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Prevalence of high risk obstructive sleep apnoea by Berlin questionnaire in patients with hypertension: study from a tertiary care hospital

Ozaifa Kareem¹, Masood Tanvir² and G. N. Bader^{1*} 

Abstract

Background: Obstructive Sleep Apnoea (OSA), a condition characterized by a complete or partial cessation of airflow during sleep, can cause various cardiovascular disorders including hypertension. The aim of the study was to determine the prevalence of OSA in patients with hypertension.

Methods: A cross-sectional prospective cohort study of 504 patients with hypertension was undertaken at a tertiary care hospital of India for a period of 6 months. OSA was evaluated using the Berlin questionnaire while the daytime sleepiness was determined using Epworth Sleepiness Scale. Data analysis was done using SPSS v. 20.

Results: High risk of OSA was identified in 120 (23.8%) patients and the prevalence of sleepiness (Epworth Sleepiness score >16) was found to be 32.5% (95% CI, $p < 0.001$) in these patients. The mean neck circumference, waist circumference and waist-to-hip ratio for high-risk OSA group were 37.41 ± 3.396 cm, 105.90 ± 11.28 cm and 1.01 ± 0.065 respectively while for the low-risk group, these parameters were 35.45 ± 2.652 cm, 98.75 ± 10.87 cm and 0.99 ± 0.080 respectively (95% CI, $p < 0.001$). The mean blood pressure (BP) $\geq 133.52/84.37$ mmHg was recorded in patients with a high risk of OSA (95% CI, $P < 0.05$), and resistant hypertension (3.3%) was significantly associated with the risk of OSA (95% CI, $P < 0.05$).

Conclusion: In the tertiary health care setting, the prevalence of high-risk of OSA in patients with hypertension is high. Screening for OSA should be a part of the hypertensive medical investigation and patients may benefit from a proper evaluation of OSA.

Keywords: Obstructive sleep apnoea, Hypertension, Berlin questionnaire, Epworth sleepiness scale

Background

Obstructive Sleep Apnoea (OSA) is a sleep-related breathing disorder that involves complete or partial cessations in airflow due to the collapse of the upper airway, despite an ongoing effort to breathe (Guilleminault and Abad 2004). The obstruction of the upper airway occurs because of the inadequate motor tone of the tongue and/or airway dilator muscles, (Park et al. 2011)

that is associated with fragmented sleep pattern, arousals from sleep and fall in oxygen saturation (Pien et al. 2015). Nocturnal oxygen desaturations cause sympathetic surges conducive to the development of acute cardiovascular events (i.e., stroke, myocardial infarction, and nocturnal sudden death) and chronic conditions such as systemic hypertension, coronary artery disease, and heart failure (Bradley and Floras 2003; Leung and Bradley 2001; Peppard et al. 2000). Hypertension is an important public health challenge worldwide because of its high frequency and concomitant risk of cardiovascular (CV)/cerebrovascular morbidity and mortality (Kearney et al. 2005; Lawes et al. 2008).

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It is estimated to cause 7.5 million deaths that are 12.8% of the total number of deaths worldwide (Global Health Observatory 2018).

Globally, various epidemiological studies report that about 30% of patients with OSA have hypertension, (Bouloukaki et al. 2018; Lavie et al. 2000; Marin et al. 2012; Mubarik et al. 2017) while in patients with resistant hypertension the prevalence of OSA is reported to be 80% (Min et al. 2015; Muxfeldt et al. 2014).

Epidemiological studies from Asia have shown that the prevalence of OSA in patients with hypertension varies from 14 to 75% (Ip et al. 1999; Pensuksan et al. 2014; Shirani et al. 2016; Wali et al. 2017). A number of studies from India have garnered data regarding the overall prevalence of OSA in general population (Sharma et al. 2006; Reddy et al. 2009; Sharma et al., 2010; Udwadia et al. 2004). However, there is insufficient data to determine the prevalence of OSA in patients with hypertension. This lack of epidemiological aspects confirming relation if any, of hypertension with OSA has remained an unmet research need. The current study investigates the prevalence of OSA in confirmed hypertensive cases and correlates the severity of hypertension and OSA in terms of Berlin and Epworth scores.

