free T3, free T4,anti-TPO, anti- TG and TSH. Thyroid ultrasound was done at baseline. The patients were assessed by an endocrinologist. Results: The average age of UC group (42 women, 33 males) was 40 ± 11 years. The control group (16 males and 4 females) was 32 ± 6 years average age. At time of recruitment, the 89.3% of UC group there were in remission and 10.7% had active disease. 58.7% had left side colitis UC, 26.7% extensive colitis and 14.7% had proctitis. After thyroid assessment, 58 patients had normal thyroid (77.3%), 1 patient had subclinical hypothyroidism (1.3%), 13 patients had subclinical hyperthyroid (17.3%) and 3 patients were diagnosed as Graves' disease (3.2%). Of the controlgroup, one was diagnosed with subclical hyperthyroid. The difference of prevalence of thyroid diseases between studied groups was insignificant (X^2 p-value was 0.347). 94.67% of UC patients have normal ultrasound (71 from 75 UC patients) and 4%.of UC patients have Nodules showing on ultrasound .**Conclusion:** The prevalence of thyroid disorders in UC might be higher than normal population. However, this association could not be confirmed.

Keywords: ulcerative colitis, thyroid disorders

Introduction

Ulcerative colitis (UC) is diseases that is caused by dysregulation of immune system in patients with genetic predisposition and characterized by chronic inflammation with relapse and remission periods. Ulcerative colitis is associated with a wide range of extra intestinal complications that influence the course and therapy of the disease. Although extrain-testinal complications of UC including rheumatologic, ocular, dermatologic and hepatobiliary complications are well understood, the data regarding the relationship between UC and thyroid disorders are not completely established [1, 2, 3]. In previous studies, the relationship between UC and thyroid diseases is well established. The rate of thyroid diseases is reported to be higher in UC patients compared to normal population [3, 4]. The incidence of thyrotoxicosis is reported as 0.8% - 3.7% in UC patients [2, 3, 5, 6]. UC is a long-term condition that results in inflammation and ulcers of the colon and rectum [8, 9]. The primary symptom of active disease is abdominal pain and diarrhea mixed with blood. The disease carchtraized by periods of activity and periods of remission [8].Complications may include megacolon , colon cancer , extra intestinal manifestations may include inflammation of the eye, joints, or liver and skin [8,10].

Thyroid disorders are generally classified into hyperthyroidism, subclinical hyperthyroidism, hypothyroidism, subclinical hypothyroidism. The most common causes of hyperthyroidism are Graves' disease (GD or Basedow disease [11, 12]. The rate of thyroid disorders is reported to be increased in patients with Ulcerative Colitis (UC) than the normal population [7].Previous investigations have clearly suggested the association between thyroid diseases and ulcerative colitis (UC): epidemiological studies have demonstrated an increased prevalence of hyperthyroidism (1.34%),[16] while the incidence of thyrotoxicosis was between 0.82%4 and 3.7%.[17,18]. The prevalence of thyroiditis was 0.23% in UC patients and 0.19% in CD

(versus 0.15%–0.20% in controls). M. Cesarini et al 2009 reported that if consider UC patients separately, it found that among the UC population 28 cases of thyroid disorders (28/445 UC patients, 6.29%; male 5/28, 17.86%; female 23/28, 82.14%) [20].

Patients and Methods

Study design: case control, **setting**: Assiut University Hospitals

Patients: seventy five patients who are diagnosed with ulcerative colitis who were admitted to Internal medicine department and who attend outpatient clinics in Assuit University Hospital will be involved in this study compared with 20 normal control subjects selected from general population at random. The patients were 42 females and 33 males and their ages ranged from 18 to 70 years.

Exclusion criteria: Patients with diabetes mellitus, patients with cardiac heart failure, patients with renal failure and patients with liver disease.

Methods: All patients included in this study will subjected to Full history taking including age, sex, duration of the disease and type of treatment , Complete clinical examination , Assessment of colonic involvement correlated with: disease activity and drugs used.

