

Expression of Vascular Endothelial Growth Factor (VEGF) in Cervical Squamous Intraepithelial Lesions and Invasive Squamous Cell Carcinoma

Jannatul Maaua^{1*}, Nousin Taslima Ferdous², Asadur Rahman³, Farzana Edib⁴, Nargis Akter⁵

ARTICLE INFO

Received: 13 July 2026
Accepted: 23 July 2026
Published Online: 27 July 2026

DOI: 10.5281/zenodo.21781577

Volume: 10, Number: 1, Page: 54-59

e-ISSN: 2789-5912
ISSN: 2617-0817

*Corresponding author



ABSTRACT

Background: Cervical cancer is the fourth most common cancer in women globally and is the second most common cancer in the women of Bangladesh. Studies have shown that development of cervical precancerous lesions and cancer is a multifactorial process in which HPV infection plays the central role. A small proportion of cervical precancerous lesions (Squamous intraepithelial lesions) progress to squamous cell carcinoma over time. Early detection and management of intraepithelial lesions can prevent invasive cancer. Tumor neovascularization plays crucial role in the development of cervical cancer like all other solid tumors. VEGF is a significant biomarker involved in tumor angiogenesis. Immunohistochemical expression of VEGF has shown to be expressed by the neoplastic cells. It has been reported that VEGF expression exhibits significant increase from low grade to high grade squamous lesions (LSIL, HSIL) to invasive carcinoma. Aim of the study: To evaluate the expression levels of VEGF in LSIL, HSIL and ISCC of cervix, and also to evaluate relationship of VEGF expression with histopathologic grades of ISCC. **Methods & Materials:** This cross-sectional study was conducted in the Department of pathology, Rajshahi Medical College, Rajshahi with support of Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period of March 2021 to February 2023. Total seventy cases were included in this study with the histopathological diagnosis of LSIL, HSIL, and ISCC of cervix. Expression of VEGF was determined semi-quantitatively by assessing staining intensity and the percentage of stained tumor cells in formalin-fixed paraffin-embedded lesionsal blocks and expression was categorized as negative and

positive. **Result:** In this study, the patients were between 30-80 years. LSIL diagnosis was more frequent in younger age group (<50 years), whereas proportion of HSIL and ISCC were more in older age group (≥50 years). The majority of the cases were ISCC of cervix 41 (58.6%) followed by HSIL 19 cases (27.2%) and LSIL 10 cases (14.3%). Positive VEGF expression was most frequently positive in ISCC (56.1%), followed by in HSIL (31.6%) and then in LSIL (10.0%). The association of the increasing grade of the cervical squamous lesions and carcinoma with VEGF expression status was statistically significant ($p=0.016$) in this study. Although positive VEGF expression was more frequently observed in Grade III ISCC (64.3%) than in Grade I (54.5%) and Grade II (50.0%), but this was not statistically significant ($p=0.729$). **Conclusion:** The study results show that positivity of VEGF expression was more frequent with invasive cervical carcinoma in comparison to HSIL and also more in HSIL in comparison to LSIL. Therefore, it can be suggested that tumour angiogenesis might be involved in progression of precancerous cervical lesions to invasive cancers.

Keywords: Vascular Endothelial Growth Factor (VEGF), Angiogenesis, Cervical Squamous Intraepithelial Lesion, High-Grade Squamous Intraepithelial Lesion, Invasive Squamous Cell Carcinoma, Immunohistochemistry.

1. Training Officer, Regional Training Centre, NIPORT, Charghat, Rajshahi, Bangladesh (ORCID: 0009-0005-9441-972X)
2. Lecturer, community medicine, Rajshahi medical college, Rajshahi, Bangladesh
3. Assistant Professor, Dept of Community Medicine, Rajshahi Medical College, Rajshahi, Bangladesh
4. Assistant Professor (Pathology) (insitu), Sirajganj Medical College, Sirajganj, Bangladesh
5. Consultant, Pathology, Islami Bank Hospital, Rajshahi, Bangladesh

