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Obstructive Sleep Apnea in Pregnant Women

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Abstract
Background: *Obstructive sleep apnea is referred to as sleep disordered breathing due to complete or partial obstruction of upper respiratory tract while sleeping by the abnormal relaxation of throat muscles lying posteriorly. The prognosis of the disease worsens in pregnancy as the airway obstruction varies due to various hormonal and physiological changes associated with pregnancy therefore causing deterioration of the quality of sleep and snoring.The purpose of this article was to give a review of the literature on the obstructed sleep apnea in pregnant women.*
Methods: *Review of articles including the case series, case reports, retrospective case control study, various clinical trials and RCTs available on pubmed, sci-hub and medline database within the range of past 10 years has been performed for better analysis excluding the articles which were not including the specifications regarding OSA in pregnancy.*
Data on women's age, ethnicity, parity, BMI, alcohol or drug use status, season, history and presentation of other diseases were taken from medical records.
Results: *The mean number of consenting women (n=451) were chosen for analysis. Therefore, it was concluded that the median of age of women at diagnosis is 27.19 years. The median of gestational age of women is found to be 24.9 weeks. There is no prevalent association with asthma(0.6%) and anemia(1.3%) but was strongly influenced by the modern prevailing smoking and drinking habits. Hypertension was common in 10% of women.*
Conclusion: *Due to some characteristics being specific to pregnancy, sleep disordered breathing and OSA are both diagnosed and treated differently in pregnant and non-pregnant women. Additionally,it is found that the risk of OSA increases with GDM in late 2nd-early 3rd trimester. Also there is a prevalent risk of gestational HTN and rare medical and surgery complications including cardiomyopathy, pulmonary edema, CHF and hysterectomy.There is no consensus on treatment of OSAS, henceforth, it should be multidisciplinary based on underlying cause.*

Keywords
Obstructive sleep apnea (OSA), pregnant women, obese, preterm, gestational diabetes, insulin resistance, pre-eclampsia, berlin questionnaire, Screening questionnaire, Stop-Bang questionnaire, hypertension, snoring, oxidative stress, sleep disordered breathing (SDB).

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I. Introduction

Obstructive sleep apnea (OSA), a common sleep-related breathing disorder, occurs when the throat muscles relax at irregular intervals and block the airway during sleep. It is characterized by recurrent collapse or blockage of the pharynx during sleep that causes intermittent cessation of airflow and a hallmark snoring-gasping pattern[1]. Women diagnosed with OSA during pregnancy likely represent one of two distinct clinical phenotypes: women with pre-existing OSA that become pregnant (chronic OSA); and pregnant women who develop OSA (gestational OSA). The prevalence of obstructive sleep apnoea in women aged 30–39 years is approximately 6.5%, with moderate or severe obstructive sleep apnoea affecting 1– 5%[2]. Women with OSA may enter pregnancy with snoring, and develop worsening airway obstruction due to physiologic and hormonal changes of pregnancy or in association with other comorbidities developed in pregnancy (multiple gestations, hypertensive disorders of pregnancy, or gestational diabetes). Patients with OSA commonly had decreased quality of life. In particular, OSA affects sleep quality and duration of sleep in pregnant women[1]. Unfortunately, 93% of women with moderate-to-severe OSA have never been diagnosed with the condition[3]. The treatment

commonly includes Continuous positive airway pressure (CPAP) therapy which is a safe and effective way to reduce the risks of sleep apnea before, during, and after pregnancy. Using a comprehensive meta-analysis, this study aimed to review and examine the risks of OSA in pregnant women.

II. Methods

Informed consent forms were used containing information about procedures, benefits and risks of participation. An explanation on how to acquire the results of the research, availability of counselling services, voluntary participation, and contact information of the researchers were taken into consideration. The purpose of the study was also on the consent form.

A systematic literature search was performed on PubMed, Medline and Google scholar database including the case series, case reports, retrospective case control studies, various clinical trials and RCTs to identify all studies published between 2012 till 2022, which investigated the association between OSA in pregnant women. Additionally, references of some systematic reviews and Randomised control trials were also explored for relevant articles. Advanced search was used in PubMed to collect all the original studies. The syntaxes which were used to collect the relevant articles were a) obstructive sleep apnea in pregnant women, b) obstructive sleep apnea in pregnant women AND clinical findings, c) obstructive sleep apnea in pregnant women AND symptoms and d) obstructive sleep apnea in pregnant women AND treatment

Inclusion criteria

The studies a) which investigated Obstructive sleep Apnea and its clinical findings, b) which examined its treatment and management plan and c) which included pregnant women met the inclusion criteria.

