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ORIGINAL ARTICLE

CONTENTS

Prevalence of thyroid dysfunction in patients with acute atrial fibrillation attending coronary care unit at Al-Sadder Teaching Hospital

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ABSTRACT

Aim: Assessment of prevalence of thyroid dysfunction in patients with acute atrial fibrillation.

Materials and Methods: A total of 110 patients participated in this cross-sectional study, admitted to the coronary care unit with AF not more than 48 hours from symptom onset and investigated by TSH, T3, and T4 to show how prevalent thyroid dysfunction in patients with acute AF, a study done at Al-Sadr Medical City – Najaf Al-Ashraf city, Iraq.

Results: This study showed Prevalence of thyroid dysfunction was 21.7% which represents 24 patients that include (one patient with subclinical hypothyroidism 0.9%, 4 patients with subclinical hyperthyroidism 3.6%, 5 patients with hypothyroidism 4.5%, 14 patients with hyperthyroidism 12.7% and patients with euthyroid represent (N=86, 78.3%) of patients.

Conclusions: For patients who admitted to the coronary care unit with acute atrial fibrillation both hypothyroidism and hyperthyroidism were frequent with the latest exceeding the prevalence in the general population necessitating screening for hidden thyroid dysfunction for early diagnosis and management to reduce morbidity and mortality.

KEY WORDS: atrial fibrillation, cardiac arrhythmia, hyperthyroidism, acute atrial fibrillationx

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INTRODUCTION

Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia worldwide, affecting over 30 million people. Its prevalence and incidence continue to rise. AF markedly increases morbidity and mortality by elevating the risks of stroke, heart failure, and hospitalization [1-2]. Notably, AF raises stroke risk by approximately fivefold, and AF-related strokes tend to be more severe and deadly than strokes in patients without AF. Clinically, AF is characterized by an irregularly irregular ventricular rhythm and absent distinct P waves on ECG. The condition is categorized by episode duration and frequency, as outlined in the 2014 AHA/ACC/HRS guidelines on AF management [3]. Paroxysmal AF (self-terminating or intermittent): AF that stops on its own or with treatment within 7 days of onset; episodes may recur. Persistent AF: AF that does not terminate spontaneously within 7 days and typically requires pharmacologic or electrical cardioversion to restore sinus rhythm. Patients with persistent AF may later have paroxysmal episodes, reflecting disease progression.

Long-standing persistent AF: AF that has been continuous for more than 12 months.

Permanent AF: Persistent AF for which the patient and clinician have agreed not to pursue further rhythm-control attempts.

Acceptance of persistent AF may shift as symptoms, treatment options, and patient–clinician preferences change. Although AF often progresses from paroxysmal to persistent forms, individuals may experience both types at different times. Despite a slightly higher prevalence in men, AF-related complications tend to be more severe in women [4]. Numerous conditions predispose to AF, including but not limited to hypertension, obesity, metabolic syndrome, diabetes, obstructive sleep apnea, ischemic heart disease, heart failure, and thyroid disorders. The thyroid is a highly vascular, brownishred gland located anteriorly in the lower neck, extending roughly from C5 to T1. It typically has an H- or U-shaped configuration, composed of two elongated lateral lobes connected by an isthmus, with an average height of 12–15 mm overlying the second to fourth tracheal rings [5]. As a key endocrine organ, the thyroid secretes hormones that regulate growth,

development, and metabolism [6]. The wide-ranging (pleiotropic) effects of thyroid hormones on metabolic pathways produce diverse, often age- and sex-related clinical presentations [6–7]. Because signs and symptoms of thyroid dysfunction are frequently nonspecific, diagnosis relies primarily on biochemical testing. Thyroid disease ranges from subclinical to overt forms, with overt disease reflecting more pronounced hormonal disturbance [7–8]. Untreated thyroid dysfunction substantially impairs well-being and can cause significant morbidity. Hypothyroidism is linked to cognitive decline, hypertension, dyslipidemia, cardiovascular and cerebrovascular events, and, in severe cases, myxedema coma [7]. Subclinical hypothyroidism increases cardiovascular morbidity and mortality in a TSHdependent manner [9]. Subclinical hyperthyroidism and overt hyperthyroidism are associated with higher risks of atrial fibrillation, heart failure, dementia, bone loss, and fractures [10]. Globally, the most common causes of thyroid dysfunction are iodine deficiency in iodinedeficient regions and autoimmune thyroid disease in iodinereplete areas; notably, about onethird of the world's population still resides in iodinedeficient regions [11]. Reported prevalence of thyroid dysfunction among patients with AF varies widely (0–24%) [12–13], likely reflecting differences in study populations' ages [14–15], geographic regions [16], comorbidities and medications [17], and laboratory methods for measuring thyroid hormones and TSH [18–19]. In hyperthyroid patients, AF prevalence is reported at 10–15%, with an incidence of 1.41 per 1,000 patients [20–21]. The link between hypothyroidism and AF remains unclear, although hypothyroidism is associated with increased cardiovascular events. Large cohort studies indicate that even variations of thyroid hormones within the reference range are related to cardiac outcomes; specifically, higher free thyroxine (T4) is associated with greater risks of heart failure, sudden cardiac death, and AF [22–24]. Overall, the influence of thyroid hormone imbalance on AF risk may be under recognized [24].

