

# Prevalence of Atrial Fibrillation among Individuals with Obstructive Sleep Apnea and Impact of Sleep Apnea on Incidence and Outcomes of Atrial Fibrillation: Systematic Review

Muhammad Adil Ramzan<sup>1</sup>, Kanwal Sartaj<sup>2</sup>, Aneela Altaf Kidwai<sup>1</sup>, Nargis Anjum<sup>1</sup>, Ali Nasir<sup>3</sup>

<sup>1</sup>Department of Medicine, Karachi Medical and Dental College, Abbasi Shaheed Hospital Karachi; <sup>2</sup>Pakistan Navy Ship (PNS) Rahat Hospital, Karachi; <sup>3</sup>Department of Medicine, Ziauddin University, Karachi

## ABSTRACT

**Objective:** This systematic review aims to evaluate the prevalence of AF in individuals with OSA and examine the impact of OSA on AF occurrence and outcomes.

**Methodology:** A systematic literature search was conducted using PubMed, Web of Science, and Google Scholar, following PRISMA 2020 guidelines and The Cochrane Handbook. Studies were selected based on predefined inclusion and exclusion criteria, focusing on human observational studies examining the relationship between OSA and AF. The risk of bias was assessed independently by two reviewers, with a third reviewer resolving discrepancies.

**Results:** Out of 200 initially identified studies, 37 met the relevance criteria, and 8 were ultimately included in the final analysis. The findings revealed a significant association between OSA and AF prevalence, with AF rates ranging from 7.2% to 49% in OSA patients, depending on the study population and OSA severity. Studies also indicated that OSA might contribute to AF development through mechanisms such as hypoxia, inflammation, and autonomic dysfunction. Furthermore, OSA was linked to a higher risk of AF recurrence post-treatment and increased hospitalization rates.

**Conclusions:** The evidence suggests that OSA is an independent risk factor for AF, contributing to its development, recurrence, and worse clinical outcomes. Early identification and management of OSA, including continuous positive airway pressure (CPAP) therapy, may help mitigate AF-related risks. However, further large-scale prospective studies are needed to establish causal relationships and optimize treatment strategies.

**Key words:** Atrial Fibrillation, Arrhythmia, Breathing, Cardiovascular, Obstructive Sleep Apnea, Sleep-disordered,

### Authors' Contribution:

<sup>1,2</sup>Conception; Literature research; manuscript design and drafting; <sup>3,4</sup>Critical analysis and manuscript review; <sup>5</sup>Data analysis; Manuscript Editing.

### Correspondence:

Muhammad Adil Ramzan  
Email: [dradilxyz@gmail.com](mailto:dradilxyz@gmail.com)

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## Introduction

Atrial Fibrillation (AF) showcases the balance of the cardiovascular system and the consequences when this balance is disrupted.<sup>1</sup> The heart functions with a beat to ensure the distribution of oxygen-rich

blood throughout the body. However, when this rhythm is interrupted in the heart chambers (atria), it is known as AF. AF refers to a heartbeat originating from the atria and can lead to several health complications if not addressed

appropriately.<sup>2</sup> To comprehend the importance of AF, examining its repercussions and identifying the risk factors that make individuals more prone to this condition is necessary. Firstly, AF should not be considered an irregularity in heartbeats. It is recognized as a leading cause of stroke within certain conditions.<sup>3</sup>

The irregular heartbeat characteristic of AF results in blood flow. This turbulence often leads to blood clot formation within the heart, increasing the likelihood of clots traveling to the brain and initiating a stroke.<sup>4</sup>