Exclusion criteria

studies a) which involved animal models and b) which were in languages other than english were excluded

Data extraction

Reviewers extracted data individually referring to all the published articles about OSA. The following information was extracted from all the relevant studies: first author, year of publication, country, study design, number of participants, age at diagnosis, gestational age, parity, neck circumference, breast circumference, mallampati class and total sleep time. Outcomes examined included morning headache, snoring, daytime sleepiness, obstructed nasal passage, anaemia, obesity, diabetes, asthma, hypertension and hyperlipidemia. progression to other diseases and symptoms were also recorded. Lab values including blood test, TSH levels, Oxygen saturation, insulin resistance, cortisol levels, spo2, AHI and ODI scores were also mentioned. Smoking and drinking habits were also considered. Discharge disposition and treatment given to the participants were recorded.

mean was the first choice during data collection of lab values. When the mean value was not available, the median of the data was calculated.

III. Results

Around 284 potentially relevant studies met our initial criteria. Out of 284 we removed the studies which were not about the topic or didn't report the desired outcome or studies which were published before 2012. 44 articles with full text were reviewed (Search flow chart is presented in fig.1. Characteristics of the included articles are summarized in table 1.

Based on geographical region, 23 studies we included were from the USA, 5 studies were from Thailand and 4 from Turkey. There were 2 studies from Taiwan and Australia as well. Apart from these, there was one study each from Canada, Peru, Korea, Egypt, France, Iran, Spain and South Africa. In terms of study design, 32 were case reports, 20 case reviews and 11 case series. There were more than 1 outcome in most of the studies.

The mean number of consenting women which were chosen for analysis were 451. The median of age of women at diagnosis was 27.19 years and the median of gestational age of women was found to be 24.9 weeks. There was cesarean delivery in some women as indicated in 12 studies.

Based on the pooled studies, snoring was significantly associated with OSA in pregnant women in 52.27% studies. Obesity, Diabetes and Hypertension also showed a significant association with data in 54.54%, 72.72% and 65.90% studies respectively. 25% studies showed association with daytime sleepiness, 15.90% with obstructed nasal passage, 40.90% with pre-eclampsia, 11.36% with anemia and 4.54% with hyperlipidemia. There was also an association of OSA in pregnant women with Smoking and Drinking as indicated in 50% and 25% studies respectively.

Apart from these, there were other diseases like sleep apnea, acute renal failure, pulmonary embolism, pulmonary edema, cardiovascular diseases like congestive heart failure, cardiomyopathy and

coronary heart disease which were associated with OSA in pregnant women. Cases of insomnia, depression, thrombocytopenia, hypoxia and restless leg syndrome were also seen in some studies.

