Reproductive Tract infections and Premalignant Lesions of Cervix: Evidence from Women Presenting at the Cancer Detection Centre of the Indian Cancer Society, Delhi, 2000–2012

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Abstract

Objectives Burden of cervical cancer (CC) is highest for women in low- and middle-income countries (LMICs).

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Human papillomavirus (HPV) is implicated as the necessary cause of CC although a number of other factors aid the long process of CC development. One among them is the presence of reproductive tract infections (RTIs). This study investigated the associations between RTIs and CC from India.

Methods This study utilized secondary data from the Cancer Detection Centre of the ICS, Delhi. Data were accessed from MS access database and were analyzed using MS Excel and SPSS 16.0. Multivariate analysis using unconditional logistic regression produced odds ratios (ORs) and 95 % confidence intervals (CIs).

Results This study used data from 11,427 women over a period of 2000–2012. Women with RTIs had Candida, Trichomonas vaginalis (TV) or coccoid infections with all having similar prevalence (~4–5 %). 9.4 % of women had premalignant lesions of cervix; ASCUS was most common (7.9 %) followed by LSIL (1.3 %). TV was significantly associated with ASCUS, LSIL and all premalignant lesions

of cervix ($P < 0.001$). Regression discovered an important association of TV with premalignant lesions of cervix (OR 2.79; 95 % CI 2.14, 3.64).

Conclusions Earlier studies have depicted associations between TV and HPV with possible enhancement of HPV virulence due to TV. Lack of awareness and hygiene, and limited access to gynecologists in LMICs lead to frequent and persistent RTIs which aid and abet HPV infection and CC occurrence. These also need to be addressed to reduce CC and RTIs among women in LMICs.

Keywords Reproductive tract infections · Trichomonas vaginalis · Premalignant lesions of cervix · Human papillomavirus (HPV) · Cervical cancer · India

Introduction

Cervical cancer (CC) is one of the commonest cancers of women in the world [1] with more than 86 % deaths occurring in the low- and middle-income countries (LMICs), a figure that is expected to increase to 91.5 % by 2030 [2]. India contributed about 23 % of CC cases and 25 % of CC deaths to the world figures in 2012 [2]. Over the years, there has been a decline in CC incidence in India even in the absence of any systematic screening program although CC still accounts for a substantial proportion of cancers among women in rural areas (29.8 % in rural registry of Barshi as compared to approximately 10 % in urban registries) [3]. A substantial portion (up to 99.7 %) of CC in India is caused due to persistent infection by the human papillomavirus (HPV) [4]. HPV infection is cleared by most women albeit for a small section of women who develop persistent infection leading to premalignant lesions with two specific HPV types (16 and 18) being the most common agents. Overall, HPV types 16, 18, 31, 33 and 45 were detected in 87.1 % of all cases in a study from India [5]. Other studies such as those by Bhatla et al. [6] found similar figures with 73.6 % cases of CC being infected with HPV 16.

Although HPV is a necessary cause of CC [4] and a lot of attention is being focused on HPV control and vaccination, the long process of CC development is aided by the presence of a number of other factors. One of the lesser studied factors related to CC development is the lack of menstrual and reproductive hygiene as evident in some studies on CC in India [7–9]. Lack of hygiene among women is one of the most important problems of LMICs, especially women belonging to low socioeconomic status (SES) [10]. Lack of hygiene ultimately leads to development and persistence of reproductive tract infections (RTIs) or lower genital tract infections (LGTIs) [10–13]

and is even associated with aiding and abetting the development of CC [7, 9]. We will use the term RTIs throughout this article.

Indeed, multiple studies highlight the clear association between RTIs and CC. Peitsidis et al. [14] in Greece discovered that women infected with chlamydia had almost twice the incidence of atypical squamous metaplasia compared to women not infected with chlamydia [14]. Similar findings were observed in a study in the UK where infection with chlamydia or bacterial vaginosis was independent risk factor for vaginal HPV infection [15]. Such associations are also seen from LMICs such as China where higher RTIs were associated with the incidence of cervical intraepithelial neoplasia (CIN) and HPV infection [16]. Another study from Beijing observed high rates of CIN among women with bacterial vaginitis [17]. Concurrent presence of RTIs might be due to the confounding role of multiple sexual partners. Alternatively, there might also be effect modification of association of HPV with CIN due to the presence of other RTIs. There is some evidence to suggest that bacterial vaginosis is not associated directly with CIN [18] and abnormal production of nitrosamines has been implicated [19]. However, biological associations such as synergism of other RTIs with occurrence of CIN cannot be ruled out emphatically [19].

