Immunization and Screening Methods for Cervical Carcinoma in Developing Nations: A Detailed Review

Dr. Saba Amin

(Ph.D).Health Management, Researcher, Faculty, SKIMS India.

Abstract:- **Objective: Cervical cancer remains a significant public health challenge in developing countries, disproportionately affecting women in these regions due to limited access to effective screening and vaccination programs. This review synthesizes the current literature on the implementation strategies, effectiveness, and challenges of cervical cancer screening and Human Papillomavirus (HPV) vaccination programs in developing countries, aiming to highlight successful models and identify gaps in current practices. Screening, for cervical cancer in developing countries faces numerous obstacles, including logistical challenges, lack of awareness, and insufficient healthcare infrastructure. Despite these hurdles, strategies such as single-visit approaches, leveraging low-cost HPV DNA testing, and utilizing mobile health units have shown promise in increasing screening coverage and early detection rates. The prerequisites for effective screening highlighted include affordability, cultural acceptability, and the ability to implement large-scale screening with limited resources. HPV vaccination presents a primary prevention measure with the potential to significantly reduce the incidence of cervical cancer. However, vaccination programs in developing countries encounter challenges in vaccine procurement, distribution, and achieving high coverage rates among the target population. Innovations in vaccine delivery, education campaigns to raise awareness, and partnerships with international health organizations are crucial for overcoming these barriers.This comprehensive review underscores the need for a multifaceted approach to cervical cancer prevention in developing countries, encompassing improvements in screening and vaccination strategies, health system strengthening, community engagement, and international collaboration. By learning from successful models and addressing identified gaps, there is a significant opportunity to reduce the burden of cervical cancer in these regions and move closer to achieving global health equity.**

Keywords:- Cervical Carcinoma, Immunization, Screening Methods, Developing Nations.

I. INTRODUCTION

Human papillomavirus (HPV) is widely known as the major cause of cervical cancer, the fourth most prevalent cancer among women worldwide. [1]. Approximately 90-100% of cervical cancer cases in women are caused by Human Papillomavirus, particularly among those under the age of 35 [2]. Approximately 11.8 crore worldwide have been targeted for Human Papillomavirus immunization. However, the number of fully vaccinated females in developing nations ranges from 10 lakh to 1.33 crore, showing low Human Papillomavirus vaccine uptake in these areas[3]. The lower uptake of Human papillomavirus vaccination is attributed to vaccine hesitancy, It is characterized by delays in vaccination approval or denial despite the availability of vaccine services, contributing to low immunization uptake. [4].

Using an example of India, cervical malignancy was the second most frequent malignancy among females in 2015, with an estimated 132,314 new cases diagnosed and 73,337 fatalities [5]. Despite accounting for roughly 1/5th of all cervical malignancy cases globally, India's healthcare system spends only 0.9% of its GDP on healthcare, and no structured cervical carcinoma programs of screening exist [6,7]. Risk factors for cervical cancer in India include illiteracy, inadequate sanitation facilities, early age of first coitus, many sexual companions, and the human papillomavirus [8]. Due to the high expense of Human papillomavirus vaccine, it is not widely available in India. However, a study in Eastern India found that 80% of parents were willing to vaccinate their daughters after receiving education about the vaccine [9]. The most common reason given for refusing the vaccine was safety concerns, followed by the perception that it would encourage sexual activity. If effective vaccination against HPV 16 and 18 were implemented in India, it could result in a 75% reduction in cervical cancer cases [10,11]. This comprehensive review examines cervical cancer vaccine awareness and methods for screening in developing nations.

II.   STAGES OF CERVICAL CANCER:

Cervical cancer is named after the type of cells it affects, primarily two types of which are common and a third type is rare. The various stages of cervical cancer are listed in Table 1.

