

# Inflammatory cervical smears and infection in Kano, Northern Nigeria

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## **Abstract**

**Background:** *Inflammation is commonly present in cervical smears for screening of pre-malignant lesions, so we undertook this study to identify microbial pathogens responsible for the inflammation.*

**Method:** *This was a prospective study of cervical smears and endocervical swabs from patients at the gynaecology, postnatal and general outpatient clinics of Aminu Kano Teaching Hospital over a 4 month period.*

**Results:** *A total of 421 women between the ages of 17 and 80 years were recruited for the study, but most (95%) were premenopausal (<50 years).*

*Two hundred and thirteen (50.6%) of the smears were inflammatory as evidenced by prominent neutrophilic infiltrate, but only 127 (30%) of the study patients had infection as demonstrated by microbial growth on culture and positive Chlamydia antigen test. Sixty one percent (78 cases) of the 127 cervical infections occurred among the 213 patients with inflamed smears. The remaining 39% (49 cases) of cervical infections occurred in patients with non-inflammatory smears. Chlamydia and candida were the most frequent microbes accounting for 68.5% of all cervical infections. Thirty nine (8.7%) of all smears were dysplastic with low grade dysplasia comprising the overwhelming majority – 35 cases.*

**Conclusion:** *As in most published studies, cervical inflammation did not correlate with infection, as infection also commonly occurs in patients without inflammatory smears. This renders patient management problematic for gynaecologists. Further research is therefore required to clarify the microbial and non-microbial causes of cervico-vaginal inflammation.*

**Keywords:** Cervical smears, Inflammation, Infection, Nigeria

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## Introduction

Although screening for dysplasia in order to prevent the development of cancer is the major reason for the widespread use of cervical smears, most studies document inflammation as the most frequent diagnosis<sup>1-3</sup>. The inflammation is not usually associated with dysplasia,<sup>1, 3, 5</sup> and its severity varies from negligible mild neutrophilic infiltrate to severe purulent exudates.

Quite disturbingly some of the patients with cytologically severe inflammation are clinically asymptomatic only being detected during routine smear screening. The long term adverse consequences of such simmering sub-clinical inflammation on female reproductive health are quite obvious – STI transmission, sub-fertility, infertility, ectopic pregnancy and miscarriages, not to mention the disruptive social impact on family and relationships.

Worse still, chronic cervical inflammation is a known predisposing factor in the progression of dysplasia to cancer<sup>3, 4, 5</sup>. It is therefore imperative that the microbial culprits of this cervical inflammation be identified and eradicated, hence the relevance of this study. Although a variety of microbes (viruses, parasites, fungi and bacteria) and non-microbial causes have been implicated in cervical inflammation, bacteria are by far the major pathogens.<sup>6-10</sup> By virtue of their peculiar diagnostic features, most of the non-bacterial pathogens can be microscopically identified during cytological examination of cervical smears. The different bacterial pathogens can however only be properly identified and eradicated by microscopy, culture and sensitivity tests, hence the bacteriological emphasis of this study.

Interestingly, some studies suggest a disconnect between cervical inflammation and infection<sup>6,11</sup> i.e. infection occurring with or

without inflammation and vice versa. It would be useful to characterize the relationship between cervical inflammation and infection in our locality, with a view to ascertaining the occurrence and pattern of microbial infections, particularly as microbial pathogens are known to differ among different populations. Such data should be of immense value to the management of patients with inflammatory smears, not just in Kano but possibly the entire Sahelian West Africa.

## Patients and Methods

This 4-month prospective study of 421 patients was approved by the ethical committee of Aminu Kano Teaching Hospital where the research was carried out. Two cervical smears and 2 endocervical swabs were collected from each of the 421 women at gynaecology, antenatal, post-natal and general outpatient clinics the hospital.

Cervical smears were stained with the usual Papanicolaou and then microscopically examined by pathologists. One of the endocervical swabs from each patient was gram stained for microscopy then cultured on blood, chocolate, MacConkay, Sabaroud and Mycoplasma agars. The blood agar plates were incubated anaerobically with Oxoid gas packs.

