Original Article

Behavioral and Psychosocial Risk Factors Associated with First and Recurrent Cystitis in Indian Women: A Case-control Study

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ABSTRACT

Background: The risk factors for urinary tract infections (UTIs) from developed countries are not applicable to women from developing world. **Objective:** To analyze the behavioral practices and psychosocial aspects pertinent to women in our region and assess their association with acute first time or recurrent UTI. **Materials and Methods:** Sexually active premenopausal women with their first (145) and recurrent (77) cystitis with *Escherichia coli* as cases and women with no prior history of UTI as healthy controls (257) were enrolled at a tertiary care hospital in India, between June 2011 and February 2013. Questionnaire-based data was collected from each participant through a structured face-to-face interview. **Results:** Using univariate and multivariate regression models, independent risk factors for the first episode of cystitis when compared with healthy controls were (presented in odds ratios [ORs] with its 95% confidence interval [CI]): Anal sex (OR = 3.68, 95% CI = 1.59-8.52), time interval between last sexual intercourse and current episode of UTI was <5 days (OR = 2.27, 95% CI = 1.22-4.23), use of cloth during menstrual cycle (OR = 2.36, 95% CI = 1.31-4.26), >250 ml of tea consumption per day (OR = 4.73, 95% CI = 2.67-8.38), presence of vaginal infection (OR = 3.23, 95% CI = 1.85-5.62) and wiping back to front (OR = 2.52, 95% CI = 1.45-4.38). Along with the latter three, history of UTI in a first-degree female relative (OR = 10.88, 95% CI = 2.41-49.07), constipation (OR = 4.85, 95% CI = 1.97-11.92) and stress incontinence (OR = 2.45, 95% CI = 1.18-5.06) were additional independent risk factors for recurrent cystitis in comparison to healthy controls. **Conclusion:** Most of the risk factors for initial infection are potentially modifiable but sufficient to also pose risk for recurrence. Many of the findings reflect the cultural and ethnic practices in our country.

Keywords: Behavioral practices, host factors, recurrent urinary tract infections, sexual behavior, urinary tract infections

Introduction

Lower urinary tract infections (UTIs) are among the most frequently seen bacterial infection and account for considerable morbidity among sexually active women.[1] *Escherichia coli* remains the predominant uropathogen, causing 80-90% of acute community acquired uncomplicated UTI.[2] More than half of all women experience at least one episode of UTI during their lifetime and about 25% of them have a second infection within six months.[3]

There is no definitive explanation for why only some women get UTIs, and why recurrences tend to occur only in some subjects.[4] The repeated infections generally occur in the absence of anatomic abnormalities in the urinary tract. Host genetic, behavioral and bacterial virulence characteristics all have been suspected to play a role in causation.[5] Host factors that might influence the risk of UTI include: Sexual history, use of barrier contraceptives with spermicides, delayed postcoital micturition, etc.[5,6] Behavioral modification is shown to reduce the risk of UTI.[7] Women with recurrent

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UTI were found to have stronger family history of UTI.[8] Most of these studies have been conducted in developed countries where the socioeconomic status is higher and a lot of behavioral practices among women differ from those in developing countries. Many of the risk factors described for the western population differ from the population in this region; for example, the use of spermicides, hot tubs and tampons. We have asked all the participants about cranberry juice, none of the women replied in affirmative. The given reference is of our previous study, where we reported similar result.[9] Therefore, the aim of the present study was to examine various host factors and identify independent risk factors that may be associated with an increased risk of first or recurrent cystitis in women in a developing country.

Materials and Methods

This was a case-control study conducted in the Department of Microbiology at a tertiary care hospital in India between June 2011 and February 2013. Patients attending gynecology outpatients department (OPD) who gave written informed consent for participation, were recruited for the study. The sample size was not formally calculated. Subjects were enrolled consecutively. The case population was sexually active premenopausal women of ≥18 years of age with symptoms suggestive of acute cystitis (i.e., two or more of the following symptoms: Dysuria, urine frequency six times per day, urgency, suprapubic pain, fever, hematuria/smoky urine, burning micturition and acute onset incontinence), who gave urine sample for examination. Non-pregnant women with bacteriologically documented *E. coli* as sole uropathogen in quantities of at least 10^2 CFU/ml,[1] with no underlying comorbidity, apparent urological abnormality, or a urethral catheter in place were included for final analysis. Control subjects were asymptomatic healthy women attending family planning clinics of the same hospital at the same time interval as cases. They came for copper-T insertion, tubal ligation, etc. and did not have any symptoms suggestive of cystitis or a past history of UTI. Controls were subjected to urine culture and, if sterile, they were included in the study. Self-report of prior UTI ever in the past was considered sufficient to exclude a potential control. The university's ethics committee approved the study protocol and informed consent.