Laboratory investigations: 1. routine investigations: Complete blood count (CBC) on ADVIA 2021, (Serum creatinine and blood urea, Random plasma glucose level, Liver function tests and Complete urine analysis) on ADVIA 1800. 2. Special investigations: Special investigations: TSH, T3, T4, Thyroid function on centaur XL semines based on chemiluminiscence and Antithyroperoxidase (Anti-TPO), Anti-thyroglobulin (anti-TG) by Architect i 1000 SR and Thyroid ultrasound by GE logiq P9 XDclear.

Normal reference ranges of TSH were 0.40–4.03 mU/L, free T4 was 0.8-1.7 ng/dL, and free T3 was 1.98-4.37 pg/mL. Anti-TPO antibody was considered negative if less than 34 IU/mL, and anti-TG antibody was considered negative if less than 4.1 IU/mL. Data were collected, coded, revised and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The data were presented as number and percentages for the qualitative data, mean, standard deviations and ranges for the quantitative data with parametric distribution and median with inter quartile range (IQR) for the quantitative data with non-parametric distribution. Chi-square test was used in the comparison between two groups with qualitative data and Independent t-test was used in the comparison between two groups with quantitative data and parametric distribution and Mann-Whitney test was used in the comparison between two groups with quantitative data and non-parametric distribution. Kruskal Wallis was done to measure correlation between quantitative variables in case of non-parametric data the confidence interval was set to 95% and the margin of error accepted was set to 5%. A significant P value was considered when it is < 0. 0.

Results

Table 1. Demographic data for all studied UC patients

		UC Patient No.= 75		**Control No. = 20**		**P- value**
		N	**%**	**N**	**%**	
Gender	**Male**	**33**	**44%**	**16**	80%	**0.005***
	Female	**42**	**56%**	**4**	**20%**	
Age (years)	**Mean ± SD**	**40 ± 11**		**32 ± 6**		**0.247**
	Range	**18 - 70**		**22 – 43**		

40 ± 11 years was the mean age of patients with UC (42 females, 33 males). The control group consists of 16 males and 4 females and 32 ± 6 years was the average age.

There were statistically significant increase with female patients (56%) compared to male patients (44%) with p value (0.005) and no statistical significant difference as regards age with p-value for 0.247.

Table 2. Distribution of UC patients according to activity and Extent of disease and type of treatment

		Activity		Treatment		Extent		
		active	in remission	Conventional	Biological	proctitis	Left side	extensive
UC Patient No.= 75	N.	8	67	59	16	11	44	20
	%	10.7%	89.3%	78.7%	21.3%	14.7%	58.7%	26.7%

The percentage of extent for all studied UC patients were 14.7% with proctitis, 58.7 with left sided colitis and 26.7% with
extensive colitis.

The results show that from 75 UC patients there were 67 patients in remission (89.3%) and 8 patients in active disease (10.7%).

Just 21.3% from all studied UC patients get biological therapy (16 from 75 patients).

Table 3. Thyroid function tests for UC patients

		T3	T4	TSH	Anti-TPO	Anti-TG
UC Patient No.= 75	Mean ± SD	3.13 ± 0.63	1.118 ± 0.471	0.844 ± 0.741	8.89 ± 29.06	4.33 ± 15.26
	Median	3.15	1.02	0.632	1.20	1.58
	Range	1.11 – 4.41	0.66 – 3.91	0.01 – 4.567	0.25 – 181.45	0.43 – 103.63
Control No. = 20	Mean ± SD	3.53 ± 0.27	1.073 ± 0.148	0.689 ± 0.229	1.30 ± 1.53	1.47 ± 0.75
	Median	3.55	1.085	0.62	0.72	1.23
	Range	3.06 – 3.95	0.89 – 1.41	0.514 – 1.417	0.3 – 5.60	0.43 – 3.16
P- value		0.004*	0.448	0.729	0.028*	0.198

The median of TSH for patients with ulcerative colitis was 0.632 and mean + SD was 0.844 + 0.741 and the median of anti -TPO was 1.2 and mean + SD was 8.89 + 29.06 and the median of T3 was 3.15 and mean + SD was 3.13 + 0.63 and the median of t4was 1.02 and mean + SD was 1.118 + 0.471 and the median of anti-TG was 1.58 and mean + SD was 4.33 + 15.26.

