The impact of occupational shift work and working hours during pregnancy on health outcomes: a systematic review and meta-analysis

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BACKGROUD: An increasing number of original studies suggest that exposure to shift work and long working hours during pregnancy could be associated with the risk of adverse pregnancy outcomes, but the results remain conflicting and inconclusive.
OBJECTIVE: To examine the influences of shift work and longer working hours during pregnancy on maternal and fetal health outcomes.
DATA SOURCES: Five electronic databases and 3 gray literature sources were searched up to March 15, 2019.
METHODS OF STUDY SELECTION: Studies of all designs (except case studies and reviews) were included, which contained information on the relevant population (women who engaged in paid work during pregnancy); exposure (rotating shift work [shifts change according to a set schedule], fixed night shift [typical working period is between 11:00 pm and 11:00 am] or longer working hours [>40 hours per week]);comparator (fixed day shift [typical working period is between 8:00 am and 6:00 pm] or standard working hours [≤40 hours per week]); and outcomes (preterm delivery, low birthweight [birthweight <2500 g], small for gestational age, miscarriage, gestational hypertension, preeclampsia, intrauterine growth restriction, stillbirth, and gestational diabetes mellitus).
TABULATION, INTEGRATION, AND RESULTS: From 3305 unique citations, 62 observational studies (196,989 women) were included. “Low” to “very low” certainty evidence from these studies revealed that working rotating shifts was associated with an increased odds of preterm delivery (odds ratio, 1.13; 95% confidence interval, 1.00—1.28, $I^2 = 31\%$), an infant small for gestational age (odds ratio, 1.18, 95% confidence interval, 1.01—1.38, $I^2 = 0\%$), preeclampsia (odds ratio, 1.75, 95% confidence interval, 1.01—3.01, $I^2 = 75\%$), and gestational hypertension (odds ratio, 1.19, 95% confidence interval, 1.10—1.29, $I^2 = 0\%$), compared to those who worked a fixed day shift. Working fixed night shifts was associated with an increased odds of preterm delivery (odds ratio, 1.21; 95% confidence interval, 1.03—1.42; $I^2 = 36\%$) and miscarriage (odds ratio, 1.23; 95% confidence interval, 1.03—1.47; $I^2 = 37\%$). Compared with standard hours, working longer hours was associated with an increased odds of miscarriage (odds ratio, 1.38; 95% confidence interval, 1.08—1.77; $I^2 = 73\%$), preterm delivery (odds ratio, 1.21; 95% confidence interval, 1.11—1.33; $I^2 = 30\%$), an infant of low birthweight (odds ratio, 1.43; 95% confidence interval, 1.11—1.84; $I^2 = 0\%$), or an infant small for gestational age (odds ratio, 1.16, 95% confidence interval, 1.00—1.36, $I^2 = 57\%$). Dose—response analysis showed that women working more than 55.5 hours (vs 40 hours) per week had a 10% increase in the odds of having a preterm delivery.
CONCLUSION: Pregnant women who work rotating shifts, fixed night shifts, or longer hours have an increased risk of adverse pregnancy outcomes.

Key words: pregnancy outcomes, shift work, working hours

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Introduction

Women of reproductive age make up a significant proportion of the workforce, and approximately 90% of women remain employed during pregnancy.[1] Data from the Sixth European Working Conditions Survey (2016) showed that more than 15% of women worked more than 41 hours per week, 21% of women were exposed to shift work, and 14% of women were engaged in night work.[2] Although definitions vary across sources, long working hours are defined as work beyond the standard hours of work,[3] whereas shift work is defined as employment in any work schedule that is not a regular daytime schedule.[4] Recent studies have found that long working hours and shift work may be associated with an increased risk of adverse pregnancy outcomes, including preterm delivery (PTD) and miscarriage.[5,6] Plausible physiological mechanisms linking altered sleep patterns and long working hours to adverse pregnancy outcomes have also started to emerge. It has been suggested that prolonged disruption of circadian rhythms as a result of shift work trigger neuroendocrine adaptations that may affect fetal growth and timing of parturition,[5] and that raised noradrenaline levels from long working hours may increase uterine contractility and the risk of preterm labor and miscarriage.[7,8]

Up to 2013, meta-analyses examining the impact of long working hours and shift work on PTD, small-for-gestational age (SGA), miscarriage, and preeclampsia reported conflicting findings.[9–12] In the subsequent 6 years, additional studies have provided evidence that may clarify the link between working hours and shift work with adverse pregnancy outcomes. Given the increasing number of women in the labor force worldwide (from 1.29 billion in 2013 to 1.36 billion in 2017),[13] synthesis of this new evidence is needed. Furthermore, no work to date has conducted risk assessments on the number of working hours per week in a continuous manner, referring instead to categorical levels of working hours (eg, >40 versus ≤40).

The purpose of this review is to evaluate the impact of shift work and long working hours during pregnancy on maternal and fetal health outcomes, and to establish whether a dose−response relationship exists between the length of working hours and these important health outcomes.

Materials and Methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,[14] and was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (Registration no. CRD42018094400).

Information sources

A structured search of MEDLINE, EMBASE, Cochrane Library, CINAHL, ClinicalTrials.gov, Science Citation Index Expanded, and Conference Proceedings Citation Index—Science up to March 15, 2019, was performed by a research librarian. The search strategies were peer reviewed by another experienced research librarian. Collaborator-nominated papers were accepted for consideration, and the reference lists of included papers and relevant systematic reviews were screened for additional, relevant papers. We also conducted forward and backward citation tracking, hand-searched Google Scholar, and obtained expert recommendations for additional relevant studies. Language restrictions were not applied. The studies published in languages other than English, Spanish, Chinese, or French that were deemed to be potentially relevant were translated by using Google Translate. (See the online supplement for complete search strategies.)

Eligibility criteria

Study design. Primary studies of any design were eligible, except case studies, narrative or systematic reviews and meta-analyses. We also excluded letters, commentaries, editorials, and abstracts.

Population. The population of interest was pregnant women (any trimester) who engaged in paid work. Some studies have suggested that paid employment and unpaid work may have different psychological, social, and biological factors that may affect health risk.[15–17] To prevent bias, we included only studies with pregnant women (any trimester) who engaged in paid work.

Exposure. Included exposures were rotating shift work, fixed night shifts, or long working hours during pregnancy. Rotating shift work was defined as working hours that rotate or change according to a set schedule.[18] Fixed night shift was defined as typical working period between 11:00 pm and 11:00 am.[19] Long working hours were defined as working more than 40 hours per week, implying either greater than a 5-day work week and/or longer than an 8-hour work day. The cut-off is also consistent with the standard hours of work (40 hours per week) under the US Department of Labor[20] and Canada Labour Code.[3]

In the event that studies reported odds ratios (ORs) for categories of working hours that were not conventional (eg, ≥45 hours reference to <45 hours), effect estimates were grouped with the nearest conventional working hour category. Studies that reported the long working hours as the referent category were not considered comparable and are therefore described only narratively.

