DOI: 10.1111/j.1471-0528.2011.03066.x
www.bjog.org

Systematic review

Shift work and pregnancy outcomes: a systematic review with meta-analysis of currently available epidemiological studies

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Accepted 30 May 2011. Published Online 27 July 2011.

Background Varying work schedules are suspected of increasing risks to pregnant women and to fetal wellbeing. In particular, maternal hormonal disturbance arising from sleep deprivation or circadian rhythm disruption might impair fetal growth or lead to complications of pregnancy. Two independent meta-analyses (from 2000 to 2007) reported a small adverse effect of shift work on the risk of preterm delivery (PTD). However, these reviews were based on few high-quality studies.

Objectives To provide an updated review of the associations of shift work with PTD, low birthweight (LBW), small-for-gestational-age (SGA) infants and pre-eclampsia.

Search strategy and selection criteria We conducted a systematic search of MEDLINE using combinations of keywords and MeSH terms.

Data collection and analysis For each relevant paper we abstracted standard details, used to summarise design features and rate methodological quality. We calculated pooled estimates of relative risk (RR) in random-effect meta-analyses.

Main results We retrieved 23 relevant studies. The pooled estimate of RR for PTD was 1.16 (95% CI 1.00–1.33, 16 studies), but when five reports of poorer methodological quality were excluded, the estimated RR decreased to 1.03 (95% CI 0.93–1.14). We also observed increased RRs for LBW (RR 1.27, 95% CI 0.93–1.74) and for SGA (RR 1.12, 95% CI 1.03–1.22), which varied little by study quality. Little evidence was found on pre-eclampsia.

Conclusions These findings suggest that overall, any risk of PTD, LBW, or SGA arising from shift work in pregnancy is small.

Keywords Meta-analysis, occupational exposures, preterm delivery, shift work, small for gestational age.

Please cite this paper as: Bonzini M, Palmer K, Coggon D, Carugno M, Cromi A, Ferrario M. Shift work and pregnancy outcomes: a systematic review with meta-analysis of currently available epidemiological studies. BJOG 2011;118:1429–1437.

Introduction

Working women form a substantial proportion of the workforce worldwide, and many continue to work during pregnancy, when they may be exposed to various occupational hazards.[1,2]

Several authors have suggested that some work schedules (including rotating shifts and night-work) may present special risks to pregnant women, including neuroendocrine changes as a consequence of sleep deprivation or disrupted circadian rhythms affecting fetal growth and the timing of parturition. In support of this, some observational studies have found a higher risk of preterm delivery (PTD) or low birthweight (LBW) among women exposed to shift work.[3] In addition, one study suggested that shift work during pregnancy carries an increased risk of pre-eclampsia,[4] whereas another suggested that it did not.[5] These pregnancy-related complications are major contributors to perinatal mortality and morbidity so identification of modifiable risk factors such as working conditions is an important priority in maternity care. Moreover, given the mounting evidence linking LBW with an increased risk of chronic diseases in adulthood,[6–8] research into the effects of workplace exposures on pregnancy is a priority also for

public health. In 2007, we published a systematic review of the epidemiological evidence relating common occupational exposures (prolonged working hours, lifting, standing, heavy physical workload and shift work) to adverse pregnancy outcomes, in which a pooled meta-analysis indicated a small but significantly increased risk of PTD in association with shift work (relative risk [RR] 1.20, 95% CI 1.01–1.42, $P = 0.002$).[9] This was in accord with the finding of a previous partially overlapping meta-analysis, published in 2000, which gave a pooled RR estimate of 1.24 (95% CI 1.06–1.46).[3] However, because of the possibility of bias and residual confounding, these meta-analyses cannot be considered conclusive.

We have now updated our earlier review of the associations of shift work with PTD and indices of fetal growth restriction, including a further 5 years (February 2005 to February 2010) of published epidemiological evidence.

