Sleep Disorders in Pregnancy

Prevalence, diagnosis and management.

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Conflict of Interest Disclosures

[X] 1. I do not have any potential conflicts of interest to disclose, **OR**

[ ] 2. I wish to disclose the following potential conflicts of interest:

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Sleep Quality in Pregnancy.

- Sleep disturbances and sleep quality decline throughout pregnancy.
- Rates range from 43.1% to 75% and up to 98% in third trimester.
- Physiological factors disturbing sleep:
  - Changes in estrogen, prolactin, progesterone and human chorionic gonadotropin.
  - Gastroesophageal acid reflux, uterine contractions, upper airway congestion and physical discomfort.
- Other risk factors:
  - Lower SES
  - Higher age
  - Parity
  - Smoking or second-hand smoke
  - Employment during pregnancy

Xu X, Liu D, Zhang Z, Sharma M, Zhao Y. Sleep Duration and Quality in Pregnant Women: A Cross-Sectional Survey in China. Int J Environ Res Public Health. 2017;14(7). pii: E817.
Oyiengo D, Louis M, Hott B, Bourjeily G. Sleep disorders in pregnancy. Clin Chest Med. 2014;35(3):571-87

Overview

Nighttime sleep variables across month of pregnancy.

	Bedtime		Sleep-onset latency (min)		Number of wakings		Duration of wakings (min)		Wake time		Nighttime sleep (h)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
≤2 months	10:17	1.33	49.25	48.98	2.34	1.20	60.18	63.09	6:50	1.48	7.01	1.58
3 months	10:08	1.36	47.62	49.45	2.47	1.18	74.11	68.82	6:53	1.55	7.02	1.65
4 months	10:23	1.30	44.06	44.27	2.50	1.23	61.73	62.18	7:06	1.44	7.10	1.55
5 months	10:15	1.37	45.59	44.07	2.56	1.16	63.30	62.98	6:46	1.54	6.93	1.53
6 months	10:33	1.36	43.75	44.27	2.53	1.13	73.59	69.33	7:01	1.40	6.75	1.53
7 months	10:29	1.19	51.20	49.00	2.84	1.24	71.06	64.88	6:54	1.51	6.63	1.45
≥8 months	10:29	1.37	51.56	48.52	3.19	1.30	79.93	68.33	6:53	1.54	6.31	1.51
Total	10:23	1.33	48.31	47.41	2.71	1.26	70.48	66.33	6:54	1.50	6.75	1.56
ANOVA	4.27***		1.67		26.14***		4.94***		1.68		14.97***	
Effect size	0.01				0.06		0.01				0.04	

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

Mindell JA, Cook RA, Nikolovski J. Sleep patterns and sleep disturbances across pregnancy. Sleep Med. 2015 Apr;16(4):483-8.

Causes of Sleep Disturbances.

Percent physical symptoms that disturbed sleep (sometimes/often) by month of pregnancy.

	Nausea	Hunger	Reflux	Leg cramps	Frequent urination	Back pain	Hip/pelvic pain	Itchy skin	Uncomfortable position	Baby movement	Contractions
<2 months	32.4	41.2	28.4	20.9	72.3	49.3	31.3	30.4	56.1	1.4	2.0
3 months	48.9	48.9	31.4	20.4	82.5	54.7	38.7	32.1	72.3	9.5	4.4
4 months	28.9	43.7	33.1	24.6	84.5	50.7	40.1	26.1	81.7	19.0	3.5
5 months	18.3	34.4	34.4	31.3	80.2	51.1	45.8	26.0	76.3	27.5	3.1
6 months	15.8	34.6	49.6	42.1	78.9	60.9	55.6	28.6	81.2	55.6	5.3
7 months	10.8	35.7	55.4	47.8	86.0	68.2	64.3	21.0	86.0	64.3	12.1
8 months +	21.6	38.7	68.0	50.0	91.9	70.3	74.8	28.8	94.1	68.0	31.1
Total	24.9	39.5	45.0	35.2	83.1	59.0	52.1	27.6	79.4	37.8	10.6
Chi-squared/ ANOVA	74.82***	10.09	96.48***	69.02***	28.12***	31.42***	102.11***	5.97	88.74***	308.94***	135.54***
Effect size (ϕ)	0.26		0.30	0.25	0.16	0.17	0.31		0.29	0.54	0.36

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

Mindell JA, Cook RA, Nikolovski J. Sleep patterns and sleep disturbances across pregnancy. Sleep Med. 2015 Apr;16(4):483-8.