The danger connected with stroke doesn't just lie in it happening. Its consequences often involve long-term disability and, unfortunately, even death. There are diverse factors that make individuals more prone to AF. Among these factors, advanced age is particularly noteworthy as older adults tend to be more susceptible to developing this condition. High blood pressure, also known as hypertension exacerbates the risk mentioned earlier. When we delve into the anatomy and physiology of the system, we find that underlying heart conditions, like heart diseases and congestive heart failure (CHF), are significant precursors to AF.<sup>5</sup> The increased prevalence of AF can partially be attributed to survival rates for patients with these heart conditions. To make things more complex, not all individuals with AF experience symptoms. Some may not show signs and only discover their AF during health checkups. However, those with symptoms often complain about fatigue, palpitations, and occasional chest pain. The patterns of AF can vary from disturbances to an irregular rhythm that requires medical interventions to restore normal rhythm.<sup>6</sup> Obstructive sleep apnea (OSA), a condition where a person's breathing is intermittently interrupted during sleep, is now recognized as not affecting sleep quality and daily performance.<sup>7</sup> Also, a potential risk factor for various cardiovascular diseases. One such cardiovascular condition that

has gained attention concerning OSA is AF, which is the most common cardiac arrhythmia.<sup>8</sup>

The association between obstructive sleep apnea (OSA) and atrial fibrillation (AF) is bolstered by a growing corpus of evidence, despite the challenges posed by the underdiagnosis of OSA. Recognizing and understanding this connection can open up approaches for preventing and managing fibrillation, particularly by addressing modifiable risk factors such as OSA. As research progresses in this area, hopefully, clearer strategies for intervention will emerge, benefiting several individuals affected by both conditions. This review aims to discover how common AF is in people with OSA and understand how OSA affects the occurrence and outcomes of AF.

## Literature Review

Increasing evidence suggests a link between OSA and the development of AF. A study conducted by Youssef et al. brought attention to the fact that individuals who have OSA or sleep-disordered breathing (SDB) face a risk of developing AF.<sup>9</sup> This correlation was substantiated by an investigation, concentrating on individuals identified with OSA/SDB. The analysis revealed a correlation between the presence of OSA/SDB and the occurrence of AF<sup>10</sup>, reviewed the relationship between OSA and AF as complex and involved underlying mechanisms.<sup>11</sup> It was concluded that episodes of OSA often result in decreased blood oxygen levels, triggering responses such as increased activity in the sympathetic nervous system, inflammation, and oxidative stress. These conditions contribute to remodeling, which makes individuals more susceptible to AF.

However, establishing OSA as a definitive contributor to AF poses challenges due to underdiagnosis. Moula et al., highlighted this dilemma. Although it is clear that there is a link between OSA and AF, accurately determining the prevalence of OSA among patients with AF remains

uncertain due to underdiagnoses.<sup>12</sup> This point is crucial because identifying and addressing OSA could effectively prevent or manage AF. OSA has been linked to an increased incidence of AF, and a few key studies have explored this relationship. Research cited in the StatPearls article confirms OSA's role as a condition with multiple adverse cardiovascular impacts.<sup>13</sup>

Another study delves into the complexities of OSA and highlights its direct implications for cardiovascular health.<sup>14</sup> Furthermore, the intricate connection between OSA, obesity, and cardiovascular risks has been discussed in several scientific papers. The recurrent nocturnal episodes of hypoxia (low oxygen levels) and arousals from sleep seen in OSA patients potentially serve as triggers for cardiac arrhythmias, particularly AF.<sup>15</sup>

Furthermore, a multitude of risk factors has been identified that are common to both obstructive sleep apnea (OSA) and atrial fibrillation (AF), thereby exacerbating this complex interrelationship. These factors encompass smoking habits, age, male gender, obesity, alcohol consumption, and heart failure. All are recognized as risk factors for both conditions. A study examined the relationship between OSA and its impact as a separate risk factor for cardiovascular diseases.<sup>16</sup>

The main objective of this study was to determine how common AF is in patients with OSA and identify the associated factors. The fact that these two conditions share overlapping risk factors suggests that there may be underlying mechanisms connecting them. It's not AF that has a connection to OSA. A larger study found that OSA is also linked to the occurrence of cardiovascular diseases, indicating the widespread impact of OSA on the body.<sup>17</sup>

Given the health implications and potential healthcare burden associated with AF, paying attention to its relationship with conditions like OSA, which can be modified or treated to reduce the risk of AF, is crucial.

