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Assessment of Timelines in the Management and Human Papilloma Virus (HPV) Status of Head and Neck Cancer Patients

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Abstract

Background: In Nigeria, many of the patients with Head and Neck cancers (HNCs) usually present late, with advanced disease, thereby reducing the chances of cure and survival. The commonest sites of HNCs among Nigerians are nasopharynx, sinonasal, larynx, oropharynx and oral cavity, with a total prevalence of 3-5%. Human Papilloma Virus (HPV) have been known to be associated with malignant tumours arising from these sites, but with little documentation in literature in Nigeria.

Objectives/Aim: This study is to assess the socio-demographic factors responsible for delay in hospital presentation, diagnosis and treatment and also to determine the presence of HPV which is a risk factor in head and neck cancer, among patients that presented in the Lagos University Teaching Hospital (LUTH), South West Nigeria, during the study period.

Patients/Method: This is a prospective study conducted to determine the timelines, socio-demographic factors responsible for delays in presentation, diagnosis, treatment and HPV status, among patients presenting with Head and Neck cancers in the Ears, Nose and Throat (ENT) and Oral and Maxillofacial Surgery (OMFS) clinics in the Lagos University Teaching Hospital (LUTH), South West Nigeria during the study period.

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Consecutive patients with HNC who presented to ENT and OMFS clinics were selected until the required sample size was met. Informed consent was taken from the patient. Semi-structured questionnaires were used to collect data on history, physical examination, investigation and treatment. History entailed details about the presenting complaints, duration, site of malignancy, socio-demographic, socioeconomic, time taken for symptom recognition, fear associated with treatment, hospital related delays and health related behaviour data were documented**.** The tumour type was confirmed by histopathological diagnosis and Immunohistochemistry was used to detect HPV viral particles in pathological specimen of patients. The tumour was staged according to TNM classification of the American Joint Committee on Cancer (AJCC), Head & Neck cancer sites was coded and classified according to ICD-10 (International statistical classification of diagnosis).

Results: Ninety-eight patients were recruited for this study while ninety-one (91) completed the study. The median timeline for presentation to a health facility on account of HNC symptoms was 34 weeks, timeline from hospital presentation to review by an ENT/OMF specialist was 5 weeks, from specialist review to diagnosis was 5 weeks and treatment was 6 weeks. The distribution of the Primary sites of Head and Neck Cancers includes Larynx (29.7%), Nasopharynx (28.6%), Oral cavity (16.5%), Nose and Paranasal sinuses (13.2%), Oropharynx (7.8%), Parotid (2.2%). The other sites were from the External Auditory Canal and the Mastoid. Only 14.3% of the HNCs were positive for HPV.

Conclusion: There was delay in presentation and management of patients with HNCs, the economic factor being the major cause. HPV-associated HNCs is higher in this study, compared to other studies in the sub-Saharan Africa.

Keywords: Head and Neck cancers; HPV; Delay; Histology; Staging**.**

1. Introduction

Head and neck cancers comprises of neoplasms of the oral cavity, pharynx, larynx, salivary glands, nose and paranasal sinuses.[1,2,3] There is dearth of data on the burden of Head & Neck Cancers (HNCs) in Nigeria. A hospital-based study in the Southern part of the Nigeria quoted an incidence of 6.2%[4] and the nasopharynx has been reported as the commonest site of HNC in Nigeria.[1,5]

Most of the patients in Nigeria presented late with advanced disease, leading to increased morbidity and mortality. [4,6,7]Researchers have documented various types of delay responsible for late advanced diseases as primary, secondary and tertiary delays.[8,9,10] Several studies have been conducted in different parts of the world on the causes of delay in seeking medical consultation, specialist consultation, diagnosis and initiation of treatment of head and neck cancers. [11,12,13]

The risk factors associated with HCNs includes smoking of cigarettes, alcohol consumption and chronic infection by the Human Papilloma Virus (HPV). There has been a rise in HPV- associated HNCs and HPV have been found to be responsible for 25% of HNCs and have been found to be associated with oral cancer, oropharyngeal cancer, laryngeal cancer and nasopharyngeal cancer.[14,15]The carcinogenic potential of HPV has

been attributed to the ability of the oncoproteins- E6 and E7 to inactivate tumour suppressor genes.[16,17]