A midstream urine sample from each case and control was collected and processed as described previously.[9] If the woman presenting with acute cystitis did not report any history of UTI in the past, she was considered as first cystitis case; if the woman experienced either three or more symptomatic UTI episodes in the past year, or two such episodes in the last six months (including index episode), she was included in recurrent cystitis group.[3] This was based on documented proof of UTI including previous urine culture reports. In the absence of a culture report, the demonstration of pyuria on urinalysis and two or more urinary symptoms, as well as complete and rapid resolution of urinary symptoms in response to antibiotic therapy, were taken as evidence of past UTI.[5]

Data were collected from each participant through a structured face-to-face interview during the visit to the clinic and noted on a predesigned questionnaire, which was formed after consultation with a concerned gynecologist and was pilot tested for relevance. A research assistant administrated the questionnaire in the patient's mother tongue. A separate area was provided in the gynecology OPD to conduct these interviews, and it was ensured that no males were present in that area to help ease the atmosphere. The questionnaire was divided into seven main parts: Socioeconomic status (education, employment and household income); demographic characteristics (age, marital status and parity); medical history (past history of UTIs, investigations reports, medication during previous UTI, age at first UTI, history of UTI among first-degree female relatives, interval from last episode of UTI, recent antibiotic use, stress incontinence, abnormal vaginal discharge and constipation); sexual history (age at first intercourse, frequency of sexual intercourse, new sex partner, anal sex, contraceptive use in past 12 months including exposure to spermicides, time interval between last sexual intercourse and current episode of UTI); voiding pattern (postcoital voiding, delayed/postponed voiding); personal hygiene (wiping back to front after bowel movement, use of hot tub once or more per month, douching, use of sanitary napkin/cloth during menstrual cycle and reuse of cloth after washing); fluid consumption (water, tea/coffee intake per day and cranberry juice consumption). Stress incontinence was assessed as by asking the patient if she experiences any involuntary leakage of urine on coughing/straining. Women were taken into confidence and made comfortable so that they could talk freely on these sensitive topics. Moreover women were assured of confidentiality.

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 16.0, IBM corporation. Univariate logistic regression analysis was employed to find the risk of first and recurrent cystitis in comparison to healthy controls. The risk of recurrence in comparison to first cystitis was also assessed using univariate logistic regression. The factors found significant in all the three models were entered in the multiple logistic regression models by the enter method to find significant factors affecting the outcomes. The results are presented in odds ratios (ORs) with its

95% confidence interval (CI). The *P*-value <0.05 was considered significant.

Results

A total of 710 symptomatic premenopausal women were interviewed during the study period and 635 consented to participate. 222 of these women satisfying the inclusion criteria were included in final analysis (145 women as first cystitis and 77 women as recurrent cases). 311 apparently healthy women were interviewed for control subjects and 257 fitting the inclusion criteria were included in final analysis. The case-control ratio was 0.86:1. The mean age of control population, first and recurrent cystitis cases was 30.5 ± 6.33 years (range, 18-48 years), 30.31 ± 7.91 years (range 18-50 years) and 33.2 ± 6.94 years (range 20-50 years), respectively. Cases and controls were similar with regard to socioeconomic status, marital status, etc. [Table 1].

In univariate analysis, when compared with control subjects, a significantly higher number of women with first and recurrent cystitis reported anal sex and abnormal vaginal discharge along with less intake of water. A twofold increase in risk of first episode of cystitis was found in women who used cloth during menstruation and the risk become fourfold when they reused it after washing (*n* = 79). All variables related to sexual history were significantly associated with first episode of cystitis [Table 2]. In our study, contraceptive methods practiced, age at first UTI and age at first

intercourse were not found to be associated with increased risk of cystitis. Postcoital voiding was the only variable which had a negative association (protective) with first episode of cystitis [Table 2]. In addition four variables *viz.* history of UTI in a first-degree female relative, stress incontinence, constipation and wiping back to front had stronger association with recurrence in comparison to both, women with first cystitis and control subjects.

