Human Papillomavirus (HPV) Infection in Rural and Tribal Populations of the World with a Special Focus on the Prevalence in India

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Abstract

Human papilloma virus (HPV) infection is one of the major causes of cervical cancer which is one of the common causes of death in women across the globe and is the fourth most prevalent cancer in women representing 7.5% of female cancer deaths globally and more than 85% of these occur in underdeveloped regions. In India, cervical cancer is responsible for the highest cancer deaths among women which can be attributed to multiple pregnancies, open relationships, inadequate sanitation and cleanliness, behavioral habit and lifestyle, smoking, poor nutrition, and long-term contraceptive use. These factors have been associated as risk factors for cervical cancer. This review discusses issues faced by women in tribal and rural areas of India due to poor economic conditions, different lifestyles to mainstream population, sociocultural behavior and lack of access to healthcare facilities. The review also focuses on the tribal populations of the world and the prevalence rates in these tribal groups. The current initiatives taken by government and non-government organizations (NGOs) to prevent and control the HPV infection and reduce the cervical cancer burden have also been highlighted. The review emphasizes the urgent need for preferential care for women in rural and tribal communities of the world.

Keywords: Cervical cancer; HPV; Risk factors; HPV prevalence; tribal; rural; Government initiatives; NGO-initiatives.
Introduction

The population of the world is divided into the urban, rural, and tribal populations. An area is known as the rural sector when the population of that area is less than 5,000, the density of population less than 400 per sq km, and more than 25% males are engaged in agricultural areas. The tribal population accounts for 5% of the global population [1] and about 19.3% of the global population lives in rural areas [2]. India is a diverse country that has 29 States and 7 Union Territories. The current population of India according to the 2019 Census is 1.37 billion, out of which 70 percent lives in a rural area [3,4]. India is home to a large tribal population which is approximately 8.6% of the Indian population and about 65% people live in rural areas whereas 35% people live in the urban area [5].

One of the common causes of death across the globe is cervical cancer. It is the fourth most prevalent cancer in women representing 7.5% of female cancer deaths globally with more than 85% of these occurring in underdeveloped regions [6]. About 20% of cancer deaths are caused due to Human papilloma virus (HPV) infection and it is a common cause of death for women belonging to Eastern, Middle, and Western Africa, Central America and South East Asia [7]. In India, cervical cancer is responsible for highest cancer deaths among women in rural areas.

Risk factors of cervical cancer

The common risk factors for HPV infection are age, multiple sexual partners, multiple pregnancies, poor sanitation and hygiene, underlying infectious diseases, smoking, poor diet and long-term use of oral contraceptives [8,9].

These factors are particularly more common in the rural and tribal belts of India.

Multiple pregnancies

Some tribal communities live in open relationships and in addition women are prone to having successive pregnancies in a year, which leads to higher parity, abortions, poor health, and susceptibility to infections. In a study conducted among the tribal adolescent girls of different tribes from three different states of India–Madhya Pradesh (Hoshangabad), Chhattisgarh (Narainpur and Kondagaon) and Jharkhand (Jamshedpur); it was found that they have persistent HPV infection due to several factors among which multiple pregnancies were also a major factor [8,10].

Age is another important risk factor. In many tribal communities, women become sexually active at a very early age of 10-12 years. It has been observed that women in their late teens and mid-30s are more prone to cervical cancer. Due to lack of education and poor awareness, researchers propose that engaging in sexual activity at a young age makes the cervix highly vulnerable to HPV infection as a result of the changes during puberty [11,12]. Women who undergo full-time pregnancy at a very young age are more susceptible to cervical cancer [8]. A study carried out in different tribal areas of Madhya Pradesh, Jharkhand, and Chhattisgarh, reported that the mean age of women getting married was
18.1 years, and 43% of women became sexually active before the age of 18 [10].

**Multiple partners**

It has been seen that some of the tribal communities mostly live in open relationships with multiple partners in preference to the traditional one partner marriage system, which increases their risk of acquiring HPV infection [10]. According to the study by Peedicayil et al in 2016, out of 809 women who took part in the study, 0.7% of them had multiple partners and 3% of them had used oral contraceptives [13]. A higher HPV prevalence rate has been observed in women with gynecological symptoms increasing their risk of developing cervical cancer [14].

**Poor sanitation and hygiene**

Due to poor economic conditions and decreased awareness, women in rural and tribal areas usually lack resources and information to maintain sexual hygiene particularly during menstruation. This makes them vulnerable to poor sexual health and prone to sexually transmitted infections, like HPV leading to increased risk of cervical cancer [9,15]. In a study conducted across the tribal areas of Chhattisgarh, Madhya Pradesh, Jharkhand, it was observed that most of the women who were tested positive for HPV infection had very poor sanitation and hygiene particularly during the time of menstruation, repeated use old cloth pieces along with cow dung ash and other unhygienic materials in their sanitary pad during menstrual period making them more susceptible to cervical cancer [10,16,17].