Fig.1 Search flow chart

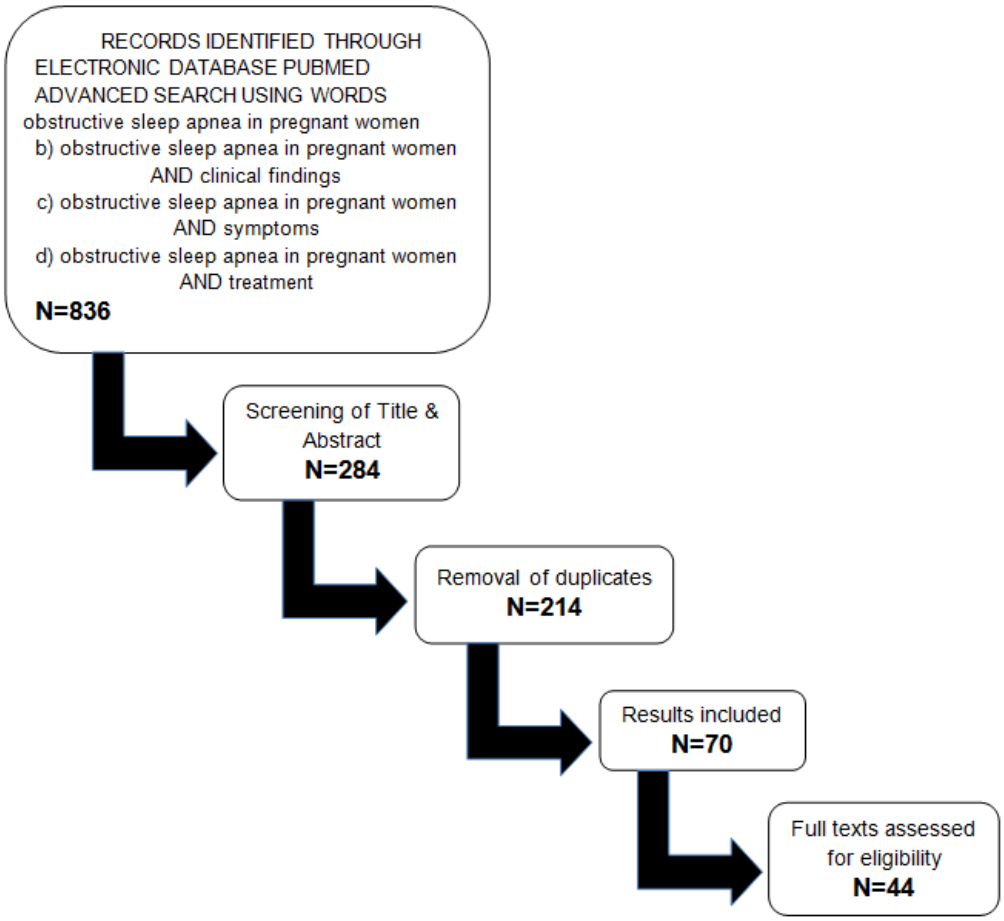

Table.1 Characteristics of the given Articles

S.No	Author	Year	No. of Participants	Age at diagnosis	Gestational Age	Month/ Season	Country
1	Yi-Hua Chen	2012	791	14-45 years	24- 41 weeks	NA	Taiwan
2	Jessica M Booth	2017	105	30-35 years	1-3rd trimester	NA	USA
3	Margaret H Bublitz	2018	25	median-30.5 years	28 weeks	NA	USA
4	Nattapong Jaimchariyatam	2019	1350	18-35 years	18.1 weeks	July	Thailand
5	L M O'Brien	2014	51	>14 years	NA	March	Canada
6	Jayne R Rice	2015	1032	mean=28.6 years	24-28 weeks	February	Peru
7	Nazia Khan	2018	64	18-42	39 weeks	NA	USA
8	Ghada Bourjeily	2015	40	28.9	n=16 1st trimester n=24 2nd trimester	NA	USA
9	Anna W Kneitel	2018	48	mean=32 years	33 weeks	April	USA
10	Visasiri Tantrakul	2015	72	mean=34.8 years	22.6 weeks	July	Thailand
11	Ellen M Lockhart	2015	293	20-30years	27 weeks	NA	USA
12	Hyun Sun Ko	2012	276	20-45	28-42 weeks	NA	Korea
13	RanaEl-Helbawy	2017	30	19-47	16-39 weeks	NA	Egypt
14	Linda M. Street	2018	73	31.8	32-35 weeks	April	North Carolina, USA

15	Bilgay Izci Balserak	2020	125	18-42 years	24-36 weeks	NA	Chicago, USA
16	Judette M	2014	NA	NA	NA	NA	USA
17	Sarah S Farabi	2019	18	20-39 years	32-34 weeks	NA	Colorado, USA
18	Farahnaz Keshavarzi	2018	38	21-35	30-39 weeks	June	Iran
19	Nattapong Jaimchariyatam	2018	136	<20 - >35	mean= 18 weeks	July	Thailand
20	L. Ghesquière	2020	67	30.5	24-32 weeks	NA	Jeanne de flandre, FRANCE
21	Mevlüt Karaduman	2016	257	30 +/- 5 years	24-28 weeks	April	Turkey
22	Dennis L.Spence	2017	266/305001	30 +/- 6 years	NA	October	Turkey
23	Ana M. Fernández Alonso	2015	367	20-30 years	39 weeks	January	Spain
24	Kunyalak Na-rungsri	2016	1345	20-35 years	14-27 weeks	July	Thailand
25	NC Lintott	2017	234	25-36 years	>20-<35	February	south africa
26	K M Antony	2014	1157	18-50 years	1-3 trimester	May	Harris country, USA
27	Alison M Fung	2013	371	36 years	24-32 weeks	May	Australia
28	K M Antony	2014	1509	18-50 years	1-3rd trimester	May	Harris country, USA
29	Fiona Pearson	2019	117	18 0r more that 18 years	20 weeks	february-august	USA
30	Ismail Arslan	2022	143	(18–40) years	36 weeks	February 2015–2016	Turkey,
31	Ayana Telerant	2018	155	34	25-27 weeks	June 2008 and December 2010	USA
32	T.Carbone	2013	115	34 years	NA	June 2009 and March 2012	USA
33	Francesca Facco	2018	34	NA	21 weeks' gestation	NA	USA
34	Karen Redhead	2020	189	>18 years	26 weeks	April- december	Australia
35	Ekasitt Wanitcharoenkul	2017	82	31.4	24-34 weeks	April 2014 to June 2016,	Thailand
36	Ghada Bourjeily	2020	1739	32.5	34-<37 weeks	NA	USA
37	Jennifer Lee	2017	27	29.6	26 weeks	NA	USA
38	Ghada Bourjeily	2017	1963	32.3	NA	NA	USA
39	Bilgay lzci Balserak	2018	126	NA	37 weeks	NA	USA
40	Yi-Hua Chen	2012	3955	(20-35) years	<37weeks	NA	Taiwan
41	Yasemin Üstündağ	2019	29	27-35 years	33-39 weeks	September	Turkey
42	Ghada Bourjeily	2016	321	28.9 years	34-42 weeks	NA	USA
43	LM O' Brien	2014	181	30-39 years	NA	NA	USA
44	Jennifer E, Dominguez	2018	108	30-39 years	24-35 weeks	NA	USA