Sleep Disorders.

Insomnia in Pregnancy.

- Insomnia worsens during the third trimester.
- Insomnia Severity Index (ISI): Higher scores on the ISI suggest more-severe insomnia, with scores between 8 and 28 suggesting some level of insomnia.
- Over 73.5% of women experience some degree of insomnia during pregnancy.

Fernandez-Alonso AM, Trabalon-Pastor M, Chedraui P, et al. Factors related to insomnia and sleepiness in the late third trimester of pregnancy. Arch Gynecol Obstet 2012; 286:55–61.

Fernandez-Alonso AM, Trabalon-Pastor M, Chedraui P, et al. Factors related to insomnia and sleepiness in the late third trimester of pregnancy. Arch Gynecol Obstet 2012; 286:55–61.

	ISI score	ESS score
Socio-demographic characteristics		
Age (years): 31.0 [7.0]		
<20 ($n = 17$)	9.0 [7.0]	6.0 [5.0]
20–30 ($n = 163$)	12.0 [7.0]	6.0 [6.0]
>30 ($n = 190$)	10.5 [9.0]	7.0 [5.0]
p*	0.04[a]	0.62[a]
Rural residency		
No ($n = 266$)	11.0 [8.0]	7.0 [5.0]
Yes ($n = 104$)	11.0 [7.0]	6.0 [5.0]
p	0.80[b]	0.31[b]
Level of education		
None ($n = 4$)	6.0 [6.0]	3.5 [3.0]
Elementary ($n = 95$)	12.0 [6.0]	6.0 [5.0]
High school ($n = 129$)	12.0 [7.0]	7.0 [5.0]
University ($n = 142$)	10.0 [9.0]	7.0 [5.0]
p	0.10[a]	0.11[a]
Employment status		
No ($n = 115$)	11.0 [6.0]	6.0 [6.0]
Yes ($n = 255$)	11.0 [8.0]	7.0 [4.0]
p	0.68[b]	0.003[b]
Church assistance		
No ($n = 322$)	11.0 [8.0]	6.5 [5.0]
Yes ($n = 48$)	10.0 [9.0]	6.0 [5.0]
p	0.72[b]	0.69[b]
Tobacco use		
No ($n = 300$)	10.0 [8.0]	6.0 [5.0]
Yes ($n = 70$)	13.0 [6.0]	6.0 [6.0]
p	0.02[b]	0.47[b]
Alcohol use		
No ($n = 367$)	11.0 [8.0]	6.0 [5.0]
Yes ($n = 3$)	17.0 [9.0]	8.0 [7.0]
p	0.09[b]	0.93[b]
Coffee consumption		
No ($n = 226$)	11.0 [8.0]	7.0 [5.0]
Yes ($n = 144$)	11.0 [8.0]	6.0 [5.0]
p	0.71[b]	0.36[b]
Isotonic drink consumption		
No ($n = 204$)	11.5 [8.0]	6.0 [5.0]
Yes ($n = 166$)	11.0 [8.0]	7.0 [5.0]
p	0.37[b]	0.72[b]
Obstetrical history and pregnancy clinical characteristics		
Parity 0.0 [1.0]		
0 ($n = 215$)	11.0 [8.0]	7.0 [5.0]
1 ($n = 119$)	11.0 [7.0]	6.0 [5.0]
≥2 ($n = 36$)	11.5 [9.0]	7.0 [4.0]
p	0.80[a]	0.70[a]
Gestational age at survey (weeks) 39.0 [1.8]		
<39 ($n = 122$)	11.0 [8.0]	6.0 [5.0]
≥39 ($n = 248$)	11.0 [7.0]	6.5 [5.0]

Complications of poor sleep in pregnancy.

