Rashmi Mulmi,<sup>1</sup> Gambhir Shrestha,<sup>2</sup> Ayodhya Pathak,<sup>1</sup> Manju Sharma,<sup>1</sup> Tara Dawadi,<sup>1</sup> Bhola Siwakoti,<sup>1</sup> Kishore Kumar Pradhananga<sup>3</sup>

<sup>1</sup>Department of Cancer Prevention, Control and Research, B.P. Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal, <sup>2</sup>Department of Community Medicine, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Maharajgunj, Kathmandu, Nepal,<sup>3</sup>Kathmandu Cancer Center, Tathali, Bhaktapur, Nepal.

# ABSTRACT

**Background:** Cervical cancer is the most common cancer among Nepalese women. Cervical cancer screening plays a vital role in reducing the morbidity and mortality of the disease. In this study, we assessed the prevalence of precancerous lesions of cervical cancer from community-based screening programs in Nepal.

**Methods:** In this cross-sectional study involving record review, data were drawn from community-based screening programs in 14 districts by B.P. Koirala Memorial Cancer Hospital in Nepal. All women who underwent cervical cancer screening using visual inspection with acetic acid between June 2017 to December 2018 were included.

**Results:** A total of 7,270 women were screened during the study period with the prevalence of cervical precancerous lesions among 153 (2.1%; 95% Confidence Interval 1.8-2.5) participants. Of which, the highest positivity rate was observed in the age group 30 years and below (46, 3%). The majority (4453, 61%) of the total women screened, were married at age below 20 years and 188 (3%) reported a history of cancer in their families. The most common presenting complaints were low abdominal pain (1236, 17%), low back pain (1152, 16%), itching in the anogenital region (828, 11%), and per vaginal discharge (818, 11%). Cervical cancer was suspected in 25 (0.3%) women.

**Conclusions:** The prevalence of precancerous lesions of cervical cancer is low but with high existing risk factors among Nepalese women of selected districts. The government should implement effective and sustained cervical cancer awareness and population-based screening programs along with a continuum of care. The national criteria for screening should also include young women with known risk factors.

Keywords: Nepal; prevention and control; screening; uterine cervical neoplasms

# **INTRODUCTION**

Cervical cancer is the fourth most common cancer among women globally with an estimated 570,000 new cases in 2018 representing 6.6% of all female cancers. Approximately 90% of deaths from cervical cancer occurred in low- and middle-income countries.<sup>1,2</sup>Cervical cancer is the topmost common cancer and the leading cause of cancer deaths among Nepalese women with an estimated 2,942 new cases and 1,928 deaths in 2018.<sup>3,4</sup>

The burden of cervical cancer has declined significantly in developed countries due to organized populationbased screening.<sup>2,5</sup> In India, a randomized controlled experiment found that cervical cancer incidence was lowered by 30% as a result of effective visual inspection of the cervix using acetic acid (VIA) screening.<sup>6</sup> Although cervical cancer screening is included in Nepal's public screening program, relatively few women undergo screening services.<sup>7.9</sup> Cervical pre-cancerous lesions can be detected and treated early on, saving lives and reducing disease burden.

This study aimed to determine the proportion of precancerous lesions of cervical cancer among women in community-based VIA screening programs in Nepal.

## METHODS

hat cervical cancer incidence was This descriptive cross-sectional study involved a record Correspondence: Dr Gambhir Shrestha, Department of Community Medicine, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Maharajgunj, Kathmandu, Nepal. Email: gamvir.stha@gmail.com, Phone: +9779841654909.

review of data from a community-based screening program conducted by B.P. Koirala Memorial Cancer Hospital (BPKMCH), the largest national-level referral cancer specialized hospital located at Bharatpur, Chitwan, central Nepal from 1<sup>st</sup> June 2017 to 31<sup>st</sup> December 2018. The camps were led by a team of health professionals of BPKMCH including medical and paramedical staff, who were trained and had an experience of more than 10 years. A standard form for screening cervical cancer developed by the Family Welfare Division, Department of Health Services was used to collect data in the camps. Women who were pregnant, history of hysterectomies, and aged more than 65 years were excluded from the screening programs. VIA positive was defined as the turning of the cervical epithelium into an aceto-white area after 1 minute of application of 3-5% acetic acid, which shows that it may have precancerous lesions.<sup>10</sup> Convenient sampling was done and it included all women screened between 1<sup>st</sup> June 2017 to 31<sup>st</sup> December 2018. The sample size was calculated by using the following formula.