IV. Discussion

In our study, we analyzed that risk factors for OSA were BMI and Insulin resistance, diabetes mellitus[65]. BMI is a strong predictor of OSA in pregnancy, approximately 15%-20% of obese pregnant women are estimated to have OSA, which is associated with more frequent pre-eclampsia and cesarean delivery[4]. CPAP therapy for OSA significantly improved maternal and fetal outcomes. Literature to support the use of CPAP to prevent adverse pregnancy outcomes for OSA patients is not yet widely available. There is 17% prevalence of OSA in a cohort consisting mainly of multigravida, multiparous, Caucasian women with GDM[5]. Although

preeclampsia-eclampsia and OSA share common risk factors such as increased maternal age and obesity. We found that high risk for OSA remained the independent risk factor for preeclampsia-eclampsia after adjustment for co-founders. These observations, when coupled with previous reports, have important clinical and replica health implications because pregnant women with symptoms of OSA are at higher risk of preeclampsia-eclampsia[6]. Snoring is considered to be an excellent marker in clinical practice for this condition. Interestingly, in women with hypertension, the timing of snoring onset appeared to be related to hypertension type. Women who reported chronic snoring were most likely to have chronic HTN, whereas those who reported the onset of snoring during pregnancy were more likely to have gestational HTN[2]. In the 2nd and 3rd trimesters, pregnant women are more likely to have frequent awakenings due to fetal movements, discomfort, backaches as well as frequent urge to urinate due to enlarged uterus[7]. Additionally, pregnancy induces many physiological changes. These include enlargement of the uterus which can elevate the diaphragm and alter respiration. These alterations, for instance, may increase the tendency for collapsing the upper airway during sleep. Changes in hormones also predispose pregnant women to episodes of sleep apnea. Notably, increased estrogen concentration has been linked to increased respiratory center sensitivity to carbon dioxide, therefore causing instability of the Respiratory Control mechanism. Oxidative stress related to repetitive episodes of hypoxia and reoxygenation has been proposed as one of the hypothetical mechanisms underlying this association[8].

Pregnant women with OSA have higher levels of antioxidant capacity and lower levels of oxidative & carbonyl stress markers in the second trimester when compared to pregnant women at low risk for OSA and sleep-disordered breathing at a similar stage in pregnancy. The effect of CPAP as a potential confounder of our results could not be evaluated. Several case reports[9] and small pilot studies[10,11] have utilized PAP therapy in pregnancy & while none has specifically investigated fetal growth. Treatment of OSA in the non-obstetric population has clear benefits including improvements in systemic HTN, ventricular function and management of non-insulin dependent diabetes mellitus[12]. The following elements were significant objective measurements [BMI, neck circumference], medical comorbidities [treatment for high blood pressure, diabetes, asthma] and symptomatic components [snoring, stop breathing during sleep, fall asleep while sitting and talking with someone, awaken from sleep with choking sensation, frequent arousals from sleep]. Screening for OSA in pregnancy is difficult because of the lack of sensitivity and specificity of tools developed in the non-pregnancy population.

Clinical Presentation

In the papers we reviewed, patients showed common symptoms such as snoring (52.2%), obesity (54.5%), hypertension (68%), diabetes (75%) and daytime sleepiness (22%). Obstructive sleep apnea affects a significant percentage of pregnant hypertensive women. In clinical practice, snoring might be a great indicator of this condition. It is suggested that pregnant women who snore and have hypertension should be thoroughly examined for underlying obstructive sleep apnea. Also, patients are more likely to develop sleep disordered breathing because of the inherent physiological changes that occur during pregnancy and because of maternal obesity that might already exist.

Some fewer common symptoms shown by pregnant women suffering from OSA were morning headache (4.5%), obstructed nasal passage (18%), anemia (11.3%), hyperlipidemia (4.5%). Some pregnant women with OSA showed significant adverse outcomes like myocardial infarction, stroke, hypertension, cesarean delivery, preterm delivery and preeclampsia–eclampsia. Predictors of decreased fetal growth include maternal OSA, particularly a slowdown in fetal growth during the third trimester. Preterm birth is also more likely in parturients with OSA, which increases the risk of maternal and neonatal morbidity and mortality overall. There is biological support for the link between OSA and preeclampsia-eclampsia, and it is most likely multifactorial. OSA causes inflammation, autonomic dysfunction, oxidative stress, and altered hormonal regulation of energy expenditure. Adverse pregnancy outcomes are also discovered to be linked to these pathways.

