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RESEARCH ARTICLE

IMPACT OF PROGNOSTIC VARIABLES ON THE SURVIVAL OUTCOME OF ORAL SQUAMOUS CELL CARCINOMA AND NASOPHARYNGEAL CARCINOMA PATIENTS AT KING FAHD MEDICAL CITY, RIYADH.

Dr. Syed Sirajul Hassan, Dr. Abdulsalam Aljabab, Dr. Syed Hammad Ahsan and Prof. Hezekiah A. Mosadomi.

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Abstract

Introduction
The reported morbidity of Oral Squamous Cell Carcinoma (OSCC) and Nasopharyngeal Carcinoma (NPC) throughout the world is high. The dilemma is that numerous patients develop OSCC and NPC who do not have a history of usage or exposure to the established risk factors.

Objectives
To extract socio-demographic, clinic pathological, histopathological and therapeutic data of OSCC / NPC patients from the online database software of King Fahd Medical City and Saudi Cancer Registry databases and to compare all of these variables with the "Overall Survival" of OSCC and NPC patients

Methods
The study was retrospective in nature. It comprised of a cohort of patients treated for Oral Squamous Cell Carcinoma (OSCC) / Nasopharyngeal Carcinoma (NPC) at King Fahd Medical City (KFMC). Frequency distribution, chi-square test and Kaplan-Meier survival analysis

Results
Following parameters had a statistically significant association with the overall survival of the subjects: Gender (p=0.022), age (p=0.001), T4 sized tumor (p=0.007), N status (p=0.037), M status (p=0.001), histological grading (p=0.043), hemoglobin (p=0.011) and cancer being the cause of death (p=0.001)

Conclusion
This study has identified clinic pathological parameters, which play an important role in determining the survival outcome of oral squamous cell carcinoma and nasopharyngeal carcinoma patients.

Introduction:-

The reported morbidity of Oral Squamous Cell Carcinoma (OSCC) and Nasopharyngeal Carcinoma (NPC) throughout the world is high. A leading journal in cancer research recorded 2,63,900 new cases and 1,28,000 deaths from OSCC worldwide in 2008[1]. The World Health Organization predicts further increase in the next few decades, as the prognosis largely remains unaltered despite the advancements in surgical, chemotherapeutic and radio therapeutic management of cancer[2]. To date; smoking, alcohol and chewable tobacco are considered as major risk

Corresponding Author:- Syed Sirajul Hassan.

factors of OSCC. In contrast, nasopharyngeal carcinoma (NPC) is comparatively rare in most parts of the world. Causative agents such as Epstein-Barr virus infection, vitamin C deficiency and dietary products containing N-nitrosamines have been considered as potential causative factors of NPC. But the dilemma is that numerous patients develop OSCC and NPC who do not have a history of usage or exposure to the above mentioned risk factors. Surprisingly the outcome of some such tumors is unpredictable. These observations indicate that apart from the formerly identified risk factors other factors yet undetermined may also influence prognosis of OSCC and NPC, which can affect the survival outcome of such patients.

Anemia is commonly associated with cancer, about 50-60% of patients suffering from cancer develop anemia at variable stages of the disease[3]. It is likely that anemia also plays a deleterious role in progression of cancer. Anemia influences progression of cancer due to the effect of hypoxia on tumor cells which leads to decreased tumor oxygenation. Decreased tumor oxygenation in turn renders the hypoxic tumor cells resistant to oncological therapies specially radiotherapy[4]. Various studies have highlighted an association of anemia with progression of cancer. For instance a study on cervical carcinoma showed anemia as a strong prognostic factor for progression of cancer & demonstrated its correlation with patient survival[5]. Furthermore a study showed increased lymph node metastasis to be associated with increase in severity of anemia in OSCC patients[6]. Anemia itself is assessed on the level of Hemoglobin (Hb) in patient's blood. Previous studies have shown that pre-treatment hemoglobin has been shown to be of clinical significance in evaluating progression of a disease[7].

The purpose of this research project is to assess the role of various socio-demographic, clinic pathological, histopathological and therapeutic variables in the progression of OSCC and NPC by comparing the level of these independent variables with Overall Survival of OSCC and NPC patients.