Methods

This cross-sectional study was conducted at the Department of General Medicine of a tertiary care hospital of India. The participants were prospectively selected for a period of 6 months. Patients 18 years and older, of both sexes, who came for consultation/treatment at the Department of General Medicine, with a known case of hypertension were enrolled for the study and a well-informed consent was taken from all the patients before enrollment in the study. Hypertension was categorized, as stage 1 (140–159/90–99 mmHg) and stage 2 ($\geq 160/100$ mmHg) based on the guidelines by the American Heart Association on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Williams et al. 2018). Resistant Hypertension was defined as the failure to control clinic BP levels, despite the use of ≥ 3 antihypertensive drugs in optimal dosages, ideally including a diuretic, or achieving it with ≥ 4 drugs (Calhoun et al. 2008), while uncontrolled hypertension was defined as an office BP $\geq 140/90$ mmHg at the day of consultation (James et al. 2014). All patients, who consented to participate, were recruited by one attending physician. The patients were asked to complete a standardized questionnaire surveying the information regarding demographics and lifestyle factors (Table 1). In addition to this, the Berlin questionnaire (Tan et al. 2017) was used to determine the risk of developing OSA, dividing the patients into high and low-risk categories (Netzer et al. 1999). The Epworth sleepiness scale (ESS) was used to

Table 1 Baseline demographic and clinical characteristics of the study patients

Variable	Low Risk Subjects N = 384	High Risk Subjects N = 120
Age – yrs	56.5 \pm 12.4	53.4 \pm 9.02
Height – m	1.60 \pm 0.092	1.61 \pm 0.099
Body Weight – kg	65.19 \pm 11.085	73.63 \pm 14.31
BMI ^a – kg/m ²	25.5 \pm 4.57	28.75 \pm 5.42
Neck Circumference – cm	35.45 \pm 2.652	37.41 \pm 3.396
Waist Circumference – cm	98.75 \pm 10.87	105.90 \pm 11.28
Hip Circumference – cm	98.85 \pm 8.59	104.25 \pm 9.99
Waist to Hip Ratio	0.99 \pm 0.080	1.01 \pm 0.065
Epworth Sleepiness Score		
Lower Normal Daytime Sleepiness	3.45 \pm 1.091	3.375 \pm 1.025
Higher Normal Daytime Sleepiness	7.73 \pm 1.330	7.94 \pm 1.279
Mild Excessive Daytime Sleepiness	11.32 \pm 0.476	11.77 \pm 0.437
Moderate Excessive Daytime Sleepiness	13.75 \pm 0.808	13.85 \pm 0.834
Severe Excessive Daytime Sleepiness	17.45 \pm 2.018	18 \pm 1.805
Total Therapy Used	1.27 \pm 0.497	1.44 \pm 0.631
Co-morbidities (No.)		
Diabetes	84	33
Sub-Clinical Hypothyroidism	31	17
Dyslipidemia	12	8
Obesity	12	8
NAFLD	6	6
Others	140	26

Data is reported as number (percentage) or mean \pm standard deviation

^aBMI Indicates body mass index

evaluate sleep propensity in patients. The scale covers the whole range of sleep propensities, from the highest to the lowest. ESS classified subjects into five groups based on the score: 0–5, Lower Normal Daytime Sleepiness; 6–10, Higher Normal Daytime Sleepiness; 11–12, Mild Excessive Daytime Sleepiness; 13–15, Moderate Excessive Daytime Sleepiness; 16–24, Severe Excessive Daytime Sleepiness (Johns 1991). After the completion of questionnaires, measurement of BP, height, weight, waist circumference (WC), neck circumference (NC), and hip circumference, were taken. BP measurement was recorded using a mercury sphygmomanometer (Speider & Keller, Jungingen, Germany) and/or oscillometric devices, according to the recommendations of the American Heart Association Council on High Blood Pressure Research (Muntner et al. 2019). Height and weight measurements were obtained to calculate BMI and to categorize underweight (BMI < 18 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), class 1 obesity (30–34.9 kg/m²), class 2

