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Obstructive Sleep Apnea: Is It a Hidden Clue for Perioperative Pulmonary Complications in Patients Undergoing Coronary Artery Bypass Grafting?

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Abstract: Background: Obstructive sleep apnea(OSA) is a common preoperative finding, sharing same demographics in patients with ischemic heart disease. Moreover, patients undergoing coronary artery bypass grafting (CABG) usually present with perioperative pulmonary complications but there is always a mysterious relationship between both. **Purpose:** We aimedto detect the relationship between preoperative OSA and peri-operative pulmonary complications in patients undergoing CABG. **Patients and Methods:** All patients enrolled in the study underwent CABG. They were allocated in two groups: control group including 21 patients without OSA and OSA group including 24 patients with preoperative OSA. Pulmonary complications for each patient were recorded when occurred and reported for analysis. **Results:** One of most remarkable significant finding was the peri-operative hypoxemia which occurred in 14 (58.3%) patients in OSA group, while it was detected in 2 (9.2%) patients in control group. We also got significant duration of mechanical ventilation (MV) with mean of 14.75±9.14 hours in OSA group, while it was 6.24±0.54 hours in control group with consequent increase in intensive care unit (ICU) and whole hospital stay. We got significant positive correlations regarding OSA parameters as AHI, OD/h, degree of ESS and SaO_2< 90% of total sleep time (TST) with the duration of MV, ICU and hospital stay. **Conclusions:** OSA is a risk factor for developing peri-operative pulmonary complications associated with CABG and consequently prolongs the duration of intensive care unit and hospital stay.
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Keywords: Obstructive sleep apnea, Coronary artery bypass, Perioperative complications.

1. Introduction:

One of the common cardiac surgeries nowadays is coronary artery bypass grafting (CABG). Different postoperative complications including cerebral, cardiovascular and pulmonary adverse events are still occur widely despite the improvement in surgical procedures [1]. One of the most important determinants of patient's prognosis is postoperative pulmonary complications (PPCs) [2]. Obstructive sleep apnea (OSA),which is recurrent attacks of obstructions of the upper airways either partial or complete and leads to disorders in sleep pattern throughout the day with excessive daytime sleeping and fragmented night sleep, is also a common finding in the pool of candidate patients for CABG [3]. Because of increasing prevalence of obesity and the ages of populations, the prevalence of ischemic heart disease (IHA) and OSA is increasing which leads to consider IHD and OSA very common heath related problems[4]. It was recorded that 40 to 45% of patients with IHD had OSA [5, 6]. This alarms for the importance to screen patients with IHD for the presence of OSA to avoid complications associated with OSA cardiac, pulmonary or cerebrovascular [7]. These complications secondary to OSA are diverse and affect the routine life leading to catastrophic events, potentiating cardiovascular complications as hypertension (HTN), and heart failure (HF). Also, OSA added to IHD increased incidence of stroke and sudden death [8]. It was previously documented that OSA can affect the prognosis of patients postoperatively and the overall morbidity and mortality following different types of operations [9]. The agreed pathophysiology in OSA leading to obstruction of the upper airways during sleep includes failure of the dilator muscles of the upper airways to overcome the negative pressure generated by the inspiratory muscles [10, 11].

It was found that general anaesthesia affects and reduces the action of these dilator muscles which favours and increases the collapse of the upper airways during surgery [12, 13] taking into consideration that most of patients have undiagnosed sleep breathing disorders which predisposes them to unexpected adverse events during and after operations [14]. Moreover, general anaesthesia impairs the arousal response that aids patients to overcome the upper airways obstruction, andrespiratorycentre depression can occur following different sedatives, hypnotics, and analgesics that are ordinary used with surgery [15]. Many considerations for CABG patients affect the prognosis more like opioids,usedfor controlling of postoperative pain, cause impairment of peripheral and central chemoreceptors which might affect the ventilatory function [16]. Besides opioids, thenecessarypostoperativesupine position could exaggerate the OSA in 50% of patients [17]. This supine position beside obesity decrease lung volumes, affect gas exchange and increase upper airways collapsibility [18,19]. As mentioned before,generalanaesthesia drugs and its residual effects associated with opioids can exacerbate apnoeic attacks and worsen hypoxemia through affecting the process of oxygenation and decreases the function residual capacity (FRC), also these drugs affect sleep pattern [20,21,22]. Finally, OSA could through different mechanisms including hypercoagulable state affect the prognosis and outcomes following CABG [23].

Aim of the work:

We aimed at detecting relationship between preoperative OSA and peri-operative pulmonary complications in patients undergoing CABG.