Aim Of Research Project

- The aim of this research project is to assess the role of socio-demographic, clinicopathological, histopathological and therapeutic variables in determining the prognosis of oral squamous cell carcinoma and nasopharyngeal carcinoma

Objectives Of Research Project

- To extract preliminary data (socio-demographic, clinicopathological, histopathological and therapeutic data of OSCC / NPC patients) from the online database software of King Fahd Medical City and Saudi Cancer Registry databases

- To compare all of these variables "socio-demographic", "clinicopathological", "histopathological" with "Overall Survival" of OSCC and NPC patients to determine the impact of these independent variables on the prognosis of OSCC and NPC

Materials & Methods

The research is retrospective and comprises a cohort of patients treated for Oral Squamous Cell Carcinoma (OSCC) / Nasopharyngeal Carcinoma (NPC) at King Fahd Medical City (KFMC) (a tertiary care hospital) located in Riyadh, Saudi Arabia. Furthermore, data will be extracted from the Dental medical records system.
The study subjects are patients who were treated for OSCC / NPC.

Sample Size Calculation with Statistical Justification:

The sample size is 420; a two-sided 95% confidence interval for a single proportion using the large sample normal approximation will extend (margin of error) 0.05 from the observed proportion for an expected proportion (OS) of 58.6%.

Inclusion Criteria:

1. Patient diagnosed and treated for Oral Squamous Cell Carcinoma / Nasopharyngeal Carcinoma via Surgical Biopsy.
2. Patient with complete Socio-demographic, Clinical, Histological, Investigative and Therapeutic Record of Oral Squamous Cell Carcinoma/ Nasopharyngeal Carcinoma.
3. Patient on a 12 month follow up basis or on a follow up from time of diagnosis to recurrence or death.

Exclusion Criteria:

1. Patient without follows up data after initial diagnosis.

2. Patient with previous malignancies or synchronous malignancies at time of diagnosis.

The Ethical Committees of Riyadh Colleges of Dentistry and Pharmacy and the RC-IRF committee of King Fahd Medical City for the study provided approval. Study requires extraction of data from the Electronic Health System in King Fahd Medical City and Saudi Cancer Registry. This data would be utilized for statistical analysis.
Data on the following variables was be utilized for statistical analysis:

- *Age*
- *Gender*
- *Tobacco Usage*
- *Chief Complaint*
- *Duration Of Symptoms*
- *Location*
- *Size Of Primary Lesion (Cm)*
- *T Status*
- *N Status*
- *M Status*
- *Histological Grading*
- *Type Of Tumor*
- *Type Of Treatment*
- *Complications*
- *Recurrence*
- *Vital Status Disease*
- *Cause Of Death*
- *Hemoglobin* (sub-categorized into separate categories titled "NORMAL Hb", "MILD ANEMIA" and "SEVERE ANEMIA" utilizing the hemoglobin (Hb) values defined by the World Health Organization (WHO), the patients were divided into a three groups: normal (female Hb≥12.0 g/dl; male Hb≥13.0 g/dl), mild anemia (female Hb = 11.0-11.9 g/dl; male Hb = 11.0-12.9 g/dl), and severe anemia (female & male Hb<11.0 g/dl)
- *Initial Biopsy To Postop Survival*

Data collection did not include collection of subject's name and every measure was taken to maintain subject's confidentiality and privacy.

Statistical Analysis
SPSS was utilized for statistical analysis. Descriptive statistics was performed to demonstrate the frequency distribution of all the measured variables. A univariate analysis (chi-square test) was performed to look for association(s) between all of the measured variables and the overall survival of the subjects. P value < 0.05 was considered to be statistically significant. Kaplan-Meier Survival Analysis was performed in order to look for an association between the "hemoglobin" variable and "Dependent Variable" namely Overall Survival to evaluate the Survival Function S(t) and Hazard Function (λ) of variable.

