

Correlation among Clinical Presentation, Staging and Histopathological Findings in Carcinoma Cervix

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Abstract

Introduction: Cervical cancer is a malignant neoplasm arising mainly in the transformation zone of the cervix. Cervical cancer is the second most common cancer among women worldwide after breast cancer. Squamous cell carcinoma and adenocarcinoma constitute the greatest burden, globally as well as in Bangladesh. Most patients in developing countries including Bangladesh present at advanced stage. Histopathological types of cervical cancer influence the treatment outcome when treated by radiation therapy. To reduce mortality from cervical cancer and improve survival, it is necessary to correlation of clinical presentation, staging and histopathological findings. **Objectives:** To find the correlation among clinical presentation, clinical staging and histopathological findings in patients with carcinoma cervix. **Materials and Methods:** This cross-sectional study was conducted in the Gynaecologic division of the Department of Obstetrics & Gynaecology, Bangabandhu Sheikh Mujib Medical University Hospital, Dhaka over a period 6 months between October 2013 to March 2014. A total of 50 patients with histologically confirmed carcinoma cervix were consecutively included in the study. Clinical presentation, staging and histopathological grading were done to see the correlations among them. All information was recorded in data collection sheet. Data were analyzed by SPSS. Data were compared and correlated among groups and presented by tables and figures. **Results:** Over two-thirds (70%) of the patients were of age 50 or > 50 years with mean age being 51.8 ± 7.7 years indicating that carcinoma cervix is disease of late middle aged or elderly women. In the present study patients were predominantly at menopausal stage (76%). Vaginal discharge was the predominant complaints (66%) followed by irregular bleeding (54%), postcoital bleeding (34%) and foul smelling discharge per vagina. Seventy percent of the cases were clinically categorised as stage IB1 followed by IB2 (16%), IA (6%), IIB2 (4%) and IIIA (4%). Histopathologically majority of the cases was ranked as Grade-II (90%) and typed as squamous-cell carcinoma (94%). Based of clinical symptoms, 42% of the carcinoma cervix were predicted as having advanced disease, but based on clinical staging and histopathological 8% and 6% of the cases respectively were considered having advanced. **Conclusion:** Present study concluded that clinical staging well-correlates with histopathological grading, but prediction of the status of the disease with mere clinical symptoms may be misleading.

Keywords: Carcinoma cervix, Clinical presentation, Staging, Histopathological findings.

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INTRODUCTION

Cervical cancer is one of the gravest threats to women's lives. It is estimated that over a million women worldwide currently have cervical cancer. Most of these women have not been diagnosed, nor do they have access to treatment that could cure them or prolong their lives. In 2020, an estimated 604 000 women were diagnosed with cervical cancer worldwide

and about 342 000 women died from the disease. Cervical cancer is the most commonly diagnosed cancer in 23 countries and is the leading cause of cancer death in 36 countries. The vast majority of these countries are in sub-Saharan Africa, Melanesia, South America and South-Eastern Asia [1]. Most women who die from cervical cancer, particularly in developing countries, are in the prime of their lives. They may be raising children, caring for their families and contributing to

the social and economic lives of their towns and villages. While less developed countries are clearly more likely to lack effective health systems and adequate financial resources compared with developed countries, it is crucial to underscore that another of the most overlooked but powerful drivers of cervical cancer is lack of equality for women in terms of access to health care in many societies [2].

Persistent infection with cancer-causing HPV types is the cause of most cervical cancer. Ninety per cent of cervical cancers are squamous cell cancers and initiate in the transformation zone of the ectocervix; the other 10% are adenocarcinomas, which arise in the glandular columnar layer of the endocervix [2]. Normal cells gradually transform to form cancer cells through several stages. More than 85% of the disease occurs in developing countries. Bangladesh, like other developing countries faces a burden of the disease [3]. It is a well-known fact that Carcinoma of Cervix is the major killer of female population more so in Bangladesh. According to Globocon report cervical cancer is the second leading malignancy, in terms of both incidence and mortality, among Bangladeshi women [4]. While incidence and treatment modalities for cervical cancer have been previously investigated in Bangladeshi populations [5], there is virtually no published information regarding outcomes among those treated from cervical cancer. There are significant challenges to the development of infrastructure for cancer care in Bangladesh.

Cervical cancer begins with a pre-cancerous stage, known as dysplasia which takes many years to develop from a normal cell. A diagnosis of cancer or a precancerous condition depends on the detection of abnormal cells on a Pap smear by cytopathologist [6]. A wide range of reactive, infectious and inflammatory conditions may give rise to cells which closely mimic that of pre-cancerous or malignant lesion which may lead to misdiagnosis, thus endangering patient lives. This may ultimately have a major impact on the management of disease. The advantage of cytology in differentiating abnormal cells from normal cells has been widely recognized and accepted in cervical screening program. However, the false negative results may unnecessarily postpone the required treatment [7]. Hence, care should be emphasized while reporting Pap smears. Cervical carcinoma in developing countries is related to a number of risk factors like early marriage, early experience of sexual activity, multiparity, poverty and high incidence of sexually transmitted diseases and HPV infection [1, 2].