Sample size (n)= Z<sup>2</sup> x p x q / e<sup>2</sup>, = (1.96)<sup>2</sup> x 0.5 x 0.5 / (0.02)<sup>2</sup>, = 2401

where, Z = 1.96 at 95% confidence interval, p = prevalence taken as 50% q= 1-p e = margin of error, 2%

Since convenient sampling was used, taking a design effect of three, the final sample size was calculated to be 7203. However, all the women screened during the study period were included. BPKMCH conducted cervical cancer screening programs at 14 different districts during this period (Figure 1). The variables used in this study were extracted from paper-based records and included age at the time of screening, age at marriage, parity, menstrual history, current contraceptive use, history of chronic diseases, tobacco use, family history of cancer, gynecological symptoms, and VIA test finding. Those forms with missing VIA test findings were excluded.

The data was entered into a Microsoft Excel spreadsheet by two researchers with one of them reading the cancer screening form aloud. A total of 100 randomly selected forms were checked for any mistake in the data entry. Data were exported and analyzed using Statistical Package for the Social Sciences version 17 software. Data were summarized using the descriptive statistics, frequency, percentage, mean and standard deviation. The prevalence ratio of VIA positivity and its 95% confidence interval (CI) were calculated by performing a binomial test. This study was approved by the Ethical Review Board of Nepal Health Research Council, Kathmandu, Nepal (Reg no. 2756 of 21 April 2019). Permission to carry out this study was also obtained from the Hospital Management Committee, BPKMCH.



Figure 1. Map of Nepal showing cervical cancer screening programs conducted by BPKMCH at various districts between June 2017 to December 2018. This map was constructed by using QGIS version 3.20.

#### RESULTS

Among 7270 women screened at 14 districts of Nepal, the prevalence of VIA positivity among the screened population was 153 (2.1%; 95% CI 1.8-2.5). The mean age of the participants was 39.3 years (SD 9.6). The most common age group was 31-40 years (2770, 38%) followed by 41-50 years (1917, 26%) and less than 31 years (1548, 21%). The mean age at first marriage was 18.9 years (SD 3.3) ranging from 12 to 41 years and a majority (4453, 61%) married at age below 20 years. Only a quarter of the participants were employed. More than half of the women had one or two children and 3275 (45%) were multiparous (>2 children). A total of 2158 (30%) women used any method of contraceptives including permanent methods. The majority (4956, 68%) had regular menstruation, 1311 (18%) had irregular menstruation and the rest were in a menopausal state. Only198 (3%) women were current smokers. A history of chronic illness was reported by 594 (8%) and 188 (3%) reported a history of cancer in their families Among the VIA-positive women, the high prevalence was seen in the age group 30 years and less (46, 3%), followed by 31-40 years (75, 2.7%) (Table 1).

Table 1. Demographic and other related characteristics of
participants screened for cervical cancer and those with
VIA positivity between June 2017 to December 2018.

Demographic and related characteristics	All participants n(%)*	VIA positive n(%) <sup>#</sup>
Total Age (in years)	7270 (100.0)	153 (2.1)
≤30	1548 (21.3)	46 (3.0)
31-40	2770 (38.1)	75 (2.7)
41-50	1917 (26.4)	19 (1.0)

