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**SCREENING FOR OBSTRUCTIVE SLEEP APNEA IN PATIENTS  
WITH TYPE 2 DIABETES MELLITUS USING STOP-BANG  
SCORING AND ITS CORRELATION WITH HSCRP LEVELS—A  
ONE YEAR CROSS SECTIONAL STUDY IN KLE'S  
DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH  
CENTRE, BELAGAVI.**

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By

REGISTRATION NO: BG0121018

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Submitted to

KAHER, Belagavi, Karnataka

In partial fulfilment

of the requirements for the degree of

**M.D.**

**IN**

**GENERAL MEDICINE**

**DEPARTMENT OF GENERAL MEDICINE**

**J. N. MEDICAL COLLEGE**

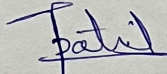
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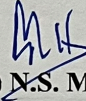
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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled  
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WITH HSCRP LEVELS.**” is ethical and justifiable. The proposed research project has been  
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## **List of abbreviations:**

ADA: American Diabetes Association

AHI: Apnea hypopnea index

ASCVD: Atherosclerotic cardiovascular disease

BMI: Body mass index

CI: Confidence interval

CPAP: Continuous positive airway pressure

CRP: C-reactive protein

CVD: Cardiovascular disease

ESS: Epworth Sleepiness Scale

GTT: Glucose tolerance tests

HOMA: Homeostatic model assessment

HSCRIP: High-sensitivity C-reactive protein

IDF: International Diabetes Federation

IH: Intermittent hypoxia

JUPITER :Justification for the Use of Statins in Prevention: an Intervention Trial  
Evaluating Rosuvastatin

MD: Mean difference

ODI: Oxygen desaturation index

OSA: Obstructive sleep apnea

PSG: Polysomnography

RCT: Randomized controlled trial

REM: Rapid eye movement

SAHS: Sleep apnea-hypopnea syndrome

SDB: Sleep-disordered breathing

SF: Sleep fragmentation

T2DM: Type 2 diabetes mellitus

UKPDS: UK Prospective Diabetes Study

UMCR: Urine microalbumin-creatinine ratio

WMD: Weighted mean difference

# ABSTRACT

**TITLE:**

Screening for Obstructive Sleep Apnea in Patients with Type 2 Diabetes Mellitus Using STOP-BANG Scoring and Its Correlation with HSCRP Levels–A One Year Cross Sectional Study In KLE’S DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, Belagavi.

**BACKGROUND:**

Higher levels of HsCRP are seen with Obstructive Sleep Apnea which indicates that OSA is an inflammatory state. Screening patients for HsCRP levels and stratifying them according to STOP-BANG criteria may help to diagnose patients suffering from OSA earlier and start treatment earlier.

**OBJECTIVES:**

To Screen for Obstructive Sleep Apnea in Patients with Type 2 Diabetes Mellitus Using STOP-BANG Scoring and Its Correlation with HSCRP Levels.

**METHOD:**

A cross-sectional study in the patients treated in the Department of General Medicine in IPD and OPD basis , at KLE Dr. Prabhakar Kore Hospital and Research Centre, Belagavi. Patients with type 2 Diabetes Mellitus were chosen as subjects, and they were stratified according to STOP-BANG scoring. Patients’ HsCRP levels were also checked and it was compares with patients’ STOP-BANG score.

**RESULT:**

A notable positive correlation between the STOP-Bang score and Hs-CRP levels was observed. The p-value of 0.0447 indicated a statistically significant association between STOP-BANG score and HsCRP levels. As the STOP-Bang score increased , indicating higher OSA risk, Hs-CRP levels also increased, possibly indicating elevated inflammation.

**CONCLUSION:**

The study highlights the necessity of assessing OSA in people with type 2 diabetes using the STOP BANG scoring system.The notable association found between STOP-Bang scores and Hs-CRP

levels indicates a possible connection between OSA severity and systemic inflammation in this group. Detecting and treating OSA early in individuals with T2DM may be vital for reducing related risks and enhancing overall health results

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## **Screening for Obstructive Sleep Apnea in Patients with Type 2 Diabetes Mellitus Using STOP-BANG Scoring and Its Correlation with HSCRП Levels**

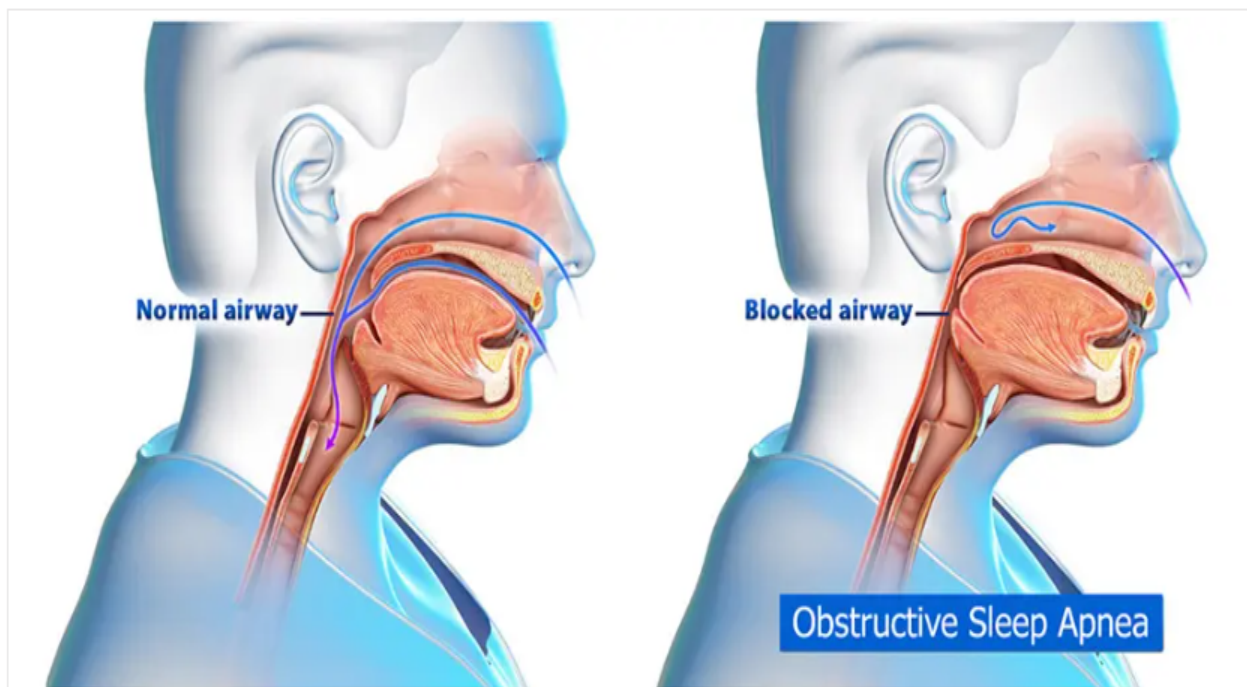
### **Introduction:**

Obstructive sleep apnea (OSA) is a common yet often underdiagnosed condition characterized by repeated episodes of partial or complete obstruction of the upper airway during sleep, leading to disrupted sleep and reduced oxygen saturation. This condition is prevalent among patients with type 2 diabetes mellitus (T2DM), a chronic metabolic disorder that impairs the body's ability to regulate blood sugar levels. The coexistence of OSA and T2DM poses significant health risks, including increased cardiovascular morbidity and mortality. Early detection of OSA in patients with T2DM is crucial for effective management and prevention of associated complications. The STOP-BANG questionnaire is a simple and effective screening tool that provides a way to identify groups at high risk for OSA. This tool assesses key risk factors such as snoring, tiredness, observed apneas, high blood Pressure, body mass index (BMI), age, neck circumference, and gender. In addition to screening for OSA, evaluating inflammatory markers such as high-sensitivity C-reactive protein (HSCRП) can provide insights into the systemic inflammation often present in both OSA and T2DM. Elevated HSCRП levels are indicative of increased inflammatory activity and are associated with a higher risk of cardiovascular events, making it a relevant marker for assessing the inflammatory burden in these patients.

The prevalence of OSA is constantly increasing due to the impact of the aging population and the increasing risk factors such as obesity, making it a widely recognized disease worldwide [1, 2]. Additionally, OSA is considered a public health problem due to its association with cardiovascular and metabolic diseases [3, 4]. Many people with OSA cases remain undiagnosed and untreated in the community [5]. OSA is usually diagnosed by laboratory or home polysomnography (PSG) [6], which provides valuable information about sleep patterns and the severity of OSA. However, PSG can be expensive, time-consuming, and uncomfortable, often disrupting patients' sleep. Additionally, PSG resources are scarce in most primary care settings, making it difficult to identify at-risk patients and ensure they receive appropriate care [7]. Consequently, screening questionnaires like the STOP-BANG and Berlin questionnaires have been recommended as alternative methods for identifying potential OSA cases in primary care settings [8]. The STOP-BANG questionnaire is especially useful for screening OSA due to its simplicity and validation in clinical settings [9]. Several studies have

shown that the STOP-BANG questionnaire is more than 80% sensitive in diagnosing all cases of OSA and more than 95% sensitive in identifying severe cases. However, the specificity is reported to be less than 50% [10-17]. On the other hand, studies examining the STOP-BANG questionnaire in the general population is limited. Existing studies suggest that this questionnaire has higher sensitivity but greater accuracy (ranging from 60% to 70%) in diagnosing severe OSA compared with inpatient findings.[18,19]

To address the shortcomings of the original survey, Tan et al. [19] modified this by lowering the cutoff value for BMI. They found that despite this change, understanding of the model and the modified model were still similar. Therefore, further research is needed to develop an improved version of the STOP-BANG questionnaire to increase its predictive power and make it more valid and widely applicable for OSA detection in the general population.



**Figure: 1 Obstructive sleep apnea (OSA)**

**Source:** <https://assets.yourpractice.online/2138/3d-images/obstructive-sleep-apnea.jpg>

The link between good sleep and overall personal health is well known, especially when it comes to serious medical conditions such as diabetes.

Studies have shown a higher prevalence of OSA in patients with type 2 diabetes [20], with a reported prevalence of 71%. The common cause of both is obesity. While treating type 2 diabetes is often about diet and exercise, the important role of good sleep is often overlooked. Obstructive sleep apnea causes periodic collapses of the airway during sleep, disrupting deep sleep and increasing the level of carbon dioxide in the blood. If left untreated, it can cause insulin resistance, increase blood

pressure, and increase the risk of cardiovascular disease; all of which contribute to the development of type 2 diabetes. This type of diabetes occurs when the pancreas does not produce enough insulin or the body cells become resistant to it, causing blood sugar levels to rise. Obesity is a risk factor for sleep apnea and type 2 diabetes.

Signs and Symptoms of OSA		
<p><b>Nocturnal Symptoms</b></p> <ul style="list-style-type: none"> <li>• Snoring</li> <li>• Choking or gasping at night</li> <li>• Observed episodes of breathing cessation during sleep</li> <li>• Night sweats</li> <li>• Maintenance insomnia</li> <li>• Erectile dysfunction</li> <li>• Nocturia</li> <li>• Heartburn</li> <li>• Awakening with nocturnal chest pain</li> <li>• Awakening with a dry mouth or sore throat</li> </ul>	<p><b>Day Time Symptoms</b></p> <ul style="list-style-type: none"> <li>• Excessive daytime sleepiness</li> <li>• Neurocognitive impairment</li> <li>• Heartburn</li> <li>• Morning headaches</li> <li>• Awakening with chest pain</li> <li>• Difficulty in concentrating during the day</li> <li>• Mood changes such as depression or irritability</li> <li>• High blood pressure</li> </ul>	<p><b>Physical Examination</b></p> <ul style="list-style-type: none"> <li>• Obesity</li> <li>• Enlarged neck circumference</li> <li>• Crowded upper airway</li> <li>• Hypertension</li> <li>• Accentuated P2 heart sounds (pulmonary hypertension)</li> <li>• Retrognathia/overjet</li> <li>• Nasal obstruction</li> <li>• Decreased oxygen saturation</li> <li>• S3 heart sound (congestive heart failure)</li> <li>• Lower extremity edema (heart failure)</li> </ul>

**Figure: 2 Signs and symptoms of OSA**

**Source:** <https://media.springernature.com>

Quality sleep is crucial for overall health, and ongoing sleep deprivation can lead to various issues, including imbalanced blood sugar levels. Chronic sleep disruption from conditions like sleep apnea can reduce insulin release after meals, while increased stress hormone production further impairs insulin function. Consequently, excess glucose remains in the bloodstream, heightening the risk of type 2 diabetes. When insulin function falters, elevated blood sugar levels can damage vital organs like the eyes, kidneys, nerves, and heart. Diabetes is just one among many health concerns stemming from inadequate sleep. Reduced insulin secretion due to sleep deprivation leads to a surge in blood sugar levels. Sleep apnea affects individuals with Type 1 and Type 2 diabetes, but only the latter can be directly linked to sleep deficiency. Even with diligent dietary and exercise regimens, persistent sleep loss can result in elevated blood sugar levels during medical check-ups. Recognizing the significance of sleep alongside diet and exercise is crucial for overall health maintenance [21].

Following a diagnosis of obstructive sleep apnea, patients may receive a prescription for continuous positive airway pressure (CPAP) therapy, widely regarded as the top-tier treatment for this condition due to its high effectiveness and minimal disruption. CPAP therapy involves wearing a mask connected to a machine during sleep, which delivers a steady stream of pressurized air to keep

airways open throughout the night. Retailers like The CPAP Shop offer affordable CPAP equipment, bypassing the hassle of insurance.

With CPAP therapy, users experience fewer nighttime disturbances caused by apneas, leading to deeper and healthier sleep, which is crucial for managing Type 2 diabetes effectively. Notably, sleep apnea is also prevalent among individuals with prediabetes, a precursor to Type 2 diabetes. Therefore, if a person has prediabetes or is suspected to have it and is experiencing sleep apnea symptoms, sleep test is beneficial, thus consider requesting a sleep test [21].

While sleep apnea treatments don't serve as a definitive remedy for Type 2 diabetes, they play a pivotal role in assisting diabetic individuals in sustaining optimal blood sugar levels. This is part of an overall regimen encompassing proper diet, exercise, and medications as directed by a healthcare provider. Sleep apnea treatments enable diabetics to reclaim restorative sleep, which was previously disrupted by the condition. Through adherence to treatment, particularly CPAP therapy, diabetic patients often experience enhanced vitality upon awakening and a reduction in blood sugar fluctuations. Furthermore, addressing sleep apnea may alleviate associated symptoms like morning dryness, headaches, irritability, mood swings, depression, and daytime fatigue. Many individuals successfully manage both diabetes and sleep apnea with the guidance of healthcare professionals, incorporating structured exercise routines, balanced diets, and potentially prescription medications into their daily lives.