Thyroid disease can affect cardiovascular physiology by increasing vascular resistance, cardiac contractility, heart rate, and left ventricular mass. Elevated thyroid hormone levels also promote arrhythmogenesis, increase atrial premature beats, and exert prothrombotic effects—mechanisms that help explain the association between hyperthyroidism and AF, though they do not fully clarify hypothyroidism's role, despite shared risk factors. Additionally, thyroid dysfunction may alter responses to anticoagulant therapy, and the safety and efficacy of standard anticoagulation in AF patients with thyroid disease are not fully defined [25]. These issues raise questions about the value of including free T4 in AF thyroid screening and about risks related to thyroid hormone replacement.

AIM

This study therefore aims to determine the prevalence of thyroid dysfunction among patients presenting with acute atrial fibrillation.

MATERIALS AND METHODS

In this cross-sectional study, 110 patients (male N=54 patient and female N=56 patient) has been admitted to the coronary care unit in al-Sadr medical city/ Najaf al-Ashraf City, Iraq during one-year period from 1 March 2022 to 1 March 2023. The data collecting during one-to-one interviews and all patients admitted to the coronary care unit has been admitted primarily to the emergency department, clinical and demographical data were obtained, these data include age, gender, residency, lifestyle, smoking state, alcohol state, BMI, Family history of thyroid disease, history of COVID 19 infection past medical history of (hypertension, heart failure, asthma, ischemic heart disease, COPD, stroke…etc.). Blood pressure measurement, electrocardiography (ECG), thyroid stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4) levels have been assessed.

1. Our study focused on patients presenting with acute atrial fibrillation to the Coronary Care Unit. We excluded patients with chronic AF, valvar heart disease, and acute decompensated heart failure to avoid confounding and to isolate the relationship with thyroid dysfunction.
2. The study was conducted in one center, Al-Sader Teaching Hospital, and data collection was limited to a one-year period. This restricts the number of cases.
3. Acute AF requiring CCU admission is less frequent compared to other cardiac conditions. Therefore, accumulating a large number in a short period from a single center is difficult.
4. Despite the moderate sample size, we performed a power calculation before starting. A sample of 110 patients was statistically adequate to estimate the prevalence with an acceptable margin of error and to detect significant associations for our primary objective.

Larger multicenter study would improve generalizability, our sample size was appropriate for a preliminary prevalence study in our hospital.

ETHICAL APPROVAL

All patients consented as per ethical approval.

INCLUSION CRITERIA

Any patient newly diagnosed with acute atrial fibrillation not more than 48 hours from symptoms onset admitted to the coronary care unit.

Table 1. Distribution of patients with atrial fibrillation according to study variables (N=110)

Study variables	Number	[%]
Residence		
Urban	69	62.7%
Rural	41	37.3%
Total	110	100.0%
Lifestyle		
Active	68	61.8%
Sedentary	42	38.2%
Total	110	100.0%
Smoking		
Active smoker	10	9.1%
Passive smoker	35	31.8%
Ex-smoker	19	17.3%
Non smoker	46	41.8%
Total	110	100.0%
Alcohol consumption		
Yes	3	2.7%
No	107	97.3%
Total	110	100.0%

Source: Compiled by the authors of this study

Table 2. The means ± SD and range of systolic and diastolic blood pressure of patients with atrial fibrillation N=110

Blood pressure	N	Mean ± SD	Range
Systolic blood pressure (mmHg)	110	143.17 ± 12.25	(123.0-175.0)
Diastolic blood pressure (mmHg)	110	80.85 ± 7.65	(67.0 - 99.0)

