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Prevalence and genotype of human papillomavirus in laryngeal cancer patients

Abstract

Introduction: Squamous cell cancer ([1] SCC) of the larynx is the most common type of cancer. Human papillomavirus ([2]HPV) is an etiological agent for head and neck cancers, especially laryngeal cancer. It is necessary to increase our knowledge about the role of HPV in the cause of laryngeal SCC, its prevalence in each geographic region, and its high-risk types in order to facilitate the development of new, specific and more targeted methods.

Objective: The present study was conducted to investigate the prevalence and genotype of human papillomavirus in laryngeal cancer patients.

Materals and Methods: The current research is a cross-sectional descriptive study. Patients were included in the study by census method. Sampling from the pathology department and medical records using patient files and samples of Laryngeal cancer referred to the medical education centers of Mazandaran University of Medical Sciences. Statistical analyzes were performed with the help of SPSS26 software.

Results: The findings of this study indicate that 14.5% of patients were HPV+ and the prevalence of high-risk genomes is type 18 (30.7%), type 31 (7.6%), type 33 (23%), and type 6 (36.3%). Also, genomes 6, 18, and 33 were the most common**.**

Conclusion: It can be stated that the role of human papillomavirus in the etiology of precancerous lesions of the larynx and laryngeal cancer is undeniable and due to its distinct clinical behavior in terms of high-risk types in each geographical region.

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Keywords: *Laryngeal cancer, human papillomavirus, genotype, prevalence*

Introduction

Laryngeal cancer is the uncontrolled growth of malignant cells in the larynx and its surrounding tissues. Laryngeal cancer is the 20th most common human cancer (1). Every year, 151,000 new cases are diagnosed worldwide and 88,000 deaths are related to it (2). Squamous cell cancer (SCC1) of the larynx is the most common cancer among head and neck cancers, which accounts for about 60% of all cancers. forms the neck (3). Like most head and neck cancers, squamous cell cancer is associated with a history of smoking <excessive alcohol consumption >improper diet <synonyms of gastroesophageal reflux disease (GERD) and laryngopharyngeal reflux (LPR) (4,5). Virus Human papillomaviruses (HPV2) are viruses with a circular double-stranded DNA genome >8000 nucleotides that can cause tumors (6). And it is an etiological factor for head and neck cancers, especially in laryngeal cancer, and it is known to be an important carcinogenic factor (7, 8). Various studies have shown the relationship between human papillomavirus infection and the process of cancer. The most common parts of the body that are attacked by the virus include the reproductive system, skin, as well as pharynx, mouth, and larynx (9). The epithelium of the larynx is sensitive to HPV infection. HPV penetrates the organ through micro-damage to the mucous membrane, which allows it to access the basal layer of the epithelium. The virus infects the absorbing and dividing cells. HPV attaches itself to the cell membrane using epidermal growth factor receptors and infects the cells in this way (10, 11). Today, more than 150 types of HPV genomes are known, which are divided into high-risk and low-risk categories based on their carcinogenic power (12). The role of human papilloma (HPV) DNA in head and neck cancer and its relationship with other risk factors have been widely investigated (13, 14). Worldwide, approximately 38,000 cases of head and neck squamous cell cancer are related to HPV (15). Studies of HPV infection in laryngeal SCC have reported a wide range of results. Some studies have reported a prevalence of 0% -80% (16) and some 20-30% (17), which may be due to the use of different techniques with different sensitivities and different sampling methods (biopsy or scraping, fixation formalin, and paraffin freezing or tissue freezing) (18). The most common diagnostic methods used include polymerase chain reaction (PCR), in situ hybridization (ISH), and immunohistochemistry ([3]IHC) (19). The best diagnostic method is to determine the presence of HPV DNA in tumor tissue samples by PCR and ISH methods. A combination of these two approaches detects HPV infection more reliably than each of these methods with a sensitivity of 97% and a specificity of 94% (20). On the other hand, studies have shown that the prevalence of HPV in LSCC can be different in terms of geography and ethnic groups, and this can be due to genetic diversity or environmental and cultural differences (8, 21). In a meta-analysis study, Kramer et al paid special attention to the geographical location of the