2. Patients and methods:

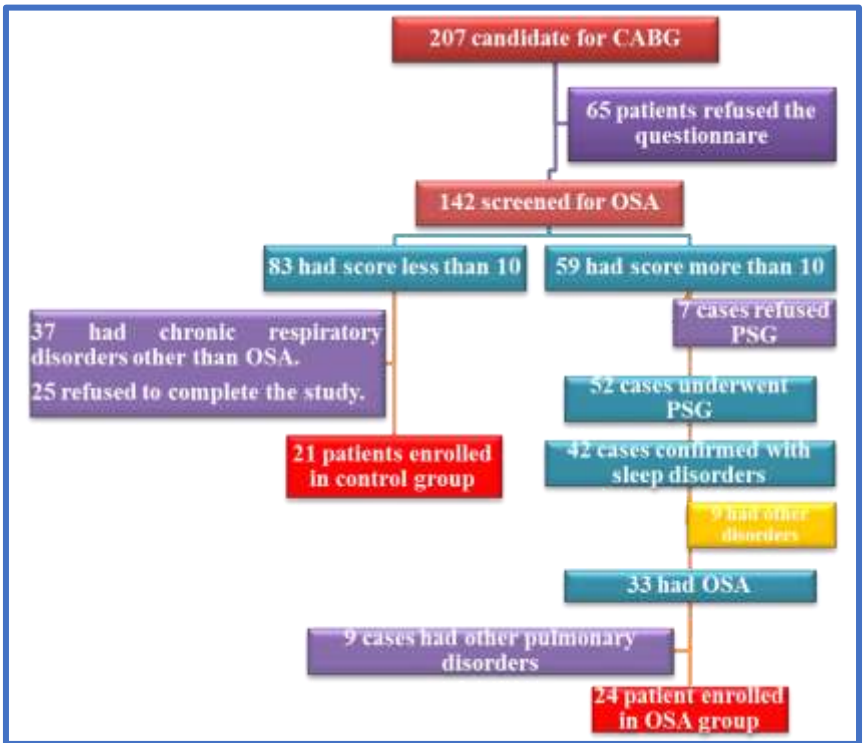

Figure (1): Flow diagram of patients allocated in the study

The study protocol was approved by the Ethics Committee of Menoufia University Hospitals and it was done at Chest and Cardiothoracic Surgery (CTS) Departments, Menoufia University Hospitals from November 2015 to August 2018 and included patients who were prepared for CABG operation and diagnosed as having OSA syndrome. Before enrolment, an informed consent was obtained from the patients. **Exclusion criteria were:** (1) Patients with chronic respiratory disorders other than OSA, (2) Patients with central or mixed sleep apnea, (3) Patients who did not complete the whole steps of the study. (4) Patients with renal, hepatic or neurological disorders. During the study period, 207 patients were prepared to undergo CABG operation at CTS department. 142 cases of them were screened for OSA using Epworth sleepiness scale (ESS) questionnaire [24]. 59 of the screened patients had score ≥ 10 and were referred to Sleep Unit at Chest Department to confirm the diagnosis of OSA using polysomnography (PSG). Of

the 59 cases, 52 cases did PSG which confirmed the presence of sleep breathing disorders in 42 cases, 33 of them had OSA. After exclusion of other pulmonary disorders, 24 of the 33 patients who had OSA only were included in the study as OSA group.83 out of 142 screened patients for OSA had score <10, 37 of them were excluded as having chronic respiratory disorders other than OSA and 25 cases refused to complete the study and so 21 patients were enrolled as control group without OSA. (Figure 1)

Preoperative assessment:

All patients were prepared for CABGare subjected to: complete history taking, clinical examination both general, cardiac, and chest examinations. Patients were referred to the sleep disorders unit at Menoufia University Hospital where the ESS was used to screen patients for OSA. The ESS questionnairedescribes eight situations as follows: sitting and reading; watching television; sitting inactive in a public place (as a passenger in a car riding for an hour without a break); lying down to rest in the afternoon when circumstances permit; sitting and talking with someone; sitting quietly after lunch without alcohol; and in a car, while stopped for a few minutes in traffic. The participant scored each situation as to its degree of sleep propensity on a scale of (0–3): 0= would never doze; 1= slight chance of dozing; 2= moderate chance of dozing; 3= high chance of dozing. A score can range from 0 through 24, with higher scores correlating to increasing degrees of sleepiness. In general, a score of ≥10 is consistent with excessive daytime sleepiness [24]. Then, overnight PSG was performed for patients with ESS score ≥10 using Embla S4000 Medicare, Iceland. The system has the following components: Somnologica studio 3.3.2 software; Pulse oximetry sensor, Airflow nasal pressure cannula; Airflow thermistor; Respiratory inductive plethysmography belts with thoracic and abdominal locks; Snoring microphone; Body position sensor; EEG electrodes with their cables; EOG electrodes; EMG electrodes for the chin and anterior tibialis muscle; and ECG electrodes with their cables. All studies were analysed by sleep physicians using the criteria of Rechtschaffen and Kales [25] and in close concordance with scoring updates given by the American Academy of Sleep Medicine [26]. Apnea was scored when there was a complete cessation of airflow or ≥90% drop in the peak thermal sensor excursion for at least 10s. Hypopneas were scored when there was a drop in the nasal pressure by ≥30% of baseline lasting at least 10s with a ≥4% desaturation from pre-event baseline, or when there was a drop in the nasal pressure signal excursion by ≥50% of baseline lasting at least 10s with a ≥3% desaturation from pre-event baseline. The apnea–hypopnea index (AHI) which is number of apnea–hypopnea events per hour was determined after the exclusion of periods with movements, which were considered to be wake periods. Patients with OSA confirmed with PSG were classified into mild OSA (AHI between 5 and <15), moderate OSA (AHI between 15 and <30), and severe OSA (≥30).

Surgical technique:

After initial assessment and groups enrolment, all patients underwent on-pump CABG through midline full sternotomy and under general anaesthesia using (propofol 2mg/kg, fentanyl 50 microgram/kg and Atracurium 0.5mg/kg) on induction,maintenance by isoflurane at 1MAC, Atracurium infusion and fentanyl. Intermittent antegrade blood cardioplegia was used for myocardial protection. Aorto- atrial cannulation, bypass initiation, coronary grafting, weaning, decannulation, and closure in layers were elaborated in sequence for every case.

Postoperative follow-up:

After surgery, patient was transferred intubated to intensive care unit and followed till full recovery, good hemodynamics, oxygenation, and accepted drainage then extubated. Every patient was monitored in ICU till hemodynamically stable without any inotropic support and adequate oxygenation, then transferred to ward. Anyperi- or postoperative pulmonary complications was recorded and followed till recovery for every patient.

Statistics:

Data entry of this study, coding and analysis were conducted using PSW (20), IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. Data of this study were of both quantitative and qualitative types . Quantitative data were expressed in Mean ($\bar{x}$), and Standard Deviation of Mean (SD), while qualitative data were expressed in frequency (number), and percent (%). Student t and ANOVA tests were used to estimate the difference in "Means" of quantitative parameters between the two studied groups and the three subdivided groups; respectively. Chi-square test was used to assess the relationship between two or more qualitative variables. Pearson correlation was used to correlate two continuous normally distributed variables.Level of significance of our data was 95%, so, p-value > 0.05 was considered a non-statistically significant difference, while p-value < 0.05 was considered a statistically significant difference and p-value < 0.01 was considered statistically a highly significant difference.

3. Results:

In this follow up case control study, the OSA group was comparable to control group without any significant difference in demographics that included age, gender, body mass index (BMI), smoking habits

or preoperative co-morbidities as hypertension (HTN), diabetes mellites (DM) and dyslipidemia (Table 1). Regarding pulmonary complications that occurred during and after CABG, Table 2 shows significant difference in rate of hypoxemia and need for non-invasive ventilation (NIV) with 58.3% of OSA group manifesting hypoxemia and 54.2% of the same group required NIV compared to 9.5% hypoxemia and 4.8% NIV in control group. Themeanduration of mechanical ventilation was statistically significant with more than double time in OSA group than control group, moreover the whole ICU stay was also significantly different with nearly double mean time in OSA group than the control. Consequently, the mean hospital stay was significantly longer by 2 days in OSA group. Regarding the effect of severity of OSA on incidence of post-CABG pulmonary complications, there was a non-significant difference with the incidence of post-operative pneumonia, pleural effusion and atelectasis. While, there were significant differences regarding peri-operative hypoxemia, duration of mechanical ventilation (MV), need of post-operative NIV, and the duration of ICU and hospital stay (Table 3). Table 4 and figures 2-6 shows the correlations between different OSA parameters and the duration of MV, ICU stay, and hospital stay. There were significant positive correlations regarding AHI, oxygen desaturation events (OD), degree of ESS and SaO2< 90% of total sleep time (TST), while there were significant negative correlations regarding average O2 and lowest O2 saturation.