- Increased risk of gestational diabetes (odds ratio, 2.24; 95% confidence interval, 1.11-4.53)[1].
- Antepartum depression and suicidal ideation[2]
  - Suicidal ideation increased 2.81 fold with poor sleep even after controlling for depression
- Postpartum depression[3]

Study factors	Regression coefficient	Standard error	95% confidence interval	P value
Sleep quality	0.85	0.13	0.61, 1.10	<0.01

- Premature birth (before 37 weeks) OR 1.3 (1.0-1.7, P=.023, 14.1%)[4]

1. Facco FL, Grobman WA, Reid KJ, et al Objectively measured short sleep duration and later sleep midpoint in pregnancy are associated with a higher risk of gestational diabetes. Am J Obstet Gynecol. 2017;217(4):447.e1-447.e13
2. Gelaye B, Addae G, Neway B, et al. Poor sleep quality, antepartum depression and suicidal ideation among pregnant women..J Affect Disord. 2017;209:195-200
3. Wu M, Li X, Feng B, Wu H, Qiu C, Zhang W Poor sleep quality of third-trimester pregnancy is a risk factor for postpartum depression. Med Sci Monit. 2014;20:2740-5.
4. Felder JN, Baer RJ, Rand L, Jelliffe-Pawlowski LL, Prather AA. Sleep Disorder Diagnosis During Pregnancy and Risk of Preterm Birth. Obstet Gynecol. 2017;130(3):573-581

Treatment of insomnia.

- Most sedative hypnotics either do not have enough human data to draw safety conclusions or have been associated with fetal developmental problems[1].
- The effects of bright light therapy have been only indirectly studied and results are equivocal[2].
- A trial for mindfulness based cognitive behavioral therapy is underway but no data from it is available yet[3].

1. Oyiengo D, Louis M, Hott B, Bourjeily G. Sleep disorders in pregnancy. Clin Chest Med. 2014;35(3):571-87.
2. van Ravesteyn LM, Lambregtse-van den Berg MP, Hoogendijk WJ, Kamperman AM. Interventions to treat mental disorders during pregnancy. PLoS One. 2017 Mar 30;12(3):e0173397
3. Tomfohr-Madsen LM, Campbell TS, Giesbrecht GF, et al. Mindfulness-based cognitive therapy for psychological distress in pregnancy: study protocol for a randomized controlled trial. Trials. 2016;17:498.

Sedative Hypnotics

Medication	Pregnancy	Lactation
Zaleplon	No increased risk of teratogenicity. Numbers too small to be conclusive	Unlikely to adversely affect the neonate, but no available studies evaluating consequences of such exposure.
Zolpidem	Increased risk of low birth weight and preterm deliveries in women but no increased risk of congenital anomalies	American Academy of Pediatrics (AAP) classifies the drug as safe for lactation
Zopiclone (no data on ezopiclone)	Crosses placental barrier and withdrawal reported at birth. No congenital anomalies	Unlikely toxicity but effects of chronic exposure unknown.
Ramelteon	Animal studies suggest dose-dependent anomalies. Human data are lacking.	No human data on lactation
Doxepin	No increased risk of animal teratogenicity. No human data.	The World Health Organization deems the drug incompatible with breastfeeding
Temazepam	Neonatal withdrawal with late third-trimester use. Concomitant use with diphenhydramine has been associated with fetal death	Occasional use of benzodiazepines in breastfeeding mothers is acceptable
Trazodone	Not likely to result in major congenital malformations	Distributed in milk in small amounts.
Diphenhydramine	First-trimester use may be associated with various anomalies	Manufacturer advises against use.
Suvorexant	No human data	No human data

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Obstructive sleep apnea & pregnancy.

- Using objective tests prevalence rates of 4.9% (higher than the general female population) have been reported[1].
- The most common risk factors of OSA in pregnancy are pre-pregnancy obesity (OR 1.85–3.01, p=0.025–0.049) and maternal age[2].
- The combination of pre-pregnancy obesity, hypertension, snoring and maternal age is the best predictor of OSA[3].

1. Antony KM, Agrawal A, Arndt ME Obstructive sleep apnea in pregnancy: reliability of prevalence and prediction estimates. J Perinatol. 2014 ;34(8):587-93.
2. Pien GW, Pack AI, Jackson N, Maislin G, Macones GA, Schwab RJ. Risk factors for sleep-disordered breathing in pregnancy. Thorax. 2014;69:371-7.
3. Facco FL, Ouyang DW, Zee PC, Grobman WA. Development of a pregnancy-specific screening tool for sleep apnea. J Clin Sleep Med. 2012 Aug 15;8(4):389-94

Table 3—Sensitivity, specificity, and positive and negative predictive values (PPV, NPV) for various cutoff values of our four-variable prediction rule