>50	)	1035 (14.2)	13 (1.3)	
Age at marriage (in years)				
<20	)	4453 (61.2)	97 (2.2)	
≥20	)	2805 (38.6)	56 (2.0)	
Not	t recorded	12 (0.2)	0 (0.0)	
Employment status				
Yes	;	1829 (25.2)	49 (2.7)	
No		5402 (74.3)	104 (1.9)	
Not	t recorded	39 (0.5)	0 (0.0)	
Parity				
0		139 (1.9)	3 (2.2)	
1-2		3820 (52.5)	98 (2.6)	
3-4	ļ	2542 (35.0)	43 (1.7)	
≥5		733 (10.1)	9 (1.2)	
Not	t recorded	36 (0.5)	0 (0.0)	
Use of any contraceptive methods				
Yes	;	2158 (29.7)	54 (2.5)	
No		5109 (70.3)	99 (1.9)	
Not	t recorded	3 (0.0)	0 (0.0)	
Menstruation pattern				
Reg	gular	4956 (68.2)	119 (2.4)	
Irre	egular	1311 (18.0)	29 (2.2)	
Me	nopause	1003 (13.8)	5 (0.5)	
Smoking habit				
Yes	;	198 (2.7)	2 (1.0)	
No		6316 (86.9)	150 (2.4)	
Not	t recorded	756 (10.4)	1 (0.1)	
History of ch	ronic disease			
Yes	;	594 (8.2)	6 (1.01)	
No		6512 (89.6)	147 (2.3)	
Not	t recorded	164 (2.2)	0 (0.0)	
Family history of cancer				
Yes	i	188 (2.6)	2 (2.1)	
No		7074 (97.3)	151 (2.1)	
Not	t recorded	8 (0.1)	0 (0.0)	
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Table 2. Presenting complaints and per speculum findings of reproductive morbidities among the screened population between June 2017 to December 2018 (n=7270).

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Characteristics	n(%)		
Presenting complaints			
Low abdominal pain	1236 (17.0)		
Lower back pain	1152 (15.8)		
Itching anogenital region	828 (11.4)		
Per vaginal discharge	818 (11.2)		
Pain during intercourse	242 (3.3)		
Post-coital bleeding	75 (1.0)		
Intermenstrual bleeding	26 (0.4)		
Per speculum examination findings			
Pelvic organs prolapse	546 (7.5)		
Cervical polyp	267 (3.7)		
Cervicitis	227 (3.1)		
Cervix bleed on touch	42 (0.6)		
Suspected cancer	25 (0.3)		
Vaginal wart	6 (0.1)		

### DISCUSSION

This study is based on the largest community-based cervical cancer screening programs using a camp approach in Nepal. One-fourth of the women who had the VIA test fall under the age group 20-30 years. This is consistent with other studies in Nepal and India.<sup>11-13</sup> Majority (61%) of the participants were married at the age of less than 20 years. This finding was in line with the Nepal Demographic Health Survey 2016 with 53% of women married before the age of 18 years.<sup>14</sup> Multiparity was reported among 45% of the women. Early age at marriage is a proxy indicator of early age at first sexual intercourse and early age at first pregnancy and high parity. This is similar to the study conducted in India.<sup>13</sup> This indicates a high prevalence of potential risk factors for cancer cervix in Nepal. Irregular menstruation poses 2-5 times more risk of cervical cancer than normal.<sup>15,16</sup> This study also found 18% of women reported irregular menstruation patterns.

The prevalence of tobacco smoking in this study was 2.7%, which is far less than the national average. The reason may be that tobacco smoking is not socially accepted mainly among women and they tend to hide the information. Also, in 10% of the women, this information was missing in the form. We found 2.5% of participants had a history of cancer in their family. Family history is also one of the risk factors for cervical cancer and they should be screened at an early age and more frequently. Reproductive tract infections suggestive symptoms were

## \*column percentage, # row percentage

The major presenting complaints among the participants were low abdominal pain (1236, 17%), low back pain (1152, 16%), itching in the anogenital region (828, 11%), and per vaginal discharge (818, 11%). Pain during intercourse and post-coital bleeding was reported by 242 (3%) and 75 (1%) of women, respectively. Pelvic organ prolapse was the most common reproductive morbidity with a prevalence of 546 (7.5%). Cervical polyp and cervicitis were found among 267 (4%) and 227 (3%) of the participants, respectively. Cervical cancer was suspected among 25 (0.3%) women (Table 2).

reported by low abdominal pain (17%), low backache (16%), and vaginal discharge (11%). Several studies have evidence that reproductive tract infection is one of the risk factors for cervical cancer.<sup>17,18</sup>

The inspection of the cervix to screen cervical cancer also allowed assessing other reproductive morbidities. The most common reproductive morbidity was the pelvic organ prolapse (7.5%). This points to the urgent need for specialized services regarding the prevention and treatment of pelvic organ prolapse. Additionally, 0.3% of the women per speculum examination were suggestive of suspected cervical cancer.