All culture plates were examined after 24 hours and biochemical tests performed on positive cultures to identify microbial genus and species. Sensitivity tests were also carried out using sensitivity discs from *Ablek Biologicals*. The second endocervical swab from each patient was for Chlamydial antigen test using *Diaspot* kit.

## Results

A total of 421 cervical smears and endocervical swabs were collected from the study patients. One hundred and fifty six (34.7%) of these

patients were postnatal, 145 (32.3%) gynaecological, 53 (11.8%) antenatal and 95 (21.1%) routine asymptomatic screening. Although their age range was broad (17 to 80 years), most patients (95%) were premenopausal ( $\leq$  50 years).

Two hundred and thirteen (50.6%) of the smears were inflammatory as evidenced by prominent neutrophilic infiltrate, but only 127 (30%) of the study patients had demonstrable infections as evidenced by microbial growth on culture and positive Chlamydia antigen test (Table 1). Sixty one percent (78 cases) of the 127 cervical infections occurred among the 213

37% (78 cases) of the 213 inflammatory smears.

All together, there were 76 pathogenic growths on microbial culture and 61 swabs positive for Chlamydia antigen test, with 10 of the positive Chlamydial infections being associated with other microbial growths on culture. Chlamydia and candida were the most frequent microbes accounting for 68.5% of all cervical infections (Table 2).

**Table 1:** Overview of cervical smears and swabs

Number of study patients	421 (100%)
Inflammatory smears	213 (50.6%)
Pathogenic microbial growths on culture	76 (18.1%)
- Bacterial growths (total)	50 (11.9%)
» Bacterial growths with inflammatory smears	39 (9.3%)
- Candida sp. (total)	26 (6.2%)
» Candida with inflammatory smears	11 (2.6%)
Chlamydia (total)	61 (14.6%)
- Chlamydia with inflammation	28 (6.7%)
- Chlamydia with other microbial growths	10 (2.4%)
High grade dysplasia	4 (0.95%)
Low grade dysplasia	35 (8.3%)
- Low grade dysplasia with inflammation	18 (4.3%)

patients with inflammatory smears. The remaining 39% (41 cases) of cervical infections occurred in patients without inflammation. Overall, infection was demonstrated in only

**Table 2:** Microbial profile of endocervical swabs in Kano

Microbe	No. of cases	%
Chlamydia only	51	37.2
Chlamydia with other microbial pathogen	10	7.3
Candida	26	19.0
Escherichia coli	14	10.2
Non-haemolytic Streptococcus	12	8.8
Enterococcus faecalis	12	8.8
Staphylococcus aureus	6	4.4
Alpha haemolytic Streptococcus	4	3.0
Mycoplasma	1	0.01
Anaerobe	1	0.01
Total	137	100

Thirty nine (8.7%) of cervical smears were dysplastic with low grade dysplasia comprising the overwhelming majority (35 cases) and high grade dysplasia accounting for just 4 cases.

## Discussion

About half (50.6%) of the 421 smears in this study were inflammatory as evidenced by prominent neutrophilic infiltrate; but only 18% (76 cases) of the accompanying endocervical swabs yielded pathogenic growths on culture. Chlamydia infection as determined by antigen test kit was demonstrated in 14.6% (61 cases) of microbial infections. Ten of these Chlamydia cases also had microbial growth on culture, so that the Chlamydia test only yielded additional 51 cases totalling 127 patients with microbial infections. This amounts to 30% of the total 421 patient population - a far cry from the 50.6% (213 cases) with inflammatory cervical smears. Thus there appears to be an obvious disconnect between inflammation in cervical smears and microbial infection, as inflammation does not appear to correlate with microbial growth. This disconnect is accentuated by the observation that more than a third (39%) of microbial infections occurred in women whose cervical smears were deemed non-inflammatory.