For sleep apnea management, maintaining consistent sleep patterns and adhering to CPAP therapy are crucial. Compliant use of CPAP devices ensures the maintenance of an open airway during sleep, facilitating quality rest. Additionally, adopting healthy lifestyle choices such as abstaining from alcohol, avoiding heavy meals before bedtime, and refraining from smoking can further support the management of both sleep apnea and diabetes. A concerted effort in managing sleep apnea stands as one of the prime methods for ensuring improved and healthier sleep for individuals suffering with the condition. Use CPAP machines as prescribed and consult healthcare providers to adjust pressure settings for changing sleep apnea needs. Many sleep apnea patients rely on sleep trackers to stay attuned to their sleep patterns. These devices, ranging from wearable wristbands to pillow attachments or bedside fixtures, have flooded the market with new iterations emerging frequently. Typically, sleep trackers employ accelerometers and motion detectors to gauge both the quantity and quality of sleep. By measuring movement during sleep, these trackers utilize algorithms to estimate sleep duration and effectiveness. However, for those seeking deeper insights into their sleep stages, relying solely on an accelerometer-based tracker may prove insufficient.

Sleep trackers struggle to accurately discern sleep stages due to minimal movement variance across stages, according to the Sleep Foundation<sup>[21]</sup>.

The purpose of this study is to examine the link between HSCRP levels and STOP-BANG scores in order to determine the prevalence of OSA in patients with T2DM. Understanding this relationship may highlight the interplay between sleep apnea, metabolic dysfunction, and inflammation, and underscore the importance of integrated care in managing patients with T2DM.

**Aim and Objective:**

To screen for Obstructive Sleep Apnea in Patients with Type 2 Diabetes Mellitus Using STOP-BANG Scoring and Its Correlation with HSCRП Levels

## **Review of literature:**

The increase in diabetes and obesity worldwide has become an urgent concern for doctors but also a major challenge for the public. The global prevalence of obesity has nearly doubled since 1980. Approximately 500 million people are currently classified as obese [22], and this number is expected to reach approximately 1.12 billion by 2030, including long-term trends [23]. The percentage of adults classed as obese in England increased significantly from 1993 to 2012; this rate increased from 13.2% to 24.4% in men and from 16.4% to 25.1% in women [24]. If current trends continue, predictions suggest obesity could reach 60% of men and 50% of women by 2050, with corresponding effects: NHS debt is expected to double to £100 billion, and social costs are also predicted. up to £49.9 billion per year [25]. The increase in obesity is closely related to the increase in type 2 diabetes. Currently, approximately 6.4% of adults worldwide have diabetes, and the condition affects approximately 285 million people. Estimates suggest that this number may rise to 7.7%, with around 439 million adults expected to be affected by 2030 [26]. Although body weight varies among people, the majority of patients with type 2 diabetes are overweight or obese [27]. Abdominal obesity, in particular, plays an important role in the pathogenesis of T2DM, making it an important target for reducing diabetes [28]. The term “diabetes” was coined to indicate the relationship between the two conditions [29]. The majority of people with type 2 diabetes are overweight or obese, which contributes to insulin resistance and disease-leading  $\beta$ -Cell dysfunction [30]. Obesity and/or diabetes can elevate the risk of various complications, including cardiovascular diseases and other obesity-related issues such as endocrine dysregulation, arthritis, and heightened cancer susceptibility. This complexity in managing these conditions is well-documented [31, 32]. Notably, sleep-disordered breathing (SDB), particularly OSA, is closely linked with both obesity and diabetes.

The interplay between obesity, diabetes, and OSA is widely acknowledged in medical literature. Obesity increases the risk of developing both diabetes and OSA. In turn, diabetes can exacerbate obesity-related complications, including OSA. The presence of OSA can also worsen glycemic control in individuals with diabetes.

Treatment strategies often involve addressing each condition holistically. Lifestyle modifications such as weight loss through diet and exercise are fundamental in managing obesity and diabetes, which can also alleviate symptoms of OSA. CPAP therapy is the primary treatment for OSA, which helps maintain an open airway during sleep. Additionally, medications and surgical interventions may be considered in specific cases.

Moreover, managing diabetes effectively with medications, insulin therapy, and blood sugar monitoring is essential to mitigate its impact on other health conditions, including OSA. Collaborative care involving healthcare professionals from multiple specialties, including endocrinologists, pulmonologists, and sleep specialists, is often necessary to tailor treatment plans to the individual's needs and optimize outcomes.

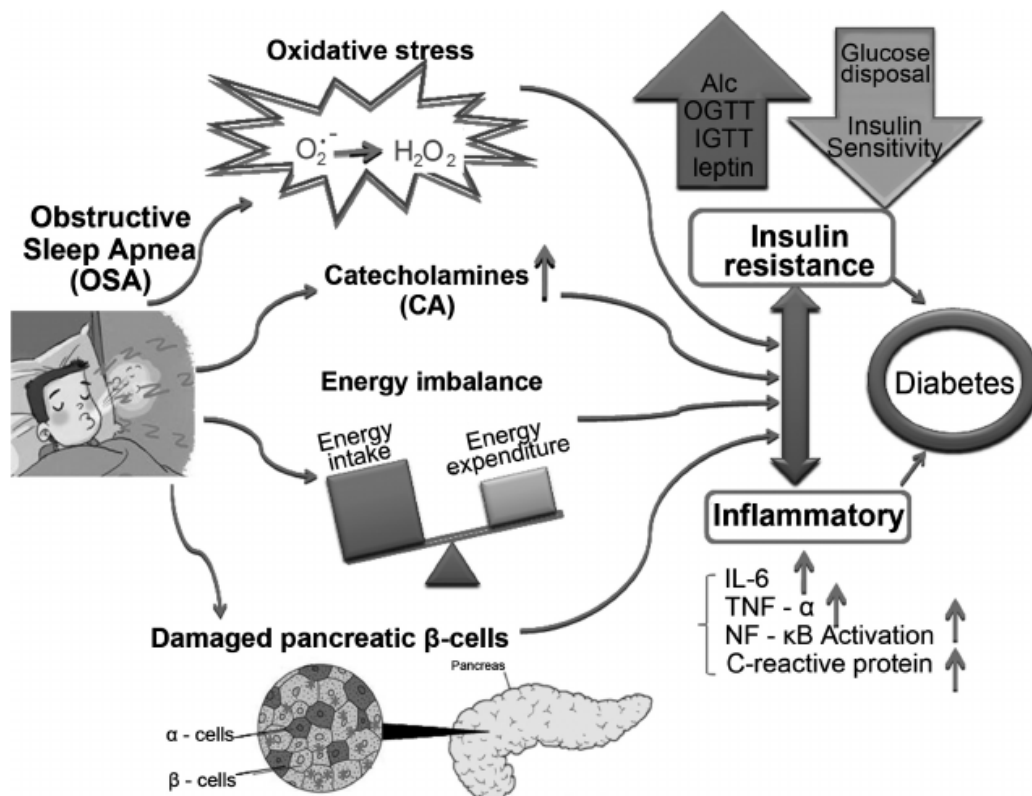
### **Role of OSA in T2DM:**

The relationship between OSA and type 2 diabetes has important implications for improving health outcomes, especially considering that the global prevalence of diabetes has increased in the past year. It is estimated that the prevalence may reach 4.4% and the number of patients is expected to reach 366 million by 2030 [33]. This analysis may facilitate important steps in cardiovascular risk management independent of CPAP therapy. Additionally, evidence suggests that OSA may be linked to microvascular complications, including diabetic retinopathy [35], nephropathy [36], and neuropathy [37]. Therefore, recognizing diabetes patients at high risk for OSA may enable targeted investigations that enhance comprehensive diabetes care.

The Taskforce on Epidemiology and Prevention of the International Diabetes Federation (IDF) released a consensus statement in 2008 suggesting a targeted strategy for screening people with type 2 diabetes and obesity for SDB [38], [39]. The IDF advises healthcare professionals to consider the possibility of OSA in patients with T2DM and collaborate with local sleep services to establish an appropriate assessment, referral, and intervention process [39].

### **The Impact of OSA on Insulin Resistance and $\beta$ -Cell Dysfunction:**

Figure 4 shows the biological pathways associated with OSA for the disruption of glucose homeostasis, ultimately leading to prediabetes and type 2 diabetes. In animal models, intermittent hypoxia (IH) reduces insulin sensitivity (also measured by blood glucose) and increases the homeostasis model (HOMA) index [40–42]. IH directly affects hepatocytes, increasing glycogen content and increasing gluconeogenesis enzyme activity in cells [42]. Chronic IH in mice increases proinflammatory cytokines (IL-1 $\beta$ , IL-6, MIP-2) and the transcription factor NF- $\kappa$ B. [43]. In addition, IH reduces proliferation and inhibits the conversion of proinsulin to insulin by increasing pancreatic beta cell apoptosis [44–46]. IH also affects adipose tissue, reducing adiponectin (an insulin-sensitizing hormone) and increasing resistance [47, 48]. IH in animals and humans is accompanied by a sympathetic reaction [49, 50].



**Figure: 3 T2DM is caused by OSA.**

**Source:www.researchgate.net**

Louis and colleagues [51] investigated the effects of IH in healthy adults by comparing normal SpO<sub>2</sub> conditions with 5-h waking IH exposure. IH was performed 24 times per hour to simulate moderate OSA. Intravenous GTT results indicate decreased insulin sensitivity and glucose levels; This indicates a decrease in blood glucose to reduce glycogen production and improve tissue absorption. Studies point to endurance caused by an increase in heart rate in response to hypoxia. Pancreatic insulin release and blood cortisol levels were unchanged. Sleep fragmentation (SF) interferes with glucose by weakening the brain due to respiratory failure and hypoxia, and cortisol contributes to obesity and insulin resistance in mice via markers of inflammation and oxidative stress. In young people, SF and IH cause insulin resistance regardless of age or obesity [52]. Studies have shown that interventions to reduce sleep deprivation in healthy adults lead to reductions in insulin levels [53, 54]. SF exacerbates glycemic control in patients with OSA and T2DM [55, 56].

### **Epidemiology:**

Insulin resistance and pancreatic beta cell dysfunction lead to prediabetes and T2DM, which are more common in individuals with OSA. Studies using tests such as rapid blood glucose or polysomnography. T2DM also increases the risk of OSA. The prevalence of OSA in type 2 diabetes

varies, with an estimated prevalence of OSA in primary care at 18%. OSA affects sleep quality and metabolism by affecting the autonomic and central nervous systems. This interaction leads to poor control of diabetes; a significant control [57] was set to reach 58% in the elderly [58] and 86% in obese individuals with T2DM [59].

### **T2DM, Prediabetes, and OSA:**

Several studies have established that Obstructive Sleep Apnea (OSA) is associated with impaired glucose tolerance, regardless of obesity [60–62], and this risk is strongly linked to the severity of nocturnal hypoxia [63]. Research following men in a community over time indicated that OSA predicts insulin resistance in individuals without diabetes [64]. Moreover, longitudinal cohort studies in North America, Europe, and Australia have shown an increased risk of developing diabetes mellitus (DM), particularly in cases of moderate to severe OSA [65–68]. These findings are further supported by a recent meta-analysis, which estimated a 63% increased risk of incident DM associated with moderate to severe OSA [69]. However, the results of these longitudinal studies vary when adjusted for confounding factors such as age, sex, and BMI, emphasizing the importance of considering shared risk factors as key moderators in the relationship between OSA and type 2 diabetes mellitus (T2DM). Therefore, these factors should be accounted for in the clinical evaluation and management of patients. Emerging evidence indicates that OSA during rapid eye movement (REM) sleep, characterized by frequent respiratory events and severe oxygen desaturation, significantly impacts insulin resistance and glycemic control [70, 71].

### **OSA's effects on Type 2 Diabetes:**

Several studies have shown that untreated OSA has a negative impact on glycemic control in patients with T2DM [71–73]. Aronson et al. [74] examined the relationship between apnea-hypopnea index (AHI) and A1C levels in 60 patients with type 2 diabetes. They found a significant association between AHI and A1C for conflict individuals even after corrective treatment. Interestingly, AHI has a greater effect on A1C than some diabetes medications. In contrast, the largest prospective analysis, the “SLEEPING AHEAD” substudy, reached a different conclusion. [75] could not establish a relationship between polysomnography-derived AHI and A1C levels in their study involving 305 participants from 4 of 16 centers. Instead, they found only a weak correlation between fasting blood sugar and sleep, a measure of sleep disruption. This study included older, obese individuals with T2DM; this may have contributed to the inconsistent results. Tamura et al [76] showed that AHI predicted long-term glycemic control (measured by A1C) in hypoglycemic

patients, but that the lowest oxygen saturation level was correlated with A1C in people with type 2 diabetes. Together, these findings support the understanding that OSA, especially moderate and severe OSA, is associated with poor metabolic control in T2DM.

### **Organ Dysfunction:**

OSA increases the risk of cardiovascular disease (CVD). It causes significant oxidative stress due to the effects of hypoxia, hypercapnia, and frequent awakenings during sleep, thus reducing the production of vasodilators such as nitric oxide [77]. OSA also causes inflammation and increases blood clotting, leading to further vascular damage [78]. These studies demonstrate why OSA severity, as measured by the AHI, is associated with stroke risk in type 2 diabetic patients (odds ratio, 2.5) [79]. This study focused on obese adults, where the prevalence of OSA is as high as 86%. Future studies should examine how OSA affects CVD in leaner, younger patients with type 2 diabetes to understand its effects on different populations. Limited evidence suggests that people with type 2 diabetes and OSA may experience poor organ function. OSA itself causes kidney damage, especially in people with diabetes [80]. In a study of approximately 500 T2DM patients, Japanese researchers used nighttime oximetry to screen for OSA [81]. In OSA, poor blood sugar is associated with high blood pressure, hyperlipidemia, microalbuminuria, and macroalbuminuria. This association persists even after taking other factors into account. A similar pattern was found in obese Britons with type 2 diabetes, suggesting that obesity is not solely responsible [82]. A recent review found an association between severe OSA and a higher risk of diabetic nephropathy, with an odds ratio of 1.73 [83]. A study in more than 200 diabetic patients examined the causes and mechanisms of peripheral neuropathy and compared patients with and without OSA. Studies have shown that patients with OSA have more peripheral neuropathy, especially when the pain is severe. Additionally, increased levels of nitrotyrosine and lipid peroxide were observed in the OSA group, indicating that nitrosative and oxidative stress are associated with nocturnal hypoxemia [37]. Many studies have shown that OSA is associated with numerous eye complications such as retinopathy and maculopathy in type 2 diabetes [84–87]. Talani et al. [36] found that type 2 diabetics with OSA had more eye problems than those without OSA.

### **Diabetes and the Impact of OSA Treatment:**

Management of OSA includes behavioral and weight management. Medical and surgical weight loss can improve OSA. Lifestyle changes may also help reduce OSA, especially in patients with type 2 diabetes [88, 89]. Improving OSA through weight loss may help control type 2 diabetes, but its

effects are not fully understood. Techniques and devices such as palatal advancement are designed to expand the airway, but there are insufficient data regarding their effectiveness in type 2 diabetic OSA for this review. CPAP treatment is the most important and effective way to treat OSA. Randomized placebo-controlled clinical trials have shown that CPAP is effective in controlling blood glucose in obese and non-obese individuals [90, 91]. Recently, RCTs have examined the metabolic effects of CPAP compared to oral placebo in patients with diabetes [90]. Importantly, CPAP oral increased insulin sensitivity during GTT and reduced 24-hour blood pressure compared to placebo. These findings are consistent with a previous meta-analysis that identified clinical trials involving approximately 240 patients without T2DM. This analysis showed that HOMA scores improved with CPAP treatment compared to placebo [92]. for diabetes management. The effect may be less than that of weight loss or medication but may still be treatment-related [93]. Importantly, this effect is frequently observed with higher CPAP adherence, particularly in individuals with severe OSA, obesity, and uncontrolled diabetes [91,94, 95]. CPAP therapy is essential for improving blood sugar control and produces significant results after three months of continuous use. Evidence favors people with type 2 diabetes over people with type 2 diabetes; This may be because less research has been done on people with type 2 diabetes. Type 2 diabetes is often associated with poor beta cell function and other health problems that are difficult to treat in older adults. Early intervention in OSA is important for treatment compliance in patients with T2DM or at risk [71].

