SYNDROMIC DIAGNOSIS VS. LABORATORY DIAGNOSIS OF REPRODUCTIVE TRACT INFECTIONS AMONG MARRIED WOMEN OF REPRODUCTIVE AGE GROUP IN URBAN SLUM OF MUMBAI

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ABSTRACT

Background: In most developing countries, STIs are managed syndromically because of lack the equipment and trained personal required for etiological diagnosis of STIs. We assessed the adequacy of syndromic diagnosis of STIs, compared with laboratory diagnosis of STIs/RTIs.

Methods: A community based, cross-sectional study was carried out among 466 women of reproductive age group during period of Jan 2007 to Jan 2008 at Urban Health Centre. Participants were selected by systematic random sampling.

Results: In the present study, 50% of women reported symptoms related to various RTI syndromes of which most common was vaginal discharge. However self reported symptoms correlated poorly with laboratory evidence of RTIs, with sensitivity of 55.06% and specificity of 57.33%. An improvement in sensitivity from 55.06% to 82.91% was observed when RTIs were diagnosed with clinical examination however specificity decreased to 53.33% from 57.33%. The sensitivity of algorithm for diagnosing cervical abnormality on clinical examination is low (56.04%) missing most true infections.

Conclusions: The control of STIs in resource poor settings remains a major challenge. The development of simple affordable diagnostic tests that can be used for case finding is highest priority.

Key Words: RTIs, Syndromic, clinical, laboratory diagnosis, Urban slum

INTRODUCTION

India has third largest HIV epidemic in the world. In 2013, HIV prevalence was an estimated 0.3%. this figure is small compared to most other middle-income countries but because of india's huge population (1.2 billion) this equates to 2.1 million people living with HIV. In the same year, an estimated 130,000 people died from AIDS-related illnesses,[1] HIV and AIDS in India/AVERT[1]. There is compelling evidence that STIs affect the transmission of

HIV. STIs facilitate the sexual acquisition and transmission of HIV infection and HIV infection increases the risk of other STIs. Hence, the recognition, treatment, and prevention of STIs to reduce the risk of HIV transmission should be a public health priority.

In order to respond to situation and for effective treatment for RTI/ STI, especially in countries with limited resources, syndromic diagnostic approach was recommended by WHO and was adopted by NACO, at the primary health centre level.[2] But it has several limitations like syndromic diagnosis relies on subjective judgment, cannot detect asymptomatic infections, and may result in overdiagnosis /overtreatment and potential drug resistance. there is still no consensus on its performance and several studies from the region have reported inconsistent results. Therefore, there is a public health need to evaluate the validity of the syndromic diagnosis of STIs using population based studies from the region, that is, the urgent need for a comparative study of syndromic and laboratory diagnosis of STIs.

So the main objective of this Urban slum community based study was to enumerating self-reported RTI/STI symptoms among study population; to Assess the clinical status by speculum examination and compare different diagnostic algorithm of STIs/RTIs like self-reporting of morbidity, syndromic diagnosis on clinical examination and etiological diagnosis.

MATERIAL AND METHODS

This is community based, cross-sectional study carried out in Urban slum area. By taking 46% prevalence of reproductive health problems among urban women (NFHS-II) [3], sample size was calculated by using formula $4pq/L^2$ and it comes as 469. By taking inclusion and exclusion criteria into consideration, total 500 married women of reproductive age groups were selected by systematic random sampling technique Urban slum area is divided into 50 plots. There are 180 houses in each plot. To cover a desired sample size of 500, 10 houses were selected from each plot. First house was selected randomly from initial 10 houses and then every 18th houses was selected. (180/10= 18th).

The study was carried out over a period of one year in 2008, among married women of reproductive age group at urban health centre, which is a field practice area of Tertiary Medical College and hospital, Mumbai.

