



## Original Article

# High-risk Human Papillomavirus Infection among Urban and Rural Women in Bangladesh



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### Abstract

**Background and objectives:** The government of Bangladesh adopted visual inspection of the cervix with acetic acid method for cervical cancer screening in the majority of the district and sub-district hospitals. Before alternative screening methods are adopted, the prevalence of high-risk human papillomavirus (HPV) genotypes among various geographical regions must be determined. Therefore, we aimed to determine the prevalence of high-risk HPV genotypes in urban and rural areas of Bangladesh.

**Methods:** This cross-sectional study was carried out at Bangabandhu Sheikh Mujib Medical University, Dhaka from July 2021 to June 2022. Using a multistage sampling method, cervical samples (N = 3,856) were collected from women aged 30–49 years attending visual inspection of the cervix with acetic acid at 16 centers (eight districts and eight sub-districts). HPV tests were performed by real-time PCR amplification. Descriptive analysis and Chi-square test/Fisher's exact test were performed for associations, and a *P* value <0.05 was considered significant.

**Results:** Among the 3,856 women, the overall prevalence of high-risk HPV was 3.6%, with 49 (1.3%) women testing positive for HPV16, 12 (0.3%) women testing positive for HPV18, and 65 (1.7%) testing positive for other high-risk HPV genotypes. There was a significant variation in the prevalence of high-risk HPV among the divisions (*P* = 0.001), with the highest infection rate (7.1%) observed among women in rural Sylhet and the lowest in rural Mymensingh (0.5%). No significant difference in high-risk HPV prevalence was found between the urban and rural women, except in Mymensingh.

**Conclusions:** The low prevalence of high-risk HPV (3.6%) among Bangladeshi women with regional variation should be considered by policymakers during the development of cervical cancer prevention policies.

### Introduction

In Bangladesh, cervical cancer (CC) is the 2nd leading female can-

cer, with about 8,268 new cases and 4,971 deaths reported in 2020 (Cancer Today (iarc.fr)). The Government of Bangladesh (GOB) has adopted the visual inspection of the cervix with acetic acid (VIA) method in all district hospitals (DHs) and the majority of the sub-district hospitals, performed by trained senior staff nurses, family welfare visitors, paramedic staff and doctors.<sup>1–4</sup> Visual methods are based on interpretations by performers and are related to wide interobserver differences, and the low specificity of VIA is an important concern.<sup>5–7</sup> Human papillomavirus (HPV) testing is a more objective test, and its use in primary screening has been established for CC prevention through a number of innovative studies.<sup>8–10</sup> Many countries are adopting the HPV test (with genotyping) for primary screening due to its better sensitivity and high negative predictive value. To achieve WHO-specified country targets for the prevention of HPV infection by 2030 (B144 28-en.pdf (who.int)), the GOB may plan to introduce the HPV DNA test (with genotyping) for primary screening. Before alternative

**Keywords:** Cervical cancer screening; HR-HPV prevalence; Bangladesh; HR-HPV in Bangladesh; HR-HPV in urban areas; HR-HPV in rural areas.

**Abbreviations:** BSMMU, Bangabandhu Sheikh Mujib Medical University; CC, Cervical cancer; DH, District hospital; GOB, Government of Bangladesh; HPV, Human papillomavirus; HR, High-risk; LMIC, Low and middle-income countries; MOHFW, Ministry of health and family welfare; PCR, Polymerase chain reaction; VIA, visual inspection of the cervix with acetic acid.

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screening methods are adopted, the GOB needs to modify the already adopted VIA-based national strategy (BGD\_B5\_s21\_National Strategy cervical ca prevention and control Bd 2017-2022. pdf (iccp-portal.org)). The global prevalence of HPV infection in women with normal cytology is around 11–12%, with a prevalence of 24% in Sub-Saharan Africa, 21% in Eastern Europe, 14% in Southeast Asia and 7.1% in Southern Asia.<sup>11</sup> Although the HPV prevalence in South-Eastern Asia and Southern Asia is known, information on the distribution of high-risk (HR) genotypes in various geographical regions in Bangladesh is necessary before adopting alternative screening methods. The objective of this cross-sectional study was to determine the prevalence of HR-HPV genotypes among urban and rural women in eight districts in eight divisions of Bangladesh.

## Materials and methods

### Study design

This cross-sectional study was carried out at the National Centre of Cervical and Breast Cancer Screening and Training of the Bangabandhu Sheikh Mujib Medical University (BSMMU) from July 2021 to June 2022. Ethical clearance for this research was obtained from the Institutional Review Board of BSMMU (IRB no. BSMMU/2021/474, 12.04.21).

### Study areas and selection of women

A multistage sampling method was used to select the study areas. Initially, eight districts were selected by simple random sampling from eight administrative divisions of Bangladesh. The residents within a 5-kilometer radius of the district hospitals were considered the urban population. Women residing within the sub-districts were considered the rural population. All eight district hospital CC screening centers were purposively selected to recruit urban population. Then, one sub-district hospital screening center from each of the eight districts was selected by simple random sampling to recruit rural population. [Figure 1](#) shows the geographical locations of the study areas in eight divisions of Bangladesh. Ever-married women aged 30–49 years attending selected screening centers were recruited purposively for data collection after counselling (N = 3,856). Pregnant women and those with a previous history of treatment for cervical disease were excluded.

### Cervical sample collection

HPV DNA specimens were collected prior to the VIA test using a cervical sampler by trained nurses/doctors and suspended in a vial of preservative (Cobas PCR collection media) for transport to the laboratory. Specimens were transported as soon as possible to BSMMU or stored in a freezer (4°C) at hospitals or at room temperature (<30°C) until transfer.

### HPV DNA detection and genotyping

HPV DNA detection and genotyping was performed using the Cobas 4800 HPV test (Roche Diagnostics, GmbH, and Mannheim, Germany), a qualitative testing device for the detection of HPV DNA. This test amplifies target DNA in cervical epithelial cells by PCR and nucleic acid hybridization to detect 14 HR-HPV types. This assay allows specific identification of HPV types 16 and 18 and pooled detection of HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.<sup>12</sup> The human beta-globulin-oriented fluorescent probe provided quality control for the whole reaction.

### Data analysis plan

The data were assessed for completeness, accuracy and consistency before analysis. Continuous variables were summarized using means and standard deviations. Categorical variables were summarized using frequency distributions. Associations between categorical variables were assessed by Chi-square test or Fisher's exact test. A *P* value of <0.05 was considered to indicate a statistically significant difference. The data analysis was performed using SPSS version 23.0.

## Results

### Socio-demographic and reproductive characteristics

Among the 3,856 women screened, 1,748 (45.3%) were from urban areas, and 2,108 (54.7%) were from rural areas. The mean age at marriage was 15.8 (±2.3) years, and the mean age at the 1st delivery was 17.9 (±2.8) years for the total population. A significant variation in monthly family income was observed among urban and rural participants. A significantly higher number of women (*P* value = 0.007) and husbands (*P* value = 0.001) in rural areas were married more than once compared to those in urban areas ([Table 1](#)).