Stages	Definition
0	Cancer only affects the surface of the cervix and does not spread to the deeper layers.
1	Cancer cells have spread from the cervix's surface to deeper tissues; tissue samples can be utilized to identify stages based on the tissue size.
1A	The malignant region measures less than 3mm in depth.
1A1	The malignant region measures between 3mm to 5mm in depth.
1A2	The tumor has developed to a large size and is still limited to the cervix's lower tissues.
1B	The tumor is at least 5mm deep but less than 2 cm.
1B1	The tumor is two centimeters or more deep and less than four centimeters wide.
1B2	The tumor is four centimeters or greater in width.
2	Cancer has grown beyond the uterus and surrounding area; the tumor is limited to the vagina and does not extend to the perimetrical area.
2A	The tumor is less than 4 centimeters broad.
2B	The tumor is 4 cm or greater in breadth.
2A2	Malignancy has progressed to the perimetrical area.
3	Malignancy has progressed to the lower portions of the vagina, damaging the kidneys and internal organs.
3A	Malignancy spreads to the lower portion of the vagina, but does not infect the pelvic wall.
3B	Malignancy had progressed to the pelvic wall.
3C	Malignancy affects lymph nodes in the pelvic area.
4A	Malignancy spread to the bladder (or) rectum.
4B	Malignancy spreads throughout the body and destroys several vital organs.

Reference: Waggoner SE (2003) Cervical cancer. The Lancet 361: 2217-25.
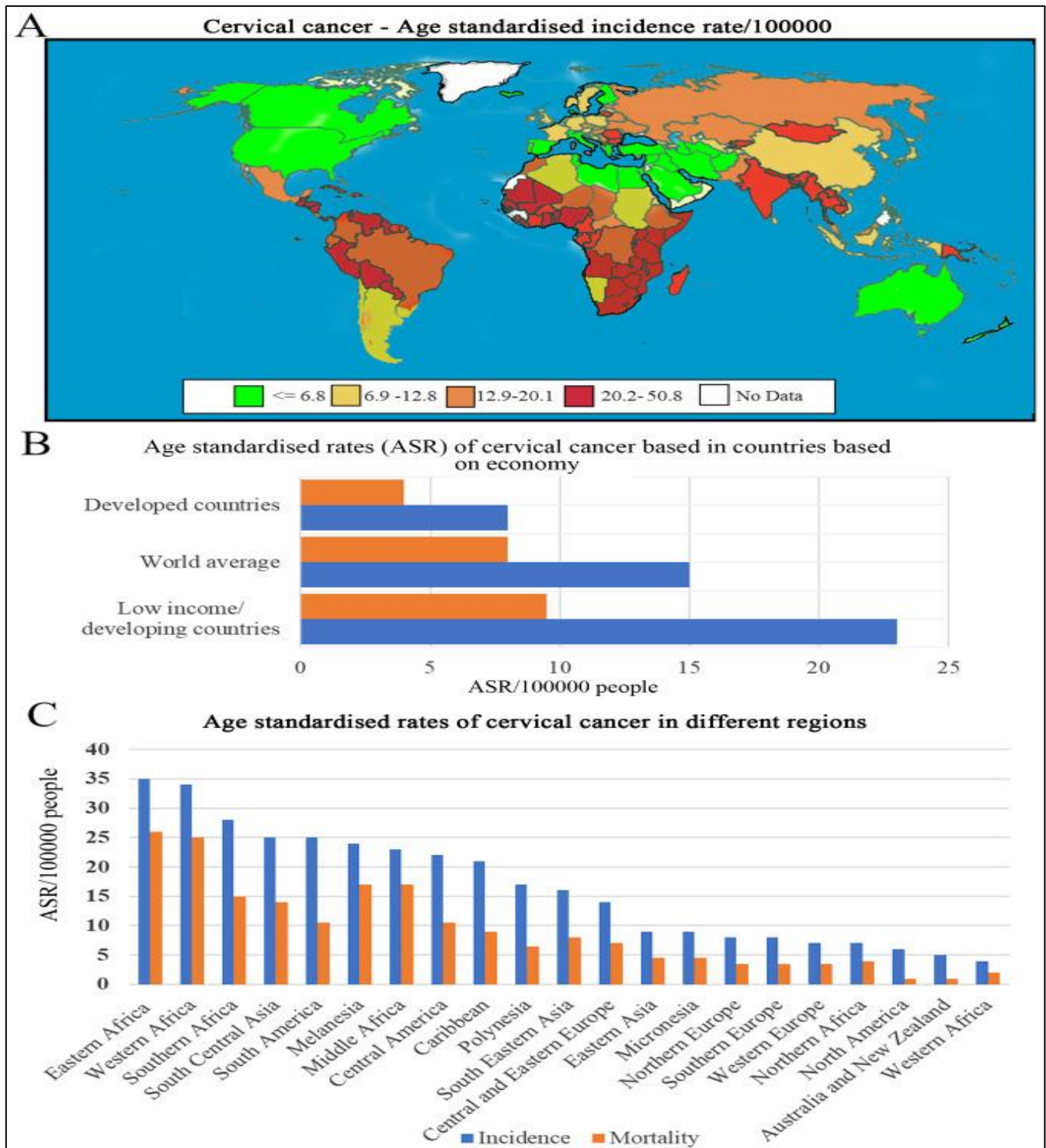
Fig 1: Cervical Cancer Incidence. (A) Global Incidence by Country. (B) The Difference in Incidence and Mortality Rates Between Countries with Varying Levels of Economic Development and the Global Average. (C) Geographically Specific Incidence and Mortality Rates.