Table (1): Demographic data of the studied groups

Variable	Control No=21	OSA No=24	Test of significance	P-value
	No (%)	No (%)		
Age (Mean ± SD)	59.05±5.14	60.46±7.96	0.69	0.49
Sex				
Male	12 (57.1)	16 (66.7)	0.43	0.55
Female	9 (42.9)	8 (33.3)		
HTN				
Present	10 (47.6)	12 (50)	0.03	1.00
Absent	11 (52.4)	12 (50)		
DM				
Present	9 (42.9)	12 (50)	0.23	0.77
Absent	12 (57.1)	12 (50)		
Dyslipidemia				
Present	13 (61.9)	14 (58.3)	0.06	1.00
Absent	8 (38.1	10 (41.7)		
BMI (Mean±SD)	40.33±5.87	40.0±7.07	0.17	0.87
Smoking				
Yes	11 (52.4)	15 (62.5)	0.47	0.56
No	10 (47.6)	9 (37.5)		

OSA: obstructive sleep apnea. HTN: hypertension. DM: diabetes mellitus. BMI: body mass index. SD: standard deviation.

Table (2): Comparison between OSA and control groups regarding CABG-associatedcomplications

Variable	Control No=21	OSA No=24	Test of significance	P-value
	No (%)	No (%)		
Aspiration pneumonia				
Present	2 (9.5)	8 (33.3)	3.68	0.08
Absent	19 (90.5)	16 (66.7)		
Peri-operative hypoxemia				
Present	2 (9.5)	14 (58.3)	11.65	0.001
Absent	19 (90.5)	10 (41.7)		
Need of NIV				
Present	1 (4.8)	13 (54.2)	12.76	<0.001
Absent	20 (95.2)	11 (45.8)		
Atelectasis				
Present	4 (19.0)	10 (41.7)	2.67	0.12
Absent	17 (81.0)	14 (58.3)		
Pleural effusion				
Present	7 (33.3)	10 (41.7)	0.33	0.76
Absent	14 (66.7)	14 (58.3)		
MV /h (Mean±SD)	6.24±0.54	14.75±9.14	4.55	<0.001
ICU stay/h (Mean±SD)	34.29±28.97	62.00±26.40	3.36	0.002
Hospital stay/d (Mean±SD)	6.43±0.51	8.63±1.58	6.43	<0.001

NIV: non-invasive ventilation. MV/h: mechanical ventilation /hour. D: day. No: numbers. ICU: intensive care unit.

Table (3): Post-operative complications in OSA group regarding degree of severity

Variable	Mild OSA No=6	Moderate OSA No=8	Severe OSA No=10	Test of significance	P-value	
	No (%)	**No (%)**	**No (%)**			
Aspirationpneumonia **Present** **Absent**	 1 (16.7) 5 (83.3)	 3 (37.5) 5 (62.5)	 4 (40) 6 (60)	1.01	0.60	
Peri-operativehypoxemia **Present** **Absent**	 1 (16.7) 5 (83.3)	 6 (75) 2 (25)	 7 (70) 3 (30)	5.76	0.05	P_1=0.03 P_2=0.04 P_3=0.06
Need of NIV **Present** **Absent**	 1 (16.7) 5 (83.3)	 4 (50) 4 (50)	 8 (80) 2 (20)	6.14	0.04	P_1=0.19 P_2=0.002 P_3=0.04
Atelectasis **Present** **Absent**	 2 (33.3) 4 966.7)	 4 (50) 4 (50)	 4 (40) 6 (60)	0.41	0.81	
MV /h **(Mean±SD)**	7.33±1.21	12.75±1.91	20.80±11.36	6.40	0.007	P_1=0.19 P_2=0.002 P_3=0.04
ICU stay/h **(Mean±SD)**	32.00±12.39	63.00±17.86	79.20±22.77	11.46	<0.001	P_1=0.007 P_2<0.001 P_3=0.09
Hospital stay/d **(Mean±SD)**	7.50±1.38	8.35±1.28	9.60±1.43	4.86	0.02	P_1=0.32 $P_2$0.007 P_3=0.05
Pleural effusion **Present** **Absent**	 2 (33.3) 4 966.7)	 3 (37.5) 5 (62.5)	 5 (50) 5 (50)	0.51	0.77	

P: comparison between all subgroups. P1: severe and mild. P2: moderate and mild. P3: severe and moderate

Table (4): Pearson correlation coefficient between OSA parameters characters and development of post-operative complications

PSG findings	Duration Of MV/h		ICU stay /h		hospital stay/day	
	r	**P-value**	**r**	**P-value**	**r**	**P-value**
AHI	0.84	<0.001	0.83	<0.001	0.87	<0.001
Lowest O2 Saturation	-0.58	0.003	-0.61	0.002	-0.66	<0.001
SaO2<90% of TST	0.52	0.009	0.56	0.005	0.65	0.001
OD/h	0.64	0.001	0.68	0.001	0.62	0.001
Average O2	-0.48	0.02	-0.44	0.03	-0.55	0.005
ESS	0.39	0.05	0.51	0.01	0.47	0.02
TST/min	-0.09	0.65	-0.12	0.57	-0.27	0.21
Sleep efficiency	-0.14	0.51	-0.19	0.38	-0.20	0.36

PSG: Polysomnography. SaO2: arterial oxygen saturation. OD/h: oxygen desaturation events/hour. ESS: Epworth sleepiness scale. TST: total sleep time.

