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Obstructive sleep apnea in pregnancy. Is it a new syndrome in obstetrics?

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ABSTRACT

Background: Sleep disordered breathing (SDB) is a frequent disorder and its severity superfats as pregnancy progresses. The exact prevalence or incidence of such disorder in pregnant women is still unknown.
Objectives: To assess the incidence and severity of OSA in pregnant women and to discover the risk factors for OSA during pregnancy.
Methods: A total of 30 pregnant women and 30 age matched controls completed Epworth Sleepiness Scale and Stop-Bang questionnaire. SDB diagnosis was based on polysomnography.
Results: The incidence of OSA among our studied pregnant women was 36.7% and 53.3% of pregnant women were snorers. They demonstrated significantly higher AHI (4.38 ± 4.45) and ODI (3.72 ± 4.03). There was a significant positive correlation between gestational age and ESS, BMI, AHI and ODI, as they are of their highest levels among cases in the third trimester. Binary logistic regression analysis showed that gestational age and body mass index were independent risk factors with odds ratio (2.23 & 4.99) and 95% CI (1.05–5.32 & 1.75–33.28) respectively while the neck circumference and ESS were considered as dependent risk factors.
Conclusion: Pregnancy is a risk condition for OSA which aggravated by neck circumference and base line BMI. The susceptibility and severity increase by increasing gestational age.

Introduction

Obstructive sleep apnea (OSA) is caused by repetitive obstruction of the upper airway during sleep, resulting in hypopnea (decreased airflow) or apnea (complete airflow cessation). Person with OSA may experience loud snoring, oxygen desaturation, frequent arousal and interruption of the sleep [1].

The prevalence of OSA is very variable according to different population groups being studied. The prevalence of OSA had been estimated to be 14% of men and 5% in women, in population based study utilizing an AHI cut off of ≥5 events/h combined with clinical symptoms to define OSA [2].

Several alternations in maternal physiology can affect breathing in pregnant women during sleep. Sleep quality is often poor. Sleep disruption due to leg cramp, low back pain, urinary frequency, or responsibilities related to child care. Total sleep time and day time sleepiness increase during the first trimester, meanwhile, sleep time diminished with increase in complain of nocturnal arousal increase in third trimester [1].

Hormonal changes of increased estrogen result in hyperaemia, upper airway narrowing and increase progesterone increase in respiratory drive, along with other physiologic changes of sleep (decreases FRC and respiratory system compliance) Predispose to alternation of sleep in pregnancy. Meanwhile snoring is more frequent in pregnant women and sleep related breathing disorders May get worse during pregnancy [3].

Polysomnography study had shown an increase in sleep latency, an increase in amount of stage 1 sleep and decease in rapid eye movement sleep and delta sleep, and also increase in number of a wakening [4].

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Although several restrictive lung factors similar to those associated with obesity are present in pregnancy, arterial oxygen saturation remains normal in pregnant women during sleep. Most sleep difficulty related to maintaining rather than initiating sleep. After child birth most parameters of sleep quality and architecture return to pre-pregnancy value, with possible exception of REM sleep [4].

Subjects and methods

A prospective cohort study was conducted on 30 pregnant cases recruited from Gynecology & Obstetric Department at Menoufia University Hospital, and 30 subjects as a control which are age matched with cases. Sleep questionnaire data were obtained from all subjects and they underwent complete diagnostic PSG evaluation in the Sleep disorders unit of Chest Department, Menoufia University hospital during the period from June 2015 to March 2017. This study was approved by the research ethics committee and a written consent was obtained from patients before the beginning of this work. There are no specific guidelines for screening pregnant women for SDB because the data are limited in this population.

Pregnant women with comorbid conditions, including chronic lung diseases, congestive heart failure, endocrinal, metabolic, hepatic, renal or neurological disorders and musculoskeletal deformities, also pregnant women with morbid obesity were excluded from our study.

On the day of the study and before electrode application the studied population completed a sleep questionnaires involved the list of their sleep-related symptoms, anthropometric measurements (height, weight & neck circumference), sleep habits, a list of their medications, STOP-BANG Questionnaire & lastly the Epworth sleepiness scale [5].