Results:-

Table 1: Frequency distribution of the studied parameters of the subjects

		n (%)
Gender	Female	146 (37.1)
	Male	248 (62.9)
	Total	394 (100.0)
Age (yr)	≤50	194 (46.6)
	> 50	222 (53.4)
	Total	416 (100.0)
	min – max	10 - 89
	Mean (SD)	51.8 (15.8)
Tobacco User	No	359 (85.5)
	Yes	61 (14.5)
	Total	420 (100.0)

Duration of symptoms (month)	min – max	1 - 240
	Mean (SD)	15.3 (37.3)
Location	Left	37 (9.9)
	Middle/anterior	1 (.3)
	Right	52 (13.9)
	Bilateral	284 (75.9)
	Total	374 (100.0)
Chief complaint	Exophytic lesion	15 (3.6)
	Leukoplakia	1 (.2)
	Other	186 (44.3)
	Pain	28 (6.7)
	Solid neck mass	96 (22.7
	Ulcer	34 (8.1)
	Headache	10 (2.4)
	Difficulty in hearing	12 (2.7)
	Epistaxis	8 (1.8)
	Nasal obstruction	37 (8.7)
	Total	420 (100.0)
Size of primary lesion (cm)	min – max	1 - 32
	Mean (SD)	4.2 (4.0)
T_Size	<2cm	55 (24.3)
	2-4cm	90 (39.8)
	>4cm	81 (35.8)
	Total	226 (100.0)
T Status	T1	55 (16.3)
	T2	89 (26.3)
	T3	75 (22.2)
	T4	111 (32.8)
	Tx	8 (2.4)
	Total	338 (100.0)
T4 sized tumor	Base of Skull	42 (37.8)
	Base of Tongue	16 (14.4)
	Alveolar bone	6 (5.4)
	Intracranial region	18 (16.2)
	Larynx	32 (28.8)
	Pharynx	22 (19.8)
	Palate	6 (5.4)
	Ocular region	9 (8.1)
	Adjacent Tissue	4 (3.6)
	Brain	1 (0.9)
	Mouth	2 (1.8)
	Lung	6 (5.4)
	Inner throat muscle	5 (4.5)
	Mandible	7 (6.3)
	Maxilla	4 (3.6)
	Neck	9 (8.1)
	Other skeletal region	7 (6.3)
N Status	N0	93 (28.0)
	N1	94 (28.3)
	N2	111 (33.4)
	N3	34 (10.2)
	Total	332 (100.0)
M Status	Missing	85 (20.2)

	M0	308 (73.3)
	M1	27 (6.4)
	Total	420 (100.0)
Scan	CT scan	328 (91.6)
	NMRI	27 (7.5)
	Nuclear medicine scan	3 (.8)
	Total	358 (100.0)
DIFFERENT INITIAL BIOPSY	Moderate	34 (26.8)
	Other	61 (48.0)
	Poor	21 (16.5)
	Well	11 (8.7)
	Total	127 (100.0)
FNAB-Lymph Node	Negative	397 (94.5)
	Positive	23 (5.5)
	Total	420 (100.0)
FNAB-Lymph Node	Negative for malignancy	4 (17.4)
	Atypical squamous epithelial cells, multinucleated giant cells	1 (4.3)
	Malignant cells	1 (4.3)
	Undifferentiated malignant cells	1 (4.3)
	Lymphoid reactive hyperplasia	1 (4.3)
	Moderately differentiated squamous cell carcinoma	1 (4.3)
	Poorly differentiated carcinoma	1 (4.3)
	Undifferentiated carcinoma	3 (13.0)
	Anaplastic carcinoma	1 (4.3)
	Metastatic squamous cell carcinoma	4 (17.4)
	Metastatic nasopharyngeal carcinoma	1 (4.3)
	Metastatic undifferentiated carcinoma	3 (13.0)
	Papillary thyroid carcinoma	1 (4.3)
Carcinoma type	Acinic cell carcinoma	1 (.3)
	Adenocarcinoma	16 (4.3)
	Ameloblastoma	3 (.8)
	Basal cell carcinoma	1 (.3)
	Squamous cell carcinoma	338 (90.1)
	DLBCL	3 (.8)
	Hemangiopericytoma	1 (.3)
	Lymphoepithelial carcinoma	2 (.5)
	Mucoepidermoid carcinoma	2 (.5)
	Osteosarcoma	3 (.8)
	Pleomorphic adenoma ex carcinoma	0 (.0)
	Rhabdomyosarcoma	2 (.5)
	Undifferentiated carcinoma	3 (.8)
	Total	375 (100.0)
Site	Alveolus	6 (1.7)
	Tongue	45 (12.8)
	Mandible	7 (2.0)
	Maxilla	5 (1.4)
	Maxillary sinus	2 (.6)
	Buccal mucosa	16 (4.5)
	Cheek	1 (.3)
	Cricoid	7 (2.0)
	Esophageal	2 (.6)
	Floor of the mouth	2 (.6)
	Glottic	9 (2.6)

