ORIGINAL ARTICLE

HBV AND HCV INFECTION IN HEAD AND NECK CANCER - A SINGLE ONCOLOGY CENTER EXPERIENCE

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ABSTRACT

Background: The present study aimed to assess the correlation between hepatitis B and hepatitis C infection in patients with head and neck cancer at a tertiary care hospital in Karachi, Pakistan.

Material and Methods: A correlation study was conducted at the medical oncology department, Jinnah Postgraduate Medical Center, Karachi, Pakistan, from April 2021 and June 2021. The study included two hundred and ninety-six patients of age greater than 18 years of either sex with a confirmed head and neck cancer diagnosis. The data regarding age, gender, ethnicity, area, education, family income, addictions, family history of any cancer, head and neck cancer history, site, type, stage and grade of tumor, nodal status, and presence of metastasis were collected from all the patients. Each patient had 15 mL of blood taken and forwarded to the laboratory for viral detection utilizing a third-generation Enzyme-Linked Immunosorbent Assay. In the laboratory, the cut-offs for hepatitis B and hepatitis C were 2.0 and 1.0, respectively. SPSS version 23 was utilized to perform data analysis.

Results: The mean age was estimated as 46.23 ± 12.42 years. Of 296 head and neck cancer patients, 82 had hepatitis B infection (27.7%), and 102 had hepatitis C infection (34.5%). Almost 61 patients were co-infected with hepatitis B and hepatitis C. There was a statistically significant association between hepatitis B and hepatitis C among head and neck cancer (p=0.0001).

Conclusion: These results suggest a significant association between hepatitis B and hepatitis C among head and neck cancer patients.

Keywords: Co-infection, Hepatitis B, Hepatitis C, Head and neck cancer, Squamous cell carcinoma, Viral infection

BACKGROUND

Head and neck cancers are the fifth most common malignancy globally, and they represent a varied collection of malignancies. According to a global study released in 2017, there were 890,000 head and neck cancer instances and 507,000 deaths worldwide, accounting for 5.3 percent of all malignancies.[1,2] Squamous cell carcinoma accounts for almost 90% of head and neck cancers, with 70% occurring in the pharynx, larynx, and oral cavity.[2] Adenocarcinomas, connective tissue tumors, melanomas, and lymphomas account for the remaining 10% of head and neck cancers.[2]

Head and neck cancers are highly prevalent among patients with alcohol and tobacco consumption. These malignancies have also been linked to viral infections such Epstein-Barr virus (EBV), human papillomavirus (HPV), hepatitis C (HCV), hepatitis B (HBV), and human immunodeficiency virus (HIV).[1,3] There is an established association of nasopharyngeal carcinoma and EBV infection and oropharyngeal carcinoma with HPV infection.[3-6] The link of head and neck squamous cell carcinoma with HBV and HCV has also been explored in a few researches.[3] Dona et al. found a positive relationship between head and neck squamous cell carcinoma and HCV (Odds ratio = 2.59; 95 % CI, 1.46-4.60) and HBV (Odds Ratio= 2.76; CI 95 %, 1.64-4.64).[7] According to Nayyar et al., the most frequent infection among patients with head and neck squamous cell carcinoma was HBV (55.1%), followed by HIV (23%) and HCV (19%).[3]

HBV and HCV are worldwide public health concerns.[8] According to the WHO, one in every three persons globally is infected with HCV or HBV, and over 1.3 million people died as a result of it in 2015.[8] Every year, over 185 million people are infected with HCV, and nearly 2 billion people are infected with HBV.[8] In

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This article can be sited as: Abro NA, Haider G, Shah A, Sarim T, Kumari R, Ramchand A. HBV and HCV infection in head and neck cancer-A single oncology center experience. Infect Dis J Pak 2022; 33(4): 108-113.

Pakistan, HBV is a highly endemic and severe public health issue affecting millions of individuals. Still, the proportion of super/co-infection with HCV in head and neck patients is generally unknown. Therefore, the current study was conducted to determine the ratios of HCV and HBV among patients with head and neck cancer and to assess the correlation between HBV and HCV infection among patients at a tertiary care hospital in Karachi, Pakistan.

MATERIAL AND METHODS

A correlational study was conducted at the medical oncology department, Jinnah Postgraduate Medical Center, Karachi, Pakistan, from April 2021-Jun 2021. By using OPENEPI sample size calculator, the sample size of 296 patients was estimated by taking the prevalence of HBV as 4.25% among patients with head and neck cancer,[7] absolute precision as 2.3%, and 95% confidence level. All the patients of age greater than 18 years of either sex with a confirmed head and neck cancer diagnosis were included in the study. Patients having chemotherapy and radiation therapy exposure, mental problems, pregnant and lactating females were excluded from the study. A Non-random convenience sampling method was employed for the selection of samples.