obesity ($35\text{--}39.9\text{ kg/m}^2$), and class 3- extreme obesity ($\geq 40\text{ kg/m}^2$) (World Health Organization 2016). The normal cut-off value for NC was taken as 35.5 cm for men and 32 cm for women (Fink, 2012). WC was defined using the new International Diabetes Federation criteria for Asians: WC ≥ 90 cm for men and ≥ 80 cm for women (International Diabetes Federation 2019). The ethical clearance for the study was obtained from the institutional review board of Government Medical College/SMHS under the investigation vide number: 108/ETH/GMC/ICM Dated 28/10/2017. A flow diagram depicting the number of subjects recruited at each step is shown in Fig. 1.

A sample size of 504 patients was calculated based on the estimated prevalence of OSA of 40% (Senaratna et al. 2017) among case-patients, with a power of 90% and an α error of 5%. The statistical analysis was done using IBM SPSS (Statistical Package for the Social Sciences), V:20.0. (Armonk, NY: IBM Corp) software. Data is expressed as mean \pm SD. The differences between means were compared using the Student t-test. Factors associated with high risk of OSA and excessive daytime sleepiness (EDS) were identified using the χ^2 test in the univariate analysis. Significant variables from the χ^2 test were then included in the multivariate logistic regression model for the assessment of the independent effect of individual factors. A p -value of <0.05 was considered statistically significant.

Results

Over a period of 6 months, 737 subjects were surveyed, of which 504 (69%) responded and completed the study. In this sample, men and women were nearly equally distributed (male 253: female 251). The mean age of the sample was 56 ± 11 years. On the basis of the Berlin questionnaire, the study population was divided into two groups according to patients exhibiting high risk and low-risk of OSA. High risk of OSA, as per the Berlin

questionnaire, was present in 23.8% ($n=120$) of the population (Fig. 3) and the severe excessive daytime sleepiness, according to the Epworth Sleepiness Scale, was present in 32.5% ($n=39$) participants of the high-risk group. The high-risk of OSA was present in 43.3% males and 56.7% females while low-risk was present in 52.3% males and 47.7% females ($p=0.05$) (Table 2).

The anthropometric indices, including BMI, NC, WC, were significantly higher in patients with high-risk of OSA ($p<0.001$; 95% CI for all comparisons). The mean BMI for the patients with high-risk of OSA was $28.75 \pm 5.4\text{ kg/m}^2$ and $25.51 \pm 4.5\text{ kg/m}^2$ ($p<0.001$; 95% CI) for the low-risk group. However, the mean WHR for the two groups was clinically insignificant. About 97% of patients in the high-risk group had abnormal WHR while only 4.7% of the low-risk group had normal WHR ($p=0.295$; 95% CI). The descriptive statistical analysis of various anthropometric parameters in study patients is given in Table 2.

The mean systolic and diastolic BP measurements were significantly higher in patients with a high risk of OSA ($p<0.05$; 95% CI) (Fig. 4). Uncontrolled hypertension was present in 50% ($n=60$) of patients with high-risk for OSA while 57.6% ($n=221$) of patients had controlled hypertension in low-risk group ($p=0.146$; 95% CI). Resistant hypertension was present in 3.3% ($n=4$) subjects in high-risk OSA category while 99.5% ($n=382$) subjects in low-risk group had non-resistant hypertension ($p<0.05$; 95% CI). The Epworth score of >10 was found in 62.5% ($n=75$) patients with high-risk for OSA and <10 was found in 86.1% ($n=331$) among low-risk group ($p<0.001$; 95% CI). The patients with high-risk for OSA tended to use more medication than the low-risk group, with 7.5% of patients in the former group using three drugs simultaneously while only 2.08% in the latter group used triple therapy ($p<0.05$; 95% CI).