One of the most common symptoms of cervical cancer is abnormal vaginal bleeding, but in some cases there may be no obvious symptoms until the cancer has progressed to an advanced stage. The diagnosis of invasive disease is usually made by biopsy of a lesion in cervix visible on gross pelvic examination. Cervical carcinoma has different

histopathological types. Squamous cell carcinoma (SCC) accounts for 75-80% of cervical cancers, adenocarcinoma 15-25% and adenosquamous carcinoma 3-5% [8]. Adenosquamous carcinoma exhibit both glandular and squamous differentiation. They may be associated with a poorer outcome than pure SCC or adenocarcinoma. In addition neuroendocrine or small cell carcinoma can originate in the cervix in women but are infrequent. Rhabdomyosarcoma of the cervix is rare, it occurs in adolescent and young women [9]. A study showed that about 90 – 95% is squamous cell carcinoma and 1 – 5% are adenocarcinoma and majority of the patients presents with stage IIB at first detection; least number patients are found in stage IV, and no patients found in stage IA [3].

Cervical cancer presents as major cause of morbidity and mortality especially in developing countries. The cause of such a high incidence is the continued negligence of benign lesion of cervix, which are common here due to early marriage, high parity, obstetrical trauma, lower socioeconomic condition, poor hygienic conditions [10, 11]. Despite of these glaring statistic, cervical cancer is a favorable site for effective control program as it is easily accessible, large number of cell exfoliated from precancerous lesion are available. There is usually long natural history of preinvasive phase, which is easily recognizable by screening techniques. Therefore aim of this study was to find out the correlation among clinical presentation, staging and histopathological findings in carcinoma cervix.

MATERIALS & METHODS

This cross-sectional study was carried out in the of Gynaecologic Oncology Division of the Department of Obstetrics & Gynaecology, Bangabandhu Sheikh Mujib Medical University Hospital, Dhaka over a period six months from October 2013 to March 2014. Patients having clinical features of carcinoma cervix and were confirmed histologically were included in the study. Patients having other pathology in cervix, and those who did not voluntarily consent to participate in the study were excluded. According to Helsinki Declaration for Medical Research Involving Human Subjects 1964, all the study subjects were informed verbally about the study design, the purpose of the study and how the study would be beneficial for the community. Patients who gave informed consent to participate in the study were included as study sample. Data were collected using a structured questionnaire (research instrument) containing the variables of interest. Using computer software SPSS (Statistical Package for Social Sciences), version 17, data were processed and analysed. The test statistics used to analyse the data were descriptive statistics. The summarized were presented in the form of tables and graphs with due interpretation.

RESULTS

According to the questionnaire, history of all the 50 selected cases were taken, the clinical examination was carried out meticulously. Demographic characteristics of the study subjects show that 70% were of age 50 or > 50 years with mean age of the subjects being 51.8 ± 7.7 years. Rural patients were a bit higher (58%) than the urban ones (42%) (Table 1).

Majority of the patients was anemic (90%) and pale (86%). About two-thirds (66%) of the patients complained of vaginal discharge followed by irregular bleeding (54%), postcoital bleeding (34%) and foul smelling discharge per vagina (Table 2).

Vaginal mucosa in majority (92%) of the cases was healthy, but cervix was ill-looking in 82% of the cases. Growth was visible in 90% of the cases with average size of the growth being 5.5 cm^2 . Most of the growths was friable (86%) with ulceration (96%) which bled on touch (90%). Fornix was free in 96% but

extension of growth was observed in 12% of the cases (Table 3).

Seventy percent of the cases were clinically classified as stage IB1 followed by IB2 (16%), IA (6%), IIB2 (4%) and IIIA (4%) (Table 4).

Histopathological grading revealed that ninety percent of the carcinoma cervix were ranked as Grade-II, 6% Grade-III and 4% Grade-I (Figure 1). Histopathological type of carcinoma revealed that 94% were squamous-cell carcinoma (Figure 2).

In table 5, clinical presentation, staging and histopathological grading were correlated. Based of clinical symptoms, 42% of the carcinoma cervix were predicted as having advanced disease, while based on clinical staging, 8% were considered having advanced disease. Histopathological grading demonstrates that 6% of the diseases were non-operable or advanced (Table 5).