Table 4. Lab investigation tests for UC patients

		UC Patient No.= 75		Control No. = 20		P-value
		N.	%	N.	%	
ESR	Normal	66	88.0%	20	100.0%	0.105
	High	9	12.0%	0	0	
CRP	Normal	66	88.0%	20	100.0%	0.105
	High	9	12.0%	0	0	

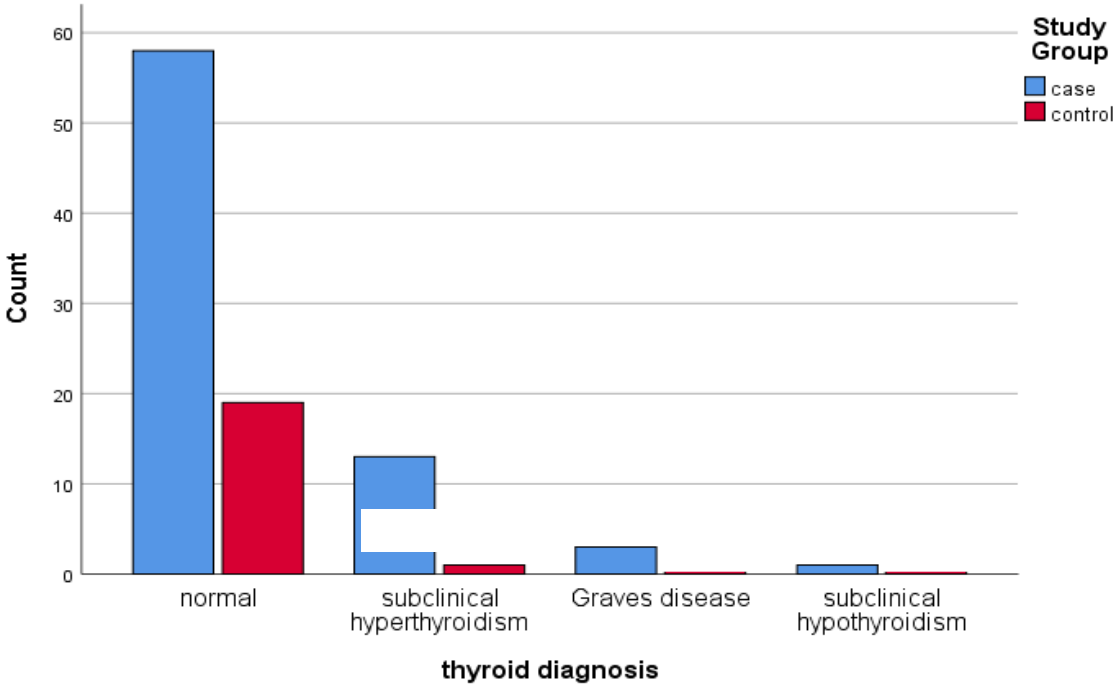
The results of ESR for 88% patients form all studied patients were normal and 12% patients have a high results.

Out of 75 patients there were 66 patients (88%) were normal for CRP test and 12% were high results.

Table 5. Thyroid state in UC and normal participants

	UC Patient No.= 75		Control No. = 20		P-value
	N	%	N	%	
Normal thyroid diagnosis	58	77.3%	20	100%	0.347
subclinical hyperthyroidism	13	17.3%			
Graves' disease	3	4.0%			
subclinical hypothyroidism	1	1.3%			

Note: the patients diagnosed as Graves' disease after consultation of endocrinologist



After thyroid assessment, 58 patients had normal thyroid (77.3%), 1 patient had subclinical hypothyroidism (1.3%), 13 patients had subclinical hyperthyroid (17.3%) and 3 patients were diagnosed as Graves' disease (3.2%). Of the control group, one was diagnosed with subclinical hyperthyroid. The difference of prevalence of thyroid diseases between study groups was insignificant (p-value was 0.347).

