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Anaerobes and septic abortion

V. O. ROTIMI* AND O. O. ABUDU†

Departments of *Microbiology and Parasitology, and †Obstetrics and Gynaecology, College of Medicine, P.M.B. 12003, Idi-Araba, Lagos, Nigeria

Summary

The bacterial flora of the genital tracts of twenty-two patients with septic abortion and twenty normal women (as controls) were studied to determine the significant aetiological agents. The predominant flora qualitatively and quantitatively in the twenty-two patients were anaerobes. *Bacteroides bivius* was isolated from all the twenty-two patients and from twelve out of twenty normal controls. The next commonest anaerobes were *B. asaccharolyticus* (fourteen out of twenty-two patients), *B. melaninogenicus* (ten out of twenty-two), *B. fragilis* (eleven out of twenty-two), *B. disiens* (eight out of twenty-two) and anaerobic cocci (six out of twenty-two); they were also isolated from nine out of twenty, twelve, zero, eight and three control subjects respectively. The commonest facultative bacteria isolated from both the patients and afebrile controls were *Escherichia coli*, *Klebsiella aerogenes* and *Streptococcus faecalis*. The comparative increase in number of patients colonized by the anaerobes and the increase in the bacteria, by quantitative assessment in the patient group, signify the importance of anaerobes in septic abortion.

Résumé

On a entrepris un étude pour déterminé la flore bacterie de la tract urogenitale chez 22 malades qui ont eut l'avartement septique et 20 femmes normale, apues la quel on a fair un analyse des agents aetiologique le plus significatif. Les flarues les plus cowraut quantitativement et

qualitativement chez les 22 malades etait les anaerobes. *Bacteroides bivius* etait isolee chez lous les 22 malades et de 12 sut 20 femmes normale. Les anaerobes suivantes les plus commue etait *B. asaccharolyticus* (14 sur 22), *B. melaninogenicus* (10 sur 22), *B. fragilis* (11 sur 22), *B. disiens* (8 sur 22) et les cocci anaerobique (6 sur 22); Ils etait aussi isolee de neuf sur vingt, 12, zero, 8 et 3 femmes controle respectivement. Le bacterice facultative les plus courrant isolee malades et controles etait *Escherichia coli*, *Klebsiella aerogenes* et *Streptococcus faecalis*. L'augmentation comparatif chez les numero des malades colonise par les anaerobes et l'augmentation chez les bacteries par l'estimation quantitaf, chez la groupe de malades, signifie l'importance des anaerobes daus l'avortement septique.

Introduction

During the last two decades sepsis complicating abortion has continued relentlessly as a prime cause of maternal morbidity and mortality world wide. In the advanced countries, where accurate statistics are available, sepsis has persisted as the most common cause of death from abortion (Gibbs *et al.*, 1975; Grimes, Cates & Selik, 1981). In Nigeria (and indeed in many West African countries), accurate data on septic abortion cases and subsequent complications is scanty. However, prevention and management of sepsis complicating abortion are important concerns in gynaecological practice in Nigeria.

Unfortunately most cases of septic abortion are not studied bacteriologically, and therefore information that could guide the empirical use of an array of antibiotics now available in the country is not easily available. Delay of antibio-

Correspondence: V. O. Rotimi, Department of Microbiology and Parasitology, College of Medicine, P.M.B. 12003, Idi-Araba, Lagos, Nigeria.

tic therapy after infection has developed may be fatal. Therefore updated knowledge of the bacteriology of this important infection is essentially vital to the prompt management of these cases in order to prevent needless mortality and serious complications such as infertility in later life.

Reports on microbiological studies on septic abortion are scanty and inconclusive. Even the available reports of microbiological studies of the genital tract in pregnancy and post-partum are often in disagreement about the role of individual potential pathogens in infections thus making any meaningful clinical deductions almost impossible. This study was therefore undertaken to investigate the bacterial flora of the genital tracts of patients with septic abortion, with particular emphasis on anaerobic bacteria and their quantitative assessments. Each patient was also investigated for possible concurrent bacteraemia.