## Methodology

**Eligibility criteria:** This section outlines the guidelines used to select and include studies. These guidelines ensured that only studies directly related to the connection between OSA and AF were included in this systematic review.<sup>18</sup>

**Inclusion Criteria:** Studies involving patients diagnosed with OSA, human studies, full-length articles about AF and OSA, observational studies associating OSA syndrome with AF, and papers written in English

**Exclusion Criteria:** Studies not specifically focusing on the relationship between OSA and AF, animal studies or in vitro studies, short communications, reviews, or abstract-only publications, studies where the primary diagnosis of OSA is unclear or not confirmed at the respective study site, studies that reported the status of AI and USA after ablation or other interventional AF treatments, studies that did not provide data on both the AF and OSA status of the participants in the study and studies involving populations with other significant confounding comorbidities that could independently affect the prevalence of AF.

**Research Strategy:** A thorough literature search followed the guidelines outlined in the PRISMA 2020 statement<sup>19</sup> and The Cochrane Handbook.<sup>19</sup> Extensive research was performed through PubMed, Web of Science and Google Scholar Databases. "Sleep Apnea Syndromes" or "sleep apnea" combined with "fibrillation" were used as keywords. Two reviewers independently evaluated bias risk in each included study. If any conflicts arose, a third reviewer was involved to resolve them. A bias assessment was performed for factors: (1) confounding. (2) classification of interventions. (3) data. (4) deviations from intended interventions. (5) measurement of outcomes. (6) overall bias evaluation. (7) selection of participants and (8) selection of reported results. The Cochrane Handbook was utilized to analyze the domains for bias.<sup>19</sup>

## Results

The original search yielded a total of 200 results. Following the inclusion and exclusion criteria implementation. 37 papers were identified that

included relevant data about the coexistence of AF and OSA. After excluding studies that did not provide separate data for individuals diagnosed with AF. 8 publications were identified that met the specified criteria for inclusion in the study (Figure.1)