Table 6. Demographic data for UC patients according to thyroid diagnosis

	Normal Thyroid diagnosis No. = 58	subclinical hyperthyroidism No. = 13	Graves' disease No. = 3	subclinical hypothyroidism No.= 1	Control No. = 20

		N	%	N	%	N	%	N	%	N	%
sex	male	18	42.9	6	46.15	0	0	0	0	16	80.0
	female	24	57.1	7	53.85	3	100	1	100	4	20.0
age	Mean ± SD	41 ± 12		30 ± 9		40 ± 9		39 ± 0		32 ± 6	
	Range	18 - 70		22 – 42		26 - 69		39		22 - 43	

Female UC patients in all thyroid cases were more than male patients with percentage 57.1% with normal Thyroid diagnosis, 53.85% with subclinical hyperthyroidism and 100% for both Graves' disease and subclinical hypothyroidism

Table 7. Distribution of all studied group with Thyroid disorders according to activity and extent of disease and type of Treatment

		Normal Thyroid diagnosis No. = 58		subclinical hyperthyroidism No. = 13		Graves' disease No. = 3		Subclinical hypothyroidism No.= 1		Control No. = 20	
		N	%	N	%	N	%	N	%	N	%
Activity	active	6	10.34%	2	15.38%	0	0.00%	0	0.00%	20	100%
	in remission	52	89.66%	11	84.62%	3	100.00%	1	100.00%		
Extent	proctitis	9	15.52%	2	15.38%	0	0.00%	0	0.00%		
	Left side	36	62.07%	6	46.15%	1	33.33%	1	100.00%		
	extensive	13	22.41%	5	38.46%	2	66.67%	0	0.00%		
Treatment	Conventional	47	81.03%	9	69.23%	2	66.67%	1	100.00%		
	Biological	11	18.97%	4	30.77%	1	33.33%	0	0.00%		

As regards UC patients in remission it was found that 11 patients with subclinical hyperthyroidism, 3 patients with Graves' disease and 1 patient with subclinical hypothyroidism.

And for UC patients in active case it was found that 6 patients with subclinical hyperthyroidism and 2 patients with subclinical hyperthyroidism and no patients with Graves ' disease or subclinical hypothyroidism.

As regards UC patients with proctitis it was found that 2 patients with subclinical hyperthyroidism and no patients with Graves' disease or subclinical hypothyroidism.

And for UC patients with left side colitis it was found that 6 patients with subclinical hyperthyroidism, 1 patient with Graves ' disease and 1 patient with subclinical hypothyroidism.

And for UC patients with extensive side it was found that 5 patients with subclinical hyperthyroidism, 2 patient with Graves' disease and no patient with subclinical hypothyroidism. As regards UC patients with conventional treatment it was found that 9 patients with subclinical hyperthyroidism, 2 patients with Graves ' disease and 1 patient with subclinical hypothyroidism.

And for UC patients with biological treatment it was found that 4 patients with subclinical hyperthyroidism and 1 patients with Graves' disease.

Table 8. Correlation between clinical parameters and prevalence of thyroid diseases in UC patients

		Age In years	Gender	extent of UC	UC activity state	type of UC treatment
thyroid diagnosis	R	-.097	.054	.300**	.030	.123
	P-value	.409	.643	.009	.798	.295

The results of p-value for Correlation between clinical parameters and prevalence of thyroid diseases in UC patients show that only significant factor is extent of UC patients.

Table 9. Distribution of UC patient according to ultrasound results

	patients No. = 75		Control No. = 20		Total No.= 95	
	N	%	N	%	N	%
Normal ultrasound	71	94.67	20	100%	91	95.79%
Nodules showing on ultrasound	3	4%	0	0	3	3.16%
Thyroidectomy	1	1.33%	0	0	1	1.05%

The results show that:
71 patients (94.67%) in normal dimensions (length 4-7 , depth 1.8 , width 2cm , isthmus less than 0.5 cm) and vascularity (89.3%) including UC patients with graves' disease.

