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ANUPDATED CLINICAL REVIEW OF ABNORMAL VAGINAL DISCHARGE AND REPRODUCTIVE TRACT INFECTION

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ABSTRACT: Vaginal discharge is the commonest symptom reported in reproductive tract infection the recognition and diagnosis of the correct cause of abnormal vaginal discharge (AVD) can be challenging due to the wide spectrum of infectious agents. Reproductive tracts infections (RTIs) can cause serious physical and psychological harm, and this harm is not limited only to the women themselves, but also a serious threat to their next generation, and may cause a heavy social and economic burden.RTI/STI wherein disclosure is associated with stigma and health-seeking is impaired by embarrassment and hesitation, particularly in women where accessibility to an empathic female health worker may not be available given the state of primary health-care. If untreated, RTIs can lead to adverse health outcomes such as infertility, ectopic pregnancy and increased vulnerability to the transmission of the Human immunodeficiency virus. It is also associated with adverse pregnancy outcomes. Clinically, the first choice to treat RTIs according to different pathogens is antibiotics. Most of the drugs used in RTIs are metronidazole, clotrimazole pessary and antibiotics like doxycycline and ciprofloxacin. This review article discusses the presentation, epidemiology, aetiology, diagnosis, and management of reproductive tract infections.

INTRODUCTION: Vaginal discharge is the commonest complaint in the reproductive age group [1-5]. That can be a normal physiologic variance or a pathological manifestation [1, 3, 6]. Further, abnormal vaginal discharge (AVD) is the second most common problem after abnormal uterine bleeding or menstrual disorder [5].

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Reproductive tract infections (RTIs) include sexually transmitted infections, endogenous infections (caused because of overgrowth of organisms normally present in the reproductive tract), and iatrogenic infections associated with medical procedures like insertion of intrauterine devices and induced abortion [2, 7].

Worldwide, the most common RTIs are endogenous infections [2]. Female RTIs frequently initiate in the lower genital tract as vaginitis or cervicitis may produce symptoms such as AVD, itching, genital pain, and burning micturition [7, 8]. RTIs if not treated can lead to complications such as pelvic inflammatory disease (PID), chronic

pelvic pain, cervical cancer, infertility, ectopic pregnancy, and pregnancy wastage [9]. Vaginitis is the commonest RTIs and it is described by vaginal discharge, malodor, vulvar itching or vulvar irritation [10]. Vaginitis mainly encompasses three main etiologies, namely bacterial vaginosis (BV), vaginal candidiasis (VVC), and trichomoniasis (TV) [5, 10], generally accounts for 90% of all etiologies [10]. The commonest being BV followed by VVC and TV though, multiple infections coexist [4, 8].

Epidemiology: "Global Burden of Disease Study estimates that 27.4% of Disability-Adjusted Life Year (DALY) lost in Indian women aged 15–44 years was attributed to reproductive ill-health" [9]. In a year, approximately, 1 in 10 women will present with vaginal discharge [5]. In the reproductive age group, vaginal discharge occurred in 1-14% of all women and India, the estimated prevalence of vaginal discharge is 30% [4]. Each year, 151 million of new cases of RTIs occur in Asia from an estimated 340 million new cases including sexually transmitted infections (STI) [11].

The prevalence of RTIs ranges from 39% to 84% as shown in various community-based studies conducted in India. The study carried out in North-East Delhi, showed the prevalence of symptoms suggestive of RTIs/STIs was higher (43.9%) as compared with urban women (27%) of Agra district of Uttar Pradesh, urban slums (35.6%) of Tirupati, Andhra Pradesh, and urban women (32%) in Sundergarh district of Orissa; and 27.8% in Punjab [12]. The prevalence, AVD because of RTIs is approximately 30% in women attending hospitals in Delhi conducted by Indian Council of Medical Research, whereas in rural Maharashtra, the prevalence was 50% [13]. Authors conducted the study among rural Chinese women in Hunchun, China to assess "the prevalence, knowledge and behaviour about reproductive tract infections (RTIs)" and found that of the 117 participants, 57.3% were diagnosed to have RTI. They concluded that the prevalence of RTI among low-income rural Chinese women were extremely high [11]. Approximately, 72.6% percent reported one or more symptoms of RTI in Bangladesh study. In Nepal, the prevalence of RTI symptom was 78.9% and the burden of the RTI among women was unpredictably high [9].