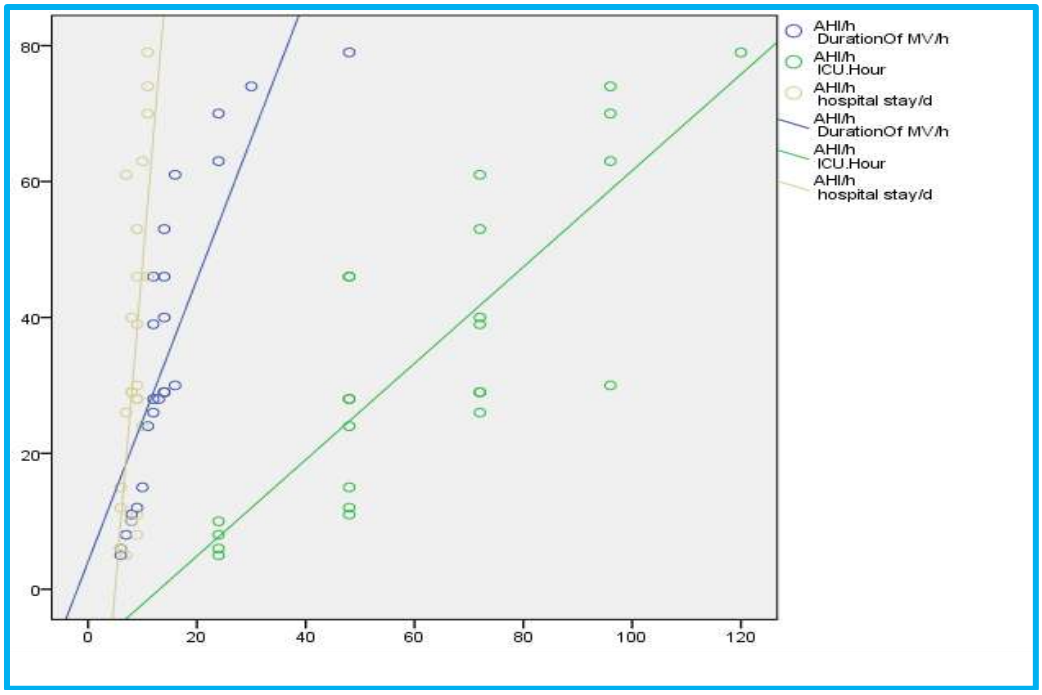

Figure (2): Correlations of apnea/hypopnea index (AHI)