Value	Sensitivity	Specificity	PPV	NPV
≥ 50	100.0% (84.9%, 100.0%)	9.7% (4.3%, 19.5%)	30.1% (21.2%, 40.6%)	100% (56.1%, 100%)
≥ 75	85.7% (66.4%, 95.3%)	73.6% (61.7%, 83.0%)	55.8% (40.0%, 70.6%)	93.0 % (82.2%, 97.7%)
≥ 100	25.0% (11.4%, 45.2%)	98.6% (91.5%, 99.9%)	87.5% (46.7%, 99.3%)	77.2% (67.0%, 65.0%)

Facco FL, Ouyang DW, Zee PC, Grobman WA. Development of a pregnancy-specific screening tool for sleep apnea. J Clin Sleep Med. 2012;8(4):389-94

Sleep apnea and pregnancy: complications.

CI 95%	Odds Ratio (OR) adjusted for socioeconomic (SE) variables	OR adjusted for SE plus obesity	OR adjusted for SE, obesity and comorbidities	OR adjusted fro SE, obesity, comorbidities and past C-Section
C-Section	2.26 (2.09–2.43)	2.05 (1.87–2.24)	1.29 (1.17–1.42)	1.12 (1.01–1.23)
Gestational diabetes	5.03 (4.50–5.62)	3.85 (3.43–4.31)	2.02 (1.79–2.28)	1.89 (1.67–2.14)
Gestational HTN	2.41 (2.04–2.85)	2.35 (1.99–2.77)	1.31 (1.11–1.56)	1.28 (1.08–1.52)
Preeclampsia	4.58 (4.05–5.18)	4.44 (3.92–5.03)	2.67 (2.35–3.05)	2.50 (2.19–2.85)
Postop wound	7.56 (4.64–12.32)	7.99 (4.88–13.06)	5.89 (3.58–9.68)	5.42 (3.29–8.92)
Hospital stay >5 days	7.54 (6.85–8.29)	6.75 (6.14–7.41)	4.30 (3.90–4.75)	3.06 (2.76–3.40)
Prematurity	1.62 (1.43–1.84)	1.40 (1.24–1.61)	1.32 (1.16–1.50)	1.20 (1.06–1.37)
IUGR	1.39 (1.10–1.74)	1.26 (1.01–1.59)	1.28 (1.02–1.62)	1.21 (0.96–1.53)
Stillbirth	1.28 (0.84–1.95)	1.04 (0.68–1.58)	1.07 (0.70–1.62)	1.01 (0.66–1.53)

The analytic sample included 55,781,965 pregnancy-related inpatient hospital discharges.

Louis JM, Mogos MF, Salemi JL, Redline S, Salihu HM. Obstructive sleep apnea and severe maternal-infant morbidity/mortality in the United States, 1998-2009. Sleep. 2014;37(5):843-9

Treatment

- No pregnancy specific guidelines.
- AutoPAP preferred to fixed CPAP.
- Positional therapy.
- No role for surgical interventions.
- Mandibular advancement not very practical.

Abdullah HR, Nagappa M, Siddiqui N, Chung F. Diagnosis and treatment of obstructive sleep apnea during pregnancy. Curr Opin Anaesthesiol. 2016;29(3):317-24.

Restless Legs Syndrome or Willis Ekbom Disease

- A sleep related movement disorder.
- Possible pathophysiology is dopaminergic neurotransmission dysregulation and iron deficiency in the brain.
- Overall Prevalence ~ 5-10% in European and North American Population based studies
- In Asian countries lower prevalence
- More common in women F/M =2/1

Diagnostic Criteria (ICSD 3)

Key RLS diagnostic criteria	✓ Supportive features
✓ Urge to move the legs – usually accompanied or caused by uncomfortable leg sensations	✓ Sleep disturbances ✓ Involuntary leg movements ✓ Positive family history for RLS
✓ Temporary relief with movement – partial or total relief from discomfort by walking or stretching	
✓ Onset or worsening of symptoms at rest or inactivity, such as when lying or sitting	
✓ Worsening or onset of symptoms in the evening or at night	
✓ The symptoms of RLS cause concern, distress, sleep disturbance, or impairment in important areas of functioning	
✓ The above features are not solely accounted for as symptoms of another medical or a behavioral condition.	