Given the above and also the fact that the literature exists from multiple epidemiological studies in India, on the associations between lack of hygiene and CC [7–9], hardly any research exists on the underlying associations between RTIs and CC in the Indian context. Pertaining to this reason, we decided to investigate the association between RTIs and CC utilizing data from women across 13 years visiting the Cancer Detection Center (CDC) of the Indian Cancer Society (ICS), Delhi.

Materials and Methods

Study Setting

This study was based on secondary analysis of data collected from the records of the CDC of the ICS, Delhi. This CDC is located at 42 Babar Road, New Delhi, and has been conducting early detection and screening for cervical, and head and neck cancers for the last 30 years for people coming voluntarily to the center or people attending cancer detection camps organized by the ICS, Delhi, upon request by organizations. All the data at this detection center originated from people getting themselves voluntarily screened, either at the center or at one of the camps. Following clinical examination and tests, the data were entered via a form into a Microsoft (MS) Access database which had 31 tables, 35 queries and one patient master

form. The patient master form described the general information asked from people at the first point of contact with the CDC personnel.

Data Management

The 31 tables contained information of different variables such as cancer type, clinical history, eating history, family history, operation or medication history, sociodemographic variables, insurance, billing, Pap smear examination details and camp venue. There were some variables which were repeated in the different tables. The number of subjects present in the database was 30,318, and the earliest subject belonged to the year 1987. After analyzing all the tables in detail, there were five tables named “Patient Master,” “Clinical History,” “Detection Report,” “Generals” and “Cytopathological Report” that were found to be useful for analysis as these were the tables containing all the relevant information about the subjects. Rest of the tables either contained duplicate, less or no information at all. Clinical History Table contained information of eating habits, medication history, family history, sexual, reproductive history, etc. Detection Report Table contained information about type of cancer, previous cancer history, already detected, referred, advice given, etc. Generals Table contained information about hemoglobin (Hb), weight (Wt), blood pressure (BP), internal viscera examination, ear, nose and throat (ENT) examination, mouth, larynx, pharynx, breast, cervix, abdomen, uterus, etc. Finally, Cytopathological Report Table contained information of Pap smear examination. These tables were combined by using commands in MS Access software, and one merged excel file was prepared by removing all the duplicate cases.

Finally, a merged Excel sheet without duplicates containing 24,931 cases and 104 variables was prepared. The merged Excel sheet contained data on 11,427 female cases and 13,504 male cases for 13 years starting from 2000 to 2012. For the purposes of this study, 11,427 female cases were included with 31 variables in total to be analyzed.

Data Analysis

Data analysis was done with the help of MS Access, MS Excel and SPSS 16. The data were tabulated in terms of frequency distribution of different variables. Cases with missing information were excluded from analysis. Chi-square and Fisher's exact tests of significance were employed for testing associations. $P < 0.05$ was considered for statistical significance. Unconditional logistic regression analysis was also performed, and odds ratios (ORs) with 95 % confidence intervals (CIs) were computed for all the relevant variables. Including sociodemographic variables did not change the estimates and thus were not

included in the final models except age which was included as a continuous variable. Inflammation is a part of the pathway as well as end result of infections as well as CC, and as such, treating it as a confounder was not yielding meaningful results. Therefore, it was not included in the multivariate model. We also ran a separate model with the composite variable—total infections, realizing that most of the effect we saw was due to *Trichomonas vaginalis* (TV) infection.

Results

Of the total 11,427 women screened at CDC of the ICS, Delhi, cytological findings were observed among 10,536 (92 %) women. Table 1 contains the distribution of cytological findings, demonstrating that majority of the cases, i.e., 2310 (29 %) had non-specific inflammation followed by atrophic vaginitis cases 963 (12.1 %). Among the RTIs, 416 (5.2 %) cases had clear diagnosis of *Candida* followed by cases of TV 353 (4.4 %), coccoid bacteria 317 (4 %) and non-specific fungal infection 71 (0.9 %). Among the premalignant lesions of cervix, the cases of atypical

Table 1 Distribution of cytological findings among 11,427 women voluntarily attending the Cancer Detection Centre of the Indian Cancer Society, Delhi, 2000–2012

