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Sleep Disordered Breathing in Patients with Chronic Heart Failure

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Abstract

Background: Chronic heart failure (CHF) is a common disease worldwide with a high morbidity and mortality rate. Sleep disordered breathing (SDB) is a common condition that frequently occurs alongside heart failure (HF) and has a significant effect on the patient's prognosis.

Aim of the work: Determining the prevalence, severity, and patterns of SDB in different types of CHF and defining the diagnostic utility of SDB scores in the prediction of SDB in HF patients.

Patient and Methods: Sixty (CHF) patients were divided into 3 equal groups based on (LVEF%) into HFrEF, HFmrEF, and HFpEF according to ESC guidelines. All patients underwent full night attended polysomnography.

Results: The three groups had a prevalence of OSA of 50%, 55%, and 60%, respectively, and a prevalence of CSA of 35%, 30%, and 5%, respectively. Patients with CSA showed a highly statistically significant ($p < 0.001$) reduction in mean LVEF%. Patients with OSA had significantly higher BMI, NC, and Mallampati scores ($p < 0.001$), all of which were statistically significant increases. While the ESS and Berlin questionnaires showed great specificity (92.3%) and low sensitivity (38.3% and 46.8%, respectively) in predicting SDB in HF patients, the STOP-BANG score showed high sensitivity (100%) but low specificity (30.7%).

Conclusion: In CHF patients, SDB was shown to be quite prevalent (78.3%). Higher BMI, NC, and Mallampati scores were associated with higher odds of OSA, whereas lower LVEF% was associated with higher odds of CSA. A good screening tool for SDB in HF patients appears to be the Berlin questionnaire in conjunction with the STOP-BANG score.

Keywords: Sleep-disordered breathing; Chronic heart failure

1. Introduction

A structural or functional anomaly in the heart can cause symptoms and/or signs of chronic heart failure (CHF), which can be verified by objective proof of congestion in the body or in the lungs, excessive levels of natriuretic peptides, or the combination of both.¹ Many breathing disorders, such as central sleep apnea and obstructive sleep apnea (OSA), are included in the category of sleep-disordered breathing (SDB). Upper airway collapse during sleep, which causes sporadic nocturnal hypoxemia and fragmented sleep, is a frequent clinical disorder that goes undiagnosed

and is associated with OSA. Airflow restriction without respiratory exertion is a hallmark of central sleep apnea.² Breathing disorders during sleep are very common in HF patients and have a significant effect on the course of treatment. Their link is reciprocal: SDB can negatively impact the development of HF, and poor cardiac function can cause SDB.³ Detecting SDB in patients with CHF has significant therapeutic implications.⁴

The current study intends to define the diagnostic value of SDB scores in predicting SDB in HF patients as well as the prevalence, severity, and patterns of SDB in various kinds of CHF.

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2. Patients and methods

The present investigation was conducted cross-sectionally at the Sleep Disorders Breathing Unit in the Chest Department of Al-Hussein and Bab Al-Shaaria University Hospitals in Cairo, Egypt.

Patients: The study was carried out on 60 patients diagnosed with chronic heart failure attending the cardiology department of Al Azhar University hospitals in the period from June 2022 to September 2023.

Inclusion criteria: Chronic compensated heart failure (HF) patients refer to individuals in stage C of HF who have structural heart disease and are currently or previously experiencing symptoms of HF.⁵ Following ESC guidelines, our patients were divided into three equal groups based on the assessment of their left ventricular ejection fraction (LVEF%).⁶ Heart failure with reduced ejection fraction, or HFrEF is a group of twenty individuals who have both a reduced left ventricular ejection fraction (~40%) and heart failure symptoms and indications. Heart failure with moderately decreased ejection fraction, or HFmrEF, is a group of 20 patients who have heart failure symptoms and signs in addition to a modestly reduced LVEF% (41–49%). With preserved ejection fraction heart failure (HFpEF): Twenty patients were identified in this cohort as having symptoms and indicators of heart failure, in addition to objective evidence of structural as well as functional abnormalities to the heart, which are consistent with increased natriuretic peptides, diastolic dysfunction, and elevated LV filling pressures.