RLS in Pregnancy or gestational RLS (gRLS)

TABLE 1. GRLS PREVALENCE STUDIES

Study, year & ref.	*Country*	*Trimester*	*Method of diagnosis*	*Prevalence*
Suzuki *et al.*, 2003[23]	Japan	All trimesters	Questionnaire	19.9%
Manconi *et al.*, 2004[24]	Italy	At delivery	Clinician interview	26%
Alves *et al.*, 2010[21]	Brazil	All trimesters	Clinician interview	13.5%
Facco *et al.*, 2010[25]	USA	All trimesters	Questionnaires	17.5% (31.2% in 3rd trimester)
Neau *et al.*, 2010[26]	France	All trimesters	Questionnaires	24%
Balendran *et al.*, 2011[27]	Australia	Third trimester	Clinician interview	22.5%
Uglane *et al.*, 2011[28]	Norway	At delivery	Questionnaires	34%
Chen *et al.*, 2012[29]	Taiwan	All trimesters	Clinician interview	10.4%
Sarberg *et al.*, 2012[30]	Sweden	All trimesters	Questionnaires	17.0% in 1st trimester 27.1% in 2nd trimester 29.6% in 3rd trimester
Hubner *et al.*, 2013[31]	Switzerland	All trimesters	Clinician interview	12%
Minar *et al.*, 2013[32]	Slovakia	Third trimester	Questionnaires	31.3%
Ramirez *et al.*, 2013[33]	Peru	All trimesters	Clinician interview	18.4%
Vandat *et al.*, 2013[34]	Iran	3rd trimester	Clinician interview	17.8%
Neyal *et al.*, 2015[35]	Turkey	Third trimester	Clinician interview	38%
Shang *et al.*, 2015[36]	China	All trimesters	Clinician interview	11.2%
Liu *et al.*, 2016[37]	China	All trimesters	Clinician interview	12.3%
Morker *et al.*, 2016[38]	USA	2nd & 3rd trimesters	Clinician interview	20.2%

gRLS, gestational restless legs syndrome; RLS, restless legs syndrome.
Note: The questionnaire used in all studies was the International Restless Legs Syndrome Study Group standardized survey form with 4 diagnostic criteria & a severity scale. Clinician interviews were face-to-face RLS–focused history gathering.

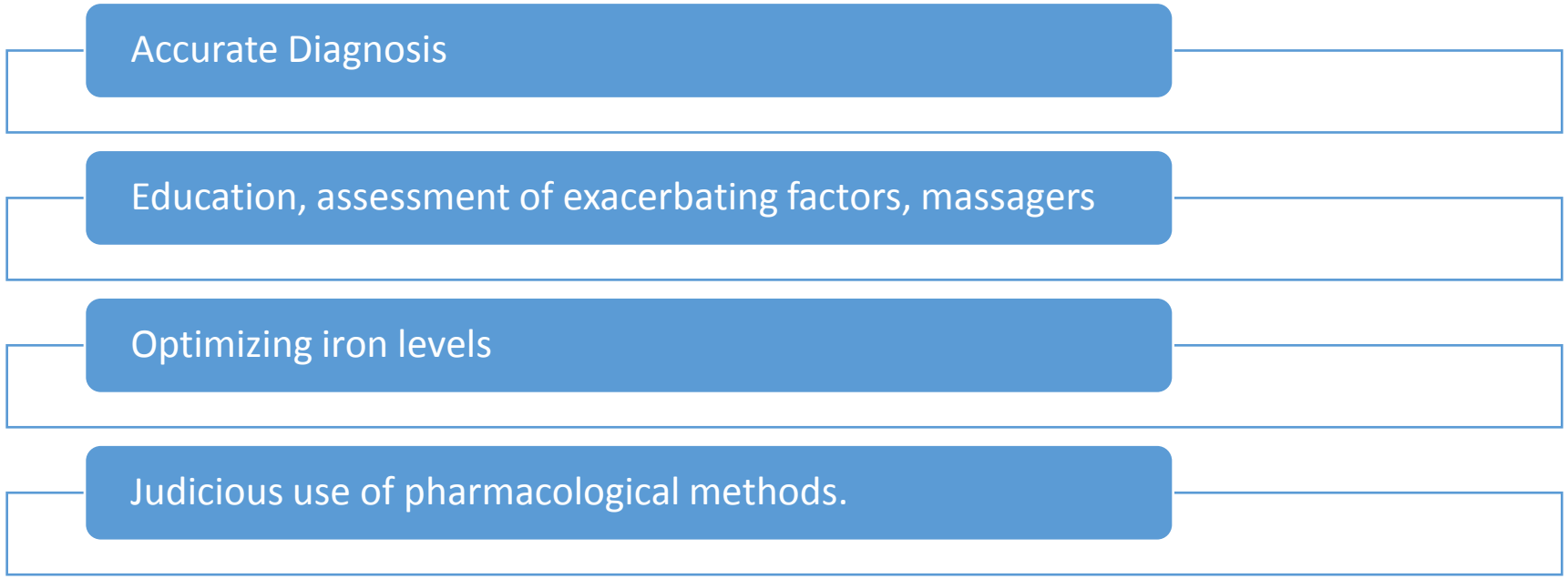
Kay-Stacey M and Attarian H Managing Sleep Disorders in Pregnancy. Gender and Genome. 2017;1(1):DOI: 10.1089/gg.2016.0006