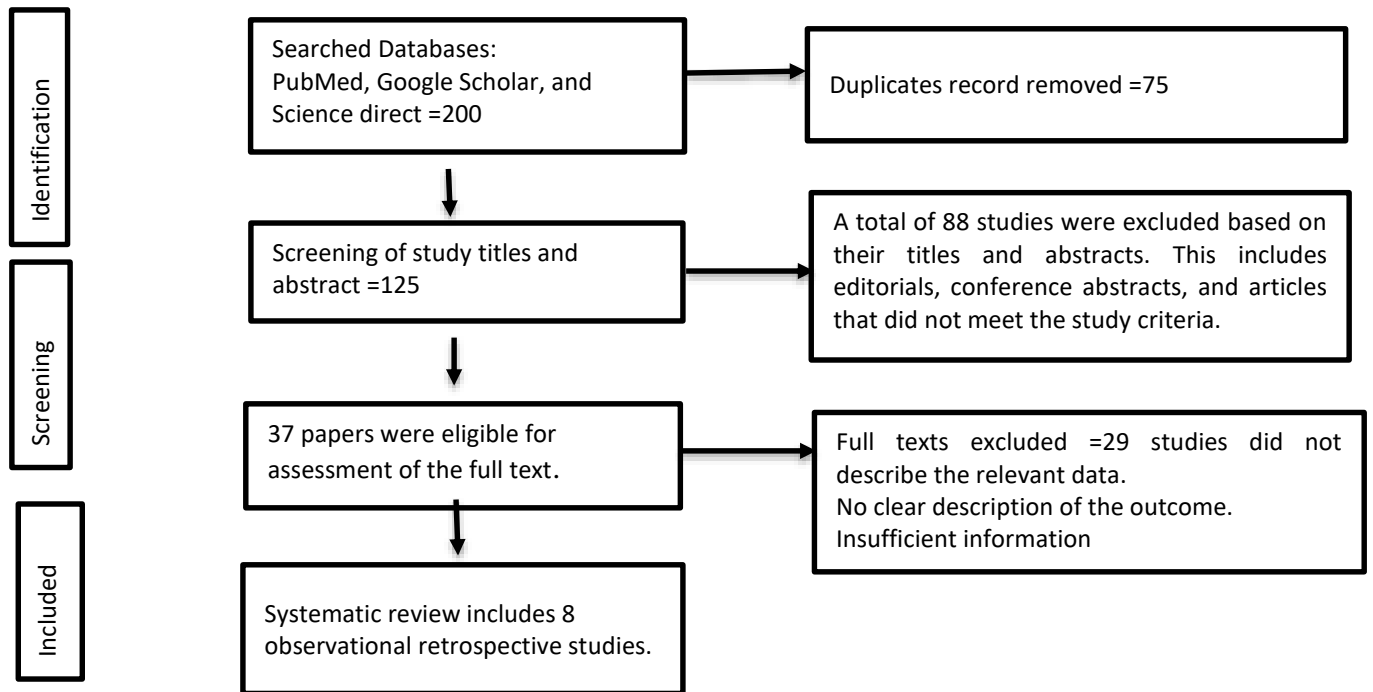


Figure.1 The PRISMA flow diagram for the selected studies

Table I. summarizes and represents the data gathered from the included investigations appropriately.					
Author	Country	Title	Participants	Methodology	Result
(Starkey et al., 2021)	Canada	Screening for Obstructive Sleep Apnea in an Atrial Fibrillation Population: What's the Best Test?	188	HSAT	According to the study, OSA is significantly under diagnosed in the community cardiology group with AF and is highly prevalent. 49% of the participants in the study had moderate to severe OSA (AHI≥15), and 86% had OSA (AHI≥ 5). <sup>20</sup>
(Oster et al., 2022)	USA	Early detection of obstructive sleep. apnea in patients with atrial fibrillation	101	EFR and Descriptive analysis	The frequency of OSA screening experienced a rise from 4.4% to 100% within the cohort

					of 68 patients constituting the comparison group and the 33 patients in the intervention group. Referrals to sleep Clinics increased from 66.7% to 93.5%. Follow-up at the sleep clinic went from 0% to 10%. <sup>8</sup>
(Xu et al., 2022a)	China	Clinical characteristics and thrombotic risk of atrial fibrillation with obstructive sleep apnea: results from a multi-center atrial fibrillation registry study	1991	PSG	The study concluded that although there was no correlation between. OSA is associated with an elevated likelihood of experiencing a stroke or TIA, and it serves as an independent risk factor for non-central nervous system embolism in individuals diagnosed with AF. <sup>21</sup>
Dhakal et al., 2020)	Nepal	Prevalence and risk factors for persistent atrial fibrillation in obstructive sleep Apnea patients in a tertiary care center	67	PSG	The incidence of AF among patients diagnosed with OSA was observed to be 10.44%, a figure that is notably elevated and more frequently encountered in individuals exhibiting severe manifestations of OSA. <sup>22</sup>
(Chen et al., 2022)	Taiwan	Association between sleep disorder and atrial fibrillation: A nationwide population-based cohort study	193288	Data based cohort study	This population-based cohort study conducted across the country shows a significant association between incident AF and SD, with insomnia having a greater effect on AF than another SD, which came out to be 1.30 higher risk of AF in such people. <sup>23</sup>
(Khamsai	Thailand.	Prevalence and	199	Cross-	Patients with OSA had

et al., 2022)		factors associated with atrial fibrillation in obstructive sleep apnea		sectional study	an AF prevalence of 15.57%. The risk of AF was higher in older individuals with renal decline, whereas it was lower in those experiencing fatigue. <sup>24</sup>
(Wang et al., 2022)	China	Prevalence and factors associated with atrial fibrillation in older patients with obstructive sleep apnea	1285	PSG	The study reported that the prevalence of paroxysmal AF was 7.2% in the overall study population, with rates increasing as the severity of OSA or age advanced. <sup>11</sup>
(Li et al., 2022)	China	Assessment of the Causal Effects of Obstructive Sleep Apnea on Atrial Fibrillation: A Mendelian Randomization Study	1030836	MR analysis	The primary study found a substantial association between OSA and an elevated risk of AF, and the replicated analysis produced similar results. This concluded to emphasize on new insights to better prevent and treat OSA, ultimately reducing the risk of developing AF. <sup>25</sup>

