

Evaluation of vaginal flora and antibiotic prophylaxis in elective hysterectomy in a rural hospital from India

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Abstract

The incidence of post-operative complications is 11.5% in developing countries and surgical site infections complicate nearly 20% of intra-abdominal procedures. Contamination of operative site with vaginal flora is unavoidable and should be treated prior to hysterectomy. This study was conducted to assess the current status of antibiotic prophylaxis in hysterectomy in a rural setting. The study was conducted at Department of Obstetrics and Gynaecology, RD Gardi Medical College, Ujjain, India. Patients of abdominal and vaginal hysterectomy for benign gynaecological diseases were included. Pre-operative vaginal swab was cultured. Patients with culture negative result received ampicillin prophylaxis while culture positive patients received antibiotic of sensitivity. Patients were observed for various post-operative morbidities. Total 109 patients with age range of 37- 76 years were analyzed in the study. Pre-operative vaginal swab culture showed non-pathogenic organisms in 67% of cultures while pathogenic bacteria in 33% of cultures. Culture positive results were more often seen in vaginal hysterectomy than in abdominal hysterectomy ($p = 0.003$). Total 25.6% (28/109) patients showed post-operative morbidities such as vaginal discharge, wound infection, urinary tract infection, and fever in decreasing order of frequency. Only 11.1% (4/36) of patients infected with pathogenic bacteria and 32.8% (24/73) of patients with non-pathogenic bacteria had complications. Complications were higher in ampicillin prophylaxis patients than in culture specific prophylaxis ($p=.014$). This study showed the beneficial effect of pre-operative vaginal swab culture in elective hysterectomy and that a culture sensitive antimicrobial coverage is more effective than ampicillin in reducing post-operative complications.

Key Words: Vagina and Microbiology; antibiotic prophylaxis; Surgical porcedures, elective; Hysterectomy; India

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Introduction

Infections and fever are the most common post-operative complications which represent a significant burden in terms of patient morbidity, mortality and cost of hospitalization. The incidence of post-operative infection and fever is 11.5% in developing countries as compared to 5% in developed countries.¹ Surgical site infections complicate up to 20% of intra abdominal procedures.²

The vagina is normally colonised with mixed aerobic and anaerobic bacteria species.^{3,4,5,6} Contamination of some operative sites with endogenous organisms from the vagina is unavoidable. The pre-surgery vaginal predominant organisms can readily be cultured to identify risk for causing pathogenic disease.⁷ The asymptomatic vaginal colonization can be treated prior to hysterectomy to avoid post surgical complications. In treated patients, reported reductions in postoperative infectious complications range from 10 to 75%.^{8,9}

As early as 1974 Ledger *et al.*¹⁰ developed guidelines for antibiotic prophylaxis in gynaecological surgery advocating laboratory and clinical evidence of effectiveness against contaminating organisms. Some data suggests that nearly 30-50% of antibiotics used in hospitals are prescribed for surgical prophylaxis and 30-90% of this prophylaxis is inappropriate.¹¹

The present study was conducted in a rural university hospital in Ujjain. Many patients undergo gynaecological procedures in our hospital but, the use of prophylactic antibiotic in hysterectomy is mainly determined by the surgeon on individual basis, rather than following an evidence based guideline. The most commonly used regimen is to give two grams of ampicillin. Though Ujjain is one of the largest districts in central India, until now due to lack of adequate baseline information on the pattern of antibiotics prophylaxis usage from our region no proper guidelines have been developed. This is the first study to assess the current status of peri-operative antibiotic prophylaxis in hysterectomy cases and identification of evidence based corrective measures for use of prophylactic antibiotics in patients undergoing gynaecological surgery.

Methodology

Setting

This study was conducted at Department of Obstetrics and Gynaecology, RD Gardi Hospital; a 600 bedded university hospital located in rural area of Ujjain, Central India. The hospital caters patients from a low socioeconomic status, nutritionally poor, low priority and poorly literate groups.