The purpose of the study was explained to each woman and informed consent was taken. Only one woman per household was enrolled. Information was collected regarding socio-economic characteristics, marital history, present clinical symptoms of reproductive tract, on preformed, pre tested interview schedule by investigator. Based on responses to the questions regarding present complaints related to RTIs; the women were labelled as symptomatic or asymptomatic. At the end of the interviews, each woman was given an appointment card, which contains unique identification number and date of appointment at the clinic (at urban health centre) for clinical examination. Co-operation of community health volunteers was sought for the same.

At the clinic, per speculum examination was carried out and samples were collected in the following order for laboratory diagnosis of cervical and vaginal infection.

1. Endocervical swab for gonococcal infection: Gram staining.
2. Vaginal swab: Two vaginal swabs were collected in sterile test tube.
- For trichomoniasis and bacterial vaginosis (saline wet preparation)
- For candidiasis (KOH wet preparation)
3. Vaginal pH was measured with a pH strip indicator (range1 to 14)

After collection sample were transported to the laboratory (at urban health Centre) for further processing.

Standardization of criteria diagnosing reproductive tract infection

Criteria used for diagnosis of RTIs on symptoms

Symptomatic

1. Vaginal discharge - associated with any one of the following complain like profuse, foul smelling, pain in abdomen, itching in vulval region, burning micturition.
2. Lower abdominal pain
3. Genital itching, lesion over genitalia
4. Inguinal Swelling

Asymptomatic: Without symptoms of disease or illness related to reproductive tract infection

Clinical criteria used for cervical infection

Cervicitis

1. Mucopurulent discharge (non-clear, yellowish discharge from endocervix)
2. Positive swab test (yellow discoloration of swab inserted in endocervix)
   – If swab appears yellow when held up against white paper.
3. Cervical Inflammation

Cervical friability: Cervical friability refers to easily induced bleeding of the cervix upon touch during a pelvic examination or cervical specimen collection.
Cervical erosion/ectopy: cervix has a red, friable ring of tissue around the os.
Cervical polyp: finger like growths originating from the mucosal surface of the cervix

Clinical criteria used for vaginal infection:

Normal vaginal discharge: usually scanty, clear or white, Nonhomogenous, Flocculent
Trichomonal vaginitis/ bacterial vaginosis: moderate or profuse, malodorous, white or gray, homogenous discharge
Candidiasis: Scanty to moderate white clumped, "cheesy" adherent, exudative plaques, erythema of vaginal wall

Criteria used for laboratory diagnosis [4]

Reproductive tract infections	Diagnostic criteria
Gonorrhoea	Identification of gram-negative intracellular diplococci in Gram-stained cervical smear
Non gonococcal Cervicitis	>30 PMNs/hpf in Gram-stained cervical smear
Trichomonas vaginitis	≥1 actively moving trichomonas (saline wet preparation) &Ph > 5
Bacterial vaginosis	Presence of "Clue" cells (saline wet preparation)& Vaginal Ph > 5
Candidiasis	Presence of Pseudohyphae and budding yeast cells (KOH wet preparation),& Ph < 5

Treatment was provided to every positive case of reproductive tract infection as per the syndromic management guidelines of RTI/STI based on per speculum examination and risk assessment criteria, provided by Mumbai District AIDS Control Society. Patients were offered specific treatment at their follow up visits on the basis of their laboratory report. Ethical approval: The study was approved by institutional ethics committee

RESULTS

Study population characteristics: In the present study, 52% of the women were in early reproductive age group and most of them belonged to Muslim community. Literate women were 60%, only 12% of women were working. More than half of women were from higher socioeconomic status.

Out of 500 women surveyed 250 did not report any symptom related to RTI at the time of survey and 250 (50%) women were diagnosed to have at least one RTI on symptoms; More than one diagnosis has been given to some women so the number of RTI per women was 1.19 (298/250), major symptom reported was vaginal discharge (Table 1).

Out of 500 women 466 women had undergone gynaecological examination and laboratory investigations at urban health Centre. On clinical examination 332 (71.2%) women were diagnosed to have at least one RTI. More than one diagnosis has been given to some women so number of RTI per women was 1.46 (485/332). Cervicitis along with other cervical abnormality was the most common infection followed by candidiasis and trichomoniasis/bacterial vaginosis (Table 2).