Methods

Search strategy

We conducted a systematic review of the epidemiological evidence relating shift work to four important pregnancy outcomes: PTD, LBW, small for gestational age (SGA) and pre-eclampsia. We systematically searched the Medline bibliographic databases for the period 1966 to February 2010, using medical subject headings (MeSH terms). Preterm birth, gestational age, small for gestational age, fetal growth restriction, pregnancy complications, pre-eclampsia and reproductive health were used to represent outcomes of interest; while work schedule tolerance, work and workload were selected to represent relevant exposures. We also supplemented our search using 'shift work' as a simple search term. We limited our search to papers with an abstract, written in English, relating to humans. We examined the abstracts, eliminated irrelevant references and obtained paper copies of all primary reports and reviews. We also cross-checked the references of all selected papers to identify other potentially relevant reports. Finally we included all papers reporting at least one risk estimate for one or more of the specified outcomes, comparing women exposed to shift work with working women who were unexposed (or less heavily exposed).

Data abstraction

For each paper that met our inclusion criteria, we extracted a standard set of information: year of publication, study location, timing of investigation, study design, strategies for exposure assessment and period of pregnancy in which exposure occurred, method of outcome assessment, and risk estimates with associated 95% CIs. If 95% CIs were not reported, we extracted the information that was needed to calculate them.

Definition of outcomes

Preterm delivery was consistently defined by the authors of primary reports, according to the World Health Organization definition, as the birth of a baby at <37 completed weeks of gestation. The definition of LBW was a birthweight $<2500 \times g$. One study also reported risk estimates for birthweight $<3000 \times g$.[10]

Authors investigating birthweight seem not to take into account specific variables such as maternal weight gain and fetal sex in defining 'normal birthweight', as suggested by Gardosi et al.[11]

The definition of SGA was a baby with a birthweight below the 10th percentile for gender and gestational age. One study considered also babies below the 5th percentile.[12] Distributions of birthweight by sex and gestational age were usually nationally or regionally based. Hence, the limit at which a baby was classed as SGA varied between studies.

Pregnancy-induced hypertension was defined as hypertension in a previously normotensive woman, with different thresholds among studies: hypertension was defined alternatively as having blood pressure ≥140/90 mmHg on at least two occasions occurring from 20 weeks of gestation onwards,[13] or having an increase of at least 20 mmHg in the mean arterial blood pressure between the mother's first and last visit.[5] Pre-eclampsia was defined as gestational hypertension in association with proteinuria/albuminuria, either occurring at some time from 20 weeks of gestation[13] or diagnosed more than once during the pregnancy;[4] no cutoffs were specified.

Quality assessment

We classed studies as high quality when reporting was complete and they were free from important bias or confounding. Completeness of reporting was evaluated as proposed by Ariens et al.[14] and van der Windt et al.[15] with modifications for studies of pregnancy outcomes,[9] using a nine-point scale covering the following items: (1) study design; (2) sampling procedure; (3) inclusion/exclusion criteria; (4) characteristics of the study population (age, social class); (5) study numbers and response rate; (6) exposure definition and assessment methods; (7) outcome assessment methods; (8) methods of statistical analysis; and (9) quantitative risk estimates with 95% CIs (and not only P values).

As reported in our previous review[9] we judged studies as prone to important bias where there was potential for recall bias that could lead to overestimation of risks. This was the case for retrospective studies investigating the association between shift work and outcomes that were both self-reported and clearly adverse (such as pre-eclampsia or PTD).

For each examined outcome, we classified reported associations as susceptible to confounding if important established risk factors were not taken into account. The importance of an established risk factor was based on the

size of the relative risk that it carried, its prevalence in the general population and the likelihood that it might vary importantly between different occupations.

Meta-analysis

For studies with sufficiently similar definitions of exposure and outcome, we calculated pooled risk estimates with a random effect meta-analysis, assuming heterogeneity of effects, following the maximum likelihood method.[16] Each risk estimate was weighted by the inverse of its variance. To increase comparability across studies, where authors presented RRs for exposures during more than one period of pregnancy, we focused on exposures during the first trimester because they were the most widely investigated. We also conducted a sensitivity analysis, checking the impact on pooled risk estimates of excluding lower quality studies, and we explored possible publication bias using funnel plots. All statistical analyses were performed using STATA software version 11.0 (Stata Corp., College Station, TX, USA).