### **Role of Hs CRP in OSA and Diabetes Type-2:**

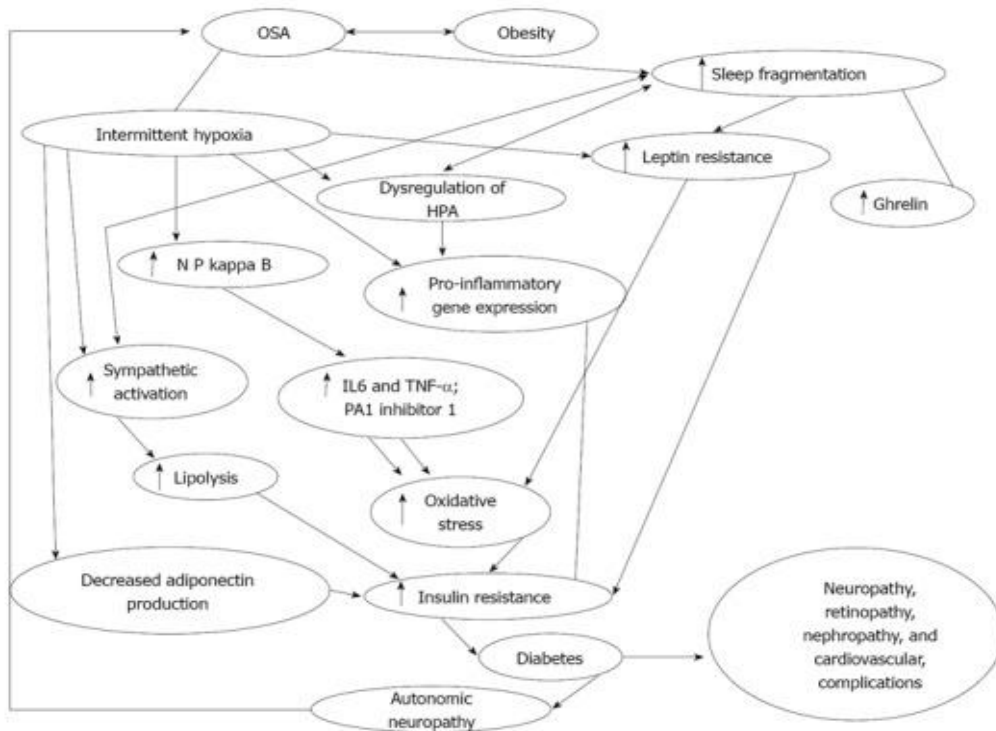
C-reactive protein (CRP) is a positive reactant produced by liver cells and released into the bloodstream in response to inflammation. It is an indicator of the ongoing inflammatory process in the body and many diseases. CRP was first found in the blood of patients with pneumonia caused by pneumococci in the acute phase [95]. Although known as a severe reactant, CRP levels are also elevated in many diseases, including autoimmune diseases, malignancies, chronic pain, inflammation and metabolic diseases [96].

Hs-CRP and normal CRP are often misunderstood separately. Hs-CRP is an advanced test that accurately measures CRP levels by detecting low blood levels in the blood, which is important for assessing inflammation in the body. It is particularly useful in predicting heart disease and stroke in healthy individuals or those unaffected [97]. The Hs-CRP test measures inflammation and indicates the risk of heart disease and stroke [98].

Sleep apnea-hypopnea syndrome (SAHS) affects 4% of middle-aged men and 2% of middle-aged women [99]. This condition involves repeated partial (hypopnea) or complete (apnea) collapse of the upper airway during sleep due to relaxation of the pharyngeal muscles [100-103]. While these people are asleep, a vicious cycle occurs: the upper airway narrows and reopens, leading to sleep and a subsequent period of apnea [103].

These conditions occur at night and are associated with the interaction between hypoxemia and hypocapnia, hyperventilation, sleep fragmentation, and excessive daytime sleepiness [100, 102]. Upper airway and recurrent nocturnal arterial desaturation leads to lower arterial pressure, which contributes to atherosclerosis and the atherosclerotic process [104, 105]. The inflammatory markers CRP, interleukin 6, tumor necrosis factor  $\alpha$  and pentraxin 3 are associated with the cardiovascular pathology seen in sleep apnea [99, 106]. Interleukin-6 (IL-6) is a pro-inflammatory cytokine that causes an inflammatory response in the liver and stimulates CRP production [99]. CRP is an uncosylated protein with a pentameric structure that migrates electrophoretically in the  $\gamma$  region. As an acute phase reactant, CRP levels rise rapidly in response to tissue damage, infection or disease, and neoplastic disease. During tissue necrosis and infection, CRP level can rise up to 300 mg/L in 12-24 hours.[107]. Fragmentation and lack of sleep are pro-inflammatory in nature. Meyer-Ewert et al. Studies have shown that 88 hours of sleep deprivation in 12 days or 10 days of sleep restriction for 4 hours per night are associated with increased CRP levels [108].

Type 2 diabetes is a chronic disease caused by insulin resistance and hyperglycemia. It can cause microvascular and macrovascular problems, especially acceleration of atherosclerosis, due to inflammation and oxidative damage caused by hyperglycemia. CRP and ESR are frequently used as markers of inflammation to assess the risk of atherosclerosis; CRP is a useful predictor of diabetes and heart disease. Other markers under investigation include serum ferritin, serum albumin, and serum fibrinogen [109].



**Figure: 4 Flow diagrams showing how diabetes, intermittent hypoxia, OSA, and sleep fragmentation interact. OSA Nucleus kappa B (NF-κB), Plasminogen activator inhibitor 1 (PA1), the hypothalamic-pituitary axis (HPA), interleukin (IL), and tumour necrosis factor-α (TNF-α).**

Source: <https://www.ncbi.nlm.nih.gov>

CRP can increase the risk of heart disease by causing atherosclerotic plaques, blood clots, and thrombosis. Previous studies have examined CRP in men, but CRP levels were generally higher in women. In middle-aged women, CRP baseline predicts cardiovascular risk and helps predict vascular events in low-risk individuals without other diseases [110].

The exact mechanism of persistent pain remains unclear. However, various vascular factors such as IL-1, IL-6, and TNFα are believed to be involved in this process. More importantly, Hs-CRP is considered a reliable indicator of vascular inflammation. As the link between diabetes, atherosclerosis, and chronic pain becomes clearer, there is interest in investigating the relationship between Hs-CRP levels and diabetes. Recently, the World Health Organization developed a new standard for measuring CRP to ensure it can be used worldwide. This development strengthens the use of Hs-CRP as a widely accepted method for the evaluation of all cardiovascular diseases. High Hs-CRP levels are associated with the risk of type 2 diabetes in patients with metabolic syndrome [111]. Primary prevention strategies can be initiated according to Hs-CRP levels to prevent

cardiovascular diseases, reduce CHD-related mortality, and reduce mortality and morbidity in diabetic patients. There is a clear link between glycosylated hemoglobin levels and Hs-CRP, and diabetes control lowers Hs-CRP. This suggests that Hs-CRP may be a useful test in diabetic patients. Studies such as the United Kingdom Prospective Diabetes Study (UKPDS) study [112], Atherosclerotic Cardiovascular Disease (ASCVD) Risk Score [113], and Fairness for Statin Prophylaxis: A Review SIGNIFICANCE OF THE RESEARCH Rosuvastatin (JUPITER) highlight this [114] showed a significant relationship between the development of atherosclerosis and Hs-CRP. These findings highlight the importance of appropriate diabetes control to lower Hs-CRP levels and reduce diabetes-related complications [115]. Acute hyperglycemia, often called prediabetes, is generally thought to be harmless, but it can cause mild inflammation, leading to the release of inflammatory markers. High-sensitivity C-reactive protein (Hs-CRP) is a strong indicator of this condition and helps identify prediabetes. This makes Hs-CRP a reliable tool for predicting heart problems in healthy individuals with high blood sugar [116]. OSA is associated with increased CRP levels. Individuals with OSA exhibit elevated IL-6 levels corresponding to the severity of their apnea-hypopnea indices. Monitoring CRP and IL-6 levels may increase the effectiveness of CPAP therapy and improve overall clinical outcomes [117, 118].

### **Stop Bang Score For OSA:**

The prevalence of OSA is on the rise, yet many individuals remain unaware they have the disorder since its symptoms predominantly manifest during sleep. Estimates suggest that up to 80% of moderate to severe OSA cases may be undiagnosed and untreated. To help identify those who could benefit from OSA testing, researchers have created an easy-to-use, eight-question survey known as the STOP-Bang Questionnaire [119].

The STOP-Bang Questionnaire is crafted to offer doctors a simple means of pinpointing potential cases of OSA. Comprising eight yes-no queries centered around prominent risk factors for OSA, this tool utilizes the acronym STOP-Bang, which encapsulates the initial letters of symptoms or physical traits often associated with the condition.

**Snoring:** Snoring loudly enough to disturb a bed partner.

**Tiredness:** Evaluates daytime fatigue, including the tendency to fall asleep during daily activities.

**Observed Apnea:** If a sleep partner has noticed episodes of stopped breathing or gasping for air during sleep.

**Pressure:** High blood pressure.

**BMI:** BMI higher than 35.

**Age:** Those over 50 years old as being at higher risk for OSA.

**Neck Circumference:** Measures neck circumference, with a measurement greater than 40 cm being a risk factor.

**Gender:** Males are more likely to have OSA.

When completing the STOP-Bang questionnaire, each symptom or risk factor adds one point to the individual's total, with a maximum score of eight. Typically, a higher total suggests a heightened likelihood of moderate or severe OSA. Research indicates a link between elevated STOP-Bang scores and the severity of OSA [120]. A STOP-Bang score of 2 or lower suggests a low risk, whereas a score of 5 or higher indicates a heightened risk for moderate to severe OSA. Individuals scoring 3 or 4 may require additional evaluation by a physician to ascertain the likelihood of OSA.

STOP-Bang Score	
<b>S</b>	Snoring
<b>T</b>	Tiredness
<b>O</b>	Observed apnea
<b>P</b>	High blood pressure
<b>B</b>	Body mass index >35 kg/m <sup>2</sup>
<b>a</b>	Age >50 years
<b>n</b>	Neck circumference >40 cm
<b>g</b>	Gender, male

**Figure: 5 STOP BANG SCORE**

Source: <https://www.anesthesiologynews.com>

The STOP-Bang questionnaire effectively assesses OSA risk, allowing further evaluation of individuals at higher risk. It is important to screen for OSA in different groups such as adults with Down syndrome, type 2 diabetics, pregnant women and people over the age of 40. The truth diminishes. Although the STOP-Bang test is more effective than other devices, failure can lead to unnecessary medical costs. The reality varies with individual characteristics and treatment, and is less effective in certain groups, such as veterans and patients with kidney failure. Although factors such as body mass index and neck circumference are given equal weight, this may still cause the test to be negative. However, the STOP-Bang test serves as an important preliminary screening tool that indicates the need for more specific testing <sup>[119]</sup>.

Future directions for addressing OSA in patients with T2DM could involve integrating the STOP-BANG scoring system with hsCRP levels, a marker of inflammation. OSA and T2DM often coexist, worsening cardiovascular risks. STOP-BANG offers a simple screening tool, useful in T2DM patients. Combining STOP-BANG scores with hsCRP levels can provide insights into underlying inflammation. This correlation aids risk assessment, treatment, and monitoring. Understanding OSA severity, T2DM, and inflammation interaction can guide personalized therapies, improving outcomes and reducing comorbidities. Future research in this area promises advancements in managing OSA in T2DM, enhancing life quality and reducing health risks.

### **Previous studies:**

In a 2016 study by Wastelake et al <sup>[121]</sup>, 294 patients with T2DM participated, completed questionnaires, and monitored sleep at home using a type IV sleep view. Of these, 31% had severe OSA, 21% had moderate OSA, and 41% had mild OSA. Various questionnaires have shown similar sensitivity and specificity for the detection of apnea-hypopnea index (AHI)  $\rightarrow$  15: Berlin Questionnaire (sensitivity 0.69, specificity 0.50), STOP (sensitivity 0.65, specificity 0.49) and STOP-Bang ( e.g. 0,5,9, sensitivity). ). Importantly, STOP-Bang performance differed between genders, with a sensitivity of 0.74 in men and 0.29 in women ( $p < 0.05$ ) and a specificity of 0.56 in men and 0.82 in women ( $p < 0.05$ ). Even the most accurate Berlin Survey failed to identify 31% of patients with moderate to severe OSA as high risk, which can affect diagnosis and treatment. Due to the heightened cardiovascular mortality risk in Type 2 diabetes mellitus patients and the prevalent moderate to severe OSA, relying solely on questionnaires for screening seems inadequate. The study suggests incorporating home sleep monitoring devices into OSA screening for more precise assessment and timely intervention.

Li et al., 2017 [122] identified 15 studies that met inclusion criteria with a total of 1,297 participants. 2.58,  $P < .01$ ). Serum hs-CRP level was significantly higher in the OSA group compared with the control group (mean difference: 1.57 mmol/L, 95% CI:  $0.96 \pm 2.18$ ,  $P < 0.01$ ). The overall weighted mean difference (WMD) between OSA and controls in this subgroup was 2.10 for CRP and 2.49 for hs-CRP. In OSA patients with a mean apnea-hypopnea index (AHI)  $\leq 15$ , the overall WMD for CRP was 2.19 and for hs-CRP was 1.70. These results showed that serum CRP and hs-CRP were elevated in OSA patients compared with controls, especially in patients with higher BMI and AHI. This suggests an inflammatory component in the pathophysiology of OSA and supports the concept of CRP and hs-CRP as potential biomarkers for this disease.

According to Vander Touw et al., 2019 [123], five studies encompassing 219 participants with OSA and 116 control participants met the inclusion criteria. The analysis found that circulating high-sensitivity CRP was, on average, 0.61 mg/dL higher in OSA participants than in controls (confidence interval: 0.38 to 0.84,  $p < 0.00001$ ). Heterogeneity between studies was low ( $df = 7$ ,  $p = 0.16$ ,  $I^2 = 33\%$ ), and there was minimal evidence of publication bias. Non-smoking OSA participants without comorbidities had elevated CRP levels compared to healthy non-smoking controls, suggesting OSA-related inflammation may raise CRP levels.

In the study by Agha et al., 2019 [124], patients exhibited significantly higher HbA1c levels compared to the control group. Among the OSA-related parameters, only the Epworth Sleepiness Scale score showed a significant positive correlation with HbA1c levels. Following three months of CPAP therapy, HbA1c levels significantly decreased from  $8.64 \pm 1.12$  to  $8.30 \pm 0.89$ . This suggests that OSA adversely impacts blood glucose control in patients with T2DM, and CPAP therapy may be beneficial in managing blood glucose levels in these patients.