Source: Compiled by the authors of this study

Table 3. The means ± SD and range of thyroid function test for patients with atrial fibrillation (N=110)

Thyroid function test	N	Mean ± SD	Range
T3 (nmol/l)	110	2.25 ± 0.84	(0.57-4.90)
T4 (nmol/l)	110	122.01 ± 38.46	(45.23 - 201.70)
TSH (µIU/ml)	110	2.79 ± 2.38	(0.08-12.90)

Source: Compiled by the authors of this study

EXCLUSION CRITERIA

- Patients who those already been diagnosed with chronic AF
- Patients with a history of malignancy on chemotherapy
- Patients with a history of radiotherapy
- Patients with sepsis and shock
- Patients with diagnosed thyroid disease

BLOOD SAMPLING

The thyroid function test is done by Roche Cobas e411 automated machine which uses the Electrochemoluminescence immunoassay method.

- Serum Thyroid stimulating hormone (TSH) has been taken by a venous sample on the same day of admission to the coronary care unit, and the normal range was used (0.40-5.0) µIU/mL.
- Serum total Triiodothyronine (T3) concentration has been taken by the venous sample during admission day, and the normal range was used (1.2-3.1) nmol/L.
- Serum total Thyroxine (T4) concentration has been taken by the venous sample during admission day, and the normal range used (66-181) nmol/L.

Thyroid dysfunction abnormalities were classified according to the above tests below:

- Overt hyperthyroidism TSH level <0.1mIU/L or undetectable with elevated T4 or T3.
- Overt hypothyroidism TSH level >4.5 mIU/L with low T4.
- Subclinical hyperthyroidism TSH level <0.1mIU/l or(0.1-0.4) mIU/L with normal T3 and T4
- Subclinical hypothyroidism TSH level >4.5mIU/L with normal T4 [26].

DATA ANALYSIS

Statistical analysis was carried out using SPSS version 27. Continuous variables are presented as mean, standard deviation, and range. Categorical variables are presented

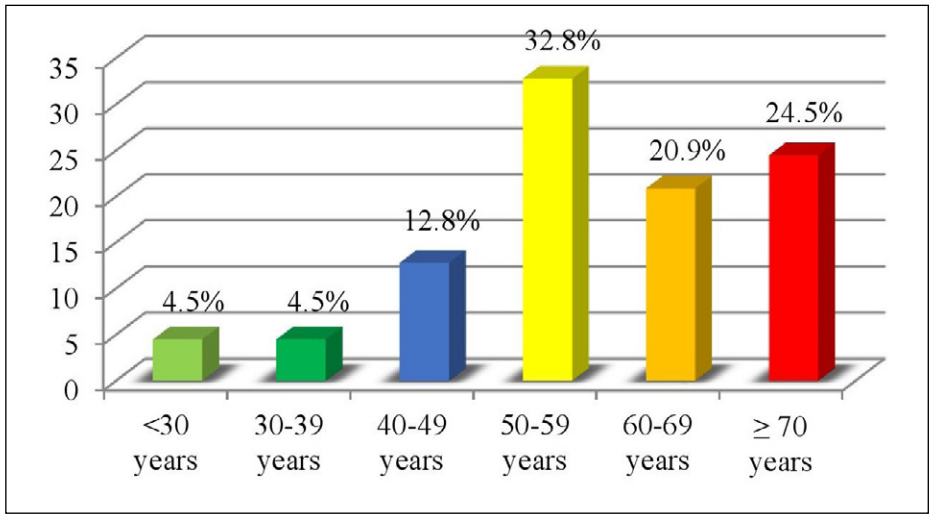


Fig. 1. Distribution of patients with atrial fibrillation according to age (years) (N=110)
Source: Own materials