Results

As set out in Tables 1–3, our search identified 17 original studies that investigated the association between shift work and PTD, including three published after 2005; ten studies concerning SGA (four published after 2005); six studies concerning LBW (one published after 2005) and three studies investigating the relationship between shift work and pre-eclampsia and/or gestational hypertension (one published after 2005). Tables 1–3 summarise quantitative risk estimates and quality assessments, with studies grouped by health outcome and then by type of study.

Sample size

Sample size varied substantially across studies—from fewer than 400 pregnancies[17,18] to more than 35 000.[19] Also, the proportion of women exposed (a determinant of the number of exposed cases) differed between studies, ranging from <5 to 20%.[10] As demonstrated by Croteau et al.,[20] the proportion of women exposed to shift work decreases over the course of pregnancy. Consequently, studies investigating the effect of exposure late in pregnancy tend to include fewer exposed cases than those investigating the effects of shift work earlier in pregnancy.

Exposure assessment

In eight cohort studies[10,12,18,19,21–24] exposure was ascertained prospectively during pregnancy, whereas in 13 studies (case–control or cross-sectional) information about occupational exposure was ascertained after delivery. Eight studies did not report the timing of exposure during pregnancy; most of the remainder focused on the first and second trimesters.

The types of shift work considered relevant varied between studies, some comparing night workers with day workers[13,21,23] and others investigating workers on rotating shifts.[19,24] Moreover, several papers did not specify what kind of shift work was investigated, or classed women as exposed if they worked either at night or in rotating shifts.

Quality of evidence

Reporting was generally satisfactory, but we judged it to be incomplete for four studies. A report by Hartikainen-Sorri and Sorri[17] did not provide information about methods of exposure assessment, inclusion criteria or the period of pregnancy for which exposure was assessed; McDonald et al.[25] did not report confidence intervals for risk estimates (only that the observed elevation of risk was statistically significant) and did not state the total number of women studied or the times during pregnancy to which exposures to shift work related. In one paper, Saurel-Cubizolles and Kaminski[26] reported only a crude analysis comparing night workers with others, indicating nonsignificant differences in the prevalence of LBW and PTD, and gave no adjusted risk estimates. Finally, a recent study by Abeysena et al.[12] evaluated the risk of SGA in women exposed not only to shift work but also to 'other occupational exposures' that were not clearly specified. Risk estimates for shift work exposure in the absence of other occupational hazards were not reported. None of the above-mentioned studies was included in the meta-analysis, which was restricted to high-quality studies.

In two studies, both exposure and relevant health outcomes (PTD or pre-eclampsia) were self-reported after delivery.[27,28] Hence, we classified these studies as susceptible to important recall bias and excluded them from our sensitivity analysis.

Various maternal characteristics have been recognised as risk factors for PTD (extremes of maternal age, maternal weight, height and ethnicity, socio-economic status, smoking and alcohol intake, substance abuse, multiparity, primiparity, diabetes, pre-eclampsia, bacterial infections during pregnancy, and other maternal diseases). However, of these, only smoking and socio-economic status (or proxies such as maternal education or income) are believed to be associated with more than small increases in risk (RR > 1.5) and are likely to differ importantly in prevalence between occupations. Three studies[17,29,30] failed to control for both smoking and social class, and were therefore classified as having a higher potential for confounding. Both LBW and SGA share most of the risk factors for PTD, but small maternal stature and low pre-pregnancy maternal weight are associated with higher RRs (>1.5). We therefore classified three studies[5,12,26] as having higher potential for confounding because they failed to control for smoking