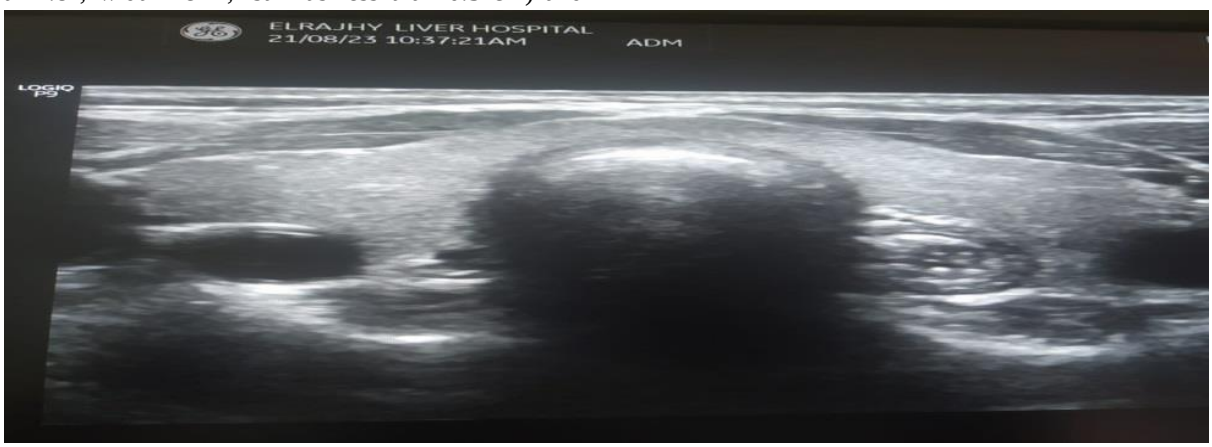


Figure.1 Normal thyroid ultrasound in patients with ulcerative colitis

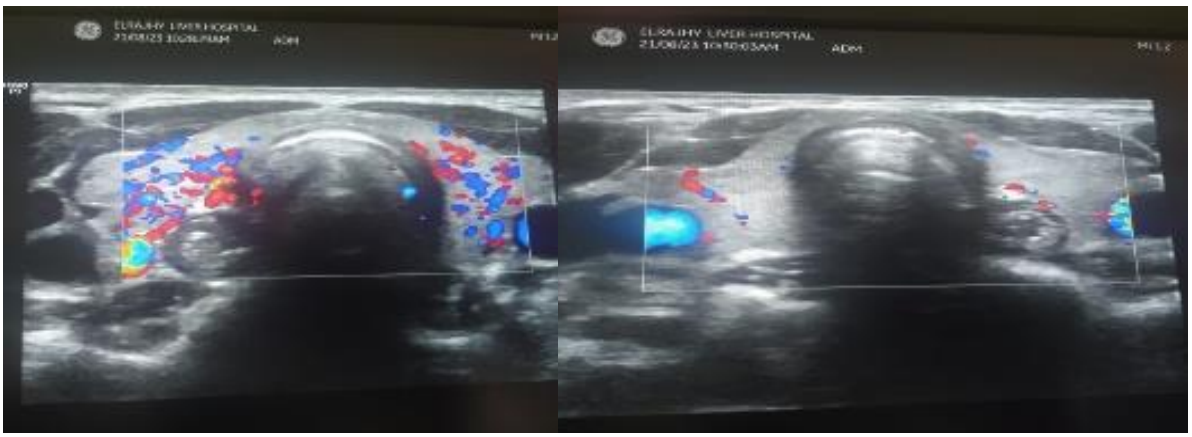


Figure. 2 Normal thyroid ultrasound with color Doppler in UC patient with Graves' disease

three patient (4.0%) with UC have nodules in there ultrasound : first patient get left lobe nodule 1.5 cm×2cm , second patient get right lobe nodule 3cm×2cm and the third patient get 2 nodules in left and 1 nodule in right lobe.