In the multivariate model, consumption of more than 250 ml tea/coffee per day increased the risk of first episode of cystitis about five times (OR = 4.73, 95% CI = 2.67-8.38). Other independent risk factors for first episode of cystitis included anal sex (OR = 3.68, 95% CI = 1.59-8.52), consumption of less than 2 L water per day (OR = 3.69, 95% CI = 2.06-6.59), abnormal vaginal discharge (OR = 3.23, 95% CI = 1.85-5.62) and use of cloth during menstrual cycle (OR = 2.36, 95% CI = 1.31-4.26) [Table 3]. When women with recurrent cystitis were compared with control subjects, family history of UTI was the strongest independent risk factor (OR = 10.88, 95% CI = 2.41-49.07). Other independent risk factors included constipation (OR = 4.85, 95% CI = 1.97-11.92), tea consumption >250 ml/day (OR = 4.14, 95% CI = 1.95-8.80), wiping back to front, less than 2 L water consumption per day, abnormal vaginal discharge and stress incontinence [Table 3]. The strongest independent risk factor for getting recurrence after first UTI was history of UTI in a first-degree female relative (OR = 4.13, 95% CI = 1.64-

Table 1: Demographic characteristics of study subjects

Variables	Healthy controls (*n* = 257)	First cystitis (*n* = 145)	Recurrent cystitis (*n* = 77)	Healthy controls *vs.* First cystitis		First *vs.* Recurrent cystitis		Healthy controls *vs.* Recurrent cystitis	
				Unadjusted OR (95% CI)	*P* value	Unadjusted OR (95% CI)	*P* value	Unadjusted OR (95% CI)	*P* value
Age in years									
18-35	196 (76.3)	114 (78.6)	53 (68.8)	1.00 (ref)	0.58	1.00 (ref)	0.11	1.00 (ref)	0.19
36-50	61 (23.7)	31 (21.4)	24 (31.2)	0.87 (0.53-1.42)		1.66 (0.89-3.11)		1.45 (0.83-2.55)	
Parity									
2	178 (69.3)	107 (73.8)	48 (62.3)	1.00 (ref)	0.33	1.00 (ref)	0.07	1.00 (ref)	0.25
>2	79 (30.7)	38 (26.2)	29 (37.7)	0.80 (0.50-1.26)		1.70 (0.94-3.07)		1.36 (0.80-2.31)	
Education									
Illiterate	107 (41.6)	57 (39.3)	35 (45.4)	1.00 (ref)	0.78	1.00 (ref)	0.50	1.00 (ref)	0.34
Primary	86 (33.5)	54 (37.2)	27 (35.1)	1.10 (0.54-2.25)	0.47	1.43 (0.50-4.07)	0.77	1.58 (0.60-4.12)	0.40
High school	35 (13.6)	20 (13.8)	9 (11.7)	1.30 (0.63-2.68)	0.69	1.16 (0.40-3.37)	0.93	1.51 (0.57-4.04)	0.71
Graduation	29 (11.3)	14 (9.7)	6 (7.8)	1.18 (0.51-2.74)		1.05 (0.30-3.62)		1.24 (0.39-3.90)	
Employment									
Homemaker	236 (91.8)	134 (92.4)	70 (90.9)	1.00 (ref)	0.83	1.00 (ref)	0.69	1.00 (ref)	0.79
Working	21 (8.2)	11 (7.6)	7 (9.1)	0.92 (0.43-1.97)		1.21 (0.45-3.28)		1.12 (0.45-2.75)	
Household income in Rs./month									
<5000	158 (61.5)	91 (62.8)	51 (66.2)	1.00 (ref)	0.13	1.00 (ref)	0.35	1.00 (ref)	0.77
5000-10000	61 (23.7)	41 (28.3)	15 (19.5)	1.68 (0.85-3.32)	0.07	0.66 (0.27-1.58)	0.09	1.11 (0.53-2.34)	0.71
>10000	38 (14.8)	13 (9.0)	11 (14.3)	1.96 (0.93-4.13)		0.43 (0.15-1.17)		0.84 (0.35-2.04)	