Exclusion criteria: Individuals at (stage D) HF are considered to have decompensated heart failure (HF) if their symptoms are severe enough to impede daily functioning, and they frequently require hospitalizations even after trying to maximize medical therapy guided by guidelines.⁵ Individuals with a history of decompensated liver and renal illness, cerebral stroke, acute coronary syndrome, and other conditions. Patients with daytime hypercapnia, such as those with SDB, neuromuscular diseases, obesity hypoventilation syndrome, severe chronic obstructive pulmonary disease (COPD), and chest wall abnormalities, were not included in the study.

Methods: Every patient had to undergo the following procedures: a thorough history, particularly for symptoms that could point to the etiology of HF and SDB. Clinical examinations with particular attention paid to BMI, neck circumference, NYHA classification, Mallampati score, and BMI. Berlin Questionnaire, STOP-BANG score, Epworth Sleepiness Scale, and SDB prediction scores. Routine tests (ECG, chest radiography, blood gases, liver, kidney, thyroid, and lipid profiles, among others). TTE stands for

transthoracic echocardiography. Attending polysomnography all night long utilizing the Neuron- Spectrum- AM model. Definition of SDB: apnea/hypopnea index (AHI) greater than five per hour of sleep. AHI>50% of central or obstructive origin was used to characterize central sleep apnea (CSA) and obstructive sleep apnea (OSA), respectively. Every patient gave their verbal consent.

Statistical analysis:

The Statistical Program for Social Science (SPSS) version 24 was used to examine the data. The frequency and proportion of the qualitative data were reported. For quantitative data that were normally distributed, the expression was mean \pm SD, and for data that were not normally distributed, it was median (IQR).

Mean (average): The central value of a discrete set of integers is the arithmetic mean, which is calculated by dividing the total of the values by the number of values.

Standard deviation (SD): Variance is the statistical measure of dispersion of a group of values. A low standard deviation (SD) suggests that the values in the set are clustered around the mean, whereas a high standard deviation implies that the values are more widely dispersed throughout a larger range.

Median: The median is the middle value obtained by arranging all data points in order and selecting the one in the middle. If there are two middle values, the median is the average of those two figures.

IQR (inter-quartile range): Variance is a statistical term that quantifies the degree of dispersion in a dataset. The term "interquartile range" refers to the numerical value obtained by subtracting the 25th percentile from the 75th percentile of a given dataset.

The subsequent examinations were conducted:

When comparing data that is regularly distributed between two groups, use the independent sample T-test (T).

When comparing two groups (for abnormally distributed data), use the Mann-Whitney U test (MW).

When comparing data that is normally distributed between more than two groups, a one-way analysis of variance (ANOVA) is used.

When comparing data from more than two groups, use the Kruskal Willis test (KW) (for erratically distributed data).

When comparing non-parametric data, the chi-square test was utilized.

Data were correlated using Pearson's correlation coefficient (r) test.

For multiple comparisons between various variables, the Post Hoc test was employed.

Cutoff value, sensitivity, specificity, positive predictive value (PPV), and negative predictive

value (NPV) were all determined using the ROC curve (Receiver Operating Characteristic Curve).

Sensitivity is the likelihood that, in the presence of the condition, a test will come back positive.

Specificity: the likelihood that a test will come out negative in the absence of the illness.

The likelihood that the disease is present when the test is positive is known as the positive predictive value.

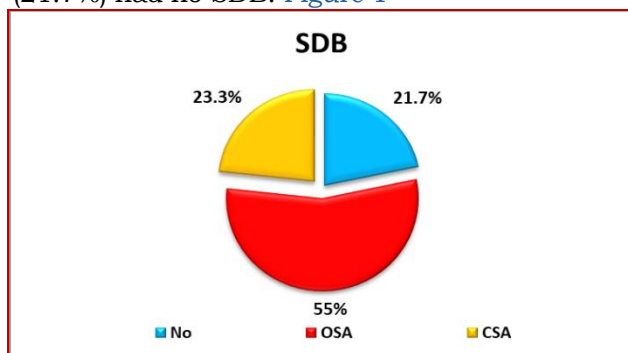
The likelihood that the illness does not exist when the test results are negative is known as the negative predictive value.

