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Gonorrhoea in pregnancy

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Summary

The role of gonorrhoea and other sexually transmitted diseases as risk factors for adverse pregnancy outcome defined as low birth weight, stillbirth and postpartum endometritis, was examined in a case control study in Nairobi, Kenya. Maternal gonococcal infection was associated with very low birth weight babies (< 1500 g; 17·1 *versus* 5·8 per cent; $P < 0{\cdot}01$; odds ratio 3·2) and with postpartum endometritis (18·2 *versus* 5·6 per cent; $P = < 0{\cdot}001$; odds ratio 4·1). The isolation rate of *Neisseria gonorrhoeae* increased with declining birth weight ($P < 0{\cdot}05$).

In addition, an association was found between maternal gonococcal infection and cervical mucopus postpartum (15·5 *versus* 3·9 per cent; $P = < 0{\cdot}001$; odds ratio 4·6). The sensitivity of a yellow cervical swab was 62 per cent and the specificity 73 per cent. In settings where laboratory facilities are not available, empirical treatment may be implemented based on the finding of cervical mucopus.

INTRODUCTION

SEXUALLY transmitted diseases in pregnancy play an important role in maternal and infant morbidity and mortality (Brunham *et al.*, 1990). We previously reported that labouring women in a large maternity hospital in Nairobi had a high prevalence of these diseases. Thus, in 1984, 7 per cent were infected with *Neisseria gonorrhoeae*, 29 per cent with *Chlamydia trachomatis* and 4 per cent had a positive syphilis serology (Laga *et al.*, 1988). The morbidity due to these infections was also high; 3 per cent of newborn babies developed gonococcal and 8 per cent chlamydial ophthalmia neonatorum (Laga *et al.*, 1988); 20 per cent of the mothers developed postpartum upper genital tract infections, which were associated with gonococcal and chlamydial infections (Plummer *et al.*, 1987).

In 1981, the incidence of low birth weight (< 2500 g) in Nairobi was 7·5 per cent, with a perinatal mortality rate of 222/1000 live births, mainly due to problems related to prematurity (Mati *et al.*, 1982). In a previous case control study on the role of sexually transmitted diseases in preterm delivery, we found an association between maternal gonococcal infection and prematurity (Elliot *et al.*, 1990). In addition, the finding of endocervical mucopus was shown to be predictive for *N. gonorrhoeae* and *C. trachomatis* in a population of pregnant women in Nairobi (Braddick *et al.*, 1990).

In order to assess further the impact of maternal gonococcal infections on pregnancy outcome in Kenya, and to validate a simple and inexpensive diagnostic test for mucopurulent cervicitis, we specifically analysed data related to maternal gonococcal infections from an ongoing project examining the impact of maternal HIV infection and sexually transmitted diseases on pregnancy outcome (Temmerman *et al.*, 1990). Low birth weight, stillbirth and postpartum endometritis were used as the indicators of poor pregnancy outcome. The colour of the cervical swab was evaluated as a diagnostic test for maternal gonococcal infection.

MATERIALS AND METHODS

The study was conducted over 9 months in 1988 at Pumwani Maternity Hospital, a large maternity hospital serving 12 health clinics and nursery homes in Nairobi. There are more than 25 000 deliveries per year at the hospital, primarily among women from lower socio-economic classes. Patients were enrolled in the study within 24 hours postpartum. Cases were defined as mothers who delivered either a live born singleton with a birth weight between 500 and 2500 g, or a stillborn fetus. Low birthweight infants were categorised as preterm babies or neonates small for gestational age, using the gestational age and Dubowitz's score (Dubowitz *et al.*, 1970). The next mother who delivered a singleton liveborn

neonate of 2500 g or more was enrolled as a control. Exclusion criteria were multiple births and, for logistic reasons, patients who had a caesarean section. Informed consent was obtained before a patient entered the study.