The most notable clinical variables in univariate analyses associated with high-risk of OSA were BP,

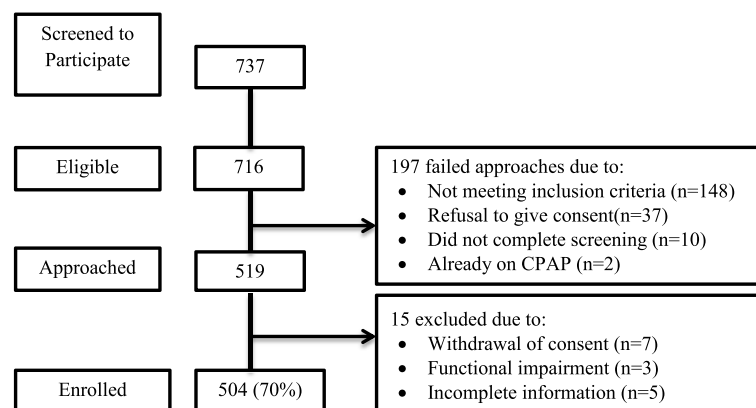


Fig. 1 Flowchart of the screened patients

Table 2 Descriptive statistical analysis of various anthropometric parameters in study patients

Parameter		Low Risk	High Risk	Total	P-value
Sex					
Male	Count	201	52	253	0.05
	% within Berlin category	52.3%	43.3%	50.2%	
Female	Count	183	68	251	
	% within Berlin category	47.7%	56.7%	49.8%	
BMI					
< 30 kg/m ²	Count	327	75	402	0.001
	% within Berlin category	85.1%	19.5%	79.8%	
≥ 30 kg/m ²	Count	57	45	102	
	% within Berlin category	14.8%	37.5%	20.2%	
Neck Circumference ^a					
Normal	Count	134	14	148	0.001
	% within Berlin category	34.9%	11.7%	29.4%	
Abnormal	Count	250	106	356	
	% within Berlin category	65.1%	88.3%	70.6%	
Waist Circumference ^b					
Normal	Count	104	12	116	0.001
	% within Berlin category	27.1%	10.0%	23.0%	
Abnormal	Count	280	108	388	
	% within Berlin category	72.9%	90.0%	77.0%	
WHR ^c					
Normal	Count	18	3	21	0.295
	% within Berlin category	4.7%	2.5%	4.2%	
Abnormal	Count	366	117	483	
	% within Berlin category	95.3%	97.5%	95.8%	

^a The cut-off for neck circumference of male and female were taken as 35.5 and 32 cm respectively

^b The WHO standards put cut-off for waist circumference for male and female at 94 and 80 cm respectively

^c A normal waist-to hip ratio is taken as 0.88 and 0.81 for male and female respectively

sleepiness, hypertension control-status, resistant hypertension, diabetes, and obesity. The most common comorbidities associated with hypertension were type 2 diabetes mellitus (23.2%), subclinical hypothyroidism (9.5%), dyslipidemia (4%), obesity (4%), and non-alcoholic fatty liver disease (2.4%) (Table 1). The high-risk group presented with disturbed sleep (29.2%), high daytime somnolence (32.5%), high fatigue/lethargy (46.7%), and loud snoring (84.2%) while these parameters were relatively normal in the low-risk group ($p < 0.001$; 95% CI). The clinical parameters of study patients are summarized in Table 3.

Discussion

The present study is a large data set furnishing information regarding the prevalence of obstructive sleep apnoea in patients with hypertension in India. The target population was identified on the basis of physician detected hypertension and the patient data was collected by a

standardized protocol on snoring, daytime sleepiness, BP, and other features associated with OSA.

Our study demonstrates that OSA is widely prevalent in patients with hypertension. Based on the standard Berlin questionnaire, 24% of the test population was found to be at high risk for OSA (i.e., 1 in every 4 hypertensive individuals). Our study is in accordance with studies by Peppard and colleagues who identified 24–28% prevalence of OSA in hypertension (Peppard et al. 2013).

The prevalence of daytime sleepiness in this sample was 62.5% by the Epworth scale result above 10 points. This prevalence in our sample is in agreement with the prevalence identified in a previous report of patients with hypertension (Ngahane et al. 2015). In that study, the authors identified the prevalence of excessive daytime sleepiness to be 62.78% (95% CI 58.08 to 67.47).

