Original Article

Comparative study of syndromic and etiological diagnosis of sexually transmitted infection except human immunodeficiency virus in sexually transmitted infection and reproductive tract infection clinic attendees in central India

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Abstract

Context: Most of the sexually transmitted infections (STIs), both ulcerative and non-ulcerative are prevalent in India. However, due to lack of adequate laboratory infrastructure in the country, information regarding STIs lies essentially on syndromic basis. Hence, there is very limited data of laboratory proven STIs. **Aims:** The aim of this study is to determine the prevalent STI and reproductive tract infection (RTI) in the region and comparison of etiological diagnosis with syndromic approach. **Settings and Design:** Cross-sectional study. **Materials and Methods:** A total of 1120 patients attending STI/RTI clinic were included in the study with one or more complaints as enunciated by World Health Organization in its syndromic approach. Depending on syndromic presentation, different samples such as ulcer swabs, genital swabs and blood samples were collected. These samples were processed by the standard guidelines of National AIDS Control Organization. Warts, *Molluscum contagiosum* and genital scabies were diagnosed clinically. **Results:** Age of acquiring STI in females (20-24 years) was lower than males (25-44 and more). Vaginal discharge syndrome (90.3%) was most common followed by cervical discharge syndrome (20%). The highest incidence of herpes (14.3%) seen in genital ulcerative diseases but clinically human papilloma virus (16.5%) was common. Overall, *Candida* was the most common isolates. Bacterial STIs like chancroid (0%) and gonorrhea (0.54%) are showing a declining trend. Laboratory confirmation of syndromic diagnosis was seen in only 409/1120 (36.5%). **Conclusions:** Viral STIs/RTIs are getting the upper hand over bacterial. Syndromic algorithms have some shortcomings and they need to be periodically reviewed and adapted to the epidemiological patterns of STIs in a given setting.

Key words: Genital discharge syndrome, genital ulcerative syndrome, sexually transmitted infection/reproductive tract infection, World Health Organization, Syndromic approach

INTRODUCTION

Sexually transmitted infections (STIs) are more dynamic than other infections prevailing in the community.[1] In India, during 1960s and 70s, bacterial infections such as syphilis, chancroid and gonorrhea were major STIs. Viral diseases such as herpes simplex virus (HSV) and human papilloma virus (HPV) were extremely rare. As in developed countries, there has been a significant rise in viral diseases and a relative fall in the incidence of traditional infections since 80s in India.[2] A total number of new cases of our major bacterial STIs are gonorrhea-88 million, genital Chlamydial infection-101 million, syphilis-11 million, *Trichomonas vaginalis*-248 million in the world as estimated by more sensitive and specific diagnostic tools such as ligase chain reaction and polymerase chain reaction.[3]

The prevalence rate are far higher in developing countries where STI treatment are less accessible.[4] Most of the STIs, both ulcerative and non-ulcerative are prevalent in India and constitute one of the major public health problems.[5] However, due to lack of adequate laboratory infrastructure in the

country, information regarding STIs lies essentially on syndromic basis. Hence, there is very limited data of laboratory proven STIs.[6]

Keeping above facts in mind, the present study was undertaken to document the common STIs in the STI/reproductive tract infection (RTI) clinic attendees of the tertiary care hospital and to compare the performance of syndromic management against their laboratory diagnosis.

MATERIALS AND METHODS

A total of 1120 patients attending STI/RTI clinic of a tertiary health-care center from June to December 2012 were included in the study with one or more complaints as enunciated by World Health Organization (WHO) in its syndromic approach for the diagnosis of STIs.[7]

All the cases were classified based on syndromic diagnosis as genito-ulcerative disease non-herpetic (GUD-NH), genito-ulcerative disease herpetic (GUD-H), urethral discharge syndrome (UDS), vaginal discharge syndrome (VDS), cervical discharge syndrome (CDS), genital warts (GW) anogenital warts (AW), *Molluscum contagiosum* (MC), genital scabies (GS). GW and AW, MC and GS were diagnosed clinically.