	Hypo pharyngeal	6 (1.7)
	Intraosseous	3 (.9)
	Laryngeal	11 (3.1)
	Lip	3 (.9)
	Lymphoid tissue	1 (.3)
	Mucoepidermoid	5 (1.4)
	Nasopharyngeal	193 (54.8)
	Oropharyngeal	1 (.3)
	Palate	2 (.6)
	Parotid gland	3 (.9)
	Pharynx	1 (.3)
	Pyriform	4 (1.1)
	Retromolar trigone	1 (.3)
	Sinonasal	3 (.9)
	Supraglottic	0 (.0)
	Tonsils	7 (2.0)
	Transglottic	2 (.6)
	Tubulo papillary	1 (.3)
	Vocal cord	3 (.9)
	Total	352 (100.0)
Histological grading	Moderately differentiated	99 (29.4)
	Poorly differentiated	13 (3.9)
	Undifferentiated	150 (44.5)
	Well differentiated	75 (22.3)
	Total	337 (100.0)
Metastasis	Keratinizing	16 (13.9)
	Non-Keratinizing	93 (80.9)
	Metastatic	6 (5.2)
	Total	115 (100.0)
MEMO Treatment	Not given	64 (15.2)
	Given	356 (84.8)
	Total	420 (100.0)
MEMO Treatment type	Nil	64 (15.3)
	Palliative	9 (2.1)
	Radiotherapy	38 (9.1)
	Chemotherapy	10 (2.4)
	Surgery	30 (7.2)
	Surgery and radiotherapy	73 (17.4)
	Surgery and chemotherapy	2 (.5)
	Radiotherapy and chemotherapy	17 (4.1)
	Surgery, radiotherapy and chemotherapy	5 (1.2)
	Neoadjuvant chemotherapy	10 (2.4)
	Neoadjuvant chemotherapy, concomittant chemoradiotherapy	42 (10.0)
	Neoadjuvant chemotherapy, surgery	5 (1.2)
	Neoadjuvant chemotherapy, surgery, concomittant chemoradiotherapy	3 (.7)
	Neoadjuvant chemotherapy, radiotherapy	64 (15.3)
	Concomittant chemoradiotherapy	29 (6.9)
	Surgery, concomittant chemoradiotherapy	18 (4.3)
	Total	419 (100.0)
MEMO Treatment Complications	No	360 (85.7)
	Yes	60 (14.3)
	Total	420 (100.0)

MEMO Treatment Complication type	Nil	360 (85.7)
	Minor morbidity	47 (11.2)
	Major morbidity	12 (2.9)
	Mortality	1 (.2)
	Total	420 (100.0)
Hemoglobin (g/dl)	min – max	7.1 - 17.8
	Mean (SD)	12.8 (1.9)
Hemoglobin	Normal	252 (69.0)
	Mild anemia	51 (14.0)
	Severe anemia	62 (17.0)
	Total	365 (100.0)
Recurrence	No	390 (92.9)
	Yes	30 (7.1)
	Total	420 (100.0)
Disease	No	131 (83.4)
	Yes	26 (16.6)
	Total	157 (100.0)
Final outcome	Survived	323 (76.9)
	Died	97 (23.1)
Cancer being the cause of death	No	376 (89.5)
	Yes	44 (10.5)
	Total	420 (100.0)
Follow up (month)	min – max	0 – 99
	Mean (SD)	44.2 (22.5)