## Discussion

Various factors influence the connection between AF and OSA. Research indicates an association between these two conditions with OSA patients having a risk of AF compared to the general population.<sup>11</sup> However, the prevalence rates may vary due to differences in the characteristics of the study population, the severity of OSA methods used, and even geographical and ethnic factors. Recognizing these variations is crucial for healthcare providers to assess risks and accurately personalize interventions. As we delve deeper into understanding the relationship between AF and OSA, it becomes increasingly important to adopt an approach that addresses both conditions simultaneously.<sup>26</sup>

This holistic approach will play a role in improving outcomes and alleviating the burden on healthcare systems. Recent research has shed light on the connection between AF and OSA, emphasizing the significance of managing both conditions comprehensively to enhance patient outcomes and quality of life.<sup>27</sup>

A study conducted at a facility aimed to investigate how common AF is among people with OSA.<sup>28</sup> The findings revealed a link between these two conditions. Likewise, another comprehensive review pointed out that we have limited knowledge about the extent of OSA in patients with AF due to significant underdiagnosis.<sup>15</sup>

Nevertheless, the existing evidence suggests a connection between AF and OSA. It is important to

consider that individuals who are obese are more prone to developing OSA, which can indirectly contribute to the prevalence of AF among this group, as indicated by the findings from the 'obesity sleep apnea study',<sup>5,16</sup> Studies conducted in sleep clinics have found that AF among patients with OSA can range anywhere from 15% to 49%.<sup>29</sup> Long-term studies following a group of individuals have shown that patients with OSA are significantly more likely to develop AF than those without OSA. These findings suggest that there may be a connection or shared mechanisms between the two conditions.<sup>30-31</sup>

It is important to examine the characteristics of the study population methodologies used to understand the variations in reported prevalence rates fully. One significant factor that influences prevalence is the severity of OSA. Studies have indicated that as OSA becomes more severe, the prevalence of AF also increases. This implies that the physiological stress and inflammation resulting from OSA could potentially contribute to the development or progression of AF.<sup>24,32-33</sup> In addition, demographic factors such as age and sex also play a role in variations in prevalence rates. Age is already recognized as an established risk factor for both AI and OSA, with studies finding higher rates of AF among older individuals with OSA.<sup>34</sup>

Furthermore, differences based on sex have been observed where certain studies report a prevalence of AI among patients with OSA while others show a more balanced distribution.<sup>30,35</sup> It is worth noting that the methods used to diagnose and assess both AF and OSA can impact reported prevalence rates. Since AF can occur intermittently (known as paroxysmal), its diagnosis can sometimes be challenging. Research that utilizes monitoring techniques tends to detect several paroxysmal AF cases compared to studies relying solely on intermittent monitoring.<sup>25</sup>

Similarly, the method used for diagnosing OSA, such as polysomnography (PSCG) or portable

monitoring, can affect the population under investigation and subsequently impact the prevalence of both conditions.<sup>36</sup>

Genetic predisposition and lifestyle factors can influence the prevalence of both AF and OSA but these factors can differ across populations.<sup>4</sup> highlighted the need to consider these factors when interpreting prevalence rates.<sup>4</sup> There is a growing awareness that OSA remains significantly underdiagnosed, which might skew prevalence statistics. When considering the prevalence of OSA in AF patients, it's evident that the lack of a standardized screening protocol for OSA across all AF patients can result in significant underreporting.<sup>19</sup>

Further variations can also arise based on the co-existence of other health conditions. For instance, diabetes is another disease that has been linked to AF. However, it is worth noting that not all studies explicitly set out to find the prevalence of AF in OSA patients or vice versa. Some studies might explore the broader relationship between the two conditions, focusing more on the underlying mechanisms rather than the exact prevalence figures.<sup>4,19,20</sup>