In the study by Shin et al., 2021 [125], 958 individuals, including 487 in an exploratory sample, were identified to have OSA. To develop a predictive model in the exploratory sample, a stepwise analysis was employed, incorporating data from the standard questionnaire along with additional variables. These variables included snoring, witnessed breathing cessation, hypertension, BMI over 25 kg/m<sup>2</sup>, age groups, gender (male), diabetes, and waist circumference over 85 cm. The final modified model derived from this analysis included these factors. When evaluating diagnostic accuracy using a validation sample, the modified model demonstrated a higher sensitivity (79.1%, 95% confidence interval [CI]: 77.3-80.9) for detecting severe OSA compared to the standard version model (66.0%, 95% CI: 64.0-68.0). Furthermore, the overall accuracy, indicated by the area under the receiver-operating characteristic curve, was significantly greater for the modified model

( $p = 0.001$ ) than for the standard version model. These results imply that the adapted STOP-BANG questionnaire may better detect severe OSA in adults overall.

In a 2021 study by Imani et al. [126], 1046 documents were found in the database, and 109 studies were selected for analysis. Of these, 96 studies examined serum hs-CRP/CRP in adults, and 13 examined these markers in children. Among the adult studies, 11 reported plasma hs-CRP levels, 44 reported serum hs-CRP levels, 9 reported plasma CRP levels, and 32 reported CRP levels. In pediatric studies, 6 reported plasma hs-CRP levels, 4 reported serum hs-CRP levels, 1 reported plasma CRP levels, and 2 reported CRP levels. The serum hs-CRP concentration was 0.09 mg/dL ( $p < 0.00001$ ), the plasma CRP concentration was 0.06 mg/dL ( $p = 0.72$ ), and the serum CRP concentration was 0.36 mg/dL ( $p < 0.0001$ ). The mean difference (MD) in plasma hs-CRP between children with OSA and controls was 1.17 mg/dL ( $p = 0.005$ ), the serum hs-CRP level was 0.18 mg/dL ( $p = 0.05$ ), the plasma CRP level was 0.08 mg/dL ( $p = 0.10$ ), and the serum CRP level was 0.04 mg/dL ( $p = 0.33$ ). Integrated regression analysis showed a significant correlation between higher AHI values and increased serum hs-CRP levels. Overall, this review, meta-analysis, and meta-regression demonstrated that plasma and serum hs-CRP and serum CRP levels were elevated in adults with OSA compared to healthy controls. Only plasma hs-CRP levels were elevated in children with OSA compared to controls.

Yadav et al., 2022[127] conducted a cross-sectional study at hospitals affiliated with BMCRI. The study assessed 100 T2DM patients per ADA guidelines using the STOP-BANG questionnaire, dividing them into low (0-2), intermediate (3-4), and high (5-8) OSA risk groups. hsCRP levels were measured. Microvascular complications were evaluated via Toronto Clinical Neuropathy Score, fundoscopy, and urine microalbumin-creatinine ratio. Results showed 16 high-risk, 68 intermediate-risk, and 16 low-risk OSA patients among the 100 screened.

In Thompson et al., 2022[128], study 27,210 participants (50.3% women) aged 45 years and above from the Canadian Longitudinal Study on Aging, researchers combined the STOP questionnaire with body fat percentage (%BF) to assess OSA risk prevalence, considering sex and age. They also investigated its link to comorbidities, menopausal status, and systemic inflammation. Our findings revealed a prevalence of 17.5% for high-risk OSA cases, with a lower occurrence among women (13.1%) compared to men (21.9%). Notably, elevated levels of high-sensitivity C-reactive protein emerged as the most significant factor linked to OSA risk, with a 1.3–2.3 times higher association in women than in men. Additionally, OSA risk demonstrated an upward trend with advancing age, presence of cardiovascular diseases, diabetes mellitus, anxio-depressive symptoms, asthma, and arthritis. Among women, post-menopausal status was notably associated with heightened OSA risk.

Study underscores that nearly one in every five adults over the age of 45 in Canada faces OSA risk. Moreover, comorbidities, menopause, and systemic inflammation, rather than age alone, appear to drive the increased prevalence of OSA. Given the substantial prevalence and its association with various medical and psychological conditions, healthcare providers should consider integrating systematic OSA screening into their clinical protocols.

According to Aashik et al., 2023[129], patients were stratified based on their STOP-BANG scores, with 16% falling into the low-risk group, 68% into the intermediate-risk group, and 16% into the high-risk group. Variations in Toronto neuropathy scores, urine microalbumin-creatinine ratio (UMCR), and diabetic retinopathy were observed across these risk groups. Notably, the high-risk group exhibited elevated neuropathy scores, increased UMCR values, and more advanced diabetic retinopathy compared to the other groups. The study found a statistically significant association between STOP-BANG scores and UMCR, Toronto neuropathy scores, and diabetic retinopathy, with respective P values of 0.002, 0.029, and 0.03. This underscores the importance of screening diabetic patients for OSA, given its simplicity and affordability. Furthermore, individuals classified as intermediate or high risk displayed more pronounced microvascular complications, suggesting the need for polysomnography and subsequent OSA treatment. Addressing OSA in these patients could lead to improved glycemic control and potentially slow the progression of microvascular complications.

In Sweed et al., 2023[130] investigation, the cohort consisted of 42 female and 17 male patients, with a mean age of  $59.76 \pm 11.13$  years. Among them, 46 patients (78%) were diagnosed with OSA. Notably, 86.8% of patients with uncontrolled glycemic levels had OSA, while 61.9% of those with controlled levels exhibited the condition, indicating a significant disparity ( $p = 0.047$ ). No significant correlation was observed between HbA1c, age, Mallampati score, or BMI and ODI (oxygen desaturation index). However, a correlation was found between the STOP-BANG questionnaire and ODI ( $P = 0.036$ ). Significant factors linked to OSA included comorbidities, Epworth sleepiness scale (ESS) score, Mallampati score, STOP-BANG responses, and specific sleep symptoms like nocturia and snoring ( $p$  values: 0.029, 0.031, 0.022, 0.005, 0.049, and 0.012, respectively). Additionally, individuals with type 2 diabetes had a notably higher OSA prevalence, especially among those with uncontrolled diabetes versus controlled cases.

## MATERIALS AND METHODS

### MATERIALS AND METHODS:

A cross-sectional study was conducted on patients treated at the Department of General Medicine, both inpatient and outpatient, at KLE Dr. Prabhakar Kore Hospital and Research Centre in Belagavi.

**STUDY DESIGN:** A Cross-Sectional study

**STUDY PERIOD:** January 2023 to December 2023

**SAMPLE SIZE:** 135

The sample size was calculated using the formula:

$$\begin{aligned}x &= Z^2 * (c/100) * r * (100 - r) \\n &= (N * x) / ((N - 1) * E^2 + x) \\E &= \text{sqrt} [ ((N - n) * x) / (n * (N - 1)) ]\end{aligned}$$

Where:

- N is the population size (N=20000)
- r is the fraction of responses of interest (r=8.8%)
- Z(c/100) is the critical value for the confidence level c (Z=1.96)

Using these values, the sample size obtained is 123 patients with type-2 diabetes mellitus, at a 95% confidence interval and 80% power of the study. Considering a 10% attrition rate, the study aims to include 135 patients with type-2 diabetes mellitus.

**SAMPLE METHOD:** This is a cross-sectional study where all consecutive patients meeting the inclusion criteria will be included. Statistical analysis will be performed using SPSS, employing descriptive analysis and the chi-square test.

**INCLUSION CRITERIA:** Patients with T2DM fulfilling the ADA criteria will be screened for Obstructive Sleep Apnoea using STOP-BANG questionnaire and will be divided into Obstructive Sleep Apnoea risk groups based on STOP-BANG score.

**EXCLUSION CRITERIA:** Patients with-

- 1) Fever
- 2) Infections

3) Neoplasms

4) Active inflammatory states

5) Connective tissue disorders

**METHODOLOGY:** Informed consent was obtained and then patients were enrolled for the study. All patients fulfilling inclusion criteria were subjected to a detailed history taking, physical examination and anthropometric measurements were taken. Then STOP BANG questionnaire was asked to the patients to grade them into risk group criteria. Patients' Serum HSCRP levels were analysed. Data was analysed and tabulated.

The STOP-BANG questionnaire was created for reliable, brief, and user-friendly screening for sleep apnea. It comprises 8 yes/no questions about sleep apnea symptoms, scoring from 0 to 8.

1. Snoring Score
2. Tiredness Score
3. Observed apnoea.
4. High Blood pressure
5. Body mass index
6. Age
7. Neck circumference
8. Male gender

Score 0-2 Low risk

Score 3-4 moderate risk. Other attributes like BMI Used for assessing risk

Score 5-8 High risk

STOP-Bang scores of  $\geq 3$  demonstrate a sensitivity of 93% for detecting moderate to severe OSA (AHI > 15) and 100% for severe OSA (AHI > 30), with negative predictive values of 90% and 100% respectively. Scores ranging from 0 to 2 indicate low risk, while 5 to 8 signify high risk for moderate to severe OSA.

**STATISTICAL ANALYSIS:**

Data is analysed using statistical software R version 4.4.0. and Microsoft Excel. Categorical variables are presented as frequency tables. Continuous variables are expressed as Mean  $\pm$  SD / Median (Min, Max). Chi-square tests determine the association of categorical variables with groups. Normality is assessed using Shapiro-Wilk test and QQ plot. Parametric tests are employed if data is normally distributed, otherwise non-parametric tests are utilized. One-way ANOVA compares variable means across final diagnosis, while Kruskal-Wallis test compares variable distribution across final diagnosis. Spearman's rank correlation assesses the correlation of STOP-Bang score with Hs-CRP. A P-value  $\leq 0.05$  denotes statistical significance.

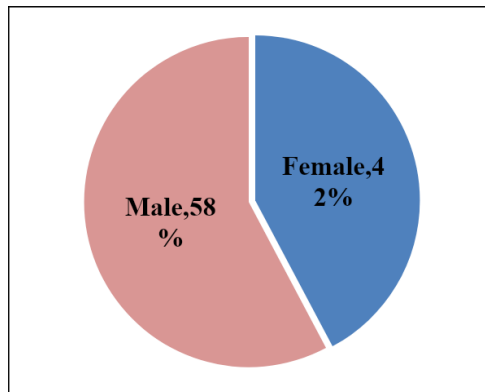
## RESULTS AND DISCUSSION

### RESULTS:

Table -1 and figure-7 displays the mean age of the participants, which is 59.44 years, accompanied by a standard deviation of 12.98 years. The middle age is 60 years, with ages ranging from 30 to 88 years. Regarding gender, the sample consisted of 57 (42.22%) females and 78 (57.78%) males. This ratio indicates a minor predominance of males among the participants.

**Table1: Distribution of subjects according to demographic details.**

Variables	Sub Category	Number of subjects (%)
Age (years)	Mean $\pm$ SD	59.44 $\pm$ 12.98
	Median (Min, Max)	60 (30, 88)
Sex	Female	57 (42.22%)
	Male	78 (57.78%)



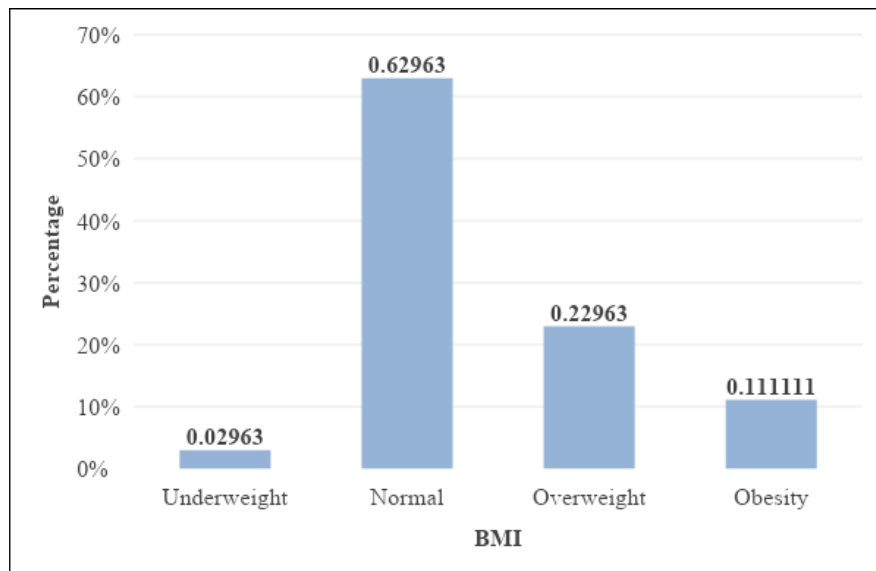
**Figure 6: Distribution of subjects according to sex.**

The table displays subjects categorized by BMI distribution. Table-2 and Figure-8 show that most of the participants, 85 (62.96%) have a BMI within the normal range. This is then followed by 31 (22.96%) participants who are considered overweight. Obesity is noted in 15 (11.11%) participants. A very small group, 4 (2.96%) participants, have a BMI that is considered underweight.

The average BMI is 24.1, with a standard deviation of 4.22. The middle BMI value is 23.56, spanning from 17.28 to 38.01.

**Table2: Distribution of subjects according to BMI.**

<b>BMI</b>	<b>Number of subjects (%)</b>
Underweight	4 (2.96%)
Normal	85 (62.96%)
Overweight	31 (22.96%)
Obesity	15 (11.11%)
Mean $\pm$ SD	24.1 $\pm$ 4.22
Median (Min, Max)	23.56 (17.28, 38.01)



**Figure 7: Distribution of subjects according to BMI.**

Table 3 displays subject distribution by clinical parameters.

**Table3: Distribution of subjects according to clinical parameters.**

<b>Variables</b>	<b>Mean <math>\pm</math> SD</b>	<b>Median (Min, Max)</b>
Haemoglobin	11.93 $\pm$ 1.88	11.7 (8.6, 17.9)
Platelet	271.39 $\pm$ 100.78	260 (117, 575)
Creatinine	0.83 $\pm$ 0.19	0.86 (0.41, 1.17)
Urea	17.59 $\pm$ 8.37	16 (4.26, 46.3)
TB	0.66 $\pm$ 0.32	0.6 (0.16, 1.83)
DB	0.33 $\pm$ 0.23	0.28 (0.07, 1.01)
Total Protein	6.78 $\pm$ 0.56	6.8 (5.1, 8.1)
Albumin	3.81 $\pm$ 0.44	3.9 (2.5, 4.8)
SGOT	25.35 $\pm$ 11.65	23 (10, 91)
SGPT	22.73 $\pm$ 12.2	20 (9, 75)
FBS	169.12 $\pm$ 51.35	155 (60, 350)
Serun Triglycerides	139.62 $\pm$ 47.98	132 (60, 381)
WBC	8.18 $\pm$ 2.07	8 (3.6, 12.6)
Hs CRP	7.5 $\pm$ 2.71	7.1 (2.1, 19)
Height	166.03 $\pm$ 13.18	167 (139, 190)
HBA1C	8.43 $\pm$ 2.14	7.7 (6.1, 15.5)
Height ft	5.45 $\pm$ 0.43	5.48 (4.56, 6.23)
Weight	66.13 $\pm$ 12.05	65 (35, 106)
Neck Circumference Quantity	30.16 $\pm$ 6.61	28 (20, 48)

Haemoglobin levels show a mean of 11.93  $\pm$  1.88 g/dL with a median of 11.7 g/dL, ranging from 8.6 to 17.9 g/dL. Platelet counts average at 271.39  $\pm$  100.78 with a median of 260, spanning from 117 to 575. Serum creatinine levels average 0.83  $\pm$  0.19 mg/dL, with a median of 0.86 mg/dL, ranging from 0.41 to 1.17 mg/dL. Blood urea levels average 17.59  $\pm$  8.37 mg/dL, with a median of 16 mg/dL, ranging from 4.26 to 46.3 mg/dL.