INTRODUCTION

Cervical cancer is the fourth most common cancer among women globally. In 2020, an estimated 604,127 cervical cancer cases were diagnosed leading to 341,831 deaths [1]. In Bangladesh, cervical cancer is the second most common cancer of females (12%) where 8268 (5.3%) new cases were diagnosed in 2020, out of which 4971 (4.6%) women died [1,2]. According to International Agency for Research on Cancer, more than 50 million Bangladeshi women are at risk of developing cervical cancer. Low grade and high grade squamous intraepithelial lesions (also referred to as CIN1, CIN2, CIN 3, CIS), usually precedes cervical squamous cell carcinoma while a small portion of squamous intraepithelial lesions progress to squamous carcinoma over time. Early detection and management of squamous intraepithelial lesions can prevent invasive cancer [2]. Human papilloma virus (HPV) infection has been

identified as the causative agent of cervical cancers and precancerous lesions in majority of cases [3]. Persistent infection specifically with high-risk HPV genotypes is considered crucial in progression from preinvasive cervical lesions to invasive cancers [4]. It has been proved that some HR-HPVs are more carcinogenic than others, particularly genotypes 16, 18 [5]. Progression of premalignant lesions to invasive carcinoma, when it occurs, takes long time, on average two decades. Approximately one third of inappropriately treated high grade squamous intraepithelial lesions (HSIL) will progress to invasive cancer over thirty years [6]. Angiogenesis has also been shown to play a vital role in tumor development and progression through the formation of new blood vessels. Angiogenesis is a double-edged sword, in spite of its central role in physiological homeostasis, it provides the oxygen and nutrition needed by tumor cells to proceed

from dormancy if pro-angiogenic factors tip the balance in favor of tumor angiogenesis. Among pro-angiogenic factors, vascular endothelial growth factor (VEGF) is a prominent target in therapeutic methods due to its strategic involvement in the formation of anomalous tumor vasculature [7]. Clinical evidence that angiogenesis plays an important role in locally advanced cervical cancer has accumulated over the past decade. Specifically, expression of VEGF has been associated with adverse oncologic outcomes in numerous solid tumors, including cervical cancer [8]. VEGF acts as the chief mediator of tumour angiogenesis and stimulates the growth of new blood vessels [9]. It has been shown that VEGF plays an important role in inducing angiogenesis in some physiological and pathological processes [10]. Moreover, VEGF expression may be induced by various factors such as altered expression of tumour suppressor genes, and altered VEGF

expression has been associated with both the advanced pathological stage of cancer and lymph node metastasis ^[11,12]. The intensity of VEGF expression has been reported to be high in poorly differentiated carcinoma as compared to well and moderately differentiated carcinoma ^[13]. This finding suggested that VEGF inhibition therapy could have an important role in cervical cancer and that VEGF might be routinely examined to predict prognosis in cervical cancer patients ^[14]. The aim of this study was to evaluate the expression of VEGF in cervical squamous intraepithelial lesions and invasive squamous cell carcinoma.

METHODS & MATERIALS

This cross-sectional observational study was conducted over a two-year period from March 2021 to February 2023. The study was carried out in the Department of Pathology at Rajshahi Medical College (RMC), Rajshahi, with support from the Department of Pathology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Immunohistochemical evaluation of vascular endothelial growth factor (VEGF) protein expression was performed in the Department of Pathology, BSMMU, Dhaka. The study population comprised all female patients who were histopathologically diagnosed with low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), and invasive squamous cell carcinoma (ISCC) of the cervix and whose paraffin-embedded tissue blocks. A total of seventy paraffin blocks were included in the study. Among them, fifty-three blocks were collected from colposcopic biopsy and loop electrosurgical excision procedure (LEEP) biopsy specimens, while the remaining seventeen blocks were obtained from total abdominal hysterectomy specimens. 70 female patients were included in the study, who were in 3 groups including LSIL (n=10), HSIL (n=19), and ISCC (n=41).

Inclusion Criteria:

- Age ≥ 30 years
- Blocks of uterine cervix, histopathologically diagnosed as LSIL, HSIL, or ISCC.

Exclusion Criteria:

- Other variants of cervical carcinoma
- Patients with recurrent cervical carcinoma
- Patients receiving chemotherapy or irradiation

Ethical Considerations

Prior to the commencement of the study, ethical clearance was obtained from the

Ethical Review Committee of Rajshahi Medical College (RMC). Written informed consent was obtained from each participant before inclusion in the study. All information collected from the participants was treated with strict confidentiality and was kept secure throughout the study period. The collected data were used solely for research purposes, and the privacy and anonymity of the participants were maintained at all stages of the investigation.