An increasing amount of evidence from clinical studies and population-based research highlights a strong association between OSA and an elevated risk of developing AF. These studies have collectively illuminated the importance of recognizing OSA as a potential risk factor for the initiation and progression of AF.<sup>35</sup> Research spanning retrospective and prospective designs has consistently indicated that individuals diagnosed with OSA are at a higher risk of developing AF. A prospective cohort study involving a large sample size and a long follow-up period demonstrated that OSA was independently associated with incident AF, even after adjusting for confounding variables.<sup>27</sup> Furthermore, a dose-response relationship has been proposed, with increasing severity of OSA correlating with a higher incidence of AF. This suggests a potential

link between the degree of OSA-related hypoxia and the subsequent arrhythmogenic substrate.<sup>37</sup> The combination of OSA and AF has sparked interest in cardiovascular research. Researchers are exploring how these two conditions interact and potentially impact outcomes. OSA and AF, being common and often interconnected, have a relationship that goes beyond coexistence. A growing body of evidence highlights the multifaceted influence of OSA on AF outcomes. Studies have delved into recurrence rates, hospitalizations, and even mortality to understand better the implications when these conditions coexist. Several investigations have explored the connection between OSA and AF recurrence after interventions like cardioversion or ablation.<sup>27,37</sup> The findings suggest that OSA may increase the risk of AF recurrence after interventions. This emphasizes the need for management strategies and provides insights into the underlying mechanisms that sustain arrhythmias in the presence of OSA.<sup>38</sup> Furthermore, studies have revealed a link between OSA and adverse outcomes during AF-related hospitalizations. It appears that OSA adds complexity to patient management during these hospital stays.<sup>29</sup> Patients with OSA often stay in the hospital for periods and are more likely to experience complications. This does not add strain to healthcare resources. Also raises the question of whether OSA could independently predict outcomes related to hospitalization in patients with AF. Additionally, the presence of both OSA and AF seems to amplify the risk of adverse cardiovascular events, including mortality.<sup>39</sup> Emerging evidence suggests that individuals affected by both conditions face a considerably higher mortality risk than those with either OSA or AF alone.

Managing OSA and its effect on fibrillation involves a diverse array of potential treatments. These encompass established methods like

continuous positive airway pressure (CPAP) therapy, lifestyle changes, and emerging pharmacological approaches. The aim is not to address OSA but to reduce the risk of developing AF and experiencing negative outcomes.<sup>34</sup> Early detection and timely intervention in patients with OSA at risk for AF can improve health and overall well-being.<sup>8</sup> A comprehensive approach that targets shared mechanisms and prioritizes patient-centered care can enhance the quality of life and outcomes for individuals affected by the interaction of OSA and AF.

Combining existing literature highlights a link between OSA and AF across prevalence, incidence and outcomes. Multiple studies consistently show a prevalence of AF in individuals with OSA, with the severity of OSA indicating a greater risk of developing AF. Moreover, the impact of OSA on outcomes related to AF—such as recurrence, hospitalization, and even mortality has gained interest. Complex mechanisms involving stress, inflammation, autonomic imbalance, and endothelial dysfunction influence the initiation and progression of AF when coupled with OSA.<sup>40-42</sup>

## Conclusion

It becomes clear that understanding the relationship between OSA and AF is essential for both practice and future research. The knowledge gained from research sheds light on the multifaceted aspects of these conditions, transforming how we diagnose, treat, and manage them. One key aspect of this transformation lies in recognizing the coexistence of OSA and AF. Their bi-directional relationship underscores the importance of screening for both conditions in patients. Early detection can lead to interventions, which can improve outcomes. For patients with AF, understanding how OSA may impact their condition can guide treatment decisions beyond managing arrhythmias by considering sleep-related interventions that may ultimately affect

the prognosis of AF. The significance of this study is not just in its existence but in its potential to redefine the future of healthcare and research.

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