Table 2: Overall survival in association with the studied parameters

		Survived	Died	p value
Gender	Female	101 (69.2)	45 (30.8)	0.022
	Male	197 (79.4)	51 (20.6)	
Age (yr)	≤50	167 (86.1)	27 (13.9)	<0.001
	> 50	152 (68.5)	70 (31.5)	
Tobacco User	No	279 (77.7)	80 (22.3)	0.339
	Yes	44 (72.1)	17 (27.9)	
Location	Left	27 (73.0)	10 (27.0)	0.817
	Middle/anterior	1 (100.0)	0 (.0)	
	Right	38 (73.1)	14 (26.9)	
	Bilateral	219 (77.1)	65 (22.9)	
T4 sized tumor	No	234 (81.0)	55 (19.0)	0.007
	Yes	76 (68.5)	35 (31.5)	
T_Size	<2cm	48 (87.3)	7 (12.7)	0.067
	2-4cm	68 (75.6)	22 (24.4)	
	>4cm	71 (87.7)	10 (12.3)	
N_Status	N0	80 (86.0)	13 (14.0)	0.037
	N1	77 (81.9)	17 (18.1)	
	N2	79 (71.2)	32 (28.8)	
	N3	24 (70.6)	10 (29.4)	
M_Status	Missing	61 (71.8)	24 (28.2)	0.001
	M0	248 (80.5)	60 (19.5)	
	M1	14 (51.9)	13 (48.1)	
Scan	CT scan	243 (74.1)	85 (25.9)	0.419
	NMRI	22 (81.5)	5 (18.5)	
	Nuclear medicine scan	3 (100.0)	0 (.0)	
DIFFERENT INITIAL	Moderate	27 (79.4)	7 (20.6)	0.825

BIOPSY	Other	44 (72.1)	17 (27.9)	
	Poor	16 (76.2)	5 (23.8)	
	Well	9 (81.8)	2 (18.2)	
FNAB-Lymph Node	Negative	305 (76.8)	92 (23.2)	0.874
	Positive	18 (78.3)	5 (21.7)	
Histological grading	Moderately differentiated	64 (64.6)	35 (35.4)	0.043
	Poorly differentiated	8 (61.5)	5 (38.5)	
	Undifferentiated	119 (79.3)	31 (20.7)	
	Well differentiated	58 (77.3)	17 (22.7)	
Metastasis	Keratinizing	12 (75.0)	4 (25.0)	0.809
	Non-Keratinizing	76 (81.7)	17 (18.3)	
	Metastatic	5 (83.3)	1 (16.7)	
MEMO Treatment	Not given	46 (71.9)	18 (28.1)	0.3
	Given	277 (77.8)	79 (22.2)	
MEMO Treatment Complications	No	277 (76.9)	83 (23.1)	0.962
	Yes	46 (76.7)	14 (23.3)	
Hemoglobin	Normal	201 (79.8)	51 (20.2)	0.011
	Mild anemia	35 (68.6)	16 (31.4)	
	Severe anemia	39 (62.9)	23 (37.1)	
Recurrence	No	304 (77.9)	86 (22.1)	0.067
	Yes	19 (63.3)	11 (36.7)	
Disease	No	127 (96.9)	4 (3.1)	0.367
	Yes	26 (100.0)	0 (.0)	
Cancer being the cause of death	No	322 (85.6)	54 (14.4)	<0.001
	Yes	1 (2.3)	43 (97.7)	

Figure 1. Kaplan-Meier curves of overall survival for patients with normal hemoglobin, mild anemia and severe anemia.