There are certain risk factors to keep in mind which can increase the chance of OSA being developed. The risk factors are smoking (50%), drinking (25%) and sedative usage. Studies have shown that pregnant women with OSA had greater rates of cesarean deliveries than pregnant women without OSA, and they also have a higher risk of preterm birth, which increases the overall risk of maternal and neonatal morbidity and mortality.

Diagnosis

Diagnosis of OSA depends on the average number of apnoeas and hypopneas episodes per hour of sleep, often referred to as apnoea hypopnoea index (AHI). OSA is diagnosed when there are clinical symptoms plus AHI ≥ 5 or AHI ≥ 15 regardless of symptoms[13]. At the initial prenatal appointment, it is frequently advised that obese pregnant women (with a BMI > 29) should be tested for OSA and it is advisable to have a proper history, perform related physical exam and any necessary clinical investigations. A first trimester assessment,

however, may not be enough, according to current study, as the symptoms of sleep disordered breathing may intensify in tandem with pregnancy's physiological changes.

A polysomnogram performed overnight is the gold standard for the diagnosis of OSA (PSG). The in-lab sleep study connects oxygen saturation, thoracic and abdominal wall motion, electroencephalogram, electromyogram, and electrooculogram activity[14]. In high-risk pregnancies such as those with preeclampsia, diabetes, or persistent hypertension, a polysomnography should be done. In such high-risk pregnancies, the sensitivity and specificity of sleep surveys also need to be assessed together[15]. The drawback of PSG is that the expectant women spend the night under observation in an unfamiliar situation, with the challenge of repeating the study in a different location if necessary[16]. The mechanism of PSG involves a RUSleeping (RUS) monitor which is placed on the face of the patient and tracks changes in nasal pressure to identify respiratory episodes. It provides an hourly and cumulative AHI score and has been categorized as a single-channel American Sleep Disorders Association (ASDA) level IV device[13]. The positive screening value, which was used to illustrate the possible advantages of additional research into OSA, was an RUS meter AHI score 15[13].

Other diagnosis methods include: (i) Exhaled nitric oxide gas has proven to be better sensitivity and specificity when combined with Malampatti score and screening tools specific to pregnancy[14]. and (ii) The most commonly used screening questionnaires for OSA include the Berlin and the Epworth Sleepiness Scale(ESS) questionnaires. The dependence on women or partners to report snoring, variability in sample characteristics (low and high risk for OSA, and type of risk), varies in the objective sleep measures[15] and the inability to determine true associations between OSA and adverse neonatal outcomes without conducting a large, prospective analysis with diagnosis confirmation by polysomnography are some of the limitations of previous studies.

S.NO.	NO. OF PARTICIAPNTS	GESTATIONAL AGE	LAB VALUES (BLOOD)(mean values)						
			LEUCOCYTES	HAEMOGLOBIN	PLATELETS	GLUCOSE	TSH LEVELS	OXYGEN SATURATION	INSULIN RESISTANCE
1.	791	24- 41 WEEKS	NA	NA	NA	NA	NA	NA	NA
2.	105	1-3RD TRIMESTER	NA	NA	NA	NA	NA	NA	NA
3.	25	28 WEEKS	NA	NA	NA	NA	NA	95.5	13.64
4.	1350	18.1 WEEKS	NA	NA	NA	NA	NA	NA	NA
5.	51	ANY	NA	NA	NA	NA	NA	NA	NA
6.	1032	24-28 WEEKS	NA	NA	NA	NA	NA	NA	NA
7.	64	39 WEEKS	NA	NA	NA	NA	NA	84%	NA
8.	40	N=16 1ST TRIMESTER N=24 2ND TRIMESTER	NA	NA	NA	NA	NA	NA	NA
9.	48	33 WEEKS	NA	NA	NA	NA	NA	NA	NA
10.	72	22.6 WEEKS	NA	NA	NA	122.4	NA	NA	CALCULATED
11.	293	27 WEEKS	NA	NA	NA	NA	NA	NA	NA
12.	276	28-42 WEEKS	NA	NA	NA	NA	NA	NA	NA