CI: Confidence interval, OR: Odds ratio, ref, reference; values in the parentheses represent percentages within the group

Table 2: Risk of first and recurrent cystitis: Univariate logistic regression analysis

Variables	Healthy controls (n=257)	First cystitis (n=145)	Recurrent cystitis (n=77)	Healthy controls vs. First cystitis		First vs. Recurrent cystitis		Healthy controls vs. Recurrent cystitis	
				Unadjusted OR (95% CI)	P value	Unadjusted OR (95% CI)	P value	Unadjusted OR (95% CI)	P value
Sexual history									
Frequency of sexual intercourse >5/month	136 (52.9)	105 (72.4)	40 (51.9)	2.33 (1.50-3.62)	**0.0001**	0.41 (0.23-0.73)	**0.003**	0.96 (0.57-1.60)	0.88
Anal sex	13 (5.1)	30 (20.7)	13 (16.9)	4.89 (2.46-9.73)	**0.0001**	0.77 (0.37-1.59)	0.49	3.81 (1.68-8.62)	**0.001**
Interval between last sexual intercourse and current episode of cystitis (<5 days)	124 (48.2)	101 (69.7)	53 (68.8)	2.46 (1.60-3.78)	**0.0001**	0.96 (0.52-1.75)	0.89	2.36 (1.37-4.06)	**0.002**
Behavioral practices									
Postcoital voiding	155 (60.3)	61 (42.1)	38 (49.4)	0.47 (0.31-0.72)	**0.0001**	1.34 (0.77-2.33)	0.29	0.64 (0.38-1.07)	**0.08**
Delayed voiding	149 (57.98)	108 (74.5)	64 (83.12)	2.11 (3.15-3.31)	**0.001**	1.68 (0.83-3.40)	0.14	3.56 (1.87-6.80)	**0.0001**
Wiping back to front after bowel movement	79 (30.7)	63 (43.5)	44 (57.1)	1.73 (1.13-2.64)	**0.01**	1.73 (0.99-3.03)	0.053	3.00 (1.78-5.07)	**0.0001**
Daily water intake ≤2L	131 (51.0)	114 (78.6)	58 (75.3)	3.53 (2.21-5.63)	**0.0001**	0.83 (0.43-1.59)	0.57	2.93 (1.65-5.20)	**0.0001**
Caffeinated beverage intake >250 ml/day	89 (34.6)	89 (61.4)	51 (66.2)	3.00 (1.96-4.57)	**0.0001**	1.23 (0.69-2.20)	0.47	3.70 (2.16-6.33)	**0.0001**
Use of cloth during menstruation	159 (61.9)	110 (75.9)	59 (76.6)	1.93 (1.22-3.05)	**0.004**	1.04 (0.54-1.99)	0.89	2.02 (1.12-3.62)	**0.01**
Reuse of cloth after washing (n=79)	29 (18.2)	32 (29.1)	18 (30.5)	1.83 (1.03-3.27)	**0.03**	1.07 (0.53-2.13)	0.84	1.96 (0.99-3.90)	**0.05**
Medical history									
Abnormal vaginal discharge	60 (23.3)	73 (50.3)	45 (58.4)	3.32 (2.15-5.14)	**0.0001**	1.38 (0.79-2.42)	0.25	4.61 (2.69-7.90)	**0.0001**
Constipation	16 (6.2)	16 (11.0)	24 (31.2)	1.86 (0.90-3.85)	**0.09**	3.65 (1.79-7.41)	**0.0001**	6.82 (3.39-13.72)	**0.0001**
Stress incontinence	51 (19.8)	55 (37.9)	44 (57.1)	2.46 (1.56-3.88)	**0.0001**	2.18 (1.24-3.82)	**0.007**	5.38 (3.12-9.29)	**0.0001**
History of urinary tract infection in a first degree female relative	3 (1.2)	9 (6.2)	18 (23.4)	5.60 (1.49-21.04)	**0.0001**	4.61 (1.95-10.85)	**0.0001**	25.83 (7.36-0.57)	**0.0001**

CI: Confidence interval, OR: Odds ratio, values in the parentheses represent percentages within the group; *P* values shown in bold are significant