Materials and methods

Patients

Twenty-two patients with septic abortion, admitted to the gynaecological wards of Lagos University Teaching Hospital (LUTH) were studied bacteriologically. They were diagnosed following the history of amenorrhoea culminating in unsuccessful termination which resulted in lower abdominal pains, offensive vaginal discharge and/or vaginal bleeding, uterine tenderness, and pyrexia of $\geq 38^{\circ}\text{C}$ at two consecutive measurements at 6-h intervals. Twenty normal adult Nigerians attending our Gynaecological Clinic out-patient department (GOP) for reasons other than infective processes and whose body temperatures on two consecutive measurements were normal, were also studied as control. All antibiotics taken by individual patients prior to admission were noted while the control subjects had not taken any antibiotics in the preceding month.

Specimen

A set of two blood cultures, high vaginal (HVS) and cervical (CS) specimens were obtained from each patient prior to any antibiotic reg-

ime; only one set of these specimens was taken from individual patients; another set of HVS and CS were taken from each control. The HVS and CS were obtained by albumen-coated swabs (Exogen Ltd, Dumbarton Road, Glasgow) under direct view using Cusco's speculum. The swabs were broken into Amies transport medium and transported immediately to our Research Laboratory where they were usually processed within 20 min of arrival.

Media

The following selective and non-selective media were used throughout the study period: (i) two blood agar (Oxoid) plates; (ii) BM-Kanamycin agar (MB agar made selective by adding 75 $\mu\text{g/ml}$ Kanamycin; Holbrook *et al.*, 1978); (iii) neomycin blood agar (Blood agar plus 75 $\mu\text{g/ml}$ neomycin); (iv) MacConkey agar (Oxoid); (v) chocolate agar; (vi) Thayer-Martin agar (Oxoid); (vii) Sabouraud's agar (Oxoid); (viii) Robertson cooked meat broth (RCM); (ix) brain-heart infusion broth (Oxoid) and Thioglycollate broth (Oxoid) for aerobic and anaerobic blood cultures.

Inoculation of media

All solid media were inoculated by rolling the swab on one sector of the agar plates to make an inoculum pool and then streaked with a sterile 2-mm wire-loop by standard method of Gillies and Dodds (1976) such that the density of growth of individual bacteria could be assessed semi-quantitatively by a method previously described (Rotimi & Duerdern, 1981). The same swab was then broken into Robertson cooked meat medium.

Incubation

The MacConkey agar, Sabouraud's agar, blood culture bottles and Robertson cooked medium were all incubated in air at 37°C . The MacConkey and Sabouraud's agar were incubated for 24 h and extended to 48 h when necessary, while the RCM was incubated for 24 h and sub-cultured onto freshly prepared and pre-reduced plain blood agar, neomycin blood agar and BMK agar. The blood culture bottles were

inspected and sub-cultured after 24 h and thereafter inspected daily for evidence of growth for 7 days after which they were discarded; any evidence of growth from the bottles were investigated by sub-culturing. One blood agar, chocolate agar and Thayer-Martin agar were incubated in air plus 10% CO₂ in a candle extinction jar for 24 h. Another blood agar, neomycin-blood agar and BMK agar were incubated anaerobically in a carefully controlled anaerobic jar (Oxoid) in the presence of 90% H₂, 10% CO₂ generated by satchets of gas generating kit (Oxoid). Each jar was controlled by anaerobic indicator (Oxoid).

Identification of isolates

The aerobes were identified by standard method of Gowan (1974) and the enterobacteriaceae by the API 20E system (API system, Montalier Fra.). The anaerobes were identified by colonial morphology, oxygen intolerance, antibiotic resistance tests, indole production, hydrolysis of gelatin and aesculin, pigment production and sugar fermentation patterns

according to the identification schemes previously described (Duerden *et al.*, 1980; Rotimi, Faulkner & Duerden, 1980).