Type of cytological finding	Present no. (%) ^b	Absent no. (%) ^b
Inflammation ^{(3466)a}	2310 (29.0)	5651 (71.0)
Atrophic vaginitis ^{(3469)a}	963 (12.1)	6995 (87.9)
Erosion ^{(3464)a}	19 (0.2)	7944 (99.8)
Bleeding ^{(3467)a}	110 (1.4)	7850 (98.6)
Fungal ^{(3465)a}	71 (0.9)	7891 (99.1)
<i>Candida</i> ^{(3465)a}	416 (5.2)	7546 (94.8)
<i>Trichomoniasis</i> ^{(3465)a}	353 (4.4)	7609 (95.6)
Coccoid ^{(3466)a}	317 (4.0)	7644 (96.0)
ASCUS ^{(3496)a}	629 (7.9)	7302 (92.1)
LSIL ^{(3466)a}	106 (1.3)	7855 (98.7)
HSIL ^{(3465)a}	11 (0.1)	7951 (99.9)
CIN ^{(3465)a}	9 (0.1)	7953 (99.9)
HPV ^{(3465)a}	13 (0.2)	7949 (99.8)
Normal ^{(3464)a}	1503 (18.9)	6460 (81.1)
NEDM ^{(3454)a}	3496 (43.8)	4477 (56.2)
NAD ^{(6872)a}	210 (4.6)	4345 (95.4)

ASCUS atypical squamous cells of undetermined significance, LSIL low-grade squamous intraepithelial lesion, HSIL high-grade squamous intraepithelial lesion, CIN cervical intraepithelial neoplasia, HPV human papillomavirus, NEDM no evidence of dysplasia or malignancy, NAD nothing abnormal detected

^a Cases with missing information for each variable—not included in the analysis

^b Row percentages of total

Table 2 Distribution of sociodemographic and hematological variables, and premalignant lesions of cervix among women ($N = 11,427$) attending the Cancer Detection Centre of the Indian Cancer society, Delhi, from 2000 to 2012

Variables	Premalignant lesions of the cervix					
	ASCUS $N = 7931$ (%)		LSIL $N = 7961$ (%)		HSIL $N = 7962$ (%)	
	Yes	No	Yes	No	Yes	No
Age ($N = 11,400$)						
Up to 35 years	158 (7.6)	1921 (92.4)	37 (1.8)	636 (98.2)	0 (0.0)	2083 (100.0)
36–45 year	173 (8.2)	2109 (91.8)	29 (1.4)	4566 (98.6)	2 (0.1)	2113 (99.9)
46–55 years	154 (8.3)	1691 (91.7)	22 (1.2)	2488 (98.8)	5 (0.3)	1851 (99.7)
Above 55 years	142 (7.6)	1732 (92.4)	18 (1.0)	141 (99.0)	3 (0.2)	1886 (99.8)
Total	627 (7.9)	7280 (92.1)	106 (1.3)	7831 (98.7)	10 (0.1)	7928 (99.9)
Marital status ($N = 11,426$)						
Married	602 (7.9)	6972 (92.1)	100 (1.3)	7502 (98.7)	11 (0.1)	7592 (99.9)
Divorced	0 (0)	2 (100)	0 (0)	2 (100)	0 (0)	2 (100.0)
Single	27 (7.6)	327 (92.4)	6 (1.7)	350 (98.3)	0 (0)	356 (100.0)
Total	629 (7.9)	7301 (92.1)	106 (1.3)	7854 (98.7)	11 (0.1)	7950 (99.9)
Occupation ($N = 8360$)						
Employed	110 (8.1)	1242 (91.9)	25 (1.8)	1327 (98.2)	5 (0.4)	1347 (99.6)
Housewife	339 (8.7)	3547 (91.3)	33 (8)	3882 (99.2)	5 (0.1)	3910 (99.9)
Student	19 (9.2)	188 (90.8)	3 (1.4)	206 (98.6)	0 (0)	209 (100)
Total	468 (8.6)	4977 (91.4)	61 (1.1)	5415 (98.9)	10 (0.2)	5466 (99.8)
Religion ($N = 11,347$)						
Hindu	579 (7.9)	6706 (92.1)	94 (1.3)	7221 (98.7)	10 (0.1)	7306 (99.9)
Sikh	22 (7.5)	270 (92.5)	7 (2.4)	285 (97.6)	0 (0)	292 (100)
Christian	3 (4.8)	59 (95.2)	1 (1.6)	61 (98.4)	1 (1.6)	61 (98.4)
Muslim	21 (9.1)	211 (90.9)	4 (1.7)	228 (98.3)	0 (0)	232 (100)
Others	1 (12.5)	7 (87.5)	0 (0)	8 (100)	0 (0)	8 (100)
Total	626 (7.9)	7253 (92.1)	106 (1.3)	7803 (98.7)	11 (0.1)	7899 (99.9)
Hb ($N = 10,952$)						
Less than 12 g	357 (8.1)	4055 (91.9)	63 (1.4)	4367 (98.6)	4 (0.1)	4426 (99.9)
12 g or more	249 (7.8)	2963 (92.2)	40 (1.2)	3184 (98.8)	7 (0.2)	3218 (99.8)
Total	606 (7.9)	7018 (92.1)	103 (1.3)	7551 (98.7)	11 (0.1)	7644 (99.9)
WBC ($N = 10,960$)						
Less than 4000	8 (6.5)	116 (93.5)	4 (3.2)	120 (96.8)	0 (0)	124 (100)