Source: Hull, R., Mbele, M., Makhafola, T., Hicks, C., Wang, S. M., Reis, R. M., Mehrotra, R., Mkhize-Kwitshana, Z., Kibiki, G., Bates, D. O., & Dlamini, Z. (2020). Cervical cancer in low and middle-income countries. *Oncology letters*, *20*(3), 2058–2074. https://doi.org/10.3892/ol.2020.11754.

➢ *Cervical Cancer in Developing Nations.*

The current situation in India highlights the leading cause of cancer mortality, which is cervical cancer. According to the Institute for HM&E's 2010 estimations, the cumulative possibility of incidence for Indian women is 1.9,

ranking second in South Asia behind Afghanistan (3.3). The World Health Organization predicts that without widespread screening and prevention efforts, the annual burden of new cases in India will increase to almost 225,000 by 2025. However, the concept of routine screening for asymptomatic

women is nearly non-existent among the Indian populace, and women are often encouraged to undergo a Pap smear only if they appear with symptoms[13,14,15].

Similarly, several developing nations are dealing with a large number of cervical cancer cases and deaths yet poor screening rates. According to 2008 research, the average coverage of cervical cancer screening in underdeveloped nations is 19%, contrary to 63% in developed nations [16]. Nwankwo et al. in Nigeria reported that merely 15.5% of respondents knew that screening services for cervical carcinoma were available, with only 4.2% having ever received Pap testing [17]. Ebu et al. in Ghana observed that only three (0.8%) of the 392 female participants in their study had received Pap testing, while 97.7% had never heard of the technique [18]. However, out of 1113 urban and 924 rural females interviewed in Bangladesh, 3.1% of urban and 0.7% of rural females underwent screeninfor cervical carcinoma.g. [19].

➤ *Importance of Cervical Cancer Screening Methods:*
Screening is pivotal for early detection, significantly increasing the chances of successful treatment and survival. Patients should be educated on the limitations of screening and recommended follow-up intervals [30, 31]. However, some women continue to ignore screening advice. Many people die of this preventable malignancy as a result of poor screening. Public health initiatives are in place to promote access to screening and adequate follow-up.[32].

➤ *Managing Women with Positive Screening Tests:*
Screening for cervical cancer aims to decrease the disease burden by identifying and treating effectively precancerous lesions early.