Stop-BANG Questionnaire is OSA screening tool. It is characterized by its feasibility and high sensitivity for OSA detection.

Epworth sleepiness scale is self-reported Questionnaire involved eight questions to assess the propensity for day time sleepiness or dozing.

Comprehensive antenatal care evaluation for pregnant cases: thorough gynecological history and physical examination that included the respiratory, cardiovascular, neurological and repro-

Table 1
Comparison between pregnant and non-pregnant females regarding all the studied parameters.

	Case N = 30	Controls N = 30	Test	P value
Age (years):			*t*-test	
X ± SD	30.4 ± 8.07	31.47 ± 6.96	0.55	0.59
Median	30.5	31.5		
Range	13–48	20–47		
Gestational age (weeks):				
X ± SD	23.03 ± 8.88			
Median	20			
Range	10–39			
ESS (0–24):			*U*	
X ± SD	7.0 ± 4.89	4.03 ± 2.52	2.32	0.02
Median	6	4		
Range	0–20	0–10		
Stop-Bang [n (%)]:			FE	
<3	23 (76.7)	30 (100)	7.93	0.01
>3	7 (23.3)	0 (0.0)		
BMI (kg/m^2):			*t*-test	
X ± SD	30.83 ± 6.43	26.77 ± 2.43	3.24	0.003
Median	29.5	27		
Range	22–44	22–32		
Neck circumference (cm):			*t*-test	
X ± SD	31.63 ± 6.45	26.23 ± 5.83	3.40	0.001
Median	33	23.5		
Range	20–39	20–36		
AHI:			U	
X ± SD	4.38 ± 4.45	1.77 ± 1.23	2.01	0.04
Median	2.5	1.5		
Range	0–15	0–4		
Oxygen desaturation index:			U	
X ± SD	3.72 ± 4.03	2.27 ± 1.11	2.30	0.02
Median	2.5	1.5		
Range	0–14.3	0–5		
Flow limitation index:			U	
X ± SD	9.48 ± 6.08	5.85 ± 4.28	2.49	0.01
Median	10	5.6		
Range	0–25	0–15.9		
Snoring index:				
X ± SD	8.19 ± 6.87	1.08 ± 1.75	4.56	<0.001
Median	8.3	0.0		
Range	0–32.9	0–7		
% of Sleeping time in supine position:				
X ± SD	48.91 ± 22.89	50.1 ± 33.94	0.04	0.97
Median	48.35	40		
Range	3–99	3–100		

FE = Fisher's Exact test, U = Mann Whitney *U* test.

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Table 2
Incidence of sleep related breathing disorders among the studied pregnant females.

	Cases N = 30	
	No	%
Sleep related breathing disorders (OSA):		
Positive	11	36.7
Negative	19	63.3
Snoring:		
Positive	16	53.3
Negative	14	46.7

ductive systems was done. Polysomnography is the standard diagnostic test for diagnosis of SDB. PSG was performed for all studied population. A full description of the study protocol was done by a well trained sleep technician was done for participant before beginning analysis. Overnight PSG was performed using (Embla S4000 Medicare, Iceland). The system has electrodes and cables to record the electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), electrocardiogram (ECG). Airflow was measured, also, nasal pressure transducer. Respiratory effort, Oximetry and Snoring were assessed. Body position was monitored using body position sensor. All studies were analyzed by trained PSG technicians and sleep physicians using the criteria of Rechtschaffen and Kales.

The apnea-hypopnea index (AHI) is number of apnea-hypopnea events per hour [6].

Statistical analysis

SPSS (Statistical package for Social Science) software was used for analysis of collected data. Quantitative data was expressed as mean, standard deviation and range, meanwhile the qualitative one was presented as number and percentage. Student *t* test was used to compare two groups of quantitative data when normal distribution of data was assumed, while Mann Whitney *U* test was used for that of non-normal distribution. When comparing three groups of not normally distributed quantitative data, Kruskal Wallis test was used. Chi square and Fisher's exact test were the tests for comparing qualitative data. Spearman correlation coefficient was used to correlate between both age & BMI and sleep disorder parameters. Finally, the multi variate regression analysis was done to assign the independent risk factors for sleep disorders in pregnant women. P value was considered significant when less than 0.05 [7].