Probability (P-value): P-value>0.05 was regarded as inconsequential, P-value<0.001 as extremely significant, and P-value<0.05 as significant.

According to the Kappa interpretation, there are four levels of agreement: poor (K<0.2), fair (K=0.2-0.4), moderate (K=0.4-0.6), good (K=0.6-0.8), and very good (K=0.8-1.0).

3. Results

Forty-seven patients (78.3%) of our studied HF patients showed SDB, 33 patients (55%) of them had OSA, while 14 patients (23.3%) had CSA. On the other hand, the remaining 13 patients (21.7%) had no SDB. [Figure 1](#)



SDB: sleep Disordered Breathing, OSA: obstructive sleep apnea, CSA: central sleep apnea
Figure 1. SDB prevalence in studied patients.

Table 3. Comparison between studied groups as regard SDB severity.

		TOTAL (N=47)		GROUPS			STAT. TEST	P-VALUE
SDB SEVERITY				HFrEF (n=17)	HFmrEF (n=17)	HFpEF (n=13)		
	Mild	10	21.3%	3	17.6%	4	23.5%	X ² =5.3
	Mod.	13	27.7%	5	29.4%	5	29.4%	
	Severe	24	51%	9	53%	8	47.1%	
								0.252 NS

X²:Chi-square test., NS:Non-significant.

No statistically significant differences were observed between SDB groups (No SDB, OSA, CSA) as regard sex, age, NYHA classification and smoking. On the other side, high statistically

Among the 47 patients (78.3%) diagnosed as SDB, 17 patients (85%) developed SDB in HFrEF group, 10 patients (50%) as OSA and 7 patients (35%) as CSA, 17 patients (85%) developed SDB in HFmrEF group, 11 patients (55%) as OSA and 6 patients (30%) as CSA. Moreover, 13 patients (65%) developed SDB in HFpEF group, 12 patients (60%) as OSA and one patient (5%) as CSA.

Table 1

Table 1. SDB types distribution in studied patients.

		TOTAL (N=60)	GROUPS					
STUDIED PATIENTS			HFrEF (n=20)		HFmrEF (n=20)		HFpEF (n=20)	
I.	NO SDB	13 21.7%	3	15%	3	15%	7	35%
II.	SDB	47 78.3%	17	85%	17	85%	13	65%
SDB TYPE	OSA	33 55%	10	50%	11	55%	12	60%
	CSA	14 23.3%	7	35%	6	30%	1	5%

HFrEF:Heart failure with reduced ejection fraction., HFmrEF:Heart failure with mild reduced ejection fraction., HFpEF:Heart failure with preserved ejection fraction .

A highly statistically significant (p-value<0.001) decline of mean LVEF% was observed in CSA patients (36.6±7.1)% when compared with OSA patients (47.3±10)% and patients without SDB (49.9±8.3)%. [Table 2](#)

Table 2. Comparison between SDB groups as regard mean LVEF%.

		TOTAL (N=60)	NO SDB (N=13)	OSA (N=33)	CSA (N=14)	STAT. TEST	P- VALUE
LVEF%	Mean	45.4	49.9	47.3	36.6	F=8.8	< 0.001 HS
	±SD	10.2	8.3	10	7.1		

F:F value of ANOVA test., HS:Highly significant.

No statistically significant difference (p-value=0.252) was observed between studied groups as regard SDB severity. [Table 3](#)

significant (p-value<0.001) increased BMI, OSA patients had larger neck circumference and higher Mallampati scores compared to CSA patients and individuals without sleep-disordered breathing (SDB). [Table 4](#)

Table 4. Comparison between SDB groups as regard socio-demographic data and anthropometric measurements.