### HR-HPV genotyping among women

Among the 3,856 asymptomatic women tested for HR-HPV, 138 (3.6%) women were HR-HPV positive. When considering single infections, among the 138 HR-HPV positive women, HPV 16 (49, 35.5%) was the most prevalent genotype, followed by HPV 18 (12, 8.7%). Another 10 (7.2%) women had HPV 16 infection as co-infection with HPV 18 or 'Other HR-HPV'. Other HR-HPV infections (65, 47.1%) were also quite common ([Fig. 2](#)).

### Distribution of HR-HPV positivity and genotypes among different divisions

[Table 2](#) and [Figure 3](#) show the division-wise distribution of overall HR-HPV infection. Almost an equal number of women were from urban and rural areas in different districts. The highest percentage of women with HR-HPV infection was in the Sylhet division (6.4%), and the lowest was in the Rajshahi division (1.7%). The HR-HPV infection rate was also high in the Barishal (5.0%) and Chittagong (4.6%) divisions. This study showed significant regional variation in overall HR-HPV prevalence among the divisions (*P* < 0.001).

[Figure 4](#) shows the division-wise distribution of overall HR-HPV infection in both urban and rural areas. Among women who had undergone HR-HPV DNA testing, 7.1% of women in rural Sylhet had the highest incidence of HR-HPV infection. In urban areas, women in the Chittagong (5.9%) division had the highest incidence of HR-HPV infection, followed by those in the Barishal (5.5%) and Sylhet (5.3%) divisions. Overall, no significant difference in HR-HPV infection distribution was found between urban and rural women (*P* = 0.9).

However, when considering urban and rural areas within each division separately, a significant difference in HR-HPV infection (*P* = 0.007) was found among women in the Mymensingh district ([Table 3](#)).

[Table 4](#) shows the division-wise distribution of HR-HPV genotypes. Among the 138 women positive for HR-HPV DNA test, the prevalence of HPV16 infection was highest in Sylhet division (2.6%), followed by the Barishal (1.8%) and Dhaka (1.7%) divisions. The prevalence of other HR-HPV infections was highest

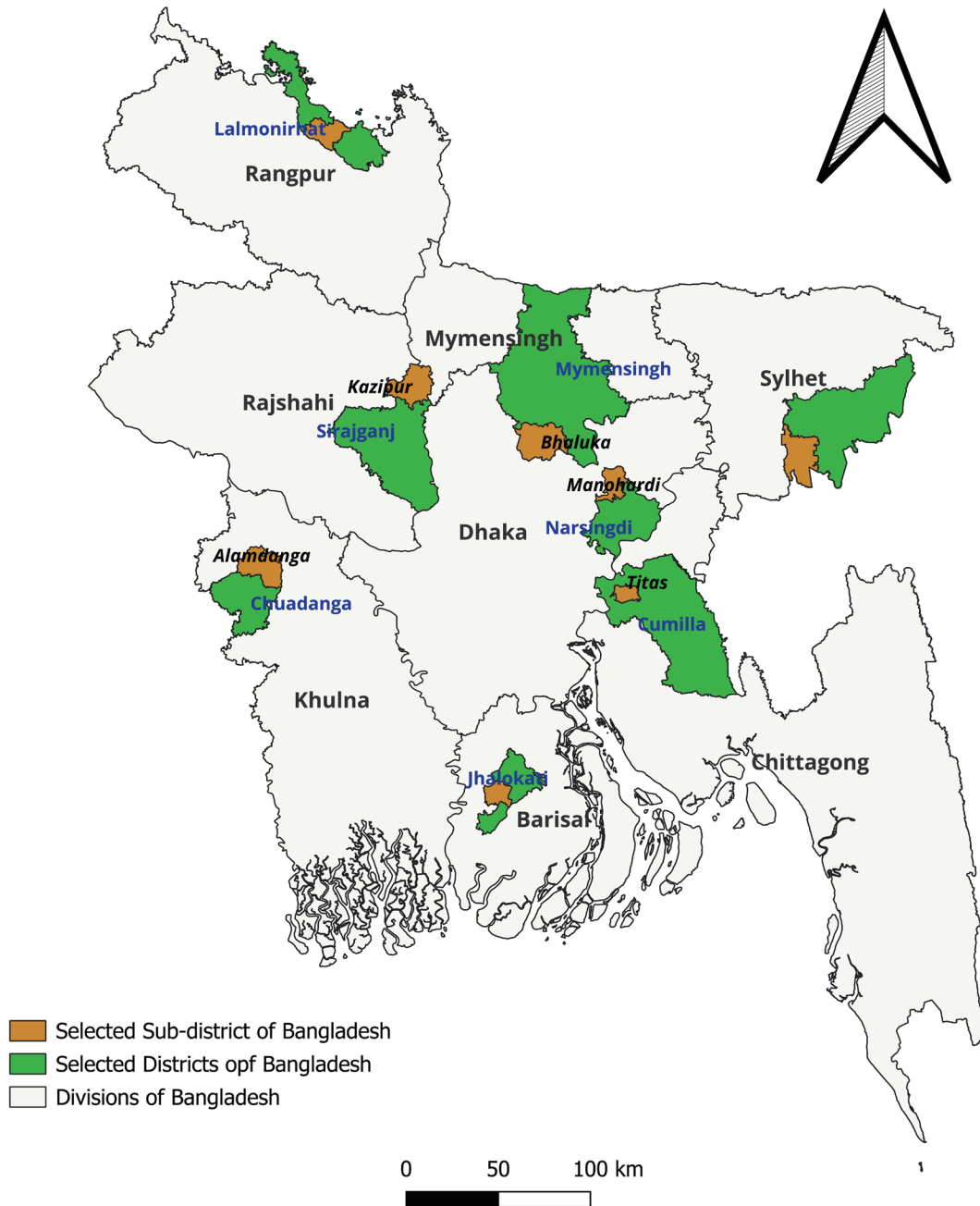


Fig. 1. Map showed the geographical location of the study areas in eight divisions of Bangladesh.

in Sylhet (13, 2.9%), followed by the Chittagong division (14, 2.8%).

**Association of viral infections with risk factors**

Figure 5 shows that the proportion of patients with HR-HPV infection was higher among the 35–39 years age group in comparison to other age groups, and this gradually decreased with age in both urban and rural areas. In rural areas, there was a continuous 2<sup>nd</sup> rise of HR-HPV infection from 40 years onwards.

Table 5 shows that age group, education level, occupation, monthly family income, parity, age of marriage, and age of the

first delivery did not show significant effect on HR-HPV infection among women.