Most of the published works on HNCs in Nigeria dealt on the pattern of these malignancies.[18] Some focused on their specific sites like nasopharynx, paranasal sinuses, larynx, oral cavity and salivary glands. [19,20] The others are on prognostic and predictive factors on survival of Head and Neck malignancies. [6] Reports have been made about the absence of some of the risks factors like alcohol, smoking, chewing of betel nut, eating of salted ungutted fish in some of the cancers like laryngeal carcinoma, nasopharyngeal carcinoma, and oral carcinoma.[21] There is dearth of data in on the timelines of presentation and management of HNCs and scanty study on the role of HPV in HNCs-in Nigeria.[2,22] This prospective study is to fill the knowledge gap on the paucity of literature in Nigeria to identify socio-demographic, socio-economic, socio-professional factors that are related to the various delay timelines from onset of symptoms to presentation to the hospital Medical consultation (Timeline 1), Specialist consultation for review (Timeline 2), Diagnosis (Timeline 3) Treatment (Timeline 4),to determine the median time interval to the timelines above and to determine the presence of HPV(P16ink4a) in the Head and Neck tumour.

2. Patients and Methods.

This was a prospective cross-sectional hospital based study conducted in the Ear Nose and Throat (ENT) and Oral & Maxillofacial surgery (OMF) clinics of Lagos University Teaching Hospital Lagos State a tertiary health centre in South West Nigeria. The clinic and theatre directories showed an average of about 68 and 40 new cases of HNCs seen in the ENT and OMF clinics annually.

The study population comprised of all patients with HNCs referred to ENT and OMFS clinics of of the hospital, for treatment during the 12 months of the study period from 26th of April 2022 to 30th of April 2023.

Sample Size was calculated using the Fischer's formula: $n = \underline{Z^2Pq} \times 1/d^2$,when the total population $N \geq 10{,}000$.Where n = sample size

Z = Standard normal deviate at 1% level of significance, = 2.33

P = prevalence in previous study = 0.04[1]

q = 1- P

d = degree of accuracy = 0.05

n is thus, $\underline{2.33^2 \times 0.04 \times (1 - 0.04)}$

0.05

n = 83

With 10% attrition, it is 91

Consecutive patients with HNCs in ENT and OMFS clinics were selected until the sample size was completed. A detailed history and physical examination which comprised complete head and neck examinations and appropriate investigations were done. The information was collected using structured interviewer questionnaire on patients. The questionnaire included age, gender, marital status, occupation, residence defined as rural or urban, educational status of patients, types of family, duration of illness, number of previous medical consultation before presenting for ENT consultation, usage of traditional medicine, cultural biases and fear, site of malignancy, and health behaviour related information, like cigarette smoking, alcohol consumption, oral sex and multiple sexual partners. Radiologic investigation- Computerised Tomography scan and/or Magnetic Resonance Imaging was done as appropriate. In addition, chest CT scan and liver function tests were carried out, where necessary for the purpose of staging. Staging of the HNC was done according to the 8th edition of AJCC (2017). Histological diagnosis was done following incisional or excisional biopsies of the sino-nasal, nasopharynx, oral cavity, oropharynx and larynx. HPV detection from the biopsy specimen was done using Immunohistochemistry of p16.

The treatments were offered and complication explained. Head & Neck cancer sites were coded and classified according to ICD-10 (International statistical classification of disease). The ICD- 10 code for oral cavity, oropharynx, nasopharynx, hypopharynx, nasal cavity and larynx are (C02-06), (C01, C09, C10), (C11), (C12,13), (30) and (C32) respectively. The following durations were calculated as previously documented with regards to the delay. [7,23,24,25,26]

The following patients with benign tumours or inflammatory lesions of head and neck and patients with HNCs that did not give consent for the study were excluded from the study. Written informed consent was obtained from each respondent and approval was obtained from the Ethical review committee of Lagos University Teaching Hospital to carry out the study.