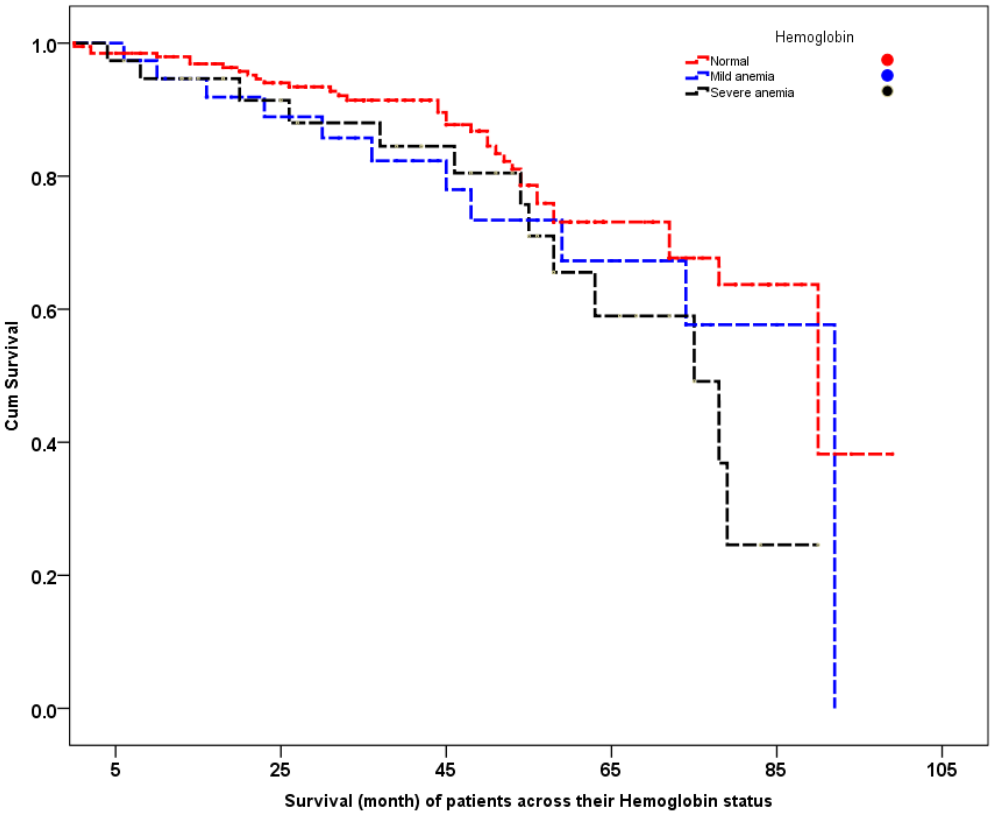

Table 3: Means for Survival Time				
Hemoglobin	Mean			
	Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Normal	78.887	2.744	73.509	84.264
Mild anemia	71.666	5.551	60.786	82.546
Severe anemia	66.252	4.660	57.119	75.385
Overall	75.859	2.289	71.372	80.345

Discussion:-

Our study comprised of a total of 420 subjects. Males comprised of 63% of the subjects, while, approximately 54% of the subjects were more than 50 years of age. Only 14.5% of the subjects were tobacco users. The duration of symptoms, on an average, was around 15 months. Only one subject presented with leukoplakia as a chief complaint, while, fifteen presented with an exophytic growth, thirty four presented with an ulcer and ninety six presented with a solid neck mass. Other chief complaints were pain (n=28, 6.7%), nasal obstruction (n=37, 8.7%), epistaxis (n=8, 1.8%), difficulty in hearing (n=12, 2.7%) and headache (n=10, 2.4%). Nasopharynx was the most common site of development of cancer (n=193, 54.8%) followed by the tongue (n=45, 12.8%) and the buccal mucosa (n=16, 4.5%). Other sites are mentioned in Table 1.

Squamous cell carcinoma was the most prevalent cancer (n=338, 90.1%) in our study. Adenocarcinoma was the second most common cancer (n=16, 4.3%). Fifty five (16.3%) subjects had T1 sized tumor, 89 (26.3%) had T2 sized tumor, 75 (22.2%) had T3 sized tumor, 111 (32.8%) had T4 sized tumor and 8 (2.4%) had Tx sized tumor. Around 33% (n=111) of the subjects had a T4 sized tumor. Amongst those who had a T4 sized tumor, 42 (37.8%) subjects had a tumor, which extended to the base of the skull, larynx (n=32, 28.8%), pharynx (n=22, 19.8%), base of the tongue (n=16, 14.4%), mandible (n=7, 6.3%) and the maxilla (n=4, 3.6%). Distant sites, which were involved, were brain and lungs. Around 95% (n=397) of the subjects had a positive nodal involvement at the time of initial diagnosis via FNAB. Ninety-three (28%) subjects had N0, while, 94 (28.3%) had N1, 111 (33.4%) had N2 and 34 (10.2%) had N3 nodal involvement. Only twenty-seven (6.4%) subjects had distant metastasis. In relevance to the histological grading of the cancer, 150 (44.5%) subjects had undifferentiated, 13 (3.9%) subjects had poorly differentiated, 99 (29.4%) subjects had moderately differentiated and 75 (22.3%) subjects had well differentiated cancer as mentioned in Table 1.