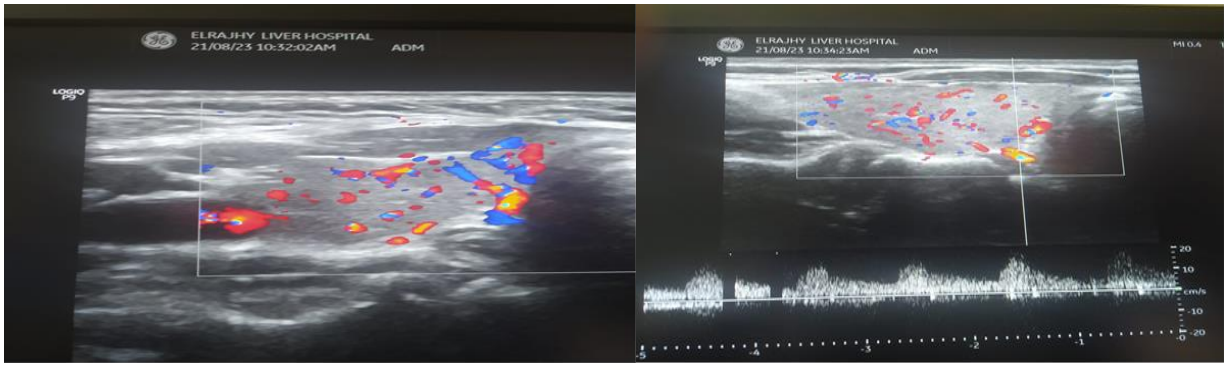


Figure.3 Another thyroid ultrasound with colour Doppler in patients with UC have 2 nodules in left and 1 nodule in right lobe

1 patient (1.3%) get total thyroidectomy with no recurrence.

Table 10. Extent OF UC for all studies group according to ultrasound

		Normal No. = 71		Nodule No. = 3		Thyroidectomy No.=1	
		N	%	N	%	N	%
Extent	proctitis	40	44.8%	3	100.0%	0	0.0%
	Left side	11	12.6%	0	0.0%	1	100.0%
	extensive	20	19.5%	0	0.0%	0	0.0%
Activity	active	8	11.27%	0	0.0%	0	0.0%
	IN remission	63	88.73%	3	100.0%	1	100.0%

Regarding extent of disease in patient with proctitis 3 of them have nodules and from patients with left side colitis there was 1 patient had total thyroidectomy and it was same result for UC patients in remission.

Discussion

- Out of 75 patient with ulcerative colitis: 42 patients are females (56%) and 33 patients are males (44%) was female predominance of the diseases and our study found that there was statistically difference between gender distribution with p-value = 0.005
  In agreement with united state statistics that found diseases slightly more common in females than males (Marc d basson et all 2023) and in agreement with serag esmat et all 2014 which stated that female to male ratio 1.6 to 1.15.
  In agreement with Baki et al 2016 that found out of 15 patients with ulcerative colitis there were 11 patients were females (73.33%) and 4 male patients (36.67%).
  In disagreement with Abdelmajiid Mosua et all 2021 which stated that male to female ratio 1.6 to 1. Also Ghersin et al 2019 disagreement with which stated that male to female ratio 2 to 1 .
- We noticed that the mean and standard deviation of age for patients with UC was 40 + 11 years and no statistical significant difference as regards age with p-value = 0.247 and study found that the range of age of patients with ulcerative colitis between 18 to 70 years.
  In agreement with Nadeem Naeem et al 2020 reported that mean age in years for ulcerative colitis patients was 43.6 + 11.5 years and reported that no statistical significant difference as regards age
- Our study found that out of 75 patients with ulcerative colitis there were 44 patients with left side colitis (58.67%) and 20 patients with extensive colitis (26.67%) which mean the percentage of left side was double percentage of extensive colitis approxmility.

In agreement with Nadeem Naeem et al 2020 that reported the distribution of patients were 44.7% left side colitis and 14.1% pan colitis.