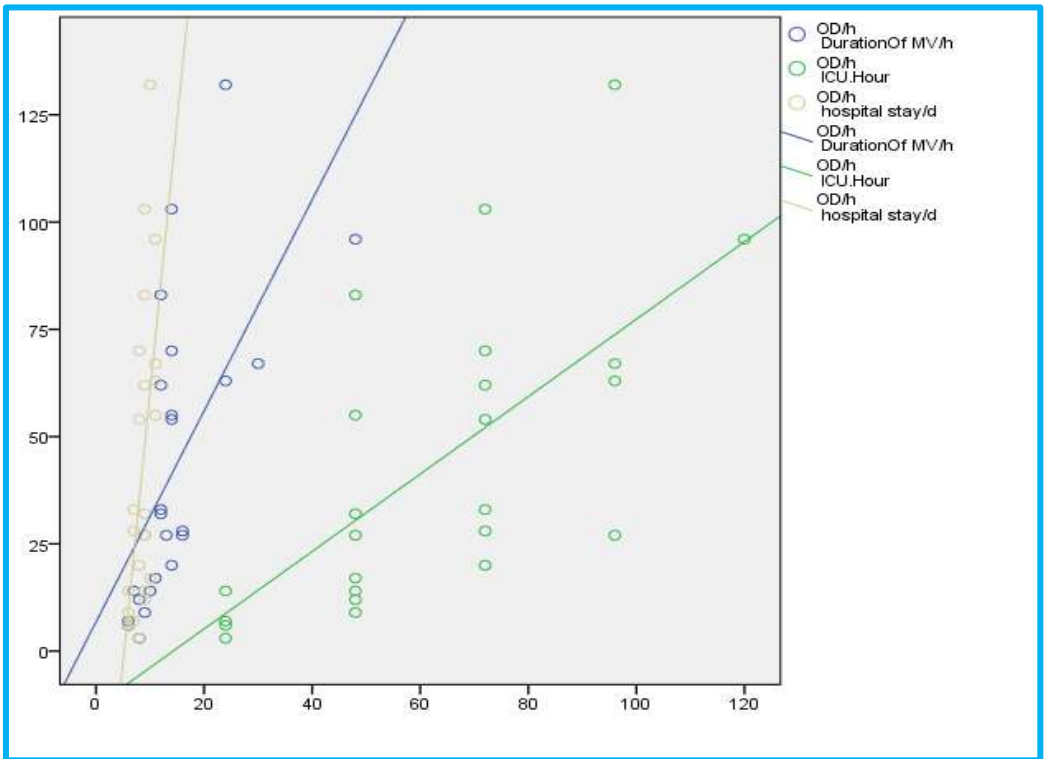

Figure (3): Correlations of oxygen desaturation (OD).

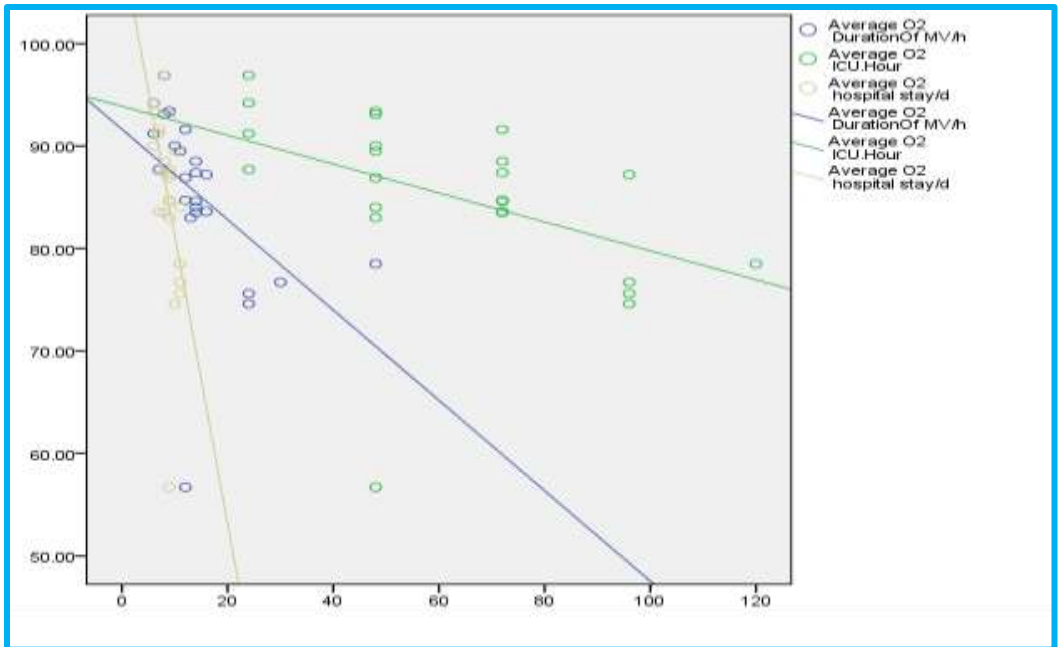

Figure (4): Correlations of average O2 saturation.