Madhivanan *et al.* (2008) reported that of the 898 women, 43.5% and 17.4% were diagnosed with ≥1 endogenous reproductive tract infection and ≥1 sexually transmitted infection respectively. BV coexisted with *T. vaginalis* and HSV-2 seropositivity [14].

Prevalence of Abnormal Vaginal Discharge According to the Cause: Vaginal discharge is the commonest reason for which women search for medical attention. Vaginal infection is the commonest gynaecological infections. It is an important public health problem due to the gynaecological and obstetric complications associated with it as well as the vaginal mucosa inflammation and the lactobacilli's reduction could make possible for the transmission of STDs, particularly HIV infection [15].

Venugopal *et al.,* (2017) examined a total of 100 women in the reproductive age group who had vaginitis in the Variyar medical college hospital, Salem. They reported that 77% cases were organism positive and among them, the most common cause of AVD was BV (27%) followed by trichomoniasis (25%), vaginal candidiasis (22%), combined infection (Candida and BV), and nonspecific cases (23%) [5].

The clinical study conducted in Brazil, the prevalence of BV was 20%, VVC was 22% and only one patient had a trichomonal infection [15].

Bacterial Vaginosis: BV prevalence differs widely from country to country and varies between ethnic groups in Europe, South America, North America, the Middle East, and Asia. Some populations in Africa have extremely low and some in Asia and Europe have higher rates of BV prevalence.[16] Bacterial vaginosis was the commonest disorder seen in 36.68% [17].

Ranjit *et al.,* (2018) showed the overall prevalence rate of BV was 24.4% among symptomatic patients based on Nugent's scoring system method upon examination of 160 nonpregnant women. A prevalence rate of BV was reported to be 24% in Kolkata, India and higher prevalence has been reported in Egypt [8]. The prevalence of BV among women of reproductive age in Mysore was 19% [14].

Candidiasis: Vulvovaginal candidiasis (VVC) is the second most common cause after bacterial vaginosis [18] and affects up to 75% of reproductive age women at least once during lifetime [10].

Trichomoniasis Vaginalis: Owing to heterogeneity for the diagnostic methods used to diagnose TV, large unpredictability in the prevalence rates of trichomoniasis has been unveiled from the literature [5]. Trichomonal vaginitis (TV) is the commonest non-viral STI caused by the parasite *Trichomonas vaginalis* in the world. The prevalence of TV differs significantly by geography and risk group. It appears to increase with age and more common among persons of African descent. The global prevalence of TV has been estimated at 8.1% for women [19]. Globally, TV affects roughly 57-180 million people and the majority lives in developing countries. Overall trichomoniasis prevalence of 2.6% in women an aged 15-64 years was reported in Nigeria (January 2006 and October 2007). The prevalence of TV in Chinese women was 2.9% (aged 36.3 ± 6.84 years), 18.2% in Palestinian women (aged 16-50 years) between 2000 and 2006, and 28.1% in Saudi Arabia for all sexually transmitted diseases (January 1995 and December 1999). In some region of Iran, the prevalence of TV ranged from 3% to 26%. Chalechale *et al.,* (2010) found the prevalence of TV was 0.9% in the Kermanshah district of Iran [20]. TV prevalence in a population of adolescents from Mexican American, non-Hispanic whites, and non-Hispanic black ethnicity was reported to be 2.1%. In the United States, two studies reported higher prevalence rates of TV 12.9% and 14.4% respectively [15].

Cervicitis: In adult females, chronic cervicitis is extremely common and at least at the microscopic level. Chronic cervicitis may lead to pelvic inflammatory disease, salpingitis, endometritis, chorioamnionitis, and other complications during pregnancy. It also plays a role in beginning or promotion of cervical neoplasia. Chronic nonspecific cervicitis was the commonest inflammatory lesion of the cervix (89.23%) and 11% of cervicitis had specific [21].

Pelvic Inflammatory Disease (PID): PID is infection and inflammation of the upper genital tract in women (the uterus, fallopian tubes and/or ovaries and pelvic peritoneum [22, 23]. It is a common disorder of the reproductive tract that is often misdiagnosed and poorly treated [22]. PID is usually a clinical diagnosis and as a result, represents a diagnostic challenge. A definitive diagnosis of PID is by laparoscopic visualization of inflamed and purulent fallopian tubes [23]. Vaginitis and cervicitis if left untreated may progress to PIDs. In the United States in 2000, there were an estimated 1.2 million medical visits for PID [23]. The US Centers for Disease Control and Prevention (CDC) estimates that more than one million women experience an episode of PID each year including missed cases of PID [22]. PID and its complications, such as chronic pelvic pain, infertility, and ectopic pregnancy are avoidable by screening asymptomatic patients for STIs and quickly treating individuals with STIs and PID [22].