Results

A prospective study was done on 30 pregnant cases and 30 age matched controls with a mean maternal age of 30.4 ± 8.07 and 31.47 ± 6.96 years respectively. The mean gestational age in the pregnant cases group was 23.03 ± 8.88 weeks. The pregnant cases demonstrated significantly higher BMI, neck circumference, ESS and AHI. Furthermore, oxygen desaturation index, flow limitation index, snoring index and STOP–BANG Questionnaire >3 had also significantly higher values among pregnant cases than controls. But there was non-significant difference between cases and controls regarding the percentage of sleeping time in supine position (Table 1).

The incidence of sleep related breathing disorders among our studied pregnant females was 11/30 (36.7%) and 16/30 (53.3%) of the pregnant cases were snorers (Table 2).

Table 3
Comparison between negative and positive pregnant cases regarding sleep related breathing disorders:

	Sleep related breathing disorders		Test	
	Positive N = 11	Negative N = 19	*U*	P value
Age (year):				
X ± SD	31.81 ± 8.18	29.57 ± 8.10	0.73	0.46
Range	19–47	13–48		
Gestational age (weeks):				
X ± SD	28.91 ± 6.92	19.63 ± 8.21	2.72	0.007
Range	16–39	10–39		
ESS (0–24):				
X ± SD	12.0 ± 2.93	4.10 ± 3.13	4.32	<0.001
Range	9–20	0–10		
STOP-BANG Questionnaire [n (%)]:			FE	
<3	4 (36.4)	19 (1 0 0)	15.77	<0.001
>3	7 (63.6)	0 (0.0)		
BMI (kg/m^2):				
X ± SD	35.09 ± 5.09	28.37 ± 5.89	2.97	0.003
Range	27–42	22–44		
Neck circumference (cm):				
X ± SD	35.0 ± 3.19	29.68 ± 7.10	4.50	<0.001
Range	30–39	20–39		
Oxygen desaturation index:				
X ± SD	9.57 ± 2.55	1.60 ± 1.19	4.50	<0.001
Range	6–14	0–4.5		
Flow limitation index:				
X ± SD	13.09 ± 6.20	7.39 ± 5.06	2.35	0.02
Range	1–25	0–15		
Snoring index:				
X ± SD	13.02 ± 7.62	5.40 ± 4.46	2.71	0.007
Range	6.5–32.9	0–11		
% of Sleeping time in supine position:				
X ± SD	47.74 ± 20.45	49.58 ± 24.71	0.26	0.80
Range	15.9–78.8	3–99.1		

FE = Fisher's Exact test, U = Mann Whitney *U* test.

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The sleep related breathing disorders were significantly related to higher gestational age, larger BMI and neck circumference, higher ESS and higher percentage of STOP–BANG Questionnaire >3. The pregnant cases with sleep related disorders showed significantly higher oxygen desaturation index, flow limitation index and snoring index (Table 3).

Pregnant snorers revealed significantly higher AHI, ODI, ESS, and Stop-BANG Questionnaire >3. However non-significant association was reported regarding age, gestational age, BMI, neck circumference, flow limitation index, and percentage of sleeping time in supine position (Table 4).

ESS, percentage of Stop-BANG Questionnaire >3, AHI, oxygen desaturation and percentage of sleep related breathing disorders increased significantly with increasing gestation age among pregnant females as they were of their highest levels among cases in the third trimester (Table 5 & Fig. 1).

A significant positive correlation between gestational age and each of ESS, BMI and oxygen desaturation index while there was non-significant correlation between gestational age and neck circumference and% of sleeping time in supine position (Table 6).

Binary logistic regression analysis for independent risk factors of SDB during pregnancy revealed that gestational age and body mass index were the independent risk factors with odds ratio (2.23 & 4.99) and 95% CI (1.05–5.32 & 1.75–33.28) respectively (Table 7).