➤ *Management of Women Positive on HPV Test:*
There is no single definitive technique for treating positive Human papillomavirus females. Management choices are typically based on available resources, logistics, and program rules. Cervical cancer is a rare result of high-risk infections, thus treatment options are built on risk criteria that identify the small number of females who are likely to develop malignancy. Additional tests (Triage tests) are recommended for risk stratification and subsequent identification of at-risk women, depending on their availability and feasibility.

Since the majority of HPV infections are transitory, most positive Human papillomavirus females will have no clinically evident illness on colposcopy. Referral of all positive Human Papillomavirus females for colposcopy will overwhelm the system, especially in LMICs with limited colposcopy facilities. This technique is also expected to raise the costs of public health programs. It should be considered in instances when doing triage tests is not practicable or assuring follow-up of positive females is difficult. [23].

Given its feasibility and affordability, VIA has been widely implemented in several LMICs in Asia and Africa.
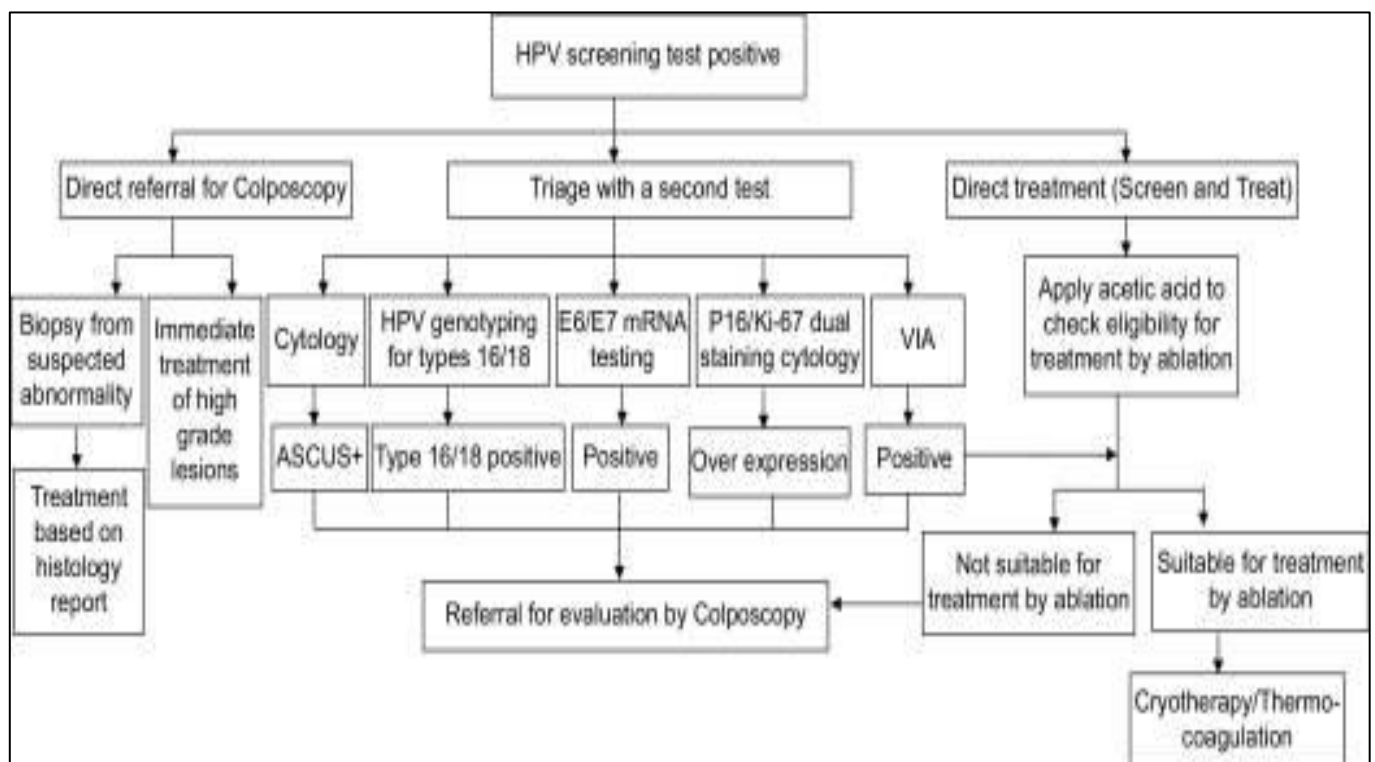

Fig 2 Illustrates Various Management Techniques For Women Who Are HPV-Positive.