- Our study found that out of 75 patients with ulcerative colitis there were 59 patients with Conventional treatment (78.67%) and 16 patients with biological treatment (21.33%).
  Abdelmajiid Mousa et al 2021 reported that 7.7% of ulcerative colitis patients were taking biological treatment.
- Our study found that out of 8 patient with ulcerative colitis on active there were 5 patients (88%) in activity with abnormally high level of CRP and ESR.
  In agreement with Abdelmajiid Mousa et al 2021 reported that the level of fecal calprotectin and serum level of ESR and CRP were increased with increase in the clinic or endoscopic severity.
- Our study found that the median of TSH for patients with ulcerative colitis was 0.632 and mean + SD was 0.844 + 0.741 and the median of anti -TPO was 1.2 and mean + SD was 8.89 + 29.06 and the median of T3 was 3.15 and mean + SD was 3.13 + 0.63 and the median of t4was 1.02 and mean + SD was 1.118 + 0.471 and the median of anti-TG was 1.58 and mean + SD was 4.33 + 15.26.
  Nadeem Naeem et al 2020 reported that the mean + SD of TSH for patients with UC mean ± SD was 1.8 ± 2.13 and the mean + SD of anti -TPO was 14.2 ± 30.25 and the mean + SD of T3 was 4.5 ± 1.42 and the mean + SD of T4 was 14.3 ± 4.015 .
  Salwa baki et al 2016 that reported the results of ulcerative colitis patient of thyroid function tests were as follows: TSH = 0.083, t3 = 5.2, t4 = 2.1.
- Our study found that out of 75 patients with ulcerative colitis there were 3 UC patients with subclinical hyperthyroid (17.3%) and 3 UC patients with GD 4 % and one UC patient with subclinical hypothyroid (1.3%).
  Nadeem Naeem et al 2020 reported that epidemiological studies have shown a higher incidence of hyperthyroidism and in an Italian study of 162 patients with ulcerative colitis hyperthyroid and hypothyroidism were reported in 2.5%.
  Matsumura k et al 2009 and Itai et al 2005 reported that prevalence of hyperthyroidism in ulcerative colitis patients was 3.7%.
  Inkuchi t et al 2005 reported that the prevalence of ulcerative colitis in patients with hyperthyroidism was 1.34%.
  Casella g et al 2008 reported that the prevalence of hyperthyroidism in Italy in ulcerative colitis patients 0.62%.
- We noticed that all cases of patients with concomitant GD were females and 53.85% of UC patients with subclinical hyperthyroidism were females.
  In agreement with Toru Shizuma 2016 which stated that of the 16 cases of concomitant GD and UC that were identified into 6 (37.5%) were male and 10 (62.5%) were female .
  Also in agreement with Bernstein CN et al 2005 that female IBD patients have a higher risk of Graves ' disease than the general population.
- Our study found that the range of age of patients with GD 26 to 69 years ago.
  In agreement with Shizuma t et all 2014 found that the diagnosis of Graves' disease was between the ages of 18 – 61 years.
  in agreement with Baki et al 2016 that reported in the study range of age for graves' disease from 18 to 61 years.
- The results show that patients with all cases of thyroid function abnormalities in remission with percentage 89.66% for normal thyroid function, 84.62% for subclinical hyperthyroidism and 100% for both Graves ' disease and subclinical hypothyroidism.
  , 62.07% from all patients with normal thyroid function with extent of disease in left side colitis
  , 46.15% from all patients with subclinical Hyperthyroidism with extent of disease in left side colitis, and 66.67% from all patients with Graves ' disease with extent of disease extensive.
  The patients with all cases of thyroid function with conventional treatment more than patients with biological treatment with percentage 81.03% for normal thyroid diagnosis, 69.23% for subclinical Hyperthyroidism, 66.67% for Graves ' disease and 100% for subclinical Hypothyroidism.
- Extent of disease is statically significant factor finding in prevalence of thyroid diseases in UC patients with p-value = 0.009.
- There were no studies show any relation between thyroid ultrasound and UC patients.
  however our study show that 94.67% of UC patients have normal ultrasound (71 from 75 UC patients) and 4%.of UC patients have Nodules showing on ultrasound.
- As regard ultra sound we reported that 44.8% of all normal ultrasound patients with extent of disease are proctitis, 100% of patients with nodules in ultrasound are proctitis case and the only patient with Thyroidectomy is left side colitis. All cases with abnormal ultrasound findings are in remission.
  Salwa Baki et al 2016 reported that thyroid

ultrasonography for UC patient revealed an enlarged thyroid and a homogenously increased activity in a moderately enlarged thyroid.

Conclusion

The prevalence of thyroid disorders in UC might be higher than normal population. However, this association could not be confirmed.

Recommendations

We recommend free T3, free T4, TSH, ANTI – TPO, ANTI – TG measurement and thyroid ultrasound procedure in the routine laboratory investigation for Graves ' disease in patients with ulcerative colitis.
A possible limitation of this study was the relatively small number of enrolled patients. So Further studies are therefore warranted, with the enrollment of a larger number of patients.
Serial measurements of free T3, free T4, TSH, ANTI – TPO, ANTI – TG are indicated in patients with ulcerative colitis after diagnosis of greaves disease and during its treatment.

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