Table 2 continued

Variables	Premalignant lesions of the cervix												
	ASCUS <i>N</i> = 7931 (%)		LSIL <i>N</i> = 7961 (%)		HSIL <i>N</i> = 7962 (%)		CIN <i>N</i> = 7962 (%)		All premalignant lesions <i>N</i> = 7930 (%)				
	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No		
4000–10,000	532 (7.9)	6195 (92.1)		86 (1.3)	6667 (98.7)		8 (0.1)	6746 (99.9)		7 (0.1)	6747 (99.9)	629 (9.4)	6097 (90.6)
More than 10,000	68 (8.7)	712 (91.3)		13 (1.7)	771 (98.3)		3 (0.4)	781 (99.6)		1 (0.1)	783 (99.9)	84 (10.8)	696 (89.2)
Total	608 (8.0)	7023 (92.0)		103 (1.3)	7558 (98.7)		11 (0.1)	7651 (99.9)		9 (0.1)	7653 (99.9)	725 (9.5)	6905 (90.5)
ASCUS atypical squamous cells of undetermined significance, HSIL high-grade squamous intraepithelial lesion, LSIL low-grade squamous intraepithelial lesion, CIN cervical intraepithelial neoplasia, Hb hemoglobin, WBC white blood cell													
^a Chi-square test													
^b Fisher's exact test													

Table 3 Distribution of sociodemographic and hematological variables, and reproductive tract infections among women ($N = 11,427$) attending the Cancer Detection Centre of the Indian Cancer society, Delhi, from 2000 to 2012