Results

The aerobic and anaerobic bacteria isolated from the HVS, CS and blood culture, are shown in Tables 1-3. Table 1 summarizes the bacterial isolates from the twenty-two patients. Except in a few patients, the same organisms, when present, were isolated from the HVS and CS specimens in each individual. The commonest organisms isolated from the septic abortion cases were the non-sporing Gram negative anaerobes, particularly the *Bacteroides* spp. *B. bivius* was isolated from the CS of all patients while the black-pigmented anaerobic bacilli mainly, *B. asaccharolyticus* and *B. melaninogenicus* were isolated from fourteen and ten out of twenty-two patients respectively. *Bacteroides fragilis*, a rare member of the normal flora of the vagina and cervix, was isolated from eleven of the twenty-two patients. *Bacteroides disiens* and anaerobic streptococci were isolated

Table 1. Bacterial isolates from twenty-two patients

Organisms	Number of patients		
	HVS	CS	Blood
Anaerobes			
<i>B. bivius</i>	21	22	2
<i>B. asaccharolyticus</i>	14	14	0
<i>B. melaninogenicus</i>	10	10	0
<i>B. fragilis</i>	10	11	2
<i>B. disiens</i>	7	8	0
Ano ₂ Streptococcus	6	6	1
<i>Cl. perfringens</i>	4	4	0
<i>Lactobacillus</i>	2	0	0
<i>Bacteroides</i> spp.	3	3	0
Aerobes			
<i>E. coli</i>	14	14	0
<i>Klebsiella</i> spp.	10	9	0
<i>Strep. faecalis</i>	13	13	0
<i>Staph. aureus</i>	3	3	2
<i>Proteus mirabilis</i>	3	3	0
Group B streptococci	3	3	0
<i>Candida albicans</i>	3	3	0
<i>N. gonorrhoeae</i>	—	2	0
<i>Ps. aeruginosa</i>	2	2	0

from eight and six patients respectively. *Bacteroides*, that could not be speciated by the conventional methods were isolated from a further three patients. The commonest facultative bacteria was *Escherichia coli* which was isolated from HVS of fourteen out of twenty-two patients. The other quantitatively significant facultative isolates were *Streptococcus faecalis* (thirteen out of twenty-two) and *Klebsiella aerogenes* (ten out of twenty-two). The isolates from seven positive blood cultures were mainly anaerobes; *B. fragilis* and *B. bivius* were isolated from two patients each, and anaerobic streptococci from one patient, while the remaining two positive blood cultures grew *Staphylococcus aureus*.

Analysis of the isolates from the twenty non-septic cases, demonstrated in Table 2, showed that *B. bivius*, *B. melaninogenicus* and *B. intermedius* relatively colonized fewer numbers of control subjects; twelve each out of twenty were colonized by these anaerobes. *Bacteroides asaccharolyticus*, *B. disiens* and lactobacilli were isolated from nine, eight and six subjects respectively, while anaerobic streptococci were isolated from only three subjects. *E. coli* (12/20) and *Strep. faecalis* (12/20) were the major facultative organisms isolated from the control subjects.

The comparative semiquantitative (density of

growth) count of the individual bacterial isolates from the CS of both patients and control is summarized in Table 3 (the counts in both HVS and CS were the same). Anaerobes predominated quantitatively over aerobes in the normal controls with counts ranging from 1+ to 4+ and with an overall mean count of 3+, while the range for aerobes was 1-3+ and a mean of 2+. In the patient group although anaerobes also predominated over aerobes the counts were significantly higher. For the anaerobes the counts ranged from 3+ to 5+ with a mean of 5+. The counts of the facultative organisms were also generally higher than in the control with a range of 1-4+ and a mean of 3+.

