Sleep disturbances in pregnant patients and the relation to obstetric outcome

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Summary

Purpose: To compare obstetric outcomes between patients with positive and negative Berlin Questionnaire results. *Methods:* An observational study comparing outcome between these two groups was carried out in seven hospitals, representing seven different regions of Turkey. In each center, pregnant women who were admitted for normal pregnancy follow-up or labor, were consecutively recruited in the study. Each participant completed a sleep apnea questionnaire from the Berlin Questionnaire. This questionnaire tests snoring and daytime sleepiness. Fetal outcome and pregnancy outcome are recorded from patient files. *Results:* A total of 465 consecutive patients who completed the Berlin Questionnaire were analyzed. Patients with a positive questionnaire had a higher BMI, pre-pregnancy medical disorder rate and cesarean rate (68% vs 51%) than the negative group. Preeclampsia and gestational diabetes were more prevalent in the positive questionnaire group than the negative questionnaire group [19 (28%) vs 18 (5%) for preeclampsia, 8 (12) vs 13 (3%) for gestational diabetes, respectively]. At logistic regression analysis, gravidity, gestational age at birth and a positive questionnaire were independent predictors for preeclampsia. BMI and history of maternal medical disorders were independent predictors of gestational diabetes mellitus. *Conclusion:* Obstructive sleep apnea may be related to preeclampsia.

Key words: Berlin Questionnaire; Sleep; Disordered breathing; Pregnancy.

Introduction

Sleep disorders are a frequent but usually unrecognized problem that seem to be related to important health topics in women of childbearing ages. Sleep disturbances have been reported to be associated with hypertension, coronary artery disease, diabetes and depression [1, 2]. Most of the trials reporting these relationships have been established in middle-aged or older populations, but younger populations are being reported to have some association in recent studies [3-5].

Pregnancy is known to be associated with several changes in the body like hormonal, anatomic and mechanical changes. These changes in pregnant women alter sleep patterns and quality of sleep [6]. Sleep disorders may be divided in two major topics as obstructive sleep apnea (OSA) and upper airway resistance syndrome. These two disorders cause upper airway obstruction and hypoxemia during sleep and they may cause more severe results in pregnant women because of the fetus's need for oxygenation. OSA is known to affect 2% of the general female adult population [7]. The true incidence is thought be higher because of the wide population of undiagnosed women. The incidence in pregnant patients and the association with adverse pregnancy outcomes are still unknown. There is no doubt about the adverse effects of hypoxemia of mothers on the fetus. Some well known pregnancy complications like intrauterine growth retardation (IUGR), preeclampsia and gestational hypertension can easily be related to maternal hypoxemia due to their pathophysiology [8, 9]. Some sleep-related problems like insomnia, snoring and restless leg syndrome are commonly reported by pregnant women [6, 10-11]. Some previous reports on sleep and pregnancy have provided important associations but there is great need for more detailed and larger studies to understand this new and underdiagnosed pregnancy problem [8, 12-18]. Life styles, socioeconomic status, physical activity degree and regional differences may affect sleep habits and pregnancy outcomes. We aimed to evaluate sleep disorder complaints and the relation to pregnancy outcome with a nationwide self-test questionnaire.

Materials and Methods

This study was conducted in seven different busy obstetrics clinics in different universities and centers. These centers were selected from different sociocultural, geographic and economic regions to be representative for all Turkey.

We conducted a prospective study comparing Berlin Questionnaire scores and pregnancy outcome between September 2010 and June 2011 in six cities (Ankara, Istanbul, Sanliurfa, Erzurum, Rize and Gaziantep). The study group consisted of pregnant women who were admitted to clinics for pregnancy follow-up or labor. All patients were interviewed by an obstetrician or midwife to obtain routine medical history and the team member used a standard verbal consent for study participation. Available and volunteer participants completed the Berlin Questionnaire (Appendix A) by themselves or with the help of a team member. The Berlin Questionnaire consists of three different categories

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Appendix A.

Center:

Name-Surname: Patient No.: Age: Gravidity: Parity: Vital:

Gestational Age: Medical History: Weight: Height:

Complications in Pregnancy: Weight gain during pregnancy:

Route of delivery: Vaginal Birth C/S Weight of the baby: APGAR: Amnion:

CATEGORY 1

1. Do you snore?
a) Yes
b) No
c) I don't know.

2. How loud do you snore?
a) A little louder than sound of breathing.
b) Like speaking voice..
c) Much louder than speaking voice..
d) Very severe- One can hear from next room.