**Behavioral pattern and lifestyle**

The prevalence of HPV in any area of inhabitation depends on the lifestyle and behavior of the inhabitants to a large extent. People living in tribal areas often live in remote areas with lack contact with the outside world [10]. Most of the rural and tribal areas in India lack health care facilities because they live in secluded and remote areas. In addition, they are less likely to access medical care due to their beliefs and prefer natural products procured locally for treatment [9,15]. Increased susceptibility to diseases such as tuberculosis, pneumonia, malaria, anemia and poor immune system are reported in the tribal areas of Madhya Pradesh, Jharkhand, and Chhattisgarh. Chlamydia infection is a kind of bacterial infection in the reproductive tract, which helps the HPV to thrive on the cervix, leading to a higher risk of cervical cancer [9,10,18,19].

**Smoking**

In rural areas, consumption of tobacco in different forms is very common among men and women. It has been observed that women who smoke are more prone to cervical cancer than non-smokers. Smoking tobacco and other such substances damage the DNA of the cervix and lower the immunity to fight HPV infection [19]. According, to a study conducted among tribal people, people in these areas consume a lot of locally fermented beverages called mahua and tadi which contain toxic chemicals and hence, maybe the reason for high HPV prevalence in this region [18].
Poor diet

Due to poor economic conditions in the tribal areas, there is lack of nutritious food specially required by women during pregnancy and childbirth which may cause anemia, malnutrition and weight loss in women and could be linked to high prevalence of HPV infection [10].

Long term use of oral contraceptives

Oral contraceptives are the hormonal medications taken to prevent pregnancy. Various studies show that women using oral contraceptives for 5 or more years are more prone to cervical cancer, as these pills induce a change in susceptibility of cervical cells and result in persistent infection [20]. Moreover, prolonged use of intrauterine contraceptive devices can lead to actinomycosis, pelvic inflammatory disease and subsequent possible malignancies [21]. However, Indian tribal women have been reported to have no or very limited knowledge about oral contraception and the use of contraceptive methods is also very limited [22].

HPV prevalence in tribal population

There are limited studies carried out to determine the HPV infection prevalence in tribal population in India and on a global level. Some major tribes/tribal groups of India and different continents are listed in Table 1 and Table 2 respectively.

<table>
<thead>
<tr>
<th>Indian States</th>
<th>Tribe/ Tribal Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andhra Pradesh</td>
<td>Nakkala, Kurvikaran, Kondhs, Kodi, Kodhu, Desaya Kondhs, Dongria Kondhs, Kottiya Kondhs, Tikiria Kondhs, Yenity Kondhs, Kuvinga, Porja, Parangiperja</td>
</tr>
<tr>
<td>Arunachala Pradesh</td>
<td>Sulung Bangni, Sulung, Laju, Havi Tangsa, Liju Nocte, Lish Monpa</td>
</tr>
<tr>
<td>Assam</td>
<td>Syntheg, Chakma</td>
</tr>
<tr>
<td>Andaman &amp; Nicobar Islands</td>
<td>Jarawas, Sentinelese, Shom Pens</td>
</tr>
<tr>
<td>Bihar</td>
<td>Banjara, Birhor, Parhayia, Korwa, Kora, Mudi-kora</td>
</tr>
<tr>
<td>Chhattisgarh</td>
<td>Saonta, Saunta</td>
</tr>
<tr>
<td>Dadra &amp; Nagar Haveli</td>
<td>Naikda or Nayaka, Kathodi</td>
</tr>
<tr>
<td>Jammu &amp; Kashmir</td>
<td>Bakarwal</td>
</tr>
<tr>
<td>Jharkhand</td>
<td>Parhaiya, Birhor, Savar, Baiga, Korwa</td>
</tr>
<tr>
<td>Kerala</td>
<td>Cholanaickan</td>
</tr>
<tr>
<td>Odisha</td>
<td>Mankirdia, Mankria, Mankidi, Koya, Gumba Koya, Koitur Koya, Kamar Koya, Musara Koya, Dharua, Dhuruba, Dhurva, Korua, Parenqa, Didayi, Didai Paroja, Didai, Bondo Poraja, Bonda Paroja, Banda Paroja, Paroja, Parja, Bodo Paroja, Barong Jhodia Paroja, Chhelia Paroja, Jhodia Paroja, Konda Paroja, Paraja, Ponga Paroja, Soda Paroja, Sano Paroja, Solia Paroja, Gandia, Omanaty, Omanatyo, Amanaty, Amanaty</td>
</tr>
<tr>
<td>Rajasthan</td>
<td>Garasia(except Rajput in that region), Kathodi, Katkari, Dhor Kathodi, Dhor Kathodi, Katkari, Son Kathodi, Son Katkari</td>
</tr>
<tr>
<td>Uttar Pradesh</td>
<td>Agariya, Baiga, Saharya, Raji</td>
</tr>
<tr>
<td>West Bengal</td>
<td>Gorait</td>
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Table 1: Tribes in each state of India [23].