Total bilirubin (TB) and direct bilirubin (DB) have means of  $0.66 \pm 0.32$  mg/dL and  $0.33 \pm 0.23$  mg/dL, respectively, with medians of 0.6 mg/dL for TB and 0.28 mg/dL for DB. Total protein averages  $6.78 \pm 0.56$  g/dL with a median of 6.8 g/dL, while albumin levels average  $3.81 \pm 0.44$  g/dL with a median of 3.9 g/dL.

Liver enzymes, SGOT and SGPT, show means of  $25.35 \pm 11.65$  U/L and  $22.73 \pm 12.2$  U/L, respectively, with medians of 23 U/L for SGOT and 20 U/L for SGPT, indicating mild variations. Fasting blood sugar (FBS) levels average  $169.12 \pm 51.35$  mg/dL with a median of 155 mg/dL, spanning from 60 to 350 mg/dL. Serum triglycerides have a mean of  $139.62 \pm 47.98$  mg/dL with a median of 132 mg/dL, ranging from 60 to 381 mg/dL.

White blood cell (WBC) counts average  $8.18 \pm 2.07$  with a median of 8. Hs CRP levels have a mean of  $7.5 \pm 2.71$  mg/L with a median of 7.1 mg/L.

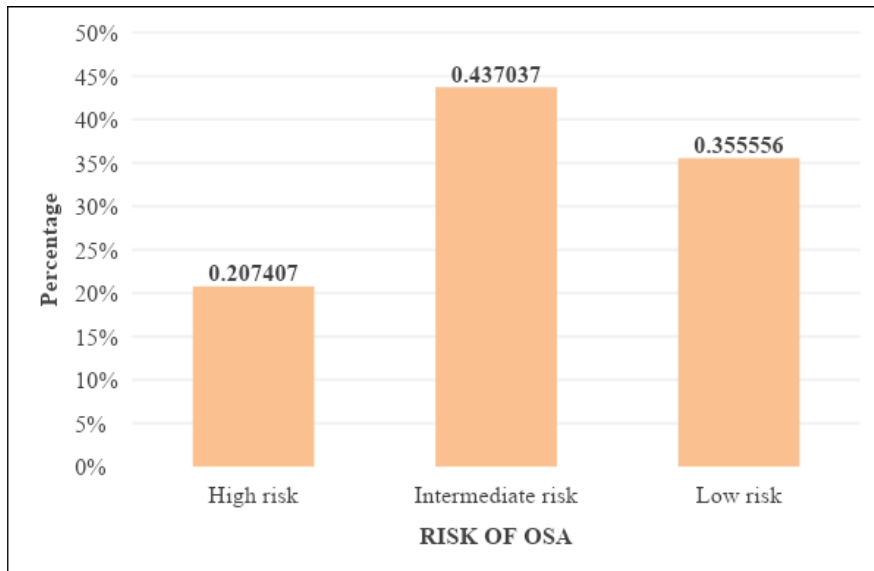
Anthropometric measurements include height with a mean of  $166.03 \pm 13.18$  cm and a median of 167 cm, weight with a mean of  $66.13 \pm 12.05$  kg and a median of 65 kg, and neck circumference with a mean of  $30.16 \pm 6.61$  cm and a median of 28 cm. Height in feet averages  $5.45 \pm 0.43$  ft with a median of 5.48 ft. Lastly, HBA1C has a mean of  $8.43 \pm 2.14$  % with a median of 7.7%, indicating a range from 6.1% to 15.5%.

The following table-4 and figure-9 gives the distribution of subjects according to STOP-Bang score indicate that out of the data, 28 individuals (20.74%) are identified as being at high risk for OSA. A bigger group, 59 individuals (43.7%) are placed in the middle risk category. The rest, 48 individuals (35.56%), are deemed to be at low risk. The average STOP-Bang score is 3.23, with a standard deviation of 1.53. The middle score is 3, with values going from a lowest of 0 to a highest of 7.

**Table4: Distribution of subjects according to STOP-Bang score.**

STOP-Bang score	Number of subjects (%)
High risk	28 (20.74%)
Intermediate risk	59 (43.7%)
Low risk	48 (35.56%)

Mean ± SD	3.23 ± 1.53
Median (Min, Max)	3 (0, 7)



**Figure 8: Distribution of subjects according to risk of OSA.**

Table-5 and figure-9 show the comparison of demographic information with the risk of OSA.

**Table5: Comparison of demographic details with risk of OSA.**

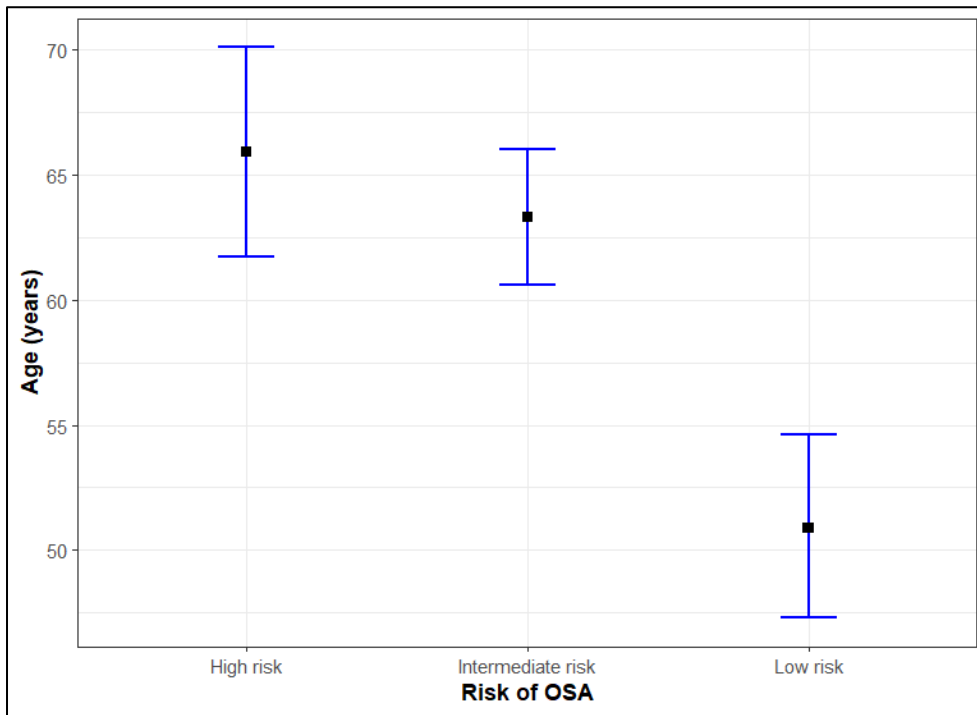
Variable s	Sub Category	Risk of OSA			p-value
		High risk	Intermediate risk	Low risk	
Age (years)	Mean ± SD Median (Min, Max)	65.89 ± 10.84 65 (42, 82)	63.31 ± 10.48 65 (40, 88)	50.94 ± 12.65 50 (30, 85)	< 0.001 <sup>A*</sup>

Sex	Female	7 (25%)	19 (32.2%)	31 (64.58%)	< 0.001 <sup>C*</sup>
	Male	21 (75%)	40 (67.8%)	17 (35.42%)	

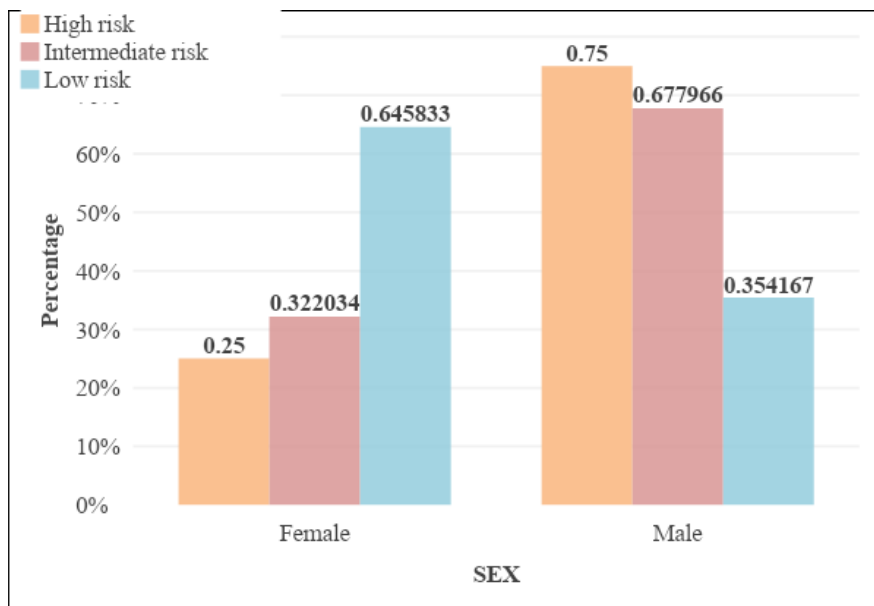
*Abbreviation: A – One-way ANOVA, C – Chi Square test, \* indicates statistical significance.*

Subjects at high risk have a mean age of 65.89 years ( $\pm$  10.84), with a median age of 65 years, ranging from 42 to 82 years. Those at intermediate risk have a mean age of 63.31 years ( $\pm$  10.48) and a median age of 65 years, with an age range from 40 to 88 years. In contrast, subjects at low risk are significantly younger, with a mean age of 50.94 years ( $\pm$  12.65) and a median age of 50 years, ranging from 30 to 85 years. Age shows a clear gradient with OSA risk. From one-way ANOVA, it is observed that, there is significant difference in age over OSA risk. Further from Tukey's HSD, it is observed that, there is significant age differences between individuals at low risk and those at high risk for OSA (p-value < 0.001), as well as between individuals at low risk and those at intermediate risk (p-value < 0.001).

Among high-risk subjects, 25% are female and 75% are male. In the intermediate-risk group, 32.2% are female and 67.8% are male. Conversely, in the low-risk category, the proportion of females increases to 64.58%, while the male proportion decreases to 35.42%. From Chi square test, it is observed that, there is significant difference in the distribution of sex over risk of OSA.



**Figure 9: Mean plot of age over risk of OSA.**



**Figure 10: Distribution of sex over risk of OSA.**

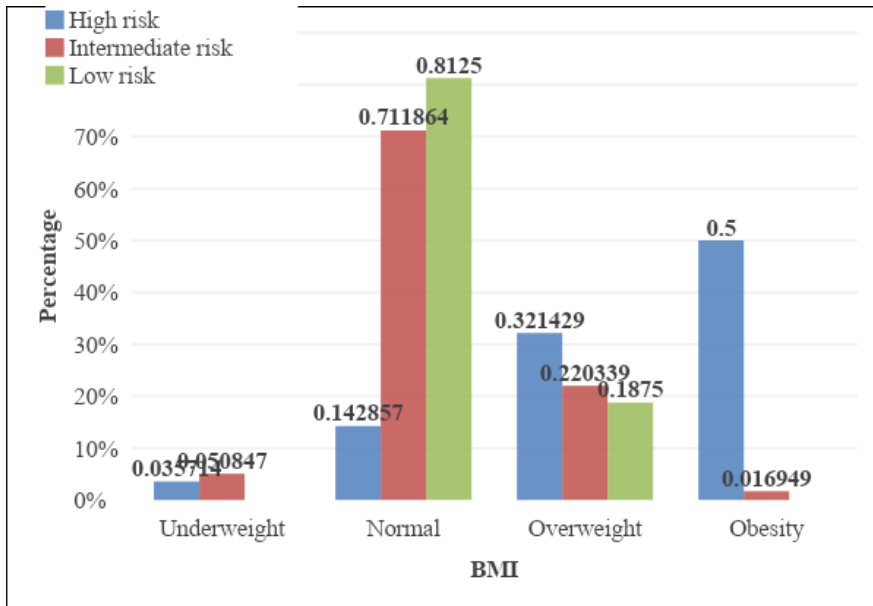
**Table6: Comparison of BMI over risk of OSA.**

<b>BMI</b>	<b>High risk</b>	<b>Intermediate risk</b>	<b>Low risk</b>	<b>p-value</b>
Underweight	1 (3.57%)	3 (5.08%)	0	<b>&lt; 0.001<sup>MC*</sup></b>
Normal	4 (14.29%)	42 (71.19%)	39 (81.25%)	
Overweight	9 (32.14%)	13 (22.03%)	9 (18.75%)	
Obesity	14 (50%)	1 (1.69%)	0	
Mean $\pm$ SD	28.79 $\pm$ 5.18	22.84 $\pm$ 3.08	22.91 $\pm$ 2.67	<b>&lt; 0.001<sup>K*</sup></b>
Median (Min, Max)	30 (17.28, 42.86)	22.66 (18.12, 31.83)	23.36 (18.52, 28.12)	

*Abbreviation: MC - Chi square test with Monte Carlo simulation, K – Kruskal Wallis test, \* indicates statistical significance.*

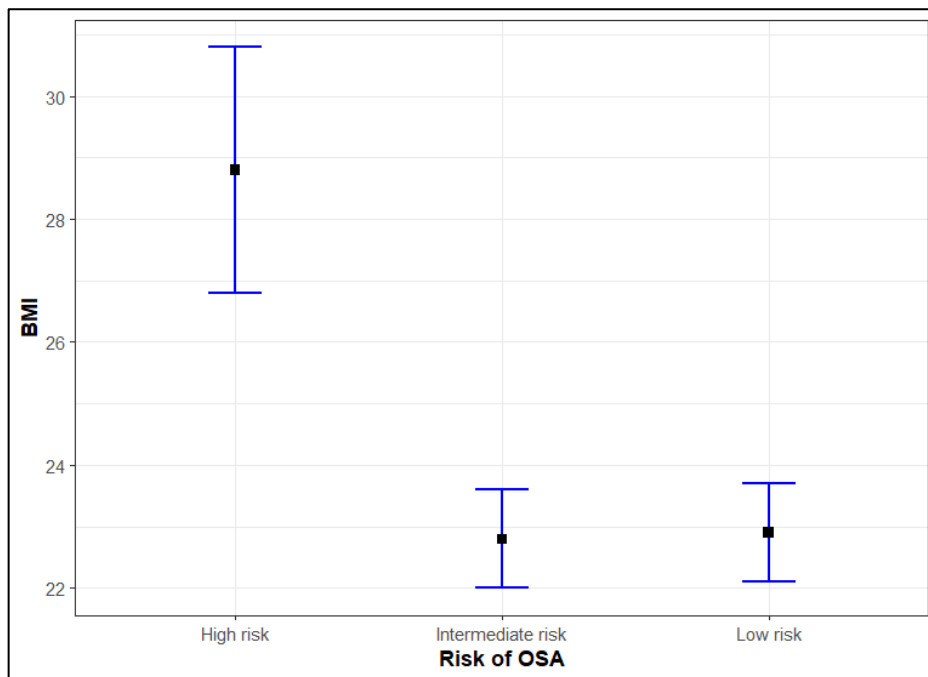
Among individuals at high risk for OSA, 50% are classified as obese, 32.14% as overweight, 14.29% as normal weight, and 3.57% as underweight. In the intermediate-risk group, the majority, 71.19%, are normal weight, followed by 22.03% overweight, 5.08% underweight, and only 1.69% obese. Conversely, in the low-risk category, 81.25% are normal weight, 18.75% overweight, and none are classified as underweight or obese. From Chi square test, it is observed that, there is significant difference in the distribution of BMI over risk of OSA.