All the variables in the data were coded and data imputed into a computer and analysed using Statistical Product and Services Solution (SPSS) version 25. Categorical variables were presented using frequency and percentages. Numeric variables were presented using mean and standard deviation or median and interquartile range when skewed.

Association between categorical data were assessed using Chi-square and Fischer exact test. In addition, survival analysis was performed to determine the duration of time between onset of symptoms to presentation, diagnosis and treatment by various level of predictor variables. All tests were performed at 5% level of significance. Charts and tables were used for data presentation where appropriate.

3. Results

Ninety-eight (98) patients were recruited into this study, out of which 91 of them completed the study.

Table 1: showed the socio-demographic characteristics of the patients.

Sixty-seven (73.6%) were males twenty-four (26.4%) were females, with a M:F ratio of 2.8:1. The age range was 15-91 years while mean age was 58.84 +/- 12.1. About 27.5% of the study group were within the age range of 50-59 years of age. Most of the patients (78%) were married with 59.3% completing Tertiary education. Only 6.6% of the patients earned over 150,000 monthly.

Table 2: showed socio-demographic factors and timeline of initial presentation (timeline 1).

Overall, 74 out of 91 patients which makes up about 81% of the participants experienced delay in initial medical consultation (Timeline 1). The male patients experienced more delay in Timeline 1 compared with the female patients (57 versus 17). The proportion of patients with tertiary education who presented early was 27.8% while only 6.1% of patients with secondary education reported early but none with only primary education presented before two months following the onset of symptoms.

About 91% of patients employed in unskilled occupation presented late for initial medical consultation as compared to patients with skilled labour in which 71.1% experienced delay for the first medical consultation. Most of the low-income earners (those that earned less than 100,000NGN/month) experienced delay in presentation while 60.7% of the middle-income earners (100,000- 150,000 NGN/month) presented later than 2 months from the onset of symptoms.

Timeline 1 has statistically significant association with the gender of patient, educational level,

occupation and patient's monthly income $P<0.05$. However, there was no statistically significant association between timeline of presentation and other socio-demographic factors, $P>0.05$.

Table 3: showed socio-demographic factors and timeline of first specialist consultation (timeline 2)

Overall, 69 patients which represents 75.8% of the entire study population experienced delay in Timeline 2 (Time for specialist review). The proportion of females who experienced delay in time of specialist review was 58.3%, compared to 82.1% in males. For the educational level, patient who had the tertiary education presented earlier for specialist review when compared to those that only completed secondary and primary schools (33% versus 12% versus 0% respectively).

About 91% of patients who were employed in unskilled occupation presented late for specialist consultation as compared to patients with skilled labour in which 64.4% experienced delay in specialist consultation. In terms of the economic status, the proportion of patients with delayed specialist consultation in low-income, middle-income and high-income earners were 94.1%, 78.2% and 52.6% respectively, which showed that low-income earners generally presented late for specialist consultation.

There was statistically significant association between the timeline of specialist consultation and gender of patient, educational level, occupation and monthly income, $P<0.05$. However, there was no statistical significant association between timeline of specialist consultation and other socio-demographic factors (age and marital

status), P>0.05.

Table 4: showed the socio-demographic factors and timeline of diagnosis (timeline 3)

Overall, 53 out of 91 (58.2%) patients experienced delay in diagnosis. Based on the gender, 41.7% of females experienced delay while 64.2% of the male participants had delay in timeline 3. In terms of the monthly income, only 33.3% of the high income earners experienced delay as against 46.4% and 66.7% observed in middle and low income earners respectively.

There was statistically significant association between timeline of diagnosis with gender of patient and monthly income of patients, P value < 0.05. The age of patients, marital status, educational level and occupation showed no statistical difference with the timeline of diagnosis, P value > 0.05.