Risk Factors: The risk factors related to bacterial vaginitis are inadequately understood. However, the use of hygiene products that modify the vaginal ecosystem, relations with sexual activity and genetic tendency have been explained. If not treated or undiagnosed, women's reproductive health might get affected by these infections. These infections are also commonly associated with gynecologic and obstetric problems, for example, PID, infertility, prematurity, premature, PROM and HIV-1 transmission. Further, the use of illegal drugs, tobacco, and alcohol was also an indirect risk factor for bacterial vaginosis [15]. PID's risk factors are similar as those for the acquisition of STIs such as young age, smoking, multiple sexual partners, illicit drug use, douching whereas oral contraceptive lowers the rate of PID infection and BV has also been associated with PID [23]. Increased rates of bacterial vaginosis occur in certain groups of women, such as black African women, lesbians, and smokers [3].

Age: The peak age group for vaginal infections was 26-35years (44%). BV was found in high frequency in the age group of 25-35 years. The most common age group affected by vaginal candidiasis was 26-35 and 18-25 years. Trichomoniasis was detected at the highest rate in the age group of 40-50 years. Nonspecific vaginitis where no organism was found was seen in high frequency in the age group of 36-40 years.

Mixed infection of candida and BV was seen in the age group 26-36 years [5]. Ray *et al.,* (2008) conducted a cross-sectional study in women attending peripheral government healthcare in four zones of Delhi over 26 months (n= 4090). They showed that 89.8% were of reproductive age group. The most predominant age group for RTIs was 14-25years (52.9%), followed by 26-25 years (36.9%) and 36-45years (7.8%).[24]Another study had reported that the majority of patients were between 20 and 30 years old.[2]Ranjit et al., (2018) revealed that the age group of 30–40 years had a high prevalence of BV (8.8%) and least for 10–20 and 50–60 years' age groups (1.3%) [8]. The high prevalence of RTIs in rural villages of China is harsh living conditions, poor personal hygiene, and a lack of accessible medical care facilities [11]. Other study showed that risk factors for the presence of STIs are age less than 25 years, not using a condom, in past 3 months, change of sexual partner or multiple contacts or frequent change of sexual partner or symptoms in a partner such as dysuria, previous history of STIs, symptoms imply complications of STIs, and sexual risk behavior of partner [3].

Contraceptives: The prevalence of RTIs is higher in IUD users within the first few weeks of use compared with those that used other methods. Females using different contraceptive methods had roughly 1-7-fold increase in the risk of acquiring RTIs in comparison to non-contraceptive users [25]. Increase duration of contraceptive use decreases the prevalence of RTIs. Among contraceptive users, *C. albicans* was the most prevalent reason for RTIs whereas among non-contraceptive users BV was the most prevalent reason for RTIs [25]. Some of the observational studies have reported hormonal contraceptives to have a reduced risk of recurrence to BV [8].

Low Socioeconomic Status: Choudhry *et al.,* (2018) conducted a hospital-based longitudinal study (n=270) between October 2012 and July 2014 who attended the obstetrics and gynaecology outpatient's department, Northern India. They observed that a complaint of vaginal discharge was from the lower socio-economic class [17]. Ray *et al.,* (2009) showed that most of the patients were from the low-socioeconomic group [24]. Philip *et al.,* (2013) found that the prevalence of the symptoms was decreased with increased monthly per capita income. It was highest in the poorest [26].

Race: BV is more common in Africans and American blacks followed by Caucasian women. TV infection prevalence was 48.9% among black females, and 0.8% among females of other races/ethnicities [27].

Sexual Behaviour: BV may be believed to be a Sexually Enhanced Disease (SED) rather than STDs, in which the incidence of intercourse plays a key role. The most important risk factors, sexual behaviour and vaginal douching are adjustable risk factors [8]. Many studies showed that vaginal discharge has also been attributed to frequent or early-onset of sexual activity, risky sexual behaviour, and sexual intercourse during menstruation [8].

Douching: Douching has been associated with many adverse outcomes including bacterial vaginosis, pelvic inflammatory disease, cervical cancer, human immunodeficiency virus transmission, ectopic pregnancy, preterm birth, low birth weight, sexually transmitted diseases, recurrent vulvovaginal candidiasis, and infertility [28].