World Health Organization has recommended VIA for low resource settings.<sup>10</sup> VIA has a sensitivity of 66% to 96% and a specificity of 64% to 98%.<sup>19</sup> The VIA positivity rate in this study was 2.1%, which is in line with the previous studies in Nepal and Bangladesh.<sup>12,20</sup> This was quite less than compared to other studies. <sup>17,21,22</sup> This finding is comparable to the results reported based on the PAP smear test in a similar setting.<sup>23</sup> Surprisingly, our results indicated a high proportion of VIA positivity (3%) among the younger women of age 30 years and less. This finding was in line with other studies.<sup>22-24</sup> The reason may be that Human Papilloma Virus (HPV) infections are more prevalent among younger married women but are usually transient in nature.<sup>10</sup> According to the national guidelines for cervical cancer screening developed in 2010, the target population for screening rate calculation is women in the age range 30-60 years and excludes younger sexually active women.<sup>25</sup> However, we found Nepalese women exposed to risk factors for cervical cancer at a younger age, suggested by early age at marriage and multiparity. This study also recommends screening criteria for cervical cancer to include young women with high risk, taking into consideration the age at sexual intercourse and parity. A similar recommendation has been suggested in the neighboring country, India.<sup>22</sup>

Studies in Nepal have reported a high prevalence of high-risk HPV infections among women in Nepal.<sup>26,27</sup> HPV infection is one of the major risk factors for cervical cancer. HPV vaccination can play a vital role in the prevention and control of cervical cancer.<sup>10,28,29</sup> Despite that, the HPV vaccine has not been still introduced in the national immunization program in Nepal.

The national guideline targeted to achieve a 50% screening rate of the target population by 2015.<sup>25</sup> But, recent data showed only 2.8% of women had their cervical cancer screening done in 2018.<sup>30</sup> Also, the incidence of cervical cancer in the largest cancer hospital, BPKMCH has remained relatively constant over

a long period.<sup>31</sup> Qualitative studies among Nepalese women and cervical cancer survivors have reported misconceptions about screening, shyness, low level of knowledge, difficult terrain, and cultural barriers as the major barriers for cervical cancer screening.<sup>32,33</sup> This evidence highlights the urgent need on raising awareness and implementation of well-organized and persistent cervical cancer screening programs.

Anecdotal evidence suggests a good response to the screening camps by the people but poor follow-up of the screened individuals. Hence, strengthening the follow-up especially screened positive individuals, and supporting the continuum of care is needed. This could have helped to know the specific diagnosis that could have come out if the patients have done other definitive tests like a biopsy, HPV DNA Polymerase chain reaction. Also, it would have helped to evaluate the effectiveness of screening programs and estimate the downstaging of cancer in the community. Second, some important variables in the report were missing. Proper documentation is very challenging in a camp, thus utilizing local human resources by orientating them to the form can fill this gap.

The study's main strength is that we utilized populationbased data from a routine cancer screening program. Furthermore, 14 different districts were included in the screening program during the period, therefore, we believe that the findings are a reflection of overall Nepalese women. The limitations of this study are: first, this study was conducted using data of cervical cancer screening camps and may not reflect the overall population, and second, we could not follow up the VIApositive patients.

We would like to recommend prospective research studies to ascertain the prevalence of cervical cancer among the screened population. Second, we recommend the inclusion of sexually active women aged less than 30 in the national guideline for cervical cancer screening. Lastly, there is a need for a nationwide program to educate and create awareness among females and the community on cervical cancer and the importance of screening.

#### CONCLUSIONS

The findings from this large community-based study indicated a low burden of precancerous lesions but high existing risk factors of cervical cancer among Nepalese women. We also identified the highest VIA positivity rate among young married women, which is of serious concern. Urgent measures need to be taken to raise awareness and implement effective cancer screening programs in the community.

### CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## REFERENCES

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424. [PubMed | FullText | DOI]
- Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Heal. 2020;8(2):e191–203. [PubMed | FullText | DOI]
- Shrestha G, Neupane P, Lamichhane N, Acharya BC, Siwakoti B, Subedi KP, et al. Cancer Incidence in Nepal: A Three-Year Trend Analysis 2013-2015. Asian Pacific J Cancer Care. 2020;5(3):145–50. [FullText | DOI]
- GLOBOCAN. The global cancer observatory: Nepal factsheet [Internet]. Lyon (France): International Agency for Research on Cancer, World Health Organization. 2019 [cited 2020 Jul 1]. Available from: http://gco.iarc. fr/today/data/factsheets/populations/524-nepal-factsheets.pdf
- Singh GK, Azuine RE, Siahpush M. Global inequalities in cervical cancer incidence and mortality are linked to deprivation, low socioeconomic status, and human development. Int J MCH AIDS. 2012;1(1):17-30. [PubMed | FullText | DOI]
- Sankaranarayanan R, Esmy PO, Rajkumar R, Muwonge R, Swaminathan R, Shanthakumari S, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. Lancet. 2007;370(9585):398–406. [PubMed | FullText | DOI]
- Ranjit A, Gupta S, Shrestha R, Kushner AL, Nwomeh BC, Groen RS. Awareness and prevalence of cervical cancer screening among women in Nepal. Int J Gynecol Obstet. 2016;134(1):37–40. [PubMed | FullText | DOI]
- Shrestha J, Saha R, Tripathi N. Knowledge, attitude and practice regarding cervical cancer screening amongst women visiting tertiary centre in Kathmandu, Nepal. Nepal J Med Sci. 2013;2(2):85–90. [Full Text | DOI]
- Pandey RA, Karmacharya E. Cervical cancer screening behavior and associated factors among women of Ugrachandi Nala, Kavre, Nepal. Eur J Med Res. 2017;22(1):32. [PubMed | FullText | DOI]

- World Health Organization. Comprehensive cervical cancer control: a guide to essential practice. 2nd ed. Geneva: World Health Organization; 2014. [PubMed | FullText]
- Shrestha A, KC S. Cervical cancer screening with pap smear in rural population in health camp. Nepal Med Coll J. 2020;22(1–2):62–6. [Full Text | DOI]
- Thapa B, Ranabhat MK, Dahal BD, Dhungana GP, Rajbanshi L. Factors associated with precancerous cervical lesion among women attending cervical cancer screening camps. Int J Health Sci Res. 2019;9(7):78-86. [Full Text]
- Yasmeen J, Qurieshi MA, Manzoor NA, Asiya W, Ahmad SZ. Community-based screening of cervical cancer in a low prevalence area of India: a cross sectional study. Asian Pac J Cancer Prev. 2010;11(1):231–4. [PubMed | Full Text]
- Sekine K, Carter DJ. The effect of child marriage on the utilization of maternal health care in Nepal: A crosssectional analysis of Demographic and Health Survey 2016. PLoS One. 2019;14(9):e0222643. [PubMed | Full Text | DOI]
- Zhang Z-F, Parkin DM, Yu S-Z, Esteve J, Yang X-Z. Risk factors for cancer of the cervix in a rural Chinese population. Int J cancer. 1989;43(5):762–7. [PubMed | FullText | DOI]
- Punyaratabandhu P, Supanvanich S, Tirapat C, Podhipak A. Epidemiologic study of risk factors in cancer of the cervix uteri in Thai women. J Med Assoc Thai. 1982;65(5):231– 9. [PubMed | FullText]
- Merera D, Jima GH. Precancerous Cervical lesions and associated factors among women attending cervical screening at Adama Hospital Medical College, Central Ethiopia. Cancer Manag Res. 2021;13:2181-9. [PubMed | FullText | DOI]
- Dey S, Pahwa P, Mishra A, Govil J, Dhillon PK. 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. J Obstet Gynecol India. 2016;66(1):441–51. [PubMed | FullText | DOI]
- Gaffikin L, Lauterbach M, Blumenthal PD. Performance of visual inspection with acetic acid for cervical cancer screening: a qualitative summary of evidence to date. Obstet Gynecol Surv. 2003;58(8):543–50. [PubMed | FullText | DOI]
- Parvin Z, Naher L, Das SK, Khanam S, Rosy N. Visual inspection of cervix with acetic acid (via) as a screening tool for early detection of cervical pre-cancer & cancer. Faridpur Med Coll J. 2018;13(1):24–7. [FullText | DOI]