The samples from the patients were collected as per the syndromic diagnosis of the patient. In brief, for GUD-NH-serous fluid from the ulcer, exudates from the ulcer base, tissue biopsy for impression smear were made. For GUD-H scrapping from the bottom of the ulcer, for UDS-two urethral swabs, for VDS-three vaginal swabs and for CDS-two endocervical swabs were taken. Sterile pure viscous swabs from Hi-Media were used to collect the sample. Samples were immediately transferred to Microbiology laboratory for further processing. One swab each from VDS and UDS were collected in Stuart's and Kupferburg's medium. All the specimens were collected and processed for culture and identification as per the standard guidelines given by National AIDS Control Organization using sheep chocolate agar in Colombia base and Saponin lysed blood agar and Sabouraud's slope.[8]

A test dose of 5ml of venous blood (without anticoagulant) was collected aseptically from all the patients. Sera was separated and stored at −20°C in screw-capped plastic vials. Venereal disease research laboratory test (Ag procured from Institute of Serology, Kolkata) and *Treponema pallidum* hemagglutination assay procured from Plasmatec, UK, was performed in GUD-NH cases. Certain other serological tests were performed i.e., from GUD-H syndromic cases HSV II immunoglobulin M (IgM) antibody (DSI, Italy) and CDS cases for *Chlamydia trachomatis* IgM antibody (Novatec, Germany).

RESULTS

A total of 1120 syndromic cases from the STI/RTI clinic attendees of a tertiary health-care center were included in this study from June to December 2012. These 1120 attendees presented with one or more of complaints as enunciated by WHO in its syndromic approach for the diagnosis of STI.[7]

Sex-wise distribution of 1120 syndromic cases showed that 91 (8.1%) were males and 1029 (91.9%) females. Age-wise distribution of total cases showed that maximum cases (84 cases-92.3%) of males belongs to 25 to more than 45 age group, whereas 885 (86%) females presented with slightly lower age group i.e., 20-44.

Out of 1120 syndromic cases, 6 (0.54%) cases of GUD-NH, GUD-H-63 (5.6%), UDS-6 (0.5%), VDS-1011 (90.3%), CDS-225 (20%), GW-14 (1.25%), MC-11 (0.09%), GS-7 (0.6%) and AW-2 (0.18%) were present. Maximum cases of syndromic presentation were females comprising of 1029 (91.9%) cases. Only 91 (8.1%) were males [Table 1].

Etiological diagnosis of syndromic cases showed that out of six GUD-NH, 2 (0.18%) were serologically confirmed syphilis (*T. pallidum*), 1 (0.09%) was donovanosis (*Calymatobacterium granulomatis*). Herpes infection was shown in 21 (1.9%) cases, *C. trachomatis* in 1 (0.09%), *T. vaginalis* in 34 (3.04%), *Candida* species in 245 (21.9%) and bacterial vaginosis in 99 (8.8%) cases [Table 2].

Comparison of syndromic approach and laboratory confirmed STIs showed that out of total 1120 syndromic cases, GUD-H (65 cases) was the most common syndrome in males (57.1%), whereas VDS (1011 cases) was common in females. In above cases, lab confirmed cases of herpes were 21 (32.3%) and in females suffering from VDS, only 378 cases (37.4%) were confirmed for pathogens in laboratory. Eighty percent laboratory confirmation is seen in UDS cases and 50% in GUD-NH cases. In total, only 409 cases (36.5%) were confirmed in the laboratory for pathogens [Table 1].

DISCUSSION

During the past two decades, sexually transmitted diseases (STDs) have undergone a dramatic transformation. STDs are superseded by STIs. The STI differs from STD in that, it includes infections that may not cause clinical diseases of genitals, but are transmitted

Table 1: Incidence of syndromes presented by STI patients (*T* = 1120)

Syndromes	Males (*n* = 91) (%)	Females (*n* = 1029) (%)	Total (*n* = 1120) (%)	Laboratory confirmed (%)
GUD NH	4 (4.4)	2 (0.2)	6 (0.54)	3 (50)
GUD H	50 (55)	13 (1.3)	63 (5.6)	21 (32.3)
UDS	6 (6.6)	—	6 (0.5)	4 (80)
VDS	—	1011 (98.2)	1011 (90.3)	378 (37.4)
CDS	—	225 (21.9)	225 (20)	3 (1.3)
GW	13 (14.3)	1 (0.1)	14 (1.25)	*
MC	9 (9.9)	2 (0.2)	11 (0.09)	*
GS	7 (7.7)	0	7 (0.6)	*
AW	2 (2.2)	0	2 (0.18)	*
				409 (36.5)

*These are clinically diagnosed cases, not confirmed in laboratory. STI=Sexually transmitted infections, GUD NH = Genito-ulcerative disease non-herpetic, GUD H = Genito-ulcerative disease herpetic, UDS = Urethral discharge syndrome, VDS = Vaginal discharge syndrome, CDS = Cervical discharge syndrome, GW = Genital warts, MC = *Molluscum contagiosum*, GS = Genital scabies, AW = Anogenital warts