Patient

All in-patients from May 2010 to Dec 2010 with benign gynaecological diseases were initially enrolled in the study. Detailed demographic information, clinical history, clinical examination findings were recorded in a pre-designed questionnaire. Pre-operative haemogram, blood urea nitrogen and sugar level, HIV test, and chest X-ray were also completed. Patients with less than 18 years of age, systemic or associated medical diseases like anaemia (haemoglobin less than 9.0gm/dl), tuberculosis, diabetes, liver or renal disease, hypertension, cardiac problem or those on anti-tuberculosis treatment, or receiving corticosteroids, immunosuppressive, anti-retroviral therapy were excluded (n=14) from the study. Patients allergic to antibiotics, currently using or used antibiotics within the week before surgery were also excluded (n=2) from the study. Hence, total 16 patients were excluded from the study.

Abdominal or vaginal hysterectomy of patients was performed. Patients were included when they were clinically diagnosed of benign gynaecological conditions, having expected length of surgery less than two hours, expected blood loss less than 100mls, elective surgery and per-speculum examination revealed no cervical or vaginal discharge.

Vaginal swab collection and culture

In lithotomy position, a vaginal swab sample was collected with sterile swab on stick from posterior vaginal fornix and external os of uterine cervix after cleaning the vulva with sterile water. The swab stick was immediately put in culture medium for aerobic and anaerobic culture, labelled, stored at 4-6°C and transported to microbiology laboratory within an hour of collection. The culture and antibiotic susceptibility was done with the standard laboratory protocol.

Antibiotic prophylaxis, surgical procedure and follow up

Patients with culture negative vaginal swab received 4g ampicillin (500 mg intravenously six hourly for two days brand SAM-500, Sarabhai Pharmaceuticals) according to the hospital policy, while culture positive patients received antibiotics depending on the sensitivity results (cefoxitin, ciprofloxacin, gentamycin, metronidazole) in standard doses for 5 days. First dose of antibiotics for all patients started half an hour prior to surgery. The abdominal or vaginal hysterectomy was performed using aseptic technique under either general (three patients) or spinal (all other patients) anaesthesia.

Patients were observed for fever and infection during the post operative period. The common causes of complication were urinary tract infection, vaginal cuff infection and surgical site infection. The outcome measures were defined as 1. Surgical site infection - dressing checked at 48 hours and five days post-operatively for any serosanguinous or purulent discharge, 2. Vaginal cuff infection - serosanguinous or purulent discharge 3. Fever - temperature $>37^{\circ}\text{C}$ on at least two

occasions, 8 hours apart, 4. Urinary tract infection - presence of > 10 pus cells per high power field of microscopy or culture positive, and 5. Symptomatic upper respiratory tract infection. Patients were discharged from the hospital at the surgeon's discretion after required nursing care. All patients were again followed after six weeks for symptoms and signs of complications.

Data analysis

Data were analyzed using SPSS Version 13 to assess differences between variables. Chi-square test was done to check the presence of associations. Bivariate logistic regression model analysis was applied to assess the risk factors. P-values <0.05 were considered statistically significant.

Ethical Consideration

Ethical approval was secured from the Institutional ethics committee. A written consent from the medical director and superintendent of the hospital was obtained for conducting the study. An informed written consent was obtained from the patients. All the procedures were conducted according to the clinical and medical need of the patient and not for the sake of study.

Table I. Clinical characteristics of patients in relation to pre-operative vaginal swab culture isolates

Clinical characteristics of patients	Vaginal swab culture isolates	
	Non-pathogenic bacteria (N=73) n (%)	Pathogenic bacteria (N=36) n (%)
Age (years)		
<50	33 (45.2)	8 (22.2)
>50	40 (54.7)	28 (77.7)
Parity		
< 2	6 (8.2)	1 (2.7)
> 2	67 (91.7)	35 (97.2)
Type of Hysterectomy		
Abdominal	40 (54.7)	9 (25)
Vaginal	33 (45.2)	27 (75)*
Length of Surgery		
> 2hrs	1 (1.3)	7 (19.4)
<2 hrs	27 (36.9)	29 (80.5)
Blood loss		
>200ml	1 (1.3)	3 (8.3)
<200ml	27 (36.9)	33 (91.6)

*p=0.003

Results

Patient details

Data from total of 109 patients were analyzed in the study. Patients from all age ranging from 37- 76 years (mean age-58 years) were seen. Patients with pre-operative diagnosis of uterine prolapse, uterine fibroid, ovarian mass and dysfunctional uterine bleeding underwent either vaginal or abdominal hysterectomy.

Culture results

Pre-operative vaginal swab culture showed non-pathogenic organisms in 67% (73/109) culture while pathogenic bacteria were isolated from 33% (36/109) cultures. Among pathogenic bacteria *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas* spp., *Klebsiella* spp., and *Enterococcus* spp. and *streptococci* were isolated in decreasing order of frequency. Patients with pathogenic bacteria were more commonly in those older than 50 years of age. Culture were positive more often in patients who underwent vaginal hysterectomy than abdominal hysterectomy ($p = 0.003$) (table I).

Pathogenic bacteria were isolated on pre-operative vaginal swab culture from most of the uterine prolapse

patients while patients with dysfunctional uterine bleeding, uterine fibroid, and ovarian tumour mainly showed non-pathogenic bacteria on culture (table II).

Post-operative morbidities

A total 25.6% (28/109) of patients showed different types of post-operative complications. Vaginal discharge, wound infection and urinary tract infection were most common followed by fever etc. The total number and type of complications varied significantly between the patients with non-pathogenic or pathogenic bacteria on vaginal swab culture. Only 11.1% (4/36) patients infected with pathogenic bacteria and 32.8% (24/73) patients with non-pathogenic bacteria showed morbidities. Wound infection and urinary tract infection were significantly common in patients with non-pathogenic bacteria on vaginal swab. After controlling for age, parity, and length of surgery using multiple linear regression, the prevalence of complication was statistically significant for blood loss, fibroids, and uterine prolapse.

Table III shows patients receiving ampicillin prophylaxis. Post-operative complications was significantly ($p=.014$) higher where ampicillin

Table II. Vaginal swab culture isolates in various gynaecological diagnosis

Gynaecological diagnosis	Vaginal swab culture isolates	
	Non-pathogenic bacteria (n=73)	Pathogenic Bacteria (n=36)
DUB (n=11)	7 (9.5)	4 (11.1)
Fibroid (n=30)	24 (33)	6 (16.6)
Prolapse (n=60)	34 (46.5)	26 (72)
Ovarian Mass (n=8)	8 (10.9)	0

DUB = Dysfunctional uterine bleeding

Table III. Different post-operative morbidities observed in relation to antibiotics used

Antibiotic Prophylaxis n(%)	Post-operative Morbidities				
	Fever	UTI	Wound infection	Vaginal discharge	URTI
Ampicillin (N=73)	3 (4.1)	5 (6.8)	6 (8.2)	7 (9.5)	3 (4.1)
Other antibiotics (N=36)	1 (2.)	1 (2.7)	0	0	2 (5.5)

UTI = Urinary tract infection

URTI = Upper respiratory tract infection

Table IV. Post-operative morbidity after Ampicillin prophylaxis

Ampicillin prophylaxis	Post-operative morbidity*	
	Absent (N=81) n (%)	Present (N=28) n (%)
Given (n=73)	49 (60.4)	24 (85.7)
Not given (n=36)	32 (39.5)	4 (14.2)

*p-value: 0.014

prophylaxis was used than in those patients who were not receiving ampicillin as prophylaxis (table IV).

Discussion

The most interesting finding of our study is that the post-operative complications were less common in patients with pathogenic bacteria on pre-operative vaginal swab culture than in those patients where no pathogens were isolated. The culture positive patients received antibiotics according to the respective sensitivity of antibiotics. These antibiotics were given either alone or in combination therapy.

The findings explain important concerns. First, our study confirms the beneficial effect of pre-operative vaginal swab culture in elective gynaecological surgery (table II) especially in uterine prolapse patients. Studies have emphasized that within colonised tissues, such as the female genital tract, organisms that are relatively dominant in numbers constitute a pathogen which can be cultured even from asymptomatic patients,⁷ whereas those species that are fewer in number may not be identified during primary isolation. Several studies confirm that the density of microbial colonisation appears to be relevant not only to the condition of asymptomatic individuals but also to the initiation of disease state.^{12,13,14}

Secondly, our study showed that a sensitive and combination antimicrobial coverage is more effective in reducing post-operative morbidities for any patient undergoing elective surgery regardless of the presence or absence of specific risk factors. In one study it was shown that a broader combination of cefazolin and metronidazole provided better efficacy with

regards to post-operative morbidity when compared with cefazolin alone.¹⁵ Various studies suggest that prophylaxis for hysterectomy should consist of an agent, or combination of agents, with activity against both aerobic and anaerobic bacteria.¹⁶ Some researchers hold the view that selective prophylaxis should be practiced instead of mass prophylaxis at least in elective gynaecological surgery as the most effective regimen of prophylaxis has yet not been established.¹⁷

Our study showed that the peri-operative ampicillin prophylaxis (administered in patients with non-pathogen on vaginal swab culture) is not sufficient to reduce post-operative complications in our setting. This could be due to ampicillin being active only against aerobic microbes, has limited spectrum thus does not meet the guidelines as an ideal agent for prophylaxis. The peri-operative antibacterial prophylaxis is effective in reducing post-operative infections only when apart from proper timing and duration, the appropriate selection of antimicrobial agents is taken into consideration. Although the majority (86%) of patients received antibiotic prophylaxis prior to surgery, surveys have shown that optimal practice is not achieved in many hospital.^{18,19,20,21} These results highlight the challenges of disseminating evidence based protocols systematically into routine clinical practice. Our study supports previous reports that Gram-negative bacilli (*E. coli*, *Klebsiella pneumoniae*, and *Proteus* species) are part of the endogenous vaginal flora.^{4,22} We isolated *S. aureus* (19.6%), and *E. coli* (11.9%), *Pseudomonas*, *Klebsiella*, *Enterococcus* and *streptococci* from asymptomatic pre-operative vaginal swab culture. The principal microorganisms that cause wound infections after gynaecologic surgery are staphylococci, streptococci and Gram-negative bacilli. Reports have shown that the Gram-negative bacilli are introduced into the upper genital tract during instrumentation and/or gynaecologic surgery,⁶ while *staphylococci* and *streptococci* are inoculated into the wound from the skin, and the latter organisms are transferred from the pelvic cavity as the surgeon closes the abdominal wound.²³

Our study design has some limitations such as the lack of microbiological data from women following surgery. This knowledge would have allowed us a better understanding of the role of the pathogen

(and the prescribed antimicrobial prophylaxis regimen) in hysterectomy. For example, presence of a microorganism in the genital tract besides infection can also be found in instances of colonisation, creating difficulty in clarifying the exact pathogenic role in instances of infection.

Despite limitations our study identifies issues of concern in developing countries. As in India and many other developing countries, routine antimicrobial sensitivity testing is not available in all the hospitals, the peri-operative prophylaxis is based on surveys of antimicrobial susceptibility test. The microbes, however, are known to vary in strains, and in the resistant patterns in post-operative infections according to geographical locations. The decision to use a particular antimicrobial agent in a setting requires access to the guidelines and a comprehensive evaluation of the patient's specific circumstances. Different studies and guidelines of prophylaxis are generally from high-income countries and of limited value to guide in developing countries.⁵ This limitation may explain the difficulties in following specific guidelines in clinical practice. We believe that the traditional surgical classification schedule should also account for patient-specific risk factors. The development of local evidence based guidelines, and an outcome based document of appropriate antibiotic may help clinicians achieve a higher certainty to improve post-operative outcomes. This approach would reduce the risk of emerging resistant bacteria, super-infection, risks of toxic reactions and cost of therapy.

In conclusion, irrational antibiotic prophylaxis leads to excessive surgical wound infection. A common error in antibiotic prophylaxis is the selection of the incorrect antibiotic. Development of a local guideline based on the knowledge of the local bacterial aetiology and susceptibility patterns may provide an updated recommendation for optimal prophylaxis. Local issues should be considered when establishing recommendations for antimicrobial selection for gynaecological surgery.

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