Table 1: Demographic characteristics of respondents, (n = 50)

Demographic variables	Frequency	Percentage
Age (years)		
< 50	15	30.0
≥ 50	35	70.0
Mean ± SD	51.8 ± 7.7	
Residence		
Rural	29	58.0
Urban	21	42.0

Table 2: Clinical presentation of the respondents, (n = 50*)

Clinical presentation	Frequency	Percentage
Pallor	43	86.0
Oedema	4	8.0
Anemia	45	90.0
P/V watery discharge	33	66.0
Irregular P/V bleeding	27	54.0
P/V foul smelling discharge	6	12.0
Postcoital P/V bleeding	17	34.0

* Multiple responses

Table 3: Distribution of respondents by pervaginal examination findings, (n=50)

Pervaginal examination	Frequency	Percentage
Vaginal mucosa		
Healthy	46	92.0
Unhealthy	4	8.0
Cervix		
Normal looking	9	18.0
Ill looking	41	82.0
Growth present in the cervix	45	90.0
Size of the growth (cm^2) (n=45)		
<10	37	74.0
≥10	8	16.0
Mean ± SD	5.5 ± 5.3	
Consistency of the growth		
Friable	43	86.0

Pervaginal examination	Frequency	Percentage
Hard	2	4.0
Ulceration	48	96.0
Bleeds on touch	45	90.0
Fornix		
Free	48	96.0
fixed	2	4.0
Extension to surrounding structures	6	12.0
Unhealthy	4	8.0
Cervix		

Table IV: Clinical staging of the disease, (n = 50)

Staging of the disease	Frequency	Percentage
IA	3	6.0
IB1	35	70.0
IB2	8	16.0
IIB2	2	4.0
IIIA	2	4.0

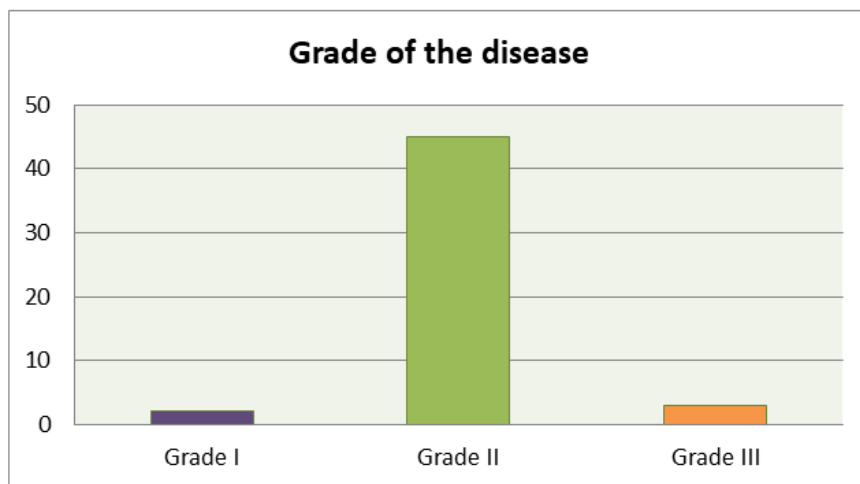


Figure 1: Histopathological grading of carcinoma cervix, (n = 50)

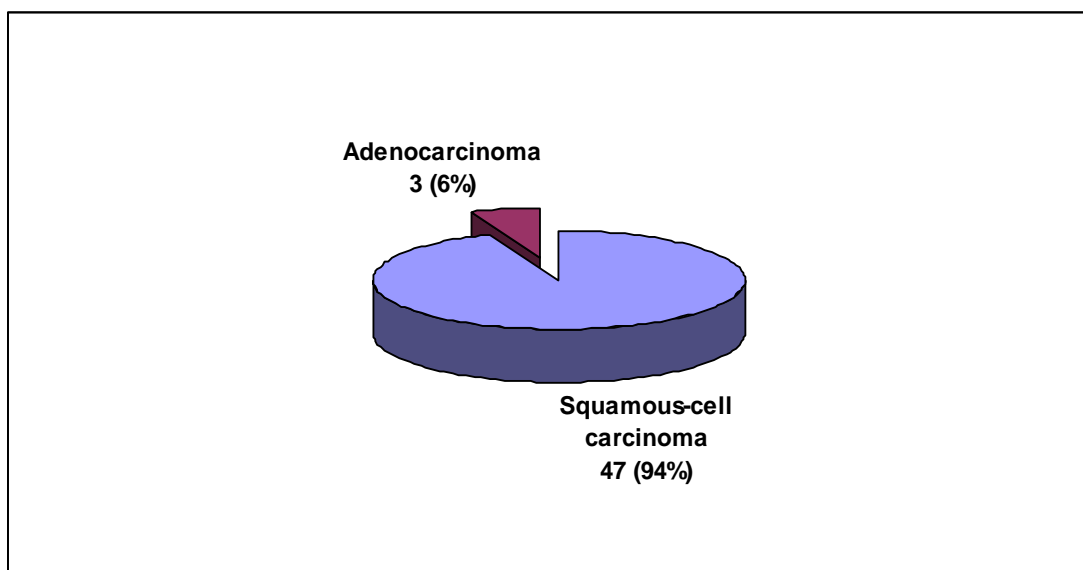


Figure 2: Histopathological types of carcinoma cervix, (n = 50)