- 21. Poli UR, Bidinger PD, Gowrishankar S. Visual inspection with acetic acid (via) screening program: 7 years experience in early detection of cervical cancer and precancers in rural South India. Indian J community Med. 2015;40(3):203-7. [PubMed | FullText | DOI]
- Vidhubala E, Shewade HD, Niraimathi AK, Ramkumar S, Ramaswamy G, Nagalekshmi G, et al. Call for Systematic Population-Based Cervical Cancer Screening: Findings from Community-Based Screening Camps in Tamil Nadu, India. Asian Pacific J cancer Prev. 2019;20(12):3703-10.
   [PubMed | FullText | DOI]
- Sherpa AT, Karki BS, Sundby J, Nygard M, Franceschii S, Clifford G. Population based study of cervical cancer screening in Bharatpur, Nepal. J Manmohan Meml Inst Heal Sci. 2015;1(4):3–8. [Full Text | DOI]
- Bongaerts THG, Ridder M, Vermeer-Mens JCJ, Plukkel JJ, Numans ME, Büchner FL. Cervical cancer screening among marginalized women: a cross-sectional intervention study. Int J Womens Health. 2021;13:549-56. [PubMed | FullText | DOI]
- Family Health Division. National Guideline for Cervical Cancer Screening and Prevention in Nepal. Kathmandu (Nepal): Ministry of Health; 2010.
- Thapa N, Maharjan M, Shrestha G, Maharjan N, Petrini MA, Zuo N, et al. Prevalence and type-specific distribution of human papillomavirus infection among women in midwestern rural, Nepal-A population-based study. BMC Infect Dis. 2018;18(1):338. [PubMed | FullText | DOI]
- Shakya S, Syversen U, Åsvold BO, Bofin AM, Aune G, Nordbø SA, et al. Prevalence of human papillomavirus infection among women in rural Nepal. Acta Obstet Gynecol Scand. 2017;96(1):29–38. [PubMed | Full Text | DOI]

- Brotherton JML, Gertig DM. Primary prophylactic human papillomavirus vaccination programs: future perspective on global impact. Expert Rev Anti Infect Ther. 2011;9(8):627–39. [PubMed | FullText | DOI]
- Armstrong EP. Prophylaxis of cervical cancer and related cervical disease: a review of the cost-effectiveness of vaccination against oncogenic HPV types. J Manag care Pharm. 2010;16(3):217–30. [PubMed | FullText | DOI]
- 30. Information Centre on HPV and Cancer. Nepal-Human Papillomavirus and Related Cancers, Fact Sheet 2018 [Internet]. Barcelona (Spain): HPV Information Centre; 2019 [cited 2021 May 2]. Available from: https:// hpvcentre.net/statistics/reports/NPL\_FS.pdf
- Mulmi R, Shrestha G, Pathak A, Sharma M, Dawadi T, Siwakoti B. Trend in Incidence of Cervical Cancer in a National Tertiary Cancer Hospital of Nepal, 2012-2017. Nepal J Cancer. 2019;3(1):5–8. [FullText | DOI]
- Darj E, Chalise P, Shakya S. Barriers and facilitators to cervical cancer screening in Nepal: A qualitative study. Sex Reprod Healthc. 2019;20(7491):20–6. [PubMed | Full Text | DOI]
- 33. Shrestha G, Mulmi R, Phuyal P, Thakur RK, Siwakoti B. Experiences of cervical cancer survivors in Chitwan, Nepal: A qualitative study. PLoS One. 2020;15(11):e0234834.
  [PubMed | FullText | DOI]