Table 5: showed socio-demographic factors and timeline of treatment (timeline 4)

Generally, 76 out of the total participants experienced delay in Timeline 4. This makes up 83.5% of total study population. A higher proportion of the high-income earners commenced treatment earlier than the middle and low-income earners (33.3%vs 25%vs10.5%). Other socio-demographic factors showed no significant association with the Timeline of treatment.

There was statistically significant association between the monthly income of the patients and the timeline of treatment. P<0.05

Figure 1 showed the mean interval of presentation, diagnosis and treatment

The median time intervals, from onset of symptoms to first presentation at a health facility is 29-45 weeks (7-11 months), while the time interval between first presentation to a health facility and review by an ENT/OMF surgeon is 5-8 weeks. However, the time interval for diagnosis and treatment are 4-6 weeks and 5-8 weeks respectively. Consequently, the median timeline for presentation to a health facility on account of HNC symptoms (Timeline 1), timeline from hospital presentation to review by an ENT/OMF specialist (Timeline 2), from specialist review to diagnosis (Timeline 3) and treatment (Timeline 4) were 34 weeks (about 8 months), 5 weeks, 5 weeks and 6 weeks respectively.

Figure 2: showed the primary sites of the head and neck cancers

The sites of Primary HNCs and their corresponding proportions are Larynx 27 patients (29.7%). Nasopharynx 26 (28.6%), Oral cavity 15 (16.5%), Nose and Paranasal sinuses 12 (13.2%), Oropharynx 7 (7.7%), Parotid gland 2 (2.2%). The Other sites are External Auditory Canal and the Mastoid. All of these have a histologic diagnosis of Squamous Cell Carcinoma. None of the patients presented with a stage I disease, with most of them presenting in advanced stage- Stage III, 56 (61.5%) and Stage IV, 29 (31.9%).

Table 6: - Showed determination of human papilloma virus status in head and neck cancers

All the 91 tissue blocks used for this study were analyzed. Antigen retrieval and immunohistochemistry was carried out in all the blocks used. Overall, 13 (14.3%) of the HNCs studied were HPV positive. Analyzing the sites of these tumors, showed that six of the HPV positive cancers are from the larynx, five from oropharynx, one from the nasopharynx and one from the oral cavity. About 71.4% of oropharyngeal cancers were HPV positive while only 22.2% of laryngeal cancers were positive for the virus.

4. Discussion

Head and neck cancer is still commoner in male, especially in the 5th & 6th decades of life. This study shows that 74 patients (81%) had delay between first onset of HNC symptoms and presentation to a medical facility while 69 patients (75.8%) experienced delay between first medical consultation and first specialist review. In addition, 53 patients (58.3%) had a delay in making histological diagnosis. The timeline from diagnosis to treatment was delayed in 76 (83.5%) of the patients. The high proportion of delay in presentation is similar to the study carried out by Ayodele and his colleagues, which revealed that 80% of the patient presented late. Also, Agarwal and his colleagues in India showed that most of the patients experienced delay in presentation due to poor socio-economic factor and poor health-seeking behaviour amongst the populace. These studies identified illiteracy, use of alternate therapy, limited access to healthcare facilities as major reasons for delayed presentation [27,28] In contrast to this, Lee and his colleagues[23] (Canada) and Nieminen and his colleagues (Finland)- found out that most of the patients with HNCs had early medical presentation. A Danish study by Lynne and his colleagues[26] also saw early timelines of diagnosis and treatment in a good proportion of the patients due to the good health insurance, high GDP and availability of health facilities and manpower.

Economic factor (monthly income) affected all the different timelines in this study. Despite the fact that a good proportion of the patient completed tertiary education, only a third earn up to $66 (100,000 naira) per month. This is a reflection of per capita income and purchasing power in the country. Hence, the inability for patients to seek prompt medical care, as payment of healthcare services is predominantly out-of-pocket. It is also important to state that those that get enrolled with Health Maintenance Organizations (HMOs) are not able to get treated for cancer cases. However, a total healthcare package, inclusive of cancer care is deployed in developed countries which is responsible for prompt presentation and management of HNCs.[26]