3. Do other people become disturbed because that you snore?
a) Yes b) No c) I don't know.

4. How often do you snore?
a) Almost every night.
b) 3-4 nights a week.
c) 1-2 nights a week.
d) 1-2 nights a month.
e) Almost never

5. Did anybody tell you that you stop breathing during your sleep?
a) Almost every night.
b) 3-4 nights a week.
c) 1-2 nights a week.
d) 1-2 nights a month.
e) Almost never

CATEGORY 2

1. How often dou you feel tired and weak when you wake up from your sleep?
a) Almost every night.
b) 3-4 nights a week.
c) 1-2 nights a week.
d) 1-2 nights a month.
e) Almost never

2. How often dou you feel tired and weak during daytime?
a) Almost every night.
b) 3-4 nights a week.
c) 1-2 nights a week.
d) 1-2 nights a month.
e) Almost never

3. Have you ever found yourself sleeping or falling asleep during driving?
a) Yes, b) No

4. How often do you fall asleep or feel very sleepy during driving?
a) Almost every night.
b) 3-4 nights a week.
c) 1-2 nights a week.
d) 1-2 nights a month.
e) Almost never

CATEGORY 3

1. Do you have a history of hypertension or obesity (BMI > 30 kg/m^2)?
a) Yes,
b) No

designed to illicit information regarding snoring (category 1), daytime somnolence (category 2) and the presence of obesity and/or hypertension (category 3). In categories 1 and 2, patients answering " almost everyday" or "3-4 times per week" were considered to have significant symptoms. The presence of obesity (body mass index -BMI- > 30 kg/m^2) and/or hypertension in category 3 was considered significant [1]. Hypertension was accepted as positive only in patients who had a "preeclampsia" diagnosis. A patient was considered to have a likelihood of sleep disordered breathing if significant symptoms existed in two out of three categories [19]. Demographic data of the patients were collected from their hospital files and medical history charts. Apgar scores and fetal data were obtained from pediatric files.

Statistical analysis

The primary outcome variable was the proportion of subjects with a high likelihood score on the Berlin Questionnaire (positive results). Categoric data were tested for significance with the χ^2 or Fisher's exact test. Continuous data were tested for significance with a 2-tailed Student's t-test or Mann-Whitney U test if not normally distributed. The Kolmogrov Smirnov test was used to test for normality of distribution. Multivariate analysis was performed by stepwise logistic regression. Results of the multivariate analysis are expressed as odds ratios with their 95% confidence intervals. A p value of 0.05 was required to reject null hypothesis. Statistical analysis was performed using SPSS software, version 14 (Chicago, IL).

Results

A total of 485 consecutive patients from seven centers were recruited for the study. Twenty patients were excluded from analysis because the Berlin Questionnaire was not filled in completely. A total of 465 patients constituted the study group. Patients' demographic characteristics are given in Table 1. The mean BMI for all patients was in the overweight range. Patients who had a positive questionnaire result were older and had higher BMI, gravidity, and parity than the negative questionnaire group. Pre-pregnancy medical disorders were more prevalent for the positive questionnaire group than the negative group. Chronic

Table 1. — *Demographic characteristics of the pregnant women by the Berlin Questionnaire for assessment of sleep disorders. Data are given as mean ± standard deviation, median (min-max), n (%) where appropiate.*

Characteristics	Total (n = 465)	Berlin Questionnaire – (n = 396)	Berlin Questionnaire + (n = 69)	*p*
Age	28.1 ± 6.2	27.6 ± 6.0	30.6 ± 6.6	< 0.001
Gravidity	2 (1-14)	2 (1-11)	3 (1-14)	0.024
Parity	1 (0-13)	1 (0-9)	2 (0-13)	0.017
Height (cm)	162.4 ± 5.3	162.3 ± 5.4	163.0 ± 5.2	0.362
Weight (kg)	75.5 ± 12.7	74.0 ± 11.1	83.5 ± 17.1	< 0.001
BMI (kg/m2)	28.6 ± 4.1	28.1 ± 3.6	31.4 ± 5.6	< 0.001
Weight gain in pregnancy	14.2 ± 5.1	14.0 ± 5.0	15.6 ± 5.3	0,027
Maternal medical disorders	44 (9)	29 (7)	15 (22)	< 0.001
Chronic hypertension	11 (2)	3 (1)	8 (12)	
Valvular heart disease	5 (1)	5 (1)	0 (0)	
Diabetes mellitus	5 (1)	2 (1)	3 (4)	
Asthma	12 (3)	9 (2)	3 (4)	
Hypothyroid	4 (1)	4 (1)	0 (0)	
Other	7 (1)	6 (2)	1 (1)	

Table 3. — *Significant independent predictors of preeclampsia with multiple logistic regression analysis.*

Variable	Odds Ratio	95% CI	*p*
Gravida	1.4	1.1-1.7	0.001
Gestational Age	0.6	0.4-0.9	0.011
+ Berlin Questionnare	12.4	4.9-31.9	< 0.001

hypertension rate was higher in patients with a positive questionnaire (p = 0.001).