Table 1. Shift work and risk of pre-term delivery

References	Women in analysis	RR (95% CI)	Exposure		Higher potential for		Incomplete reporting	In meta-analysis
			Comparison	Timing	Bias	Confounding*		
Cohort studies								
Bonzini et al.[21]	1327	1.14 (0.43–2.93)	Night vs day	Trimester 1	No	No	No	Yes**
Bonzini et al.[21]	1327	1.07 (0.37–3.05)	Night vs day	Trimester 1 and 2	No	No	No	–
Misra et al.[22]	1166	1.0 (0.59–1.69)	Shifts vs none	Trimesters 1 and 2	No	No	No	Yes
Niedhammer et al.[10]	1124	1.68 (0.44–6.34)	Shifts vs none	Trimester 2	No	No	No	Yes
Pompeii et al.[23]	1796	1.5 (1.0–2.1)	Regular night work (yes vs no)	Trimester 1	No	No	No	Yes**
Pompeii et al.[23]	1796	1.6 (1.0–2.8)	Regular night work (yes vs no)	Trimester 2	No	No	No	–
Pompeii et al.[23]	1796	1.8 (0.8–3.4)	Regular night work (yes vs no)	Trimester 3	No	No	No	–
Stinson and Lee*[18]	359	1.8 (0.93–3.53)	Night vs day	22–26 weeks	No	No	No	Yes
Xu et al.[24]	887	2.0 (1.1–3.5)	Rotating shift work (yes vs no)	Not stated	No	No	No	Yes
Zhu et al.[19]	35 662	0.97 (0.8–1.17)	Rotating shift work vs daytime work	Trimesters 1 and 2	No	No	No	Yes
Case–control studies								
Croteau et al.[20]	1606–4371	0.9 (0.7–1.2)	Night vs day	Trimester 1	No	No	No	–
Croteau et al.[20]	1606–4371	1.0 (0.9–1.3)	Rotating shift work vs daytime work	Trimester 1	No	No	No	Yes**
Croteau et al.[20]	1606–4371	1.0 (0.7–1.3)	Rotating shift work vs daytime work	Trimester 1 only	No	No	No	–
Croteau et al.[20]	1606–4371	0.8 (0.5–1.3)	Rotating shift work vs daytime work	Trimesters 1 and 2 but not Trimester 3	No	No	No	–
Croteau et al.[20]	1606–4371	1.2 (0.9–1.6)	Rotating shift work vs daytime work	All pregnancy	No	No	No	–
Hartikainen-Sorri and Sorri[17]	358	0.86 (0.51–1.45)	Shift work (yes vs no)	Not stated	No	Yes	Yes	Yes***
Luke et al.*[28]	1470	1.5 (1.1–2.1)	Evening/night vs day	Not stated	Yes	No	No	Yes***
Saurel-Cubizolles et al.[30]	6309	0.97 (0.8–1.1)	Shift work (yes vs no)	Trimester 1	No	No	No	Yes
Cross-sectional studies								
Bodin et al.[27]	1685	5.6 (1.9–16.4)	Night vs day	Trimester 2	Yes	No	No	Yes***
Fortier et al.[31]	4118	1.03 (0.72–1.48)	Shift work vs day only	Not stated	No	No	No	Yes
Mamelle et al.[29]	1928	1.6 (1.0–2.5)	Shift and night work vs none	Not stated	No	Yes	No	Yes***
McDonald et al.[25]	–	1.18 $P > 0.05$	Changing shift vs not	Not stated	No	No	Yes	No****
Nurminen[5]	–	0.9 (0.7–1.1)	Shift work (yes vs no)	'Most of pregnancy'	No	No	No	Yes
Saurel-Cubizolles and Kaminski[26]	2261	0.80 (0.16–2.51)	Night vs day	Trimester 1	No	Yes	Yes	Yes***

*As described in the text, risk estimates were classified as having a higher potential for confounding if they failed to take into account both smoking and socio-economic status (or maternal education/income as proxy).
**Risk estimate included in the pooled analysis because calculated in a period of pregnancy more comparable with others studies (first trimester).
***Excluded from sensitivity analysis.
****Risk estimate not pooled as a standard error could not be derived from the presented data.