Male gender, Unskilled occupation and Lack of education were other contributing factors to the delay experienced in these patients. This study showed that a higher proportion of the male patients had delay in presentation and management of HNCs. This is possibly due to a better health seeking behaviour in the female patients. Contrary to this, Lee and his colleagues showed that the delayed group were predominantly female (60%). This is likely due to a smaller sample size used in their study. Since payment for healthcare services is mostly out-of-pocket, it is expected that those in unskilled occupation earn less, therefore are unable to seek and pay for medical care promptly. Interestingly, all the patients that completed only primary education experienced delays in presentation and treatment. This is likely due to poor economic status in them resulting in inability to pay out-of-pocket for healthcare. This can also be linked to poor health seeking behaviour amongst them due to lack of awareness on

the importance of the symptoms. This has some similarity to the study by Agarwal and his colleagues, who also identified proximity to the hospital, fear, insufficient knowledge of disease as other factors.[27]

The median timeline for First medical presentation was (eight months) and ENT/OMFS review (five weeks). A similar study showed a median timeline of ten months and four weeks respectively.[25] The reason for this delay is as a result of poor health seeking behaviour in these patients and the need to pay Out of pocket payment for health care. However, Nieminen and his colleagues[12] showed a lower median time interval because of good health-seeking behaviour and widespread health insurance services. The median timeline for diagnosis and treatment were (five weeks) and (six weeks) respectively. Slight similarity to a Brazilian study by Fellipu and his colleagues with median time of four weeks for diagnosis and twelve weeks for treatment[25]. The shortage of manpower in developing countries limits accessibility to review by the specialist thereby constituting delay in diagnosis and treatment. As earlier mentioned, poor socio-economic indices in these countries which results to out-of-pocket payment and absence of equipment for diagnosis and treatment in these developing countries have also been fingered as likely reasons for these delays. [29,30]. Contrary to this, Lyhne and his colleagues [26] showed a lower median time interval for diagnosis and treatment.

The larynx is the commonest site, with about 29.7% of the entire HNCs. Nasopharyngeal cancer was the second commonest (28.6%). This contradicts the study by Sowunmi and his colleagues[4] which showed that the nasopharynx was the commonest site. This is because the above study was retrospective, with more tissue blocks analysed. Similar to this, Ndiaye and his colleagues [31] also showed the nasopharynx as the commonest site of HNCs.

The prevalence of HPV in this study is 14.3%. This is similar to the study by Okerosi and his colleagues[32] which revealed that 13.6% of patients with HNCs were HPV positive with Immunohistochemistry p16. However, unlike this study, Oropharyngeal cancer (20.3%), Hypopharyngeal cancer (16.7%), Oral cavity cancers (11.7%) were the commonest types of HNCs. According to a multi-centre study by Oga and his colleagues[2], involving- two hospitals in North central Nigeria (UITH and UATH), one in Mid-western Nigeria (UBTH) and one in South- South (UCTH), none of the tissue blocks was positive for HPV. This could be due to the methodology of the study in which old tissue blocks were used. Ndiaye and his colleagues also showed that oropharyngeal cancers were the most common HNCs in which HPV DNA were detected and there was similarity between E6/E7 m RNA and $p16^{ink4a}$. [31]

Ba and his colleagues reported that 39.7% of the patients were HPV positive.[33] Similarly, Abogunrin and his colleagues found out in his study that the prevalence of HPV in HNCs amongst European population is 40%.[34] The studies above were systematic reviews of various studies done within the different regions. The low prevalence of HPV in my study is attributable to the small number of patients used, compared to the studies above. Also, different methods of HPV detection were used which could have increased the prevalence of HPV. The presence of other risk factor of HNCs like smoking of cigarettes, alcohol consumption, exposure to petrochemicals may be more associated with the HNCs used for my study.