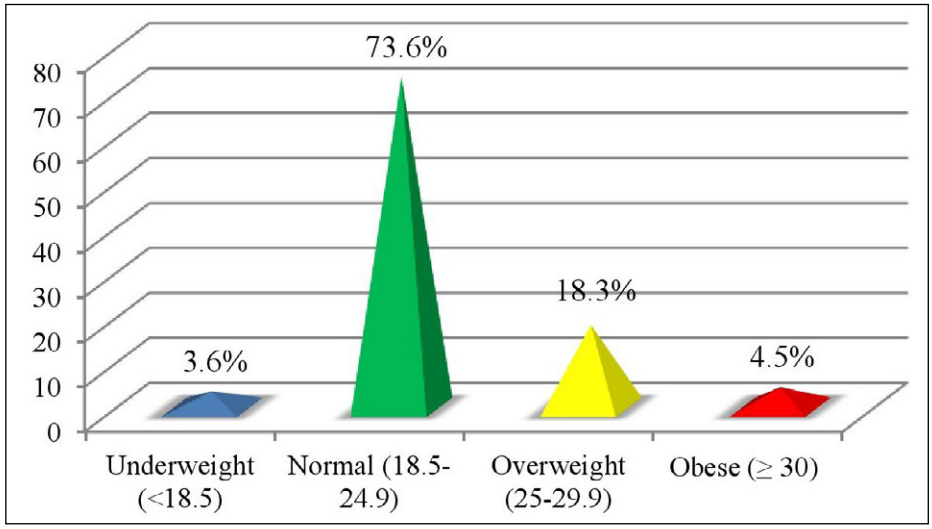


Fig. 2. Distribution of patients with atrial fibrillation according to BMI (kg/m^2) (N=110)
Source: Own materials

as frequencies and percentages. ANOVA test was used to compare means among 3 groups. Fisher's exact test was used to find the association between categorical variables. A p-value of ≤ 0.05 was considered significant.

RESULTS

In this study, 110 patients were enrolled all with confirmed atrial fibrillation by electrocardiography not more than 48 hours from symptom onset, distribution of patients with atrial fibrillation according to age including (<30 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and ≥ 70 years). Age <30 years represents only five patients 4.5%, age of 30-39 years represents only five patients 4.5%, age of 40-49 years represents N=14, 12.8%, age of 50-59 years represent N=36, 32.8%, age of 60-69 years represent N=23, 20.9% and age of ≥ 70 years represent N=27, 24.5% of patients. The mean age of patients was 57.82 ± 13.03 with an older patient was 79 years and a younger patient was 27 years (Fig. 1). The patients' BMI was also considered (Fig. 2).

Table 1 shows the distribution of patients with atrial fibrillation according to study variables including (residence, lifestyle, smoking habit, and alcohol consumption). Patients from urban areas represent N=69, 62.7% and patients from rural areas represent N=41, 37.3%. Patients with active lifestyles represent N=68, 61.8% and patients with sedentary lifestyles represent N=42, 38.2%. Active Smokers represent only ten patients 9.1% and only three patients 2.7% had a history of Alcohol use (two of them were ex-alcoholic and one still alcoholic).

Figure 3 shows the distribution of patients with atrial fibrillation according to the history of COVID-19 infection including (positive and negative). Patients with a positive history of COVID-19 infection represent N=74, 67.3% and patients with negative family history represent N=36, 32.7% of patients.

Figure 4 shows the distribution of patients with atrial fibrillation according to past medical history including (positive and negative). Patients with positive past medical history represent N=85, 77.3% and patients with negative past medical history represent N=25, 22.7% of patients.

In table 2 means, standard deviations, and range of systolic and diastolic blood pressure of patients with

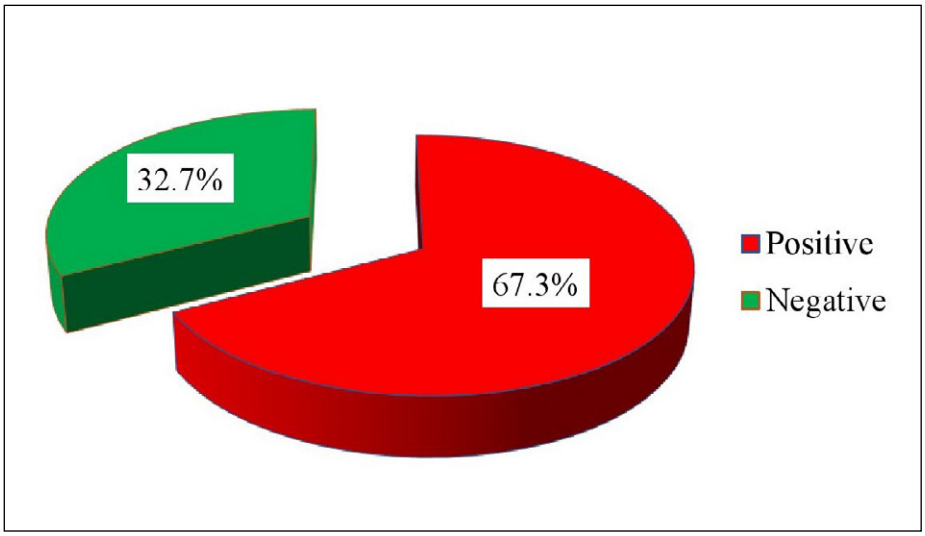


Fig. 3. Distribution of patients with atrial fibrillation according to the history of COVID-19 infection N=110
Source: Own materials