Table 2: Etiological agents in syndromes (*T* = 1120)

Etiological agents	Males (*n* = 91) (%)	Females (*n* = 1029) (%)	Total (*n* = 1120) (%)
T. pallidum	2 (2.2)	0	2 (0.18)
C. granulomatis	1 (1.1)	0	1 (0.09)
Herpes II virus	13 (14.3)	8 (0.78)	21 (1.9)
N. gonorrhoeae	4 (4.4)	2 (0.1)	6 (0.54)
C. trachomatis	0	1 (0.1)	1 (0.09)
T. vaginalis	0	34 (3.3)	34 (3.04)
Candida species	0	245 (23.9)	245 (21.9)
G. vaginalis	0	99 (9.65)	99 (8.8)
Human papilloma virus	15 (16.5)	1 (0.1)	16 (1.4)
Molluscum contagiosum	9 (9.9)	2 (0.2)	11 (1)
Ectoparasite	7 (7.7)	0	7 (0.6)

T. pallidum = Treponema pallidum, C. granulomatis = Calymatobacterium granulomatis, N. gonorrhoeae = Neisseria gonorrhoeae, C. trachomatis = Chlamydia trachomatis, T. vaginalis = Trichomonas vaginalis, G. vaginalis = Gardnerella vaginalis

by sexual interactions like all STDs and hepatitis B, human immunodeficiency virus (HIV) infections, etc. However for all practical purposes, both STIs and STDs are used synonymously.[9]

In the present study, a total 1120 STI/RTI clinic attendees were included, which were mainly dominated by females (91.9%). A study in Himachal Pradesh also reported the number of female attendees almost 3 times the number of males.[10] This probably is due to scaled-up intervention, effective contact tracing, spouse screening, better female literacy rate, changed definitions of STIs in the light of syndromic case management, clubbing of RTIs and media aware ness campaigns. This trend has also been observed by other workers in some other states as well.[10,11]

An important observation in the present study is that STI in females is noted at lower age (20 years) as compared with males. Male patients presented at 25 years and above. Similar result was observed by Okonko *et al*.[12] Age wise distribution of male patients shows that approximately 92% cases belongs to 25-44 years and above 45 years age group, where as in females, STI is noticed more in 20-44 years age. But one thing was common in both sexes that the peak age for maximum cases of STI was 25-44 years (79.1% in males and 64% in females), which is similar to several other studies.[5,10,11] This is the sexually active group and at a high risk of behaviorally more vulnerable to STI acquisition.[5]

In the present study, the overall prevalence for STIs in syndromic and clinically diagnosed cases was 39.5%. There is variation in reports showing low prevalence of STI ranging 6-8.3%.[11,13] Our study is comparable with Okonko *et al*.[12] who showed 39% prevalence of STIs in their study.

The most commonly reported syndrome in males was GUD-H (57.1%) followed by genital and AW (16.5%) and in females was VDS (98.2%) followed by CDS (21.9%). Similar findings are shown by a Nigerian study.[14] Overall, genital discharge syndrome (VDS, CDS and UDS) was reported in 90.7% patients and genitoulcerative syndrome (GUD-NH and GUD-H) in 71 cases (6.34%). Thomas *et al*.[13] found genital discharge in 41.7% and genital ulcers in 2.8% cases. Ganju and Sharma[10] reported 29% genital discharges and 5.6% genital ulcer diseases. Choudhry *et al*.[15] reported a low percentage of genital discharge syndrome (39%) and high percentage of genitor-ulcerative syndrome (30%). This is a matter of concern in the context of HIV transmission as genital ulcer facilitates the transmission and enhances susceptibility to HIV infection by sexual contact. Also, non-ulcerative STIs like *Neisseria gonorrhoeae, C. trachomatis* and *T. vaginalis* increases the shedding of HIV virus in the genital tract by recruiting HIV infected inflammatory cells as part of normal host response.[15]

In our study, genital and anogenital wart accounted for 16 cases (1.43%). Several studies[5,11] have reported an increase in incidence of GW (7.6-25.2%), whereas Ganju and Sharma[11] reported only 0.68%. The reason for these variable results probably lies in the study design, data source and computational method. The data presented by our study is from STI clinics of tertiary care hospital.

We found 1% cases of MC and 0.6% cases of GS. Choudhry *et al*.[15] and Devi *et al*.[11] reported slightly higher percentage of these condition i.e., 4.7% and 2.76% respectively. Devi *et al*.[11] reported 0.92% and Narayanan[6] found 1.8% incidence of GS respectively. The variation noted may be due to the hygienic habits and socioeconomic status of the study population.