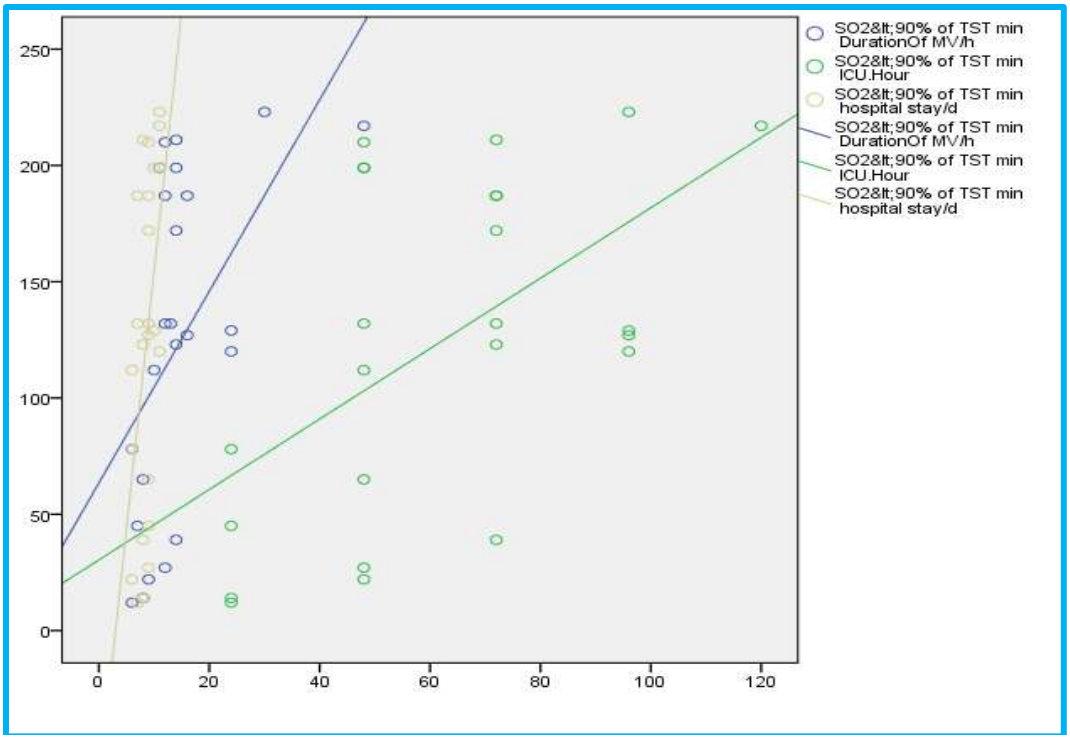

Figure (5): SaO2<90% of total sleep time (TST) correlations

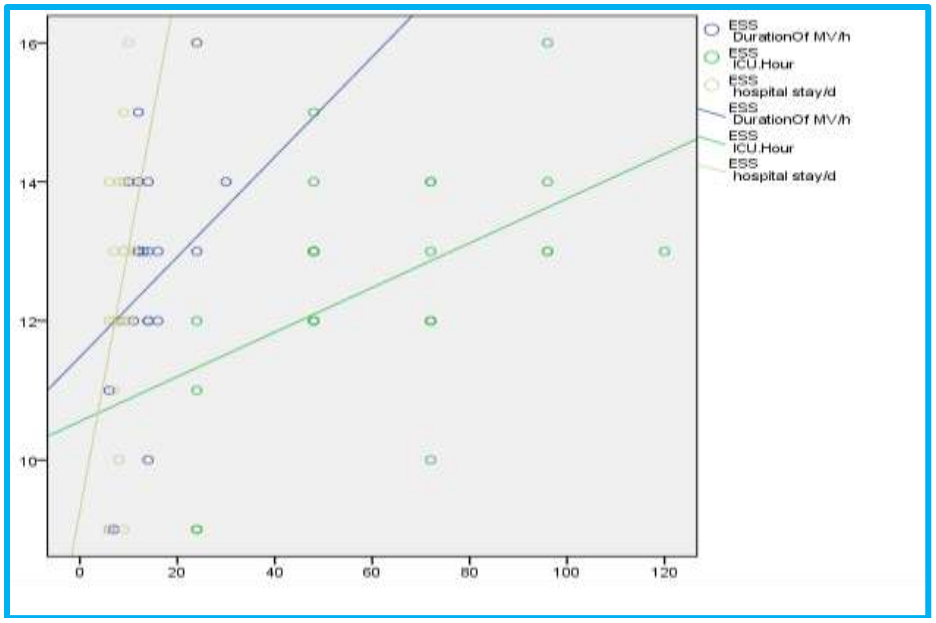

Figure (6): Correlations of Epworth sleepiness scale(ESS).