		TOTAL (N=60)	NO SDB (N=13)	OSA (N=33)	CSA (N=14)	STAT. TEST	P- VALUE
SEX	Male	41 68.3%	8 61.5%	24 72.7%	9 64.3%	X ² =0.67	0.713
	Female	19 31.7%	5 38.5%	9 27.3%	5 35.7%		NS
AGE (YEARS)	Mean	58.2	57.5	58.0	59.1	F=0.68	0.509
	±SD	3.7	4.4	3.4	3.7		NS
BMI (KG/M ²)	Mean	31.4	23.8	35.1	29.6	F=130.5	<0.001
	±SD	5.1	1.6	2.6	1.5		HS
NC (CM)	Mean	40.5	34.0	44.0	38.1	F=126.1	<0.001
	±SD	4.6	1.2	2.4	1.7		HS
MALLAMPATI SCORE	I	22 36.6%	12 92.3%	0 0%	10 71.4%	X ² = 45.3	<0.001
	II	25 41.6%	1 7.7%	20 60.6%	4 28.6%		HS
	III	13 21.6%	0 0%	13 39.4%	0 0%		HS
NYHA CLASSIFICATION	I	5 8.3%	2 15.4%	3 9.1%	0 0%	X ² =3.9	0.407
	II	51 85%	10 76.9%	29 87.9%	12 85.7%		NS
	III	4 6.7%	1 7.7%	1 3%	2 14.3%		NS
SMOKING	No	35 58.3%	8 61.5%	19 57.6%	8 57.1%	X ² =0.07	0.965
	Yes	25 41.7%	5 38.5%	14 42.4%	6 42.9%		NS

X²:Chi-square test., F:F value of ANOVA test., NS:Non-significant., HS:Highly significant.

An analysis of the data revealed a statistically significant increase in the percentage of hypertension (HTN) as a cause of heart failure (HF) in patients with obstructive sleep apnea (OSA) (78.8%) compared to patients with central sleep apnea (CSA) (41.9%) and patients without sleep-disordered breathing (SDB) (53.8%). The p-value associated with this finding was 0.039.

Table 5

Table 5. Comparison between SDB groups as regard causes of HF.

		TOTAL (N=60)	NO SDB (N=13)	OSA (N=33)	CSA (N=14)	STAT. TEST	P- VALUE
CAUSES	IHD	44 73.3%	10 76.9%	25 75.8%	9 64.3%	0.77	0.680
	HTN	39 65%	7 53.8%	26 78.8%	6 42.9%	6.4	0.039 S
	DCM	11 18.3%	1 7.7%	5 15.2%	5 35.7%	4.03	0.133
	VHD	9 15%	2 15.4%	5 15.2%	2 14.3%	0.008	0.996

X²:Chi-square test, NS:Non-significant, S:Significant. IHD:Ischemic heart diseases, HTN:Hypertension, DCM:Dilated cardiomyopathy VHD:Valvular heart diseases.

DM was the most common co-morbidity among studied patients, no statistically significant differences were observed between SDB categories as regard co-morbidities. Table 6

Table 6. Comparison between SDB groups as regard co-morbidities.

		TOTAL (N=60)	NO SDB (N=13)	OSA (N=33)	CSA (N=14)	X ²	P- VALUE
CO-MORBIDITIES	D.M	38 63.3%	7 53.8%	22 66.7%	9 64.3%	0.66	0.716
	Hyper-lipidemia	36 60%	7 53.8%	22 66.7%	7 50%	1.4	0.497
	AF	11 18.3%	3 23.1%	5 15.2%	3 21.4%	0.5	0.776
	Hypothyroidism	4 6.7%	0 0%	4 12.1%	0 0%	3.5	0.173

X²:Chi-square test, NS:Non-significant, DM:Diabetes mellitus, AF:Atrial fibrillation.

ACEI/ARBs was the most common administrated drug No statistically significant differences were revealed between SDB categories as regard HF medications. Table 7

Table 7. Comparison between SDB groups as regard HF medications.

		TOTAL (N=60)	NO SDB (N=13)	OSA (N=33)	CSA (N=14)	X ²	P- VALUE
DRUGS	ACEI/ARBs	48 80%	9 69.2%	28 84.8%	11 78.6%	1.44	0.486
	Diuretics	41 68.3%	6 46.2%	23 69.7%	12 85.7%	4.9	0.085
	B blockers	39 65%	8 61.5%	23 69.7%	8 57.1%	0.76	0.681
	Digitalis	7 11.7%	2 15.4%	2 6.1%	3 21.4%	2.4	0.29 NS

X²:Chi-square test, NS:Non-significant.