**Discussion**

This cross-sectional study demonstrated the prevalence and distribution of HR-HPV genotypes among urban and rural Bangladeshi populations in selected eight districts of eight divisions. The overall HR-HPV infection rate (3.6%) among women aged 30–49 years was relatively low, and a similar finding (4.2%) was observed in a population-based study in the Dhaka division.<sup>13</sup> The HR-HPV

**Table 1. Distribution of the study population by socio-demographic characteristics (n = 3,856)**

| Characteristics                | Rural        | Urban        | P value <sup>a</sup> |
|--------------------------------|--------------|--------------|----------------------|
| Age of Women                   | No. (%)      | No. (%)      | <0.001               |
| 30–34 years                    | 561 (26.6)   | 486 (27.8)   |                      |
| 35–39 years                    | 782 (37.1)   | 542 (31.0)   |                      |
| 40–44 years                    | 432 (20.5)   | 441 (25.2)   |                      |
| 45–49 years                    | 333 (15.8)   | 279 (16.0)   |                      |
| Education of women             |              |              |                      |
| Not educated                   | 881 (41.8)   | 799 (45.7)   | 0.141                |
| Up Primary                     | 890 (42.2)   | 696 (39.8)   |                      |
| SSC                            | 198 (9.4)    | 140 (8.0)    |                      |
| HSC                            | 120 (5.7)    | 96 (5.5)     |                      |
| Graduate & above               | 19 (0.9)     | 17 (1.0)     |                      |
| Occupation of the Women        |              |              |                      |
| Housewife                      | 2,101 (99.7) | 1,742 (99.7) | 0.952                |
| Service Holder                 | 7 (0.3)      | 6 (0.3)      |                      |
| Occupation of the Husband      |              |              |                      |
| Farming                        | 1,417 (67.2) | 1,107 (63.3) | 0.041                |
| Service Holder                 | 170 (8.1)    | 180 (10.3)   |                      |
| Business                       | 314 (14.9)   | 295 (16.9)   |                      |
| Living abroad                  | 114 (5.4)    | 74 (4.2)     |                      |
| Driver                         | 44 (2.1)     | 42 (2.4)     |                      |
| Others                         | 21 (1.0)     | 25 (1.4)     |                      |
| Not alive                      | 28 (1.3)     | 25 (1.4)     |                      |
| Religion of the women          |              |              |                      |
| Muslim                         | 1,936 (91.8) | 1,632 (93.4) | 0.158                |
| Hindu                          | 169 (8.0)    | 116 (6.6)    |                      |
| Buddhist                       | 3 (0.1)      | 0 (0.0)      |                      |
| Monthly family income          |              |              |                      |
| Up to 5,000                    | 1,036 (49.1) | 756 (43.2)   | 0.003                |
| Taka 5,001–10,000              | 750 (35.6)   | 710 (40.6)   |                      |
| Taka 10,001–20,000             | 172 (8.2)    | 135 (7.7)    |                      |
| Taka 20,001–50,000             | 147 (7.0)    | 144 (8.2)    |                      |
| Taka 50,001 and above          | 3 (0.1)      | 3 (0.2)      |                      |
| Number of Marriages of Women   |              |              |                      |
| One                            | 2,085 (98.9) | 1,742 (99.7) | 0.007                |
| More than one                  | 23 (1.1)     | 6 (0.3)      |                      |
| Number of Marriages of Husband |              |              |                      |
| One                            | 2,090 (99.1) | 1,746 (99.9) | 0.001                |
| More than one                  | 18 (0.9)     | 2 (0.1)      |                      |

Low class = ≤ 6,827 BDT and middle class = 6,828–2,6852 BDT (World Bank and UNDP, 2016). <sup>a</sup>Pearson chi-square test was performed.

prevalence in Punjab (1.5%) and Karachi (0.7%) of Pakistan showed an even lower prevalence.<sup>14,15</sup> Suburban areas of Thailand (5.6%), Vietnam (9.5%), North India (8.2%), Andhra Pradesh of India (10.3%), Southern India (12.5%), and China (12.1%) had

relatively higher prevalence of HR-HPV.<sup>16–21</sup> The prevalence of HR-HPV in Kolkata, India (5.8%) was comparatively lower than in other parts of India and close to the prevalence observed in the present research.<sup>22</sup> This may be related to the geographical, cul-

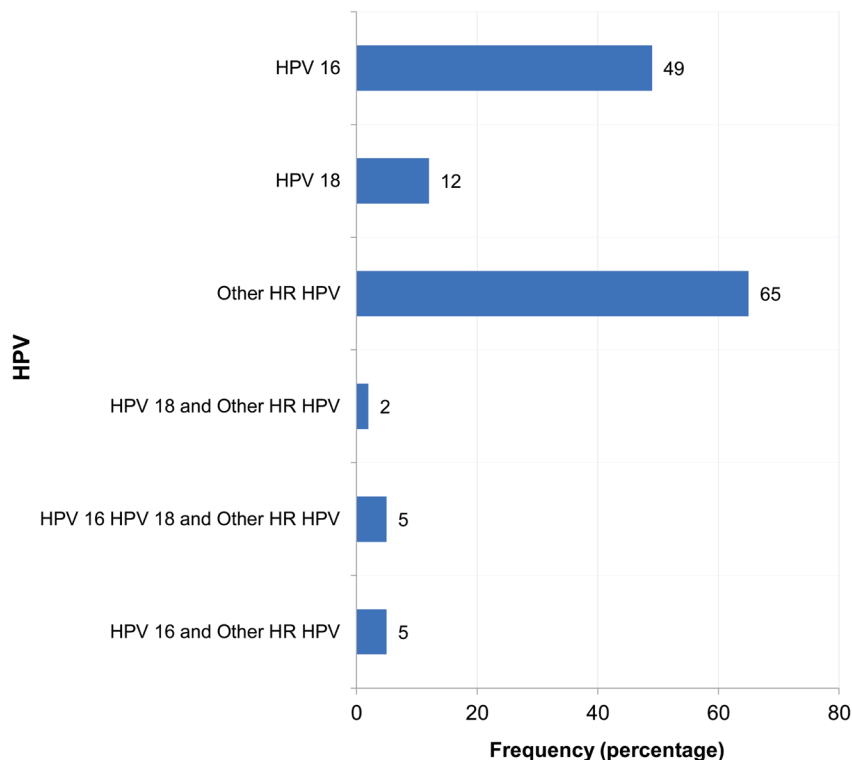


Fig. 2. HR-HPV (high-risk human papillomavirus) genotypes among women with positive screening results (n = 138).

tural and behavioral similarities between Kolkata and Bangladesh. Therefore, the prevalence of HR-HPV infection may vary from country to country, and in the majority of Asian countries, including Bangladesh, the HR-HPV prevalence is relatively lower than that in Western countries (13.7%–28.3%).<sup>23–25</sup>

Even though Bangladesh is a small country, significant regional variation of HR-HPV prevalence was observed among different divisions ( $P < 0.001$ ). Sylhet (6.4%), Barishal (5.0%), and Chittagong (4.6%) divisions had higher prevalence of HR-HPV and Rajshahi (1.7%) had the lowest infection rate. Sylhet, Barishal, and Chittagong divisions need more attention during the formulation of larger population-based implementation research. Regional

variation of HR-HPV prevalence within the country was observed in Thailand between Lampang (9.1%) and Songkla (3.9%),<sup>26</sup> in India between North India (8.2%) and Andhra Pradesh (10.3%),<sup>18,19</sup> in China between Xinjiang (9.7%),<sup>27</sup> Han (11.5%) and Mongolia (32.6%).<sup>28</sup>