13.	30	16-39 WEEKS	NA	NA	NA	NA	NA	NA	NA
14.	73	32-35 WEEKS	NA	NA	NA	NA	NA	NA	NA
15.	125	24-36 WEEKS	NA	NA	NA	NA	NA	NA	NA
16.	NA	NA	NA	NA	NA	NA	NA	NA	NA
17.	18	32-34 WEEKS	NA	NA	NA	76	NA	NA	18129.6
18.	38	30-39 WEEKS	NA	NA	NA	NA	NA	NA	NA
19.	136	MEAN= 18 WEEKS	NA	NA	NA	NA	NA	NA	NA
20.	67	24-32 WEEKS	NA	NA	NA	NA	NA	NA	NA
21.	257	24-28 WEEKS	NA	NA	NA	NA	NA	NA	NA
22.	266/305001	NA	NA	NA	NA	NA	NA	NA	NA
23.	367	39 WEEKS	NA	NA	NA	NA	NA	NA	NA
24.	1345	14-27 WEEKS	NA	NA	NA	NA	NA	NA	NA
25.	234	>20-<35WEEKS	NA	NA	NA	NA	NA	NA	NA
26.	1157	1-3 TRIMESTER	NA	NA	NA	NA	NA	NA	NA
27.	371	24-32WEEKS	NA	NA	NA	NA	NA	>3% PER HOUR	NA
28.	1509	1-3 TRIMESTER	NA	NA	NA	NA	NA	NA	NA
29.	117	20 WEEKS	NA	NA	NA	76	NA	>5/HOUR	NA
30.	143	36 WEEKS	NA	LBW=11.69 ± 1.02 ; NBW=11.72 ± 1.35	LBW 239.6 ± 54.2; NBW 241.5 ± 65.4	LBW=88.27 ± 19.89 NBW =81.56 ± 13.82	NA	NA	NA
31.	155	25-27 WEEKS	NA	NA	NA	NA	NA	NA	NA
32.	115	NA	NA	NA	NA	NA	NA	NA	NA
33.	34	21 WEEKS	NA	NA	NA	NA	NA	NA	NA
34.	189	26 WEEKS	NA	NA	NA	NA	NA	NA	NA
35.	82	24-34WEEKS	NA	NA	NA	NA	NA	NA	NA
36.	1739	34-<37 WEEKS	NA	NA	NA	NA	NA	NA	NA
37.	27	26 WEEKS	NA	NA	NA	NA	NA	NA	NA
38.	1963	NA	NA	NA	NA	NA	NA	NA	NA
39.	126	37 WEEKS	NA	NA	NA	NA	NA	NA	NA
40.	3955	<37 WEEKS	NA	NA	NA	NA	NA	NA	NA
41.	29	33-39 WEEKS	NA	NA	NA	NA	0.8-3.6	NA	NA
42.	321	34-42 WEEKS	NA	NA	NA	NA	NA	NA	NA
43.	181	NA	NA	NA	NA	NA	NA	NA	NA
44.	108	24-35 WEEKS	NA	NA	NA	NA	NA	NA	NA

Table 1: presents the mean values of leucocytes, Hemoglobin, Platelets, Glucose, TSH levels, Oxygen saturation and insulin resistance amongst the studied population.

S.NO.	NO. OF PARTICIAPNTS	GESTATIONAL AGE	LAB VALUES (BLOOD)(mean values) CORTISOL LEVEL	SP02	AHI	ODI	DBP	SBP
1.	791	24- 41 WEEKS	NA	NA	NA	NA	NA	NA
2.	105	1-3RD TRIMESTER	NA	<90%	>5	NA	NA	NA
3.	25	28 WEEKS	0.15	<90%	0.9	NA	NA	NA
4.	1350	18.1 WEEKS	NA	NA	NA	NA	NA	NA
5.	51	ANY	NA	96	MEAN= 6	NA	NA	NA
6.	1032	24-28 WEEKS	NA	NA	NA	NA	NA	NA
7.	64	39 WEEKS	NA	90	15.4	NA	NA	NA
8.	40	N=16 1ST TRIMESTER N=24 2ND TRIMESTER	NA	NA	5-15	NA	NA	NA
9.	48	33 WEEKS	NA	NA	16-18.5	NA	NA	NA
10.	72	22.6 WEEKS	NA	NA	11.7	5.3	77.3	121.4
11.	293	27 WEEKS	NA	NA	NA	NA	NA	NA
12.	276	28-42 WEEKS	NA	NA	NA	NA	NA	NA
13.	30	16-39 WEEKS	NA	NA	NA	NA	NA	NA
14.	73	32-35 WEEKS	NA	NA	NA	NA	NA	NA
15.	125	24-36 WEEKS	NA	NA	3.51	NA	NA	NA
16.	NA	NA	NA	NA	NA	NA	NA	NA
17.	18	32-34 WEEKS	NA	NA	16.1	7.4	NA	NA
18.	38	30-39 WEEKS	NA	NA	17	NA	83.3	118.2
19.	136	MEAN= 18 WEEKS	NA	NA	NA	NA	NA	NA
20.	67	24-32 WEEKS	NA	NA	NA	NA	NA	NA
21.	257	24-28 WEEKS	NA	NA	NA	NA	NA	NA
22.	266/305001	NA	NA	NA	NA	NA	NA	NA
23.	367	39 WEEKS	NA	NA	NA	NA	NA	NA
24.	1345	14-27 WEEKS	NA	NA	NA	NA	NA	NA