Histopathological and Immunohistochemical Evaluation

All microscopic examinations and photomicrographs were performed using an Olympus multiheaded microscope (Model u-MDO10R3, Olympus Corporation, Tokyo, Japan). Histopathological slides were reviewed to confirm the diagnosis and classify lesions as low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), or invasive squamous cell carcinoma (ISCC). Cases of invasive carcinoma were further graded as well-differentiated (Grade I), moderately differentiated (Grade II), or poorly differentiated (Grade III).

For immunohistochemical analysis, a monoclonal mouse anti-human VEGF primary antibody (Catalog No. MA1-16629, Invitrogen, Thermo Fisher Scientific, UK) was used. Placental tissue, known to express VEGF, served as the positive control, and a control sample was included in each staining batch. VEGF immunoreactivity was assessed semi-quantitatively based on both staining intensity and the proportion of positively stained tumor cells. Immunostaining was predominantly cytoplasmic, although occasional nuclear staining was observed. Five representative high-power fields (400 $\times$ magnification) showing the highest density of VEGF expression were selected for evaluation. Staining intensity was scored as 0 (negative), 1 (weak), 2 (moderate), or 3 (strong). The proportion of positive tumor cells was scored as 0 (0%), 1 (<30%), 2 (30–60%), or 3 (>60%). The final VEGF expression score was obtained by adding the intensity score and distribution score, yielding a total score ranging from 0 to 6. Cases with a total score of 0–2 were considered negative for VEGF expression, whereas those with a score of 3 or higher were regarded as positive for VEGF expression.

Data Collection

Data were collected using a structured Case Record Form (CRF) designed for the study. The variables included in this study were categorized as demographic, clinical, and

laboratory-related variables. Demographic variables included age of the patients. Clinical variables comprised age at menarche, age at marriage, parity, and menopausal status. Laboratory-related variables included histopathological diagnosis, tumor grade, and immunohistochemical (IHC) expression of VEGF. Detailed clinical information was obtained from the patients through direct interviews and review of relevant clinical records and investigation reports. In cases where direct information was unavailable, data were collected from attendants accompanying the patients. Paraffin-embedded tissue blocks and corresponding histopathological reports were collected from the Department of Pathology, Rajshahi Medical College and BSMMU. Hematoxylin and eosin (H&E) staining was performed according to the standard protocol followed in the Department of Pathology, Rajshahi Medical College. Immunohistochemical staining for VEGF expression was carried out in the Department of Pathology, BSMMU, using formalin-fixed, paraffin-embedded tissue sections of 3–4 μ m thickness.

Statistical Analysis

Data were entered in to Excel worksheet to generate a master sheet. Then they were fed into SPSS-23.0 for processing and analysis. Qualitative variables were expressed as frequency, percentage and compared between groups by Chi-square test. Continuous variables were expressed as mean $\pm$ SD and independent sample t test was used to test the difference between two means. P value less than 0.05 was considered statistically significant.

RESULT

Table I showed the age distribution of the study population according to histopathological diagnosis (N=70). In the LSIL group (n=10), 40.0% of patients belonged to both the 30–39 and 40–49 years age groups, while 10.0% were aged 50–59 and 60–69 years each. The mean age was 41.80 ± 9.73 years. In the HSIL group (n=19), the highest frequencies were observed in the 40–49 years and 50–59 years groups (31.6% each), followed by 60–69 years (21.1%) and 30–39 years (15.8%), with a mean age of 50.42 ± 9.50 years. Among ISCC patients (n=41), most cases were aged 40–49 years (34.1%), followed by 50–59 years and 60–69 years (17.1% each), while 12.2% were aged ≥ 70 years. The mean age was 53.78 ± 10.67 years.

Table I
Distribution of the study population according to age (*n*=70).

Variables	LSIL (n=10)		HSIL (n=19)		ISCC (n=41)	
	n	%	n	%	n	%
Age in years						
30-39	4	40	3	15.8	2	4.9
40-49	4	40	6	31.6	14	34.1
50-59	1	10	6	31.6	7	17.1
60-69	1	10	4	21.1	7	17.1
≥ 70	0	0	0	0	5	12.2
mean age ± SD	41.80±9.73		50.42±9.50		53.78±10.67	

Among the 70 patients, ISCC constituted the majority with 58.6% cases, followed by HSIL with 27.2% cases and LSIL with 14.3% cases (*Figure 1*).