Table 3: Factors associated with first and recurrent cystitis: Multivariate logistic regression analysis

Variables	Healthy controls *vs*. First cystitis		First *vs*. Recurrent cystitis		Healthy controls *vs*. Recurrent cystitis	
	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Sexual history						
Frequency of sexual intercourse >5 per month	1.60 (0.85-2.99)	0.14	0.44 (0.23-0.83)	**0.01**	—	—
Anal sex	3.68 (1.59-8.52)	**0.002**	—	—	2.20 (0.63-7.66)	0.21
Interval between last sexual intercourse and current episode of cystitis (<5 days)	2.27 (1.22-4.23)	**0.01**	—	—	1.75 (0.84-3.64)	0.12
Behavioral practices						
Postcoital voiding	0.31 (0.18-0.53)	**0.000**	—	—	—	—
Delayed voiding	1.61 (0.92-2.81)	0.09	—	—	2.25 (0.94-5.41)	0.06
Wiping back to front after bowel movement	2.52 (1.45-4.38)	**0.001**	1.30 (0.70-2.41)	0.39	3.82 (1.84-7.91)	**0.000**
Daily water intake ≤2L	3.69 (2.06-6.59)	**0.000**	—		3.32 (1.51-7.32)	**0.003**
Caffeinated beverage intake >250 ml/day	4.73 (2.67-8.38)	**0.000**	—		4.14 (1.95-8.80)	**0.000**
Use of cloth during menstruation	2.36 (1.31-4.26)	**0.004**	—		1.32 (0.60-2.89)	0.47
Medical history						
Abnormal vaginal discharge	3.23 (1.85-5.62)	**0.000**	—	—	2.99 (1.48-6.04)	**0.002**
Constipation	1.29 (0.51-3.24)	0.58	3.40 (1.58-7.32)	**0.002**	4.85 (1.97-11.92)	**0.001**
Stress incontinence	1.59 (0.89-2.84)	0.11	1.88 (1.02-3.47)	**0.04**	2.45 (1.18-5.06)	**0.01**
History of urinary tract infection in a first degree female relative	2.99 (0.71-12.50)	0.13	4.13 (1.64-10.40)	**0.003**	10.88 (2.41-49.07)	**0.002**

CI: Confidence interval, OR: Odds ratio, *P* values shown in bold are significant

10.40), followed by constipation (OR = 3.40, 95% CI = 1.58-7.32) and stress incontinence (OR= 1.88, 95% CI=1.02-3.47) [Table 3].

Discussion

The study was conducted to address some of the gaps in our understanding of risk factors for first and recurrent cystitis amongst sexually active women in developing countries. In the present study, majority of women attending the hospital came from rural and semi-urban areas and belonged to lower socio-economic strata with poor literacy rates. Increased consumption of tea/coffee was found to be associated with an increase in UTI among women, as reported earlier.[6,10] There was a 3.5 times increased risk of first episode of cystitis among those who have anal sex. This is because the female urethra is short, located fairly close to the anus and small amounts of fecal flora could be transferred to the urethra;[11] significant association of anal sex with acute UTI and pyelonephritis has been reported.[11,12] Low water intake was an independent risk factor for UTI; consistent with other studies.[7,13] Water diuresis serves to "flush" the urinary tract of infecting organisms and frequent voiding reduces bacterial multiplication in the bladder.[13] The presence of abnormal vaginal discharge indicating vaginal infection was significantly high in cystitis cases when compared with control subjects. Vaginitis has been reported as a risk factor for UTI.[14] In our study, the percentage of vaginal infection amongst both cases and controls though was higher than reported in literature from developed countries.[5] This may be because of poor personal hygiene in low socioeconomic

strata in our study population. Wiping back to front was an important behavioral risk factor for UTI and so was the recent sexual intercourse (<5 days from index infection). Both these factors enhance entry of bowel bacteria in to the urethral opening.[10,15,16] Many studies in past have demonstrated an association between frequency of sexual intercourse and risk of UTI,[8,15] for the same reasons,[17] but we did not find this association in multivariate analysis for either first or recurrent cystitis. In fact, in recurrent cases, frequency of sexual intercourse was actually less than the first episode of cystitis cases in our study. One plausible explanation could be that this factor may be important for first infection and there after the bacteria may persist in urinary bladder and produce relapse.[18] This may also points towards possible genetic predisposition of the host for bacterial attachment.[19]

