# **ORIGINAL ARTICLE**

# Prevalence of Hyperthyroidism in Patients with Atrial Fibrillation

INAM ULLAH<sup>1</sup>, SHAKIR GHAFFAR<sup>2</sup>, MUHAMMAD ILYAS<sup>3</sup>, FALAK ZEB<sup>4</sup>, SULAIMAN TAHIR<sup>5</sup>, MUHAMMAD HAIDAR ZAMAN<sup>6</sup>

<sup>1</sup>Department of Cardiology, First Affiliated Hospital of Nanjing Medical University, China

<sup>2</sup>Department of Cardiology, Hayatabad Medical Complex, Peshawar

<sup>3</sup>Cardiology Department, Pakistan Institute Of Medical Sciences (PIMS), Islamabad
<sup>4</sup>Department Of Nutrition and Dietetics, National University of Medical Sciences, Islamabad

<sup>5</sup>College of physicians and surgeons Pakistan (CPSP)

<sup>6</sup>IBD, Nan Shi Fu Zhang (NSFZ), Nanjing Normal University, China

Corresponding author: Muhammad Haidar Zaman, Email: dr.mhaidarzaman@gmail.com

## ABSTRACT

**Background:** Hyperthyroidism causes a rise in cardiovascular disease and dysrhythmias, leading to increased mortality. Low serum thyrotropin levels are a known independent risk factor for atrial fibrillation (AF). The frequency of hyperthyroidism in patients with AF is still unknown.

**Objectives:** To determine the prevalence of hyperthyroidism in patients with AF admitted to a tertiary care hospital in Peshawar. **Methodology:** This was a cross sectional observational study that included 155 patients with AF. The study was conducted in the cardiology department of a tertiary care hospital in Peshawar, Pakistan, from December 2019 to May 2020.

**Results:** Hyperthyroidism was found in 13(8.39%) patients with atrial fibrillation, while 142(91.61%) patients were without hyperthyroidism. There were 94 (60.65%) males and 61(39.35%) females. The ratio of male to female was 1.6: 1. The mean age of the patients enrolled was 50.35 years+14.95SD, with a range of 18-75 years. Patients were divided into three age groups, and atrial fibrillation was common in the 41-60 (years) age group.

**Conclusion:** Hyperthyroidism is a recognized cause of atrial fibrillation. Every new-onset atrial fibrillation should be investigated with serum TSH levels. It can result in cerebral embolic episodes, particularly in the elderly and people with other risk factors. **Keywords:** Atrial fibrillation, Hyperthyroidism, Arrhythmia

## INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia, which is more frequent in older people. About 1% of patients under the age of 60 and 8% of patients over the age of 80 experience it. Younger people can also have AF, even though it typically affects those over 60.AF<sup>1-3</sup>. AF is a supraventricular tachyarrhythmia characterized by unsynchronized atrial activity and subsequent mechanical atrial function deterioration. Electrocardiographic findings include oscillatory or fibrillatory waves of various sizes, amplitudes, and timing replacing regular P waves (which reflect synchronous atrial activity). Unless additional conduction anomalies exist, the QRS complex stays narrow (e.g., bundle branch block, accessory pathways). Ventricular response is usually fast, extending from 90 to 170 beats per minute. Because AF reduces cardiac function and increases the risk of stroke, it can greatly increase the risk of morbidity and mortality<sup>4, 5</sup>.

AF is a common type of arrhythmia. In the United States of America, about 2.3 million people develop AF, and 160,000 new cases are diagnosed annually<sup>6, 7</sup>. Approximately 9 out of 100 people over the age of 65 years have AF<sup>8</sup>. AF is an independent risk factor for mortality<sup>9</sup>; it can also lead to or worsen heart failure and increase mortality in patients with myocardial infarction<sup>10, 11</sup>.

AF can be a source of heart symptoms and complications of embolism. So the main focus in treatment is control of heart rate and prevention of embolic complications. AF is also the primary goal of therapy in patients with heart failure comorbid with atrial fibrillation. Uncontrolled ventricular response aggravates symptoms and debility in heart failure patients and presents a challenge for managing the condition<sup>12</sup>. AF management requires understanding the pattern of presentation (paroxysmal, chronic, or permanent) and decisions concerning sinus rhythm restoration and maintenance, ventricular rate control, and antithrombotic treatment<sup>3, 9</sup>.

Hyperthyroidism occurs in 9–15% of patients with AF patients according to the published literature. the depleted level of thyrotropin in serum is an sovereign risk factor for AF<sup>13</sup>. The thyroid bestows to arrhythmogenic activity by shifting atrial myocyte's electrophysiological features through shortening the action potential duration, enhancing automaticity, and triggering activity in the pulmonary vein cardio myocytes<sup>14</sup>. Excess mortality is associated with hyperthyroidism due to the increased frequency of cardiovascular disease and arrhythmias<sup>15, 16</sup>.

