Obstetrics and gynaecology

Comorbidity a key factor in maternal deaths from pregnancy complications

An analysis from the National Perinatal Epidemiology Unit has estimated that almost 50% of the population attributable risk of maternal mortality is associated with the presence of a medical comorbidity.

Using data from the Confidential Enquiry into Maternal Deaths, 135 cases of direct maternal death were identified between 2009 and 2012 from five major causes.

Data from the UK Obstetric Surveillance System was used to identify 1,661 women who survived one of these five complications i.e. eclampsia, pulmonary embolism, severe sepsis, amniotic fluid embolism and peripartum haemorrhage. These survivors formed an unmatched control group.

Analysis revealed that six factors were more commonly observed in the women who died, see table 1, below.

Inadequate antenatal care was nearly 16 times more common in those who died compared with controls. Substance misuse was ten times more common and medical comorbidity almost five fold higher.

Previous pregnancy problems, pregnancy-induced hypertension and being of Indian ethnicity were all twice as common in cases. The excess mortality attributed to Indian ethnicity was confined to sepsis and haemorrhage.

On a population basis, almost 70% of the raised risk associated with maternal death was attributed to these six risk factors, see table 2 below. The leading risk factor was medical comorbidities accounting for almost half the population attributable risk.

Eighteen medical comorbidities were studied of which eight were significantly more commonly present in the women who died compared with survivors (musculoskeletal disorders, inflammatory and atopic conditions, autoimmune disease, infections e.g. TB and group-B streptococcus, haematological disorders, essential hypertension, mental health problems and asthma.

Women with these comorbidities were more likely to be older, nulliparous, obese, smokers and have pregnancies complicated by gestational diabetes and hypertension. This study did not address individual avoidable case factors.

The authors estimated that almost 50% of the population attributable risk of mortality was associated with the presence of a medical comorbidity.

They concluded that their findings should encourage all of us involved in any way with pregnancy to minimise adverse consequences with 'extra vigilance and proactive management'.

Table 1

Risk factors independently associated with maternal death

Risk factor	Adjusted odds ratio (95% CI)
Inadequate use of antenatal care	15.87 (6.73-37.41)
Substance misuse	10.16 (1.81-57.04)
Medical comorbidities	4.82 (3.14-7.40)
Previous pregnancy problems	2.21 (1.34-3.62)
Hypertensive disorders of pregnancy	2.44 (1.31-4.52)
Indian ethnicity	2.70 (1.14-6.43)

Table 2

Population attributable risks

Risk factor	% Population attributable fraction (95% CI)
Medical comorbidities	48.9 (40.5-56.2)
Previous pregnancy problems	21.1 (11.7-29.5)
Hypertensive disorders of pregnancy	12.0 (7.7-16.1)
Inadequate use of antenatal care	10.5 (9.7-11.4)
Indian ethnicity	2.9 (0.3-5.5)
Substance misuse	1 (0.03-1.40)
Risk factors score	**69.8 (66.1-73.0)**

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● Nair M, Kurinczuk JJ, Brocklehurst P et al. Factors associated with maternal death from direct pregnancy complications: a UK case-control study. *BJOG* 2015;122:653-662

Diabetes

Shift work may raise risk of diabetes

A meta-analysis published in the *Journal of Occupational and Environmental Medicine* has concluded that shift work is associated with an increased risk of diabetes mellitus, especially in men and in those working rotating shifts.

The authors searched PubMed, Embase, Web of Science and Proquest for relevant studies. Overall, 448 potential studies were identified. Of »

these 434 were excluded on various grounds, including inappropriate inclusion criteria, lack of observational study design, lack of diabetes outcomes, absence of shift work exposure, subjects already with a diagnosis of diabetes or a study design that did not allow the association between diabetes and shift work to be assessed.

Fourteen studies remained, of which one had been reported in two or more papers. This left 12 eligible studies with 28 independent reports involving 226,652 participants and 14,595 patients with diabetes.

The studies were from a range of countries (Japan, Sweden, United States, Belgium and China), eight studies included men only and two women only. There were seven prospective cohort studies, one retrospective cohort study and four cross-sectional studies. The number of participants ranged from 475 to 107,915.

Four studies were classified as rotating shifts, two irregular or unspecified shifts, three night shifts and three mixed or evening shifts only.