The lack of hygiene during menstrual cycle is reported to pose a greater risk of both vaginitis and UTI.[20] The use of cloth during menstruation is common among women in low socio-economic strata in developing countries. Women often use cotton cloth (torn piece of old saree/ rag), change it infrequently and reuse the cloth after washing.[20] A twofold-increased risk of the first episode of cystitis in multivariate analysis was found among women who were using cloth during their menstrual cycle. Micturition after sexual intercourse (post-coital voiding) was associated with decreased risk of first episode of cystitis in multivariate analysis. Micturition can flush out bacteria that might have moved to urethral opening because of sexual intercourse.[6] Although in present study it did not protect against recurrent cystitis,

indicating probably a stronger bacterial attachment and hence host cellular predisposition for recurrence. A family history of UTI in a first-degree female relative was a strong and consistent risk factor for both initial and recurrent cystitis, although the association was stronger with the recurrent UTI. Increased risk estimates of recurrent cystitis with stronger family history have been noted previously, suggesting a genetic predisposition to infection.[5,8] Overall we found the percentage of women with family history of UTI to be less in our study population as compared to western countries. This may be because in our country these topics are not discussed openly in the family and women may well be unaware of other female relatives with similar problems. Constipation was a significant finding amongst women with recurrent cystitis. This has been studied extensively in children and postmenopausal women and found to be an important risk factor;[21,22] however, in premenopausal women though there is not much published literature on this.[4] Constipation causes urinary dysfunction by anatomic distortion and displacement of the bladder by the rectum and the sigmoid colon is loaded with feces. In addition, chronic pelvic floor spasms prevent complete relaxation during voiding and may attribute to post-void residues.[21,23] Stress incontinence was an independent risk factor for recurrence of infection, though the risk was not very high as the average age of our study population was around 30 years. It has been reported as an important risk factor for UTI in peri and postmenopausal women.[24] Studies from western countries report contraceptive use as an important risk factor for UTI;[5,15] we did not find this association. In our study population (both cases and controls), more than half of the women did not use any methods of contraception and none reported use of diaphragms or spermicides. Delayed voiding was significantly associated with the first and recurrent cystitis in univariate model but it disappears in multivariate model in our study. This factor has been reported in literature to be an important risk factor for UTIs.[7,13] Not many women (in both the case and control populations) in our study population reported having a new sexual partner in last one year, while this is a common risk factor in many studies from developed countries.[5]

The strength of our study is that we compared both first and recurrent cystitis with each other and with healthy controls so that we could analyze risk factor for both. Its large sample size allowed us to analyze the independent contribution of several risk factors applicable to developing countries. We would like to add that most of the women were very patient and forthcoming with their answers. Some limitations of the present study, however, need to be considered. Constipation, anal sex and history of UTI in a first-degree female relative emerged as significant risk factors; however, since the actual number of participants who answered positively for these variables was small, these need to be further validated by a larger study sample. Among recurrent cystitis cases, it is possible that some of the behaviors of interest were modified in response to the occurrence of repeated infections. Recall bias and case-control comparability, however, were appropriately addressed as the survey was collected at the time of event and both cases and controls were collected from close proximity.

Conclusion

Independent risk factors for first episode of cystitis when compared with healthy controls identified in the present study includes anal sex, the time interval between last sexual intercourse and current episode of UTI <5 days, use of cloth during menstrual cycle, >250 ml of tea consumption per day, presence of vaginal infection and wiping back to front. Along with the latter three, history of UTI in a first degree female relative, constipation and stress incontinence were additional independent risk factors for recurrent cystitis in comparison to healthy controls. This study shows that major risk factors for lower UTI differ from those identified in the western world. Since most of the women in our study belonged to rural and semi-urban background with low socioeconomic status, these findings can be applied to a larger population of India as well as other developing countries with similar demographic characteristics. We also found that several risk factors for initial infection although potentially modifiable were sufficient to also pose risk of recurrence. Women can easily adopt most of these behavior modifications. More such studies from developing countries are required to validate these findings and the formulation of appropriate preventive strategies.

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