Variables	Reproductive tract infections														
	Fungal <i>N</i> = 7962 (%)			Candida <i>N</i> = 7962 (%)			Trichomoniasis <i>N</i> = 7962 (%)			Coccoid <i>N</i> = 7961 (%)			All infections <i>N</i> = 7962 (%)		
	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value
Age (<i>N</i> = 11,400)			0.252 ^b			0.484 ^a			0.929 ^a			0.226 ^a			0.613 ^a
Up to 35 years	15 (0.7)	2068 (99.3)		121 (5.8)	1963 (94.2)		95 (4.6)	1988 (95.4)		78 (3.7)	2005 (96.3)		286 (13.7)	1798 (86.3)	
36–45 years	15 (0.7)	2098 (99.3)		109 (5.2)	2004 (94.8)		95 (4.5)	2017 (95.5)		78 (3.7)	2034 (96.3)		279 (13.2)	1833 (86.8)	
46–55 years	23 (1.2)	1833 (98.8)		95 (5.1)	1761 (94.9)		77 (4.1)	1779 (95.9)		89 (4.8)	1767 (95.2)		253 (13.6)	1603 (86.4)	
Above 55 years	18 (1.0)	1868 (99.0)		89 (4.7)	1796 (95.3)		84 (4.5)	1803 (95.5)		70 (3.7)	1816 (96.3)		234 (12.4)	1652 (87.6)	
Total	71 (0.9)	7867 (99.1)		414 (5.2)	7524 (94.8)		351 (4.4)	7587 (95.6)		315 (4.0)	7622 (96.0)		1052 (13.3)	6886 (86.7)	
Marital status (<i>N</i> = 11,426)			1.000 ^b			0.455 ^b			0.108 ^b			0.382 ^b			0.330 ^b
Married	68 (0.9)	7535 (99.1)		394 (5.2)	7209 (94.8)		337 (4.4)	7266 (95.6)		307 (4)	7295 (96)		1011 (13.3)	6592 (86.7)	
Divorced	0 (0)	2 (100)		0 (0)	2 (100)		1 (50)	1 (50)		0 (0)	2 (100)		1 (50.0)	1 (50.0)	
Single	3 (0.8)	353 (99.2)		22 (6.2)	334 (93.8)		15 (4.2)	341 (95.8)		10 (2.8)	346 (97.2)		46 (12.9)	310 (87.1)	
Total	71 (0.9)	7890 (99.1)		416 (5.2)	7545 (94.8)		353 (4.4)	7608 (95.6)		317 (4)	7643 (96)		1058 (13.3)	6903 (86.7)	
Occupation (<i>N</i> = 8360)			0.660 ^b			0.410 ^a			<0.001 ^a			0.462 ^b			0.002 ^a
Employed	8 (0.6)	1344 (99.4)		74 (5.5)	1278 (94.5)		78 (5.8)	1274 (94.2)		51 (3.8)	1301 (96.2)		199 (14.7)	1153 (85.3)	
Housewife	34 (0.9)	3881 (99.1)		179 (4.6)	3736 (95.4)		105 (2.7)	3809 (97.3)		162 (4.1)	3752 (95.9)		434 (11.1)	3480 (88.9)	
Student	1 (0.5)	208 (99.5)		10 (4.8)	199 (95.2)		9 (4.3)	200 (95.7)		5 (2.4)	204 (97.6)		24 (11.5)	185 (88.5)	
Total	43 (0.8)	5433 (99.2)		263 (4.8)	5213 (95.2)		192 (3.5)	5283 (96.5)		218 (4.0)	5257 (96.0)		657 (12.0)	4818 (88.0)	
Religion (<i>N</i> = 11,347)			0.723 ^b			0.352 ^b			0.702 ^b			0.266 ^b			0.691 ^b
Hindu	66 (0.9)	7250 (99.1)		387 (5.3)	6929 (94.7)		325 (4.4)	6991 (95.6)		302 (4.1)	7013 (95.9)		985 (13.5)	6331 (86.5)	
Sikh	4 (1.4)	288 (98.6)		15 (5.1)	277 (94.9)		17 (5.8)	275 (94.2)		8 (2.7)	284 (97.3)		41 (14)	251 (86)	
Christian	0 (0)	62 (100)		0 (0)	62 (100)		3 (4.8)	59 (95.2)		3 (4.8)	59 (95.2)		6 (9.7)	56 (90.3)	
Muslim	1 (0.4)	231 (99.6)		14 (6)	218 (94)		8 (3.4)	224 (96.6)		4 (1.7)	228 (98.3)		26 (11.2)	206 (88.8)	
Others	0 (0)	8 (100)		0 (0)	8 (100)		0 (0)	8 (100)		0 (0)	8 (100)		0 (0)	8 (100)	
Total	71 (0.9)	7839 (99.1)		416 (5.3)	7494 (94.7)		353 (4.5)	7557 (95.5)		317 (4)	7592 (96)		1058 (13.4)	6852 (86.6)	
Hb (<i>N</i> = 10,952)			0.793 ^a			0.979 ^a			0.029 ^a			0.433 ^a			0.274 ^a
Less than 12 g	41 (0.9)	4389 (99.1)		234 (5.3)	4195 (94.7)		218 (4.9)	4211 (95.1)		171 (3.9)	4258 (96.1)		609 (13.8)	3819 (86.2)	
12 g or more	28 (0.9)	3197 (99.1)		170 (5.3)	3056 (94.7)		125 (3.9)	3101 (96.1)		136 (4.2)	3089 (95.8)		416 (12.9)	2811 (87.1)	
Total	69 (0.9)	7586 (99.1)		404 (5.3)	7251 (94.7)		343 (4.5)	7312 (95.5)		307 (4.0)	7347 (96.0)		1025 (13.4)	6630 (86.6)	
WBC (<i>N</i> = 10,960)			0.402 ^b			0.941 ^a			0.794 ^b			0.042 ^a			0.613 ^a
Less than 4000	1 (0.8)	123 (99.2)		6 (4.8)	118 (95.2)		5 (4.0)	119 (96.0)		8 (6.5)	116 (93.5)		18 (14.5)	106 (85.5)	
4000–10,000	58 (0.9)	6696 (99.1)		355 (5.3)	6399 (94.7)		307 (4.5)	6447 (95.5)		257 (3.8)	6496 (96.2)		894 (13.2)	5860 (86.8)	

Table 3 continued

Variables	Reproductive tract infections														
	Fungal <i>N</i> = 7962 (%)			Candida <i>N</i> = 7962 (%)			Trichomoniasis <i>N</i> = 7962 (%)			Coccoid <i>N</i> = 7961 (%)			All infections <i>N</i> = 7962 (%)		
	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value
More than 10,000	10 (1.3)	774 (98.7)		43 (5.5)	741 (94.5)		31 (4.0)	753 (96.0)		42 (5.4)	742 (94.6)		113 (14.4)	671 (85.6)	
Total	69 (0.9)	7593 (99.1)		404 (5.3)	7258 (94.7)		343 (4.5)	7319 (95.5)		307 (4.0)	7354 (96.0)		1025 (13.4)	6637 (86.6)	

Hb hemoglobin, *WBC* white blood cell^a Chi-square test^b Fisher's exact test

0.29; 95 % CI 0.20, 0.42). In a separate model, women with premalignant lesions of cervix had a higher odds overall of having RTIs (OR 1.52; 95 % CI 1.25, 1.86), an effect most likely due to TV infection.