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Cervical cancer is one of the most common cancers in women in India especially in rural and tribal areas, where the HPV infection is increasing at an alarming rate. However, the HPV prevalence and incidence studies reported in rural and tribal populations of India are limited. In India, the initial reports of the incidence of cervical cancer were reported from the rural areas of Barshi in Maharashtra in 1987 [28]. Other rural areas affected in the state of Maharashtra included Paranda and Bhum Tahsils [28]. In 2007, rural areas of Ahmedabad and Gujrat were reported to be affected by cervical cancer. About 700 different cases were reported from Ratnagiri district in Mumbai in 2009. In the following years, several rural areas such as Sevagram, Konkan in Maharashtra reported the incidence of cervical cancer [29]. In Aizawl district of Mizoram, the prevalence of HPV virus was reported to be 15.94% and 11.08% in rural areas of Meghalaya [30]. A population-based study was conducted in the tribal areas of southern coastal Karnataka, reported a higher prevalence of HPV infection among tribal women (40.6%) than general population (14.3%) [31]. HPV infection with type 16 type was found in indigenous Nicobarese tribe, in Andaman and Nicobar Islands, with a prevalence of 2.3% [32]. In rural areas of West Bengal, a higher prevalence of risk factors related to cervical cancer was reported by Gupta et al, (2012). The prevalence of HPV 16 and 18 in rural areas of eastern India was found to be 7.5% and 9.6% respectively [33]. A study carried out by Sharma et al. (2015) in tribal areas of three Indian states: Madhya Pradesh, Jharkhand and Chhattisgarh reported 12.9% overall prevalence of HPV infection in tribal girls of these regions with more than 65% of them infected with HR-HPV types predominantly HPV16 indicating. The study reported a very high prevalence of HPV infection in adolescent and young adult tribal girls possibly due to different socio-sexual behavior, indicating a serious health

<table>
<thead>
<tr>
<th>Continent</th>
<th>Tribe/ Tribal Groups</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>Veddas (Sri Lanka), Jarawa (Andaman Islands, India), Naga (north-eastern India and north-western Myanmar), Lhop (northwest Bhutan), Bodo (Nepal), Giraavaru (Maldives). Burmans, Karen, Shan, Rakhine, Karenri, Chin, Kachin and Mon (Burma/Myanmar) Tibetans, Uighurs (China), Ainu, Okinawans (Japan), Orang asli (Malaysia), Igorot, Lumad, Mangyan (Philippines)</td>
<td>[24]</td>
</tr>
<tr>
<td>Africa</td>
<td>Zulu (South Africa), Maasai (East Africa), San Bushmen (Western Botswana and Makgadikgadi), Yoruba (Nigeria and Southern Benin), Xhosa (Eastern-Cape-Province of South Africa), Hausa (West Africa), Himba (Northern Namibia), Oromo (southern parts of Ethiopia, Northern Kenya, some parts of Somalia), Kalenjin (Western highlands of Kenya), Chaga (Tanzania)</td>
<td>[25]</td>
</tr>
<tr>
<td>Europe</td>
<td>Saami (Scandinavia and Russia)</td>
<td>[26]</td>
</tr>
<tr>
<td>South America</td>
<td>Mapuche, Kolla, Toba, Guarani, Wichi, Mocovi, Haurpe, Comechingen, Tehuelche, Charrua, Pilaga (Argentina), Quechua, Aymara, Chiquitano, Mojeno (Bolivia), Atacama (Chile), Awa, Chachi, Tsachila (Ecuador), Wayuu, Pemon, Warao (Venezuela)</td>
<td>[27]</td>
</tr>
<tr>
<td>North America</td>
<td>Alaska natives, Pacific islands American (United States), Nahua Mazahua, Otomi, Mixtecs (Mexico)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Tribal groups present in different continents of the world.
concern for Indian tribal women. Apart from India, cervical cancer is the second most common cancer after breast cancer to affect women aged 15–44 years in the European Union with 33,000 cases of cervical cancer and 15,000 deaths each year [34]. It is twice as high in Latin America compared with the worldwide average and is associated with 68,220 new cases of cervical cancer per year with incidence rates ranging from 20 to 80 per 100,000 women and 31,712 cervical cancer-associated deaths occur each year [35]. The incident rates of HPV in sub-Saharan Africa are very high, especially in Abuja, Nigeria, (with HPV prevalence of 37%), where the proportion of HPV positive women is same in all groups, from 10 years to 65 years of age (or more) [36,37]. The higher HPV rate was due to the high tobacco use, lack of cervical cancer screening, and unattended precancerous lesions [38]. The sub-Saharan Africa regions of Guinea, Zambia, Tanzania, Malawi, and Mozambique are affected by high incidences of invasive cervical cancer and HPV appears to be more common among women with normal cytology than in more developed parts of the world, with a prevalence of 24 percent on average [39]. According to the WHO report, the rate of cervical cancer is found to be higher in Eswatini, followed by Malawi in regions of sub-Saharan Africa [40]. It was due to the lack of technical, infrastructural, financial and human resources needed for the cytological screening of HPV and the method of Visual Inspection using acetic acid (VIA) used for cytological screening due to low income, resulting in higher HPV [41]. The main reason for this difference in incidence rates is the effective implementation of HPV screenings and vaccination programs by the developed countries compared to developing countries [42]. Table 3 lists the major studies carried out in the rural and tribal populations of the world.