In this study, HPV 16 (35.5%) was the most prevalent single infection among HR-HPV positive cases, followed by HPV 18 (8.7%). Another study in Bangladesh revealed a similar prevalence of HPV 16 (28.7%).<sup>13</sup> In Vietnam, the prevalence of HPV 16 (31.6%) and HPV 18 (8.2%) was similar to that in Bangladesh.<sup>17</sup> In Pakistan, HPV 16 (18%) and HPV 18 (6%) were less prevalent.<sup>29</sup> In a Chinese population, HPV 16 was the major genotype

Table 2. Distribution of HR-HPV DNA Results by Division (n = 3,856)

| Divisions  | Districts   | Sub-districts | N (%)         | HPV DNA      |              | P value             |
|------------|-------------|---------------|---------------|--------------|--------------|---------------------|
|            |             |               |               | Negative (%) | Positive (%) |                     |
| Dhaka      | Narshingdi  | Monohardi     | 516 (13.4)    | 496 (96.1%)  | 20 (3.9)     | <0.001 <sup>a</sup> |
| Mymensingh | Mymensingh  | Bhaluka       | 395 (10.2)    | 384 (92.7)   | 11 (2.8)     |                     |
| Rangpur    | Lalmonirhat | Kaliganj      | 499 (12.9)    | 488 (97.8)   | 11 (2.2)     |                     |
| Chittagong | Cumilla     | Titas         | 501 (13.0)    | 478 (95.4)   | 23 (4.6)     |                     |
| Barishal   | Jhalokathi  | Rajapur       | 400 (10.4)    | 380 (95.0)   | 20 (5.0)     |                     |
| Rajshahi   | Sirajganj   | Kazipur       | 521 (13.5)    | 512 (98.3)   | 9 (1.7)      |                     |
| Khulna     | Chuadanga   | Alamdanga     | 570 (14.8)    | 555 (97.4)   | 15 (2.6)     |                     |
| Sylhet     | Maulvibazar | Sreemangal    | 454 (11.8)    | 425 (93.6)   | 29 (6.4)     |                     |
| Total      |             |               | 3,856 (100.0) | 3,718 (96.4) | 138 (3.6)    |                     |

<sup>a</sup>Chi-square test. HR-HPV, high-risk human papillomavirus.

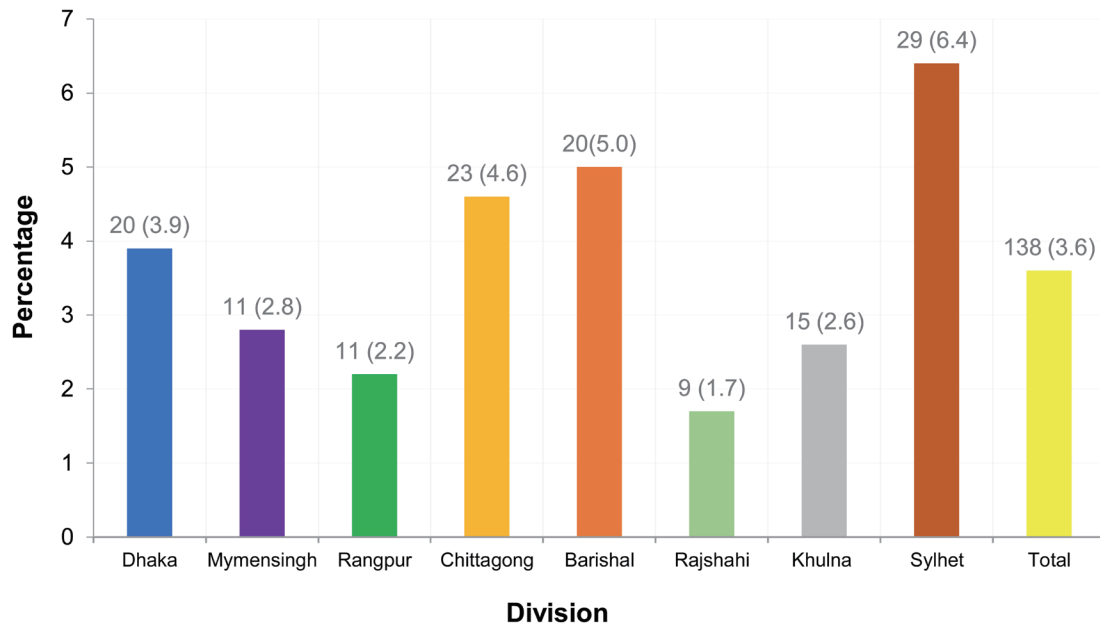


Fig. 3. Percentage distribution of patients with HR-HPV (high-risk human papillomavirus) infection in different divisions.

observed.<sup>30</sup> Therefore, the prevalence of HPV 16 and HPV 18 varies in different geographical regions. HPV genotyping is presently being mentioned for better risk assessment, and currently, only types 16 and 18 are commonly described for direct clinical management.<sup>31</sup> The prevalence of HPV 16 infection was high in Sylhet (2.6%), Barishal (1.8%) and Dhaka (1.7%) divisions, and these

divisions need particular attention during implementation policy.

Among the 138 HR-HPV positive cases, other HR-HPV infection (65, 1.7%) was more prevalent than HPV 16 infection (49, 1.3%). This indicates the necessity of a larger population-based longitudinal study to determine the fate of this high proportion of ‘other HR-HPV types’.

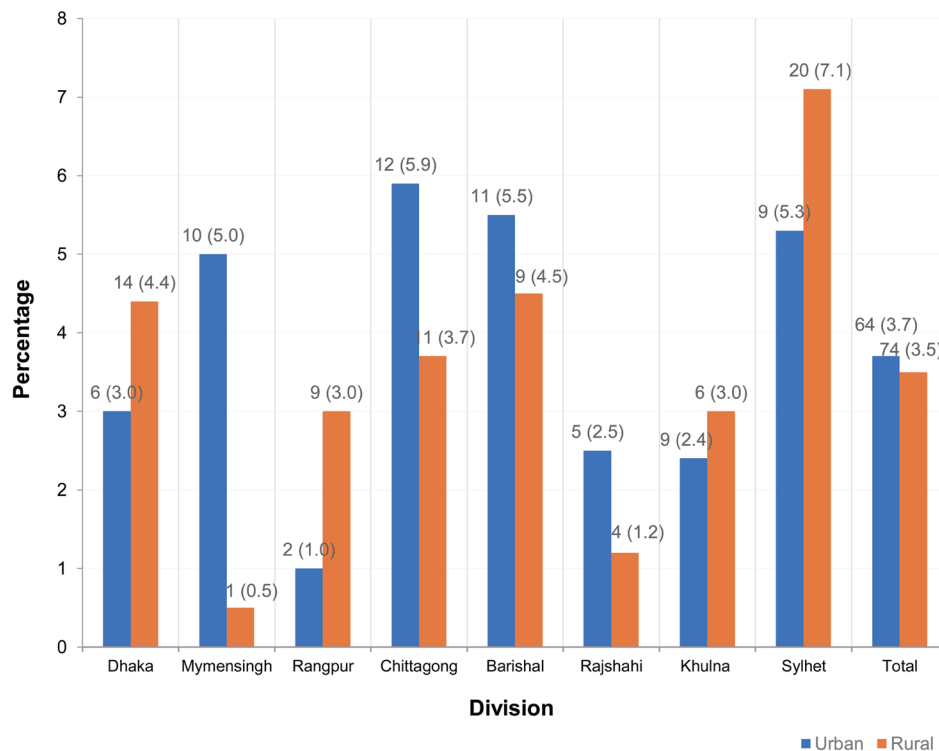


Fig. 4. Percentage distribution of patients infected with HR-HPV (high-risk human papillomavirus) in urban and rural areas in different divisions.



