Research Article

Role of C reactive protein and Erythrocyte sedimentation rate in Obstructive Sleep Apnea

Lamiaa H. Shaaban*, Nezar R. Tawfike, Zainab H. Saeed* and Hadeer E. Refaat***
* Department of Chest Diseases, Faculty of medicine, Minia university, Egypt
** Department of Chest Diseases, Faculty of medicine, Assuit university, Egypt

Abstract
Background: Obstructive sleep apnea (OSA) is a condition characterized by repeated episodes of partial or complete obstruction of the respiratory passages(1) The standard diagnostic procedure for establishing the presence of OSA is the overnight polysomnography(2) **.** The development of simple, and reliable biomarkers that permit precise screening of at-risk populations is required. So , special interest has centered around potential OSA biomarkers. The ideal biomarker should be highly sensitive , specific and correlate to severity of OSA.(3) **Patients and methods**: This study was performed on 35clinically suspected OSA patients, and15 non-smoker healthy control persons . Patients were recruited from of Minia cardiothoracic university hospital during the period from September 2018 to September 2019. All patients were assessed for excessive day time sleepiness by Epworth sleepiness score and STOPBANG score, pulmonary function tests (FEV1, FVC and FEV1/FVC)% predicted, ABG, and measurements of C reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) were done for all patients and control. **Results:** This study were performed on 50 patients 35 cases and 15 control group and showed a Significant elevation in CRP and ESR in the case group compared to the control group. **Conclusion:** The current study showed that there was a significant elevation in CRP and ESR in case group versus control group.
Keyword: OSA, Obstructive sleep apnea, CRP:C-reactive protein
FEV1: Forced expiratory volume at the first second, **FVC:** Forced Vital Capacity

Introduction
Obstructive sleep apnea (OSA) is a condition characterized by repeated episodes of partial or complete obstruction of the respiratory passages at the sleep . The body's response to obstructed breathing leads to arousal of the brain, sympathetic activation, and oxygen desaturation in the blood. Repeated episodes of upper airway obstruction during sleep may result in sleep fragmentation and non-restorative sleep **(3)**.
The standard diagnostic procedure for establishing the presence of OSA is the overnight polysomnography **(4)**

PSG are sometimes inconvenient and relatively inaccessible to patients, waiting times between referral for evaluation to diagnosis commonly take 3–6 months across the United States and around the world **(5)**.

The development of simple, and reliable biomarkers that permit precise screening of at-risk populations is required. So, special interest has centered around potential OSA biomarkers. The ideal biomarker should be highly sensitive , specific and correlate to severity of OSA. **(6)**

C-reactive protein (CRP) is synthesized in the liver and regulated by cytokines. Unlike cytokines, CRP levels are stable in the same individual over 24 h and may reflect the level of inflammatory response**.(7)**

Erythrocyte sedimentation rate (ESR) can assess the ability of red blood cells to aggregate and reported to be increased in different inflammatory diseases, Although ESR is low cost, simple and applicable test, few studies were done on the relationship between the degree of plasma ESR level and OSA **(8).**

Patients and methods
This case control study has been performed on 35 clinically suspected OSA patients , and15 non-smoker healthy control persons. Patients were recruited from of Minia Cardiothoracic

University hospital during the period from September 2018 to September 2019. The study was approved by the hospital research ethics board of Minia University. Informed consent was obtained from each patient.

Inclusion criteria

Patients diagnosed as OSAS proven by PSG (35 patients).

The study also included 15 non-smoker healthy control persons.

Exclusion criteria

- Smokers
- Medical disorder as left sided heart failure.
- (COPD, ILD and OHS).
- Drugs e.g anti-inflammatory, analgesics, insulin, antineoplastic, anti-psychotic drugs in the previous 2 weeks before the study.

All patients were assessed for excessive day time sleepiness by Epworth sleepiness score and STOPBANG score, pulmonary function tests (FEV1, FVC and FEV1/FVC)% predicted, ABG, and measurements of C reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) were done for all patients and control.

Results

Table (1): Demographic data of all cases**.**

		Case	Control	P- value
		N=35	N=15	
Age	Range Mean ± SD	(38-76) 59.4±8.3	(36-76) 56.9±13.6	0.428
Sex	Male Female	8(22.9 %) 27(77.1 %)	5(33.3%) 10(67.7 %)	0.493
Special habit	Smoking Current Ex-smoker Non smoker	 0(0%) 2(5.7%) 33(94.3%)	 0(0%) 2(13.3%) 13(86.7%)	0.574
BMI	Range Mean ± SD	(20-34) 27.2±2.6	(24-30) 26.9±1.8	0.687
Neck circumference	Range Mean ± SD	(34-67) 47.5±7.7	(33-44) 46.6±3.1	0.295

- Independent samples T test for parametri quantitative data between the two groups
- Chi square test (if < 20% of cells have expected count less than 5) or Fisher exact test (if >20% of cells have expected count less than 5)
- Significant level at P value < 0.05

Table (1): shows demographic data of the 2 groups. The mean age in the OSA group was 59.4 ranging from 38 to 76, about 77.1% were females and 22.9% were males. In the control group , the mean age was 55.9 ranging from 40 to 66 , 86.7% were females and 13.3% were males. No significant difference between the 2 groups as regard the demographic data.

