Obstetrics and gynaecology

Miscarriage associated with raised risk of premature death

A history of one or more miscarriages appears to be associated with an increased risk of dying before the age of 70, an analysis of data from the US Nurses' Health Study II has found.

The researchers analysed data, from 1993 to 2017, on 101,681 participants in the Nurses' Health Study II, who had ever been pregnant.

Participants completed questionnaires on reproductive history, lifestyle factors and health every two years. In the first questionnaire participants reported their lifetime history of pregnancies, including outcomes, and subsequent events were updated every two years.

By 2009 most of the participants had reached the menopause and were asked to report the outcome and year of all their pregnancies. Women were followed up until death or 2017 whichever came first.

Covariates assessed included gestational diabetes and hypertensive disease of pregnancy. Race or ethnicity, height, and body weight were recorded at baseline and current weight recorded on subsequent questionnaires.

Use of oral contraceptives, lifestyle factors such as smoking, diet, alcohol consumption, physical activity, marital status and parental history of myocardial infarction and stroke before the age of 60 were also tracked.

Deaths before the age of 70 were defined as premature and cause of death was established by autopsy reports, physician review of medical records, or death certificates.

During 24 years of follow-up, 2,936 premature deaths were recorded, including 1,346 deaths from cancer and 269 from cardiovascular disease.

After adjusting for confounding factors, dietary and lifestyle factors miscarriage was associated with a hazard ratio (HR) of 1.19 (95% CI: 1.08-1.30) for premature death.

The HR values were higher for those women who had had more miscarriages.

Compared with women who had had no miscarriages:

- 1 miscarriage HR 1.16 (95% CI: 1.05-1.28)
- 2 miscarriages HR 1.23 (95% CI: 1.0-1.50)
- 3 or more miscarriages HR 1.59 (95% CI: 1.17-2.15)

($P < 0.001$ for all comparisons)

Younger age at miscarriage was also associated with increased risk of premature death when compared with those who had had no miscarriages.

- Women aged ≤ 23 years HR 1.32 (95% CI: 1.14-1.53), $P < 0.001$

When the cause of death was examined, the strongest association was with cardiovascular disease: HR 1.48 (95% CI: 1.09-1.24), independent of several shared risk factors (e.g. BMI, smoking, diet, and physical activity), followed by all other causes combined HR 1.25 (95% CI: 1.09-1.44). Miscarriage did not appear to be associated with early death from cancer.

The investigators state that miscarriage 'could be an early marker of future health risk in women, including premature death.'

They speculate that there may be common pathways contributing to miscarriage and cardiovascular disease.

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Wang Y-X, Minguez-Alarcon L, Gaskins AJ et al. Association of spontaneous abortion with all cause and cause specific mortality: prospective cohort study. *BMJ* 2021;372:n530

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