The overall prevalence of reproductive tract infections by laboratory investigations was 67.81 % (316/466). Total Positive laboratory tests being 505. Thus, the number of RTIs per woman was shown to be 1.59 (505/316). Prevalence of candidiasis was highest (37.6%) among all infections diagnosed. It was followed by Non-gonococcal Cervicitis (36.3%) (Table 3)

Table: 1 Reproductive tract infections by Syndromic approach, based on symptoms (N = 500)

Symptoms	Symptoms (%)
Vaginal discharge	221(44.2)
Lesion over genital area	5(1.0)
Lower abdominal pain	68(13.6)
Inguinal swelling	4(0.8)
Total (Reported RTI symptoms)	298(59.6)
No symptoms	250(50)

Table: 2 Reproductive tract infections by Syndromic approach based on clinical examination (N = 466)

Clinical Diagnosis	STI/RTIs (%)
Cervicitis and other cervical abnormality	184(39.5)
Candidiasis	148(31.8)
Trichomoniasis & / or Bacteria Vaginosis	110(23.6)
Genital ulcer disease	5(1.1)
Pelvic inflammatory disease	31(6.7)
Inguinal bubo	5(1.1)
Genital warts	2(0.4)
Total (clinically abnormal)	485 (symptoms)
Clinically normal	134(28.8)

Table: 3 Reproductive tract infections by laboratory investigation (N = 466)

Reproductive tract infection	Women testing positive
Gonococcal cervicitis	33(7.1)
Non-gonococcal cervicitis	169(36.3)
Trichomonas Vaginalis	63(13.5)
Bacterial vaginosis	65(13.9)
Candidiasis	175(37.6)
Total (RTIs present)	505
RTIs absent	150(32.19)

Table: 4 Sensitivity, Specificity and Positive Predictive values of Syndromic approach based on Symptoms and clinical examination in diagnosing different RTIs taking laboratory diagnosis as gold standard

	Infected (RTI) (n=316) (on lab diagnosis)	Not infected (n=150) (on lab diagnosis)	Total (n=466)	Sensitivity	Specificity	PPV
Symptoms (self reported)						
Present	174	64	238	55.06%	57.33%	73.10%
Absent	142	86	228			
Observed morbidity(clinical examination)						
Yes	262	70	332	82.91%	53.33%	78.91%
No	54	80	134			

Table: 5. Sensitivity, Specificity and Positive Predictive values of clinical examination in diagnosing different RTIs

On clinical examination Differential diagnosis	Sensitivity	Specificity	PPV
Trichomoniasis/ BV	53.65%	87.17%	60%
Candidiasis	62.28%	86.59%	73.64%
Cervical abnormality	56.04%	71.12%	55.43%

Table: 6: Sensitivity, Specificity and Predictive values of Syndromic approach based on clinical examination and > 1 Risk Assessment Criteria for Diagnosing STIs (Gonococcal & Non gonococcal infection)

Clinical examination + > 1 Risk Assessment	Infected with STI	Not infected with (STI)	Total	Sensitivity	Specificity	PPV
Positive	123	128	251	67.58%	54.92%	49.00%
Negative	59	156	215			
Total	182	284	466			

Self reporting Vs Lab. Diagnosis: For the sensitivity analysis to compare the different diagnostic methods to diagnose RTI/STI laboratory diagnosis is taken as gold standard method. In the present study, 50% of women reported symptoms related to various RTI syndromes. However self reported symptoms correlated poorly with laboratory evidence of RTIs, with sensitivity of 55.06% and specificity of 57.33%. Thus only half of the cases of RTI reported symptoms of RTIs and about 42.67% (64/150) of uninfected cases reported symptoms.