Obstetric outcomes of patients are shown in Table 2. Cesarean rate was higher in patients with a positive questionnaire. Although number of fetuses with an Apgar score lower than 7 was higher in the positive questionnaire group it was the same at 5 min. Preeclampsia and gestational diabetes were more prevelant in the positive questionnaire group than the negative group. All other obstetric outcomes did not differ between groups.

At logistic regression analysis, gravidity, gestational age at birth and a positive questionnaire were independent predictors for preeclampsia. The regression model correctly predicted 25% of patients with preeclampsia and 99.4% of normal patients.

BMI and history of maternal medical disorders were independent predictors of gestational diabetes mellitus. The regression model, however, predicted 5% of patients with gestational diabetes and all the normal patients.

Discussion

There are few studies that evaluate sleep disorders in pregnancy and the relation between these disorders and pregnancy complications. Examining this relation between sleep problems and pregnancy and mother's

Table 2. — *Obstetric outcomes of pregnant women by the Berlin Questionnare for assessment of sleep disorders. Data are given as mean ± standard deviation, median (min-max) where appropiate.*

Characteristics	Berlin Questionnaire – (n = 396)	Berlin Questionnaire + (n = 69)	*p*
Gestational age (weeks)	38.6 ± 1.3	38.5 ± 1.1	0.530
Meconium staining	21 (5)	7 (10)	0.161
Apgar score at 1 min < 7	13 (3.3)	9 (13)	< 0.001
Apgar score at 5 min < 7	3 (1)	1 (1)	0.475
Cesarean	203 (51)	47 (68)	0.01
Birth weight	3280.3 ± 458.9	3155.2 ± 650.8	0.055
Preeclampsia	18 (5)	19 (28)	< 0.001
GDM[b]	13 (3)	8 (12)	0.002
IUGR[a]	6 (2)	2 (3)	0.415
Oligohydramnios	8 (2)	1 (1)	0.751
Placenta previa	4 (1)	0 (0)	1
Other	2 (1)	1 (1)	0.366

[a]Intrauterine growth retardation; [b]Gestational diabetes mellitus.

Table 4. — *Significant independent predictors of gestational diabetes mellitus with multiple logistic regression analysis.*

Variable	Odds Ratio	95% CI	*p*
BMI*	1.1	1.02-1.2	0.013
Maternal medical disordes	6.6	2.4-18.3	< 0.001

*Body mass index (kg/m^2)

demographic variables may give us some hints about the pathophysiology of some pregnancy complications like IUGR, preeclampsia and preterm labor. It is well known that age, obesity, ethno racial origin, geographic region, employment and pre-pregnancy sleep habits are all related to some pregnancy complications [20-24]. In our study we found similar associations for these complications and a high sleep disorder rate in pregnant women.

Short sleep duration and sleep disordered breathing have been linked to obesity, diabetes, hypertension and coronary heart disease in the non-pregnant population [3, 20, 25-31]. Pathophysiology for these health problems is reported to be elevated proinflammatory cytokines and oxidative stress markers in sleep disordered patients. The hypothesis is that enhanced inflammatory and oxidative stress response caused by these sleep disorders promote endothelial damage and metabolic dearrangements, which ultimately lead to conditions such as hypertension and non-insulin dependent diabetes mellitus [32-35]. Many authors report short sleep duration and sleep-disordered breathing symptoms in pregnancy as frequent problems, and that these may be the cause of obstetric complications like preterm birth, preeclampsia and IUGR as a result of inflammation and oxidative stress [36-38]. There are some limited data from retrospective and case control studies pointing to these mechanisms as the cause of preeclampsia [8, 39, 40]. The main problem for this important topic is the testing method for sleep disorders; the Berlin Questionnaire is not the gold standard for this diagnosis,

and an overnight polysomnographic study is required for an exact diagnosis [41]. This test may be cumbersome and also expensive for the patient and many physicians prefer to use the questionnaire instead of this test.

We believe sleep disorders, especially OSA, are an important problem in pregnant women and related to some pregnancy complications based on our results. Larger and polysomnographic prospective studies are needed to show the relation between these two entities.

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