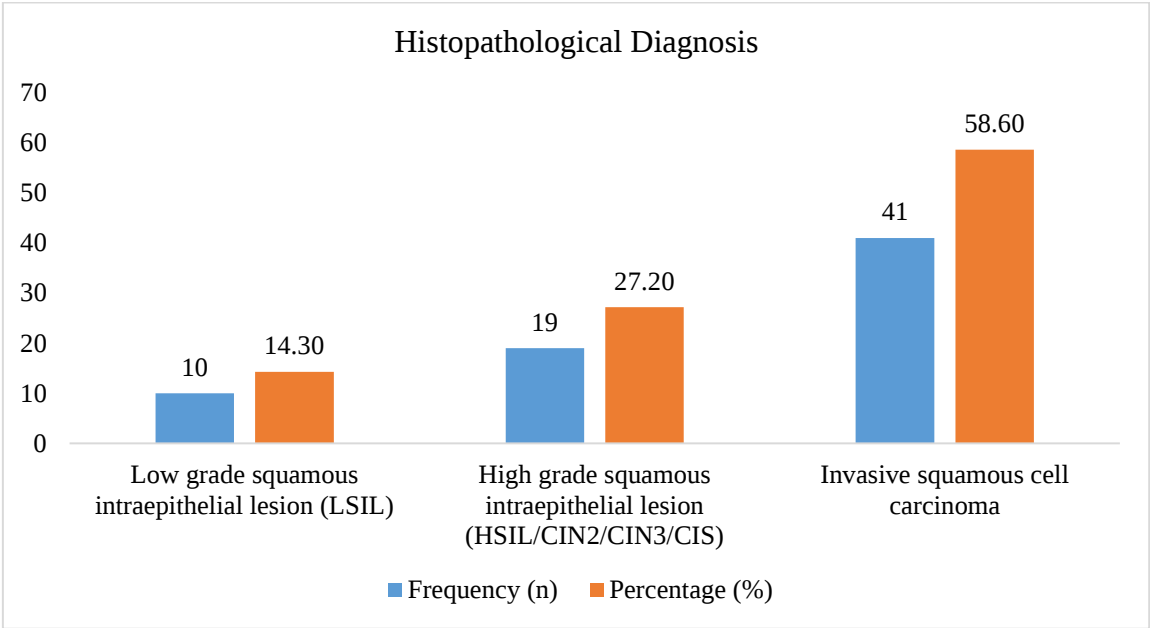


Figure 1 Histopathological diagnosis of the study population (*n*=70)

Age at menarche <13 years was observed in 60.0% of LSIL, 63.2% of HSIL, and 68.3% of ISCC patients. Marriage before 18 years occurred in 70.0%, 57.9%, and 73.2% of LSIL, HSIL, and ISCC groups, respectively. Multiparity was common, found in 80.0% of LSIL, 94.7% of HSIL, and 95.1% of ISCC patients. Menopausal/postmenopausal status predominated in HSIL (73.7%) and ISCC (73.2%), whereas 60.0% of LSIL patients were premenopausal (*Table II*).

Table II
Reproductive profile of the study subjects (*n*=70).

Reproductive characteristics	Histopathological diagnoses		
	LSIL, n (%)	HSIL, n (%)	ISCC, n (%)
Age at menarche (years)			
<13	6 (60.0)	12 (63.2)	28 (68.3)
≥13	4 (40.0)	7 (36.8)	13 (31.7)
Age at marriage (years)			
<18	7 (70.0)	11 (57.89)	30 (73.2)
≥18	3 (30.0)	8 (42.11)	11 (26.8)
Parity			
Nulliparous	2 (20.0)	1 (5.30)	2 (4.90)
Multiparous	8 (80.0)	18 (94.70)	39 (95.10)
Menopausal status			
Premenopausal	6 (60.0)	5 (26.30)	11 (26.8)
Menopausal/ postmenopausal	4 (40.0)	14 (73.70)	30 (73.2)