Comparison. Eligible comparators were fixed day shift or "standard" working hours. Fixed day shift was defined as typical working period between 8:00 am and 6:00 pm. Standard working hours was defined as ≤40 working hours per week, or the nearest cut-off reported by the studies.

Outcomes. Relevant outcomes were PTD (<37 weeks of gestation), low birthweight (LBW, birthweight <2500 g), SGA (a weight below the 10th percentile for the gestational age), miscarriage (or spontaneous abortion, defined as loss of a fetus prior to 20 weeks' gestation),[21] stillbirth (a fetal

AJOG at a Glance

Why was this study conducted?

- Concerns have been expressed that shift work and longer working hours may expose pregnant workers to higher risks of adverse pregnancy outcomes.

Key findings

- Rotating shift work, fixed night shifts, and working >40 hours per week increased the odds of preterm delivery by 13%, 21%, and 21%, respectively.
- Fixed night shifts and working >40 hours per week increased the odds of miscarriage by 23% and 38%, respectively.
- Women working more than 55.5 hours per week had a 10% increase in the odds of having a preterm delivery compared to working 40 hours per week.

What does this add to what is known?

- Updated evidence now demonstrates that pregnant women who work rotating shifts, fixed night shifts, or longer hours have an increased risk of adverse pregnancy outcomes.

death occurring after 20 completed weeks of pregnancy),[22] gestational hypertension (new-onset elevated blood pressure [≥140/90 mm Hg] after 20 weeks of gestation without proteinuria or end-organ involvement) and preeclampsia (the development of hypertension with evidence of end-organ effects or proteinuria after 20 weeks of pregnancy),[23] intrauterine growth restriction (IUGR, failure of the fetus to attain its expected fetal growth [<10th percentile] at any gestational age),[24] and gestational diabetes mellitus (GDM, any degree of glucose intolerance with onset or first recognition during pregnancy as defined by the criteria used by the study).[25] The definitions of miscarriage, gestational hypertension, preeclampsia, IUGR, and GDM that were used for inclusion were based on the regional standards in place at the time of each study.

Study selection and data extraction

Titles and abstracts of articles identified by the search were assessed by 2 independent reviewers. Studies meeting eligibility criteria by at least 1 reviewer were selected for full-text review. Two independent reviewers examined all full-text articles for eligibility. If there was a discrepancy between reviewers, eligibility was decided based on discussion between the reviewers and by decision of a third reviewer when needed. Data were extracted by 2 reviewers independently. For each primary study, the most recent or complete publication was selected; however, relevant data from all publications related to each unique study were extracted. Study characteristics (eg, study period, study design, country) and population characteristics (eg, number of participants, age, prepregnancy body mass index [BMI], parity), exposure (eg, work schedules, weekly working hours) and clinical outcomes (eg, PTD, LBW, SGA, miscarriage, gestational hypertension, preeclampsia, IUGR, stillbirth, and GDM) were extracted (see online supplement Table 1). If data were not available for extraction, attempts were made to contact the corresponding authors for additional information.

Quality of evidence assessment and GRADE

Two reviewers independently assessed the quality of the studies. The Cochrane Risk of Bias Tool (version 1) was used for randomized controlled trials (RCT). We assessed study quality of prospective cohort, case-control, and cross-sectional studies using the Joanna Briggs Institute Critical Appraisal of Evidence Effectiveness tool.[26] Risk of bias across studies was rated as "serious" when studies with the greatest influence on the pooled result (contributing >50% of the weight of the pooled estimate in forest plots) presented "high" risk of bias.

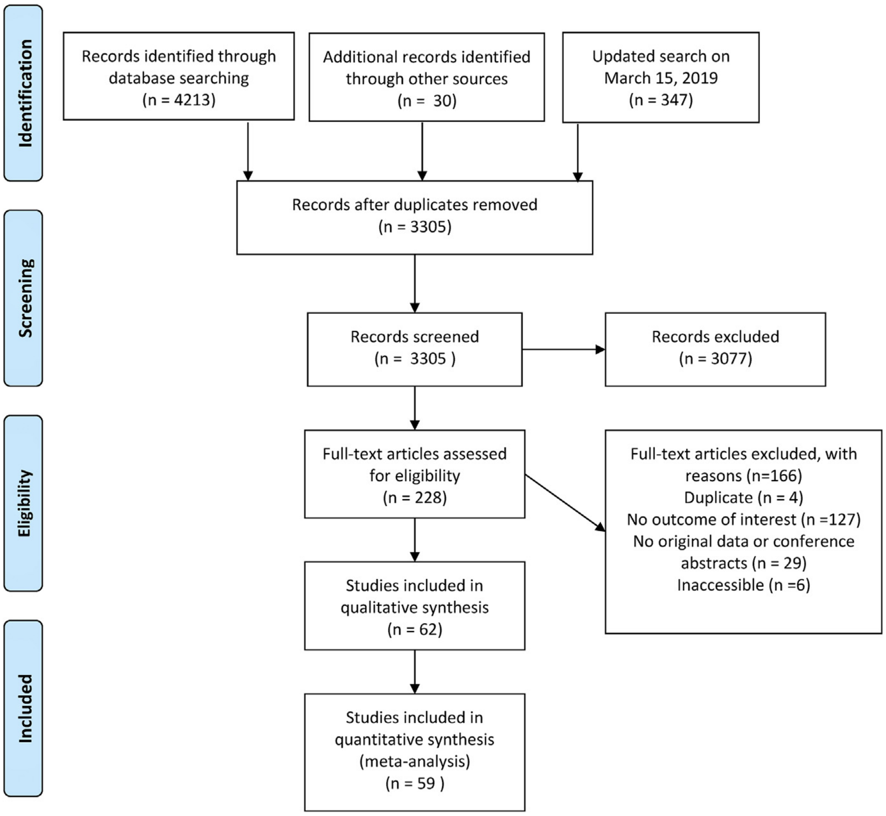
The Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool[27] was used to assess the certainty of the evidence across each outcome. Evidence from RCTs began with a "high" certainty of evidence rating and was downgraded if there were concerns of risk of bias, indirectness, inconsistency, or imprecision. Evidence from all observational studies began with a "low" certainty rating. The initial "low" rating was upgraded when there was evidence for large magnitude of effect, evidence of dose-response, counteracting plausible residual bias, or confounding.[28] Inconsistency across studies was considered serious when heterogeneity was high ($I^2 \geq 50\%$) or when only 1 study was assessed (I^2 unavailable). Imprecision was considered serious when the 95% confidence interval (CI) crossed the line of no effect. Imprecision was not considered serious when only 1 study was assessed, because the study would have already been downgraded for inconsistency for this reason. Finally, publication bias was assessed via funnel plots when more than 10 studies were included in the forest plot. Publication bias was not downgraded when there were fewer than 10 studies. The GRADE assessment is presented in online supplementary tables.