One study stated that vaginal douching was linked with an increased prevalence of BV. Fonck *et al.* reported that general douching and douching with soap and water in female sex workers in Kenya was significantly related to BV. Royce *et al.,* in their prospective study found that douching was associated with BV. Scholes *et al.* found that the frequency of douching increases, the probability of chlamydial infection also increases. Vaginal douching might encourage the ascend of lower genital tract infections to the upper genital tract and thereby increases the risk of PID. Further, change in the vaginal environment also increases the susceptibility to reproductive tract infections that precede PID. Douching may introduce the nonpathogenic vaginal bacteria into the characteristically sterile upper genital tract. However, some others report doubts about the association douching and PID [28]. It is reported douching is not needed for routine vaginal hygiene. However, it is useful in symptomatic vaginitis or vaginosis. Vinegar-containing douches could help

treat vaginal infections and it has selectively inhibitory against vaginal pathogens linked with BV, group B streptococcal vaginitis and candidiasis [28].

Personal and Menstrual Hygiene: One of the studies showed that the prevalence of the symptoms of RTIs was higher in those who used ordinary cloth during menstruation as compared with those who used sanitary pads [25]. A study found that poor personal hygiene, harsh living conditions contribute to the high prevalence of RTIs among rural Chinese women [11].

Stress: In primary care settings, common mental disorders (CMD), characterized by medically unexplained physical symptoms, are amongst the commonest health problems. A study in India reported higher rates of depression in women who attended the gynaecological clinic compared to women who attended a general medical clinic. A community-based study in Goa, India reported that stress was the most common attribution for vaginal discharge. They concluded that psychosocial factors have the strongest association with the complaint of vaginal discharge [27].

Smoking: Cigarette smoking is strongly associated withthe risk factor for bacterial vaginosis and frequently found in a dose-dependent relationship.

It is well recognized that the vaginal microenvironment is influenced by endogenous estrogen. The increase in bacterial virulence, physiological and structural changes and dysregulation of immune function are three mechanisms by which tobacco affects the human body. It is also theorized that smoking predisposes a woman to BV as smoking escorts to an accumulation of vaginal amines which combined with the antiestrogenic effect. Further, the study showed that women who smoke have considerably lower levels of mid-cycle and luteal phase estradiol than nonsmokers. Brotman *et al.,* (2014) conducted a pilot study on the association between cigarette smoking and the vaginal microbiota. They concluded smokers had a lower proportion of vaginal Lactobacillus spp. compared to non-smokers. The anti-estrogenic effect of smoking and trace amounts of benzo[a]pyrenediol epoxide (BPDE) may predispose women to BV [29].

Obstetric History: Philip *et al.,* (2013) found thatthe prevalence of RTIs is highest in those with gravidity >4, and those with a history of abortion [26]. Kafle *et al.,* (2016) found that the prevalence of symptoms of RTIs higher among women who had three or more children, and it increased with increase in parity, he also discussed the women who delivered a baby at their own home and conducted delivery by non-health worker were at significant risk of RTI symptoms [9].

Mixed Infections: Bacterial vaginosis (BV), which is a disturbance in the vaginal flora, frequently coexists with cervicitis. In one study, 50% of women had cervicitis associated with BV [30]. Bacterial vaginosis is having high co-infection rates with other STIs [10]. Bacterial vaginosis and cervicitis are strongly associated with pelvic inflammatory diseases [31]. A strong association between abnormal vaginal flora and HIV acquisition has been studied in two prospective longitudinal studies. Moodley *et al.,* (2002) studied the association among HIV, BV, yeast, and Trichomoniasis. They concluded a positive linear association between HIV-1 infection and bacterial vaginosis [32].

Aetiopathogenesis:

Physiological Discharge: Normal vaginal flora (lactobacilli) colonizes the vaginal epithelium and plays a role in defence against infection. They help to maintain the normal vaginal pH of vagina (between 3.8 and 4.4). The quantity and quality of vaginal discharge could vary in the same woman in cycles and over time. Further, each woman has her sense of normality and what is acceptable or excessive for her. The normal physiologic vaginal discharge comprises exfoliated cells, vaginal secretions, and cervical mucus. The occurrence of vaginal discharge varies with the menstrual cycle, age, pregnancy and use of oral contraceptives [33].

Pathological Vaginal Discharge:

Non-infective: Physiological, endocervical polyp, cervical ectopy, foreign bodies (retained tampon), vulvar dermatitis**,** vesicovaginal or uterovaginal fistula [1, 32].