III. DISCUSSION

With a high incidence and death rate, particularly in poor nations, cervical cancer is a serious global health concern. [33,34]. Early detection is critical to properly treating and controlling cervical cancer. The Pap smear test has long been used to detect cervical cancer. It analyzes cervical cells under a microscope to detect abnormalities. Human Papillomavirus is a common STD, affecting up to 80% of sexually active females. The majority of infections clear up on their own and offer little long-term health concern. There are several types of Human papillomavirus, with some more likely to cause malignancy than others. However, this method is subjective and may overlook precancerous lacerations, resulting in inaccurate results and a delayed diagnosis. As a result, there has been increased interest in developing strategies to improve the screening of cervical carcinoma. CAD technology for cervical carcinoma diagnosis has been substantially surveyed during the last few years. [35,36]. Significant progress has been made in this area between 1996 and 2022, which has enhanced the CAD approaches' accuracy, sensitivity, and specificity. Early CAD systems analyzed digital pictures of cervical cells to find abnormal cells and lesions using image processing and pattern recognition techniques. However, because of their poor sensitivity and specificity, these early systems were not very successful. In the early 2000s, machine learning techniques were first used in the field of CAD to detect cervical cancer.ML algorithms can evaluate and learn from enormous data sets, allowing them to recognize patterns and make predictions. This enabled more accurate and automatic analysis of digital images of cervical cells. Several studies indicated that ML-based CAD systems have better sensitivity and specificity when compared to traditional screening approaches[37,38].

IV. CONCLUSION

The review underscores the critical gap in knowledge, awareness, and application of cervical cancer screening and vaccination in developing countries. Despite the proven effectiveness of Human Papillomavirus vaccinations and screening of cervical carcinoma in preventing the disease, these preventative measures are significantly underutilized in these regions. Studies indicate a dire need for increased awareness and education regarding cervical cancer prevention methods, alongside improved access to these crucial health services. Innovations in screening and treatment methods, including self-sampling and Human Papillomavirus DNA testing, offer promising avenues to enhance early detection and treatment of precancerous conditions, potentially reducing the cervical cancer burden. Future efforts should focus on integrating these advancements into public health strategies, ensuring equitable access, and fostering collaborations that leverage local and global resources to combat cervical cancer effectively in developing countries.

➤ *Telecommunication*

With the aid of modern digital technology, tele-VILI, tele-VIA, tele-cervicography or even tele-colposcopy, ei-ther as still digital images or even real-time teleconference images is a reality of the modern era. Utilisation of digital cameras linked to the internet via laptop or even multime-dia messaging system (MMS) via mobile phones, especial-ly modern smartphones, will enable non-physician health.

REFERENCES

[1]. GLOBOCAN 2012: Estimated Cancer Incidence, M. A. P. W. *Cervical Cancer*, *Estimated Incidence*, *Mortality and Prevalence Worldwide in* 2012, http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx (2012).

[2]. Bruni L, Diaz M, Castellsagué X, Ferrer E, Bosch FX, de Sanjosé S. Cervical human papillomavirus prevalence in 5 continents: Meta-analysis of 1 million women with normal cytological findings. *J Infect Dis.* 2010; 202:1789–1799. doi: 10.1086/657321.

[3]. Bruni, L. *et al.* Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. *The Lancet Global Health* **4**, e453–e463, https://doi.org/10.1016/S2214-109X(16)30099-7.