4. Discussion:

The repeatedly encountered post CABG pulmonary complications and its impact on short and long-term prognosis aroused many researchers to study that problems and trying to detect its preoperative predisposing factors to help preventing and minimizing incidence of such deleterious complications. Arozullah A et al [27] and Arozullah AM et al [28] in their studies about risk factors of post-operative pulmonary complications concluded that age more than 60 is a risk factors for developing post-operative pulmonary complications as respiratory failure (RF) and pneumonia. Others noted that smoking is a well-known risk factor for post-operative pulmonary complications even in patients without chronic pulmonary disorders. Warner et al [29] in their study, they reported more PPCs in patients with active smoking or who quitted smoking less than 2 months before surgery, and it is recommended to quit smoking 2 months before operations [30]. Also, increased body mass index (BMI) or obesity is associated with post-operative complications. Some researchers suggested OSA as pre-operative risk factor for PPC. They stated that the prevalence of undiagnosed OSA in patients who are candidates for CABG is high. Obesity, old age, smoking and comorbidities as Diabetes Mellitus (DM), HTN or dyslipidaemia are similar co-factors in patients with OSA and coronary artery disease (CAD). Moreover, Memtsoudis et al [31] who reported in their case-control study, increased PPCs in their patients with sleep apneas following orthopaedic and general surgery. Opperer M et al [32] in their study concluded that OSA remains a major risk factor for PPCs in general surgical procedures despite the marked improvement in methods of surgery and anaesthesia. Another two meta-analyses studies [33,34] reported 2-3 folds increase in post-operative cardiopulmonary complications in patients with OSA. Also, D'Apuzzo and Browne [35] in their study on patients with OSA undergoing total hip and knee revision arthroplasty found 2 folds increase in post-operative adverse events. In a similar way, in the study of Kaw R et al [36], reported higher rates of longer ICU and hospital stays and post-operative hypoxemia in patients with OSA, all of that arouse need to study the OSA effect in cardiac surgery specially CABG with shared patients' characteristics. The OSA and control groups in our study were comparable with no significant difference in other preoperative risk factors as age, sex, BMI, HTN, DM, dyslipidaemia, and smoking. Regarding perioperative pulmonary complications, there were significant differences between both groups regarding intraoperative hypoxemia, duration of MV, duration of ICU and hospital stay. There was higher incidence of post-operative pneumonia, atelectasis and pleural effusions in OSA group, but these differences didn't reach level of statistical significance. These findingsagree with that of Gupta et al [37] who reported increased post-operative complications (39% vs 18%), increased rates of ICU admissions (24% vs 9%), and increased hospital stay in patients with OSA compared with their comparable control. Also, they added that the effect of treated OSA preoperative markedly reduced the incidence of post-operative complications and hospital stay compared with untreated patients. Liao et al [38] reported a higher

rate of post-operative complications in patients with OSA (44% vs 28%), they noted that non-compliant patients with their CPAP were the group with highest rates of post-operative complications. In their study on the effect of OSA on post-operative outcomes, Kaw et al [39] reported higher rates of post-operative complications and increased ICU length of stay among patients with OSA. Bhama JK et al [40] who found that patients with OSA had longer hospital stay ranged from 13 to 24 days than patients without OSA.In disagreement with our results and all the previous studied [31-39], Mokhlesi B et al [41] reported lower rates of post-operative complications following orthopaedic, general surgery, and cardiovascular operations and they explained these finding with the special care that patients with OSA were taken than patients without. As regards the effect of OSA severity on occurrence of post-CABG pulmonary complications, there was a slight non-significant increase of the incidence of post-CABG pneumonia, atelectasis and pleural effusion with increased degree of OSA. On the other hand, we got significant increase in incidence of intraoperative hypoxemia, duration of mechanical ventilation, need of post-operative NIV, and the duration of ICU and hospital stay. That's exactly opposite to Kaw R et al [39] whodid not find any correlation between the severity of OSA and the incidence of PPCs. We tried to study which parameter should be in consideration in preoperatively assessing the OSA prepared for CABG to minimize the post-operative complications specially the most noted of prolonged MV, ICU and hospital stay. We analysed the correlations between different OSA parameters and the duration of MV/h, ICU stay/h and hospital stay/ddetectingsignificant positive correlations regarding AHI, OD/h, degree of ESS and SaO_2< 90% of TST, while there were significant negative correlations regarding average O_2 and lowest O_2 saturation. The previous findings agree with that of Hwang et al [42] on their study of 172 patients who were assessed for elective surgery and had home nocturnal oximetry, they reported that patients with high oxygen desaturation events per hour developed more post-operative complications. Also, they found a positive correlation between the number of oxygen desaturation events and a higher rate of post-operative complications. Agreeing with Tafelmeier M et al [43], who concluded that patients with OSA had a significantly prolonged length of hospital stay (LOS) and theyreported that AHI of ≥ 15/h was associated with prolonged hospital stay by 4 days, and on analysis, they found that prolonged LOS after CABG was significantly associated with AHI, diagnosis of OSA, the oxygen desaturation index (ODI) time of SaO_2 < 90% with insignificant difference regarding post-operative pneumonia.

Conclusions:

OSA is a risk factor for developing peri-operative pulmonary complications in patients who are candidates for CABG as other surgeries. Not only the degree of OSA is important in pre-CABG risk assessment but special parameters as AHI, OD/h, degree of ESS and SaO_2< 90% of TST are very important to assume risk for postoperative pulmonary complications.

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