It is important to create awareness to the population on the symptoms of HNCs, while educating health care

providers at primary and secondary health facilities on the signs of these malignancies, in order to ensure prompt referral to tertiary centres where diagnosis and treatment can be quickly done. Also, there need to be a re-awakening of the National Health Insurance Scheme, in order to promote unhindered presentation and management of these diseases as it has been shown that Out-of-pocket payment is not sustainable for the treatment of cancers. In Nigeria, Immunohistochemistry is not done routinely for malignancies in many centres because tissue blocks are usually sent out of the country for review. Hence, there is a need for equipping pathology laboratories with the necessary kits for this test to be run locally. In the same vein, there it is necessary to ensure adequate coverage of HPV immunization in the country. Currently, the immunization is more tilted towards prevention of cervical cancers therefore not freely available for the male.

5. Conclusion

This study established that most of the patients that presented to the ENT/OMFS clinic experienced delay in presentation, diagnosis and treatment. It also showed that sociodemographic factors which includes patient's educational level, type of occupation and monthly income had significant effect on their timeline for first hospital presentation and also review by ENT/OMFS specialist. Meanwhile, the timelines for diagnosis and treatment were only affected by the patient's income. Laryngeal cancer is the commonest HNC in the Lagos University Teaching Hospital and only about 14.3% of HNCs were positive for HPV. Cancers of laryngeal origin had the highest absolute value of HPV-positivity but the proportion was highest in oropharyngeal cancers.

6. Limitation of Study

1. The durations given by patients for Timelines 1 and 2 may not be exact, as approximate durations were documented.
2. Over-expression of p16 in some HPV negative tumours which may make them appear positive.

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Table 1: Sociodemographic Characteristics of the Patients

Variable	Frequency (n=91)	Percentage(%)
Age groups (Years)		
10-19	4	4.4
20-29	4	4.4
30-39	13	14.3
40-49	17	18.7
50-59	25	27.5
60-69	22	24.2
≥70	6	6.6
Mean±SD	54.84±12.1	
Gender		
Male	67	73.6
Female	24	26.4
Marital status		
Single	16	17.6
Married	71	78.0
Others	4	4.4
Educational level		
Primary	4	4.4
Secondary	33	36.3
Tertiary	54	59.3
Occupation		
Unskilled	31	34.1
Skilled	45	49.5
Non-employed	15	16.5
Patients' income per months		
≤100,000	57	62.6
101,000-150,000	28	30.8
>150,000	6	6.6

Table 2: Sociodemographic Factors and Timeline of Initial Presentation (Timeline 1)

	Timeline of presentation in hospital		χ^2	**p-value**
	≤ 8 weeks	**>8 weeks**		
Age group				
<40	7(33.3)	14(66.7)	4.250	0.119
40-59	5(11.9)	37(88.1)		
≥60	5(17.9)	23(82.1)		
Gender			3.359	**0.035***
Male	10(14.9)	57(85.1)		
Female	7(29.2)	17(79.8)		
Marital status				
Single	6(37.5)	10(62.5)	5.124	0.077
Married	11(15.0)	60(84.5)		
Others	0(0.0)	4(100.0)		
Educational level				
Primary	0(0.0)	4(100.0)	7.320	**0.026***
Secondary	2(6.1)	31(93.3)		
Tertiary	15(27.8)	39(72.2)		
Occupation				
Unskilled	2(6.5)	29(93.5)	6.421	**0.040***
Skilled	13(28.9)	32(71.1)		
Non-employed	2(13.3)	13(86.7)		
Patients' income per month				
≤100,000	5(8.8)	52(91.2)	11.525	**0.003***
101,000-150,000	11(39.3)	17(60.7)		
>150,000	1(16.7)	5(83.3)		

Table 3: Sociodemographic Factors and Timeline of First ENT/OMFS Specialist Consultation (Timeline 2)