Table 2. Shift work and risk of being small-for-gestational-age or having a low birthweight at delivery

References	Women in analysis	RR (95% CI)	Exposure		Higher potential for		Incomplete reporting	In meta-analysis
			Comparison	Timing	Bias	Confounding*		
Cohort studies								
Abeysena et al.[12]	690	3.2 (0.95–10.7)	Shift work with other occupational exposures (not stated) (yes vs no)	Trimesters 2 and 3	No	Yes	Yes	Yes***
Bonzini et al.[21]	1327	0.92 (0.43–1.97)	Night vs day	Trimester 1	No	No	No	Yes**
Bonzini et al.[21]	1327	0.92 (0.41–2.06)	Night vs day	Trimester 2	No	No	No	–
Niederhammer et al.[10]	1124	1.32 (0.50–3.46)	Shifts vs none	Trimester 2	No	No	No	Yes
Pompeii et al.[23]	1796	1.3 (0.8–2.2)	Regular night work (yes vs no)	Trimester 1	No	No	No	Yes**
Pompeii et al.[23]	1796	1.4 (0.9–2.4)	Regular night work (yes vs no)	Trimester 2	No	No	No	–
Zhu et al.[19]	35 662	1.07 (0.94–1.21)	Rotating shift work vs daytime work	Trimesters 1 and 2	No	No	No	Yes
Cross-sectional studies								
Bodin et al.[27]	1685	0.8 (0.4–1.8)	Night vs day	Trimester 2	No	No	No	Yes
Fortier et al.[31]	4118	0.98 (0.75–1.27)	Shift work vs day only	Not stated	No	No	No	Yes
Hanke et al.[37]	1064	1.0 (0.19–3.26)	Shift work (yes vs no)	Not stated	No	No	No	Yes
Nurminen[5]	738	1.5 (1.0–2.4)	Shift work (yes vs no)	'Most of pregnancy'	No	Yes	No	Yes
Case–control studies								
Croteau et al.[20]	1606–4371	0.8 (0.7–1.0)	Night vs day	Trimester 1	No	No	No	–
Croteau et al.[20]	1606–4371	1.2 (1.0–1.4)	Rotating shift work vs daytime work	Trimester 1	No	No	No	Yes**
Croteau et al.[20]	1606–4371	1.0 (0.7–1.2)	Rotating shift work vs daytime work	Trimester 1 only	No	No	No	–
Croteau et al.[20]	1606–4371	1.5 (1.0–2.1)	Rotating shift work vs daytime work	Trimester 2 but not Trimester 3	No	No	No	–
Croteau et al.[20]	1606–4371	1.3 (1.0–1.7)	Rotating shift work vs daytime work	All pregnancy	No	No	No	–
LBW								
Cohort studies								
Niederhammer et al.[10]	1124	0.92 (0.26–3.26)	Shifts vs none	Trimester 2	No	No	No	Yes
Xu et al.[24]	887	2.1 (1.1–4.1)	Rotating shift work (yes vs no)	Not stated	No	No	No	Yes
Zhu et al.[19]	35 662	1.02 (0.68–1.51)	Rotating shift work vs daytime work	Trimesters 1 and 2	No	No	No	Yes
Cross-sectional studies								
Bodin et al.[27]	1685	1.9 (0.6–5.8)	Night vs day	Trimester 2	No	No	No	Yes
McDonald et al.[25]	–	1.38 $P < 0.01$	Changing shift vs not	Not stated	No	No	No	No****
Saurel-Cubizolles and Kaminski[26]	2392	1.28 (0.4–3.21)	Night vs day	Trimester 1	No	Yes	Yes	Yes***

*As described in the text, risk estimates were classified as having a higher potential for confounding if they failed to take into account both smoking and at least one of: socio-economic status, maternal height, or pre-pregnancy weight.
**Risk estimate included in the pooled analysis because calculated in a period of pregnancy more comparable with others studies (first trimester).
***Excluded from sensitivity analysis.
****Risk estimate not pooled as a standard error could not be derived from the presented data.

Table 3. Shift work and the risks of pre-eclampsia and/or pregnancy-induced hypertension

References	Numbers in analysis	RR (95% CI)	Exposure		Higher potential for		Incomplete reporting
			Comparison	Timing	Bias	Confounding	
Pregancy-induced hypertension							
Cross-sectional studies							
Nurminen[5]	890	0.9 (0.4–1.9)	2 or 3 shift work vs none	'Most of pregnancy'	No	Yes	No
Case–control studies							
Haelterman et al.[13]	540	1.0 (0.5–2.0)	Night vs day	Trimester 1	No	No	No
Pre-eclampsia							
Cross-sectional studies							
Wergeland and Strand[4]	3281	1.3 (0.8–1.9)	Shift work (yes vs no)	Trimester 1	No	No	No
Case–control studies							
Haelterman et al.[13]	540	1.0 (0.5–2.0)	Night vs day	Trimester 1	No	No	No

and at least one of social class, maternal height and pre-pregnancy weight. Finally, the only known risk factors for pre-eclampsia and gestational hypertension that we considered to be both common and carrying a substantial RR were primiparity and maternal weight. One study took into account neither of these variables and was therefore classified as a poor-quality study.[5]