<table>
<thead>
<tr>
<th>Continents/ Countries</th>
<th>Tribe/ Tribal Groups</th>
<th>Prevalence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Southeast Asia</td>
<td>Tibetan group, Hani women (China)</td>
<td>14%</td>
<td>[43]</td>
</tr>
<tr>
<td>South America</td>
<td>Guarani (Argentina)</td>
<td>64%</td>
<td>[44]</td>
</tr>
<tr>
<td>Tanzania (Eastern-Africa)</td>
<td>Mwanza</td>
<td>11.60%</td>
<td>[45]</td>
</tr>
<tr>
<td>Europe</td>
<td>North Sami (sami group) (Finland)</td>
<td>21%</td>
<td>[43,46]</td>
</tr>
<tr>
<td>Latin America</td>
<td>Alaska Native tribal women</td>
<td>16%</td>
<td>[43,47]</td>
</tr>
</tbody>
</table>

**Table 3: Prevalence of HPV in different continents/ countries**

**Government and Non-Government initiatives**

The government of India has developed specific programs and initiatives to screen and manage the increasing rate of HPV infection among rural and tribal women in India to reduce the cervical cancer burden in this population. Indian Council of Medical Research (ICMR) established the National Cancer Registry program, which acts as a surveillance system for cancer and collects information about the cancer prevalence from various rural and urban registries [48]. This provides the map for designing and implementing screening and management programs effectively. Another committee that works on the cancer control is the Indian Academy of Pediatrics committee. Its purpose is to raise awareness, educate patients and parents on HPV infection and risk of cervical cancer and sensitizing pediatricians to play an active role in cervical cancer prevention program [49]. The three prophylactic vaccines: quadrivalent HPV vaccine, bivalent HPV vaccine, and the monovalent HPV
vaccines are available commercially are for the prevention of HPV infection against HPV genotypes 16,18,6 and 11 [50]. Gardasil, Gardasil 9, and Cervarix are used for the prevention of HPV infection from HPV genotypes 16 and 18. Apart from these HPV genotypes, Gardasil prevents infection caused by HPV 6 and 11, which is responsible for 90% of genital warts. Gardasil 9 prevents HPV 31,33,45,52, and 58 besides 6,11,16, and 18 [51,52]. In India, Gardasil was the first HPV vaccine approved for use in 2006 [53]. HPV vaccination is recommended for women from 9 to 26 years before the onset of any sexual activity [54]. However, these vaccines provide protection for only certain HPV types but not all [54]. Also, some side effects like pain, redness, or swelling in the arm where the shot was given and fever, dizziness, nausea, headache or feeling tired, muscle or joint pain have been reported after the vaccination.