The mean BMI differs significantly across the risk groups, with those at high risk having the highest mean BMI of 28.79  $\pm$  5.18, followed by individuals at low risk with a mean BMI of 22.91  $\pm$  2.67, and those at intermediate risk with a mean BMI of 22.84  $\pm$  3.08. From Kruskal Wallis test, it is observed that there is significant difference in the distribution of BMI over risk of OSA. Further, from Dunn's test, it is observed that, there is significant difference in BMI between individuals at low risk and those at high risk for OSA (p-value < 0.001), as well as between individuals at high risk and those at intermediate risk (p-value < 0.001).



**Figure 11: Distribution of BMI over risk of OSA.**

Figure-12 displays the average BMI graph in relation to the risk of OSA.



**Figure 12: Mean plot of BMI over risk of OSA.**

The following Table 7 presents a comparison of clinical parameters across different risk levels of OSA.

**Table7: Comparison of clinical parameters over risk of OSA.**

Variables	Risk of OSA			p-value
	High risk	Intermediate	Low risk	
Haemoglobin	11.82 ± 2.04 11.45 (8.6, 16.1)	12.02 ± 1.89 11.8 (9.3, 17.9)	11.9 ± 1.81 11.8 (9, 15.9)	0.9197 <sup>K</sup>
Platelet	266.39 ± 92.14 270.5 (117, 553)	258.61 ± 95.21 250 (123, 575)	290.02 ± 110.98 273 (147, 561)	0.4106 <sup>K</sup>
Creatinine	0.86 ± 0.18 0.87 (0.5, 1.17)	0.87 ± 0.17 0.9 (0.52, 1.13)	0.75 ± 0.2 0.75 (0.41, 1.1)	<b>0.0050<sup>K*</sup></b>
Urea	20.85 ± 9.12 21.5 (7.64, 45)	17.42 ± 8.46 16 (5.24, 43.7)	15.9 ± 7.38 14.6 (4.26, 46.3)	0.0651 <sup>K</sup>
TB	0.68 ± 0.31 0.62 (0.23, 1.28)	0.69 ± 0.35 0.63 (0.18, 1.83)	0.6 ± 0.29 0.6 (0.16, 1.57)	0.4341 <sup>K</sup>
DB	0.35 ± 0.22 0.31 (0.09, 0.8)	0.34 ± 0.24 0.26 (0.07, 0.94)	0.32 ± 0.21 0.26 (0.08, 1.01)	0.9300 <sup>K</sup>
Total Protein	6.81 ± 0.56 6.95 (5.4, 7.7)	6.78 ± 0.55 6.7 (5.1, 7.9)	6.76 ± 0.59 6.8 (5.5, 8.1)	0.9290 <sup>A</sup>
Albumin	3.73 ± 0.4 3.85 (2.9, 4.5)	3.76 ± 0.48 3.8 (2.5, 4.6)	3.92 ± 0.4 4 (3, 4.8)	0.0996 <sup>A</sup>
SGOT	24.82 ± 9.94 23.5 (10, 54)	26.78 ± 13.26 23 (10, 91)	23.9 ± 10.41 22.5 (11, 63)	0.6178 <sup>K</sup>
SGPT	20.25 ± 6.87 20 (12, 37)	25.66 ± 13.82 20 (10, 66)	20.56 ± 11.93 18 (9, 75)	0.0656 <sup>K</sup>
FBS	189.39 ± 55.86 189 (88, 321)	168.53 ± 49.23 153 (60, 316)	158.02 ± 48.6 147.5 (84, 350)	<b>0.0194<sup>K*</sup></b>
Serum Triglycerides	154.54 ± 60.79 145.5 (79, 381)	138.39 ± 45.81 139 (60, 271)	132.44 ± 40.8 118 (76, 253)	0.2985 <sup>K</sup>

WBC	8.46 ± 2.23 8.2 (3.9, 12.6)	8.29 ± 1.97 8.2 (3.7, 12.5)	7.88 ± 2.09 7.75 (3.6, 11.4)	0.4240 <sup>A</sup>
Hs CRP	8.62 ± 3.94 8.35 (3.7, 19)	7.38 ± 2.45 7.1 (3.6, 18)	6.99 ± 1.89 6.95 (2.1, 12.3)	0.2454 <sup>K</sup>
Height	162.14 ± 10.52 160 (139, 187)	166.95 ± 13.81 167 (139, 190)	167.17 ± 13.61 167 (139, 190)	0.1927 <sup>K</sup>
HBA1C	9.92 ± 2.75 9.65 (6.1, 15.5)	8.27 ± 1.96 7.8 (6.3, 15.3)	7.76 ± 1.49 7.15 (6.4, 12.8)	< 0.001 <sup>K*</sup>
Height ft	5.32 ± 0.35 5.25 (4.56, 6.14)	5.48 ± 0.45 5.48 (4.56, 6.23)	5.48 ± 0.45 5.48 (4.56, 6.23)	0.1927 <sup>K</sup>
Weight	75.36 ± 14.06 76.5 (48, 106)	63.68 ± 11.35 64 (35, 102)	63.77 ± 8.82 64 (43, 81)	< 0.001 <sup>K*</sup>
Neck Circumference	37.71 ± 6.69 39.5 (20, 48)	28.32 ± 5.15 28 (20, 45)	28.02 ± 4.81 28 (20, 40)	< 0.001 <sup>K*</sup>

*Abbreviation: K – Kruskal Wallis test, A – One way ANOVA, \* indicates statistical significance.*

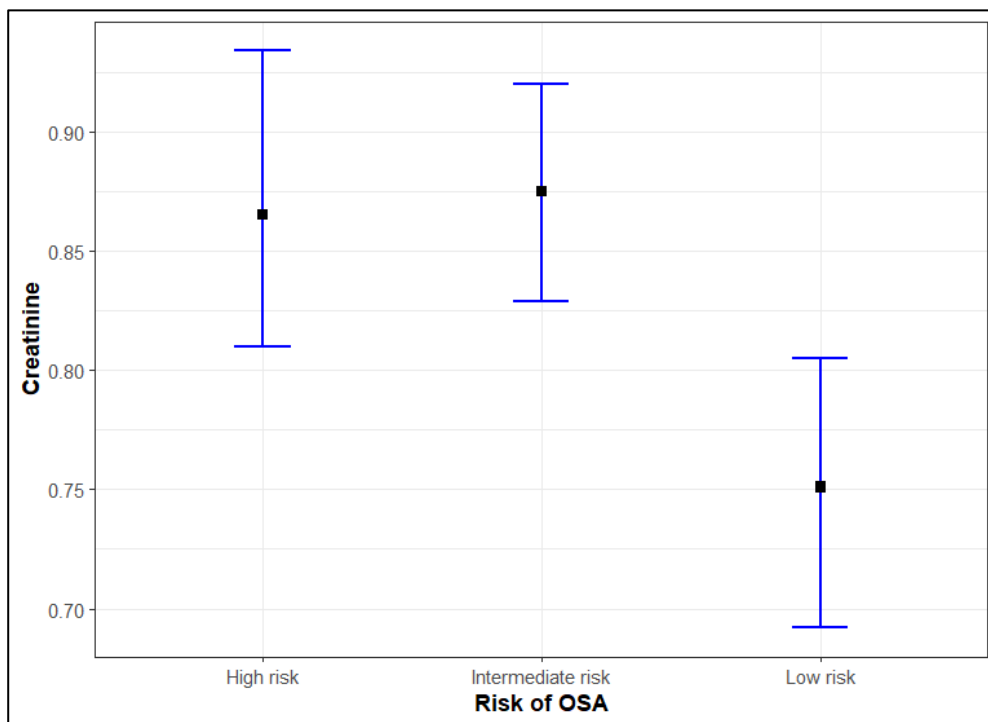
From Kruskal Wallis test, it is observed that, there is no significant difference in the distribution of Haemoglobin, Platelet, Urea, TB, DB, SGOT, SGPT, Serum Triglycerides, Hs CRP, Height and Height ft over risk of OSA. However, significant differences were found in the distribution of Creatinine, Fasting Blood Sugar (FBS), HBA1C, weight, and Neck Circumference Quantity among individuals with different OSA risk levels.

Further analysis from Dunn test, it is observed that, there is significant difference in Creatinine between individuals at low risk and those at high risk for OSA (p-value = 0.0423), as well as between individuals at low risk and those at intermediate risk (p-value = 0.0060). Similarly, there is significant difference in Creatinine between individuals at low risk and those at high risk for OSA (p-value = 0.0153). Additionally, there is significant difference in HBA1C between individuals at low risk and those at high risk for OSA (p-value < 0.001), as well as between individuals at high risk and those at intermediate risk (p-value = 0.0150). Similarly, there is significant difference in weight between individuals at low risk and those at high risk for OSA (p-value = 0.0013), as well as

between individuals at high risk and those at intermediate risk (p-value < 0.001). Also, there is significant difference in Neck Circumference Quantity between individuals at low risk and those at high risk for OSA (p-value < 0.001), as well as between individuals at high risk and those at intermediate risk (p-value < 0.001).

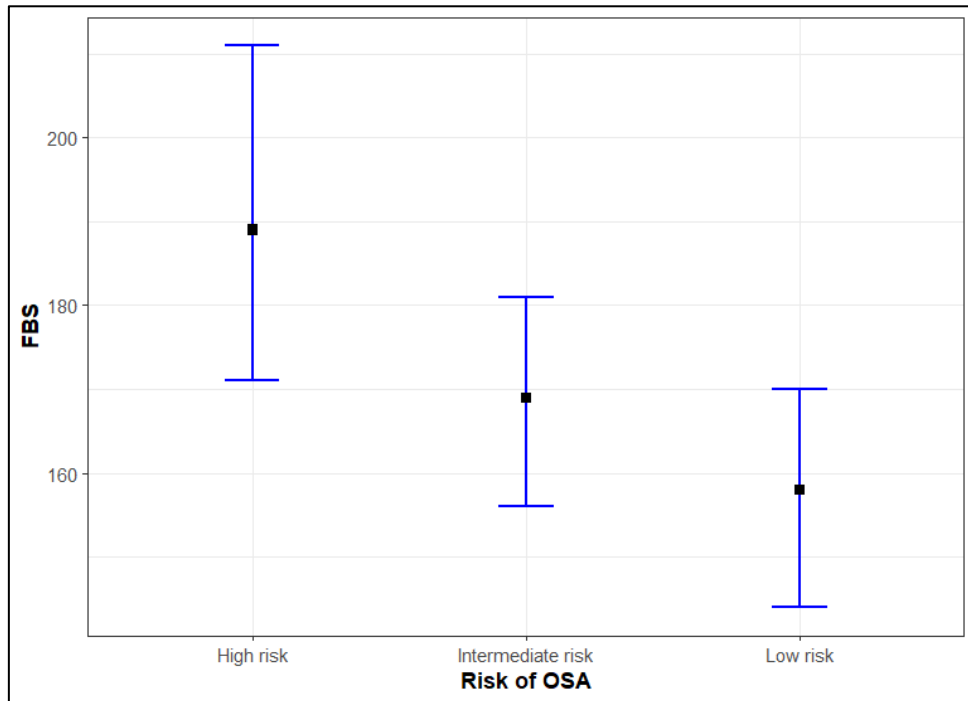
From one way ANOVA, it is observed that, there is no significant difference in Total Protein, albumin and WBC over risk of OSA.

Figure 13 depicts the mean plot of creatinine levels across different OSA risk categories.



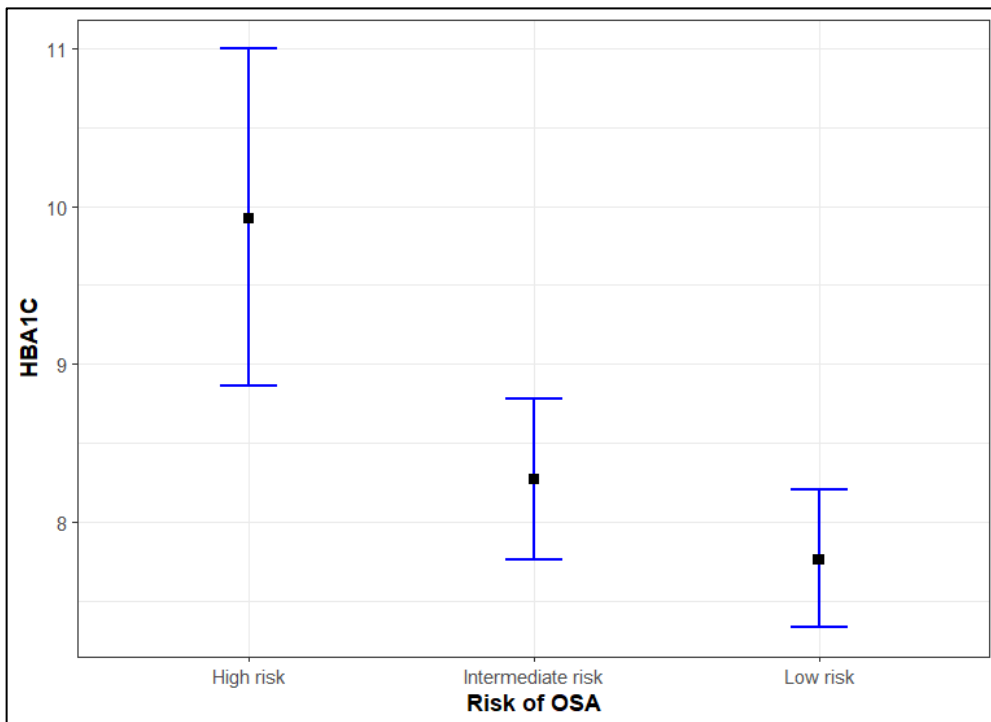
**Figure 13: Mean plot of creatinine over risk of OSA.**

Figure 14 presents the mean fasting blood sugar (FBS) levels across different OSA risk categories.