Summary of evidence

Preterm delivery

The possible association between shift work and PTD was examined in 17 studies (seven of which were prospective cohorts in which exposure was ascertained before delivery). Most papers reported several risk estimates covering different time windows of exposure during pregnancy, so that there were a total of 24 time-specific risk estimates.

Most of the studies[10,18,20,21,23–25,27–29,31] indicated elevated risks, but only two found significantly elevated RRs of 2 or higher.[24,27] One study gave an RR estimate >5, but was weakened by possible recall bias, both exposure and outcome being self-reported retrospectively.

Studies showing more than moderate adverse effects (RR > 1.5)[10,23,24,27] tended to be smaller than the negative ones, with the four largest studies finding RRs close to one,[5,19,20,30] suggesting that publication bias may have occurred with the exclusion of small studies with negative results.

We pooled 16 studies in a random effect meta-analysis (see Figure 1), and we obtained a pooled RR estimate of 1.16 (95% CI 1.00–1.33, test for heterogeneity $P = 0.006$).

When we excluded five studies that did not meet our criteria for high quality,[17,26–29] the pooled estimated risk reduced and was no longer statistically significant (RR 1.03, 95% CI 0.93–1.14, test for heterogeneity $P = 0.023$).

Small for gestational age

Ten studies analysed the possible association between shift work and the risk of delivering an SGA baby, including five prospective cohort investigations. Studies tended to rule out a more than moderate effect, with RRs ranging from 0.8 to 1.5, an exception being a recent investigation by Abeysena et al.[12] in Sri Lanka which found an RR > 3.0 for women exposed to the combination of shift work and other occupational hazards.

A pooled risk estimate (based on ten studies) was calculated as 1.12 (95% CI 1.03–1.22, test for heterogeneity $P = 0.39$; Figure 2). When the one poor-quality study was removed[12] in a sensitivity analysis, the revised risk estimate was 1.10 (95% CI 1.00–1.20).

Low birthweight

Risk of delivering an LBW baby at term was analysed in six studies. Among these, only one of the three cohort studies showed a significantly elevated risk. When all of the results were pooled in a meta-analysis, the combined risk estimate was 1.27 (95% CI 0.93–1.74, test for heterogeneity $P = 0.39$). Exclusion of the study by Saurel-Cubizolles and Kaminski,[26] which did not present an RR estimate adjusted for important potential confounders, did not change this finding materially.

Pre-eclampsia or pregnancy induced hypertension

We found only two studies investigating pre-eclampsia and two investigating pregnancy-induced hypertension. None of them was prospective. No studies showed a significantly