**Table 3. Distribution of HR-HPV infection in urban and rural areas of different divisions (n = 3,856)**

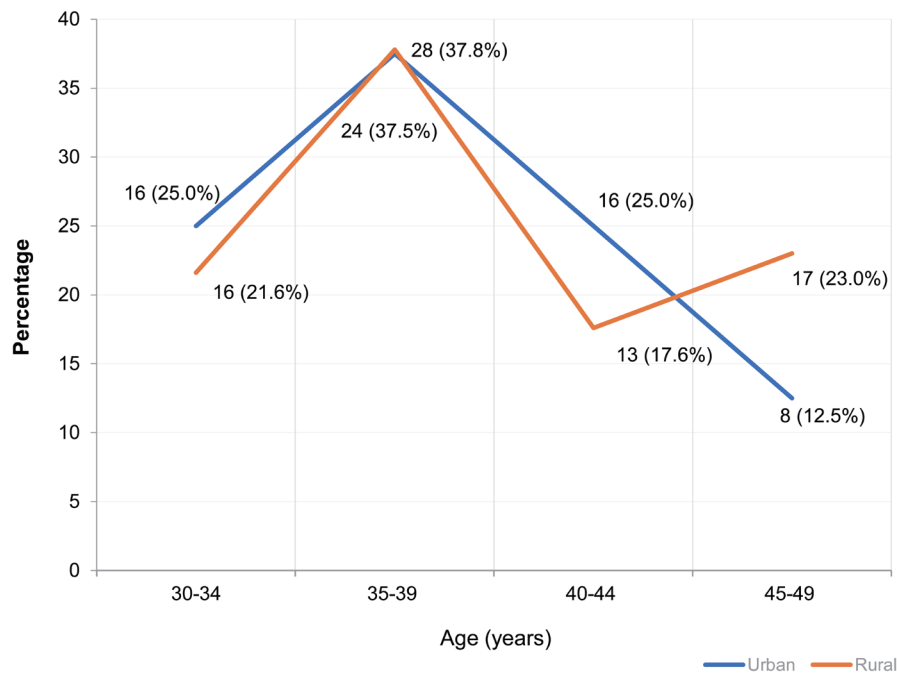
| Name of Division |       | HR-HPV         |                | Total | P value            |
|------------------|-------|----------------|----------------|-------|--------------------|
|                  |       | Positive N (%) | Negative N (%) |       |                    |
| Dhaka            | Urban | 6 (3.0)        | 195 (97.0)     | 201   | 0.402              |
|                  | Rural | 14 (4.4)       | 301 (95.6)     | 315   |                    |
|                  | Total | 20 (3.9)       | 496 (96.1)     | 516   |                    |
| Mymensingh       | Urban | 10 (5.0)       | 190 (95.0)     | 200   | 0.007              |
|                  | Rural | 1 (0.5)        | 194 (99.5)     | 195   |                    |
|                  | Total | 11 (2.8)       | 384 (97.2)     | 395   |                    |
| Rangpur          | Urban | 2 (1.0)        | 198 (99.0)     | 200   | 0.213 <sup>a</sup> |
|                  | Rural | 9 (3.0)        | 290 (97.0)     | 299   |                    |
|                  | Total | 11 (2.2)       | 488 (97.8)     | 499   |                    |
| Chittagong       | Urban | 12 (5.9)       | 193 (94.1)     | 205   | 0.261              |
|                  | Rural | 11 (3.7)       | 285 (96.3)     | 296   |                    |
|                  | Total | 23 (4.6)       | 478 (95.4)     | 501   |                    |
| Barishal         | Urban | 11 (5.5)       | 189 (94.5)     | 200   | 0.646              |
|                  | Rural | 9 (4.5)        | 191 (95.5)     | 200   |                    |
|                  | Total | 20 (5.0)       | 380 (95.0)     | 400   |                    |
| Rajshahi         | Urban | 5 (2.5)        | 194 (97.5)     | 199   | 0.313 <sup>a</sup> |
|                  | Rural | 4 (1.2)        | 318 (98.8)     | 322   |                    |
|                  | Total | 9 (1.7)        | 512 (98.3)     | 521   |                    |
| Khulna           | Urban | 9 (2.4)        | 363 (97.6)     | 372   | 0.664              |
|                  | Rural | 6 (3.0)        | 192 (97.0)     | 198   |                    |
|                  | Total | 15 (2.6)       | 555 (97.4)     | 570   |                    |
| Sylhet           | Urban | 9 (5.3)        | 162 (94.7)     | 171   | 0.446              |
|                  | Rural | 20 (7.1)       | 263 (92.9)     | 283   |                    |
|                  | Total | 29 (6.4)       | 425 (93.6)     | 454   |                    |
| Total            | Urban | 64 (3.7)       | 1,684 (96.3)   | 1,748 | 0.802              |
|                  | Rural | 74 (3.5)       | 2,034 (96.5)   | 2,108 |                    |
|                  | Total | 138 (3.6)      | 3,718 (96.4)   | 3,856 |                    |

<sup>a</sup>Fisher's exact test, Pearson chi-square test. S = significant, NS = non-significant. HR-HPV, high-risk human papillomavirus. Data were expressed as frequency and percentage.

**Table 4. Distribution of HR-HPV genotypes among 8 divisions**

| Name of Divisions | Negative N (%) | HPV 16 N (%) | HPV 18 N (%) | Other HR-HPV N (%) | HPV 16/18 and Other HR-HPV N (%) | HPV 16 and Other HR-HPV N (%) | HPV 18 and Other HR-HPV N (%) | Total |
|-------------------|----------------|--------------|--------------|--------------------|----------------------------------|-------------------------------|-------------------------------|-------|
| Dhaka             | 496 (96.1)     | 9 (1.7)      | –            | 10 (1.9)           | –                                | –                             | 1 (0.2)                       | 516   |
| Mymensingh        | 384 (97.2)     | 4 (1.0)      | –            | 7 (1.8)            | –                                | –                             | –                             | 395   |
| Rangpur           | 488 (97.8)     | 4 (0.8)      | 2 (0.4)      | 5 (1.0)            | –                                | –                             | –                             | 499   |
| Chittagong        | 478 (95.4)     | 3 (0.6)      | 3 (0.6)      | 14 (2.8)           | 1 (0.2)                          | 2 (0.4)                       | –                             | 501   |
| Barishal          | 380 (95.0)     | 7 (1.8)      | 2 (0.5)      | 7 (1.8)            | 1 (0.2)                          | 2 (0.5)                       | 1 (0.2)                       | 400   |
| Rajshahi          | 512 (98.3)     | 2 (0.4)      | 1 (0.2)      | 4 (0.8)            | 2 (0.4)                          | –                             | –                             | 521   |
| Khulna            | 555 (97.4)     | 8 (1.4)      | 2 (0.4)      | 5 (0.9)            | –                                | –                             | –                             | 570   |
| Sylhet            | 425 (93.6)     | 12 (2.6)     | 2 (0.4)      | 13 (2.9)           | 1 (0.2)                          | 1 (0.2)                       | –                             | 454   |
| Total             | 3,718 (96.4)   | 49 (1.3)     | 12 (0.3)     | 65 (1.7)           | 5 (0.1)                          | 5 (0.1)                       | 2 (0.1)                       | 3,856 |

HR-HPV, high-risk human papillomavirus.