The overall mean age of the high risk for OSA respondents was 53.4 ± 9.02 years. The prevalence of OSA was highest between 51 and 60 years of age and this risk

Table 3 Descriptive statistical analysis of various clinical parameters in study patients

Parameter		Low Risk	High Risk	Total	P-value
Blood Pressure (mm Hg)					
Systolic		130.21 ± 17.244	133.52 ± 17.503		< 0.05
Diastolic		82.69 ± 9.531	84.37 ± 7.425		
Hypertension Control					
Controlled	Count	221	60	281	0.146
	% within Berlin category	57.6%	50.0%	55.8%	
Uncontrolled	Count	163	60	223	
	% within Berlin category	42.4%	50.0%	44.2%	
Resistant Hypertension					
Non-Resistant hypertension	Count	382	116	498	< 0.05
	% within Berlin category	99.5%	96.7%	98.8%	
Resistant hypertension	Count	2	4	6	
	% within Berlin category	0.5%	3.3%	1.2%	
Epworth Score					
0–5	Count	205	16	221	<0.001
	% within Berlin category	53.4%	13.3%	43.8%	
6–10	Count	126	29	155	30.8%
	% within Berlin category	32.8%	24.2%	30.8%	
11–12	Count	25	17	42	8.3%
	% within Berlin category	6.5%	14.2%	8.3%	
13–15	Count	17	19	36	7.1%
	% within Berlin category	4.4%	15.8%	7.1%	
16–24	Count	11	39	50	9.9%
	% within Berlin category	2.9%	32.5%	9.9%	
Therapy					
Off Therapy	Count	1	0	1	< 0.05
	% within Berlin category	0.26%	0.0%	0.26%	
Monotherapy	Count	284	77	361	71.6%
	% within Berlin category	73.9%	64.1%	71.6%	
Double Therapy	Count	91	34	125	24.8%
	% within Berlin category	23.6%	28.3%	24.8%	
Triple Therapy	Count	8	9	17	3.37%
	% within Berlin category	2.08	7.5%	3.37%	

increased exponentially from 0.8% at ≤30 years of age to 41.7% at 51–60 years of age ($p < 0.001$) (Fig. 2). This finding is in agreement with the previous studies demonstrating the effect of age on OSA status (Deng et al. 2014; Ip et al. 1999).

The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recognizes both the independent role of OSA in the development of hypertension and OSA in association with obesity (Chobanian et al. 2003). In our study, patients with high-risk of OSA had significantly higher BMI, WC, WHR, and NC values

statistically as compared to the patients with low-risk of OSA (Fig. 3). All of the anthropometric indices (NC, WC, and BMI) were significantly correlated with the risk of OSA. These results are similar to those of previous studies. Kang et al. reported that NC [95% CI; $p < 0.001$], WC (95% CI; $p < 0.001$), and BMI (95% CI; $p < 0.001$) were significantly associated with the presence of OSA (Kang et al. 2014). Hiestand and colleagues reported that among obese subjects (BMI ≥30 kg/m²), 59% of subjects were at high risk of OSA (Hiestand et al. 2006). In our study, only 37.5% of subjects were at high risk of OSA among obese patients (BMI ≥30 kg/m²).