Based on our results, Epworth sleepiness scale (ESS) and Berlin questionnaire showed high specificity (92.3%) for both, but low sensitivity (38.3% and 46.8%) respectively in the diagnosis of SDB in HF patients. In contrary, STOP-BANG score displayed higher sensitivity (100%) but lower specificity (30.7%). Table 8

Table 8. Diagnostic utility of Epworth sleepiness scale, STOP-BANG score and Berlin questionnaire in the diagnosis of SDB among HF patients.

	ESS (N=60)	STOP- BANG SCORE	BERLIN QUESTIONNAIRE
TRUE POSITIVE	18 30%	47 78.3%	22 36.7%
FALSE POSITIVE	1 1.7%	9 15%	1 1.7%
FALSE NEGATIVE	29 48.3%	0 0%	25 41.7%
TRUE NEGATIVE	12 20%	4 6.7%	12 20%
SENSITIVITY	38.3%	100%	46.8%
SPECIFICITY	92.3%	30.7%	92.3%
PPV	94.7%	83.9%	95.6%
NPV	29.3%	100%	32.4%

PPV:Positive predictive value., NPV: Negative predictive value.,

ESS:Epworth sleepiness scale.

4. Discussion

Patients with chronic heart failure (CHF) are prone to sleep disordered breathing (SDB). According to recent research, up to 80% of CHF patients may have either central or obstructive sleep apnea or SDB7.

Among the studied patients, the mean age

was (58.2 ± 3.7) years; 41 (68.3%) of them were males, while 19 (31.7%) were females. Patients with SDB in the current study were older than those without SDB; the mean age was (58 ± 3.4) years in OSA patients, (59.1 ± 3.7) years in CSA patients, and (57.5 ± 4.4) years in patients without SDB. Male superiority was observed in all SDB groups; (72.7%) in OSA, (64.3%) in CSA, and (61.5%) in non-SDB, with no statistically significant differences noticed regarding age and sex (p -value=0.509 and 0.713), respectively.

Merging with our observations, Samaha et al. reported no significant differences considering age and sex (p -value=0.63 and 0.168), respectively.⁸

Although Daniel et al. reported an insignificant relationship between SDB and age in CHF patients, a significant one between SDB and masculinity in the same cardiovascular disease.⁹

In the HF patients under study, the prevalence of SDB was 78.3%; this was split between those with OSA (55%) and CSA (23.3%) and those without SDB (21.7%). In the HFrEF, HFmrEF, and HFpEF groups, the prevalence of SDB was, respectively, 85%, 85%, and 65%. The three groups had a prevalence of OSA of 50%, 55%, and 60%, respectively, and a prevalence of CSA of 35%, 30%, and 5%, respectively.

As well, Wang et al. indicated that 70% of the study population had this prevalence. Of the patients, (48%) had a diagnosis of OSA, and (22%) had a diagnosis of CSA. In the HFrEF, HFmrEF, and HFpEF groups, the prevalence of SDB was 86%, 86%, and 62%, respectively. The three groups had corresponding OSA prevalences of 42%, 47%, and 49%, and CSA prevalences of 44%, 40%, and 13% among the same groups¹⁰. Kishan et al. showed that the frequency of SDB was slightly greater in HF patients (81.5%), with OSA predominating (59.2%) as opposed to CSA (22.33%). The HFrEF group's SDB prevalence was 84.4%, quite similar to our own, whereas the HFpEF groups' SDB prevalence was noticeably higher (79.3%).¹¹

Unlike the high prevalence of SDB in previous studies, The German SchlaHF-XT registry reported that the overall prevalence of SDB in HF patients was (39.4%), distributed as (48%) in HFpEF group, (41%) in HFmrEF group and (36%) in HFrEF group. SDB was determined using Type 3 polygraphic devices, with a target AHI of ≥ 15 events/hour.¹² The extremely low prevalence of SDB among HF patients in the former study compared with ours could be referred to ignoring mild cases of the disease in which AHI ranges from 5 to <15 events/hour, in addition to using a different, less sensitive diagnostic tool.