Self reporting Vs clinical Diagnosis: Compared to Syndromic approach based on symptoms, an improvement in sensitivity from 55.06% to 82.91% was observed when RTIs were diagnosed with the help of clinical examination however specificity decreased to (53.33%) from (57.33%) (Table 4)

The sensitivity of algorithm is low (53.65%) for identification of Trichomoniasis and Bacterial Vaginosis, though specificity and PPV are 87.17% and 60% respectively. The sensitivity of algorithm for diagnosing candidiasis is low (62.28%) but specificity is high (86.59%) and PPV is 73.64%. The sensitivity of algorithm for diagnosing cervical abnormality on clinical examination is low (56.04%) missing most true infections and low PPV (55.43%) leading to overtreatment of women who did not have the disease. Specificity is 71.12% (Table 5).

Improvement in sensitivity from 56.46% to 67.58% is observed when risk assessment criteria and clinical examination both were used to diagnose cervical infection but specificity remains the problem. PPV decrease from 58.69% to 49.00% (Table 6).

DISCUSSION

Based on clinical examination, Prevalence of RTIs was 71.2%. On laboratory examination, 316 (67.81%) women showed positive results for RTIs, the total number of positive tests being 505. Thus, the number of RTIs per woman was shown to be 1.59 (505/316). Candidiasis being most prevalent infection (37.6%) followed by Non-gonococcal cervicitis (36.3%) and bacterial vaginosis (13.9%). P.T.Lane et al[5] had done a study in rural district of Vietnam. In this study aetiologically confirmed RTI/STI was identified in 39% of the women. Endogenous infection were more prevalent (candidiasis 26%, BV 11%) followed by, Chlamydia trachomatis 4.3%, Trichomonas Vaginalis 1%.

The high prevalence of RTI/STIs in women, in the present study, supports the current consensus that young adults should constitute a priority target group in the STI Control Programme. The physiological risk of increased susceptibility to infection among young adults is due to the presence of greater cervical ectopy, making the cervix more

susceptible to gonorrhoea, chlamydia and HPV. The present study population consisted mostly of illiterate women, of low socioeconomic status, with a history of low use of contraceptives and poor treatment-seeking behaviour. All these factors might have contributed to the high RTI/STI endemicity in the study areas.

On sensitivity specificity analysis, self reported symptoms correlated poorly with laboratory evidence of RTIs, with sensitivity of 55.06% and specificity of 57.33%. Thus only half of the cases of RTI reported symptoms of RTIs and about 42% (64/150) of uninfected cases reported symptoms. These values imply that treatment on the basis of reported symptoms alone would have missed half of the infected women, but would also have resulted in unnecessary treatment of uninfected cases.

A study done by Roochika Ranjan[6] in New Delhi found that WHO Syndromic approach based on symptoms had low sensitivity (53.6%) and low PPV (53.1%) in diagnosing RTIs among women which lead to over treatment who did not have the disease taking laboratory diagnosis as a Gold standard.

Jasmin Helen Prasad[7] et al. had done a study in Tamil Nadu among young married women. The study found that the WHO algorithms based on reported vaginal discharge alone had poor sensitivity (50%), specificity (60%), and predictive value (47%).

These results add to the growing body of evidence that treatment on the basis of reported symptoms is inadequate in the Indian setting. Women do not seek care or do not report symptoms such as vaginal discharge because they do not perceive the implications of these symptoms for health.

In the present study, it is also seen that compared to Syndromic approach based on symptoms, an improvement in sensitivity from 55.06% to 82.91% was observed when RTIs were diagnosed with the help of clinical examination however specificity decreased to (53.33%) from (57.33%).

The sensitivity of algorithm is low (53.65%) for identification of Trichomoniasis and Bacterial Vaginosis, though specificity and PPV are 87.17% and 60% respectively. The low sensitivity of algorithm may relate to the fact that around 50% of trichomoniasis infections remain asymptomatic, but 30% of this group develops symptoms when they are observed for 6 months.

The sensitivity of algorithm for diagnosing candidiasis is low (62.28%) but specificity is high (86.59%) and PPV is 73.64%. the low sensitivity of the algorithm may be related to the fact that overgrowth of candida albicans in the vagina is not always associated with discharge.