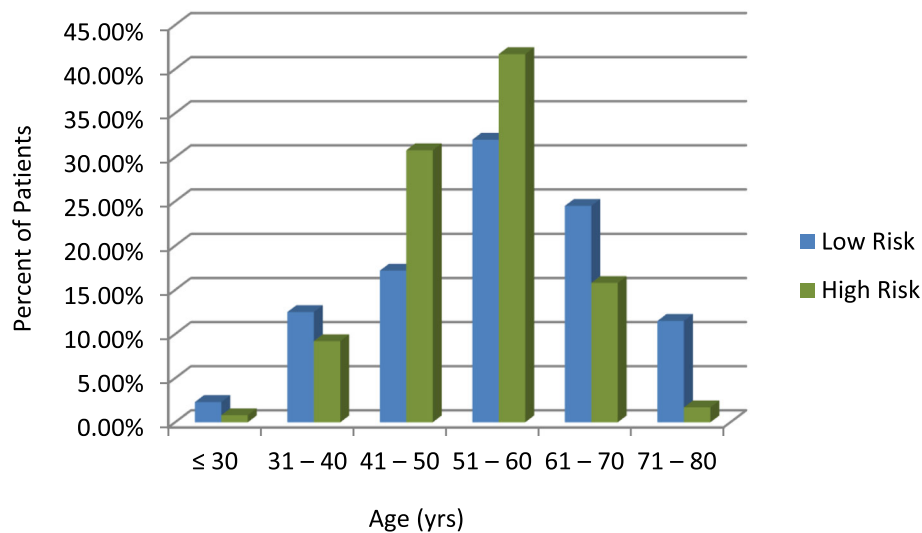


Fig. 2 Comparison between age and the risk of Obstructive Sleep Apnoea

In a study by Endeshaw and colleagues the mean BP values among older adults with sleep-disordered breathing were 133 ± 16 and 71 ± 8 mmHg for systolic and diastolic BP, respectively ($p < 0.001$) (Endeshaw et al. 2009). In our study, the average systolic and diastolic BP was 133.52 ± 17.503 and 84.37 ± 7.425 mmHg (Fig. 4).

In our study, OSA was found to be strongly associated with resistant hypertension. Though our sample size was not large enough to justify a meaningful conclusion on this, another case-control study by Gonçalves et al. reported that OSA is a strong independent risk factor for resistant hypertension (Gonçalves et al. 2007). This study represents an advanced approach in the understanding of the risk factors of hypertension and gives an insight into the prevalence of high-risk of OSA in patients with

hypertension. The Berlin Questionnaire, used in our study, is a validated method that has been used widely to identify individuals who are at risk for OSA (Gus et al. 2008). Our assessment of excessive daytime sleepiness was based on the ESS score, which is a well-tested international tool for the evaluation of daytime sleepiness (Boyes et al. 2017). With the increasing problem of hypertension, the impact of undetected or under-diagnosed OSA as a healthcare burden cannot be undermined. Therefore, this study can help reduce CV outcomes and healthcare costs of a rigorous anti-hypertensive regimen by treating the underlying cause.

There are a few limitations in our study that need to be considered. Firstly, the collection of data has been from a single tertiary care hospital for a limited period