In India, the National Technical Advisory Group on Immunization recommended the HPV vaccine for young women to be included in the National Immunization Program [55] to ensure easy access and affordability for the economically and socially deprived sections of the society. However, factors like high vaccine costs, duration of vaccine use, vaccine acceptance, and disease prioritization have prevented the vaccine to become a part of the National Immunization Program [56]. For a mass HPV vaccination program, affordability and accessibility are of major concern and for region-specific issues; a cost-effective second-generation vaccine may be needed [17]. WHO recommends that HPV vaccination must be included in the National Immunization Program and the operational difficulties can be discovered only after the true implementation of these vaccines in India [57]. Some of the states in India have initiated HPV screening and vaccination programs. Delhi was the first state in India to launch free HPV vaccination as a part of the Public Health Program for girls of the age of 11-13 years at Delhi State Cancer Institute through its framework in the east and west regions of Delhi [58], WHO has supported the Government of Punjab (Bhatinda) for HPV vaccination programme in 2016 [59]. In 2009, a vaccination trial for cervical cancer was conducted by Andhra Pradesh Minister for Health and Family Welfare in collaboration with ICMR and PATH, a non-profit organization in the USA in Khammam district. A similar project was also launched by the Gujrat government in Vadodara district. Most of the vaccinated girls belonged to the tribal communities whose parents were agricultural laborers [60]. However, this trial was suspended by the state governments when six deaths of young girls were reported in the weeks following the vaccination. It was later discovered that the reason for their death was due to other factors unrelated to the HPV vaccine, such as poisoning, drowning, malaria, or snakebite [55]. Various non-governmental organizations (NGOs) like Biocon Foundation and SAMA work to spread awareness about HPV infection and its vaccination. Biocon Foundation provides Pap smears tests to economically poor communities in India and it conducted its first test in Karnataka in 2016. Since then, it has been successful in screening more than 3000 women in India [55]. SAMA is a research group that works for the health and welfare of women. In 2010, SAMA reported the side
effects of the HPV vaccine given to young girls, which included cramps, heavy bleeding, and early onset of menstruation [53].

To encourage the research into HPV, the National Institutes of Health, USA and National Cancer Institutes, UK provides grants and funds to enhance the healthcare delivery system and studies its characteristics [8].

Many countries across the world have introduced HPV vaccination in their National Immunization Program, including Australia, Canada, USA, and various other European countries [61]. In 2007, Australia commenced the National HPV vaccination program and National HPV vaccination Register (NHPVR) that delivers HPV vaccine to young girls and monitors and reports the coverage of HPV vaccine [62]. Along with it, the National Cervical Screening Program was also introduced by the Australian government to review cervical screening in different areas [63]. In European countries, the Council of the European Union recommends that the screening programs for cervical cancer are implemented using a systematic population-based approach with quality assurance at all appropriate levels and the test to be used should be the pap test with age groups not less than 20 and not more than 30 [64]. In the United States, the Advisory Committee on Immunization Practices recommends that all the young girls (between age groups of 11-12) should receive the HPV vaccine [61]. Following this, the Cervical Cancer Prevention Act was also introduced which proposed that girls should be given HPV vaccination as soon as enter seventh grade of their school [65].

The Government schemes and initiative can have both positive and negative impact on people worldwide. The prophylactic vaccines for HPV have met with mixed acceptance globally. However, policy-level interventions have been effective in increasing public health benefit. Government policies and mandates may result in improved HPV vaccination coverage and reduced disease burden and alternative policies that improve unhindered access to HPV vaccination may allow success as well [65]. The HPV vaccines have been licensed almost in all the countries across the globe. More than 80 countries have introduced HPV vaccine in the National Immunization Programs. In most programs, a school-based approach is used to deliver the vaccine to the targeted adolescents with additional efforts using field clinics, and primary health centers to cover girls who missed vaccination and do not attend schools [59,66].

**Conclusion**

The review highlights the status of HPV prevalence in rural and tribal areas of India and at global level. Most of the tribal populations of the world live in secluded and inaccessible areas and follow more open sexual relationships with women becoming sexually activity early, after menarche; and have multiple sexual partners and are multiparous. As these population groups are located in distant areas and are economically deprived, they have limited access to healthcare facilities and may follow different
social norms and religious beliefs which is compounded by poverty, illiteracy, ignorance, hostile environment, poor sanitation, lack of safe drinking water, blind beliefs and prejudices particularly in developing and underdeveloped countries. As the economic and socio-cultural milieu of this population is different; the women are at an increased risk of HPV infection. In order to improve the health and reduce mortality in women in these rural and tribal areas, government organizations should adopt rigorous measures to create awareness and promote screening by setting up awareness workshops and screening camps about HPV infection and cervical cancer and the importance of maintaining good sexual health and hygiene. The government should develop policies to ensure the screening and vaccination of adolescent girls and young women in these areas and also improve the health care facilities in the rural and tribal areas of the country. The government organizations can support and work along with non-governmental organizations and NGOs to promote the awareness and help reduce cancer burden in rural and tribal women.

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