Data synthesis

All statistical analyses were conducted using Review Manager v5.3 (Cochrane Collaboration, Copenhagen, Denmark).

ORs and corresponding 95% CIs were used to assess the association between the clinical outcomes and work exposures. Significance was set at $P < 0.05$. Inverse-variance weighting was applied to obtain ORs using a random-effects model. For observational studies, sensitivity analyses were performed to evaluate whether the effects were different between adjusted ORs vs crude ORs for the outcomes of interest. If adjusted data

FIGURE 1
Study flow diagram



Cai. Prenatal work schedules and pregnancy complications. Am J Obstet Gynecol 2019.

were available, we calculated the natural logarithms of the effect measure and corresponding standard errors; otherwise, we included the unadjusted estimate. Heterogeneity between the studies was assessed using the I^2 statistic. In the case of I^2 >50%, heterogeneity was explored further with subgroup and sensitivity analyses. If data were not suitable for meta-analysis, authors were contacted to obtain additional information, and data were synthesized narratively if authors were unable to provide additional data. The 95% prediction intervals were also calculated for the distribution of true effects.[29]

To identify a clinically meaningful improvement in pregnancy outcomes with working hours and shift work, a dose−response meta-regression was carried out using the drmeta command in STATA 14.2.[30] A random-effects maximum-likelihood approach was used for both linear and quadratic models on the log ORs. A likelihood ratio test was used to determine nonlinearity. As an accepted cut-point for a clinically meaningful increase does not exist in the literature, an increase of 10% was chosen based on expert opinion.

Results

The literature search identified 3305 unique citations, with 62 observational studies (16 longitudinal studies,[31−46] 27 cross-sectional studies,[47−73] and 19 case-control studies[74−92]; N = 196,989 women) from 33 countries included in this systematic review. A PRISMA diagram of the search and study selection results is shown in Figure 1. Three corresponding authors were sent letters requesting additional information or clarification of data from 4 studies.[39,40,45,93] One author responded to the e-mails.[93] However, no additional data were obtained for the meta-analysis (see the online supplemental document for the detailed list).

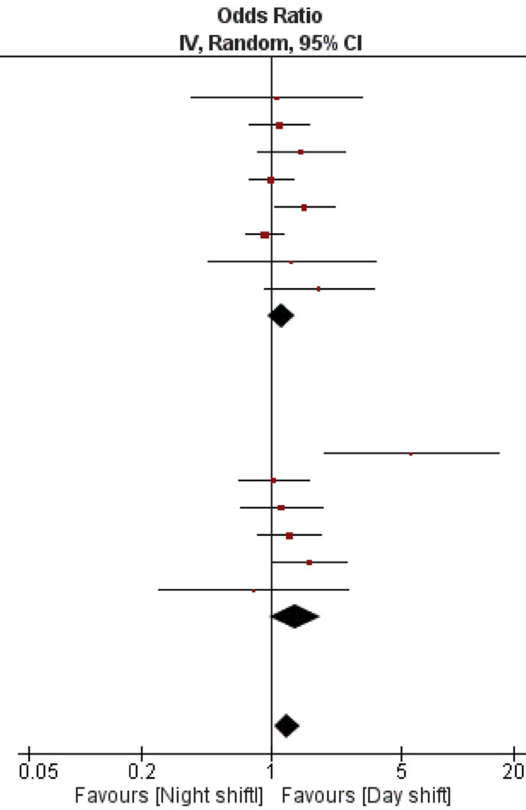
Twenty studies examined specific occupational groups, including midwives,[50,51] nurses,[56,58−60,66,84] physicians,[70] physiotherapists, cosmetologists,[57,91] lawyers,[65] veterinarians,[67,68] hospital administrators/workers,[49,54] pharmaceutical workers,[48] workers from semiconductor companies,[69] military personnel,[42] and textile workers,[72] whereas the other 42 studies assessed the general population. All studies reported category of working hours and shift work assessed by self-report (questionnaires or interviews). Fifteen studies reported pregnancy outcomes assessed by self-report,[41,50,52,58−60,62,65−68,70,72,76,84] another 6 studies used birth registry or certification,[32,51,54,63,90,91] and the other 42 studies used medical records or hospital reports. The majority of studies used the same outcome definition with the exception of miscarriage. Half of the studies defined the miscarriage as the loss of a fetus prior to 20 weeks of gestation; the rest either defined it as the loss of a fetus prior to 28 or 29 weeks of gestation or lacked a clear definition. Individual study characteristics can be found in the online supplement tables. Excluded studies, with reasons for their exclusion, are presented in the online supplement.

Quality of evidence and GRADE

All the included studies were observational studies, which began with a "low" certainty assessment. No studies were upgraded, and the most common reasons for downgrading the certainty of evidence were (1) serious risk of bias, (2) inconsistency, and (3) imprecision. Overall, the certainty of evidence ranged from "low" to "very low" (see online supplement tables). Common sources of bias were performance bias and detection bias, which included imprecise measurement of both the exposure and outcomes. No evidence of publication bias was observed.

FIGURE 2
Effects of fixed night shift compared with day shift on odds of preterm delivery