RLS in pregnancy: complications and determinants

- RLS is associated with higher prevalence of preeclampsia, hypertension, daytime sleepiness and poorer quality of life[1].
- Determinants of RLS in pregnancy include multi-parity, anemia, hormonal fluctuations[2], vitamin D1 and folic acid[3] levels as well as personal and family history of RLS.
- None of the variables above except for personal and family history have been consistently associated with pregnancy induced RLS.

1. Liu G, Li L, Zhang J, et al Restless legs syndrome and pregnancy or delivery complications in China: a representative survey. Sleep Med. 2016;17:158-62
2. Chen PH, Liou KC, Chen CP, Cheng SJ. Risk factors and prevalence rate of restless legs syndrome among pregnant women in Taiwan. Sleep Med. 2012;13:1153–7.
3. Morker M, Gossett D, McKnight T, Patel B, Patel M, Attarian H,. J Reprod Med. 2017; 62(6): 593-597.

RLS treatment and pregnancy



Picchietti DL, Hensley JG, Bainbridge JL Consensus clinical practice guidelines for the diagnosis and treatment of restless legs syndrome/Willis-Ekbom disease during pregnancy and lactation. Sleep Med Rev. 2015;22:64-77.

RLS Medications

Medication	Safety in Pregnancy	Lactation
Pramipexole	• Animal studies show no increased risk of malformations. • Human safety data are limited but do not show evidence of malformations.	No human studies assessing levels in breast milk are available. Pramipexole is known to reduce the secretion of prolactin, and it is possible that it could significantly reduce milk Therefore should probably not be used in breastfeeding mothers
Ropinirole	• Same as above	• Same as above
Rotigotine	• Teratogenic effect unknown. • No animal data exists	• Same as above
Gabapentin	• There are case reports of normal pregnancy outcomes also reports of malformations. • It is not known if the risk of malformations in increased with this medication.	Data reveal that the infant plasma levels following exposure to gabapentin through breastfeeding are probably too low to cause untoward effects in the breastfed infant.
Pregabalin	• Pregabalin has adverse effects on embryo development in animals. • Human data are limited.	There are no data available on the transfer of pregabalin into human milk. However, due to the kinetics of the drug bioavailability to the infant would be high. Infant risk cannot be ruled out.
Opiates	• Neonatal withdrawal after maternal use has occurred. • Oxycodone use in the first trimester was associated with an increase in pulmonary valve stenosis	Small amounts are secreted in breast milk. Sedation of the newborn may be observed
Levodopa	• Adverse pregnancy and fetal outcomes in animals • Case reports in humans have not identified abnormal fetal development. • Theoretic concern about placental perfusion. • Current data do not support the safety of this drug in pregnancy	Reduced prolactin levels by dopamine may reduce milk production
Clonazepam	• Not thought to increase the risk of congenital malformations. • Risk of transient respiratory distress and hypotonia in women taking clonazepam in combination with paroxetine	One case report of apnea, cyanosis, and hypotonia in a newborn exposed to clonazepam via breast milk
Clonidine	Not expected to increase the risk of structural malformations. Possible behavioral effects reported in children and animals exposed prenatally	Clonidine is minimally excreted in human milk. No pediatric concerns reported, but newborns may need to be observed for hypotension. Clonidine may reduce milk production by reducing prolactin secretion.
Cabergoline	Human studies of more than 500 pregnancies suggest no increase in risk of congenital malformations.	Decreases prolactin levels. If lactation can be maintained, watch infant for ergot effects.