	Timeline Of Specialist Consultation		χ^2	**p-value**
	≤4 weeks (n=22)	**>4 weeks (n=69)**		
Age group				
<40	4(19.0)	17(81.0)	0.599	0.741
40-59	10(23.8)	32(76.2)		
≥60	8(28.6)	20(71.4)		
Gender				
Male	12(17.9)	55(82.1)	5.440	**0.020***
Female	10(41.7)	14(58.3)		
Marital status				
Single	2(12.5)	14(87.5)	1.450	0.484
Married	19(26.8)	52(73.2)		
Others	1(25.0)	3(75.0)		
Educational level				
Primary	0(0.0)	4(100.0)	6.362	**0.042***
Secondary	4(12.1)	29(87.9)		
Tertiary	18(33.3)	36(66.7)		
Occupation				
Unskilled	5(16.1)	26(83.9)	6.783	**0.034***
Skilled	16(35.6)	29(64.4)		
Non-employed	1(6.7)	14(93.3)		
Patients' income per months			8.846	0.**012***
≤100,000	1(5.9)	16(94.1)		
101,000-150,000	12(21.8)	43(78.2)		
>150,000	9(47.4)	10(52.6)		

Table 4: Sociodemographic Factors and Timeline of Diagnosis (Timeline 3)

	Timeline of diagnosis		χ^2	**p-value**
	≤2 weeks	**>2 weeks**		
Age group				
<40	8(39.1)	13(61.9)	0.395	0.821
40-59	19(45.2)	23(54.8)		

≥60	11(39.3)	17(60.7)		
Gender				
Male	24(35.8)	43(64.2)	3.682	**0.045***
Female	14(58.3)	10(41.7)		
Marital status				
Single	8(50.0)	8(50.0)	0.933	0.627
Married	29(40.8)	42(59.2)		
Others	1(25.0)	3(75.0)		
Educational level				
Primary	2(50.0)	2(50.0)	4.467	0.107
Secondary	9(27.3)	24(72.7)		
Tertiary	27(50.0)	27(50.0)		
Occupation				
Unskilled	11(35.5)	20(64.5)	0.784	0.676
Skilled	20(44.4)	25(55.6)		
Non-employed	7(46.7)	8(53.3)		
Patients' income per months			4.801	**0.047***
≤100,000	19(33.3)	38(66.7)		
101,000-150,000	15(53.6)	13(46.4)		
>150,000	4(66.7)	2(33.3)		

Table 5: Sociodemographic Factors and Timeline of Treatment (Timeline 4)

	Timeline of treatment		χ^2	**p-value**
	≤2 weeks	**>2 weeks**		
Age group			0.286	0.867
<40	4(19.0)	17(81.0)		
40-59	6(14.3)	36(85.7)		
≥60	5(17.9)	23(82.1)		
Gender			0.448	0.503
Male	10(14.9)	57(85.1)		
Female	5(20.8)	19(79.2)		
Marital status				
Single	3(18.8)	13(81.3)	0.858	0.651
Married	12(16.9)	59(83.1)		
Others	0(0.0)	4(100.0)		
Educational level				
Primary	1(25.0)	3(75.0)	4.107	0.128
Secondary	2(6.1)	31(93.9)		

Tertiary	12(22.2)	42(77.8)		
Occupation				
Unskilled	3(9.7)	28(90.3)	4.165	0.125
Skilled	11(24.4)	34(75.6)		
Non-employed	1(6.7)	14(93.3)		
Patients' income per months				
≤100,000	6(10.5)	51(89.5)	4.182	**0.044***
101,000-150,000	7(25.0)	21(75.0)		
>150,000	2(33.3)	4(66.7)		