The ethical approval was taken from the ethical review committee before the conduct of study (ERC approval NO.F.2-81/2021-GENL/58456/JPMC). Verbal informed permission was acquired from all of the eligible individuals. The data regarding age, gender, ethnicity, area, education, family income, addictions like smoking, tobacco, naswar, betel nuts, betel leaf and alcohol consumption, family history of any cancer, family history of head and neck cancer, site, type, stage and grade of tumor, nodal status and presence of metastasis were collected from all the patients. Each patient had 15 mL of blood taken and forwarded to the laboratory for viral detection. Antibodies to hepatitis B (HBV) and hepatitis C (HCV) were found utilizing a third-generation Enzyme-Linked Immunosorbent Assay (ELISA). In the laboratory, the cut-offs for HBV and HCV were 2.0 and 1.0, respectively. All data was collected using a predefined pro forma.

Statistical Package for the Social Sciences (SPSS) version 27 was used to analyze data. Mean and SD was computed for numeric variables like age. Frequency and percentage were computed for categorical variables like gender, ethnicity, area, education, family income, addictions like smoking, tobacco, naswar, betel nuts, betel leaf and alcohol consumption, family history of any cancer, family history of head and neck cancer, site, type, stage and grade of tumor, nodal status, presence of metastasis, HBV and HCV infection. Chi-square/Fisher exact test was applied to check the correlation between the presence of HBV and HCV infection. The proportions of HBV and HCV were stratified concerning site, type, stage, and grade of tumor, nodal status, and presence of metastasis using Chi-square/Fisher exact test. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

The study comprised a total of 296 head and neck cancer patients. The average age was estimated as 46.23 ± 12.42 years (range: 16-76 years). Urdu was spoken by the majority of the patients (n=138, 22%), followed by Sindhi (n=65, 22%). The majority of the patients were men (n=220, 74.3%), from urban areas (n=211, 71.3%), no formal education (n=132, 44.6%), and had a household monthly income of less than 15,000 PKR (n=181, 61.1%). Among the 296 patients, 104 were betel nut users (35.1%), 84 were smokers (28.4%), 66 were betel leaf consumers (22.3%), 63 were tobacco users (21.3%), 57 were naswar consumers (19.3%), and 9 were alcoholics (3%). Of the 296 patients, 46 had a family history of cancer (15.5%) and 13 had a family history of head and neck cancer (4.4%). The oral cavity was the most common location of malignancy (n=248, 83.8 percent), followed by the nasopharynx (n=19, 6.4%). Squamous cell carcinoma was found in 285 individuals (96.3%), while adenocarcinoma was found in 11 patients (3.7%). Of 296 patients, 133 had T3 tumor size (44.9%), 198 had at least one lymph node involved (66.9%), 257 had grade II of tumor (86.8%) and 295 had no metastasis (99.7%) (Table-1).

Of 296 head and neck cancer patients, 82 had HBV infection (27.7%) and 102 had HCV infection (34.5%). Almost 61 patients were co-infected with hepatitis C (HCV) and hepatitis B (HBV). There was a statistically significant association between HBV and HCV among patients with head and neck cancer (p=0.0001) (Table-2).

Statistically, no significant association was found between proportions of HBV and HCV infection and site, type, grade of tumor, nodal status, and metastasis (p>0.05) (Table-3).

Table-1: Descriptive analysis of study variables (n=296)