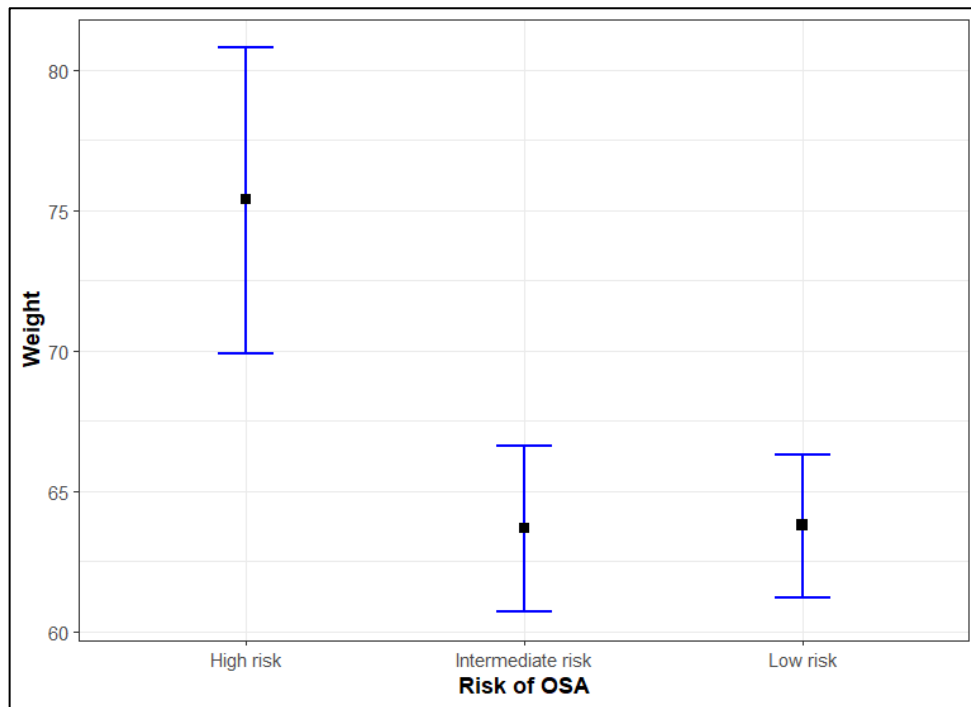
**Figure 14: Mean plot of FBS over risk of OSA.**

Figure 15 illustrates the mean HbA1c levels across different OSA risk categories.



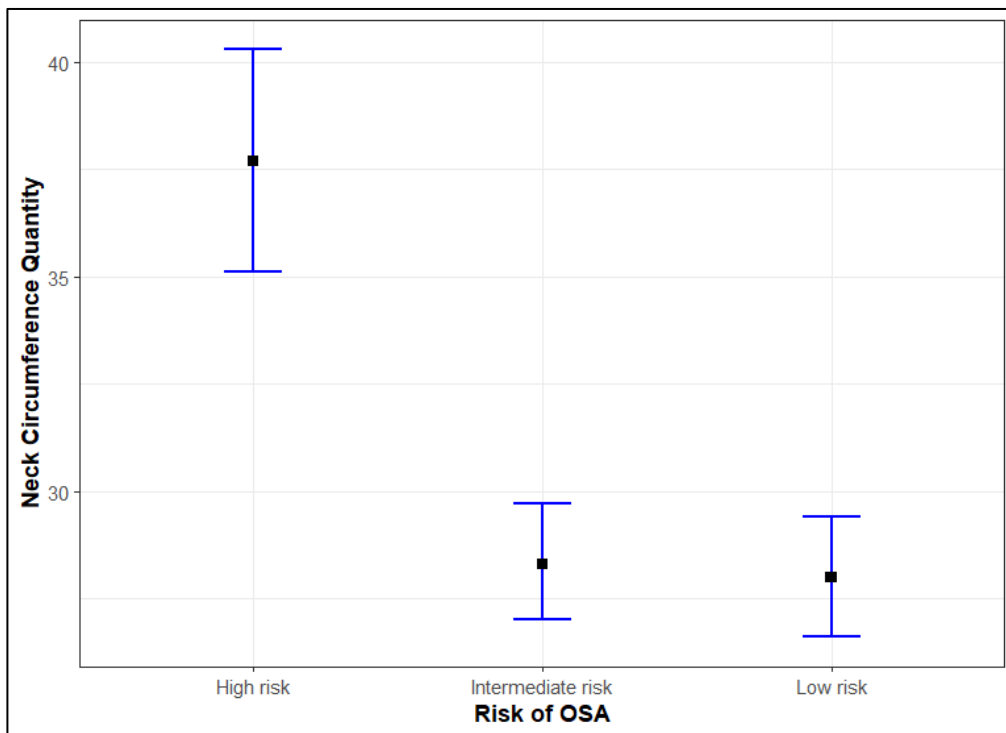
**Figure 15: Mean plot of HBA1C over risk of OSA.**

Figure 16 illustrates the mean plot of weight across different OSA risk levels.



**Figure 16: Mean plot of weight over risk of OSA.**

Figure 17 illustrates the mean plot of neck circumference measurements across different levels of OSA risk.



**Figure 17: Mean plot of neck circumference quantity over risk of OSA.**

The correlation between STOP-Bang scores and Hs-CRP levels is presented in Table 8.

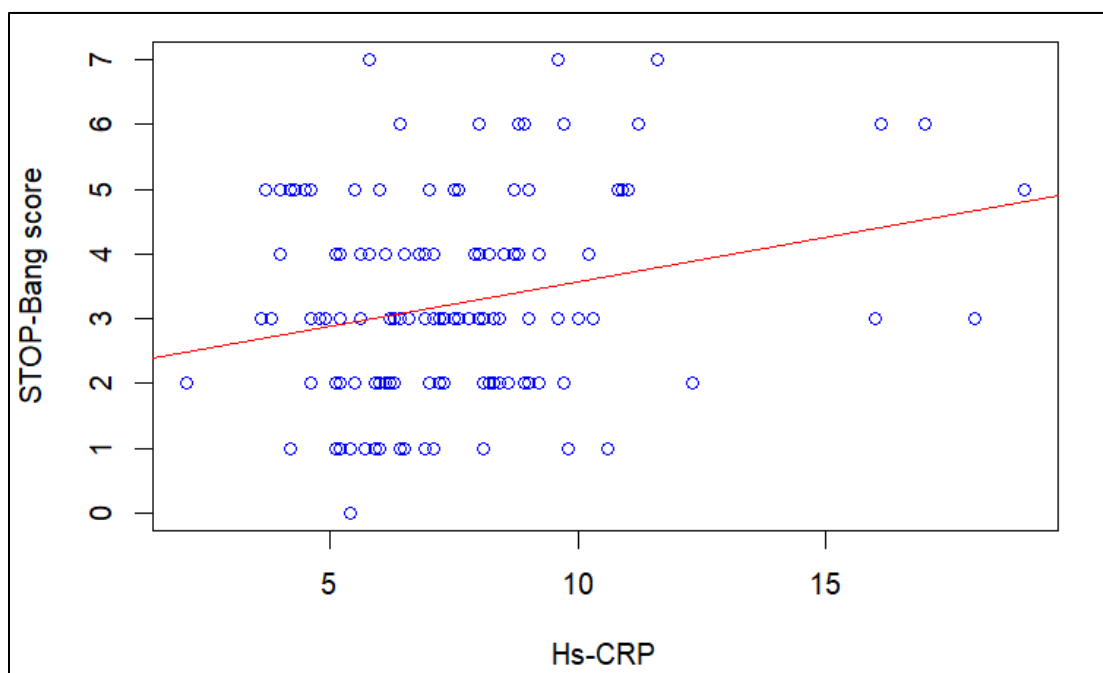
**Table 8: Correlation of STOP-Bang score with Hs-CRP.**

Variables	Correlation coefficient	p-value
STOP-Bang score & Hs-CRP	0.1731	<b>0.0447<sup>SP*</sup></b>

*Abbreviation: SP – Spearman’s rank correlation test, \* indicates statistical significance.*

From Spearman’s rank correlation test, it is observed that, there is significant positive correlation of STOP-Bang score with Hs-CRP (p-value = 0.0447).

Figure 19 illustrates a scatter plot depicting the correlation between the STOP-Bang score and Hs-CRP levels.



**Figure 18: Scatter plot of STOP-Bang score with Hs-CRP.**

## **Discussion:**

A study at KLE Dr. Prabhakar Kore Hospital and Research Centre in Belagavi assessed OSA prevalence in type 2 diabetes patients using the STOP BANG scoring system and explored its link with HSCRP levels. The research conducted from January 2023 to December 2023, involving a sample size of 135 participants.

We are discussing this study under the following headings

### **1. Distribution of subjects according to demographic details.**

In our study, participant's average age was 59.44 years, with a standard deviation of 12.98 years. The median age was 60 years, and the ages ranged from 30 to 88 years. In terms of gender distribution, the sample included 57 females (42.22%) and 78 males (57.78%), indicating a slight predominance of males among the participants. In another study conducted by Sweed et al., 2023 [130], the participants included 42 females and 17 males, with an average age of  $59.76 \pm 11.13$  years. Morsy et al., 2023[131] conducted research involving 125 Egyptian patients diagnosed with T2DM, with an average age of  $54.63 \pm 9.47$  years. Among the participants, 35.2% were male and 64.8% were female. According to Mirghani et al. (2023) [132], the study involved 208 patients with type 2 diabetes, with an average age of 51.98 years and a standard deviation of 12.90 years. Barbosa et al., 2022[133] examined 77 patients 88.3% female and found that 36 were at risk for OSA.

### **2. Distribution of subjects according to BMI.**

In our study, 85 participants (62.96%) had a normal BMI. This was followed by 31 participants (22.96%) who were classified as overweight. There were 15 participants (11.11%) who were considered obese, and a very small group of 4 participants (2.96%) who were classified as underweight. The average BMI was 24.1, with a standard deviation of 4.22. The median BMI was 23.56, with a range from 17.28 to 38.01. Obesity poses a significant risk for developing OSA. According to Grunstein et al., 2007 [134], adopting a low-calorie diet or undergoing bariatric surgery can mitigate OSA severity. Newman et al., 2005 [135] demonstrated that weight gain correlates with increased AHI. Pusuroglu et al., 2022 [136] found a significant link between rising BMI and OSA severity in univariate analysis, though this association didn't hold in multivariate analysis.

The findings of Shin et al., 2021 [125] indicate that a predictive model incorporating risk factors such as daytime drowsiness, snoring, witnessed pauses in breathing, high blood pressure, BMI over 25 kg/m<sup>2</sup>, individuals aged 51–64 years and over 65 years, male gender, waist circumference over

85 cm, and diabetes mellitus demonstrated significantly improved diagnostic performance compared to the standard model. Notably, this predictive model exhibited higher sensitivity (79%) for detecting severe OSA compared to the standard model (66%), suggesting its potential utility in identifying high-risk OSA cases among the general adult population. According to Mirghani et al., (2023) [132], the average body mass index was 32.28 with a standard deviation of 9.38. Barbosa et al., 2022 [133] examined average body mass index =  $32.7 \pm 5.8$  kg/m<sup>2</sup>; average postoperative period =  $9.9 \pm 3.1$  years).

### 3. Distribution of subjects according to clinical parameters.

In our research, hemoglobin averaged  $11.93 \pm 1.88$  g/dL (median 11.7, range 8.6–17.9), while platelet counts averaged  $271.39 \pm 100.78$  (median 260, range 117–575). Serum creatinine averaged  $0.83 \pm 0.19$  mg/dL (median 0.86, range 0.41–1.17). Blood urea averaged  $17.59 \pm 8.37$  mg/dL (median 16, range 4.26–46.3). Total bilirubin and direct bilirubin averaged  $0.66 \pm 0.32$  mg/dL and  $0.33 \pm 0.23$  mg/dL (medians 0.6 and 0.28). Total protein averaged  $6.78 \pm 0.56$  g/dL (median 6.8), and albumin  $3.81 \pm 0.44$  g/dL (median 3.9). SGOT and SGPT averaged  $25.35 \pm 11.65$  U/L and  $22.73 \pm 12.2$  U/L (medians 23 and 20), showing mild variations. Fasting blood sugar averaged  $169.12 \pm 51.35$  mg/dL (median 155, range 60–350). Serum triglycerides averaged  $139.62 \pm 47.98$  mg/dL (median 132, range 60–381). WBC counts averaged  $8.18 \pm 2.07$  (median 8). Hs CRP levels averaged  $7.5 \pm 2.71$  mg/L (median 7.1). Height averaged  $166.03 \pm 13.18$  cm (median 167), weight  $66.13 \pm 12.05$  kg (median 65), and neck circumference  $30.16 \pm 6.61$  cm (median 28). Height in feet averaged  $5.45 \pm 0.43$  ft (median 5.48). HbA1C averaged  $8.43 \pm 2.14$  % (median 7.7, range 6.1%–15.5%). Barbosa et al., 2022 [133] study showed a positive correlation with high-sensitivity C-reactive protein levels ( $r^2 = 0.270$ ;  $p = 0.025$ ), triglycerides ( $r^2 = 0.338$ ,  $p = 0.004$ ), total cholesterol ( $r^2 = 0.262$ ;  $p = 0.028$ ), and HbA1c ( $r^2 = 0.332$ ;  $p = 0.005$ ). Compared to their counterparts, those who self-reported witnessed apnea had higher basal insulin and triglycerides ( $12.8 \pm 6.5$  vs  $8.1 \pm 3.8$ ,  $p = 0.013$ ;  $136.4 \pm 41.1$  vs  $88.5 \pm 34.8$ ,  $p = 0.001$ , respectively). Additionally, participants reporting tiredness had higher levels of total cholesterol and LDL-C ( $183.9 \pm 27.0$  vs  $164.8 \pm 33.4$ ,  $p = 0.005$ ;  $105.9 \pm 24.4$  vs  $92.0 \pm 26.6$ ,  $p = 0.018$ ), while those with snoring exhibited higher triglycerides ( $107 \pm 41.1$  vs  $83.7 \pm 33.9$ ,  $p = 0.010$ ).

### 4. Distribution of subjects according to STOP-Bang score.

In our study, the STOP-Bang score showed that 28 individuals (20.74%) were at high risk for OSA, 59 individuals (43.7%) were at moderate risk, and 48 individuals (35.56%) were at low risk. The average score was 3.23 with a standard deviation of 1.53, ranging from 0 to 7, with a median of 3. In Westlake et al., 2016 [121], the questionnaires exhibited similar levels of sensitivity and specificity for identifying individuals with an AHI of 15 or higher: 0.69 sensitivity and 0.50 specificity for Berlin, 0.65 sensitivity and 0.49 specificity for STOP, and 0.59 sensitivity and 0.68 specificity for STOP-Bang. However, there were differences in the performance of the STOP-Bang questionnaire between men and women. Specifically, sensitivity was higher in men at 0.74 compared to 0.29 in women ( $p < 0.05$ ), while specificity was higher in women at 0.82 compared to 0.56 in men ( $p < 0.05$ ).