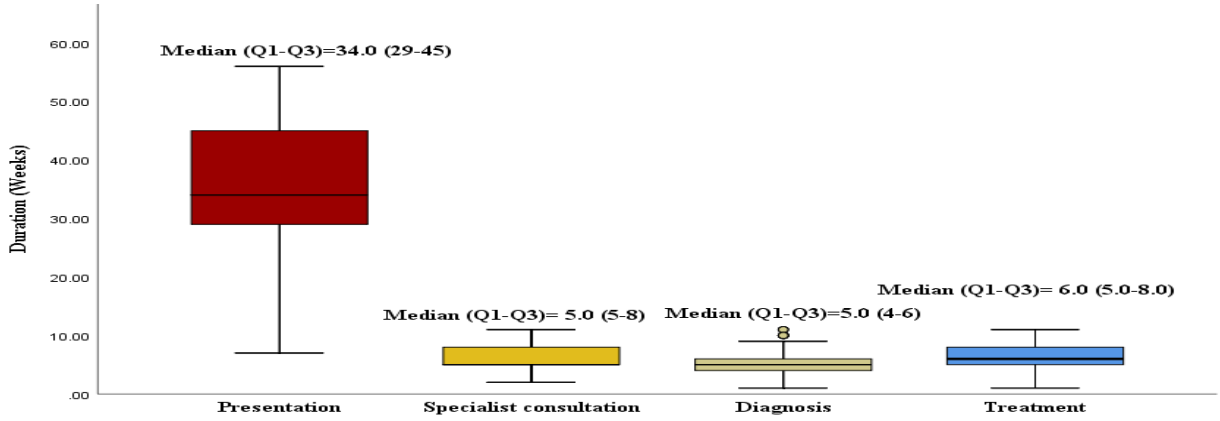

Figure 1: Mean Interval of Presentation, Diagnosis and Treatment

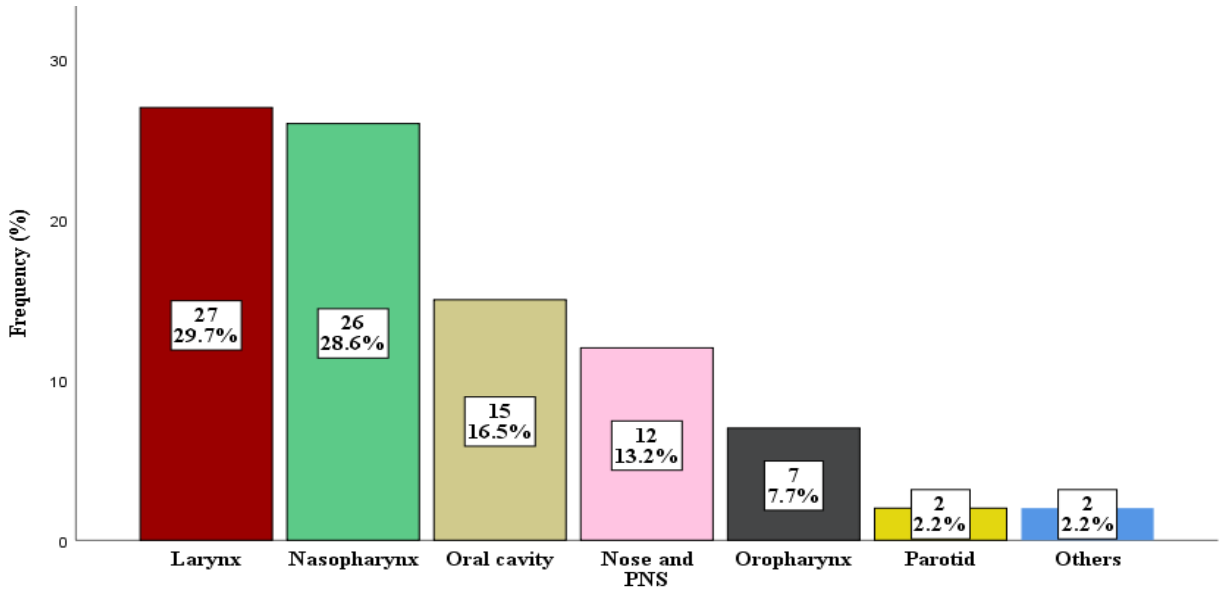

Figure 2: Primary Sites of the Head and Neck Cancers

Table 6: Determination of Human Papillomavirus Status in Head and Neck Cancers

	HPV status		χ^2	**p-value**
	Positive (n=13)	**Negative (n=78)**		
Primary site of cancer				
Nose and PNS	0(0.0)	12(100.0)	25.747	<0.001*
Nasopharynx	1(3.8)	25(96.2)		
Oral cavity	1(6.7)	14(93.3)		
Oropharynx	5(71.4)	2(28.6)		
Larynx	6(22.2)	21(77.8)		
Parotid	0(0.0)	2(100.0)		
Others	0(0.0)	2(100.0)		