[1]Squamous cell carcinoma
[2]Human Papilloma Virus

studies conducted on the relationship between HPV infection and head and neck cancer, especially laryngeal cancer, and confirmed that the prevalence of HPV infection in head and neck cancer cases depends on the geographical area where the patients are. It depends. The prevalence of HPV in laryngeal infection is higher in Asia and accounts for 38.2% of squamous cell cancers (22). Laryngeal cancer associated with viral infections has a long course of progression resulting from a persistent and latent infection. Meanwhile, other HPV-related head and neck cancers have less severe disease periods, respond better to radiation therapy and chemotherapy, and lead to long-term patient survival (23, 24). Currently, the main factor of clinical prognosis in these patients is determined by the spread of the tumor(25) and the knowledge about how to better respond to the treatment of patients with HPV related to laryngeal cancer and its importance in the prognosis of patients is weak, and more research on It is needed on this topic (26). Since there are 2 types of preventive vaccines against the HPV virus, bivalent (HPV 16 and HPV18) and quadrivalent (against HPV 16, 18, 11, and 6) are available and the vaccines are designed to induce the production of antibodies against the viral protein. and do not have viral DNA(26), as a result, knowing the high-risk types of this virus in any society can be effective in choosing the correct type of vaccine to prevent infection in the at-risk group. The role of human papillomavirus in the etiology of precancerous lesions of the larynx and laryngeal cancer. It is undeniable and due to its distinctive clinical behavior in terms of high-risk types in each geographical region, it is a subject that has a lot of scope for research. It is necessary to increase our knowledge about the role of HPV in the cause of laryngeal SCC, its prevalence in each geographic region, and its high-risk types in an attempt to the prevalence and genotype of human papillomavirus in cancer patients. Laryngology was performed in hospitals affiliated with Mazandaran University of Medical Sciences. Facilitate the development of new, specific, and more agreed methods and to identify and plan more features of each tumor. For more specific treatment. As a result, according to the search of available sources and databases, extensive evidence was not found regarding the prevalence and high-risk types of human papillomavirus in laryngeal cancer patients in the hospitals of the country, the present study aims to investigate

Materials and Methods:

This present research is a cross-sectional descriptive study that was conducted in the form of data extraction using a checklist from the files of laryngeal cancer patients referred to hospitals affiliated with Mazandaran University of Medical Sciences during the years 2018-2021. Patients were included in the study by census method. To collect data, the researcher's checklist and the patient's pathology sample were used. Sampling from the pathology department and medical records using patient files and samples Laryngeal cancer referred to the medical education centers of Mazandaran University of Medical Sciences was investigated and patients' information was checked and forms were completed, and the samples in the pathology department were used to perform PCR and then determine the genotype. The informed consent form for entering the study was completed for all participants and then statistical analyzes were performed with the help of SPSS26 software.

Results:

During the 3-year study period from September 2018 to August 2021, 90 patients were examined by the pathology department and their information was entered within the specified period. In this study the most cases were men (92.5%). Mean and standard deviation of age at patients was 62.30±11.85 years, with the youngest and the oldest patients as 35 years and 88 years, respectively. Also 55.6% of the patients had a history of alcohol consumption. The stage of cancer in most patients was in stage 1A,67 (74.4%). (Table 1)

Based on the results of the study, 13 patients' secretions were PCR positive for the HPV virus, and in 77 people of patients, PCR was negative, which includes 14.5% and 85.5% of patients, respectively.