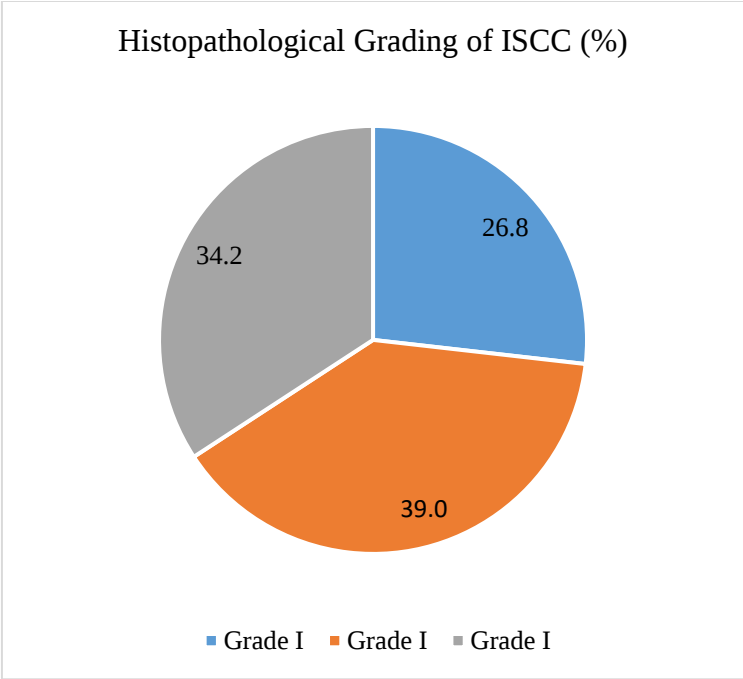


Figure 2 Histopathological Grading of ISCC among patients (n=41)

Grade II tumors were most common (39.0%), followed by Grade III (34.2%) and Grade I (26.8%) (Figure 2). VEGF positivity increased progressively from LSIL (10.0%) to HSIL (31.6%) and was highest in ISCC (56.1%). Negative VEGF expression was observed in 90.0% of LSIL, 68.4% of HSIL, and 43.9% of ISCC cases. The association between histopathological diagnosis and VEGF expression was statistically significant (p=0.016) (Table III).

Table III
Positive VEGF expression status in LSIL, HSIL, and ISCC of cervix.

Histopathological diagnosis	VEGF expression status		p-value
	Negative	Positive	
LSIL (n=10)	9 /10 (90.0%)	1/10 (10.0%)	0.016
HSIL (n=19)	13/19 (68.4%)	6/19 (31.6%)	
ISCC (n=41)	18 /41 (43.9%)	23/41 (56.1%)	

Positive VEGF expression was found in 54.5% of Grade I, 50.0% of Grade II, and 64.3% of Grade III tumors. No significant association was observed between tumor grade and VEGF expression (p=0.729) (Table IV).

Table IV
Frequency of VEGF Positivity in different grades of ISCC of cervix (n=41).

Tumour grade	Number of cases	VEGF expression status		p-value
		Negative	Positive	
Grade I	11	5/ 11 (45.5%)	6/11 (54.5%)	0.729
Grade II	16	8/16 (50.0%)	8/16 (50.0%)	
Grade III	14	5 /14 (35.7%)	9 /14 (64.3%)	

DISCUSSION

In the present study, LSIL was proportionately higher in the younger age group (<50 years) in comparison to that of HSIL and ISCC. However, the age group 40-49 years show all three diagnoses show more or less even distribution (40.0% in LSIL vs 31.6% in HSIL vs 34.1% in ISCC). Number of HSIL and ISCC cases were more in the older age group (>50 years). Nessa *et al.* found in their study that HSIL was more frequent in the age 30-39 years and ISCC was proportionately higher after 50 [15]. Sharma and Pattanshetty (2018) found that

ISCC was most prevalent in the age group 51-60 years. This discrepancy was due to relatively small sample size, heterogeneity of patient population [16]. Our study revealed that ISCC constituted the majority of cases (58.6%), followed by high-grade squamous intraepithelial lesions (HSIL/CIN2/CIN3/CIS) (27.2%), while LSIL accounted for only 14.3% of cases. Chaivirattana and Lomdee (2012) reported that among women with LSIL cytology who underwent histopathological evaluation, approximately 66.5% were confirmed as LSIL and 16.5% as HSIL, while no invasive

carcinoma was identified [17]. Khuakoonratt et al. reported that among women with LSIL cytology, histological examination demonstrated LSIL in 58.8%, HSIL in 15.0%, and invasive carcinoma in only 1.3% of cases [18]. The higher proportion of LSIL in their study is likely attributable to the screening-based nature of the population, allowing detection of lesions at an earlier stage before progression to high-grade dysplasia or invasive cancer. Based on reproductive profile of the study population, LSIL, HSIL and ISCC diagnoses were higher in patients who had