Data collection at enrolment included demographic background and sexual, medical and obstetric histories. Clinical examination was performed and 5 ml blood was taken for HIV and syphilis serology. All mothers were scheduled to attend the follow up clinic 14 days postpartum. At this occasion, women were asked about the presence of fever, abdominal pain, and the quality of lochia. An abdominal, vaginal speculum and bimanual examination was performed. Uterine tenderness, cervical motion tenderness, adnexal tenderness, and the quality of the lochia were assessed. Lochia was defined as purulent if it was yellow or green. The severity of tenderness was graded on a scale of 0 to 3. After cleaning the cervix with cotton wool cervical swabs were obtained for culture for *N. gonorrhoeae* and *C. trachomatis*. The first swab was assessed for the colour of the endocervical secretion. Postpartum endometritis was diagnosed if at least two of the following symptoms were present: fever of more than 38°C, foul lochia and uterine tenderness.

Specimens for *N. gonorrhoeae* were inoculated directly on to Thayer-Martin medium and incubated for 48 hours at 37°C in humidified candle-extinction jars. *N. gonorrhoeae* was identified by colony morphology, Gram stain appearance, oxidase reactivity and carbohydrate fermentation. Chromogenic cephalosporin (Nitrocefin, Becton Dickinson, Cockeysville, Maryland, USA) was used to assay the production of β-lactamase. *C. trachomatis* was isolated on cycloheximide treated McCoy cells read with fluorescent monoclonal antibodies. HIV-1 antibody was determined in an enzyme immunoassay (Du Pont, Geneva, Switzerland) and confirmed in a Western blot assay as described previously (Temmerman *et al.*, 1990). Syphilis serology included a rapid plasma reagin test (Wellcome, London, UK) and a *Treponema pallidum* haemagglutination assay (TPHA, Wellcome).

The χ^2 test with Yates' correction was used to compare proportions. The odds ratios and the 95 per cent confidence interval were used to measure strength of associations. The χ^2 test for trend in proportions was used to test the association between maternal gonococcal infection and the categorised baby's birth weight. Logistic regression was used to compute odds ratios adjusted for other risk factors (SYSTAT program).

RESULTS

A total of 17412 singleton deliveries occurred during the study. The incidence of singleton liveborn low birth weight babies, vaginally delivered, was 5·1 per cent. The stillbirth rate was 2·2 per cent. Overall, 1507 mothers were enrolled in the study, including 796 cases and 711 controls. The case group consisted of 373 mothers who delivered a preterm baby, 234 who delivered a neonate small for gestational age, and 189 who had a stillborn baby. The follow-up rate at 1–2 weeks postpartum was 67 per cent. Hence, clinical data on postpartum endometritis and culture results for *N. gonorrhoeae* and *C. trachomatis* were available for this proportion of the study group only.

The maternal gonococcal infection rate in the different outcome groups is shown in Table I. The prevalence of gonococcal infection was not demonstrably higher in the preterm group as compared to the controls (8·6 *versus* 5·8 per cent; odds ratio 1·5; 95 per cent confidence interval 0·8–2·9). On examination of the subset of preterm babies with a birth weight less than 1500 g, we found that 7 out of 41 mothers (17·1 per cent) were infected with *N. gonorrhoeae* as compared

Table I. Prevalence of *N. gonorrhoeae* in the different outcome groups

Pregnancy outcome	*Number*	*Difference from controls*		
			Odds ratio	*95% confidence interval*
Preterm				
500–1499 g	7/41 (17·1%)	$P < 0·05$	3·2	1·2–8·0
1500–2499 g	14/203 (6·9%)	—	1·2	0·6–2·5
Small for gestational age	14/168 (8·3%)	—	1·5	0·7–3·1
Stillbirth	7/149 (4·7%)	—	0·8	0·3–2·0
Controls	26/451 (5·8%)			