**Fig. 5.** Age-specific prevalence of HR-HPV (high-risk human papillomavirus) infection in urban and rural study populations.

The major strengths of this study lie in the inclusion of samples from all divisions of the country, the use of a well-validated HPV test, and the collection of samples from both urban and rural areas. However, no significant variation in HR-HPV prevalence between rural and urban women was found, except in Mymensingh. Nahar *et al.* also found no significant variation between rural and urban women in the Dhaka division,<sup>13</sup> indicating the necessity of equal attention to both rural and urban populations during the implementation of the CC screening program. This study included women aged 30 to 49 years only; the sample size was relatively small, and these were important limitations of this study.

The proportion of HR-HPV infection was highest among the 35–39 years age group, with a second rise after 40–44 years onwards in rural areas. Studies from Costa Rica and Colombia also revealed a second peak,<sup>32–34</sup> which may be a cohort effect, due to exposure of older women to HPV or reactivation of latent HPV infection for women infected with human immunodeficiency virus. However, the prevalence of human immunodeficiency virus infection is very low in Bangladesh,<sup>35</sup> and further research is necessary to explore the cause of the second rise in the older population of rural women, including factors related to immune suppression and other unknown carcinogenic potential. The second increase in HR-HPV infection indicates the usefulness of screening among older women. A population-based survey identified that in the rural population of Bangladesh, the prevalence of HR-HPV infection was 5.0% among the 45–64 years age group.<sup>13</sup> Other studies in Bangladesh reported that 19.23% of HR-HPV positive women were between 45–60 years of age,<sup>36</sup> and 26.7% of HR-HPV positive women were between 40–70 years of age.<sup>37</sup> It was also revealed that among CC patients, the highest number were older than 50 years (43.4%).<sup>38</sup> Based on these findings, the age for CC screening can be extended to more than 60 years of age.

In this study, age, education level, occupation, monthly family income, parity, age of marriage, and age of first delivery did not show any significant influence on HR-HPV infection. However, a

significant association of HR-HPV infection with education levels and early age of sex initiation was observed in other studies.<sup>30,39</sup> A small sample size and the inclusion of women aged 30 to 49 years only may be related to the low influence of all these known risk factors. However, further investigations with larger sample sizes and wider age groups are needed.

**Conclusions**

The prevalence of HR-HPV infection was comparatively low, with significant variation among the divisions in Bangladesh. HPV 16 infection was high in Sylhet, Barishal and Dhaka divisions and these divisions need particular attention during the planning of larger implementation research. During the introduction of the HR-HPV test for primary screening, similar attention should be given to both rural and urban populations. The rebound to higher HR-HPV prevalence among older women suggested that this group should also be targeted for screening.

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**Table 5. Association of different socioeconomic and reproductive factors with HR-HPV prevalence (n = 3,856)**

|                              |                     | HR-HPV               |                    | Total        | P value            |
|------------------------------|---------------------|----------------------|--------------------|--------------|--------------------|
|                              |                     | Negative (n = 3,718) | Positive (n = 138) |              |                    |
| Age of Woman (years)         | 30–34               | 1,015 (27.3)         | 32 (23.2)          | 1,047 (27.2) | 0.59 <sup>a</sup>  |
|                              | 35–39               | 1,272 (34.2)         | 52 (37.7)          | 1,324 (34.3) |                    |
|                              | 40–44               | 844 (22.7)           | 29 (21.0)          | 873 (22.6)   |                    |
|                              | 45–49               | 587 (15.8)           | 25 (18.1)          | 612 (15.9)   |                    |
| Residence                    | Urban               | 1,684 (45.3)         | 64 (46.4)          | 1,748 (45.3) | 0.802 <sup>a</sup> |
|                              | Rural               | 2,034 (54.7)         | 74 (53.6)          | 2,108 (54.7) |                    |
| Education                    | No schooling        | 1,622 (43.6)         | 58 (42.0)          | 1,680 (43.6) | 0.895 <sup>a</sup> |
|                              | Up Primary          | 1,524 (41.0)         | 62 (44.9)          | 1,586 (41.1) |                    |
|                              | SSC                 | 328 (8.8)            | 10 (7.2)           | 338 (8.8)    |                    |
|                              | HSC                 | 209 (5.6)            | 7 (5.1)            | 216 (5.6)    |                    |
|                              | Graduate & above    | 35 (0.9)             | 1 (0.7)            | 36 (0.9)     |                    |
| Occupation                   | Housewife           | 3,705 (99.7)         | 138 (100.0)        | 3,843 (99.7) | >0.99 <sup>a</sup> |
|                              | Service Holder      | 13 (0.3)             | 0 (0.0)            | 13 (0.3)     |                    |
| Monthly family income (Taka) | Up 5,000            | 1,737 (46.7)         | 55 (39.9)          | 1,792 (46.5) | 0.389 <sup>a</sup> |
|                              | 5,001–10,000        | 1,399 (37.6)         | 61 (44.2)          | 1,460 (37.9) |                    |
|                              | 10,001–20,000       | 298 (8.0)            | 9 (6.5)            | 307 (8.0)    |                    |
|                              | 20,001–50,000       | 278 (7.5)            | 13 (9.4)           | 291 (7.5)    |                    |
|                              | 50,001 and above    | 6 (0.2)              | 0 (0.0)            | 6 (0.2)      |                    |
| Parity                       | Nulliparous         | 71 (1.9)             | 4 (2.9)            | 75 (1.9%)    | 0.858 <sup>a</sup> |
|                              | Primipara           | 551 (14.8)           | 20 (14.5)          | 571 (14.8%)  |                    |
|                              | Multi para          | 2,795 (75.2)         | 102 (73.9)         | 2,897 (75.1) |                    |
|                              | Grand multipara     | 301 (8.1)            | 12 (8.7)           | 313 (8.1)    |                    |
| Age of marriage              | <18 years           | 2,774 (74.6)         | 109 (79.0)         | 2,883 (74.8) | 0.245 <sup>a</sup> |
|                              | 18 years and above  | 944 (25.4)           | 29 (21.0)          | 973 (25.2)   |                    |
| Age of first delivery        | Less than <18 years | 1,648 (44.3)         | 71 (51.4)          | 1,719 (44.6) | 0.098 <sup>a</sup> |
|                              | 18 years and above  | 2,070 (55.7)         | (48.6)             | 2,137 (0.4)  |                    |

<sup>a</sup>Pearson chi-Square test. HR-HPV, high-risk human papillomavirus.

based Cervical and Breast Cancer Screening Programme” (Code no. 16201-224259800). All the research activities, including participant recruitment, HPV sample collection, and VIA procedures, were conducted within the framework of the government infrastructure. The MOHFW’s funding covered essential laboratory expenses, ensuring the successful implementation of the study.