early menarche (<13 years), age of marriage <18 years of age, multiparous, and postmenopausal. Confirming these findings of the present study Nessa *et al.* found that early age of marriage and multiparity had individual influence on cervical neoplasia [15]. The results of the present study demonstrated that VEGF expression had progressively increased from LSIL (10%) to HSIL (31.6%) to ISCC (56.1%). The association between the severity of the cervical neoplasia (LSIL to HSIL to ISCC) and VEGF expression status was statistically significant ($p=0.016$). Similarly, Mandic *et al.* reported positive VEGF expression more frequently in patients with cervical cancer (60.87%) than in patients with HSIL (33.33%) ($p<0.05$) [19]. Regarding VEGF expression, Hammes *et al.* found a direct relationship between the increasing grade of the lesions and VEGF expression in both neoplastic epithelium and in stroma [20]. Normal epithelium, low-grade CIN, high-grade CIN and SCC lesions expressed VEGF in 11.5%, 39.3%, 53.3% and 75% of the cases, respectively. Regarding the expression of VEGF, the positive expression rates in the CIN I (10%), CIN II (18.2%) and CIN III (35.7%) groups were significantly lower compared with that in the ISCC group (73.8%; $P<0.05$) in the study of Li and Zhao (2018) [21]. According to this study, positive VEGF expression was 56.1% in case of invasive squamous cell carcinoma of cervix. The VEGF positivity was 63.07% in cervical carcinoma in the study of Rahmani *et al.* [13]. The positive staining for VEGF was determined in 89% of investigated cervical cancers in the study of Goncharuk *et al.* [22]. Li and Zhao (2018) found that VEGF expression was positive in (73.8%) cases of cervical squamous cell carcinoma [21]. Relatively less positivity of VEGF expression among ISCC cases in this study might have been due to small sample size, use of different antibodies, differences in methods for evaluating VEGF expression and heterogeneity in the population of SIL and invasive carcinoma. In the present study, positive expression of VEGF was higher in cervical squamous cell carcinoma than in squamous intraepithelial lesions. This indicates that angiogenesis serves an important role in tumorigenesis as the positivity of VEGF increases with the progression of cervical intraepithelial lesions to invasive carcinoma.

LIMITATIONS

- Small sample size
- Use of only one antibody to explore tumour angiogenesis rather than a panel of antibodies.
- Examination of limited clinicopathological parameters like association with age and reproductive profile

CONCLUSION

VEGF expression shows significant relationship with tumor progression as has been shown by higher percentage of positive VEGF expression in ISCC than in HSIL and LSIL. This finding support VEGF expression is associated with tumorigenesis. However, difference in VEGF expression among three grades of ISCC were not statistically significant. This may be due to small sample size, heterogeneity of population and differences in VEGF detecting methods.

RECOMMENDATIONS

- Further studies with larger samples size including all histological types of cervical carcinoma are recommended.
- Further prospected studies with larger sample size may provide data regarding significance of VEGF expression with tumorigenesis and the clinical trials targeting anti-VEGF therapy.