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.2.1 Adjusted odds ratio				
Bonzini 2009	0.0677	0.5381	2.0%	1.07 [0.37, 3.07]
Croteau 2007	0.0953	0.1923	9.9%	1.10 [0.75, 1.60]
Fortier 1995	0.3716	0.2772	6.2%	1.45 [0.84, 2.50]
Lawson 2009	0	0.1428	13.3%	1.00 [0.76, 1.32]
Pompeii 2005	0.4055	0.1893	10.1%	1.50 [1.04, 2.17]
Saurel-cubizolle 2004	-0.0834	0.1153	15.5%	0.92 [0.73, 1.15]
Snijder 2012	0.2546	0.5284	2.1%	1.29 [0.46, 3.63]
Stinson 2003	0.5878	0.3403	4.5%	1.80 [0.92, 3.51]
Subtotal (95% CI)			**63.6%**	**1.13 [0.96, 1.33]**
Heterogeneity: Tau² = 0.01; Chi² = 8.71, df = 7 (P = 0.27); I² = 20%				
Test for overall effect: Z = 1.44 (P = 0.15)				
1.2.2 Unadjusted odds ratio				
Bodin 1999	1.7228	0.5499	2.0%	5.60 [1.91, 16.45]
El-Gilany 2016	0.0281	0.2177	8.6%	1.03 [0.67, 1.58]
Heaman 2005	0.1222	0.2557	6.9%	1.13 [0.68, 1.87]
Luke1995	0.2227	0.2	9.5%	1.25 [0.84, 1.85]
Mamelle 1984	0.47	0.2338	7.8%	1.60 [1.01, 2.53]
Saurel-Cubizolles 1987	-0.2198	0.5974	1.7%	0.80 [0.25, 2.59]
Subtotal (95% CI)			**36.4%**	**1.34 [0.97, 1.85]**
Heterogeneity: Tau² = 0.07; Chi² = 9.98, df = 5 (P = 0.08); I² = 50%				
Test for overall effect: Z = 1.77 (P = 0.08)				
Total (95% CI)			**100.0%**	**1.21 [1.03, 1.42]**
Heterogeneity: Tau² = 0.03; Chi² = 20.31, df = 13 (P = 0.09); I² = 36%				
Test for overall effect: Z = 2.38 (P = 0.02)				
Test for subgroup differences: Chi² = 0.86, df = 1 (P = 0.35), I² = 0%				



Sensitivity analyses were conducted with studies reported adjusted odds ratio for confounders and unadjusted odds ratio.

CI, confidence interval; *df*, degrees of freedom; *IV*, inverse-variance method.

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Obstetric outcomes

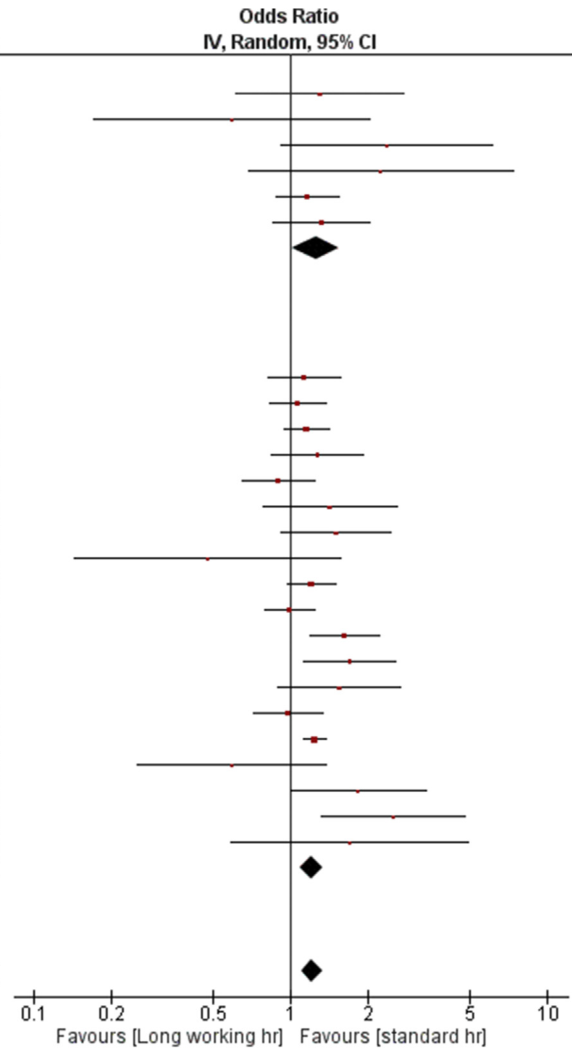
Preterm delivery. Overall, there was "low" certainty evidence from 15 observational studies (n = 26,677) regarding the association between rotating shift work and PTD.[33,36,38,47,51,53,58,61,72,75,80,81,87,90,92] The pooled estimate demonstrated that working a rotating shift was associated with a 13% increase in the odds of PTD compared with working a day shift (OR, 1.13; 95% CI, 1.00−1.28; I^2 = 31%; see online supplement Figure 1). There was "low" certainty evidence from 14 studies (n = 39,714)[31,33,40−42,51,53,58,61,64,75,81,84,87] showing that working a fixed night shift was associated with a 21% increase in the odds of PTD compared with working a day shift (OR, 1.21; 95% CI, 1.03−1.42; I^2 = 36%; Figure 2). There was "low" certainty evidence from 25 studies (n = 66,184) regarding the association between working long hours and PTD.[31,33−35,37,38,40,43,51−53,58,61,63,64,68,70,73,75,78,81,83,84,86,87] Overall, working long hours was associated with a 21% increase in the odds of PTD compared with working regular hours (OR, 1.21; 95% CI, 1.11−1.33, I^2 = 30%; Figure 3). The single study that was not included in the pooled estimate because the data could not be converted into a useable form indicated that working 16−32 hours per week was associated with a 47% decrease in the odds of PTD compared with working >32 hours per week (n = 2264; OR, 0.53; 95% CI, 0.33−0.86).[45]

Miscarriage. Overall, there was "very low" certainty evidence from 12 studies (n = 118,376)[44,48−50,56,59,62,66,69,79,82,94] showed that no association between rotating shifts and miscarriage (OR, 1.05; 95% CI, 0.85−1.29, I^2 = 64%; see online supplement Figure 2). The certainty of evidence was downgraded from "low" to "very low" because of serious risk of bias, inconsistency, and imprecision. However, pregnant women who worked fixed night shifts had higher rates of miscarriage than women who worked regular day shifts (10 studies, n = 62,877; OR, 1.23; 95% CI, 1.03−1.47, I^2 = 33%; "very low" certainty, downgraded because of serious risk of bias; Figure 4).[44,49,50,59,66,69,77,79,82,94] Meanwhile, women who worked >40 hours per week had a 38% increase in the odds of miscarriage compared to women who did not (8 studies, n = 73,855; OR, 1.38; 95% CI, 1.08−1.77, I^2 = 73%; "very

FIGURE 3

Effects of working more than 40 hours per week compared with working 40 hours or less per week on the odds of preterm delivery