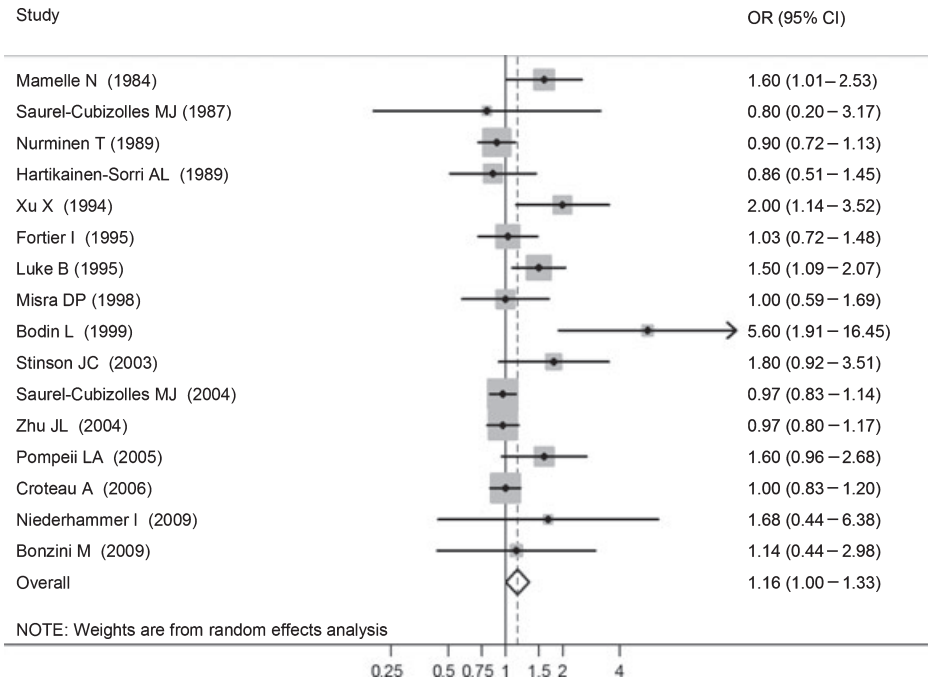

Figure 1. Studies investigating PTD risk and shift work exposure. Random effects meta-analysis.

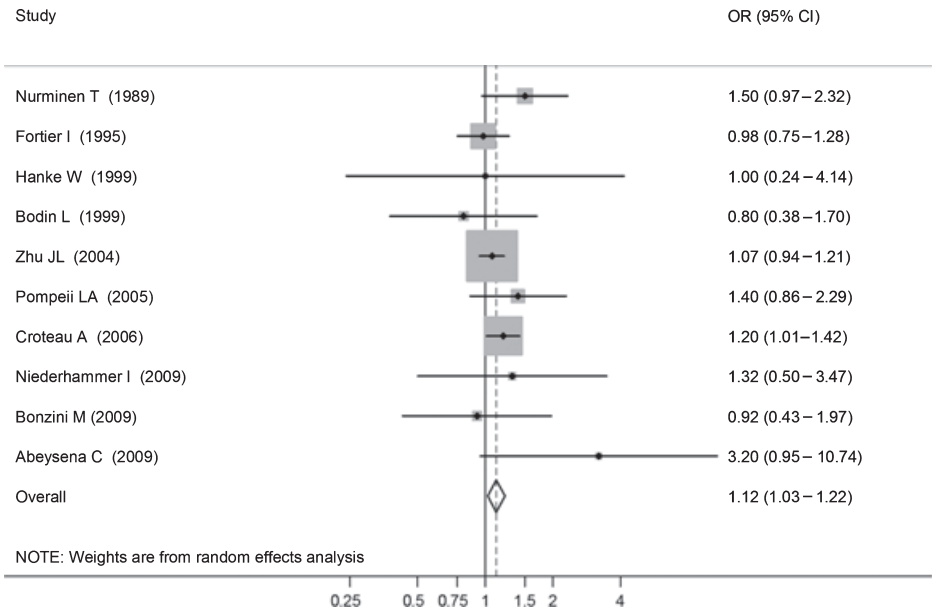

Figure 2. Studies investigating the association between shift work exposure and the risk of delivering an SGA baby. Random effects meta-analysis.

increased risk. Formal meta-analysis was not performed because of the small number of retrieved papers.

Discussion

In our study we calculated pooled risk estimates for three clinically important pregnancy outcomes (PTD, SGA and LBW) among women exposed to shift work, after systematically reviewing all available epidemiological studies. We found small elevations of risk (pooled RRs between 1.1 and 1.3).

Our risk estimate for PTD was based on a reasonable number of studies, but may have been exaggerated by publication bias, with more complete reporting of positive than

non-positive findings from smaller studies. Moreover, when poorer quality studies were excluded, the pooled risk estimate did not differ significantly from unity. Regarding SGA and LBW, the number of studies identified was smaller, but results were more homogeneous across studies, and exclusion of poor-quality studies did not materially change the pooled risk estimates. However, the pooled risk estimates were not sufficiently high to allow confident conclusions about a hazard, and spurious associations from bias or residual confounding cannot be ruled out. For pregnancy-induced hypertension and pre-eclampsia too few studies were available to allow any firm conclusion to be drawn. Our findings are largely consistent with those of previous reviews[3,9] and indicate that any effects of shift work on PTD, SGA and LBW are likely to be small.