FUNDING

No funding sources

CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. 2021 May;71(3):209-49.
2. World Health Organization International Agency for Research on Cancer (IARC). GLOBOCAN 2020: Bangladesh fact sheets. 2021. Available from: <http://gco.iarc.fr/today/data/factsheets/population/50-Bangladesh-fact-sheets.pdf>
3. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Muñoz N. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *The Journal of pathology*. 1999 Sep;189(1):12-9.
4. Nicolás I, Marimon L, Barnadas E, Saco A, Rodríguez-Carunchio L, Fusté P, Martí C, Rodríguez-Trujillo A, Torne A, Del Pino M, Ordi J. HPV-negative tumors of the uterine cervix. *Modern Pathology*. 2019 Aug 1;32(8):1189-96.
5. Mateos Lindemann ML, Sánchez Calvo JM, Chacón de Antonio J, Sanz I, Díaz E, Rubio MD, de la Morena ML. Prevalence and Distribution of High-Risk Genotypes of HPV in Women with Severe Cervical Lesions in Madrid, Spain: Importance of Detecting Genotype 16 and Other High-Risk Genotypes. *Advances in preventive medicine*. 2011;2011(1):269468.
6. McCredie MR, Sharples KJ, Paul C, Baranyai J, Medley G, Jones RW, Skegg DC. Natural history of cervical neoplasia and risk of invasive cancer in women with cervical intraepithelial neoplasia 3: a retrospective cohort study. *The lancet oncology*. 2008 May 1;9(5):425-34.
7. Ghalehbandi S, Yuzugulen J, Pranjol MZ, Pourgholami MH. The role of VEGF in cancer-induced angiogenesis and research progress of drugs targeting VEGF. *European journal of pharmacology*. 2023 Jun 15;949:175586.
8. Eskander RN, Tewari KS. Targeting angiogenesis in advanced cervical cancer. *Therapeutic advances in medical oncology*. 2014 Nov;6(6):280-92.
9. Kajdaniuk D, Marek B, Borgiel-Marek H, Kos-Kudła B. Vascular endothelial growth factor (VEGF)—part 1: in physiology and pathophysiology. *Endokrynologia Polska*. 2011;62(5):444-55.
10. Bergers G, Benjamin LE. Tumorigenesis and the angiogenic switch. *Nature reviews cancer*. 2003 Jun 1;3(6):401-10.
11. Kieser A, Weich HA, Brandner G, Marmé D, Kolch W. Mutant p53 potentiates protein kinase C induction of vascular endothelial growth factor expression. *Oncogene*. 1994 Mar 1;9(3):963-70.
12. Shariat SF, Youssef RF, Gupta A, Chade DC, Karakiewicz PI, Isbarn H, Jeldres C, Sagalowsky AI, Ashfaq R, Lotan Y. Association of angiogenesis related markers with bladder cancer outcomes and other molecular markers. *The Journal of urology*. 2010 May;183(5):1744-50.
13. Rahmani AH, Babiker AY, Alsahli MA, Almatroodi SA, Husain NE. Prognostic significance of vascular endothelial growth factor (VEGF) and Her-2 protein in the genesis of cervical carcinoma. *Open access Macedonian journal of medical sciences*. 2018 Feb 10;6(2):263.
14. Zhang S, Xu H, Zhang L, Qiao Y. Cervical cancer: Epidemiology, risk factors and screening. *Chinese Journal of Cancer Research*. 2020 Dec 31;32(6):720.
15. Nessa A, Ara R, Fatema P, Nasrin B, Chowdhury A, Khan KH, Barua AR, Rashid MH. Influence of demographic and reproductive factors on cervical pre-cancer and cancer in Bangladesh. *Asian Pacific journal of cancer prevention: APJCP*. 2020 Jul;21(7):1883.
16. Sharma P, Pattanshetty SM. A study on risk factors of cervical cancer among patients attending a tertiary care hospital: A case-control study. *Clinical Epidemiology and Global Health*. 2018 Jun 1;6(2):83-7.
17. Chaivirattana S, Lomdee T. Histological diagnosis of conventional Pap smear with Low grade squamous intraepithelial lesion (LSIL) in Chon-Buri Hospital. *Thai Journal of Obstetrics and Gynaecology*. 2012;34-40.
18. Khuakoonratt N, Tangjitgamol S, Manusirivithaya S, Khunnamong J, Pataradule K, Thavaramara T, Suekwattana P. Prevalence of high grade squamous intraepithelial lesion (HSIL) and invasive cervical cancer in patients with low grade squamous intraepithelial lesion (LSIL) at cervical pap smear. *Asian Pac J Cancer Prev*. 2008 Jan 1;9(2):253-7.
19. Mandic A, Usaj Knezevic S, Kapicl Ivkovic T. Tissue expression of VEGF in

- cervical intraepithelial neoplasia and cervical cancer. J BUON. 2014 Oct 1;19(4):958-64.
20. Hammes LS, Tekmal RR, Naud P, Edelweiss MI, Kirma N, Valente PT, Syrjänen KJ, Cunha-Filho JS. Up-regulation of VEGF, c-fms and COX-2 expression correlates with severity of cervical cancer precursor (CIN) lesions and invasive disease. Gynecologic oncology. 2008 Sep 1;110(3):445-51.
21. Li Y, Zhao S. The expression and underlying angiogenesis effect of DPC4 and VEGF on the progression of cervical carcinoma. Oncology Letters. 2018 Feb 1;15(2):2534-40.
22. Goncharuk IV, Vorobjova LI, Lukyanova NY, Chekhun VF. Vascular endothelial growth factor expression in uterine cervical cancer: correlation with clinicopathologic characteristics and survival. Exp Oncol. 2009 Sep 1;31(3):179-81.