### Conflict of interest

The authors declare no competing financial and non-financial interests related to the publication of this article.

### Author contributions

Conceptualization of the study was done by AN and SAB. NF and AC developed the data collection tools and coordinated and performed the field activities. FB and SUM arranged and super-

vised laboratory work. AN and SAB performed data validation and supervised analysis. All authors participated in drafting and revising the manuscript and approved the final version before submission.

### Ethical statement

Ethical clearance was received from the Institutional Review Board of BSMMU Ethics and Scientific Review Committee (IRB no. BSMMU/2021/474, 12.04.21). This study was performed following the principles of the Declaration of Helsinki. All participants provided written informed consent.

### Data sharing statement

Most of the data collected were analyzed and are contained within this published article. To maintain data privacy, the data used are

not publicly available. The data can be made available after a rational request from the researchers.

## References

- [1] Ahmed T, Ashrafunnessa, Rahman J. Development of a visual inspection programme for cervical cancer prevention in Bangladesh. *Reprod Health Matters* 2008;16(32):78–85. doi:10.1016/S0968-8080(08)32419-7, PMID:19027625.
- [2] Nessa A, Hussain MA, Rahman JN, Rashid MH, Muwonge R, Sankaranarayanan R. Screening for cervical neoplasia in Bangladesh using visual inspection with acetic acid. *Int J Gynaecol Obstet* 2010;111(2):115–118. doi:10.1016/j.ijgo.2010.06.004, PMID:20674919.
- [3] Nessa A, Naud P, Esmay PO, Joshi S, Rema P, Wesley R, *et al*. Efficacy, safety, and acceptability of thermal coagulation to treat cervical intraepithelial neoplasia: pooled data from Bangladesh, Brazil and India. *J Clin Gynecol Obstet* 2017;6(3-4):58–64. doi:10.14740/jcgo464w.
- [4] Bhatla N, Nessa A, Oswal K, Vashist S, Sebastian P, Basu P. Program organization rather than choice of test determines success of cervical cancer screening: Case studies from Bangladesh and India. *Int J Gynaecol Obstet* 2021;152(1):40–47. doi:10.1002/ijgo.13486, PMID:33205399.
- [5] Gaikwad V, Gaikwad S, Yalla S, Salvi P. A prospective comparative study between pap smear, visual inspection with acetic acid, visual inspection with lugol's iodine, colposcopy and histopathology for diagnosis of cervical intraepithelial neo-plasia and early carcinoma cervix. *J Pharm Negat Results* 2023;14:1817–1826. doi:10.47750/pnr.2023.14.S02.219.
- [6] Jain R, Jatav J, Jain A. Diagnostic utility of pap smear and visual inspection of acetic acid for the detection of various cervical lesions. *Asian J Med Sci* 2022;13(9):213–218. doi:10.3126/ajms.v13i9.44448.
- [7] Srivastava A, Sinha P, Vatsal P, Khatoun F, Lal N. Visual Inspection with Acetic Acid Versus Papanicolaou Test in Cervical Cancer Screening. *Indian J Gynecol Oncol* 2020;18:86. doi:10.1007/s40944-020-00438-z.
- [8] Wright TC, Stoler MH, Behrens CM, Sharma A, Zhang G, Wright TL. Primary cervical cancer screening with human papillomavirus: end of study results from the ATHENA study using HPV as the first-line screening test. *Gynecol Oncol* 2015;136(2):189–197. doi:10.1016/j.ygyno.2014.11.076, PMID:25579108.
- [9] Zhao Y, Bao H, Ma L, Song B, Di J, Wang L, *et al*. Real-world effectiveness of primary screening with high-risk human papillomavirus testing in the cervical cancer screening programme in China: a nationwide, population-based study. *BMC Med* 2021;19(1):164. doi:10.1186/s12916-021-02026-0, PMID:34261463.
- [10] Arbyn M, Simon M, Peeters E, Xu L, Meijer CJLM, Berkhof J, *et al*. 2020 list of human papillomavirus assays suitable for primary cervical cancer screening. *Clin Microbiol Infect* 2021;27(8):1083–1095. doi:10.1016/j.cmi.2021.04.031, PMID:33975008.
- [11] Bosch FX, Broker TR, Forman D, Moscicki AB, Gillison ML, Doorbar J, *et al*. Comprehensive control of human papillomavirus infections and related diseases. *Vaccine* 2013;31(Suppl 7):H1–31. doi:10.1016/j.vaccine.2013.10.003, PMID:24332295.
- [12] Liu SS, Chan KKL, Wei TN, Tse KY, Ngu SF, Chu MMY, *et al*. Clinical performance of the Roche Cobas 4800 HPV test for primary cervical cancer screening in a Chinese population. *PLoS One* 2022;17(8):e0272721. doi:10.1371/journal.pone.0272721, PMID:35930575.
- [13] Nahar Q, Sultana F, Alam A, Islam JY, Rahman M, Khatun F, *et al*. Genital human papillomavirus infection among women in Bangladesh: findings from a population-based survey. *PLoS One* 2014;9(10):e107675. doi:10.1371/journal.pone.0107675, PMID:25271836.
- [14] Aziz H, Iqbal H, Mahmood H, Fatima S, Faheem M, Sattar AA, *et al*. Human papillomavirus infection in females with normal cervical cytology: Genotyping and phylogenetic analysis among women in Punjab, Pakistan. *Int J Infect Dis* 2018;66:83–89. doi:10.1016/j.ijid.2017.11.009, PMID:29138009.
- [15] Raza SA, Franceschi S, Pallardy S, Malik FR, Avan BI, Zafar A, *et al*. Human papillomavirus infection in women with and without cervical cancer in Karachi, Pakistan. *Br J Cancer* 2010;102(11):1657–1660. doi:10.1038/sj.bjc.6605664, PMID:20407442.
- [16] Phoolcharoen N, Kantathavorn N, Sricharunrat T, Saeloo S, Krongthong W. A population-based study of cervical cytology findings and human papillomavirus infection in a suburban area of Thailand. *Gynecol Oncol Rep* 2017;21:73–77. doi:10.1016/j.gore.2017.06.003, PMID:28725677.
- [17] Van SN, Khac MN, Dimberg J, Matussek A, Henningsson AJ. Prevalence of Cervical Infection and Genotype Distribution of Human Papilloma Virus Among Females in Da Nang, Vietnam. *Anticancer Res* 2017;37(3):1243–1247. doi:10.21873/anticancer.11440, PMID:28314288.
- [18] Aggarwal R, Gupta S, Nijhawani R, Suri V, Kaur A, Bhasin V, *et al*. Prevalence of high-risk human papillomavirus infections in women with benign cervical cytology: a hospital based study from North India. *Indian J Cancer* 2006;43(3):110–116. doi:10.4103/0019-509x.27932, PMID:17065768.
- [19] Sowjanya AP, Jain M, Poli UR, Padma S, Das M, Shah KV, *et al*. Prevalence and distribution of high-risk human papilloma virus (HPV) types in invasive squamous cell carcinoma of the cervix and in normal women in Andhra Pradesh, India. *BMC Infect Dis* 2005;5:116. doi:10.1186/1471-2334-5-116, PMID:16371167.
- [20] Franceschi S, Rajkumar R, Snijders PJ, Arslan A, Mahé C, Plummer M, *et al*. Papillomavirus infection in rural women in southern India. *Br J Cancer* 2005;92(3):601–606. doi:10.1038/sj.bjc.6602348, PMID:15668709.
- [21] Bao HL, Jin C, Wang S, Song Y, Xu ZY, Yan XJ, *et al*. Prevalence of cervicovaginal human papillomavirus infection and genotypes in the pre-vaccine era in China: A nationwide population-based study. *J Infect* 2021;82(4):75–83. doi:10.1016/j.jinf.2021.02.017, PMID:33610682.
- [22] Basu P, Mittal S, Bhaumik S, Mandal SS, Samaddar A, Ray C, *et al*. Prevalence of high-risk human papillomavirus and cervical intraepithelial neoplasias in a previously unscreened population—a pooled analysis from three studies. *Int J Cancer* 2013;132(7):1693–1699. doi:10.1002/ijc.27793, PMID:22907663.
- [23] Bonde J, Rebolj M, Ejegod DM, Preisler S, Lynge E, Rygaard C. HPV prevalence and genotype distribution in a population-based split-sample study of well-screened women using CLART HPV2 human papillomavirus genotype microarray system. *BMC Infect Dis* 2014;14:413. doi:10.1186/1471-2334-14-413, PMID:25064473.
- [24] Coupé VM, Berkhof J, Bulkman NW, Snijders PJ, Meijer CJ. Age-dependent prevalence of 14 high-risk HPV types in the Netherlands: implications for prophylactic vaccination and screening. *Br J Cancer* 2008;98(3):646–651. doi:10.1038/sj.bjc.6604162, PMID:18182990.
- [25] Heard I, Tondeur L, Arowas L, Falguières M, Demazoin MC, Favre M. Human papillomavirus types distribution in organised cervical cancer screening in France. *PLoS One* 2013;8(11):e79372. doi:10.1371/journal.pone.0079372, PMID:24244490.
- [26] Sukvirach S, Smith JS, Tunsakul S, Muñoz N, Kesaratat V, Opasatian O, *et al*. Population-based human papillomavirus prevalence in Lam-pang and Songkla, Thailand. *J Infect Dis* 2003;187(8):1246–1256. doi:10.1086/373901, PMID:12696004.
- [27] Wang J, Tang D, Wang K, Wang J, Zhang Z, Chen Y, *et al*. HPV genotype prevalence and distribution during 2009–2018 in Xinjiang, China: baseline surveys prior to mass HPV vaccination. *BMC Womens Health* 2019;19(1):90. doi:10.1186/s12905-019-0785-3, PMID:31286939.
- [28] Wang X, Ji Y, Li J, Dong H, Zhu B, Zhou Y, *et al*. Prevalence of human papillomavirus infection in women in the Autonomous Region of Inner Mongolia: A population-based study of a Chinese ethnic minority. *J Med Virol* 2018;90(1):148–156. doi:10.1002/jmv.24888, PMID:28661048.
- [29] Minhas S, Kashif M, Rehman Z, Pasha MB, Idrees M, Ansari F. Distribution of High-risk Human Papillomavirus Genotypes in Cervical Secretions in Punjab. *J Coll Physicians Surg Pak* 2021;30(7):786–791. doi:10.29271/jcpsp.2021.07.786, PMID:34271777.
- [30] Niyazi M, Husaiyin S, Han L, Mamat H, Husaiyin K, Wang L. Prevalence of and risk factors for high-risk human papillomavirus infection: a population-based study from Hetian, Xinjiang, China. *Bosn J Basic Med Sci* 2016;16(1):46–51. doi:10.17305/bjbm.2016.593, PMID:26773182.
- [31] Demarco M, Egemen D, Raine-Bennett TR, Cheung LC, Befano B, Poiras NE, *et al*. A Study of Partial Human Papillomavirus Genotyping in Support of the 2019 ASCCP Risk-Based Management Consensus Guidelines. *J Low Genit Tract Dis* 2020;24(2):144–147. doi:10.1097/