Atrial fibrillation is induced by hyperthyroidism and is one of the main contributors to destabilizing patient symptoms of heart failure. Our study aims to find the frequency of hyperthyroidism in a patient with atrial fibrillation.

## MATERIAL AND METHODS

This cross-sectional observational study assessed the relationship between hyperthyroidism and AF. The ethics committee approved the study of the Hayatabad medical complex Peshawar. Informed consent was signed and obtained from each patient.

**Study population:** All patients meeting the inclusion criteria with atrial fibrillation and low serum TSH of less than 0.3miu/ml with serum T4 greater than 14.1mcg/dl and T3 greater than 2.0ng/ml performed through electrochemiluminescence immunoassay (ELCIA) from Hayatabad medical complex Peshawar were enrolled in the study through outpatient department and cardiac care unit and were admitted to the ward for further evaluation.

The patients were evaluated with complete history, physical examination, routine investigations, and conditions mentioned in the exclusion criteria to control confounding variables and bias in the study results.

All patients with AF on ECG were subjected to undergo thyroid functions test, and those with hyperthyroidism, according to operational definition, were included in the study after evaluation by an expert endocrinologist with at least five years' experience.

**Statistical Analysis:** The statistical analysis was done using SPSS 25.0. Continuous variables like age and duration of AF were expressed as means ± standard deviations or medians. Categorical variables such as gender were presented as frequencies. A statistically significant p-value of 0.05 was used. Age and gender were used to stratify AF to examine the effects of changes. Tables and graphs are used to illustrate all of the results.

### RESULTS

A total of 155 patients were included in this study. The study was conducted at the cardiology department of the MTI-Hayatabad Medical Complex Peshawar. 60.65% (94) of study patients were male, and 39.35% (61) were female. The male-to-female ratio was 1.6:1, as shown in Fig 1.

The mean age of the patient enrolled in this study was 50.35 years+14.95SD with a range of 18-75 years. Patients were divided into three age groups; AF was common in the 41-60 age group. There were 47(30.3%) patients with age  $\leq 40$  years, 59(38.1%)

patients were in the age range of 41-60 years, and 49(31.6%) presented were of more than 60 years of age Table 1



Figure 1: Gender wise distribution of the study population



Figure 2: Frequency of Hyperthyroidism in patients with atrial fibrillation (n=155).

0			
Age (years)	Frequency	Percent	Mean +SD
<= 40.00	47	30.3	
41.00 - 60.00	59	38.1	50.35 years+14.95
61.00+	49	31.6	
Total	155	100.0	

Table 1: Age-wise distribution of the patients with atrial fibrillation.

Table 2:	Age-wise	distribution	of	hyperthyroidisn	n in	patients	with	atrial
fibrillation	1							

Age					p-value
(in years)		Hyperth	Hyperthyroidism		
		Yes	No	Total	
	<= 40.00	4	43	47	0.348
		8.5%	91.5%	100.0%	
	41.00-60.00	7	52	59	
		11.9%	88.1%	100.0%	
	61.00+	2	47	49	
		4.1%	95.9%	100.0%	
Total		13	142	155	
		8.4%	91.6%	100.0%	

Table 3: Gender, smoking,	and	BMI-wise	distribution	of	Atrial	fibrillation
patients having hyperthyroidi	sm					

		Hyperthyroidism		p-value
		Yes	No	
Gender	Male	7	87	0.600
		7.4%	92.6%	
	Female	6	55	
		9.8%	90.2%	
Smoking	Yes	3	29	0.821
		9.4%	90.6%	
	No	10	113	
		8.1%	91.9%	
Body Mass Index (kg/m)	<= 30.00	7	90	0.4977
		7.2%	92.8%	
	31.00+	6	52	
		10.3%	89.7%	

Hyperthyroidism was found in 13(8.39%) patients having atrial fibrillation, while 142(91.61%) patients were not having hyperthyroidism, as shown in Fig 2

Age-wise distribution of hyperthyroidism in our study showed that it was observed in most patients having the age group 41-60 years, although it was not significant with p-value=0.348. Hyperthyroidism was found in four (8.5%) patients of the age group  $\leq$  40 years, in the age group of 41-60 years, 11.9% of patients were found with hyperthyroidism, and the age group with more than 60 years of age had 4.1% of patients with hyperthyroidism. Table 2

Gender-wise distribution of hyperthyroidism shows that gender also has no significant role over them with p-value=0.600. There were 7.4% hyperthyroidism in male patients and 9.8% observed in female patients included in our study. Smoking and BMI also have no significant effect, although it was greater in smokers and obese patients Table 3.