	Mean ± SD		n (%)
Age in years	46.23±12.42	**Family history of cancer**	
		Yes	46 (15.5%)
Gender	**n (%)**	No	250 (84.5%)
Male	220 (74.3%)	**Family history of head and neck cancer**	
Female	76 (25.7%)	Yes	13 (4.4%)
Ethnicity		No	283 (95.6%)
Urdu	138 (46.6%)	**Site of tumor**	
Sindhi	65 (22%)	Oral cavity	248 (83.8%)
Punjabi	30 (10.1%)	Nasopharynx	19 (6.4%)
Balochi	24 (8.1%)	Larynx	17 (5.7%)
Pashto	20 (6.8%)	Hypopharynx	8 (2.7%)
Others	19 (6.4%)	Oropharynx	4 (1.4%)
Locality		**Type of tumor**	
Urban	211 (71.3%)	Squamous cell carcinoma	285 (96.3)
Rural	85 (28.7%)	Adenocarcinoma	11 (3.7)
Education		**Tumor size**	
No formal education	132 (44.6%)	T1	4 (1.4%)
Primary	85 (28.7%)	T2	57 (19.3%)
Matric	31 (10.5)	T3	133 (44.9%)
Intermediate	32 (10.8%)	T4	102 (34.5%)
Graduate	14 (4.7%)	**Nodal status**	
Postgraduate	2 (0.7%)	No	42 (14.2%)
Family income		N1	198 (66.9%)
<15,000 PKR	181 (61.1%)	N2	56 (18.9%)
15,000-30,000 PKR	105 (35.5%)	**Grade of tumor**	
>30,000 PKR	10 (3.4%)	I	24 (8.1%)
Addiction		II	257 (86.8%)
Betel nuts	104 (35.1%)	III	15 (5.1%)
Smoking	84 (28.4%)	**Metastasis**	
Tobacco	63 (21.3%)	Mo	295 (99.7%)
Betel leaf	66 (22.3%)	M1	1 (0.3%)
Naswar	57 (19.3%)		
Alcohol	9 (3%)		

Table-2. Correlation of HBV with HCV in patients with head and neck cancers (n=296)

HBV	HCV		Total	p-value
	Yes	No		
Yes	61	21	82	<0.0001
No	41	173	214	
Total	102	194	296	

Table-3: Stratification of HBV and HCV with respect to the site, type, grade of tumor, nodal status, and metastasis

	HCV			HBV		
	Yes	No	p-value	Yes	No	p-value
Site of tumor						
Oral cavity	84	166		68	182	
	33.6%	66.4%		27.2%	72.8%	
Larynx	4	13		4	13	
	23.5%	76.5%		23.5%	76.5%	
Hypopharynx	2	6		1	7	
	25.0%	75.0%	0.762	12.5%	87.5%	

Oropharynx	2	2		1	3	
	50.0%	50.0%		25.0%	75.0%	
Nasopharynx	8	12		6	14	
	40.0%	60.0%		30.0%	70.0%	0.950
Histological type						
Adenocarcinoma	0	2		0	2	
	0.0%	100.0%		0.0%	100.0%	
Squamous cell carcinoma	99	192		79	212	
	34.0%	66.0%	0.551	27.1%	72.9%	0.9990
Size of tumor						
T1	3	1		1	3	
	75.0%	25.0%		25.0%	75.0%	
T2	21	35		19	37	
	37.5%	62.5%		33.9%	66.1%	
T3	42	94		34	102	
	30.9%	69.1%		25.0%	75.0%	
T4	35	70		27	78	
	33.3%	66.7%	0.278	25.7%	74.3%	0.600
Nodal status						
No	11	31		9	33	
	26.2%	73.8%		21.4%	78.6%	
N1	64	138		57	145	
	31.7%	68.3%		28.2%	71.8%	
N2	26	31		15	42	
	45.6%	54.4%	0.086	26.3%	73.7%	0.69
Grade of tumor						
I	5	18		5	18	0.22
	21.7%	78.3%		21.7%	78.3%	
II	88	175		69	194	
	33.5%	66.5%		26.2%	73.8%	
III	8	7		7	8	
	53.3%	46.7%	0.127	46.7%	53.3%	
Metastasis						
Mo	99	198		80	217	
	33.3%	66.7%		26.9%	73.1%	
M1	1	0		1	0	
	100.0%	0.0%	0.366	100.0%	0.0%	0.272

DISCUSSION

Head and neck cancer are some of the common malignancies in South Asian countries including Pakistan.[9,10] It has also been found that Pakistan has a huge population suffering from viral diseases like hepatitis B (HBV) and hepatitis C (HCV).[11,12] HCV infection has a prevalence of 7%-14%, while HBV infection has the prevalence of 6.7% in Sindh province respectively.[12,13] Studies showed that HCV and HBV infection are correlated with head and neck cancer. [1,3,7,14,15] but there is a lack of Pakistani literature in this regard. Therefore, we have evaluated the proportions of HCV and HBV among patients with head and neck cancer and assessed the correlation between HBV and HCV infection among those patients presenting at a tertiary care hospital of Karachi, Pakistan.