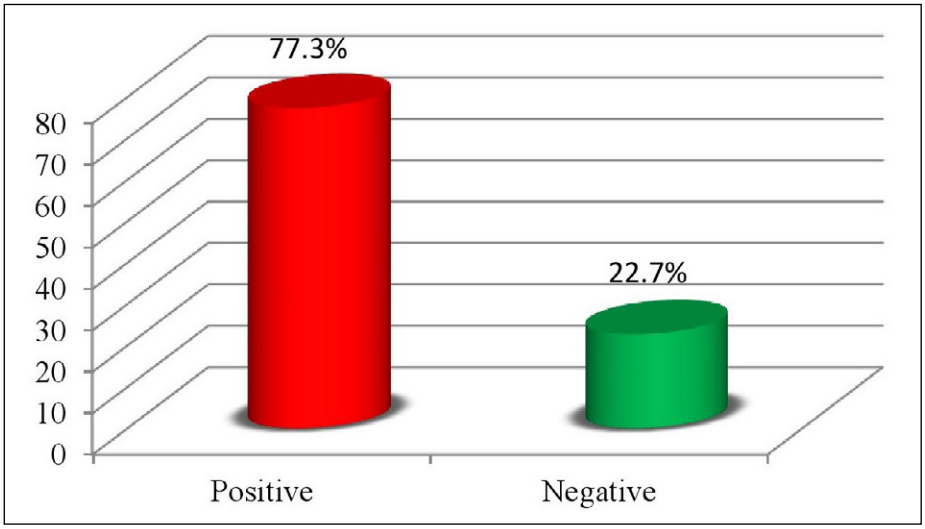


Fig. 4. Distribution of patients with atrial fibrillation according to past medical history (N=110)
Source: Own materials

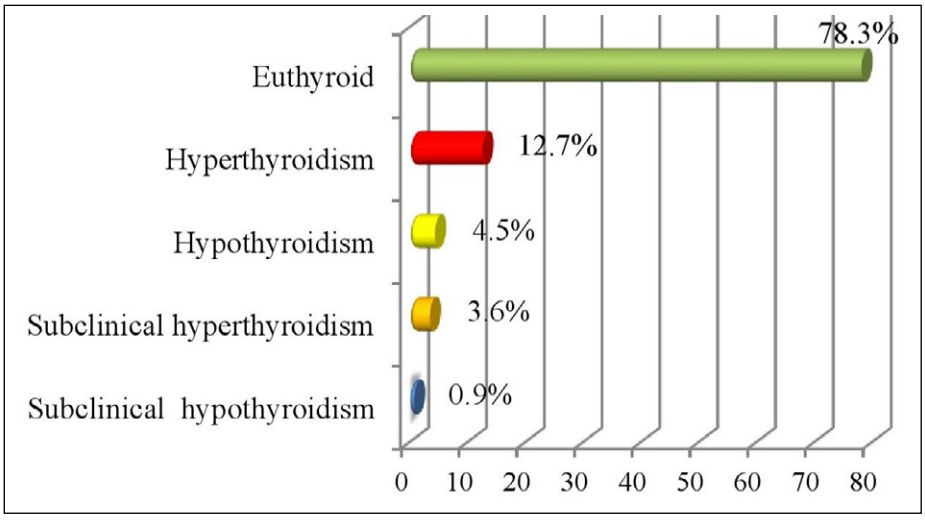


Fig. 5. Distribution of patients with atrial fibrillation according to thyroid function test (N=110)
Source: Own materials

atrial fibrillation. The mean systolic blood pressure was (143.17 ± 12.25) mmHg and the mean diastolic blood pressure was (80.85 ± 7.65) mmHg.

In table 3 the means, standard deviations, and range of thyroid function test including T3 (nmol/l), T4 (nmol/l), and TSH (μIU/ml) for patients with atrial fibrillation. Mean T3 was 2.25 ± 0.84 nmol/l and mean T4 was 122.01 ± 38.46 nmol/l and mean TSH was 2.79 ± 2.38 μIU/ml.