- LGT.000000000000530, PMID:32243309.
- [32] Herrero R, Hildesheim A, Bratti C, Sherman ME, Hutchinson M, Morales J, *et al.* Population-based study of human papillomavirus infection and cervical neoplasia in rural Costa Rica. *J Natl Cancer Inst* 2000;92(6):464–474. doi:10.1093/jnci/92.6.464, PMID:10716964.
- [33] Molano M, Posso H, Weiderpass E, van den Brule AJ, Ronderos M, Franceschi S, *et al.* Prevalence and determinants of HPV infection among Colombian women with normal cytology. *Br J Cancer* 2002;87(3):324–333. doi:10.1038/sj.bjc.6600442, PMID:12177803.
- [34] Castle PE, Schiffman M, Herrero R, Hildesheim A, Rodriguez AC, Bratti MC, *et al.* A prospective study of age trends in cervical human papillomavirus acquisition and persistence in Guanacaste, Costa Rica. *J Infect Dis* 2005;191(11):1808–1816. doi:10.1086/428779, PMID:15871112.
- [35] Azim T, Rahman M, Alam MS, Chowdhury IA, Khan R, Reza M, *et al.* Bangladesh moves from being a low-prevalence nation for HIV to one with a concentrated epidemic in injecting drug users. *Int J STD AIDS* 2008;19(5):327–331. doi:10.1258/ijsa.2007.007269, PMID:18482963.
- Nessa A. *et al.*: HR HPV infection among women in Bangladesh
- [36] Shahida SM, Chowdhury M, Shajahan F, Rifat JA, Lubaba AS, Shamsuzzaman SM, *et al.* Distribution of High-Risk Human Papillomavirus Genotypes among Women with Colposcopic Diagnosis of Cervical Intraepithelial Neoplasia in Bangladesh. *J Cancer Ther* 2023;14(6):277–290. doi:10.4236/jct.2023.146023.
- [37] Rahman T, Tabassum S, Jahan M, Nessa A, Ashrafunnessa. Detection and estimation of human papillomavirus viral load in patients with cervical lesions. *Bangladesh Med Res Counc Bull* 2013;39(2):86–90. doi:10.3329/bmrcb.v39i2.19648, PMID:24930198.
- [38] Nessa A, Ara R, Fatema P, Nasrin B, Chowdhury A, Khan KH, *et al.* Influence of Demographic and Reproductive Factors on Cervical Pre-Cancer and Cancer in Bangladesh. *Asian Pac J Cancer Prev* 2020;21(7):1883–1889. doi:10.31557/APJCP.2020.21.7.1883, PMID:32711411.
- [39] Kang LN, Castle PE, Zhao FH, Jeronimo J, Chen F, Bansil P, *et al.* A prospective study of age trends of high-risk human papillomavirus infection in rural China. *BMC Infect Dis* 2014;14:96. doi:10.1186/1471-2334-14-96, PMID:24559293.