The sensitivity of algorithm for diagnosing cervical abnormality on clinical examination is low (56.04%) missing most true infections and low PPV (55.43%) leading to overtreatment of women who did not have the disease. Specificity is 71.12%. Clinical diagnosis of cervicitis is weakly linked with laboratory diagnosis of gonococcal and non gonococcal infection. This is not surprising, because of its asymptomatic nature, cervicitis can have a non specific cause, and can be caused by pathogens other than those assessed. To improve the sensitivity of cervical infection we can add risk assessment criteria to diagnostic algorithm.

Nandan D[8], conducted a study on reproductive tract infection in women of reproductive age group in Sitapur/Shahjahanpur district of Utter Pradesh. He reported that, compared to syndromic approach based on symptoms, an improvement in the sensitivity (81.8%) and predictive accuracy (74.1%) was noted when cases were detected with help of clinical examination.

A study done by Sarah Hawkes et al[9] in Matlab, Bangladesh showed that the sensitivity of WHO algorithm (clinical examination) for bacterial vaginosis was (32%), trichomonas vaginosis (33%) and for candiasis (59%). Specificity for bacterial vaginosis (82%), trichomonas vaginosis (80%) and for candiasis (79%)

A study done by Roochika Ranjan[5] in New Delhi found that WHO syndromic approach based on clinical examination had low sensitivity in diagnosing trichomoniasis(21.3%) and bacterial vaginosis (32.5%) but high specificity (76.3%) for trichomoniasis and (85.6%) for bacterial vaginosis. Sensitivity for diagnosing candidiasis is 56.2% and specificity (82.7%).

In preset study, it shows that addition of risk assessment criteria increases the sensitivity for diagnosing cervical infection but specificity and PPV remains the problem leading to overtreatment and erroneous labelling of women as having a serious STI. The risk assessment criteria used in present study are Under age 21, Single, Diagnosed with an STI in last three months, Partner with an STI symptoms, More than one sexual partner in last three months without always using condoms, Unprotected sex with partner who has had more than one partner in last three months, Situation suggestive of risky behaviour-e.g. man work far from home for long period of time

A study done by Vuylesteke et al[10]. in Zaire among pregnant women attending antenatal clinics. Results showed that simple hierarchical algorithm (WHO) based only on reported symptoms was found to have a sensitivity of 48% and a specificity of 75.2% for the screening of pregnant women.

Speculum examination yielded a lower sensitivity of 29.3% percent and a higher specificity of 85.3% percent. Using risk score plus clinical examination the sensitivity was 72%and the specificity was 73.5% percent.

A study conducted by Behets F et al[11]. in Cite Soleil, Haiti shantytowns among pregnant women visiting antenatal clinics showed sensitivity (71%) and specificity (62%) and PPV (22%) only on risk assessment score, which includes the number of sexual partners in the past three months, the age of "coital debut" of the patient, whether or not she is living with her current sexual partner, and whether or not partner has an STD. when this risk assessment score combined with speculum examination yielded an 89% sensitivity and 43% specificity, and PPV of 18.8%.

A study conducted by Behets et al[12]. at Jamaican sexually transmitted disease clinic to evaluate diagnostic algorithms versus laboratory test showed that, use of clinical algorithms for diagnosing cervical infection was 73% sensitive and 55% specific when compared with laboratory testing. The risk assessment inclusive flow chart developed by WHO was 84% sensitive and 40% specific for diagnosing cervical infection. Therefore we can say that for the control of cervical infection, syndromic management of vaginal discharge is not an efficient approach.

CONCLUSION

This study highlights the wide variation between self-reporting of morbidity and syndromic- and etiology-based diagnosis in women from urban settings. This has implications for the syndromic approach to STI case management. These observations call for a review of the diagnostic policy for RTIs/STIs by national authorities in order to avoid the overuse of antimicrobials. The study also highlights the need for the introduction and/or strengthening of facilities for simple diagnostic tests for RTIs/STIs, and effective partner management especially at the peripheral healthcare level.

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