- The results showed a pooled adjusted odds ratio (OR) for the association between any exposure to shift work and diabetes risk of 1.09 (95% CI: 1.05-1.12)
- Sub-group analysis showed a stronger association between shift work and diabetes for men OR 1.37 (95% CI: 1.20-1.56), than for women OR 1.09 (95% CI: 1.04-1.14)
- Further sub-group analysis showed that evening shifts and mixed shifts did not increase the risk of diabetes, but all other shift patterns did
- The rotating shift pattern showed the highest risk OR 1.42 (95% CI: 1.19-1.69)

Several observational studies had previously noted an increased risk of diabetes in shift workers, but none had used quantitative techniques to estimate risk.

The headline finding from the analysis is that exposure to shift work increases the risk of diabetes by 9%, and that men may be more at risk than women.

Shift work can disturb health in two main ways. First, it has an effect on physiology, when normal circadian rhythms are overridden. There is some evidence that insulin resistance is increased and that circadian disruption can increase the development of type 2 diabetes in susceptible individuals.[1]

Second, it interferes with normal social interaction, and may be associated with less exercise and unhealthy patterns of eating, as well as continual low-level stress.

This meta-analysis did include a very heterogeneous group of research papers, and although I am not a statistical expert, I would be cautious about the strength of the results. Allowing for this, the findings appeal strongly to the commonsense of those of us who work on the front line with diabetes patients. Achieving good control always seems more of a challenge in patients who work shifts, at every level of diabetes treatment. The complex regimens of insulin-dependent shift workers would suggest that diurnal rhythms might well have a significant effect on this aspect of metabolism.

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- **Gan Y, Yang C, Tong X et al. Shift work and diabetes mellitus: a meta-analysis of observational studies. *Occupat Environ Med* (2014) doi:10.1136/oemed -2014-102150**

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Mental health

Antidepressants may increase suicide risk

Patients prescribed mirtazapine or venlafaxine are more likely to attempt or complete suicide, a UK study has found.

Data were obtained from more than 600 contributing practices that use the EMIS medical records system. There were 238,963 participants who were aged between 20 and 64 years and had a first recorded diagnosis of depression between 1 January 2000 and 31 July 2011. The follow-up period ended on 1 August 2012.

Antidepressant exposure was measured from electronic prescribing data. Suicides were identified from linked death certificates; both open and suicide verdicts were classified as suicide. Attempted suicide or self-harm events recorded using the appropriate Read codes were identified from the medical records.

During follow-up (median 5.2 years), 87.7% of the cohort received at least one prescription for antidepressants. The median duration of treatment was 221 days (7.3 months). During the first five years of follow-up, there were 198 cases of suicide and 5,243 cases of attempted suicide or self harm.

- Compared with SSRIs, the suicide rate was significantly increased during periods of treatment with 'other antidepressants' (mainly mirtazapine and venlafaxine; adjusted hazard ratio (HR) 2.64 (95% CI: 1.74-3.99) but not with tricyclics
- The absolute annual risk of suicide was highest with mirtazapine (0.19%) and lowest with amitriptyline (0.02%)
- Similarly, when compared with SSRIs, the rate of attempted suicide or self harm was significantly increased with 'other antidepressants' adjusted HR 1.80 (95% CI: 1.61-2.00) but not with tricyclics

Compared with citalopram, the adjusted HRs for attempted suicide or self harm were significantly increased:

- Venlafaxine 1.85 (95% CI: 1.61-2.13)
- Trazodone 1.73 (95% CI: 1.26-2.37)
- Mirtazapine 1.70 (95% CI: 1.44-2.02)

The majority of open verdicts are thought to be suicides and it is standard practice to include them in studies of suicide. However, not all open verdicts are suicides and it has been suggested that those cases in which suicide is unlikely on the grounds of probability should be excluded.[1] This does not appear to have been attempted in the present study. Even with the inclusion of open verdicts, the total number of suicides was low and the results for completed suicide should be treated with caution. For example, the 95% confidence intervals for absolute suicide risk with mirtazapine and amitriptyline overlap.

The variation in suicide rates was not explained by the relative toxicity of antidepressants in overdose. A UK study found that tricyclics were by far the most toxic (case fatality rate ratio of 13.8 as compared with 2.5 for venlafaxine, 1.9 for mirtazapine and 0.5 for SSRIs).[2] »