Discussion

This study aptly demonstrates that the high vaginal fornices (HVS) and cervix (CS) of afebrile normal women contain abundant bacteria that are essentially similar in composition (except for a few species) to the flora of patients with septic abortion. However, significantly, the quantity of each bacterial isolates was different in the two populations. Some species that are potentially pathogenic, were also found in the CS of patients but absent in the afebrile control.

Table 2. Predominant vaginal flora of twenty normal healthy adults

Organisms	Number of specimens	
	High vaginal swab	Cervical swab
Anaerobes		
<i>B. melaninogenicus</i>	12	12
<i>B. intermedius</i>	11	12
<i>B. asaccharolyticus</i>	9	9
<i>B. bivius</i>	11	12
<i>B. disiens</i>	8	8
Anaerobic cocci	3	3
Lactobacilli	6	3
Aerobes		
<i>E. coli</i>	12	12
<i>Strep. faecalis</i>	12	11
<i>K. aerogenes</i>	5	5
<i>Staph. albus</i>	6	5
<i>Candida</i> spp.	4	3

Table 3. Semiquantitative assessment of the significant bacterial isolates

Organisms	Predominance of bacteria (bacterial count)			
	Patients (CS)*		Control (CS)	
	Range	Mean	Range	Mean
<i>B. bivius</i>	3-5+	5+	1-4+	3+
<i>B. asaccharolyticus</i>	2-5+	5+	1-3+	3+
<i>B. melaninogenicus</i>	3-5+	5+	1-4+	3+
<i>B. fragilis</i>	3-5+	5+	0	0
<i>B. disiens</i>	3-5+	5+	1-3+	3+
Anaerobic cocci	1-4+	4+	1-3+	3+
<i>Cl. perfringens</i>	1-3+	2+	0	0
Lactobacilli	1-4+	3+	1-3+	2+
<i>Bacteroides</i> spp.	3-5+	5+	0	0
<i>E. coli</i>	1-4+	3+	1-3+	2+
<i>Klebsiella aerogenes</i>	1-3+	2+	1-3+	2+
Group B streptococci	2-3+	2+	0	0
<i>Ps. aeruginosa</i>	2-3+	3+	0	0
<i>Staph. aureus</i>	1-3+	2+	0	0

*(CS) = Cervical swab specimen.

Of special interest was the high number of patients from whom *B. bivius* was isolated — unlike its relatively lower isolation rate in afebrile normal subjects. All patients with clinical diagnosis of septic abortion harboured the *Bacteroides* whereas only 60% of controls did. The high number of normal subjects colonized by this organism make the interpretation of the results obtained by sampling through the cervix and high vagina difficult, as contamination by normal vaginal flora cannot be ruled out. It is clear that the mere presence of the organism in the cervix or HVS does not necessarily constitute infection. However, despite these reservations the pathogenic potential of *B. bivius*, and of other anaerobes, isolated from septic abortion cases was demonstrated by the profuse increase in their quantity when assessed semi-quantitatively. For example, the mean count of *B. bivius* and other anaerobes in afebrile controls was 3+ (approximately 10^6 cfu/ml) and 5+ ($\geq 10^{10}$ cfu/ml) in septic abortion cases. Besides, *B. bivius* and *B. disiens*, as in this study, have recently been implicated as the most important pathogen in endometritis (Syndman *et al.*, 1980) and particularly *B. bivius* as the only pathogen in some

abscesses especially breast abscesses (Leach *et al.*, 1979).

Anaerobes are opportunistic pathogens. They only become infective when the host defence mechanism is compromised, such as when there is a breach in the mucous lining of the cervix and endometrium as was the case in these patients. The pathogenic potential of some of the anaerobes was also demonstrated by their isolation, albeit occasionally, from blood cultures of the patients. *B. bivius*, *B. fragilis* and anaerobic cocci were isolated from the blood of five out of seven patients with positive blood cultures while the remaining two yielded *Staphylococcus aureus*, whose pathogenicity was never in doubt.