Infective: It can be broadly categorized as non-sexually transmitted and sexually transmitted infections. Non-sexually transmitted infections are

bacterial vaginosis, candida infections, mucopurulent cervicitis, and pelvic inflammatory disease. Sexually transmitted infections are *Chlamydia trachomatis, Neisseria gonorrhoea, and trichomonas vaginalis.*[34]Further, it can be classified according to the common and less common causes. The common cause includes bacterial vaginosis, vulvovaginal candidiasis, trichomoniasis, cervicitis or cervical ectropion, and pelvic inflammatory diseases. Less common causes include human papillomavirus (HPV), primary syphilis and fistulas [3].

The epithelium of vagina, ectocervix, and endocervix differs cytologically and depending on other factors in microenvironment, the aforementioned structures are susceptible to various pathogens. Candida species and *Trichomonas vaginalis* (TV) infections infect the stratified squamous epithelium of the vagina and ectocervix, whereas the columnar epithelium of endocervix is infected by *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Both types of epitheliums are susceptible to Herpes simplex virus. Infection with any of the above-mentioned organisms can cause vaginal discharge. Furthermore, identifying its specific cause is a difficult task as a large number of pathogens leads to vaginal and cervical infections, and sometimes coexistence of numerous infections may be present [5, 35].

Vaginal cells that contain glycogen continually shed into the lumen of the vagina and as the cells autolyze, glycogen depolymerizes to glucose. This serves as an energy source for bacteria known as lactobacilli. Lactobacilli produce hydrogen peroxide that is bactericidal alone. Lactobacilli in combination with physiologic amounts of myeloperoxidase and chloride are highly bactericidal. Loss of the normal lactobacillus precipitate changes in the normal activities of the vagina and increases the exogenous infection after exposure to sexually transmitted pathogens and also increases the risk of endogenous infection [8, 36].

Pathophysiology: BV is responsible for the presence of enzymes that reduce the ability of host leukocytes to fight infection and for an increased release of endotoxins that cytokine & prostaglandin production within vagina [36]. The endocervix is lined by columnar epithelium which is susceptible to infectious agents leading to cervicitis [35]. Most cases of pelvic inflammatory disease are due to ascending infections of the genital tract transversing through the endocervix into the uterus, fallopian tubes, and adjoining structures of the uterus. Subclinical PID is defined as inflammation of the upper reproductive tract in the absence of signs and symptoms of acute PID. According to the CDC 2015 Sexually Transmitted Diseases Treatment Guidelines, any young sexually active woman or woman at risk for STIs with unexplained lower abdominal or pelvic pain and at least one of the following clinical criteria noted on pelvic examination should receive presumptive treatment for PID(cervical motion tenderness, uterine tenderness, and adnexal tenderness) [22].

Among all patients, organisms responsible for abnormal vaginal discharges were found in 94.8% of the cases [35].

Diagnosis and Differential Diagnosis: The prevalence of symptoms suggestive of RTIs/STIs in the study population (17.3%) is low as compared with the country as a whole (40%). The prevalence of RTIs in India was 27% in urban women of Agra district of Uttar Pradesh, 35.6% in reproductive-age women living in urban slums of Tirupati, Andhra Pradesh, 32% in urban women in Sundergarh district of Orissa and 27.8% in Punjab. This suggests that many women in the study population may be asymptomatic or have symptoms that are considered “normal” for women. This is further suggested by the fact that the majority of the women sufferers under study (64.4%) did not seek any treatment [26].

Symptoms: Physiological discharge is characteristically white or clear and has a minimal odourthatvaries with the menstrual cycle.[34] Pathological or abnormal vaginal discharge is often accompanied by symptoms like vaginal itching, soreness, and foul odour [13]. Vaginal discharge is considered to be abnormal if it is yellowish, greenish or curdy white, mixed with blood [1]. Pathological vaginal discharge predominantly caused by vulvovaginitis, from which BV is the commonest cause of abnormal vaginal discharge followed by candidiasis and trichomoniasis. In BV the discharge is profuse, malodorous which is more

pronounced after sexual intercourse and associated with dysuria, dyspareunia and vaginal pruritus [8]. Whereas in VVC discharge is cheese-like and associated with other symptoms like vulvar itching, vulvar burning, soreness and irritation, dysuria and dyspareunia. All symptoms worsen during the week before menses [5]. TV can cause an offensive yellow vaginal discharge, which is often profuse and frothy, along with associated symptoms of vulvar itch and soreness, dysuria, and superficial dyspareunia [34].