In table 4 the mean differences of study variables including age (years) and body mass index kg/m^2 according to thyroid function test including (hypothyroidism, hyperthyroidism, and Euthyroid status). There were no

Table 4. The mean differences of study variables according to the thyroid function test (N=110)

Study variables	Thyroid function test	N	Mean ± SD	F	P-value
Age (years)	Hypothyroidism	6	58.67 ± 16.08	0.356	0.702
	Hyperthyroidism	18	55.44 ± 13.19		
	Euthyroid	86	58.26 ± 12.90		
Body mass index (kg/m^2)	Hypothyroidism	6	25.46 ± 3.80	1.273	0.284
	Hyperthyroidism	18	23.16 ± 3.65		
	Euthyroid	86	23.62 ± 2.89		

Source: Compiled by the authors of this study

Table 5. Association between thyroid function test and study variables (N=110)

Study variables	Thyroid function test			Total (N=110) n(%)	P-value
	Hypothyroidism (N=6)	Hyperthyroidism (N=18)	Euthyroid (N=86)		
Sex					
Female	4 (66.7)	10 (55.6)	42 (48.8)	56(50.9)	0.724
Male	2 (33.3)	8 (44.4)	44 (51.2)	54(49.1)	
Total	6 (100.0)	18 (100.0)	86 (100.0)	110(100)	
Residence					
Urban	2 (33.3)	13 (72.2)	54 (62.8)	69 (62.7)	0.25
Rural	4 (66.7)	5 (27.8)	32 (37.2)	41 (37.3)	
Total	6 (100.0)	18 (100.0)	86 (100.0)	110(100.0)	
Lifestyle					
Active	3 (50.0)	14 (77.8)	51 (59.3)	68 (61.8)	0.276
Sedentary	3 (50.0)	4 (22.2)	35 (40.7)	42 (38.2)	
Total	6 (100.0)	18 (100.0)	86 (100.0)	110 (100.0)	
Smoking					
Active smoker	1 (16.7)	2 (11.1)	7 (8.1)	10 (9.1)	0.442
Passive smoker	4 (66.7)	4 (22.2)	27 (31.4)	35 (31.8)	
Ex-smoker	0 (0.0)	3 (16.7)	16 (18.6)	19 (17.3)	
Non-smoker	1 (16.7)	9 (50.0)	36 (41.9)	46 (41.8)	
Total	6 (100.0)	18 (100.0)	86 (100.0)	110 (100.0)	
Alcohol consumption					
Yes	0 (0.0)	0 (0.0)	3 (3.5)	3 (2.7)	1.000
No	6 (100.0)	18 (100.0)	83 (96.5)	107 (97.3)	
Total	6 (100.0)	18 (100.0)	86 (100.0)	110 (100.0)	

Source: Compiled by the authors of this study

significant differences between means of age and body mass index according to the thyroid function test.

The table 5 shows association between thyroid function test including (hypothyroidism, hyperthyroidism and Euthyroid status) and study variables including (sex, residence, lifestyle, smoking habit and alcohol consumption). There was no significant association between thyroid function test and study variables.

DISCUSSION

Thyroid disease burden in patients with atrial fibrillation can be predicted from the systemic effects of thyroid hormones that contribute to increased vascular resistance, cardiac contractility, heart rate, and left ventricular mass [1]. In this study, hyperthyroidism was 16.3%which was more prevalent than the general population which is estimated to be 0.2% to 1.3% in iodine-sufficient parts of the world [27-28], compared to another study done by Auer J et al showed that the prevalence of hyperthyroidism in AF was 13.8% [29], another study found that 8.3% developed new AF or flutter within 30 days of diagnosis of hyperthyroidism [30], whereas study found that AF in hyperthyroidism patients around 10-25% [31], while the prevalence of hypothyroidism in this study was 5.4%for both overt and subclinical hypothyroidism, The prevalence of overt hypothyroidism in the general population ranges from between 0.2% and 5.3% in Europe and 0.3% and 3.7% in the USA [32-34] which is comparable to the results of the current study. Another study revealed that