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.3.1 Adjusted odds ratio				
Bodin 1999	0.2627	0.3837	1.3%	1.30 [0.61, 2.76]
Bonzini 2009	-0.528	0.6327	0.5%	0.59 [0.17, 2.04]
El-Gilany 2016	0.8587	0.4811	0.8%	2.36 [0.92, 6.06]
Niedhammer 2009	0.8109	0.6025	0.5%	2.25 [0.69, 7.33]
Rodrigues 2008	0.1484	0.1428	6.3%	1.16 [0.88, 1.53]
Snijder 2012	0.2776	0.2221	3.3%	1.32 [0.85, 2.04]
Subtotal (95% CI)			**12.7%**	**1.25 [1.01, 1.55]**
Heterogeneity: Tau² = 0.00; Chi² = 4.45, df = 5 (P = 0.49); I² = 0%				
Test for overall effect: Z = 2.09 (P = 0.04)				
1.3.2 Unadjusted odds ratio				
Bell 2008	0.1177	0.1658	5.1%	1.12 [0.81, 1.56]
Ceron-Mireles 1996	0.0643	0.1262	7.3%	1.07 [0.83, 1.37]
Croteau 2007	0.1414	0.1043	8.9%	1.15 [0.94, 1.41]
Escribà-Agüir 2001	0.2392	0.2075	3.7%	1.27 [0.85, 1.91]
Fortier 1995	-0.109	0.1674	5.1%	0.90 [0.65, 1.24]
Heaman 2005	0.3507	0.3052	1.9%	1.42 [0.78, 2.58]
Henriksen 1994	0.4068	0.2512	2.7%	1.50 [0.92, 2.46]
Hickey 1995	-0.7437	0.61	0.5%	0.48 [0.14, 1.57]
Lawson 2009	0.1868	0.1089	8.5%	1.21 [0.97, 1.49]
Lee 2016	-0.0094	0.1165	7.9%	0.99 [0.79, 1.24]
Luke1995	0.4832	0.1573	5.5%	1.62 [1.19, 2.21]
Mamelle 1984	0.5306	0.2094	3.6%	1.70 [1.13, 2.56]
Nguyen 2004	0.4347	0.2814	2.2%	1.54 [0.89, 2.68]
Peoples-Sheps 1991	-0.0267	0.1578	5.5%	0.97 [0.71, 1.33]
Saurel-cubizolle 2004	0.2157	0.0539	13.5%	1.24 [1.12, 1.38]
Saurel-Cubizolles 1987	-0.528	0.4288	1.0%	0.59 [0.25, 1.37]
Shirangi 2009	0.6055	0.3101	1.9%	1.83 [1.00, 3.36]
Takeuchi 2014	0.9216	0.3295	1.7%	2.51 [1.32, 4.79]
Tuntiseranee 1998	0.5306	0.5409	0.7%	1.70 [0.59, 4.91]
Subtotal (95% CI)			**87.3%**	**1.21 [1.09, 1.34]**
Heterogeneity: Tau² = 0.02; Chi² = 29.82, df = 18 (P = 0.04); I² = 40%				
Test for overall effect: Z = 3.73 (P = 0.0002)				
Total (95% CI)			**100.0%**	**1.21 [1.11, 1.33]**
Heterogeneity: Tau² = 0.01; Chi² = 34.41, df = 24 (P = 0.08); I² = 30%				
Test for overall effect: Z = 4.32 (P < 0.0001)				
Test for subgroup differences: Chi² = 0.09, df = 1 (P = 0.77), I² = 0%				



Sensitivity analyses were conducted with studies reporting adjusted odds ratio for confounders and unadjusted odds ratio.

CI, confidence interval; *df*, degrees of freedom; *IV*, inverse-variance method.

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low" certainty, downgraded due to serious risk of bias and inconsistency; see online supplement Figure 3).[57,59,62,65,67,69,79,94]

Stillbirth. Only 1 study (n = 41,769) reported the association between shift work and stillbirth, and indicated that rotating shifts or fixed night shift was not associated with stillbirth (rotating shifts, hazard ratio [HR], 0.81; 95% CI, 0.38−1.70; fixed night shift, HR, 1.92, 95% CI, 0.82−4.5).[44]

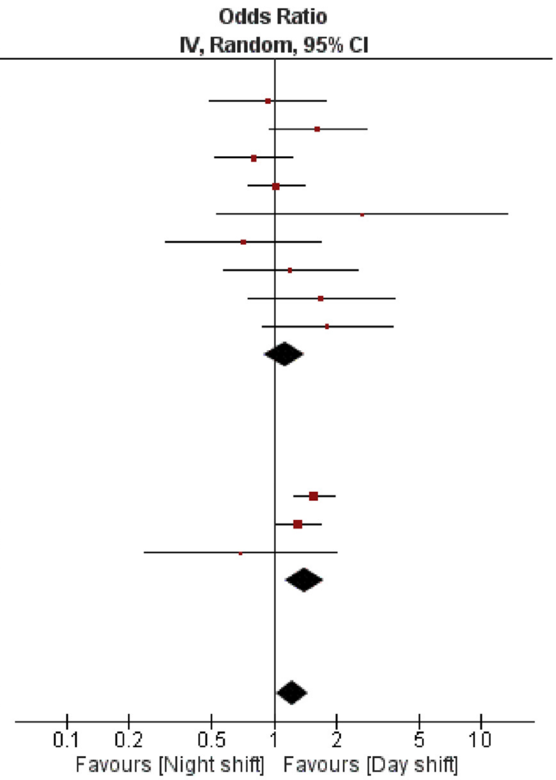
Maternal outcomes

Preeclampsia. There was "very low" certainty evidence from 2 studies (n = 29,588) found that rotating shifts was associated with a 75% increase in the odds of preeclampsia compared with working a day shift (OR, 1.75; 95% CI, 1.01−3.01; I^2 = 75%; see online supplement Figure 4).[32,95] The certainty of evidence was downgraded from "low" to "very low" because of serious risk of bias, and inconsistency. However, there was no association between working a night shift and preeclampsia (3 studies, n = 33,247; OR, 1.05; 95% CI, 0.63−1.75; I^2 = 0%, "very low" certainty, downgraded because of imprecision; see online supplement Figure 5).[32,39,76] Long working hours were also not associated with preeclampsia (5 studies, n = 34,650; OR, 1.27; 95% CI, 0.74−2.19; I^2 = 84%; "very low" certainty, downgraded due to inconsistency and imprecision; see online supplement Figure 6).[32,39,76,85,88]