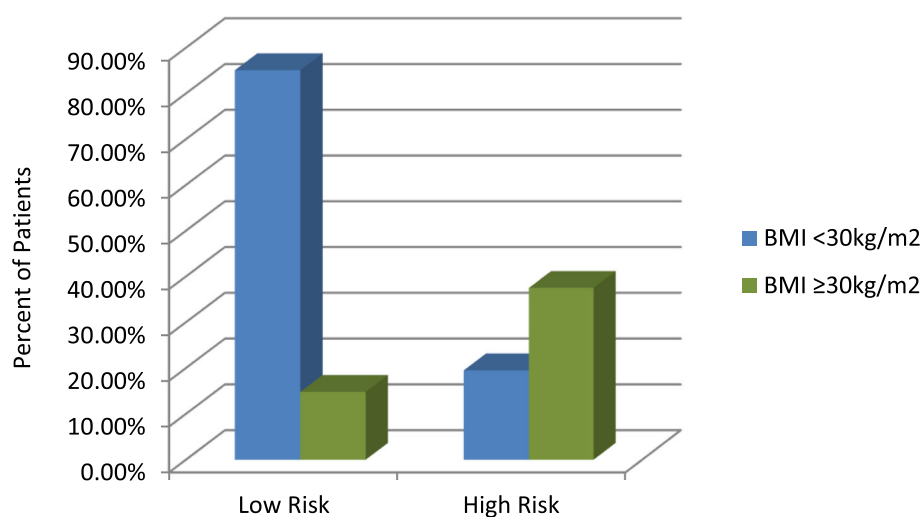


Fig. 3 Comparison between BMI and the risk of Obstructive Sleep Apnoea

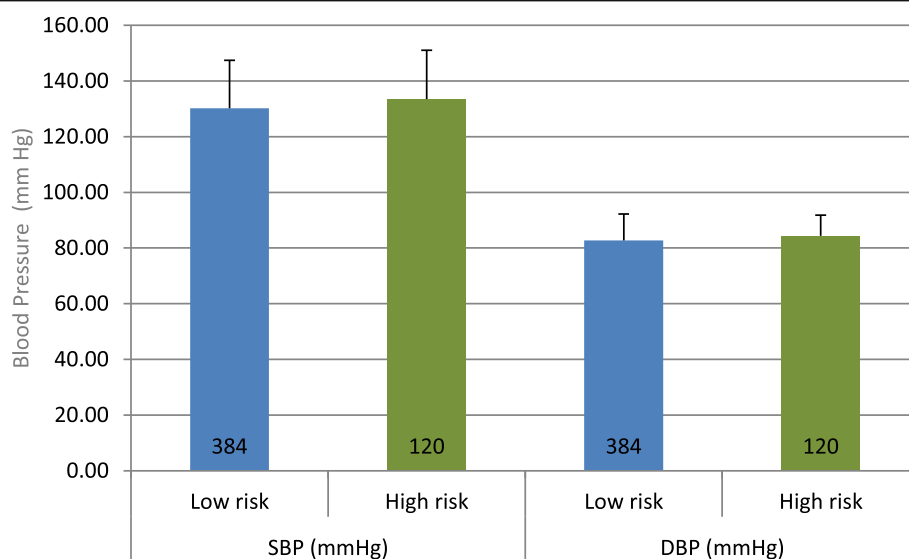


Fig. 4 Comparison of SBP and DBP in high and low risk subjects

of time yielding a small size of the patient population. Secondly, the Berlin Questionnaire was used to identify high risk for OSA instead of polysomnography which is the gold-standard test for the diagnosis of OSA in clinical settings (Pang and Terris 2006). However, it is complex, expensive, time-consuming, and is not available for the general population in India. The Berlin Questionnaire is a reliable tool and has been found to generate comparable results to that of polysomnography, yet there is a possibility of variation in the precision of results (Amra et al. 2018). We believe further studies using overnight polysomnography are warranted to exhaustively elucidate the bidirectional association between OSA and hypertension from different healthcare facilities of the state.

Conclusion

OSA is one of the most underdiagnosed and overlooked conditions in the health care system. The screening of OSA must be done in every suspected case, such as uncontrolled BP, unexplained hypertension, resistant hypertension, and obese patients. Our study concludes that nearly one in every four hypertensive patients is at high risk of OSA and most of them are obese and have a large neck circumference. Therefore, patients who feel very dizzy, fatigued and lethargic during the day should consult the physician, while the health-care personnel involved in the management of hypertensive patients should screen OSA and EDS and consider life-style modifications in patients who are at a high risk of developing OSA. The current study strengthens the acceptance of OSA as a risk factor for hypertension, in terms

of essential hypertension and resistant hypertension. The results of the study suggest new and possibly modifiable variables that can be targeted in future trials focusing on hypertensive medication.

Abbreviations

BMI: Body mass index; BP: Blood pressure; ESS: Epworth sleepiness scale; HC: Hip circumference; mm Hg: Millimeters of mercury; NC: Neck circumference; OSA: Obstructive sleep apnoea; SPSS: Statistical Package for the Social Sciences; WC: Waist circumference; WHR: Waist-to-hip ratio

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Authors' contributions

GNB and MT initiated the idea and designed the study protocol. OK performed the research at the hospital under the active involvement of MT. GNB and MT supervised the overall work. GNB and OK drafted the manuscript. All authors contributed to the writing of the final manuscript and approved the final version.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Ethics Committee of Government Medical College/Shri Maharaja Hari Singh (IEC-GMC/SMHS), in accordance with Indian Council of Medical Research (ICMR) guidelines. Institutional Ethical Registration Number: 108/ETH/GMC/ICM Dated 28/10/2017.

A well informed written as well as verbal consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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