In the current study, the average age of patients with head and cancer was 46 years, and the majority of the patients were men (74.3%). According to Aziz et al., study's the average age of head and neck cancer patients was 50 years, and most of the patients were men (76%).[16] According to global statistics from various socio-demographic backgrounds, head and neck cancer has a linear connection with advancing age, with the average age being 51 to 55 years. Furthermore, men are more impacted than women, with a male to female ratio of 1.5 in Pakistan, since men are more exposed to risk factors for head and neck cancer in our region than women.[17]

Various studies have shown a high frequency of HCV and HBV in head and neck cancer patients when compared to healthy controls. In Brazil, the HCV proportion was reported as 34.5% among patients with head and neck cancer.[1] In India, the most frequent infection among patients with head and neck squamous cell carcinoma was HBV (55.1%), followed by human immunodeficiency virus (HIV) (23%) and HCV (19%).[3] Takata and colleagues found an increased prevalence of HCV in patients with oral cancer.[15,18] A study conducted in China reported 59% higher oral cancer incidence among HBV-positive patients.[19] A Turkish study reported the prevalence of HBV as 5.9% in patients with head and neck cancer as compared to healthy controls (3.3%).[20] In the current study of patients with head and neck cancer from single-center sample of Karachi Pakistan, we found that 27.7% had HBV infection, 34.5% had HCV infection and 20.3% were co-infected with HCV and HBV. We also discovered a link between HBV and HCV in individuals with head and neck cancer. In contrast, Su et al. discovered that co-infection/alone HBV infections were not significant among patients with oral cancer.[15] Another Japanese study found a significant proportion of HBV infection in individuals with benign oral tumors but not in patients with oral cancer that required resection.[21] These findings suggest that viral infections are unlikely to play a significant part in head and neck tumor formation. Few other studies also reported co-infected patients with the phenomenon of HCV or HBV dominant effect.[15,22-24] This mutual inhibition between HCV and HBV may also explain the failure of one of the two viruses to replicate in our HCV + HBV group to enhance the occurrence of head and neck cancer.[25] To validate this finding, further prospective cohort studies are necessary. Additionally, physicians or surgeons managing patients with head and neck cancer should also consider testing patients for viral infections in order to start early therapy and prevent increasing liver damage.

LIMITATIONS

The present study is limited by a small sample size as due to this, the findings of the study cannot be generalized to a larger population. Therefore, we recommend that further studies should be undertaken with multicenter and a larger sample.

CONCLUSION

The current study suggests a substantial relationship between HBV and HCV among patients with head and neck cancer. More research is needed to determine the causative relationship, however knowledge of the potential for higher head and neck cancer risk can lead to earlier diagnosis and improved results for HBV and HCV patients.

AUTHOR CONTRIBUTION

Nargis Aalam Abro: Conception, the acquisition, data collection, interpretation of data and manuscript writing

Aamera Shah, Ghulam Haider: Data analysis, conception**:**

Tooba Sarim: Literature review and revisions

Reeta Kumari: Data interpretation

Aakash Ramchand: Reviewed critically for important intellectual content

REFERENCES

1. Rangel JB, Thuler LCS, Pinto J. Prevalence of hepatitis C virus infection and its impact on the prognosis of head and neck cancer patients. Oral Oncol 2018; 87: 138-43. DOI: 10.1016/j.oraloncology.2018.10.024
2. Aupérin A. Epidemiology of head and neck cancers: An update. Curr Opin Oncol 2020;32(3):178-86. DOI: 10.1097/CCO.0000000000000629
3. Nayyar SS, Thiagarajan S, Malik A, D'Cruz A, Chaukar D, Patil P, et al. Head and neck squamous cell carcinoma in HIV, HBV and HCV seropositive patients - Prognosis and its predictors. J Cancer Res Ther 2020; 16(3): 619-23. DOI: 10.4103/jcrt.JCRT_166_19
4. Tsao SW, Tsang CM, Lo KW. Epstein-Barr virus infection and nasopharyngeal carcinoma. Philos Trans R Soc Lond B Biol Sci 2017; 372(1732). 20160270. DOI: 10.1098/rstb.2016.0270
5. Zil ER, Baig S, Zaman U, Lucky MH. Human papillomavirus 16/18: Fabricator of trouble in oral squamous cell carcinoma. Int J Infect Dis 2018; 69: 115-9. DOI: 10.1016/j.ijid.2018.02.003
6. More P, Kheur S, Patekar D, Kheur M, Gupta AA, Raj AT, et al. Assessing the nature of the association of human papillomavirus in oral cancer with and without known risk factors. Transl Cancer Res 2020; 9(4): 3119-25. DOI: 10.21037/tcr.2020.03.81
7. Donà S, Borsetto D, Fussey J, Biscaro V, Vian E, Spinato G, et al. Association between hepatitis C and B viruses and head and neck squamous cell carcinoma. J Clin Virol 2019; 121: 104209. DOI: 10.1016/j.jcv.2019.104209
8. Jefferies M, Rauff B, Rashid H, Lam T, Rafiq S. Update on global epidemiology of viral hepatitis and preventive strategies. World J Clin Cases 2018; 6(13): 589-99. DOI: 10.12998/wjcc.v6.i13.589