[4]. World Health Organization. Report of the Sage Working Group on Vaccine Hesitancy, http://www.who.int/immunization/sage/meetings/2014/october/1 Report WORKING_GROUP_vaccine_hesitancy_final.pdf (2014).

[5]. Mishra GA, Pimple SA, Shastri SS. Prevention of cervix cancer in India. *Oncology.* 2016;91(Suppl 1): S1–S7. doi: 10.1159/000447575.

[6]. Senapathy JG, Umadevi P, Kannika PS. The present scenario of cervical cancer control and HPV epidemiology in India: An outline.

[7]. Gheit T, Vaccarella S, Schmitt M, Pawlita M, Franceschi S, Sankaranarayanan R, Sylla BS, Tommasino M, Gangane N. Prevalence of human papillomavirus types in cervical and oral cancers in central India. *Vaccine.* 2009; 27:636–639. doi: 10.1016/j.vaccine.2008.11.041.

[8]. Deodhar K, Gheit T, Vaccarella S, Romao CC, Tenet V, Nene BM, Jayant K, Kelkar R, Malvi SG, Sylla BS, et al. Prevalence of human papillomavirus types in cervical lesions from women in rural Western India. *J Med Virol.* 2012; 84:1054–1060.

[9]. Chatterjee S, Chattopadhyay A, Samanta L, Panigrahi P. HPV and cervical cancer epidemiology-current status of HPV vaccination in India. *Asian Pac J Cancer Prev.* 2016; 17:3663–3673.

[10]. Mattheij I, Pollock AM, Brhlikova P. Do cervical cancer data justify HPV vaccination in India? Epidemiological data sources and comprehensiveness. *J R Soc Med.* 2012;105: 250–262. doi: 10.1258/jrsm.2012.110343.

[11]. Senapathy JG, Umadevi P, Kannika PS. The present scenario of cervical cancer control and HPV epidemiology in India: An outline. *Asian Pac J Cancer Prev.* 2011;12: 1107–1115.

[12]. Waggoner SE (2003) Cervical cancer. The Lancet 361: 2217-25.

[13]. Institute for Health Metrics and Evaluation. The challenge ahead: Progress and setbacks in breast and cervical cancer. Seattle, WA: IHME, 2011.

[14]. Krishnan S, Madsen E, Porterfield D, Varghese B, Poehl-man J, Taylor O. Advancing Cervical Cancer Prevention in India. Health, nutrition, and population global practice knowledge brief. World Bank, Washington, DC. https:// openknowledge.worldbank.org/handle/10986/21765License: CC BY 3.0 IGO.

[15]. World Health Organization. Strategic framework for the comprehensive control of cancer cervix in south-east Asia. Retrieved from http://apps.who.int/iris/bitstre-am/handle/10665/152098/9789290224723-MRH.pdf?sequence=1&isAllowed=y on 30th July 2019.

[16]. Gakidou E, Nordhagen S, Obermeyer Z. Coverage of cer-vical cancer screening in 57 countries: low average levels and large inequalities. PLoS Med 2008: 5: e132.

[17]. Nwankwo K, Aniebue U, Aguwa E, Anarado A, AgunwahE. Knowledge attitudes and practices of cervical cancer screening among urban and rural Nigerian women: a call for education and mass screening. Eur J Cancer Care 2011; 20: 362-367.

[18]. Ebu N, Mupepi SS, Mate-Siakwa P, Sampselle C. Knowledge, practice, and barriers toward cervical cancer screening in Elmina, Southern Ghana. Int J Womens Health 2014; 7:31-39.

[19]. Islam JY, Khatun F, Alam A, Sultana F, Bhuiyan A, Alam N, Reichenbach L, Marions L, Rahman M, Nahar Q. Knowledge of cervical cancer and HPV vaccine in Bangladeshi women: a population-based, cross-sectional study. BMC Womens Health 2018; 18: 15.