hypothyroidism is associated with decreased risk of AF [35], these results are compatible with a study done in Brazil by Barbisan, Juarez Neuhaus et al., [36], which found a prevalence of hyperthyroidism 6.9% and hypothyroidism 5.6% in AF patients. Among patients with hyperthyroidism both overt and Subclinical, 10 patients were female vs. 8 male patients, while in the hypothyroidism arm, 4 were female vs. 2 male patients .this female predominance may be explained by the observation that the prevalence of both conditions more in females. This may be explained by more autoimmune diseases and the role of sex hormones in females [37]. In this study percentage of patients with af increased with increasing age with most age group affected being (50-59) years, Mean age of patients was (57.82 ± 13.03) this age relationship was documented in many studies as noted in the ATRIA study [38], number of patients according to gender is about equal in this study. In our study, no significant association was found between thyroid dysfunction and systolic, diastolic measurements of blood pressure whereas a study done by Dernellis et al found an increase in diastolic blood pressure in hypothyroidism patients which is reversible in 50% of patients with thyroxine treatment [39], on the other hand, a study conducted by Marcisz et al showed that systolic blood pressure higher than the healthy control which normalized after a short treatment with anti-thyroid medication while diastolic blood pressure was lower [40]. Patients with hypothyroidism had a mean BMI of 25.46 which is overweight in contrast to hyperthyroidism patients mean BMI of 23.16 within the normal range for BMI but without significant p-value for both conditions and BMI .same findings were in a study published in India [41]. In our study, no significant association was found among lifestyle, smoking, alcohol consumption, and thyroid dysfunction.in contrast to this, a study done in China found that smoking, alcohol consumption, and exercise were associated with decreased incidence of hypothyroidism, alcohol consumption was associated with decreased probability of hyperthyroidism, hypothyroidism, as well as positive TPOAb, The amounts of cigarettes smoked daily displayed a positive correlation with hyperthyroidism among smokers, Accordingly, smoking seemed to be associated with decreased risk for hypothyroidism and positive TPOAb. This study was done on a minor ethnic group in China [42]. Around 67.3% of patients had a history of (SARS-CoV-2) of them 6 were hypothyroid and 12 were hyperthyroid with no significant p-value found, in a study published in 2021 found around 13.1% of patients with COVID 19 had thyroid dysfunction but these findings were transient and tested during hospitalization for COVID infection [43]. Another study done on severe COVID 19 patients show mild transient thyroiditis and areas of focal hypoechogenicity on thyroid ultrasound with no residual abnormalities on long term follow up [44]. In our study 25.5% had a past medical history of thyroid disease, one patient was hypothyroid and six had hyperthyroidism with no significant p-value found, compared to this study a multicenter cohort study showed different results with half of the patients of both hypothyroidism and Graves' disease had family history of thyroid disease [45]. This may be explained by the large study sample used and different populations also the lack of data systems in our hospitals. In Our study, although hypertension, Dm, IHD, and CVA were frequent no significant relationship between past medical history and thyroid dysfunction regardless of the type of the disease the patient had was found, contrary to this a study done by Nearmeen M. Rashad et al found that hypertension was significantly prevalent in hypothyroid patients compared to hyperthyroid patients and DM especially type 2 where significant throughout the spectrum of thyroid dysfunctions encountered [46].

LIMITATIONS OF THE STUDY

1. Single-Center Design was conducted only at Al-Sader Teaching Hospital. Therefore, results may not be generalizable.
2. Cross-Sectional Study can determine prevalence but cannot establish a causal relationship between thyroid dysfunction and acute atrial fibrillation.
3. Sample Size, sample of 110 patients is considered moderate. A larger sample is needed to detect smaller differences between subgroups.
4. Patients were not followed after discharge from CCU. So the effect of treating thyroid dysfunction on AF recurrence could not be assessed.

CONCLUSIONS

High prevalence of thyroid function abnormalities was common among patients with acute atrial fibrillation especially hyperthyroidism exceeding that of the general population with the female being more affected in this study. Although many comorbidities were frequent, the same as other patients' variables, No significant associations were present between thyroid dysfunction and these variables.

RECOMMENDATIONS FOR FUTURE RESEARCHES

1. Multicenter study, a multicenter study across different governorates in Iraq to increase sample size and generalizability.
2. Longitudinal cohort design, a prospective cohort study with long-term follow-up is recommended

to evaluate the causal relationship and the impact of thyroid treatment on AF outcomes.

3. Screening protocol: screening for thyroid function tests in all patients admitted with acute atrial fibrillation to CCU is recommended for early detection and management.
4. Larger sample size needed to evaluate the difference between hyperthyroidism and hypothyroidism as risk factors for AF.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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