The presence of a purulent or mucopurulent discharge that is visible in the endocervical canal and other signs of inflammation such as oedema and easily induced endocervical bleeding suggestive of cervicitis [30]. In the case of PID typically, women present with lower abdominal pain, or pelvic pain, although it may be mild. Other symptoms include abnormal vaginal discharge, fever or chills, cramping, dysuria, abnormal or postcoital bleeding, low back pain, nausea, vomiting, deep dyspareunia, and secondary dysmenorrheal [22]. The majority of the participants (92.3%) reported that they suspected having an RTI, with unusual vaginal discharge, perineal itching, lower back pain, is the most commonly reported symptoms, affecting more than half of the respondents [11].

Bimanual and Speculum Examination: In case of BV, normal appearance of tissue, discoloured discharge with abnormal odour, homogenous discharge that adheres to the vaginal wall is seen [8]. A study observed greyish white homogeneous vaginal discharge in 87% of women with BV [11]. In VVC vulvar and vaginal erythema, oedema and fissures are present along with the thick curdy white discharge that adheres to the vaginal wall. Vulvar, vaginal oedema, erythema and the strawberry cervix is seen in up to 25% of affected women and frothy, purulent discharge in TV [34, 4, 5]. In cervicitis, the cervix is friable with mucopurulent discharge. It is suggestive of PID if it is associated with cervical motion, uterine, or adnexal tenderness [22].

Investigation: Sowjanya *et al.,* (2015) on the comparison of visual and clinical methods with the microbiological method, the sensitivity of visual diagnosis for bacterial vaginosis was 81.48% and specificity was 45.8%. The sensitivity of clinical diagnosis for bacterial vaginosis was 94.4% and specificity was 66.6% [38].

Vaginal pH: A normal vaginal pH is between 3.8 and 4.2. In the case of BV and TV, pH is elevated >4.5, whereas it is normal in VVC. pH had low values of both sensitivity (61%) and specificity (60%) [39].

Whiff Test or KOH Preparation: The whiff test is positive if a 'fishy' or amine odour is detected when 10 % KOH is added to the vaginal discharge. A positive whiff test is suggestive of BV. However, in the case of TV it can be positive [2, 3, 12, 16]. The whiff test had the highest sensitivity (74%) while specificity was moderate (72%) [39].

Wet Mount Preparation: Microscopic examination of a wet mount preparation can detect 'clue cells' which are vaginal epithelial cells coated with coccobacillus, few lactobacilli, and occasional motile, curved rods in case of BV [2, 3, 16]. Clue cells specificity (75%) was higher than its sensitivity (66%) [39]. The examination may also detect fungal hyphae, mycelia tangles in VVC, mobile trichomonads many polymorphonuclear cells in TV [33].

Some authors concluded that the presence of ≥1 neutrophil per 1000x field saline wet mount of vaginal discharge had 91% sensitivity and 26.3% specificity for endometritis. In a cohort of women at high risk for pelvic infections, absence of vaginal white blood cells had 95% negative predictive value. It is suggested that if there are no white blood cells in wet mount/ vaginal smear then an alternative diagnosis to PID should be considered [40].

Triple Swabs: High vaginal swab to identify BV, VVC and TV, endocervical swab in transport medium to diagnose gonorrhoea and endocervical swab for a Chlamydia DNA amplification test to diagnose Chlamydia [34].

One of the RCTs conducted by Melville *et al.,* (2005) concluded that women presenting with the vaginal discharge with the addition of a high vaginal swab for culture provided a more accurate final diagnosis than the use of microscopy alone [41].

Diagnostic Criteria: Amsel diagnostic criteria for BV for clinical diagnosis are the presence of three of the 4 criteria required are a thin white, homogenous discharge, clue cells on microscopy, pH of vaginal fluid > 4.5 and Whiff test (release of a fishy odour after adding on alkali solution (KOH) [40]. The sensitivity of Amsel criteria was 77% and specificity was 91% with positive predictive value was 97 % while false negative value was 53 %. Taj *et al.,* examined Amsel criteria and other microbiological methods to diagnose BV and showed that Amsel criteria are acceptable for diagnosing BV [39].

Nugent diagnostic criterion for BV is a gold standard study. It relies upon estimating the relative proportions of bacterial morphotypes on a gram-stained vaginal smear to give a score between 0 and 10. A score of <4 is normal, 4-6 is intermediate and >6 is BV [30, 40]. Mengistie *et al.* compared various diagnostic methods for BV and suggested Amsel clinical criteria to have a sensitivity of 85.7% and a specificity of 98% compared with the Nugent scoring system. They indicated the presence of clue cells as the individual Amsel criterion with the highest specificity and sensitivity [42].