Table (2): Spirometer results of all cases

		Case	Control	P value
		N=35	N=15	
FVC	Range Mean ± SD	(33-78) 54.3±12.7	(80-95) 88±4.3	**<0.001***
RATIO	Range Mean ± SD	(66-99) 82.3±9.9	(70-99) 87.7±8.8	**0.076**
FEV1	Median IQR	55 (44-67)	94 (88-99)	**<0.001***

- Independent samples T test for parametri quantitative data between the two groups.
- Mann Whitney test for non-parametric quantitative data (expressed as median) between the two groups.
- *: Significant level at P value < 0.05.

Table (2): shows spirometry results and sleep questionnaire of the OSA group. FVC ranged from 33-78, FEV1/FVC ranged from 66-99 and FEV1 median was 55and show significance between case and control in FVC and FEV1.

Table (3): Comparison of CRP and ESR markers between the study group and the control group.

		Case	Control	P- value
		N=35	N=15	
ESR1st hr	Median IQR	30 (20-50)	10 (5-20)	**<0.001***
ESR 2nd hr	Median IQR	70 (50-80)	20 (10-30)	**<0.001***
CRP	Median IQR	34 (20-66)	12 (10-13)	**<0.001***

- Mann Whitney test for non-parametric quantitative data (expressed as median) between the two groups
- *: Significant level at P value < 0.05.

Table (3): shows a comparison between the OSA group and control group regarding the level of the CRP and ESR markers. both markers were significantly higher in the case group when compared to the control group (p value <0.001).

Discussion

The association of CRP with OSAS has been a subject of debate in recent years with differing conclusions in various studies that have explored the relationship .[9]

The strong relationship between CRP levels and obesity may have influenced some studies investigating CRP levels in adult patients with OSAS where the populations investigated were not optimally matched for BMI [10] .

After the index report in 2002 on a pilot trial suggesting that CRP level might be related to OSAS severity Shamsuzzaman, et al., observed that CRP levels in the OSA patients were significantly higher as compared with that in normal individuals. Furthermore, significant differences in CRP levels were detected between mild and severe OSA patients.[11]

In the present study we assessed the value of ESR and CRP biomarkers in patients with Obstructive sleep apnea .

Our study included 35 cases of OSA were referred to chest department at cardiothoracic university hospital at Minia governorate from September 2018 to September 2019.

This study was designed to be open labeled, case control group matched; 35 adult OSA patients and 15 control persons were screened for by history, clinical examination ,sleep study, ABG, pulmonary function test, CRP and ESR .

In the present study there was no significant difference between the case group and the control group regarding age, sex, BMI and neck circumference. Regarding gender distribution, females were significantly more frequently affected than males. This comes in agreement with Pumarega, et al., who denoted a higher incidence of OSA among females than among males.[(12)]

Although it is known that OSAS is much more in males than females .[(13,14)]
The exclusion of smokers in our inclusion criteria seems to be another cause as smoking is less common in Egyptian females.

we found that 100% of group I was complaining of snoring and 88% of group I was complaining of daytime sleepness,65% of group I was complaining of witness apnea , and65% of group I was complaining of morning headache Patil ,et al study showed that snoring, excessive daytime sleepiness, and hypertension were found to be the most typical characteristics of OSAS[(15).]

Our study showed that there was significant elevation in CRP marker in case group versus control group in agreement with Visser, et al., who observed that the strong relationship between CRP levels and obesity may influence some studies investigating CRP levels in adult patients with OSAS where the populations investigated were not optimally matched for BMI.[(16)]

In our study there was also significant elevation in ESR marker in case group versus control group in agreement with Lee, et al Who observed that ESR was more closely correlated with PSG parameters recorded during sleep hypoxic episodes. Moreover, the ESR may be useful to predict the OSA severity because moderate and severe OSA were independently associated with an elevated ESR.[(17)]

Conclusion

Our study showed that there was significant elevation in CRP and ESR markers in case group versus control group.

Recommendation

It is known that our study had limited numbers of patients so, we recommend making studies on larger scale.

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