25.	234	>20-<35WEEKS	NA	NA	NA	NA	NA	NA
26.	1157	1-3 TRIMESTER	NA	NA	NA	NA	>90 MM HG	>140 MM HG
27.	371	24-32WEEKS	NA	NA	NA	NA	NA	NA
28.	1509	1-3 TRIMESTER	NA	CALCULATED	>5	NA	NA	NA
29.	117	20 WEEKS	NA	NA	NA	2.2	71	117
30.	143	36 WEEKS	NA	NA	NA	NA	NA	NA
31.	155	25-27 WEEKS	NA	NA	14.4	NA	NA	NA
32.	115	NA	NA	NA	NA	NA	NA	NA
33.	34	21 WEEKS	NA	NA	>5	NA	NA	NA
34.	189	26 WEEKS	NA	NA	>5	3% AND 4%	NA	NA
35.	82	24-34WEEKS	NA	89	5.3	2	NA	NA
36.	1739	34-<37 WEEKS	NA	NA	NA	NA	NA	NA
37.	27	26 WEEKS	NA	NA	NA	NA	NA	NA
38.	1963	NA	NA	NA	NA	NA	NA	NA
39.	126	37 WEEKS	NA	NA	NA	NA	NA	NA
40.	3955	<37 WEEKS	NA	NA	NA	NA	NA	NA
41.	29	33-39 WEEKS	NA	NA	NA	NA	80	120
42.	321	34-42 WEEKS	NA	NA	20.2	NA	NA	NA
43.	181	NA	NA	<_80%	>_30	NA	NA	NA
44.	108	24-35 WEEKS	NA	NA	> 5 PER HOURS	NA	NA	NA

Table 2: presents the mean values of cortisol levels, spo2, AHI,ODI,SBP,DBP calculated amongst the studied population.

Treatment

OSA has been associated with many complications leading to severe outcomes which worsens if not managed timely. Therefore, an early detection and therapy requires manifolds. The treatment includes wide-spectrum methods which treat other constitutional causes simultaneously. First line treatment and prophylactic measures include physical training and weight loss, avoid sleeping in supine position, elevate the head by a specific angle of 45 degrees while sleeping and restricting alcohol, sedatives and other CNS relaxing drug consumption[14]. In cases of severe obstruction wherein the conservative management proves to be less effective, CPAP, oral appliances and Mandibular enhancement devices are used which has proven to be a safe and effective management. In some cases airway surgeries are also performed. The use of medications has not been proven effective enough.

CPAP

Continuous Positive Airway Pressure commonly abbreviated as CPAP is considered to be the treatment of choice for OSA in pregnant females. It works on the principle of applying positive airway pressure above the atmospheric pressure thereby keeping the upper airway tract open while sleeping. CPAP normalizes the apnea-hypopnea index, prophylaxis of hypoxemia episodes, prevents the symptoms of related sleep apnea, improves sleep quality and lowers the risk of cardiac arrest and strokes.

Therefore, it is considered to be a safe treatment with demonstrated safety and compliance in pregnancy with proven compliance and safety throughout pregnancy.

Follow-up duration:

Women who have been using CPAP for some time should not terminate throughout their pregnancies, with a reassessment at 24 weeks gestation owing to BMI changes and increasing nasal congestion[14]. To accommodate fluctuations in severity as the pregnancy's several trimesters proceed, auto-titrating CPAP may be the best option. Positional treatment includes elevation of the upper body by 45° while sleeping which results in an increase of upper airway size[18]. Risk factors associated with CPAP are rhinitis, skin lesions, xerostomia and aerophagia. The results may be impacted due to altered risk-benefit ratio (in terms of fetus) and fast weight gain during pregnancy[19].

Anesthesia and C-section Guidelines

Early consultation with an anesthesiologist helps to prepare a peripartum strategy that includes early labor analgesia, the avoidance of respiratory depressants, and more intensive oxygenation monitoring. A previously implanted epidural catheter can help laboring patients with OSA who need cesarean deliveries avoid the requirement for general anesthesia in critical or urgent situations. To dose epidural catheters for surgical delivery, local anesthetics like chloroprocaine or lidocaine are frequently employed[2]. There isn't yet a pregnancy-specific recommendation for the treatment of SDB or its effects on maternal or newborn morbidity. The guidelines of providing ten free prenatal care visits to medical facilities contracted under the NHI programme cannot be relied upon exclusively by the government and authority. Health authorities should encourage screening so that pregnant women with OSA can be identified and receive the best possible therapy. Furthermore, we anticipate that closer monitoring of pregnant women with OSA would reduce the likelihood of unfavorable pregnancy outcomes.