CDC Criteria for PID Diagnosis (2015): "Minimum criteria at least one needed for diagnosis i.e. cervical motion tenderness, uterine tenderness, and adnexal tenderness. Additional criteria support a diagnosis of PID includes oral temperature >101ºF, abnormal vaginal or cervical discharge, white blood cells on the saline wet mount (>10), elevated ESR, elevated C-reactive protein, elevated white blood cell count. A definitive criterion includes histopathologic evidence of endometritis, imaging showing thickened, and fluid-filled tubes, with or without pelvic free fluid, Doppler studies suggesting pelvic infection, intraabdominal findings consistent with PID on laparoscopy" [22].

Nucleic Acid Amplification Tests: NAATs such as polymerase chain reaction and ligase chain reaction are molecular biological techniques that amplify DNA and other genetic material. These tests can detect tiny amounts of cells or viruses and are highly sensitive and specific [34]. Sensitivity and specificity of NAATs approaching 100% have been reported. Vijayalakshmi and colleagues found that the prevalence of BV was identified more by the clinical diagnostic approach than the microbiological approach. Out of 200 cases, clinically, BV was found to be positive in 108 cases and microscopically positive for BV [4].

Management: Syndromic management is the main strategy recommended by the National AIDS Control Organization in India for the effective management of reproductive tract infections. As per WHO (2004), RTI/STI symptoms are usually managed by the syndromic approach. This approach has-been recommended by NACO, India, at the primary healthcentre (PHC) level, 2 as it is feasible, adaptable, and cost-effective. Syndromic diagnosis is mostly carried out without offering any laboratory-based diagnosis, because of the high costs involved and the lack of facilities countrywide. The symptom of AVD is highly indicative of vaginal infection, however poorly predictive for cervical infection. Therefore, all women presenting with vaginal discharge should receive treatment for trichomoniasis and BV [24]. A cluster-randomized trial concluded that STI syndromic package improved STI case management at a reasonable cost and should widely be used [24].

The management recommended by CDC (2015) is as follows.

Bacterial Vaginosis: The drug of choice for BV is metronidazole at a dose of 500 mg orally twice a day for 7 days is administered orally or as a single, 2g oral dose of metronidazole or metronidazole gel 0.75%, one full applicator (5g) intravaginally once a day for 5 days or clindamycin cream 2%, one full applicator (5g) intravaginally at bedtime for 7 days. The alternative regimen is tinidazole 2 g orally once daily for 2 days or tinidazole1 g once daily for 5 days or clindamycin 300mg twice daily for 7 days or clindamycin ovules 100mg intravaginally once at bedtime for 3 days [42].

Vulvovaginal Candidiasis: The treatment for uncomplicated VVC is clotrimazole 1% cream 5g intravaginally daily for 7-14 days or clotrimazole 2% cream 5g daily for 3 days. Miconazole 2% cream or 4% cream 5g intravaginally daily for 7 days or 3days respectively or miconazole100mg vaginal suppository once daily for 3 days.

Tioconazole 5% ointment 5g intravaginally in a single application or butoconazole 2% cream 5g intravaginally in a single application or terconazole 0.4% cream 5g intravaginally daily for 7 days or fluconazole 150mg orally in a single dose.

In complicated and recurrent VVC, 100mg, 150mg or 200mg oral doses of fluconazole every third day for a total of 3 doses (day 1, 4 and 7) or oral fluconazole weekly for 6 months for RVVC [42]. Short term local therapy or single-dose oral treatment is effective for treating 90% of uncomplicated VVC whereas complicated and recurrent cases of VVC require prolonged treatment [18].

Trichomoniasis: Metronidazole 500 mg orally twice a day for 7 days or metronidazole 2g orally in a single dose or tinidazole 2g orally in a single dose [42].

PID: Ceftriaxone 250 mg IM single dose or cefoxitin 2 g IM one dose with probenecid 1g orally or other parenteral 3rd generation cephalosporin and doxycycline 100mg orally twice daily for 14 days with or without metronidazole 500mg twice daily for 14 days [42].

Management of Partner: In BV and candida routine screening and treatment of male partners are not indicated [42]. In trichomoniasis, current sexual partners should be screened for STIs and treated for TV regardless of the results of their tests.[42]In pelvic inflammatory disease, men who have had sexual contact with a woman with PID during the 60 days preceding her onset of symptoms should be evaluated, tested, and presumptively treated for chlamydia and gonorrhoea, regardless of the aetiology of PID [42].