Discussion

Since the first retrieved case report of OSA in pregnancy in 1978 [8], there are several association between OSA and pregnancy. The exact prevalence of OSA in pregnant women is unknown. The severity of SDB increases as pregnancy progresses.

The aim of this work was to assess the incidence and severity of (OSA) in the pregnant population, and to explore the risk factors for OSA in pregnancy.

A prospective study was done on 30 pregnant cases and 30 age matched control with mean maternal age (30.4 ± 8.07 & 31.47 ± 6.96) year respectively. While mean Gestational age was (23.03 ± 8.88) week. All were primigravid. Based on BMI: BMI mean was 29.5 (range 22–44) and 27 (26.77 ± 2.43) for pregnant and non-pregnant women respectively, Sleep characteristics: sleep apnea diagnosis was made on PSG, 11/30 (36.7%) of pregnant women had mild OSA, while16/30 (53.3%) were snorer. Mean AHI, DI, snoring index were 2.5 (range 0–15), 2.5 (range 0–14.3), 8.3 respectively in pregnant women, compared to non-pregnant women (1.77 ± 1.2), (2.27 ± 1.11), and (1.08 ± 1.75) respectively, The cases demonstrated significantly higher BMI, AHI, ODI, furthermore snoring index. However mean AHI was (1.60 ± 1.56) in first trimester, (3.35 ± 4.08) in second, and (6.80 ± 4.76) in third trimester. Our data revealed that AHI increased significantly with increasing gestational age among pregnant female as they were of their highest level among cases in third trimester.

Data from 22 papers containing information on 47 pregnancies among 43 women. Baseline characteristics: Mean age was 29.1 yr (range 22–39 yr). All pregnancies were singleton. 57% were obese or morbidly obese, 14% were overweight, 24% had normal weight, and 5% were underweight. Sleep apnea diagnosis was made on clinical grounds alone in 12, on polysomnography and clinical features prior to pregnancy in 12; in the first trimester in 5, in the last trimester in 5, postpartum in 6. All but three had obstructive sleep apnea. Two had exclusively central apneas. One had mixed pre-

Table 4
Comparison between negative and positive pregnant cases regarding snoring.

	Snoring		Test	
	Positive N = 16	Negative N = 14	U	P value
Age (years)				
X ± SD	31.63 ± 7.54	29.0 ± 0.69	1.06	0.29
Range	13–48	13–48		
Gestational age (weeks):				
X ± SD	25.19 ± 8.62	20.19 ± 8.85	1.42	0.16
Range	10–39	11–39		
ESS (0–24):				
X ± SD	9.38 ± 5.04	4.29 ± 3.05	2.82	0.005
Range	1–20	0–10		
Stop-BANG questionnaire [n (%)]:			FE	
<3	9 (56.2)	14 (1 0 0)	7.93	0.01
>3	7 (43.8)	0 (0.0)		
BMI (kg/m^2):				
X ± SD	32.94 ± 7.07	28.43 ± 4.78	1.77	0.08
Range	22–44	23–38		
Neck circumference (cm):				
X ± SD	31.81 ± 6.74	31.43 ± 6.35	0.21	0.84
Range	20–39	20–39		
AHI:				
X ± SD	6.81 ± 4.84	1.60 ± 1.23	1.58	0.01
Range	0–15	0–4		
Oxygen desaturation index:				
X ± SD	6.92 ± 4.60	1.79 ± 1.22	2.71	0.007
Range	0–14.3	0–4.5		
Flow limitation index:				
X ± SD	11.03 ± 6.77	7.71 ± 4.83	1.33	0.18
Range	0–25	1–15		
% of Sleeping time in supine position:				
X ± SD	45.73 ± 20.86	52.53 ± 25.3	0.89	0.37
Range	15.6–78.8	3–99.10		

FE = Fisher's Exact test, U = Mann Whitney *U* test.

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Table 5
Comparison between pregnant cases regarding the gestational age.

