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Placenta praevia and sex ratio at birth

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Abstract

The ratio of male to female sex among infants born to 391 women with and 114 079 without placenta praevia was analysed by parity. In the women without placenta praevia the sex ratio decreased significantly with increasing parity, whereas in the women with placenta praevia it increased. Overall, the sex ratio was increased among the women with placenta praevia, particularly multiparas.

An increase in the sex ratio at birth is associated with insemination early or late in the menstrual cycle, which may result in delayed development and implantation of the blastocyst; this may be a predisposing factor in placenta praevia.

Introduction

Several complications of pregnancy, including pre-eclampsia¹ and premature labour,² are associated with an increase in the ratio of male to female sex at birth. As placenta praevia is believed to be due to delayed development and implantation of the blastocyst, and as abnormalities in the development of the blastocyst are associated with alterations in the sex ratio, we investigated the sex ratio in women with placenta praevia.

Subjects, method, and results

We determined the sex ratio at delivery in 114 470 singleton pregnancies (391 women with and 114 079 women without placenta praevia) in the Peninsula Maternity and Neonatal Service region in Cape Town between 1976 and 1983. The women were divided into three groups according to parity (para 1, para 2 and 3, and para 4), those who were para 2 and para 3 being grouped together to ensure adequate numbers in each group (table).

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In the reference population without placenta praevia the sex ratio showed a significant decrease with increasing parity ($p < 0.02$, Bartholemew's test for proportions qualitatively ordered³). In women with placenta praevia, however, the sex ratio showed a progressive increase with increasing parity, but this trend was not significantly different from zero owing to the smaller numbers. The proportion of male births by parity in the two groups was compared by ridit analysis.⁴ The mean ridit for the group with placenta praevia was 0.634 (SE 0.022), which was significantly greater than the reference ridit value of 0.5 ($p < 0.0001$) with an odds ratio of 7.4 that multiparas with placenta praevia would have a higher proportion of male births than the reference group. Furthermore, in multiparas with four or

Ratio of male to female sex at birth among women with and without placenta praevia

Parity	Without placenta praevia			With placenta praevia		
	No of male infants	No of female infants	Male:female ratio	No of male infants	No of female infants	Male:female ratio
1	22 601	21 229	1.065	34	31	1.097
2 and 3	24 172	23 027	1.050	95	78	1.218
≥4	11 671	11 379	1.026	90	63	1.429
Total	58 444	55 635	1.050	219	172	1.273

more pregnancies the sex ratio in those with placenta praevia was 1.429, which was significantly greater than the ratio of 1.026 in the women without placenta praevia ($p < 0.043$, G^2 test).⁵ The increase in the sex ratio with increasing birth order among women with placenta praevia compared with those without was thus highly significant.

Discussion

An increased ratio of male to female sex at birth among women with placenta praevia, particularly multiparas, is a new observation. Moreover, the progressive increase in sex ratio with increasing parity in placenta praevia contrasts with the decrease found in normal pregnancy.

One of the main factors influencing the sex ratio at birth is the time of insemination during the menstrual cycle, more male infants being delivered when insemination occurs two or more days before or after ovulation.⁶ Early and late insemination and alterations in sex ratio are also associated with an increased incidence of miscarriage.⁷

When insemination occurs early in the menstrual cycle the sperm may be over-ripe, and when fertilisation occurs later the ova may be over-ripe. Both over-ripe sperm and over-ripe ova are associated with an increased incidence of chromosomal abnormalities, blighted ova, and death of the blastocyst, and it has been suggested that in such cases female embryos may have a higher incidence of abnormalities and death.⁸ When early or late insemination results in fertilisation of an over-ripe ovum or by an over-ripe sperm the survival of male embryos may thus be relatively increased, resulting in an increased male to female sex ratio at birth. Similarly, the development of the embryo from an over-ripe sperm or ova may be impaired, resulting in delayed and low implantation of the embryo in the uterus and hence placenta praevia.

Placenta praevia may thus be due to delayed development and implantation of the blastocyst resulting from early or late insemination, which is associated with an increase in the male to female sex ratio. The progressive increase in the sex ratio with increasing parity in women with placenta praevia is difficult to explain unless increasing parity is in some way associated with an increase in the incidence of fertilisation of over-ripe ova or by over-ripe

sperms. The significant increase in the sex ratio nevertheless suggests that early or late insemination and impaired development of the embryo may be a predisposing factor in placenta praevia.

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An epidemiological study of the immunogenetic aetiology of pre-eclampsia

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Abstract

A population based case-control study of the association between dissimilar race of parents and risk of pre-eclampsia was undertaken. Data on singleton births in Washington State in 1981 were available for analysis from birth certificates. All mothers recorded as having pre-eclampsia and a sample of mothers who did not have pre-eclampsia were eligible for comparison with regard to racial dissimilarity between parents. Women with previously diagnosed cardiovascular disease and diabetes were excluded. After the confounding effects of maternal parity and race had been controlled for, racial dissimilarity of parents was associated with a 1.9-fold increased risk of pre-eclampsia (95% confidence interval=1.3-2.8; number of cases=973, of controls=1480).

This finding supports the theory that genetic dissimilarity of father and mother has a role in pre-eclampsia and is consistent with an immunogenetic aetiology.

Introduction

Previous studies have linked paternal factors with pre-eclampsia.^{1,2} Several reports have indicated that change of paternity is associated with an increased occurrence of pre-eclampsia among multiparous women,^{3,5} while others have suggested that exposure to paternal spermatic antigens may protect against pre-eclampsia.⁶ Such observations support the theory that pre-eclampsia may represent a disorder in the maternal immune response to paternally inherited antigens expressed by the fetus.

Some investigators believe that paternal antigens may increase the risk of pre-eclampsia through genetic dissimilarity from the mother, which results in "immunological" incompatibility between fetus and mother.⁷ This theory is supported by a large epidemiological study of a highly consanguineous population, which found that paternal unrelatedness to the mother was associated with an increased risk of pre-eclampsia.⁸ Other investigators, however, believe that the depression of the maternal immune response in pre-eclampsia may result from inadequate stimulation of the immune response owing to genetic similarity of the father and mother.⁹

We designed a population based case-control study to re-examine the relation between pre-eclampsia and a global measure of genetic dissimilarity of mother and father. Dissimilar race of parents, rather than lack of consanguinity, was used as the indicator of genetic dissimilarity.

Methods

Birth certificates for all single births that occurred in Washington State in 1981 were used to identify subjects and provide data for analysis. All women who were recorded as having pre-eclampsia on the birth certificate were eligible for inclusion in the study. According to protocol, the birth certificate is completed within two days of birth by a nurse or doctor who was present at the birth or by a member of staff at the hospital who has been trained by the state health department. If the attending doctor has diagnosed pre-eclampsia a box labelled pre-eclampsia is to be ticked on the certificate. This protocol is followed closely, as shown by a recent study, which found that after the

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