Surgery and radiotherapy was the most common treatment modality (n=73, 17.4%) which was utilized for the treatment of cancer in our subjects, followed by neoadjuvant chemotherapy and radiotherapy (n=64, 15.3%), neoadjuvant chemotherapy and concomittant chemo radiotherapy (n=42,10.0%), radiotherapy (n=38, 9.1%) and surgery (n=30, 7.2%). Rest of the treatment modalities are listed in the Table 1. Only sixty (14.3%) subjects encountered complications because of the treatment, which was provided to them. Amongst those who encountered complications, 47 suffered from minor morbidity, 12 suffered from major morbidity and 1 died because of the complications. Of all the subjects in our study only 30 (7.1%) had a recurrence.

Subjects were contacted via telephonic interview. Approximately 77% (n=323) of our subjects were alive when they were contacted, while, 23% (n=97) had deceased. Cancer was the cause of death of 44 (10.5%) subjects (Table 1).
One of the objectives of our study was to look for any association(s) of the studied parameters with the overall survival of our subjects. Following parameters had a statistically significant association with the overall survival of the subjects: Gender (p=0.022), age (p=0.001), T4 sized tumor (p=0.007), N status (p=0.037), M status (p=0.001), histological grading (p=0.043), hemoglobin (p=0.011) and cancer being the cause of death (p=0.001) (Table 2). In addition to that, Kaplan-Meier survival analysis showed that low haemoglobin levels were associated with poor overall survival outcome of the subjects (Figure 1).

In our study, males comprised of majority of the subjects (63%), while, more than half of the subjects (54%) were greater than 50 years of age. This in agreement with the literature as in a cohort study of OSCC patients the male-to-female ratio was 5.3:1 and the average age at the time of the diagnosis of the patients was 56 years[8]. OSCC is considered as a type of cancer which usually affects men more commonly than women and affects individuals between the fifth and sixth decade of life[9], although, the male-to-female ratio and the age might vary from region to region and might be dependent on other factors.

Tobacco is considered as one of the leading causative factors of OSCC[9]. For instance, a study reported that 72.6% of the OSCC patients were tobacco users[8]. However, tobacco is used in different forms and the affect of these forms of tobacco might vary on upper aero-digestive tract cancers. In some studies, oral cavity seems to be the least affected site of the entire upper aero-digestive tract by the carcinogenic effect of smoked tobacco, whereas, larynx seems to be the most affected site [10,11]. In contrast, pipe smoking and cigar are considered as a leading cause of development of cancer in the oral cavity[11]. While, chewable tobacco causes a six fold increase in the risk of oral cancer (OR 5.8), as compared to oropharyngeal cancer which has been shown to have a minute risk (OR 1.2) [12]. Surprisingly, in our study only 14.5% of the subjects had a history of tobacco usage. The presence of different types of cancers in our sample including NPC might be a reason behind the less number of tobacco users in our sample, as other cancers including NPC might have different etiological factors as compared to OSCC. However, numerous patients develop OSCC and NPC who do not have a history of usage or exposure to the established causative factors, which raises an interesting prospect regarding the role of other clinicopathological factors in the development of these cancers.
Around 95% (n=397) of the subjects in our study had a positive nodal involvement at the time of initial diagnosis. In some of the previous studies the incidence of occult metastases was 28%[13], 23%[14] and 21%[15].

The treatment modalities of OSCC are still the same; surgery being the main treatment modality, it might be the only treatment performed or it might be followed by radiotherapy, radiotherapy might be performed only or in combination with chemotherapy (chemo radiotherapy) which is used as an adjuvant treatment to surgery or as a palliative treatment[16]. Technological advances in surgery, postoperative radiotherapy and concurrent chemo radiotherapy has remarkably improved the survival outcome of OSCC patients during the last decade [17,18]. Surgery and postoperative radiotherapy was the most common treatment modality (n=73, 17.4%) in our study, followed by neoadjuvant chemotherapy and radiotherapy (n=64, 15.3%), neoadjuvant chemotherapy and concomittant chemo radiotherapy (n=42,10.0%), radiotherapy only (n=38, 9.1%) and surgery only (n=30, 7.2%).

Of all the subjects in our study only 30 (7.1%) had a recurrence. Recurrence significantly reduces survival in oral cancer patients[19]. Previous studies have shown that numerous OSCC patients die for reasons not related to the cancer itself[20]. For instance, the main causes of death in a study based on OSCC patients were other malignancies, cardiac, vascular and pulmonary diseases[19]. Our findings are in line with these studies, as cancer was the cause of death of only 10.5% of the subjects in our study. Although it might be plausible that post treatment complications (as shown in Table 1) might have contributed to the decline in the quality of life of subjects as at least one subject died because of the complications caused by the treatment.