FIGURE 4

Effects of fixed night shift compared with day shift on odds of miscarriage

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.3.1 Adjusted				
Axelsson 1989	-0.0726	0.3291	6.0%	0.93 [0.49, 1.77]
Axelsson 1996	0.4886	0.2757	7.8%	1.63 [0.95, 2.80]
Eskenazi 1994	-0.2231	0.2233	10.5%	0.80 [0.52, 1.24]
Fenster 1997	0.0296	0.161	15.3%	1.03 [0.75, 1.41]
Infante-Rivard 1993	0.9858	0.8246	1.1%	2.68 [0.53, 13.49]
Swan 1995	-0.3425	0.4425	3.6%	0.71 [0.30, 1.69]
Swan 1995 I	0.1823	0.3817	4.7%	1.20 [0.57, 2.54]
Swan 1995 II	0.5306	0.414	4.1%	1.70 [0.76, 3.83]
Zhu 2004	0.5933	0.3677	5.0%	1.81 [0.88, 3.72]
Subtotal (95% CI)			**58.1%**	**1.13 [0.91, 1.41]**
Heterogeneity: Tau² = 0.02; Chi² = 9.63, df = 8 (P = 0.29); I² = 17%				
Test for overall effect: Z = 1.07 (P = 0.28)				
4.3.2 Unadjusted				
El Metwalli 2001	0.4525	0.116	20.1%	1.57 [1.25, 1.97]
Lawson 2012	0.2781	0.1227	19.3%	1.32 [1.04, 1.68]
Shagheibi 2016	-0.3715	0.5422	2.5%	0.69 [0.24, 2.00]
Subtotal (95% CI)			**41.9%**	**1.40 [1.13, 1.75]**
Heterogeneity: Tau² = 0.01; Chi² = 2.89, df = 2 (P = 0.24); I² = 31%				
Test for overall effect: Z = 3.02 (P = 0.003)				
Total (95% CI)			**100.0%**	**1.23 [1.03, 1.47]**
Heterogeneity: Tau² = 0.03; Chi² = 16.43, df = 11 (P = 0.13); I² = 33%				
Test for overall effect: Z = 2.32 (P = 0.02)				
Test for subgroup differences: Chi² = 1.87, df = 1 (P = 0.17), I² = 46.6%				



Sensitivity analyses were conducted with studies reporting adjusted odds ratio for confounders and unadjusted odds ratio.

CI, confidence interval; *df*, degrees of freedom; *IV*, inverse-variance method.

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Gestational hypertension. Evidence from 2 studies (n = 25,675) demonstrated that rotating shifts was associated with a 19% increase in the odds of gestational hypertension compared with working a day shift (OR, 1.19; 95% CI, 1.10–1.29; I^2 = 0%; "low" certainty; see online supplement Figure 7).[32,92] There was "very low" certainty evidence from 4 studies (n = 51,971) found that working a night shift was not associated with gestational hypertension (OR, 1.19; 95% CI, 0.97–1.45; I^2 = 2%; "very low" certainty, downgraded because of imprecision; see online supplement Figure 8).[32,39,54,76] Working long hours was also not associated with gestational hypertension (5 studies, n = 34,650; OR, 0.99; 95% CI, 0.72–1.37, I^2 = 62%; "very low" certainty, downgraded because of inconsistency and imprecision; see online supplement Figure 9).[32,39,76,85,88] The single study that was not included in the pooled estimate because the data could not be converted into a usable form demonstrated that working 16–32 hours per week was not associated with gestational hypertension compared with working >32 hours per week (n = 2264; OR, 0.83; 95% CI, 0.62–1.12).[45]

Gestational diabetes mellitus. Only 1 study reported the association between working hours and GDM, and demonstrated that working 16–32 hours per week was not associated with GDM compared with working >32 hours per week (n = 2264; OR, 0.81; 95% CI, 0.43–1.54).[45]

Fetal outcomes

Small for gestational age. There was "low" certainty evidence from 7 studies (n = 18,230) found that working rotating shifts was associated with a 18% increase in the odds of SGA compared with working a day shift (OR, 1.18; 95% CI, 1.01–1.38; I^2 = 0%; see online supplement Figure 10).[33,38,51,55,74,92] However, there was no association between night shift work and the risk of having an SGA neonate (6 studies, n = 20,861; OR, 1.08; 95% CI, 0.86 to 1.35; I^2 = 0%; "very low" certainty, downgraded due to imprecision; see online supplement Figure 11).[31,33,40,41,51,74] Meanwhile, working long hours was associated with a 16% increase in the odds of SGA compared with not working long hours (12 studies, n = 38,246; OR, 1.16; 95% CI, 1.00–1.36; I^2 = 57%; "very low" certainty, downgraded because of inconsistency; see online supplement Figure 12).[31,33,34,38,40,41,43,51,52,73,74,83] Two studies were not included in the pooled estimate because data could not be converted into a usable form. One study found that working ≥32 hours per week was not associated with SGA compared with working 8–23 hours per week (OR, 1.1; 95% CI, 0.8–1.5).[46] The other study indicated that working 16–32 hours per week was not associated with SGA compared with working >32 hours per week (n = 2264; OR, 0.86; 95% CI, 0.6–1.25).[45]

Low birthweight. There was "very low" certainty evidence from 3 studies (n = 3750) demonstrated that no association between rotating shifts and LBW (OR, 1.41; 95% CI, 0.82–2.41; I^2 = 20%; see online supplement Figure 13).[38,51,72] The certainty of evidence was downgraded from "low" to "very low" because of serious risk of bias, and imprecision. There was "very low" certainty evidence from 3 studies (n = 8442) indicating no association between fixed night shift and LBW (OR, 1.44; 95% CI, 0.76–2.75; I^2 = 0%; see online supplement Figure 14).[40,51,64] The certainty of evidence was downgraded from "low" to "very low" because of imprecision. However, working more than 40 hours per week was associated with a 43% increase in the odds of LBW compared with not working more than 40 hours per week (6 studies, n = 14,074; OR, 1.43; 95% CI, 1.11– 1.84; I^2 = 0%; "low" certainty, see online supplement Figure 15).[38,40,43,51,63,64] The single study that was not included in the pooled estimate because data could not be converted demonstrated that working more than 30 hours per week was not associated with LBW compared with working 30 hours or less per week (n = 283; OR, 1.43; 95% CI, 0.82–2.49).[96]

Intrauterine growth restriction. One study reported the association between working hours and IUGR and demonstrated that long working hours were not associated with IUGR (n = 1047; OR, 1.62; 95% CI, 0.93–2.85; "very low" certainty, downgraded because of inconsistency).[89]

Ninety-five percent prediction intervals

Overall, the 95% prediction intervals were wider than the 95% CIs but provided the information in the distribution of true effects (see online supplement Table 10).

Meta-regressions

Meta-regression analyses were conducted when at least 10 studies with sufficient data[97] were available. In this review, only the meta-analysis relating working hours and the risk of PTD met this criterion. Linear models were presented unless the fit of the spline was significantly better ($P < 0.05$). Thirteen observation studies (n = 38,849) were included in the dose–response analysis using a linear model. Compared to a 40-hour work week, working at least 55.5 hours per week was associated with a 10% increase in the odds of having a preterm delivery (see online supplement Figure 16).