Our findings were broadly similar to several published studies around the world which found no correlation between cervical infection and inflammatory cervical smears<sup>11-15</sup>, as significant proportion of infection also occurred in patients without inflammatory smears.

In a BMJ commentary, Mali and Josh (1993) postulated that infection in patients without inflammation could be due to recent infection in which inflammatory response was not yet fully developed.<sup>14</sup> This is particularly likely because some of the smears deemed non-inflammatory actually had scanty neutrophilic infiltrate.

Cervical infection in published reports varied from 29% to 48% of patients with inflammatory smears.<sup>11-15</sup> In this study only 37% of patients with inflammatory smears had demonstrable evidence of infection - bacteria

(including Chlamydia) & Candida. In other words most women with inflamed cervical smears had no evidence of infection.

This absence of demonstrable infection in many women with inflammatory smears has so far defied explanation. One remote possibility is that viruses or some other yet to be identified pathogen may be responsible. This is particularly likely as unusual pathogens like cytomegalovirus and Human T-lymphotropic virus have been implicated as aetiological factors in some studies.<sup>15-16</sup>

Cytologically, apart from the 38 cases of dysplasia (9.3%) usually due to Human Papilloma Virus (HPV), no cytopathic changes indicative of viral infections were present in the cervical smears. However, more sensitive molecular diagnostic techniques like nucleic acid hybridization for viruses were not undertaken in this appraisal. Another possible explanation is that inflammation in cervical smears is indicative of vaginal infection rather than cervical.

The ectocervix from which smears are mostly taken is bathed with vaginal fluid and is directly continuous with the vagina, which is more vulnerable to infection by virtue of the fact it directly communicates with the exterior via the introitus, and is the receptacle for the penis during STI transmission.

This vaginal inflammation hypothesis is supported by the observation that neutrophilic infiltrate in cervical smears is often not accompanied by reactive changes in cervical epithelial cells (squamous & endocervical) indicative of cellular injury.

Furthermore, although acute inflammation with neutrophilic infiltrate is common in cervical smears, such neutrophilic infiltrates are relatively uncommon in histological sections of the cervix. Histologically, cervical

inflammation is usually of the chronic variety with lymphocytic rather than neutrophilic infiltrate.

A comparative study by Vural *et al* (1995) in Sweden similarly demonstrated that cytological inflammation of the cervix did not correlate with histopathology.<sup>17</sup> Thus high vaginal swabs rather than the endocervical might prove to be more useful in evaluating inflammatory cervical smears. But a study of both vaginal and endocervical swabs by Tibaldi *et al* (2009)<sup>18</sup> failed to demonstrate infection in nearly half of symptomatic women.

Perhaps because inflammation in cervical smears does not appear to have any clinical significance, the newer liquid based cytology (LBC) deliberately dispenses with inflammatory cells to enhance clarity in the cytological evaluation of epithelial cells for dysplasia.

But this extreme of removing leukocytes from LBC cervical smears deprives the pathologist of useful information that might be relevant for evaluating cervical smears. For instance the presence or absence of inflammation sometimes aids the distinction of Atypical Squamous Cells of Undetermined Significance (ASCUS) from marked reactive cellular change in the 2001 Bethesda diagnostic classification.

With regards to the microbial profile of cervical infections, *Chlamydia trachomatis*, *Candida sp* and *Escherichia coli* were the most frequent pathogens in this review. This is somewhat at variance with published studies from the Europe & United States where *Chlamydia Trachomatis* and *Neisseria gonorrhoea* appear to be major culprits.<sup>19-22</sup> Significantly, gonorrhoea was conspicuously absent from this review.

Thus the significance of inflammation in cervical smears remains problematic particularly for gynaecologists who have to decide whether or not to investigate and treat patients with inflamed smears. This problem is compounded by the observation that cervical inflammation often persists even after antibiotic treatment.<sup>21-22</sup>

More studies are therefore required to further define the infectious and non-infectious causes of cervico-vaginal inflammation with a view to enhancing patient management.

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