The findings of this study indicate that 14.5% of patients were HPV+ and the high-risk genomes is type 18 was the most case. (Table 2)

Table 1: The cancer stage of patients

Stage of cancer	N	%
1A	1	1.1
2A	67	74.4
2B	4	4.4
3A	3	3.3
4A	15	16.7

Table 2: Virus genotype of patients

Virus Genotype	N	%
6	5	38.4
18	4	30.7
31	1	7.6
3	3	23

Discussion and conclusion:

squamous cell cancer of the larynx is the most common type of cancer of the head and neck, which accounts for about 60% of It forms head and neck cancers (3). Various studies have shown the relationship between human papillomavirus infection and the process of cancer. The most common parts of the body that are attacked by the virus include the reproductive system, skin, as well as pharynx, mouth, and larynx (9). Today, more than 150 types of HPV genomes are known, which are divided into high-risk and low-risk categories based on their carcinogenic power (12). Studies have reported the prevalence of HPV infection in laryngeal SCC with a wide range of results. Some studies have reported a prevalence of 0% -80% (16) and some 20-30% (17), which may be due to the use of different techniques with different sensitivities and different sampling methods (biopsy or scraping, fixation formalin, and paraffin freezing or tissue freezing) (18). The best diagnostic method is to determine the presence of HPV DNA in tumor tissue samples by PCR and ISH methods. On the other hand, studies have shown that the prevalence of HPV in LSCC can be different in terms of geography and ethnic groups, and this can be due to genetic diversity or environmental and cultural differences (8, 21). In a meta-analysis study, Kramer et al paid special attention to the geographical location of the studies conducted on the relationship between HPV infection and head and neck cancer, especially laryngeal cancer, and confirmed that the prevalence of HPV infection in head and neck cancer cases depends on the geographical area where the patients are. It depends. The prevalence of HPV in laryngeal infection is higher in Asia and accounts for 38.2% of squamous cell cancers (22). Currently, the main factor of clinical prognosis in these patients is determined by the spread of the tumor(25) and the knowledge about how to better respond to the treatment of patients with HPV related to laryngeal cancer and its importance in the prognosis of patients is weak, and more research on this issue is needed (26). Since there are 2 types of preventive vaccines against the HPV virus, bivalent (HPV 16 and HPV18) and quadrivalent (against HPV 16, 18, 11, and 6) are available and vaccines for They are designed to induce antibody production against viral protein and do not contain viral DNA (26), as a result, knowing the high-risk types of this virus in any society can be effective in choosing the correct type of vaccine to prevent infection in the at-risk group. The role of human papillomavirus in the etiology of precancerous lesions of the larynx and laryngeal cancer is undeniable, and due to its distinct clinical behavior in terms of high-risk types in each geographical region, it is a subject that has a lot of scope for research. It is necessary to increase our knowledge about the role of HPV in the cause of laryngeal SCC, its prevalence in each geographic region, and its high-risk types in order to facilitate the development of new, specific, and more targeted methods and to identify and plan more features of each tumor. For more specific treatment. Therefore, considering the importance of the mentioned cases, this study was conducted to investigate the prevalence and genotype of human papillomavirus in laryngeal cancer patients referred to hospitals affiliated with Mazandaran University of Medical Sciences. The findings of this study indicate that 13 patients were HPV+ and 77 patients were HPV-, which includes 14.5% and 85.5% of patients, respectively. Also, based on the results of the prevalence of high-risk genomes, type 18 in 4 cases, type 31 in 1 case, type 33 in 3 cases, and type 6 genome in 5 cases, which include 30.7%, 7.6%, 23% and 38.4% of the positive cases, respectively. Thus, genomes 6, 18, and 33 were the most common in Mazandarani patients of the study population.

Suggestions:

conducting a more comprehensive study with higher sample size and by different experts,

conducting a systematic review and meta-analysis in the scope of the present study, and giving a

on vaccination to prevent infection in the at-risk group with a quadrivalent vaccine (against HPV 16, 18, 11, and 6) after further studies and investigation, conducting more

studies that the diagnostic method used in their study is a combination of PCR and ISH methods and therefore has a higher and more reliable diagnostic capability than a specific method.

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