B. fragilis, the type-species of the *B. fragilis* group, is the commonest anaerobe implicated in post-surgical wound infections following abdominal and gynaecological operations (Holland, Hill & Altermeier, 1977; Duerden, 1980a). Possession of polysaccharide capsules (Kasper *et al.*, 1977; Onderdonk *et al.*, 1977), ability to resist phagocytosis and prevent opsonization of aerobic bacteria (Kasper *et al.*, 1979), and to survive the bactericidal action of human serum (Rotimi & Eke, 1984) are said to

be responsible for its pathogenicity. Even though the organism is not a member of the normal flora of the vagina (Duerden, 1980b), it is noteworthy that it is isolated from the CS of about 50% of the patients. This is a significant finding which lends weight to the important role played by anaerobes in septic abortion. The source of *B. fragilis* may have been the cervix which, in some people, is said to be transiently colonized by *B. fragilis*, in the first trimester (J. G. Bartlett, John Hopkins; pers. comm.).

The importance of anaerobes in septic abortion is similar to its importance in puerperal sepsis and post-partum endometritis. A number of earlier reports indicated that the anaerobic cocci followed by *Bacteroides* spp. were the most common pathogens isolated in the lochia and cervix of patients with post-partum endometritis and puerperal sepsis (Gibbs *et al.*, 1975; Soto *et al.*, 1974). Ulson *et al.* (1979) also found a preponderance of anaerobes in the cervix of their septic abortion and puerperal sepsis cases, which is in accord with our present findings.

In this study, the significance of isolation of aerobic bacteria is relatively indistinguishable between the patients and the afebrile controls. Some earlier studies stressed the significance of facultative Gram negative bacilli, particularly *E. coli*, in puerperal sepsis and endometritis even when anaerobic techniques were used (White & Koontz, 1973; Sweet & Ledger, 1973). Our present findings and those of others (Ulson *et al.*, 1979), do not support this assertion. The increase in number of some normal flora aerobes, e.g., *E. coli* and *Klebsiella aerogenes*, should be expected in this type of infection which is essentially polymicrobial in aetiology with the anaerobes preventing their opsonization and subsequent phagocytosis. Obviously anaerobes appear to be more important than aerobes in septic abortion as shown by the totality of their quantitative and qualitative predominance. Moreover, anaerobes were isolated more frequently than aerobes from positive blood cultures of the patients by a ratio of 3:1.

Our present report indicates that the most common pathogens present in septic abortion cases were the Gram negative non-spore-forming anaerobic bacteria, especially *B. bivius*, black-pigmented *B. asaccharolyticus* and *B. melaninogenicus*, *B. fragilis* and anaerobic cocci. In

the reports of Gibbs *et al.* (1975) and Soto *et al.* (1974), anaerobic cocci were the predominant organisms in cases of clinical endometritis they investigated. Other potential pathogens, including *Klebsiella* spp. and *Streptococcus faecalis* were present almost as frequently as *E. coli*. *Neisseria gonorrhoeae* was isolated from two patients, a significant finding which with the raw surfaces on the cervix may lead to disseminated gonococcal infections.

The usefulness of prophylactic antibiotics in reducing the risk of post-abortion sepsis is not certain. Most studies that evaluated antibiotic prophylaxis in such cases reported findings on sepsis secondary to legal abortions where utmost care and necessary precautions are taken in the management of cases. Abortions complicated by sepsis seen in our hospital are usually illegal and are performed by unqualified and inexperienced practitioners. It is desirable to carry out urgent prophylactic antibiotic trials on legal or illegal abortions in order to prevent complications such as morbidity and mortality. Also adequate information in a form of clinical trials, on broad spectrum single agents or a combination of bactericidal agents is needed to help in guiding our colleagues in the use of empirical antibiotic regimes.

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