Follow-up: Only in women with persistent or recurrent symptoms of BV or candida requires follow-up. All such women should have at least one culture. Consider other diagnoses e.g., vulvar dermatitis. In TV, once men and women become asymptomatic or who are initially asymptomatic after treatment follow-up is unnecessary for men and women [42].

Complications: BV is associated with a 2-fold increases risk of serious health complications including susceptibility to and transmission of HIV and herpes simplex type 2 virus; acquisition of other sexually transmitted infections, including *Neisseria gonorrhoeae* and *Chlamydia*. BV is also associated with upper genital tract infections like pelvic inflammatory disease [16]. One of the studies has shown that spontaneous abortion, preterm labour, premature birth, preterm rupture of the membranes, amniotic fluid infection, postpartum endometritis, and post-cesarean wound infections are increased because of infection with BV [4]. Women with PID have an increased risk of ectopic pregnancy, infertility and chronic pelvic pain [22, 23]. Trichomoniasis causes significant morbidity if infections are not treated during pregnancy, including preterm delivery, low birth weight infants, and premature rupture of membranes [10]. Complications of vulvovaginal candidiasis are chorioamnionitis in pregnancy and vulvar vestibulitis syndromes have been reported [18]

Most healthcare workers advocate regarding infertility as the most important reproductive health and social issue confronting Nigerian women and gynaecologists frequently report that infertility constitutes 60%-70% of their consultations in tertiary institutions. In Nigeria, most cases of infertility follow RTIs.[7]

Complementary and Alternative Medicine (CAM): Tabassum *et al.,* (2017) in a randomized, single-blind, standard controlled study on the efficacy of *Tamarindus ind*icus, *Melia* and *Santalum album* against the combination of azithromycin, fluconazole and secnidazole in syndromic management of abnormal vaginal discharge found no significant differences between the two groups. The Unani formulation was effective to alleviate the disease with associated symptoms without any side effects and was useful in syndromic management of vaginal discharge [43]. A comparative randomized controlled study between a polyherbal pessary with ginlac-V pessary for treatment of women with symptomatic vaginal discharge found that both provided symptomatic relief in most of the women [44].

Salhan *et al.,* (2017) also conducted a phase II randomized controlled trial to evaluate the efficacy and safety of parneem polyherbal vaginal tablets compared with betadine vaginal pessary in women with symptoms of abnormal vaginal discharge.

They found that 92% of women using parneem were relieved of their symptoms of AVD against 81.6% women using betadine [13].

A study reported that management of chronic PID after nine shortwave diathermy (SWD) treatments using a modified crossfire technique showed that patient was completely relieved of abdominal and back pain [45]. Another study carried out to evaluate the role shivagutika administered twice daily with honey after meals for 60 days in the pelvic inflammatory disease that clinical features of PID progressive reduced with time, indicating the efficacy of the formulation in PID [45].

A comparative study on the therapeutic effects of *Zataria multiflora* vaginal cream versus metronidazole vaginal gel on BV showed that *Z. multiflora* had a similar effect as metronidazole [40]. Motlagh *et al.*, (2018) conducted a randomized controlled clinical trial treated with oral metronidazole plus *Prangosferulacea* vaginal cream and the other with oral metronidazole plus a placebo vaginal cream for seven days. This trial showed that *Prangosferulacea* vaginal cream accelerated the recovery of bacterial vaginosis of patients with bacterial vaginosis. It can be used effectively as a complementary treatment with oral metronidazole in cases of medication resistance and also in people wishing to use herbal remedies [46]. A study showed that the effects of feilin vaginal Gel (FVG), a Chinese herbal formula, on the treatment of cervicitis in the mouse model could significantly inhibit the cervicitis. FVG could down-regulate the bacterial load, mitigate the pathological injury [47].

CONCLUSION: Vaginal discharge is the common symptom of a variety of diseases each of which has a distinct treatment. Incorrect diagnosis has medical and social consequences. Many women with vaginal discharge self-treat incorrectly with over-the-counter drugs. Abnormal vaginal discharge is usually related to the three conditions, such as bacterial vaginosis, candidiasis, and trichomoniasis. Vaginal discharge may be either physiological or pathological in origin. It is recommended that prevention, early diagnosis, and prompt treatment of abnormal vaginal discharge especially among the sexually active women should be done to avoid complication. This review article gives a detailed description of physiological/ pathological vaginal discharge as well as evidence-based herbal medicine.

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