9. Waqar M, Nawaz Abro M, Soomro Q, Shahban M, Khatoon S. Retrospective incidence analysis of head and neck cancer patients in rural areas of Sindh, Pakistan. Jundishapur J Chronic Dis Care 2019; 8(4): e95530. DOI: 10.5812/jjcdc.95530
10. IARC Monograph. Available from: https://monographs.iarc.fr/wp-content/uploads/2018/06/mono85-6B.pdf. [Last accessed on 2021 Jun 13].
11. Butt AS, Sharif F. Viral hepatitis in Pakistan: Past, present, and future. Euroasian J Hepatol Gastroenterol 2016; 6(1): 70-81. DOI: 10.5005/jp-journals-10018-1172
12. Mahmud S, Al Kanaani Z, Abu-Raddad LJ. Characterization of the hepatitis C virus epidemic in Pakistan. BMC Infect Dis 2019; 19(1): 809. DOI: doi.org/10.1186/s12879-019-4403-7
13. Samo AA, Laghari ZA, Baig NM, Khoso GM. Prevalence and Risk Factors Associated with Hepatitis B and C in Nawabshah, Sindh, Pakistan. Am J Trop Med Hyg 2020; 104(3): 1101-5. DOI: 10.4269/ajtmh.20-1228
14. Komori MF, Kimura T, Kariya S, Onoda T, Takeda S, Mizukawa N, et al. Epidemiological correlations between head and neck cancer and hepatitis B core antibody positivity. Anticancer Res 2020; 40(4): 2393-403. DOI: 10.21873/anticanres.14209
15. Su FH, Chang SN, Chen PC, Sung FC, Huang SF, Chiou HY, et al. Positive association between hepatitis C infection and oral cavity cancer: a nationwide population-based cohort study in Taiwan. Plos One. 2012;7(10):e48109. DOI: 10.1371/journal.pone.0048109
16. Aziz A. Study on environmental factors causing head and neck cancer in Karachi, Pakistan. Int J Cur Res Rev 2019; 10(8): 2. DOI: 10.7324/IJCRR.2018.10801
17. Baig MS, Bhutto RA, Muhammad S, Siddiqui MI. Epidemiology of oral cancer in Southern Punjab, Pakistan. Pakistan J Medical Health Sci 2015; 9: 1269-71.
18. Nagao Y, Tanaka J, Nakanishi T, Moriya T, Katayama K, Kumagai J, et al. High incidence of extrahepatic manifestations in an HCV hyperendemic area. Hepatol Res 2002;22(1):27-36. DOI: 10.1016/s1386-6346(01)00114-0
19. Song C, Lv J, Liu Y, Chen JG, Ge Z, Zhu J, et al. Associations between hepatitis B virus infection and risk of all cancer types. JAMA Netw Open 2019; 2(6): e195718. DOI: 10.1001/jamanetworkopen.2019.5718
20. Kocoglu H, Karaca M, Tural D, Hocaoglu E, Okuturlar Y, Fetullahoglu Z, et al. Hepatitis B and C rates are significantly increased in certain solid tumors: A large retrospective study. J Cancer Res Ther 2018; 14: S774-s8. DOI: 10.4103/0973-1482.174544
21. Takata Y, Takahashi T, Fukuda J. Prevalence of hepatitis virus infection in association with oral diseases requiring surgery. Oral Dis 2002; 8(2): 95-9. DOI: 10.1034/j.1601-0825.2002.1o794.x
22. Mavilia MG, Wu GY. HBV-HCV coinfection: Viral interactions, management, and viral reactivation. J Clin Transl Hepatol 2018; 6(3): 296-305. DOI: 10.14218/JCTH.2018.00016
23. Konstantinou D, Deutsch M. The spectrum of HBV/HCV coinfection: Epidemiology, clinical characteristics, viral interactions and management. Ann Gastroenterol. 2015; 28(2): 221-8.
24. Caccamo G, Saffioti F, Raimondo G. Hepatitis B virus and hepatitis C virus dual infection. World J Gastroenterol. 2014;20(40):14559-67. DOI: 10.3748/wjg.v20.i40.14559
25. Yu G, Chi X, Wu R, Wang X, Gao X, Kong F, et al. Replication inhibition of hepatitis B virus and hepatitis C virus in co-infected patients in Chinese population. Plos One. 2015; 10(9): e0139015. DOI: doi.org/10.1371/journal.pone.0139015