	Trimester			Test	
	First N = 6	Second N = 12	Third N = 12	U	P value
Age (years)					
X ± SD	29.0 ± 5.18	30.67 ± 9.15	30.83 ± 8.62	1.06	0.29
Range	21–36	13–47	19–48		
ESS (0–24):					
X ± SD	2.33 ± 2.07	5.83 ± 3.97	10.50 ± 4.34	12.42	0.005
Range	0–6	0–12	3–20		
Stop hanging [n,%]:				FE	
<3	6 (1 0 0)	12 (1 0 0)	5 (41.7)	13.70	0.001
>3	0 (0.0)	0 (0.0)	0 (58.3)		
BMI (kg/m^2):					
X ± SD	26.67 ± 1.63	29.67 ± 6.83	34.08 ± 6.21	1.77	0.08
Range	25–29	22–39	27–44		
Neck circumference (cm):					
X ± SD	27.83 ± 6.85	31.25 ± 6.86	33.92 ± 5.25	0.21	0.84
Range	21–36	20–39	22–39		
AHI:					
X ± SD	1.60 ± 1.56	3.35 ± 4.08	6.80 ± 4.76	1.58	0.01
Range	0–4	0–12	0.7–15		
Oxygen desaturation index:					
X ± SD	1.38 ± 1.48	3.91 ± 4.08	6.71 ± 4.45	2.71	0.007
Range	0–3.6	0.5–12	0.6–14.3		
Flow limitation index:					
X ± SD	1.67 ± 2.79	5.38 ± 4.12	8.4 ± 3.29	1.71	0.09
Range	0–7.3	0.2–15	4.3–15.9		
% of Sleeping time in supine position:					
X ± SD	52.8 ± 22.85	50.15 ± 21.75	45.73 ± 25.50	0.89	0.37
Range	32–85.9	3–81	15.6–99.1		
Sleep related breathing disorders:					
Positive	0 (0.0)	3 (25.0)	8 (66.7)	8.83	0.01
Negative	6 (1 0 0)	9 (75.0)	4 (33.3)		
Snoring:					
Positive	2 (33.3)	5 (41.7)	9 (75.0)	3.88	0.14
Negative	4 (66.7)	7 (58.3)	3 (25.0)		

FE = Fisher's Exact test, U = Mann Whitney *U* test.

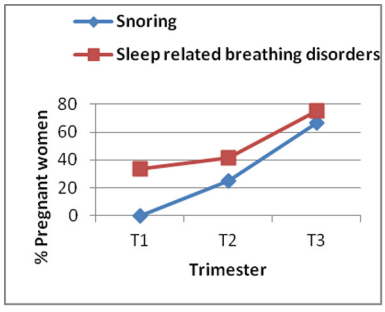

Fig. 1. Prevalence of sleep related breathing disorders and snoring among pregnant women in relation to the gestational age.

Table 6
Correlation between gestational age and (AHI – OD – snoring index – flow limitation index – % of sleep in supine position).

	Gestational age	
	R	P value
ESS:	0.58	0.001
BMI:	0.48	0.008
Neck circumference:	0.25	0.19
Oxygen desaturation index:	0.45	0.02
Flow limitation index:	0.69	<0.001
Snoring index:	0.34	0.07
% of sleeping time in supine position:	−0.07	0.72

senting in the context of hypothyroidism combined with a lingual thyroid66.polysomnography results, OSA was severe in 16, moderate in 9, mild in 4, unspecified in three. The saturation was below 90% in 27of 28 parturient, below 80% in 13, and below 50% in 6 [9–12].

Louis et al. [13] also reported that Obstructive sleep apnea rates rise to 11–20% of pregnant women, with the highest rates seen in obese women.

Izci et al. [14] postulated that the incidence of habitual snoring increases in pregnancy, affecting 10–35% of pregnant women especially during the third trimester.

There are several studies on snoring and other symptoms suggestive of OSA during pregnancy, conducted in different countries, all confirming the increase in snoring and OSA symptoms from pre-pregnancy status to the end of pregnancy or among pregnant women compared to non-pregnant women [15,16].