Discussion

This study used data from 11,427 women over a period of 2000–2012, from the CDC of the ICS, Delhi. Most women were middle-aged, married, Hindu and housewives with more than half being anemic. The occurrence of inflammation was quite high among women. Women with RTIs had Candida, TV or coccoid infections with professionally employed women and anemic women having higher incidence of TV. Among the premalignant lesions of cervix, ASCUS had a high prevalence followed by LSIL. TV was significantly associated with ASCUS, LSIL and all premalignant lesions of cervix.

A high prevalence of 7.9 % for ASCUS observed in our study was more than that observed in other studies conducted in the community in India [20]. Overall, multiple studies across the world have found an ASCUS prevalence varying from 0.6 to 4.5 % [21], with higher prevalence of as much as 10.5 % observed among adolescents [22]. Some researchers have discovered as much as a fivefold difference in ASCUS prevalence in two different cities of the same country (Brazil) [23], but have not been able to explain the cause for it. We are also unable to pinpoint the exact reason for the high prevalence of ASCUS we observed except for the fact that we did have women in younger ages in our study. Nevertheless, this finding of ours needs to be further elaborated by larger studies in the community.

The prevalence of TV infection in this study was comparable to existing figures of 2–7 % for India [24]. The most notable finding in this study was the high association of TV infection with women having premalignant lesions of cervix. None of the other infections, which had similar proportion of occurrence as TV infection, were as closely associated. TV is an anaerobic, flagellated parasitic protozoan and is the most prevalent curable sexually transmitted infection (STI) in the world [25] with 89 % prevalent cases being women [25]. Although up to 80 % of TV infections remain asymptomatic [25], it does not reduce the extent to which TV is a public health concern. TV increases the risk of human immunodeficiency virus (HIV) acquisition by as much as 2.7 times [25], preterm labor by up to 1.3 times [25] and pelvic inflammatory disease (PID) by 4.7 times [25]. Evidence also exists of possibly more virulent pseudocystic forms of TV existing with and exacerbating CC [26].

In addition, TV has been regularly found to be associated with HPV and CC in human studies in various parts of