We showed a substantial statistical drop (p -value <0.001) in the mean LVEF% in CSA, but no

statistically significant distinction (p -value=0.252) was seen between the HF groups under study in terms of SDB severity.

Wang et al. revealed that LVEF% was an independent risk factor for CSA in HF patients, with a significant negative correlation with the central apnea index (p -value <0.001).¹⁰

In OSA patients, we found a statistically significant (p -value <0.001) rise in BMI. On the same path, Huang et al. and Herrscher et al. reached similar results.^{13,14}

The mean NC for the studied population was (40.5 ± 4.6) cm, with high statistically significant (p -value <0.001) increased NC observed in OSA patients. Also, Ferreira et al. showed a significantly higher median NC in HF patients OSA.¹⁵

We observed a high statistically significant increase (p -value <0.001) as regards Mallampati score among OSA patients. In the study done by Samaha et al., class II/ III Mallampati was found in (87.5%) of OSA patients, which almost resembles ours.⁸

In our study, no statistically significant difference was noticed among SDB groups (p -value=0.407) regarding NYHA classification in HF patients. Consistent with these results, Kishan et al., and Bekfani et al., found no statistically significant difference regarding NYHA classification between OSA, CSA, and no SDB patients with HF.^{11,16}

HTN showed a statistically significant (p -value=0.039) increased percentage in our OSA patients. Similarly, Huang et al. stated that significantly higher prevalence of HTN (76.8%) in HF patients with OSA; they view HTN as one of the most reliable indicators of OSA in individuals with heart failure.¹³

In our study, no statistically significant differences were discovered among HF and SDB groups as regards other co-morbidities and administrated drugs (p -value >0.05). Our findings agreed with Kishan et al., as they reported no statistically significant differences among HF and SDB groups as regards co-morbidities and administrated drugs (p -value <0.05).¹¹

Based on our results, ESS and Berlin questionnaires showed high specificity (92.3%) for both but low sensitivity (38.3% and 46.8%), respectively, in the prediction of SDB in HF patients. On the contrary, the STOP-BANG score displayed higher sensitivity (100%) but lower specificity (30.7%). Given that certain symptoms of CHF and SDB overlap, the low specificity of the STOP-BANG score may be explained

Identically, Samaha et al., featured that the most sensitive SDB diagnostic standard in the context of CHF was the STOP-BANG score (100%), followed by the Berlin questionnaire (39%) and finally ESS (21.2%). The Berlin

questionnaire and ESS had the highest specificity (100% for each), followed by the STOP-BANG score, which had the lowest specificity (0%)^{.8}

As well a systematic review and meta-analysis of multiple studies in different countries explored that the STOP-BANG score had high pooled sensitivities in screening for mild, moderate, and severe OSA in cardiovascular patients (89.1%, 90.7%, and 93.9%), respectively. However, the pooled specificities of the score for the same purpose were relatively low (32.3%, 22.5%, and 18.3%), respectively.^{.17}

Additionally, Amra et al. demonstrated that the STOP-BANG score had the highest sensitivity (97.55% and 98.7%, respectively) for predicting mild and severe OSA in the general population. However, the Berlin questionnaire had the best specificity (90 and 80 percent) for identifying mild and severe OSA. Correspondingly.^{.18}

Conversely, Kishan et al. revealed that the Berlin questionnaire, STOP-BANG score, and ESS were not very useful in finding SDB in HF patients (p-values=0.182, 0.184, and 0.293, respectively). This departure from the majority of research may be because these people don't have normal symptoms or risk factors.^{.11}

4. Conclusion

Our study displayed a high prevalence of SDB in chronic heart failure patients (78.3%). OSA was the most common SDB and constituted (55%) of studied HF patients, while (23.3%) had CSA. OSA was more common with higher BMI, neck circumference, and Mallampati score. CSA was more common with lower LVEF%. The degree of SDB showed no discernible correlation with LVEF%. The Berlin questionnaire and ESS were more specific in their assessment of SDB in patients with HF, although the STOP-BANG score was more sensitive.

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