to 26/451 (5·8 per cent) of those who had a baby with a birth weight of 2500 g or more ($P < 0·05$; odds ratio 3·2; 95 per cent confidence interval 1·2–8·0). In addition, we found an inverse relationship between the isolation rate of *N. gonorrhoeae* and the birth weight, when birth weight was classified into 7 categories ($P < 0·05$; Table II). The isolation rate of *N. gonorrhoeae* was 4·7 per cent in the still births, 8·3 per cent in the small for dates babies, and 5·8 per cent in the controls. Variables including age, marital status, the number of sexual partners during the previous two years, coitus during pregnancy, antenatal clinic attendance, hypertension, maternal syphilis and HIV-1 antibody results and *N. gonorrhoeae* and *C. trachomatis* culture results in the very low birth weight babies were used for multiple logistic regression analysis. Lack of antenatal care (odds ratio 5·4; 95 per cent confidence interval 1·8–20·4), maternal HIV-1 infection (odds ratio 2·1, 95 per cent confidence interval 1·0–36·5) and maternal gonococcal infection (odds ratio 4·1, 95 per cent confidence interval 1·9–28·8) were independently associated with very low birth weight.

The association between postpartum endometritis and gonococcal infection in the different outcome groups is shown in Table III. The overall prevalence of postpartum endometritis was 6·9 per cent (66 out of 960) and the odds ratio for mothers infected with *N. gonorrhoeae* was 4·1 (95 per cent confidence interval 2·0–8·4). *C. trachomatis* was not associated with postpartum endometritis in this study; 5 out of 63 patients (7·9 per cent) with clinical signs and symptoms of postpartum endometritis had a positive culture result for *C. trachomatis* compared to 18 out of 190 patients (10·4 per cent) without postpartum endometritis.

The colour of the cervical swab was recorded during the second part of this study in cases and controls ($n = 510$). A mucopurulent swab was strongly associated with *N. gonorrhoeae* (15·5 *versus* 3·9 per cent; $P < 0·001$; odds ratio 4·6; 95 per cent confidence interval 2·2–9·7). The sensitivity of a yellow, mucopurulent swab in the diagnosis of gonococcal infection in the postpartum period was 62·2 per cent and the specificity 72·8 per cent. In contrast, the colour of the swab was no indicator for infection with *C. trachomatis*; 14 out of 36 patients (38·9 per cent) with chlamydial infection had a purulent swab compared to 125 out of 433 (28·9 per cent) of non-infected mothers (odds ratio 1·7, 95 per cent confidence interval 0·8–3·6; Table IV).

Table II. Maternal gonococcal infection in relation to categorised birth weight

Birth weight (g)	*N. gonorrhoeae*
< 1000	2/22 (9·1%)
1000–1499	7/52 (13·5%)
1500–1999	10/125 (8·0%)
2000–2499	21/283 (7·4%)
2500–2999	10/149 (6·7%)
3000–3499	13/224(5·8%)
> 3500	5/145 (3·6%)

$P < 0·05$ (test for trend)

DISCUSSION

There is a strong association between gonococcal infection during pregnancy, and very low birth weight babies (< 1500 g), which is the group of neonates with the highest mortality rate (41·4 per cent; Temmerman *et al.*, 1990).

Although the point is still controversial, most authors have demonstrated some evidence of an effect of maternal gonorrhoea on prematurity (Sarrel and Pruett, 1968; Handsfield *et al.*, 1973; Amstey and Steadman, 1976; Edwards *et al.*, 1978). Drawbacks in these studies include small

Table III. Maternal gonococcal infection in women with and without postpartum endometritis

	Postpartum endometritis		*Differences*		
	Yes	*No*		*Odds ratio*	*95% confidence interval*
Preterm	3/12 (25·0%)	15/221 (6·8%)	—	4·6	0·8–21·5
Small for gestational age	3/9 (33·3%)	11/159 (6·9%)	$P < 0·05$	6·4	1·1–35·1
Stillbirths	2/21 (9·5%)	4/108 (4·8%)	—	2·7	0·1–19·4
Controls	4/24 (16·7%)	20/406 (4·9%)	$P = 0·05$	3·9	1·0–13·6
Total	12/66 (18·2%)	50/896 (5·6%)	$P < 10^{-6}$	4·1	2·0–8·4