Despite several improvements in the diagnostics and treatment modalities of head and neck cancer, the 5-year survival rate seems to be unaltered over the last two decades[6]. Various clinicopathological parameters might affect the overall survival of such patients. For instance, in our study a statistically significant association was observed between age and overall survival of the subjects (p=0.001). Numerous studies support our findings that age is significantly associated with disease-specific survival[8]. Some studies showed higher mortality in elderly patients when compared to younger patients[21], while, others reported higher death rate in younger patients. E.g.; under 40 years of age[22].

Previous studies suggested primary tumour size as reliable indicator of patient's survival outcome [23,24]. Our study showed a statistically significant relationship (p=0.007) between large sized tumors. E.g.; T4 stage tumor and overall survival of the subjects.

Although the size of the primary tumour plays a cardinal role in determining the potential of a tumour to metastasize, it is plausible that cancers of minuscule size can metastasise, while, some large cancers never metastasise[19]. Studies have shown nodal involvement as an important predictor of the overall survival of the patients[23,24,] so much so that patients with occult metastasis had 5-fold increased risk of dying from cancer as compared to patients with no occult metastases[13]. The negative effect of occult nodal metastases on the survival outcome of patients is evident by the fact that when patients with occult metastases receive radiotherapy, their disease specific survival is still poorer as compared to patients with pathologically negative necks (DSS rate, 60% vs. 87%)[13]. Our findings support the findings of previous studies, as a statistically significant relationship (p=0.037) was seen between N status and overall survival of the subjects.

In addition to the size of the primary tumor and nodal involvement, other indicators of patient's survival outcome are the histological grade and distant metastases[25]. A statistically significant association was observed between M status (p=0.001), histological grading (p=0.043), and overall survival of our subjects.

In the current study, low haemoglobin levels were found to be associated with poor survival outcome of the subjects (p=0.011) (figure 1). Studies have shown anemia to be a prognostic factor for the development of local recurrence (p= 0.001) and ultimately poor prognosis of the patients[6]. Anemia causes resistance to radiation because most likely the haemoglobin level affects tumor response to radiation through the delivery of oxygen to the tumor [26].

The findings of this study will aid the clinician in diagnosing and treating future cancer patients. This study has identified clinicopathological parameters, which play an important role in determining the survival outcome of oral squamous cell carcinoma and nasopharyngeal carcinoma patients.

Limitations of this study
Following are some of the limitations of this study:
1) Retrospective nature of the study
2) Availability of some of the online data in the form of notes. Extraction of this type of data was time consuming
3) Data for some subjects was missing
4) Some of the patients were referred from other hospitals. Data of those hospitals was not obtainable
One of the major problems which we faced was cleaning and organization of data. Rigorous efforts were made to organize the data for the purpose of statistical analysis
Our work is still in process. We plan to use Kaplan Meier survival analysis to determine the impact of tumor size and nodal involvement on the survival outcome of patients. But a Future research project can focus on some of the parameters which were missing in this study, such as role of molecular markers e.g; HPV 16, HPV 18, EBV, htert gene, VEGF etc. in the prognosis of cancers. In addition to that, some of the important parameters which were lacking in this study such as depth of invasion of the tumor and involvement of margins, neuro-invasion (the online data was missing) can be investigated to see their impact on the prognosis of patients.

Conclusion:-

This study has identified clinicopathological parameters, which play an important role in determining the survival outcome of oral squamous cell carcinoma and nasopharyngeal carcinoma patients. This study showed a statistically relationship between age, gender, tumor size, nodal involvement, distant metastasis, histological grading, level of hemoglobin and survival outcome of the oral squamous cell carcinoma and nasopharyngeal carcinoma patients. In addition to that, this study also showed the significance of different level of hemoglobin in determining the overall survival outcome of the patients.

Further more studies can focus on some of the parameters which were missing in this study, such as role of molecular markers e.g; HPV 16, HPV 18, EBV, htert gene, VEGF etc. in the prognosis of cancers. In addition to that, some of the important parameters which were lacking in this study such as depth of invasion of the tumor and involvement of margins, neuro-invasion (the online data was missing) can be investigated to see their impact on the prognosis of patients

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