Table 5: Correlation among clinical presentation, staging and histopathological grading, (n = 50)

Disease stratification	Frequency	Percentage
Clinical symptoms		
Early	29	58.0
Advanced	21	42.0
Clinical staging		
Operable	46	92.0
Non-operable	4	8.0
Histopathological grading		
Grade-II	47	94.0
Grade-III	3	6.0
Grade-II	47	94.0
Grade-III	3	6.0

DISCUSSION

It appears from the findings of the study that over two-thirds (70%) of the patients were of age 50 or > 50 years with mean age being 51.8 ± 7.7 years indicating that carcinoma cervix is disease of late middle aged or elderly women. Rural patients were a bit higher (58%) than the urban ones (42%). In a study at BSMMU, majority of the patients suffering from cervical carcinoma had mean age of 45.21 ± 9.75 years, (range 26-80 years) and frequency of rural patients were a bit higher (58%) than the urban ones (42%) [3] More than 45% of the patients were within the age range of 36-45 years.

In the present study patients were predominantly at menopausal stage (76%). Nearly 55% of the patients' age of menarche was 13 years and the rest was 12 years. In majority (84%) of the patients, past menstrual cycle was regular and 50% of the patients delivered their first child before 18 years of age with mean age being 17.2 years. Majority of the patients was anemic (90%) and pale-looking (86%). Vaginal discharge was the predominant complaints (66%) followed by irregular bleeding (54%), postcoital bleeding (34%) and foul smelling discharge per vagina. Vaginal mucosa was healthy in 92% of the cases, but cervix was ill-looking in 82% of the cases. Ninety percent of the patients exhibited visible growth with average size of the growth being 5.5 cm^2 . Most of the growths was friable (86%) with ulceration (96%) which bled on touch (90%). Fornix was free in 96% but extension of growth to the surrounding structures was observed in 12% of the cases. Seventy percent of the cases were clinically categorised as stage IB1 followed by IB2 (16%), IA (6%), IIB2 (4%) and IIIA (4%). Histopathologically majority of the cases was ranked as Grade-II (90%) and typed as squamous-cell carcinoma (94%).

Based on clinical symptoms, 42% of the carcinoma cervix were predicted as having advanced disease, but based on clinical staging and histopathological grading 8% and 6% of the cases respectively were considered having advanced disease indicating that clinical staging well-correlates with

histopathological grading, but prediction of the status of the disease with mere clinical symptoms may be misleading. Literatures suggest that advanced stage of the disease usually presents with postcoital bleeding, pelvic or sciatic pain, and foul smelling vaginal discharge [1, 2]. In the present study 21(42%) patients presented with postcoital bleeding and/or foul smelling vaginal discharge, but more than 80% of them did not have advanced stage of the disease. Ferdous *et al.*, [3] in a similar study also reported that clinical staging of the disease are not fairly comparable with histologic grading of the disease.

Proper staging of the disease is key to planning ensuring optimal treatment [11, 12]. The International Federation of Gynecology and Obstetrics (FIGO) recommends a clinical staging system for cervical carcinoma which, among others includes inspection, palpation, endocervical curettage, cystoscopy, proctoscopy, intravenous urography, and radiographic evaluation of lungs and skeleton. However, the accuracy of FIGO staging system is questionable as in this system 24-39% cases may erroneously be classified into stage when they are actually not. Staging of the disease using FIGO staging system depends on the experience of the examining physician [13]. In spite of that it is commonly used for treatment planning. But is no more adequate in the evaluation of prognostic factors like tumor volume and nodal status. The most important prognostic factors for cervical cancer are tumor stage and size [1, 2, 11]. Although not included in the International Federation of Gynecology and Obstetrics (FIGO) staging, the presence and extent of nodal involvement is an another important prognostic factor.

CONCLUSION

Cervical cancer is one of the leading causes of cancer death among females worldwide and its behavior epidemiologically likes a venereal disease of low infectiousness. Early age at first intercourse and multiple sexual partners have been shown to exert strong effects on risk. From the findings of the study it can be concluded that majority of the patients presented with symptoms of advanced disease (postcoital

bleeding and/or foul smelling vaginal discharge), may not have advanced disease in the clinical staging and histopathological grading. So the clinical staging well-correlates with histopathological grading, but prediction of the status of the disease with mere clinical symptoms may be erroneous.

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