[20]. Operational Framework Management of Common Cancers. Ministry of Health and Family Welfare Government of India. Retrieved from https://mohfw.gov.in/sites/default/files/ Operational%20Framework%20Management%20of%20Common%20Cancers_1.pdf on 30th August 2019.

[21]. Bobdey S, Sathwara J, Jain A, Balasubramaniam G. Burden of cervical cancer and role of screening in India. Indian J Med Paediatr Oncol 2016; 37: 278-285.

[22]. Lee. H, Kang. Y, Ju. W, Cervical Cancer Screening in Developing Countries: Using Visual Inspection Methods (2016), CJON 2016, 20(1), 79-83. DOI: 10.1188/16.CJON.79-83.

[23]. Karimi-Zarchi M, Peighmbari F, Karimi N, et al. A comparison of 3 ways of conventional pap smear, liquid-based cytology and colposcopy vs cervical biopsy for early diagnosis of premalignant lesions or cervical cancer in women with abnormal conventional Pap test. *Int J Biomed Sci.* 2013;9:205–10.

[24]. Adamson PC, Huchko MJ, Moss AM, et al. Acceptability and accuracy of cervical cancer screening using a self-collected tampon for HPV messenger-RNA testing among HIV infected women in South Africa. *PLoS One.* 2015;10:1–12.

[25]. Sumarmi S, Hsu YY, Cheng YM, et al. Factors associated with the intention to undergo Pap smear testing in the rural areas of Indonesia: a health belief model. *Reprod Health.* 2021; 18: 1–10.

[26]. Mesafint Z, Berhane Y, Desalegn D. Health Seeking Behavior of Patients Diagnosed with Cervical Cancer in Addis Ababa, Ethiopia. *Ethiop J Health Sci.* 2018;28:111–6.

[27]. Geneva, Switzerland: 2013. WHO guidelines: WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention,

[28]. Geneva, Switzerland: 2013. WHO Guidance Note. Comprehensive cervical cancer prevention and control: a healthier future for girls and women.

[29]. Geneva, Switzerland: 2013. WHO Guidelines: WHO Guidelines for Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention WHO.

[30]. Practice Bulletin No. 168: Cervical Cancer Screening and Prevention. Obstet Gynecol. 2016 Oct;128(4):e111-e130.

[31]. Committee on Gynecologic Practice. Committee opinion No. 534: well-woman visit. Obstet Gynecol. 2012 Aug;120(2 Pt 1):421-4.

[32]. Benard VB, Thomas CC, King J, Massetti GM, Doria-Rose VP, Saraiya M., Centers for Disease Control and Prevention (CDC). Vital signs: cervical cancer incidence, mortality, and screening - United States, 2007-2012. MMWR Morb Mortal Wkly Rep. 2014 Nov 07;63(44):1004-9.

[33]. Siegel, R.L.; Miller, K.D.;Wagle, N.S.; Jemal, A. Cancer statistics, 2023. CA A Cancer J. Clin. **2023**, 73, 17–48.

[34]. American Cancer Society. Statistics for Cervical Cancer. J. Gynecol. Womens Health **2021**, 2, 1–9.

[35]. Das, D.K. Promising Deep Learning-Based CAD System for Cervical Cancer. Oncol. Times UK **2022**, 44, 30.

[36]. Purwono, R.R.P.A.; Purwanti, E.; Rulaningtyas, R. Segmentation of cervical cancer CT-scan images using K-nearest neighbors method. AIP Conf. Proc. **2020**, 2314.

[37]. Alsmariy, R.; Healy, G.; Abdelhafez, H. Predicting Cervical Cancer using Machine Learning Methods. Int. J. Adv. Comput. Sci.Appl. **2020**, 11, 110723.

[38]. Tanimu, J.J.; Hamada, M.; Hassan, M.; Kakudi, H.; Abiodun, J.O. A Machine Learning Method for Classification of Cervical Cancer. Electronics **2022**, 11, 463