Estimates of risk for PTD have tended to reduce with inclusion of more recent studies in meta-analyses: Mozurkewich[3] in 2000 pooled risk estimates from six studies and found a 24% elevation of risk among exposed women; in our previous review[9] (2007, based on 13 studies), we calculated a 20% increase in risk; and with the addition of three further studies published over the past 5 years, the excess RR has fallen to 15%. If there is a hazard, then one explanation of this time trend could be that in most countries, precautionary legislation was introduced, allowing pregnant workers to be assigned to other tasks (without shift work) or to take earlier antenatal leave, so that fewer women continued shift work during the later stages of pregnancy. An occupational exposure such as night shifts may have been voluntarily suspended if women suspected that it could be detrimental to their pregnancy. In this situation, risks in women who continue to work shifts late in pregnancy might be underestimated because of a healthy pregnant worker effect,[32] healthier women with uncomplicated pregnancies being less likely to modify their work schedules. In support of this, in two studies[20,21] the risk of PTD associated with shift work was higher in women whose work conditions did not change in the course of pregnancy. Finally, in a study comparing European countries, significant associations of PTD with shift work were mainly observed in countries where long prenatal leaves were infrequent and legal support for preventive measures was weaker.[30]

An important limitation of the available epidemiological evidence is that many authors have not properly distinguished between different types of shift work. There is a possibility that rotating shifts (with or without work at night) may have varying levels of job demand or could lead to a different degree of misalignment of maternal endogenous circadian rhythms compared with fixed night work. We did not calculate pooled estimates of risk for specific patterns of work-schedule because of the small number of studies available with sufficient information. However, Croteau et al.[20] presented risk estimates separately for night workers and for rotating shift workers (both compared with fixed day-time workers), and found that for both SGA and PTD the risks were elevated only among rotating shift workers.

The mechanisms whereby shift work might result in adverse pregnancy outcomes are not entirely understood. Both direct (through disturbances of circadian rhythm) and indirect (through psychosocial stresses and sleep disruption) mechanisms have been proposed to explain a causal relationship between shift work and obstetric complications that are inherently multifactorial in nature. There is a sound basis for the notion that stressors may impact on PTD and LBW through several intersecting pathways, which include neuroendocrine, behavioural, immune and vascular mechanisms.[33,34] Moreover, shift work modifies peak values and rhythm amplitudes of serum melatonin, whose function seems essential for successful pregnancy.[35] Recently, melatonin was found to act synergistically with oxytocin to increase membrane-bound phospholipase C activity and associated signalling mechanisms, thereby enhancing myometrial contractility and gap junction-associated intercellular communication.[36] Further investigation is needed to ascertain whether and to what extent disruption of sleep, circadian rhythms and daylight–night working cycles pose a significant threat to pregnant women and their fetuses.

On balance, the evidence currently available about the investigated birth outcomes does not make a compelling case for mandatory restrictions on shift-working in pregnancy. Further studies are needed to address the question whether adverse birth outcomes are related to different types of rotating work schedules (separating between night and day-time shift), or to fixed night work. In the meantime, we suggest that, it would be prudent, insofar as job circumstances allow, to permit pregnant women who wish to do so, to reduce their exposure to shift and night working.

Disclosure of interests

The authors declare that they have no competing interests.

Contribution to authorship

MB, KTP and DC designed the study protocol, developed search strategies and established selection criteria. MB, KTP and MC performed the data collection and applied quality score, MB and KTP performed the meta-analyses; MB and CA wrote the manuscript under the supervision of MMF and DC. MC, DC and KTP contributed to the data interpretation and critical revision of the manuscript.

Funding

No funding was obtained for this research activity.

Acknowledgements

MB presented an earlier version of this paper to the Scientific Symposium on the Health Effects of Shift Work, held in Toronto, Canada on 12 April 2010, when he was the invited speaker on the topic shift work and pregnancy. ■

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