### DISCUSSION

Thyroid hormones affect the cardiovascular system differently and play an essential role in regulating cardiovascular homeostasis under physiologic and pathologic conditions. The heart is particularly prone to changes in local tri-iodothyronine (T3) levels<sup>17</sup> because T3 is essential for maintaining cardiac morphology. Sinuous tachycardia is the most typical arrhythmia associated with hyperthyroidism. Our study showed that hyperthyroidism in patients with atrial fibrillation was found in 13(8.39%) patients, while 142(91.61%) patients did not have hyperthyroidism. In the age group of 41-60 years, hyperthyroidism was found in (11.9%) of patients. Hyperthyroidism was more common in male patients (60.65%) than female patients (39.35%), with a male-to-female ratio of 1.6:1.

In a study<sup>20</sup> about 21% of people with Grave's disease also had AF. Similar to our findings, the prevalence of AF was substantially higher in those over 40 than in those under 40 (31% versus 0%)<sup>18</sup>. Krahn et al. revealed that 1% of all new occurrences of AF were caused by hyperthyroidism. In order to rule out hyperthyroidism, serum thyrotropin should be assessed in all those patients with new onset of AF, according to the published literature. This connection is remarkable in the lack of further hyperthyroidism symptoms and signs<sup>19</sup>. However, according to another study, biochemical evidence of hyperthyroidism was present in 13% of patients with unexplained atrial fibrillation. <sup>19</sup>.

Iwasaki and coworkers reported that more severe Hyperthyroidism biochemically (higher serum thyroxin and triiodothyronine levels) could increase the chances of AF<sup>20</sup>. However, this study did not contain biochemical information about the severity of hyperthyroidism. In 40,628 patients from the Danish National Registry over 20 years, Lars Frost et al. discovered that 8.3% of patients experienced AF or flutter within 30 days of diagnosis. This is very similar to our findings<sup>21</sup>.

Auer J et al. Investigated 23,638 individuals and observed that 13.8 % of participants with overt hyperthyroidism developed atrial fibrillation, compared to 2.3 % of euthyroid. Patients with low blood thyrotropin concentrations had a 13.3% ratio of AF, compared to 2.3% in those with normal concentration<sup>22</sup>. Sawin C T and his group found a 2.8-fold higher risk of AF in subclinical hyperthyroid patients over the age of 60 years. The history of smoking was taken, and its association was determined with hyperthyroidism in our study. The rate of hyperthyroidism was not significantly different between smokers and non-smokers (9.4 % vs. 8.1 %)23. In an extensive prospective population survey, smokers were found to have a higher risk of atrial fibrillation in nonthyrotoxic individuals. The link between thyrotoxic AF and smoking was less apparent. One research looked at the link between smoking and chronic thyrotoxic atrial fibrillation, and no association was observed 24.

#### CONCLUSION

Hyperthyroidism is one of the critical reversible causes of atrial fibrillation in patients with no cardiac valvular lesions. It can be caused by both overt and subclinical hyperthyroidism.

**Recommendation:** Every patient with a new onset of atrial fibrillation should have their serum TSH levels tested. In severe conditions, anti-thyroid medication and beta-blockers should be used. Treatment is also recommended in subclinical hyperthyroidism with atrial fibrillation.

#### REFERENCES

- Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV and Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. Jama. 2001;285:2370-5.
- Feinberg WM, Blackshear JL, Laupacis A, Kronmal R and Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. Archives of internal medicine. 1995;155:469-73.
- Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE and Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). The American journal of cardiology. 1994;74:236-41.
- Psaty BM, Manolio TA, Kuller LH, Kronmal RA, Cushman M, Fried LP, White R, Furberg CD and Rautaharju PM. Incidence of and risk factors for atrial fibrillation in older adults. Circulation. 1997;96:2455-61.
- Stewart S, MacIntyre K, MacLeod MM, Bailey AE, Capewell S and McMurray JJ. Trends in hospital activity, morbidity and case fatality related to atrial fibrillation in Scotland, 1986--1996. European heart journal. 2001;22:693-701.
- Jaïs P, Haïssaguerre M, Shah DC, Chouairi S, Gencel L, Hocini M and Clémenty J. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. Circulation. 1997;95:572-6.
- Leone O, Boriani G, Chiappini B, Pacini D, Cenacchi G, Martin Suarez S, Rapezzi C, Bacchi Reggiani ML and Marinelli G. Amyloid deposition as a cause of atrial remodelling in persistent valvular atrial fibrillation. European heart journal. 2004;25:1237-41.
- Goette A, Staack T, Röcken C, Arndt M, Geller JC, Huth C, Ansorge S, Klein HU and Lendeckel U. Increased expression of extracellular signal-regulated kinase and angiotensin-converting enzyme in human

atria during atrial fibrillation. Journal of the American College of Cardiology. 2000;35:1669-77.