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Narcolepsy and primary hypersomnias.

- Whether narcolepsy leads to significantly increased mortality remains uncertain.
- Profoundly disabling condition with a hefty economic and QoL burden.
- Narcolepsy is also associated with major societal stigma, leading to more QoL issues.

1 Ozaki A, Inoue Y, Hayashida K, et al. Quality of life in patients with narcolepsy with cataplexy, narcolepsy without cataplexy, and idiopathic hypersomnia without long sleep time: comparison between patients on psychostimulants, drug-naive patients and the general Japanese population. Sleep Med 2012;13:200–206.
2 Kapella MC, Berger BE, Vern BA, et al. Health-related stigma as a determinant of functioning in young adults with narcolepsy. PLoS One 2015;10:e0122478.

Narcolepsy and Pregnancy

- No significant increase in complications.
- Very few, however, take medications during pregnancy and lactation.
- Depending on the medication, 59%–73% of physicians advise their patients who had narcolepsy and were trying to conceive to stop their stimulants and anticataplexy medications
- Another 5%–15% of the physicians advised a reduction in the dose, and 19%–28% did not advise any change in dosing.

1 Maurovich-Horvat E, Kemlink D, Hogl B, et al. Narcolepsy and pregnancy: a retrospective European evaluation of 249 pregnancies. J Sleep Res 2013;22:496–512.
2 Thorpy M, Zhao CG, Dauvilliers Y. Management of narcolepsy during pregnancy. Sleep Med 2013;14:367–376.

More Physician Advice.

- During actual pregnancy and breastfeeding, 70%–94% of the physicians advise stopping the medications
- Another 3%–19% advised reductions in doses.
- Zero-11% advised no changes in dosing.
- Medication advice also depended on the trimester of the pregnancy.
  - Approximately 50% of the responding physicians stopped the medications throughout the 3 trimesters
  - About 33%–43% stopped medication only during the first trimester
  - About 4%–12% stopped the medications during the first 2 trimesters.

Thorpy M, Zhao CG, Dauvilliers Y. Management of narcolepsy during pregnancy. Sleep Med 2013;14:367–376.

Meds for Narcolepsy and Cataplexy

Medications	Pregnancy	Lactation
Modafinil	Ongoing registry. No congenital abnormalities reported	No human data
Armodafinil	Ongoing registry. Rare skeletal abnormalities reported	No human data
Sodium Oxybate	There are no available studies to support safe use of this drug to date. When sodium hydoxybutirate was used as an anesthetic there were 12% fetal complications and high risk of maternal seizures and blood loss.	No human data
Amphetamines	Increased risk of minor malformations.	Not compatible with breast feeding
Methylphenidate	Possible increase in risk of prematurity, growth restriction, and neonatal withdrawal.	Small amount transferred in milk no adverse events reported
TCAs	Possible increase risk of cardiac malformations and transient neonatal complications.	Small amount transferred in milk. May be of concern
SSRIs	No significant association with birth defects. Transient neonatal complications with third trimester use. Risk of social-behavioral abnormalities in childhood	Small amount transferred in milk
SNRIs	Some reports of small birth weight. Transient neonatal problems no congential abnormalities	Small amount transferred in milk

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Recommendations.

(1) Have a clear and detailed discussion with the patients during preconception about the risk vs. benefits of taking the medications used to treat narcolepsy and cataplexy.

(2) If it is feasible to manage EDS with naps, have flexible work hours, go on short-term disability and rely on others for transportation, then patients should stop the medications used to treat narcolepsy and cataplexy altogether, at least for the first trimester and ideally for as long as possible during pregnancy and lactation. Patients with type 1 narcolepsy should be warned of the potential of labor-induced cataplexy.

(3) Prenatal vitamins and folic acid at 0.4–4 mg per day should be recommended to mitigate the potential of teratogenicity if the patient is to continue on medications.

(4) If stimulant medications are required, then use the minimal effective dose, and use it sparingly preferably after the first trimester.

(5) Perform a targeted anatomical ultrasound (a ‘‘level II ultrasound’’) at 20 weeks.

Kay-Stacey M and Attarian H Managing Sleep Disorders in Pregnancy. Gender and Genome. 2017;1(1):DOI: 10.1089/gg.2016.0006