Table IV. *N. gonorrhoeae, C. trachomatis* and the colour of the cervical swab

	Yellow swab (n)	*White swab (n)*	*Differences*		
				Odds ratio	*95% confidence interval*
N. gonorrhoeae	23/148 (15·5%)	14/362 (3·9%)	$P < 0·001$	4·6	2·2–9·7
C. trachomatis	14/139 (10·1%)	22/330 (6·7%)	—	1·6	0·7–3·3
N. gonorrhoeae **and** C. trachomatis	1/135 (0·7%)	2/320 (0·6%)	—	1·2	0·6–2·3
N. gonorrhoeae **or** C. trachomatis	32/135 (23·7%)	32/320 (10·0%)	$P < 0·001$	2·8	1·6–4·9

sample sizes, the possible bias in selection of cases and comparison groups, lack of a control group, or their retrospective nature. In a previous case control study on the role of sexually transmitted diseases in preterm delivery conducted at the same maternity centre in Nairobi, an association (odds ratio 2·9; 95 per cent confidence interval 1·1–8·0) between maternal gonococcal infection and prematurity was demonstrated (Elliot *et al.*, 1990). Our finding of an odds ratio of 1·5 with a 95 per cent confidence interval of 0·8 to 2·9 indicates a similar weak overall effect of gonococcal infection on preterm delivery. Nevertheless, we found an independent association between maternal gonorrhoea and very low birth weight preterm babies, even after controlling for confounding factors. Although the very low birth weight group represents only 15 per cent of the preterm babies, its early neonatal mortality rate was 41 per cent and therefore accounts for a disproportional fraction of the overall early neonatal mortality.

The finding that the prevalence of maternal gonococcal infection decreases gradually with birth weight supports a role for *N. gonorrhoeae* in low birth weight. One hypothesis for this inverse relationship could be a progressive increase of the inhibitory capacities of amniotic fluid with gestational age, reflected in the birth weight. This hypothesis has never been tested for *N. gonorrhoeae*, but Schlievert *et al.* (1975) observed a maximum inhibitory capacity of amniotic fluid for *Escherichia coli* between 36 and 40 weeks, while all fluid samples obtained before 20 weeks were capable of supporting bacterial growth.

In addition, our data confirm that gonococcal infection carries a high risk for the development of postpartum endometritis. Bernstine and Bland (1948) described a puerperal morbidity rate of 32 per cent among 292 women with gonorrhoea. Fransen *et al.* (1985) reported that 17 per cent of mothers of babies with ophthalmia neonatorum developed postpartum pelvic infections. These were most commonly mothers with infection due to *N. gonorrhoeae*. Plummer *et al.* (1987) showed an association between upper genital tract infections and gonorrhoea. So far, the consequences of postpartum endometritis are not fully understood. A high prevalence of this disorder might explain the high rate of secondary infertility due to tubal scarring in many sub-Saharan African countries (Walton and Mati, 1976; Cates *et al.*, 1985). The type of infertility should be susceptible to intervention programmes focusing on sexually transmitted diseases in antenatal clinics.

Antenatal case detection and treatment for gonorrhoea during pregnancy is the obvious solution to this problem but there are major logistic impediments to its implementation. Populations with a high prevalence of sexually transmitted diseases often lack the resources to finance extensive screening programmes to control the spread of these infections. Case detection of gonococcal infections cannot be based on laboratory confirmation in most developing countries, because of economic constraints. Our data show a sensitivity of 60·5 per cent, a specificity of 73·5 per cent, a predictive value of a positive yellow cervical swab test of 10·8 per cent, and a predictive value of a negative test of 67·1 per cent, for a prevalence of 7 per cent. Since the test is poorly predictive we suggest that case identification by recognition of mucopurulent cervicitis may be recommended only in areas where no laboratory facilities are available. In contrast to the data presented by Braddick *et al.* (1990) cervical mucopus was not associated with *C. trachomatis* in this group of postpartum women. These findings underline the urgent need to validate this simple approach in different populations and to determine its impact on adverse pregnancy outcome.

The study confirms that maternal gonococcal

infection is associated with very low birth weight babies, who have a high neonatal mortality rate, and with postpartum endometritis. Simple and cheap diagnostic methods should be developed for antenatal case detection. Finally, further larger case control and intervention studies should be performed to optimise control measures and to quantify the risk of gonococcal infection in poor obstetric outcome, since gonorrhoea is still a common infection in many parts of the world, and is prone to intervention.

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