Prognosis

Untreated obstructive sleep apnea (OSA) in pregnant women is associated with adverse clinical outcomes. With an increase in body mass index, the prevalence of obstructive sleep apnea rises. Significant obstetric concerns are brought on by the rising incidence of maternal and fetal morbidity and mortality among pregnant women who are obese. The development of OSA in the third trimester was also found to be substantially correlated with maternal age and first trimester BMI[14].Numerous studies show that a significant percentage of hypertensive pregnant women also have obstructive sleep apnea. Pregnant women with OSA had greater rates of gestational diabetes, gestational hypertension, preterm delivery, cesarean delivery and hypertensive problems. Limiting weight gain, avoiding sleep in supine position, elevating the head while sleeping, and restricting alcohol and sedative usage are some of the conservative treatment options for OSA. However, there hasn't been any evidence linking OSA to rates of stillbirth or small for gestational age neonates[14]. OSA in pregnant women is a sign of poor fetal growth. When compared to mothers without the condition, mothers with OSA had a higher likelihood of cesarean delivery, preeclampsia, gestational diabetes, gestational hypertension, low birth weight, and small for gestational age newborns.

V. Conclusion

OSA was related to various pregnancy related health outcomes, such as gestational diabetes, gestational hypertension, pre-eclampsia, C-section and preterm birth[20]. A study by Louis et al found that women with OSA were more likely to have preterm births than obese controls and normal weight controls [30% vs 10% & 12% respectively; $P<0.01$][1]. Pregnant women with high risk of OSA as estimated using the Berlin questionnaire have an increased risk for preeclampsia-eclampsia[6]. Current screening questionnaires for OSA were originally developed for non-pregnant populations that use only a single point of testing[21]. Pregnant women with symptoms of OSA are at higher risk of adverse pregnancy and perinatal outcomes[7]. SGA occurred in 71% of mothers with frequent snoring, compared with 2.6% of mothers without frequent snoring[1]. Women presenting with hypertension during pregnancy who also report snoring are at particularly high risk for moderate to severe obstructive sleep apnoea, with clinically significant oxyhaemoglobin desaturation[2]. Pregnant women who demonstrate excessive daytime sleepiness are more likely to have sleep disturbances associated with snoring[22]. Oxygen consumption increases during pregnancy by 20%, in addition, minute ventilation also increases by 30%-50%, therefore, the needed increased diaphragmatic effort will create negative inspiratory pressure on the hyperaemic upper airway that may induce obstructive respiratory events[17]. Pregnant women with OSA have lower levels of carbonyl stress markers compared to pregnant controls[8]. OSA is associated with reduced serum uE3 levels, independently of BMI, possibly indicating fetal distress[23]. An interaction was found between OSA and history of depression[24]. CPAP, a treatment for upper airway narrowing during sleep, appears to represent a safe treatment with minimal adverse effects[1]. CPAP therapy in pregnancy is safe, with the most common side effects being rhinitis, skin abrasion, mouth dryness and aerophagia[19]. CPAP therapy significantly reduced the incidence of severe forms of hypertensive syndrome in pregnant women with OSA. Early diagnosis and effective management may significantly diminish adverse outcomes associated with OSA during pregnancy[4]. Among early postpartum women, 45 degrees upper body elevation increased upper airway CSA and mitigated sleep apnoea. Elevated body position might improve respiratory safety in women early after delivery[18]. Management of obesity by lifestyle and dietary changes can be tried in these women preventively before conception, especially if other comorbidities are present (older age, chronic hypertension) to reduce the risk of OSA and of the obstetric complications that can be associated with it[25].

VI. Limitations

Several limitations needed to be noted in this meta-analysis. To begin with, the results were possibly impacted by potential confounding factors. We extracted median from included studies when they were available and calculated mean when only raw data was accessible. Our meta-analysis was limited to publications

written in English and there is the possibility of unidentified articles in other databases. Also, we did not include unpublished literature. Snoring is linked to obesity and the major predisposing factor for OSA is excess body weight. However, OSA and obesity commonly coexist and even have similar clinical consequences such as insulin resistance and oxidative stress. Thus, it was a huge challenge to separate the effects of OSA from obesity. large heterogeneity was found in this meta-analysis, which may derive from characteristics of population, study design, measurement of sleep disturbances and outcomes and clinical stage of pregnancy. Sleep disturbances were mainly derived from subjective reports or questionnaires, with the exception of OSA which was diagnosed based on objective findings. In addition, some other factors which may also have great impact such as chemo sensitivity and ethnicity are not fully considered. Sleep apnea prevalence is known to be different among various ethnicities.

Abbreviations
AHI- Apnea-Hypopnea Index
ODI- Oxygen Desaturation Index
DBP- Diastolic Blood Pressure
SBP- Systolic Blood Pressure
CPAP- Continuous Positive Airway Pressure
HTN- Hypertension
GDM- Gestational Diabetes Mellitus
RDI- Respiratory Disturbance Index
VEGF- Vascular Endothelial Growth Factor
FENO- Fraction of Exhaled Nitric Oxide

Conflict of Interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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