Premalignant lesions of the cervix																
Variables		ASCUS <i>N</i> = 7931 (%)			LSIL <i>N</i> = 7961 (%)			HSIL <i>N</i> = 7962 (%)			CIN <i>N</i> = 7962 (%)			All premalignant lesions <i>N</i> = 7930 (%)		
		Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value	Yes	No	<i>P</i> value
Fungal (<i>N</i> = 7962)				1.000 ^b			0.616 ^b			1.000 ^b			1.000 ^b			0.778 ^a
Yes		5 (7.0)	66 (93.0)		1 (1.4)	70 (98.6)		0 (0)	71 (100)		0 (0)	71 (100)		6 (8.5)	65 (91.5)	
No		622 (7.9)	7236 (92.1)		105 (1.3)	7785 (98.7)		11 (0.1)	7880 (99.9)		9 (0.1)	7882 (99.9)		741 (9.4)	7116 (90.6)	
Total		627 (7.9)	7302 (92.1)		106 (1.3)	7855 (98.7)		11 (0.1)	7951 (99.9)		9 (0.1)	7953 (99.9)		747 (9.4)	7181 (90.6)	
Candida (<i>N</i> = 7962)				0.180 ^a			0.377 ^b			1.000 ^b			1.000 ^b			0.502 ^a
Yes		40 (9.6)	375 (90.4)		3 (0.7)	412 (99.3)		0 (0)	415 (100)		0 (0)	415 (100)		43 (10.4)	372 (89.6)	
No		587 (7.8)	6926 (92.2)		103 (1.4)	7442 (98.6)		11 (99.9)	7535 (99.9)		9 (0.1)	7537 (99.9)		704 (9.4)	6808 (90.6)	
Total		627 (7.9)	7301 (92.1)		106 (1.3)	7854 (98.7)		11 (1)	7950 (99.9)		9 (0.1)	7952 (99.9)		747 (9.4)	7180 (90.6)	
Trichomoniasis (<i>N</i> = 7962)				<0.001 ^a			<0.001 ^a			1.000 ^b			1.000 ^b			<0.001 ^a
Yes		61 (17.3)	291 (82.7)		17 (4.8)	335 (95.2)		0 (0)	352 (100)		0 (0)	352 (100)		78 (22.2)	274 (77.8)	
No		566 (7.5)	7010 (92.5)		89 (1.2)	7519 (98.8)		11 (0.1)	7598 (99.9)		9 (0.1)	7600 (99.9)		669 (8.8)	6906 (91.2)	
Total		627 (7.9)	7301 (92.1)		106 (1.3)	7854 (98.7)		11 (0.1)	7950 (99.9)		9 (0.1)	7952 (99.9)		747 (9.4)	7180 (90.6)	
Coccoid (<i>N</i> = 7961)				0.281 ^a			1.000 ^b			1.000 ^b			1.000 ^b			0.249 ^a
Yes		20 (6.3)	297 (93.7)		4 (1.3)	313 (98.7)		0 (0)	317 (100)		0 (0)	317 (100)		24 (7.6)	293 (92.4)	
No		607 (8)	7004 (92.0)		102 (1.3)	7541 (98.7)		11 (0.1)	7633 (99.9)		9 (0.1)	7635 (99.9)		723 (9.5)	6887 (90.5)	
Total		627 (7.9)	7301 (92.1)		106 (1.3)	7854 (98.7)		11 (0.1)	7950 (99.9)		9 (0.1)	7952 (99.9)		747 (9.4)	7180 (90.6)	
Atrophic vaginitis (<i>N</i> = 7958)				<0.001 ^a			<0.001 ^b			1.000 ^b			0.299 ^b			<0.001 ^a
Yes		26 (2.7)	937 (92.7)		2 (0.2)	961 (99.8)		1 (0.1)	962 (99.9)		2 (0.2)	961 (99.8)		29 (3.0)	934 (97.0)	
No		601 (8.6)	6361 (91.4)		104 (1.5)	6890 (98.5)		10 (0.1)	6985 (99.9)		7 (0.1)	6988 (99.9)		718 (10.3)	6243 (89.7)	
Total		627 (7.9)	7298 (92.1)		106 (1.3)	7851 (98.7)		11 (0.1)	7947 (99.9)		9 (0.1)	7949 (99.9)		747 (9.4)	7177 (90.6)	
Inflammation (non-specific) (<i>N</i> = 7961)				<0.001 ^a			<0.001 ^a			0.740 ^b			0.462 ^b			<0.001 ^a
Yes		373 (16.4)	1899 (83.6)		53 (2.3)	2251 (97.7)		2 (0.1)	2303 (99.9)		1 (0.1)	2304 (99.9)		427 (18.8)	1844 (81.2)	
No		253 (4.5)	5398 (95.5)		53 (0.9)	5598 (99.1)		9 (0.2)	5642 (99.8)		8 (0.1)	5643 (99.9)		319 (5.6)	5332 (94.4)	
Total		626 (7.9)	7297 (92.1)		106 (1.3)	7849 (98.7)		11 (0.1)	7945 (99.9)		9 (0.1)	7947 (99.9)		746 (9.4)	7176 (90.6)	
Erosion (<i>N</i> = 7963)				0.049 ^b			0.023 ^b			1.000 ^b			1.000 ^b			0.001 ^a
Yes		4 (22.2)	14 (77.8													

Table 4 continued

Variables	Premalignant lesions of the cervix					
	ASCUS <i>N</i> = 7931 (%)		LSIL <i>N</i> = 7961 (%)		HSIL <i>N</i> = 7962 (%)	
	Yes	No	Yes	No	Yes	No
Total	627 (7.9)	7302 (92.1)	106 (1.3)	7855 (98.7)	9 (0.1)	7953 (99.9)
All infections (<i>N</i> = 7962)						
Yes	121 (11.5)	935 (88.5)	23 (2.2)	1033 (97.8)	0 (0)	1056 (100)
No	506 (7.4)	6365 (92.6)	83 (1.2)	6820 (98.8)	11 (0.2)	6895 (99.8)
Total	627 (7.9)	7300 (92.1)	106 (1.3)	7853 (98.7)	11 (0.1)	7949 (99.9)
ASCUS atypical squamous cells of undetermined significance, HSIL high-grade squamous intraepithelial lesion, LSIL low-grade squamous intraepithelial lesion, CIN cervical intraepithelial neoplasia						