Sensitivity analyses

The pooled estimates of PTD, miscarriage, preeclampsia, SGA, or LBW for the adjusted odds ratio were not significantly different from the pooled estimate for the unadjusted odds ratio for worked with rotating shifts, fixed night shifts, or longer hours. However, the pooled estimate examining the impact of long working hours on risk of gestational hypertension was significantly different between the adjusted OR (1 study, n = 4465; OR, 1.57; 95% CI, 0.20–0.91; "very low" certainty evidence, downgraded because of inconsistency)[39] and unadjusted OR subgroups (4 studies, n = 30,185; OR, 1.11; 95% CI, 0.86–1.43; "very low" certainty evidence, downgraded because of imprecision).[32,76,85,88]

Subgroup analyses

The association between long working hours, rotating shifts, or fixed night shifts and gestational hypertension, SGA, or LBW (see online supplement Tables 5–7) were not dependent on the cut-off value for long working hours, study design, or study population.

The association between long working hours, rotating shift work, or fixed night shift and PTD were not dependent on study design or study population (Table 1). The test for subgroup differences of cut-off values for long working hours was statistically significant ($P <$ 0.05). Results showed that compared to working 35 hours or less per week, working more than 35 hours per week increased the odds of PTD by 59%; compared to working 40 hours or less per week,[34,51,68,84] working more than 40 hours per week increased the odds of PTD by 13%.[31,33,35,37,38,43,52,53,58,61,63,70,73,75,78,83,86,87]

The association between rotating shift or fixed night shift work and miscarriage were not dependent on study design or study population (online supplement Table 7). The test for subgroup differences of long working hours by study types and study population were both statistically significant ($P < 0.05$). Results from retrospective studies showed that long working hours increased the odds of miscarriage by 46%.[57,59,62,65,67,69,79] Results from 1 prospective study showed that long working hours was not associated with miscarriage.[94] Results from general population studies showed that long working hours were not associated with miscarriage.[79,94,98] Results from specific occupations studies showed that long working hours increased the odds of miscarriage by 64%.[57,59,65,67,69]

The association between long working hours or fixed night shift and preeclampsia was not dependent on the specific cut-off value for long working hours, or study design (online supplement Table 8). The test for subgroup differences of rotating shift work by study types was statistically significant. Results from 1 retrospective study showed rotating shift work was not associated with preeclampsia,[92] whereas the other prospective study showed rotating shift work increased the odds of preeclampsia by 127%.[32]

A series of subgroup analyses were performed for subsets of rotating shift work (ie, studies that included night shift as part of rotating shift work and studies that did not provide the information). No significant difference was detected between groups in across all outcomes (see online supplement Figure 23–26).

Comment

Main findings

In this systematic review and meta-analysis of 62 studies, despite "low" to

TABLE 1
Associations among long working hours, shift work, and preterm delivery

Subgroup factor	Subgroups	OR (95% CI)	Test for subgroup difference χ^2	*P* value
Long working hours				
Cut-off value for long working hours	≤35 vs >35 h	1.59 (1.26–2.00)		
	≤40 vs >40 h	1.13 (1.02–1.25)		
	Overall	1.19 (1.07–1.31)	7.28	0.007
Study design	Retrospective	1.19 (1.07–1.32)		
	Prospective	1.20 (0.92–1.56)		
	Overall	1.19 (1.08–1.31)	0.00	0.96
Study population	General population	1.12 (1.02–1.22)		
	Specific occupation groups	1.46 (1.11–1.93)		
	Overall	1.19 (1.08–1.31)	3.26	0.07
Rotating shift work				
Study design	Retrospective	1.11 (0.96–1.28)		
	Prospective	1.25 (1.02–1.52)		
	Overall	1.13 (1.00–1.28)	0.88	0.35
Study population	General population	1.13 (1.02–1.26)		
	Specific occupational groups	1.13 (0.69–1.86)		
	Overall	1.13 (1.00–1.28)	0.00	1.00
Fixed night shift				
Study design	Retrospective	1.17 (0.94–1.46)		
	Prospective	1.34 (1.08–1.68)		
	Overall	1.21 (1.03–1.42)	0.76	0.38
Study population	General population	1.12 (0.98–1.29)		
	Specific occupation groups	1.53 (0.94–2.49)		
	Overall	1.21 (1.03–1.42)	1.46	0.23

CI, confidence interval; *OR*, odds ratio.

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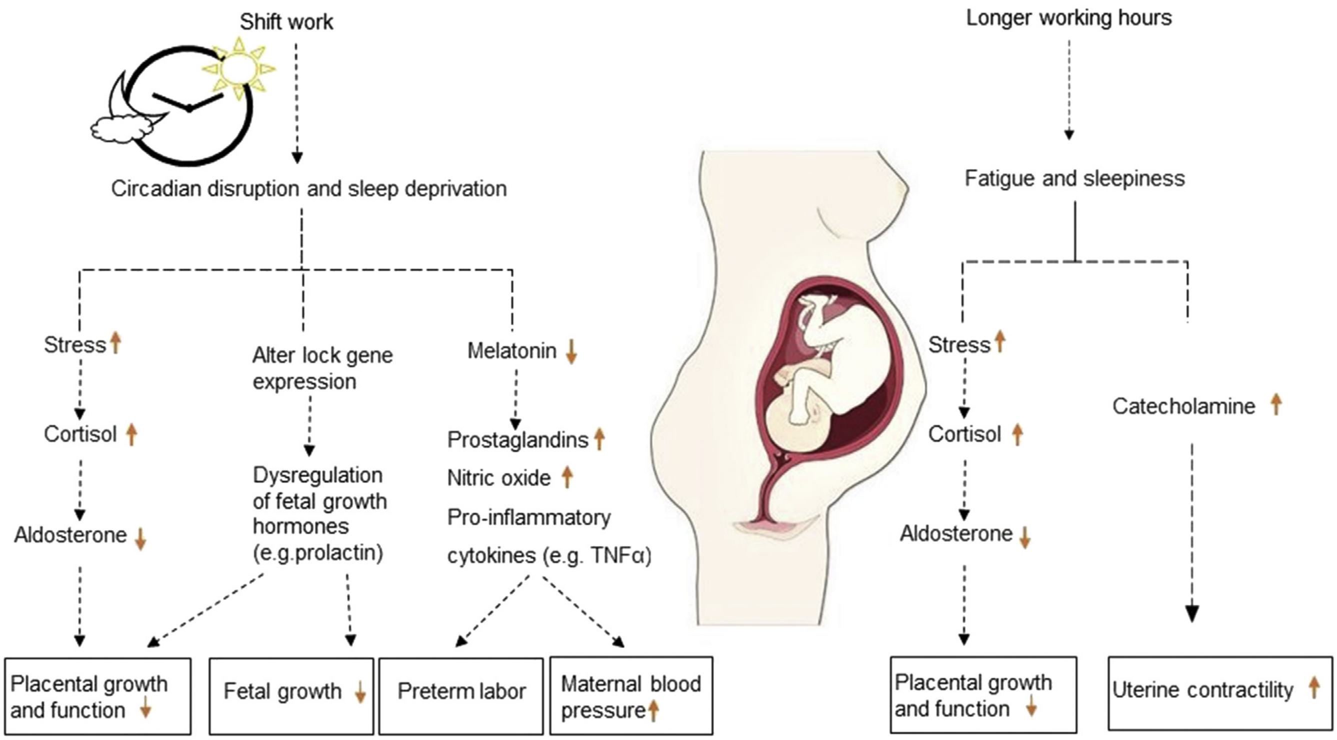
"very low" certainty evidence from observational studies, the data demonstrated that compared with working a fixed day shift, working rotating shifts was associated with a 13% increase in the odds of PTD, a 18% increase in the odds of having an SGA infant, a 75% increase in the odds of preeclampsia, and a 19% increase in the odds of gestational hypertension. Compared to working a fixed day shift, working a fixed night shift was associated with a 21% increase in the odds of PTD and a 23% increase in the odds of miscarriage. Compared with working standard hours, working longer hours was associated with an increase in the odds of PTD by 21%, miscarriage by 38%, having an LBW infant by 43%, and having an SGA infant by 16%.