- De Ferrari GM, Klersy C, Ferrero P, Fantoni C, Salerno-Uriarte D, Manca L, Devecchi P, Molon G, Revera M, Curnis A, Sarzi Braga S, Accardi F and Salerno-Uriarte JA. Atrial fibrillation in heart failure patients: prevalence in daily practice and effect on the severity of symptoms. Data from the ALPHA study registry. European journal of heart failure. 2007;9:502-9.
- Le Heuzey JY, Paziaud O, Piot O, Said MA, Copie X, Lavergne T and Guize L. Cost of care distribution in atrial fibrillation patients: the COCAF study. American heart journal. 2004;147:121-6.
- 11. Scherf D, Schaffer AI and Blumenfeld S. Mechanism of flutter and fibrillation. AMA archives of internal medicine. 1953;91:333-52.
- Röcken C, Peters B, Juenemann G, Saeger W, Klein HU, Huth C, Roessner A and Goette A. Atrial amyloidosis: an arrhythmogenic substrate for persistent atrial fibrillation. Circulation. 2002;106:2091-7.
- Sawin CT, Geller A, Wolf PA, Belanger AJ, Baker E, Bacharach P, Wilson P, Benjamin EJ and D'Agostino RB. Low Serum Thyrotropin Concentrations as a Risk Factor for Atrial Fibrillation in Older Persons. New England Journal of Medicine. 1994;331:1249-1252.
- Chen Y-C, Chen S-A, Chen Y-J, Chang M-S, Chan P and Lin C-I. Effects of thyroid hormone on the arrhythmogenic activity of pulmonary vein cardiomyocytes. Journal of the American College of Cardiology. 2002;39:366-372.
- Kahaly GJ, Bartalena L, Hegedüs L, Leenhardt L, Poppe K and Pearce SH. 2018 European Thyroid Association Guideline for the Management of Graves' Hyperthyroidism. European Thyroid Journal. 2018;7:167-186.
- Gorenek B, Boriani G, Dan G-A, Fauchier L, Fenelon G, Huang H, Kudaiberdieva G, Lip GYH, Mahajan R, Potpara T, Ramirez JD, Vos MA, Marin F and Group ESD. European Heart Rhythm Association (EHRA) position paper on arrhythmia management and device therapies in endocrine disorders, endorsed by Asia Pacific Heart Rhythm Society (APHRS) and Latin American Heart Rhythm Society (LAHRS). EP Europace. 2018;20:895-896.
- 17. Grais IM and Sowers JR. Thyroid and the heart. The American journal of medicine. 2014;127:691-8.
- Van Gelder IC, Crijns HJ, Van Gilst WH, Verwer R and Lie KI. Prediction of uneventful cardioversion and maintenance of sinus rhythm from direct-current electrical cardioversion of chronic atrial fibrillation and flutter. The American journal of cardiology. 1991;68:41-6
- Gürdoğan M, Ari H, Tenekecioğlu E, Ari S, Bozat T, Koca V and Melek M. Predictors of Atrial Fibrillation Recurrence in Hyperthyroid and Euthyroid Patients. Arquivos brasileiros de cardiologia. 2016;106:84-91.
- Iwasaki T, Naka M, Hiramatsu K, Yamada T, Niwa A, Aizawa T, Murakami M, Ishihara M and Miyahara Y. Echocardiographic studies on the relationship between atrial fibrillation and atrial enlargement in patients with Hyperthyroidism of Graves' disease. Cardiology. 1989;76:10-7.
- Frost L, Benjamin EJ, Fenger-Grøn M, Pedersen A, Tjønneland A and Overvad K. Body fat, body fat distribution, lean body mass and atrial fibrillation and flutter. A Danish cohort study. Obesity (Silver Spring, Md). 2014;22:1546-52.
- Auer J, Scheibner P, Mische T, Langsteger W, Eber O and Eber B. Subclinical hyperthyroidism as a risk factor for atrial fibrillation. American heart journal. 2001;142:838-42.
- Sawin CT, Geller A, Wolf PA, Belanger AJ, Baker E, Bacharach P, Wilson PW, Benjamin EJ and D'Agostino RB. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. The New England journal of medicine. 1994;331:1249-52.
- Siu CW, Pong V, Zhang X, Chan YH, Jim MH, Liu S, Yiu KH, Kung AW, Lau CP and Tse HF. Risk of ischemic stroke after new-onset atrial fibrillation in patients with hyperthyroidism. Heart rhythm. 2009;6:169-73.