Several studies[10,15] reported a high incidence of UDS; however, our study shows only 0.5% cases of UDS. The reason may be that ours being a tertiary hospital, the males of the urban area may be going to private practitioners due to social stigma attached with STIs, which is reflected by lower UDS in males.

HSV (15%) was the most common laboratory diagnosed and HPV (17%) as the most common clinically diagnosed etiological agent of STIs in males in the present study. These findings are close to observations of Choudhry *et al*.[15] Slightly higher incidence of HSV (24.5%) was reported by Devi *etal*.[11] as the most common etiological agent of STIs in males and HPV in 1.8% cases. Choudhry *et al*.[15] found 19% of males to be affected by genital herpes and 16% by HPV as the next most common viral STIs in STI attendees in Delhi. Overall they found genital herpes (28.7%) as the most common and HPV (20%) as 3rd most common STI in the total population. They suggested this rising incidence of viral STIs as a result of increased usage of antibiotics.[15]

Candida was the commonest etiological agent in female STI comprising of 245 (23.9%) followed by *Gardenella vaginalis* (8.9%) and *T. vaginalis* (3.04%), which is similar to Okonko *et al*.[12] who also showed *Candida* (27%) to be the commonest infection in females followed by *G. vaginalis* (10.5%) and *T. vaginalis* (1.5%). A marked decrease in bacterial STIs resulting in an apparent increase in fungal

and viral STIs has been reported from different regions.[11,15]

Neisseria gonorrhoea was found in 6 (0.54%) cases in the present study. Though the isolates were six only, all were resistant to Nalidixic acid and ciprofloxacin and four were intermediate resistant to Penicillin. In India, the prevalence of Gonococci among STI clinic attendees in different regions varies from 3% to 19%. However, it has been on the decline over the past decade, probably due to availability of medical facilities at the primary health-care level, indiscriminate use of potent over the counter drugs, prophylactic use of antibiotics after sexual exposure and growing awareness about acquired immune deficiency syndrome.[16]

C. trachomatis and *C. granulomatis* (Donovanosis) are confirmed in 1 (0.09%) of cases each respectively. A high prevalence of *C. trachomatis* (16.5%) was reported by Choudhry *et al*.[15] and 3.9% by Thomas *et al*.[13] A wide variation in *Chlamydia* infection rate is reported due to differences in sensitivity and specificity of different tests used. The low prevalence of *C. granulomatis* is comparable to 0.013% in Tezpur and 0.43% in Cuttack.[17]

In our study, no case was confirmed with *Haemophilus ducreyi* which is similar to Choudhry *et al*.[15] This may be due to the availability of newer antibiotics, their indiscriminate use before and after sexual exposure, greater awareness regarding early diagnosis and treatment of STIs and condom promotion campaigns.[16]

Only two cases (0.18%) from the genital ulcers were confirmed for *T. pallidum* in the present study. Choudhry *et al*.[15] confirmed 4.7% genital ulcers with primary syphilis, whereas Bruisten *et al*.[18] reported only 1.9%.Overall, there is a marked decline in bacterial STIs resulting in an apparent increase in viral and fungal STIs, which is found by most of Indian[10,15] as well as foreign studies.[12,14]

Laboratory confirmation was found in 409/1120 cases (36.5%). Documented incidence of *C. trachomatis* is 3.9-16.5%, but in our study, it was very low, i.e., 0.09%. This may be due to low sensitivity and specificity of the test used in the study. Even if we consider maximum incidence (16.5%) of *C. trachomatis* in India, the total laboratory confirmed cases will come near about 50%. Are we over diagnosing the overall cases by syndromic approach? May this is one of the cause to lead the increasing resistance in bacterial STI like gonococcal infections.

CONCLUSION

Bacterial STDs like chancroid and gonorrhea are showing a declining trend, but viral STIs like herpes genitalis and HPV and fungal STIs like candidiasis constitute a major burden of STI clinic in this region. This may be due to prophylactic use of broad spectrum antibiotics. However, these increasing viral STIs enhance the susceptibility of an individual to acquire or transmit HIV through sexual contact.

The emphasis on the syndromic approach to the management of STDs might have increased the accessibility to healthcare for these patients with STDs. Though the syndromic approach has been a major step forward in rationalizing and improving the management of STIs, but syndromic algorithms have some short comings and they need to be periodically reviewed and adapted to the epidemiological patterns of STIs in a given setting.

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