^a Chi-square test^b Fisher's exact test

the world. Lazenby et al. [27] discovered more than sixfold higher risk of women with TV being infected with HPV type 16 infection. We saw an association of TV with ASCUS and LSIL which was similar to the findings of a Belgian study where such associations were seen among women with high-risk HPV infection [28]. Depuydt et al. [29] in their study done in Antwerp also demonstrated a higher association between TV and HPV infections. Studies from India also show a presence of TV infection among women who were HPV positive [30] or who had dysplastic changes [31]. There have been few other studies from India which did not detect links between TV and HPV [32, 33]. However, the number of studies investigating the link between RTIs, HPV and CC in India is quite low. There is a need for more such studies to better define the epidemiology of RTIs in the Indian context.

There is also the need for more awareness among women, especially in rural areas of India, regarding menstrual and genital hygiene, STIs and accessing gynecological services. Multiple studies from India have repeatedly pointed out the lack of hygiene among women [7, 8, 10–13, 20] and the very low utilization (31 % of symptomatic rural women sought care) of gynecological services [34] which lead to persistence of RTIs resulting in worsening of any HPV infections that might be present. Adding to the above scenario is the low rates of barrier contraception usage in rural areas of India as is evident from the low usage of condoms (~9 %) [35]. Also, the Indian government has woken a little late with regard to women's health in rural areas. It has been only couple of years that the National Rural Health Mission (NRHM) began the Promotion of Menstrual Hygiene Scheme in India wherein rural adolescent girls are provided sanitary napkins at a price of rupee 1 (~2 cents) [36], a step which might be too little and definitely late, as far as women's health is concerned. Similar steps are also needed for women in urban areas since urban women from low SES might be facing similar issues as rural women.

To conclude, CC, which is still the most common cancer among rural women and second most common cancer among urban women of India, is probably being aided and abetted by the high presence of RTIs. These RTIs persist in an environment of low awareness and lack of hygiene in women, especially in rural areas. In the absence of any population-level screening for CC and lack of adequate steps being taken to increase awareness or hygiene among women, the fight against CC in India is on the back step. The cost of HPV vaccine is quite high to be included as routine immunization, and in the absence of screening services, even HPV vaccination will not be meaningful. We need large primary studies from India, mainly in rural women, regarding the link between RTIs, HPV and CC. More also is needed to be done to improve the status of

Table 5 Unconditional logistic regression analysis depicting adjusted odds ratios (ORs) and 95 % confidence interval (95 % CI) comparing women ($N = 7895$) with and without premalignant lesions of cervix attending the Cancer Detection Centre of the Indian Cancer Society, Delhi, from 2000 to 2012

Variables	OR (95 % CI) ^b	OR (95 % CI) ^c	OR (95 % CI) ^d
Age ^a	0.998 (0.993, 1.004)	0.999 (0.993, 1.004)	0.998 (0.993, 1.004)
Fungal infection	0.89 (0.38, 2.05)	0.82 (0.34, 1.96)	
Candida	1.12 (0.81, 1.55)	1.06 (0.76, 1.49)	
Trichomoniasis	2.94 (2.26, 3.83)	2.79 (2.14, 3.64)	
Coccoid	0.78 (0.51, 1.19)	0.69 (0.45, 1.06)	
Atrophic vaginitis	0.27 (0.19, 0.39)	0.29 (0.20, 0.42)	0.29 (0.20, 0.42)
Erosion	4.84 (1.81, 12.93)	5.08 (1.89, 13.68)	4.91 (1.82, 13.22)
Total infections	1.64 (1.35, 1.99)		1.52 (1.25, 1.86)
Inflammation ^c (non-specific)	3.87 (3.32, 4.52)		

^a Age has been treated as continuous variable in the model^b Unadjusted ORs^c ORs are adjusted for all the variables in this table except total infections and inflammation^d ORs are adjusted for the following variables—age, atrophic vaginitis, erosion and total infections^e Multivariate model with inflammation was not created since it is correlated with all other variables in this table except age

women's health in India to reduce the incidence of CC as well as other reproductive morbidities associated with recurrent and persistent RTIs.

Compliance with Ethical Standards

Conflict of interest None of the authors have any conflicts of interest that might influence this work.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors. Exemption from full ethical review for this secondary analysis was obtained from the Public Health Foundation of India (PHFI) Institutional Ethics Committee (IEC) via letter no. TRC-IEC-184/13.

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