Comparison with existing literature

Previous systematic reviews examining the impact of long working hours and shift work on pregnancy outcomes had methodologic limitations, such as including women doing unpaid work in the home,[9,10,12] restricting searches by language,[9,11,12] and reporting on studies published only to 2013.[9–12] The current study updates these reviews by providing evidence from 62 observational studies (196,989 women) and is, to our knowledge, the first to quantify the dose–response relationship between working hours and risk of PTD. The dose–response analysis showed a positive gradient of preterm delivery risk with long working hours. Compared to working less than 40 hours per week, a 10% increase in preterm delivery rates corresponds to working more than 55.5 hours per week.

An important difference with previous systematic reviews is that we included only studies with pregnant

FIGURE 5
Potential mechanism for the impact of shift work and longer working hours on pregnancy health



Shift work may cause circadian disruption and sleep deprivation, which may result in increased stress, alter lock gene expression, and decrease melatonin production. Evidence suggests that low aldosterone and enhanced cortisol availability due to stress might mutually affect placental growth and function. Altering lock gene expression is associated with dysregulation of fetal growth hormones that may impair the placental and fetal growth. Decreasing melatonin production may lead to the release of prostaglandins, nitric oxide, and pro-inflammatory cytokines, which are associated with preterm labor and increased maternal blood pressure. Fatigue and sleepiness caused by working longer hours may also increase stress. They will also increase the release of catecholamine, which may increase uterine contractility.

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women in paid employment. We found concordance across study types, long working time cut-offs, and adjusted vs unadjusted analyses. This systematic review and meta-analysis demonstrated a significant association between shift-work status (both rotating shifts and night shift) and PTD and preeclampsia. The pathophysiologic mechanism linking the 2 phenomena may relate to circadian rhythm disturbances, which pose a significant challenge to pregnant women and their fetuses through related neuroendocrine, vascular, and immune pathways[5,7,99–101] (Figure 5). In particular, we found an increased odds of miscarriage in night shift but not in rotating shift workers. Repeated disruption of circadian rhythm and exposure to light in night workers leads to reduced secretion of melatonin and sleep deprivation, which may interfere with maternal and fetal hormone homeostasis, placental implantation, and fetal growth.[102] Maternal melatonin passes through the placenta to the embryo and the fetus, which is involved in the placental function of both animals and humans.[103,104] Studies from rats have suggested that the association between melatonin and miscarriages may be due to melatonin's role in weakening uterine contractions by decreasing the production of prostaglandins and in the prevention of the immunologic rejection of trophoblasts by stimulating the production of progesterone.[105,106] These adverse effects can be resolved when the mother receives melatonin.[106,107]

Our analysis also showed a higher odds of PTD, LBW, SGA, and miscarriage in women who worked more than 40 hours per week as compared with women who worked fewer hours. In nonpregnant populations, long working hours may increase fatigue, sleepiness, and stress.[108,109] These outcomes may result from the dysregulation of biochemical and neurophysiological function, including increased release of catecholamine.[8,110–113] Raised catecholamine levels from long working hours may increase uterine contractility[114,115] and the risk of preterm labor and miscarriage.[116,117] Further investigation is needed to examine whether and to what extent sleep disruption, stress, and fatigue affect the health outcomes of pregnant women and their fetuses.

Strengths and limitations

This study provided in-depth analyses of up-to-date evidence including meta-regression to identify dose-response between the amount and type of occupational activity with adverse pregnancy outcomes. Rigorous methodological standards (following GRADE guidelines) were used to assess the certainty of the evidence, and to further decrease bias we examined the grey literature and did not limit our search to a single language.

Nevertheless, several limitations should be noted. This study used observational data and, as such, cannot eliminate potential unmeasured confounders, including socioeconomic status of the participants, which may related both to type of work hours as well as to clinical outcomes. Only 14 studies have considered socioeconomic status as an independent factor and included it as a confounder in their adjusted models. The majority of the included studies did not consider the independent effect of socioeconomic status on clinical outcomes. As a result, we cannot identify the independent link of socioeconomic status with poor pregnancy outcomes. Despite the lack of randomized studies, our study adjusted for a variety of clinical risk factors and subgroup analysis, and did not find significant differences between unadjusted and adjusted models. In addition, the majority of the studies assessed shift work and working hours through self-reported measures, which increases the risk of recall bias. Another limitation of this research is that work hours are not standardized, and thus the individual studies examined differed somewhat in their definitions of shift work and long working hours. However, this review attempted to minimize this variation by grouping hours into similar ranges. Furthermore, some studies were limited to a single ethnic group, and the majority of the included studies did not detail the type of work performed, limiting the generalizability of the study findings. Finally, few studies were also available on the specific outcomes of gestational hypertension, preeclampsia., IUGR, GDM, and stillbirth, thus limiting the ability to draw firm conclusions on work patterns and these outcomes.

Conclusions and Implications

Women who work longer hours or who work night shifts or rotating shifts have higher risks of experiencing adverse pregnancy outcomes than those working standard hours or regular daytime shifts. Our findings suggest that working 55.5 or more hours per week is associated with a 10% increase in the odds of preterm delivery compared to working fewer than 40 hours per week. Adverse health outcomes, such as preterm delivery and SGA, are associated with long-term neurodevelopment impairment and chronic health problems in the offspring.[118–120] Taken together, longer work hours and shift work may have major implications for the short-term and long-term health of both women and their children. These novel findings may help to inform decision making on occupational directives or workplace design for the prevention of adverse pregnancy outcomes. ■

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