Teng et al., (2018) [137] found that the STOP-Bang questionnaire's effectiveness in screening for OSA in Chinese patients with T2DM, findings revealed: AHI  $\geq 5$ /hour had AUC of 0.825 (95% CI: 0.763–0.887,  $p < 0.05$ ), sensitivity 85.6% (95% CI: 85.55–85.65%,  $p < 0.05$ ), specificity 60% (95% CI: 59.85–60.15%,  $p < 0.05$ ); AHI  $> 15$ /hour had AUC of 0.856 (95% CI: 0.799–0.913,  $p < 0.05$ ), sensitivity 88.6% (95% CI: 88.55–88.65%,  $p < 0.05$ ), specificity 38.4% (95% CI: 38.30–38.49%,  $p < 0.05$ ); AHI  $> 30$ /hour had AUC of 0.891 (95% CI: 0.836–0.946,  $p < 0.05$ ), sensitivity 90.5% (95% CI: 90.44–90.56%,  $p < 0.05$ ), specificity 27% (95% CI: 26.94–27.07%,  $p < 0.05$ ).

Similarly Butt et al., (2021) [138] in type 2 diabetic patients, OSA prevalence via polysomnography was 65.5%. STOP-BANG showed highest sensitivity for mild, moderate, and severe OSA (84.2%, 90.3%, 100% respectively). Berlin questionnaire had 100% sensitivity for severe OSA, and specificity for mild and moderate OSA (70%, 63% respectively). Epworth Sleepiness Scale had highest specificity for severe OSA (53.3%).

Yadav et al., (2022) [127] a study examined 100 patients diagnosed with T2DM by ADA criteria, who were screened using the STOP-BANG questionnaire. Subsequently, they were categorized into different groups based on their STOP-BANG scores: 0-2 indicated low risk, 3-4 denoted intermediate risk, and 5-8 indicated high risk for OSA. According to Mirghani et al. (2023) [132], the Stop-Bang scores varied between 1 and 7, with an average score of  $4.37 \pm 1.61$ . The HbA1c levels averaged  $9.44 \pm 1.67$ .

## 5. Comparison of demographic details with risk of OSA.

In our study, high-risk subjects have a mean age was found 65.89 years, intermediate-risk subjects 63.31 years, and low-risk subjects 50.94 years, with significant age differences between these groups. One-way ANOVA and Tukey's HSD show significant age differences, especially between

low-risk and high-risk or intermediate-risk groups ( $p < 0.001$ ). High-risk group: 25% female, 75% male; intermediate-risk: 32.2% female, 67.8% male; low-risk: 64.58% female, 35.42% male. Chi-square test indicates a significant sex distribution difference across OSA risk levels.

As per study conducted by Westlake et al., 2016 [121], they discovered severe OSA in 31 patients (10%), moderate OSA in 61 patients (21%), and mild OSA in 121 patients (41%).

Yadav et al., (2022) [127] reported that among a sample of 100 patients, 16 were categorized as high risk, 68 fell into the intermediate risk category, and the remaining 16 were classified as low risk.

#### **6. Comparison of BMI over risk of OSA.**

In our study, among individuals at high risk for OSA, 50% were obese, 32.14% were overweight, 14.29% were of normal weight, and 3.57% were underweight. In the intermediate-risk group, 71.19% were of normal weight, 22.03% were overweight, 5.08% were underweight, and 1.69% were obese. For those at low risk, 81.25% were of normal weight, 18.75% were overweight, with no individuals underweight or obese. The Chi-square test showed a significant difference in BMI distribution across OSA risk levels. The mean BMI also varied significantly among risk groups: high-risk individuals had the highest mean BMI ( $28.79 \pm 5.18$ ), followed by low-risk ( $22.91 \pm 2.67$ ) and intermediate-risk ( $22.84 \pm 3.08$ ) individuals. The Kruskal-Wallis test confirmed significant BMI differences across risk groups. Dunn's test further revealed significant BMI differences between low and high-risk groups ( $p < 0.001$ ) and between high and intermediate-risk groups ( $p < 0.001$ ).

#### **Comparison of clinical parameters over risk of OSA**

In our present study, the Kruskal-Wallis test showed no significant difference in Hemoglobin, Platelet, Urea, TB, DB, SGOT, SGPT, Serum Triglycerides, Hs CRP, Height, and Height ft across OSA risk levels. However, significant differences were found in Creatinine, Fasting Blood Sugar (FBS), HBA1C, weight, and Neck Circumference. The Dunn test revealed significant differences in Creatinine between low and high risk ( $p = 0.0423$ ), and low and intermediate risk ( $p = 0.0060$ ). HBA1C showed significant differences between low and high risk ( $p < 0.001$ ) and high and intermediate risk ( $p = 0.0150$ ). Weight differed significantly between low and high risk ( $p = 0.0013$ ) and high and intermediate risk ( $p < 0.001$ ). Neck Circumference differed significantly between low

and high risk ( $p < 0.001$ ) and high and intermediate risk ( $p < 0.001$ ). The one-way ANOVA indicated no significant difference in Total Protein, Albumin, and WBC across OSA risk levels. Sweed et al., 2023 [130] conducted a study on hospitalized diabetic patients, categorizing them as uncontrolled if their HbA1c levels were above the recommended threshold. The study found that 38 patients (64.4%) had uncontrolled diabetes, while 21 patients (35.6%) had their condition under control. This outcome aligns with a large-scale outpatient multicenter survey in China, which included nearly 240,000 patients and revealed that many with T2DM did not achieve the HbA1c target of less than 7% set by the American Diabetes Association (ADA) and the Chinese Medical Society. According to Ji et al., 2013 [139], less than one-third of T2DM patients reached the glycemic control goal of HbA1c  $< 7.0\%$ . Similarly, Borgharkar et al., 2019 [140] reported comparable findings in a study conducted in India.

Reis et al., 2015 [141] reported a notable rise in neck circumference. In contrast, Morsy et al. (2023) [131] discovered that patients with OSA and those without OSA had comparable body mass index (44.15% vs. 40.89%) and neck circumference (44.41% vs. 43.66%).

#### **7. Correlation of STOP-Bang score with Hs-CRP.**

Our study found a significant positive correlation between the STOP-Bang score and Hs-CRP using Spearman's rank correlation test ( $p = 0.0447$ ).

Shamsuzzaman et al., 2002 [142] examined 22 OSA patients (18 males, 4 females) without other health conditions or treatments, compared to 20 matched controls, OSA patients showed significantly higher CRP levels (median [range] 0.33 [0.09 to 2.73] vs 0.09 [0.02 to 0.9] mg/dL,  $P < 0.0003$ ). Multivariate analysis revealed an independent correlation between CRP levels and OSA severity ( $F=6.8$ ,  $P=0.032$ ), suggesting a link between OSA and elevated CRP levels, indicative of inflammation and cardiovascular risk, with severity of OSA positively associated with CRP levels.

## Summary:

A cross-sectional study was carried out among patients receiving medical care at the Department of General Medicine, encompassing both inpatient (IPD) and outpatient (OPD) settings at JAWAHARLAL NEHRU MEDICAL COLLEGE, BELAGAVI. The objective was to Screen for Obstructive Sleep Apnea in Patients with Type 2 Diabetes Mellitus Using STOP-BANG Scoring and Its Correlation with HSCRП Levels. The research spanned from January 2023 to December 2023, involving a total of 135 participants.

The key findings of the study are summarised here. The median age was 60 years, ranging from 30 to 88 years. The sample comprised of 57 females (42.22%) and 78 males (57.78%), indicating a slight male predominance among the participants. The majority of participants, comprising 85 individuals (62.96%), had a BMI falling within the normal range. Following this, 31 participants (22.96%) were classified as overweight. Obesity was observed in 15 participants (11.11%). A small fraction of the group, consisting of only 4 participants (2.96%), were categorized as underweight based on BMI criteria. The median BMI value was 23.56. The Hs CRP levels showed Mean of  $7.5 \pm 2.71$  mg/L and a Median of 7.1 mg/L. The HBA1C levels showed a mean of  $8.43 \pm 2.14$  % and a median 7.7%.

Among the studied population, 28 individuals (20.74%) were classified as high risk for Obstructive Sleep Apnea (OSA) based on the STOP-Bang score, 59 individuals (43.7%) fell into the intermediate risk category and the rest 48 individuals (35.56%) were considered to be at low risk for OSA. The average STOP-Bang score in the samples was 3.23, with a standard deviation of 1.53. The median score was 3, ranging from a minimum of 0 to a maximum of 7.

Among individuals at high risk for OSA, 50% were obese, 32.14% were overweight, 14.29% were normal weight, and 3.57% were underweight.

Spearman's rank correlation test revealed a notable positive correlation between the STOP-Bang score and Hs-CRP levels. The p-value of 0.0447 indicated a statistically significant association between STOP-BANG score and HsCRP levels. As the STOP-Bang score increased, indicating higher OSA risk, Hs-CRP levels also increased, possibly indicating elevated inflammation.

**Conclusion:**

Our research highlights the necessity of assessing OSA in people with type 2 diabetes using the STOP BANG scoring system. The notable association found between STOP-Bang scores and Hs-CRP levels indicates a possible connection between OSA severity and systemic inflammation in this group. Detecting and treating OSA early in individuals with T2DM may be vital for reducing related risks and enhancing overall health results. More studies are needed to understand the mechanisms behind this association and to investigate how addressing OSA in diabetic patients could benefit them therapeutically.

**Limitations:**

One drawback of this research was its dependence on the STOP BANG scoring system for assessing the occurrence of OSA in people with T2DM. While the STOP BANG system is a widely accepted screening tool, it may not capture entire spectrum of OSA severity or account for all risk factors, potentially leading to under- or over-estimation of OSA prevalence. Additionally, the cross-sectional design of the study limits the ability to establish causality between OSA and elevated HSCR levels. The study's sample size and population demographics might also limit the generalizability of the findings to broader, more diverse populations. Furthermore, other confounding factors that could influence HSCR levels, such as concurrent infections or inflammatory conditions, were not controlled for, which could affect the accuracy of the correlation observed between OSA and HSCR levels.

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**Screening For Obstructive Sleep Apnoea In Patients With Type 2 Diabetes Mellitus Using Stop Bang Scoring And Its Correlation With Hscrp Levels - A One Year Cross Sectional Study In KleS Dr.Prabhakar Kore Hospital And Medical Research Centre, Belagavi.**

**PROFORMA**

**CASE NO:**

**NAME:**

**AGE/SEX:**

**IP NO.:**

**ADDRESS:**

**OCCUPATION:**

**COMPLAINTS AT PRESENTATION:**

**Past history:**

**Family history:**

**Personal history:**

**Treatment history:**

**PHYSICAL EXAMINATION:**

GENERAL CONDITION:

- PALLOR- YES/NO
- ICTERUS-YES/NO
- LYMPHADENOPATHY-YES/NO
- CYANOSIS- YES/NO
- CLUBBING-YES/NO
- EDEMA-YES/NO

**VITALS:**

- TEMPERATURE:
- PULSE:

- RESPIRATORY RATE:
- BLOOD PRESSURE:

**Anthropometry-**

- WEIGHT
- HEIGHT
- BODY MASS INDEX
- NECK CIRCUMFERENCE

**STOP BANG QUESTIONNAIRE-**

Criteria	Score 0 or 1
snoring	
tiredness	
observed apnea	
high BP	
BMI	
Age	
Neck circumference	
Male gender	
	Total score- /8

**SYSTEMIC EXAMINATION:**

R. S.:

C.V.S.:

C.N.S.:

P.A.:

## INVESTIGATIONS

- CBC, Fasting lipid profile, Serum creatinine
- FBS ,PPBS ,HBAIC
- HSCR

## **INFORMED CONSENT FORM**

Dear Mr. /Mrs. /Dr. \_\_\_\_\_, you are kindly requested to enrol yourself in a research study titled, “Screening for obstructive sleep apnoea in patients with type 2 diabetes Mellitus using STOP BANG Scoring and it’s correlation with HSCRП levels” being conducted by Dr. Shubham Kapshe, a post graduate student in M.D. General Medicine and the study will be carried out under the direct supervision and guidance of Dr. ARATHI DARSHAN, Professor, Department of General Medicine, Jawaharlal Nehru Medical College, Belgaum.

You have been requested to participate in this as you fit into the laid out criteria for a study ‘subject’/ participant.

Your participation in study is voluntary. During the study you will be asked some questions and you are supposed to answer to the best of your knowledge. Your decision whether or not to participate in the study will not affect your treatment in any form. If you decide to participate you are free to withdraw at any time.

### TITLE OF THE STUDY:

“Screening for obstructive sleep apnoea in patients with type 2 diabetes Mellitus using STOP BANG Scoring and it’s correlation with HSCRП levels”

PURPOSE OF THE STUDY: To screen for obstructive sleep apnoea in patients with type 2 diabetes mellitus using STOP BANG Scoring and correlate the risk with the patients’ HSCRП levels.

PROCEDURES INVOLVED: If you agree to enrol yourself in my study, you will be interviewed regarding your present, past and family history then you will be clinically examined in detail and investigated accordingly.

Then you will be subjected to a few blood investigations, namely CBC, FBS OR PPBS OR HbA1C, HSCRП.

RISKS AND BENEFITS: There are no potential risks involved in this study.

Benefits of taking part in this research: By taking part in this study, you shall help me determine whether a patient with type 2 diabetes mellitus has of also suffering from obstructive sleep apnoea and help me correlate the risk scores with patients HSCRП levels.

VOLUNTARY PARTICIPATION / WITHDRAWAL FROM THE STUDY: Taking part in the study is voluntary. You may choose not to enrol yourself in this study and may choose to leave the study anytime in between.

ALTERNATIVES: Your decision regarding participation in study will not change present or future health care services offered to you at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum. You would simply be excluded from the study if you wish to, and all your details shall be kept confidential and you will get the routine line of management.

PRIVACY AND CONFIDENTIALITY: All data collected or disclosed by you during the course of participation of study, will be kept fully confidential. If however during the course it becomes necessary for the progress of the course to disclose the identity, it would be done so only after your informed & written consent. The only people to know that you are a research subject are members of the research team. No information about you will be disclosed to other without your written permission except:

In emergency to protect your rights AND welfare.

If required by law.

AUTHORISATION TO PUBLISH RESULT: The results of the study may be used to publish an article. When the results of research published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information obtained in connection with this study and that can be identified with you will remain confidential.

FINANCIAL INCENTIVES FOR PARTICIPATION: No additional costs shall be incurred upon you for the purpose of this study. It is purely being done with the idea of research and all the cost of study will be borne by the investigator.

COMPENSATION: In the event that you become injured as a result of taking part in this study, treatment will be offered to you at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum, or you will be given information about where to receive medical care. However, no reimbursement, compensation or free medical care will be given.

QUESTIONS/CONTACT DETAILS: You shall be free to contact the below mentioned name & addresses anytime during the study period for any clarification or help as you may desire for.

PRINCIPAL INVESTIGATOR: BG0121018

MD (Post Graduate Student), Department of General Medicine,,Jawaharlal Nehru Medical College,Nehru Nagar, KLE Hospital Road Belagavi 590010

**GUIDE:**

Professor, Department of General Medicine, Jawaharlal Nehru Medical College,  
Nehru Nagar, KLE Hospital Road, Belagavi 590010

Dr. Harsha Hegde, Chairman, J.N.M.C Ethical Committee for Human Research

**CONSENT FORM**

I, voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has been read to me, this consent form and have had all the questions answered.

.....

Name of the Participant

.....

Signature of the participant  
or Left-Hand Thumb impression

.....

Name of Investigator

Signature of investigator  
or Left-Hand Thumb impression

.....

Name of Witness

.....

Signature of Witness  
or Left-Hand Thumb impression

Date:

Place:

