CHAPTER 1

INTRODUCTION

Background

Infectious vaginitis is the most common gynecologic diagnosis, accounting for a substantial percentage of ambulatory visits. It involves a wide range of organisms: group B Streptococci, *Escherichia coli*, anaerobes, herpes, candida, chlamydia, mycoplasma, gonococcus, chancroid and treponemas. It also leads to a variety of morbidities namely infertility, abortion, malformation, congenital infection,growth retardation, stillbirth, prematurity, sepsis and shock[1].

Vaginitis can present with a variety of symptoms and signs depending on the underlying pathogenic organism. Typical manifestations, occurring alone or in combination, include abnormal vaginal discharge, vaginal discomfort, pruritus, and abnormal odour. The evaluation should have an accurate history, physical examination and microscopic examination. The study by Holme KK. of lower genital tract infection in women show that most of the diagnosis were made by microbiological examination (30/167 were diagnosed by clinical examination, 105/167 were diagnosed by microscopic examination), thus negative clinical examination alone cannot rule out infection[2]. Microbiological studies are particularly crucial in diagnosing infectious vaginitis.

Various organisms cause vaginitis in pregnant women, which could lead to some pregnancy complications as described in the followings:

i) Bacterial vaginosis (BV)

BV is characterized by nonpurulent, homogenous, malodorous vaginal discharge, increased vaginal pH, presence of characteristic amines and organic acids in vaginal fluid, and polymicrobial changes in vaginal flora. Changes in vaginal flora include a decrease in H_2O_2-producing facultative lactobacilli, increase in *Gardnerella vaginalis* and several anaerobic species. BV and BV-associated microorganisms have been found to be correlated with amniotic-fluid-infection syndrome, prematurity and puerperal infection. A study by Eschenbach DA et al[3]. revealed that 47% of BV were diagnosed by clinical examination while 81% were diagnosed by microscopic examination. This indicates that BV usually can only be diagnosed by microscopic examination.

ii) Gonococcal cervicitis

Detection of *N. gonorrhoea* by screening cultures during the initial antenatal visit is justified in most population[4] since gonococcal cervicitis causes adverse effects on pregnancy and increase risk of neonatal infection. The majority of women with gonorrhea (pregnant and non-pregnant) are asymptomatic. Thus, the diagnosis of these infections depends upon sampling of specimen from potentially infected sites. The major site of primary infection in women is the endocervix. Unfortunately, microscopic examination of a gram-stained specimen from the infected site produces a diagnosis of gonorrhea in only 60% of women compared with 95% of men[5]. In women,

the diagnosis of *N. gonorrhoea* infection requires isolation of the organism by culture. Ideally, all sexually active women should have been screened for *N.gonorrhoea* at every opportunity (i.e., annual routine pelvic examinations, presenting with gynecologic complaints).

iii) Chlamydial infection during pregnancy

The detection and treatment of Chlamydial infection of the genital tract in pregnant women is certainly not less important than in non-pregnant women. In fact, Chlamydial infection also caused complications of pregnancy and postpartum pelvic infection[6]. The clinical spectrum and epidemiology of *C. trachomatis* infection in women are similar to those associated with gonococcal infection. However, there are also major differences. Chlamydial infection is generally more frequent (5 times), may be asymptomatic, may be associated with nonspecific symptoms, or may exist in the absence of any visible signs of infection. The diagnosis can be proven only by culture or use of antigen detection methods such as monoclonal antibody staining or immunoassay[7].

iv) Group B streptococcus (GBS)

Antenatal culture screening for GBS and treatment of carrier has been proposed for prevention of GBS morbidity in the neonate and perhaps for prevention of obstetrical complications as well. The gold standard for diagnosing maternal asymptomatic genitourinary tract colonization with GBS

is the culture. Rapid diagnostic test for GBS are based upon gram stain, antigen detection[8]

v) Trichomonas Vaginalis (TV)

Trichomonas is the most common non viral sexually transmitted diseases. It plays a role in preterm labour and premature rupture of membranes. As with other sexually transmitted diseases, symptoms and signs of trichomoniasis are neither adequately sensitive nor specific enough to preclude diagnostic testing. Trichomonal infections are asymptomatic in as many as 50% of male and female patients. In pregnancy, this number is even higher as in a recent literature. The diagnosis of trichomonas is made by directly observing the motile parasites.

Although it is recommended that common genital tract infection should be screened in all pregnant women in current practice[9], but most of health care centers do not have enough facility to do so, even in the hospital of this study, a tertiary care center. It is not a cost-effective modality to screen vaginitis in all pregnant women in a low prevalence area either. A rapid screening test would be useful to improve the accuracy of diagnosis particularly in situation of limited time and medical personnel to obtain an accurate history, physical examination and laboratory investigation to diagnose infectious vaginitis. The vaginal fluid pH screening might serve this purpose. Pregnant women may be the group of patient that require a more careful

assessment of vaginitis. Because antenatal vaginitis will affect not only patients themselves but also their fetuses. The early detection and prompt treatment of maternal reproductive tract infection may result a relatively simple and cost-effective opportunity to significantly reduce pregnancy complication since the other causes are not easily preventable[10].

Related findings

Physiology of vagina and vaginal pH

Vaginal physiology depends on an appropriate hormonal and bacteriologic milieu. The vagina is a target organ for ovarian estrogen[11]. Estrogen induces proliferation and maturation of the stratified squamous epithelium, enhances glycogen storage in the superficial cells, and increase blood flow through the paravaginal tissues. The increase thickness of the epithelium and good blood supply acts to create an effective mechanical barrier between the vagina and the environment. The stored glycogen participates in the information of a microbiologic barrier.

Vaginal squamous epithelium consists of three layer, parabasal cells, intermediate cells and superficial cells, that demonstrate progressive maturation as they are displaced upward by proliferation of basal cell[12]. Estrogen stimulation results in a predominance of the more mature superficial cells. Glycogen storage in the intermediate and superficial cells is promoted by estrogen. It serves as a substrate for carbohydrate metabolism by the bacterium lactobacillus vaginalis. The product of fermentation is lactic acid,

which maintains a low vaginal pH (normal 3.5 - 4.5). The acidity favors continued growth of the nonpathogenic lactobacillus and inhibits colonization by more virulent organisms[13].

A wide variety of bacteria can be cultured from the normal vagina[14]. The number and type depend in part on the culture media used. Lactobacillus, staphylococcus epidermidis, diphtheroids, and aerobic and anaerobic streptococci are most frequently isolated from culture. These organisms are normally present in numbers insufficient to cause clinical infection and do not require treatment.

Vaginal acidity

Because of the action of estrogen on the vaginal epithelium, glycogen is produced, the lactobacillus thrives, and the ensuring lactic acid production lower the pH of vagina to between 3.5-4.5, a level which inhibits growth of other bacteria. Pregnancy is normally associated with a progressively more acidic environment, because of estrogen as well[15]. In elderly women normally levels of circulating estrogens gradually decline following menopause. The high vaginal pH and mucosal atrophy are secondary to a decreased steroid production following menopause[16]. Vaginal acidity can be reduced by cervical ectropion and chronic cervicitis, ovulation (because of excessive alkaline mucous production), amniotic fluid, seminal fluid, menstrual blood, douching and progestin therapy. Lactobacilli may be eliminated by antibiotic therapy[17].

Infection and vaginal pH

Vaginitis can be caused by many types of pathogenic organism. It is important to consider the nature of growth promoting substances used by microorganism. Protein catabolism may result in the production of basic end products, where as fermentation of carbohydrates is characterized by acidic end products. Amino acid may be fermented by some anaerobic bacteria to produce organic acids and ammonia[18]. Alkalinization volatizes two amines, putrescine and cadaverine in Gardnerella associated vaginitis which results in an elevated of vaginal pH above 4.5 in virtually all cases[19].

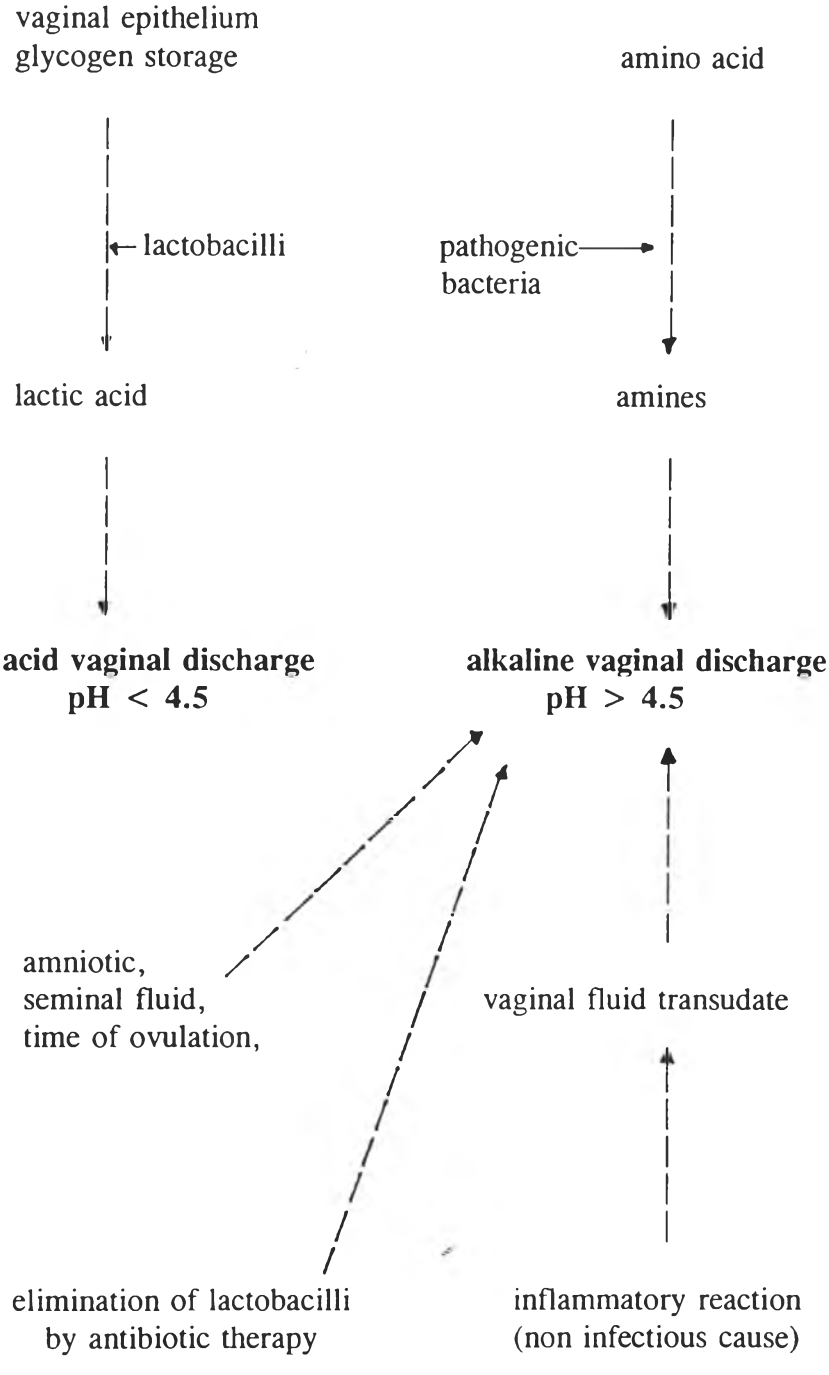
Another property of many frankly pathogenic microorganism in their ability to cause damage to some host structure or function by means of the production of toxic end products. These may be metabolic end products or macromolecular toxins. The biologic properties of these toxins include its ability to interfere with viability and function of human leukocytes. Leukocytic infiltration may play a role in the control of bacterial flora and protect against invasive exogenous microorganisms. Some of the functional attributes of the polymorphonuclear leukocytes were altered by exposure to the toxin, including their chemotactic ability, ability to ingest and kill bacteria[18]. The presence of toxin and inflammatory reaction may be an erotic stimuli to increase vaginal fluid transudate across the epithelium and result in an elevated vaginal pH. A study of the relation between vaginal pH and the microbiological status in vaginitis found that vaginal fluid pH greater than 6.0 is strongly predictive of infection this may be more useful than the appearance of discharge in

suggesting a need for confirmatory microbiological test[20].

Most vaginal infections are asymptomatic[2], which is difficult to be screened by clinical examination alone. The common pathogens of vaginitis, if present, will elevate vaginal pH. This clinical clue may be useful to screen for vaginitis.

Conceptual framework (from infection to vaginal pH)

Fig. 1: Conceptual framework



Research questions

Primary research question

What is the diagnostic performance of vaginal fluid pH in detecting infectious vaginitis in pregnant women?

Secondary research question

What is the prevalence of infectious vaginitis in pregnant women attending antenatal care clinic at Srinagarind hospital?

Research objectives

1) To assess diagnostic performance of vaginal fluid pH as a screening test for antenatal infectious vaginitis.

2) To determine the prevalence of infectious vaginitis in pregnant women attending antenatal care clinic at Srinagarind hospital.

3) To determine the proportion of asymptomatic vaginitis cases detected by vaginal pH.