Increased airway resistance may occur due to increased estrogen and progesterone hormonal levels that induce mucosal edema of the upper airway [15]. These changes may lead to narrowing of upper airways [17]. Thus, pregnant women with narrowed airways are more likely to snore and more liable to have obstructed breathing during sleep compared to non-pregnant women and the snoring frequency and severity increase with increasing gestational age [18]. Larger neck circumference and high baseline BMI in pregnant women will increase symptoms of SDB [15]. Hirnle et al. [17] clarified the physiologic changes in pregnancy which increase the risks of SDB like weight gain, increased edema and mucus production in

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Table 7
Multivariate analysis regarding the factors that leads to sleep disorders breathing in pregnant women.

	SE	Wald X^2	P value	Odds ratio	95% CI (lower-upper)	
Gestational age:	0.08	6.70	0.01	2.23	1.05	5.32
BMI:	0.97	2.76	0.009	4.99	1.75	33.28
Neck circumference:	0.09	1.63	0.09	1.01	0.23	4.33
ESS (Epworth sleepiness score):	0.12	0.89	0.45	0.99	0.44	7.65

CI = confidence interval.

the nasopharyngeal passages and upper airway narrowing in the third trimester. These changes decreased functional reserve capacity by 10–20% at term.

Regarding cardiovascular changes, maternal blood volume also expands by 40–50% over baseline by the third trimester. The combination of increased blood volume, interstitial fluid and recumbent position during sleep leads to nasal congestion and displaces fluid that could diminish upper airway patency [15].

In late pregnancy, airway closure results in ventilation–perfusion mismatch and diminished gas exchange [18], especially in the supine position, due to gravity, intra-abdominal pressure and loss of muscle tone during sleep [14,15].

Oxygen consumption increases during pregnancy by 20%, in addition, minute ventilation also increases by 30–50%, there for the needed increased diaphragmatic effort will create negative inspiratory pressure on the hyperaemic upper airway that may induce obstructive respiratory events [18,19], along with consequential respiratory alkalosis, may give rise to instability in respiratory control pathways and relatively increase the likelihood of central apnea episodes at sleep onset and during sleep [16,19].

Predictors of pregnancy related SDB

The results of the current work showed, by Binary logistic regression analysis, that gestational age and body mass index were the independent risk factors for SDB with odds ratio (2.23 & 4.99) and 95% CI (1.05–5.32 & 1.75–33.28) respectively.

Similar results were found by Louis et al. [14] & Facco et al. [18], they documented that, Epworth Sleepiness Scale is poorly predictive of a positive test for OSA in pregnancy. Conversely, several studies have documented that the combined presence of snoring and elevated BMI increases predictive value of OSA and the risk increases in the third trimester.

Data from larger observational and international studies to assess association between pregnancy and sleep disordered breathing, Schoenfeld et al. [19], had studied Eleven pregnant women with a BMI > 30 were compared to 11 pregnant women with a normal BMI for OSA as determined by a polysomnography performed at 15 and 34 week of gestation. The mean AHI were higher for the obese group though every woman had an index below 10 on the first polysomnography, On the second polysomnography, the mean AHI was higher for obese and one reached an index above 10, the threshold for OSA in the study [19,20]. One abstract reports the preliminary results of a longitudinal study on incident OSA during pregnancy. Seventy-one pregnant women with a mean body mass index of 28 had a polysomnography in the first and again in the third trimester, the incidence of OSA increase by 3 folds in the third trimester than the base line measures in the first trimester [20].

This suggests that obstructive sleep apnea is rare in healthy, normal women with low-risk pregnancy and that pregnancy is a risk factor for incident OSA, especially among obese women [4].

Limitation of the study

Our research study that evaluated SDB during pregnancy was limited by small sample size and limitations of study design to draw definite conclusions. PSG requires pregnant women to spend the night under observation in foreign environment, with difficulty to repeat the study in another setting if needed. Our study excluded pregnant women with comorbid condition including cardiopulmonary diseases, endocrinal metabolic or neurological disorders.

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