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Original Article.

Different Ttreatment Modalities of Head and Neck Cancer (Retrospective Study)

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ABSTRACT

Background: Surgery, radiation therapy, and chemotherapy are the approved methods for curing head and neck cancer. While radiation therapy is the gold standard right now, other targeted therapies are receiving more attention and may soon replace it. This study aimed to assess the different treatment modalities of head and neck cancer in the Clinical Oncology and Nuclear Medicine Department at Zagazig University Hospitals.

Methods: This was a retrospective cross-sectional study performed at the Zagazig University Hospitals' Clinical Oncology and Nuclear Medicine Department. For this study, we used the medical records of all long-term head and neck cancer (HNC) cases stored in the Clinical Oncology and Nuclear Medicine Department between 201٦ and 2021.

Results: We found that 30.3% of the studied cases had radical surgery. The frequency of chemotherapy was as follows: definitive (5.5%), induction (4.1%), concurrent (43.5%), adjuvant (22.2%) and palliative (1.1%). Regarding radiotherapy 93% of the cases had radiotherapy most frequent was definitive (64.9%). The median of regional recurrence-free survival among Non-Nasopharyngeal carcinoma (NPC) differed significantly when compared to NPC cases ($p<0.001$). There was a statistically significant increase in median overall survival among cases less than 50 years old, stage II AJCC, CR cases, and cases with absent local recurrence ($p<0.001$).

Conclusion: Cancer of the head and neck has become an urgent public health issue in Zagazig. Due to the high rates of tobacco use and HPV infection, screening programs and patient monitoring of various treatment modalities are crucial for the early diagnosis of HNC.

Keywords: Treatment Modalities; Cancer; Head and Neck.

INTRODUCTION

Lip, throat, oral cavity, nose, ear, salivary glands, paranasal sinuses, and larynx can all be affected by head and neck cancer (HNC). Squamous cell carcinomas account for 90% of HNC, making it one of the top 10 incidence malignancies in males worldwide [1]. Squamous cell carcinoma of

the head and neck (HNSCC) is the sixth most common kind of cancer in both men and women. Around 560,000 new cases and 300,000 deaths are attributed to HNC annually [2].

The epithelial lining of the oral cavity, oropharynx, larynx, and hypopharynx is the most common site of origin for (HNSCC). Tobacco and alcohol use, for example, have been linked to an increased chance of developing these cancers, and there is good evidence that these two risk factors interact [3]. Multiple human papillomavirus (HPV) strains have been linked to the emergence of a new disease in recent years (HPV 16,18) [4]. These patients have a much better prognosis than those with cigarette use. Forty to fifty percent of patients with HNSCC will be alive after five years. Thirty-five percent of patients were diagnosed with an early stage (T1-2, N0) [5]. Previous hospital-based studies in Egypt found that between 17 and 20% of all cancers have HNC [6]. When compared to other Middle Eastern countries, Egypt's rate of oral cavity and pharynx cancer incidence (5.5/105) was among the highest [7].

This study aimed to investigate the different treatment modalities of head and neck cancer among cases of the Clinical Oncology and Nuclear Medicine Department in Zagazig University Hospitals.

METHOD

This was a retrospective study that was performed at the Clinical Oncology department in Zagazig University Hospitals by reviewing the registrar's files during the study period. All cases that fulfill the inclusion and exclusion criteria were included from the year 2016 to 2021, (312 cases) as a comprehensive sample.

Inclusion criteria:

All (HNC) patient's files in the Clinical Oncology and Nuclear Medicine Department medical records room from (2016 to 2021). All files of Head and neck cancer were selected with no inclusion criteria, and we select squamous cell carcinoma as they represent 95% of pathological types of Head and neck cancer.

Exclusion criteria:

None of the files were excluded.

Data Collection*:*

Operational design:

Sample size: The sample size will be all (HNC) patients diagnosed from (2016 to 2021). Process: Personal identification, certain demographics, the date and most reliable basis of diagnosis, the place, and the morphology of the tumor were all part of the foundational data for Head and Neck Cancer.

Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Institutional Review Board approval (ZUIRB#: 9300/ 5-6-2022) was obtained.

Treatment modalities:

1st surgical procedures, chemotherapeutic agent, concurrent chemoradiation, and radiotherapy treatment.

Response of the treatment; one for those who had complete response (CR), two for those who had partial response (PR), three for those

who had stable Disease (SD), four for those who had progressive disease (PD).

STATISCAL ANALYSIS

For this data analysis, we used SPSS 23. Quantitative evidence supports a qualitative argument. Moment to death or the last known date of survival (OS) was measured from the time of operation (censored). RFS was determined by subtracting the date of primary treatment from the date of recurrence or metastasis, or the date on which the patient was last known to be relapse-free (censored). The date of initial treatment until recurrence or the date last known to be recurrence-free was used to determine Locoregional Recurrence Free Survival (LRFS) (censored from the primary treatment date to the date when distant metastasis was identified (or the date on which distant metastasis-free status was last reported), we determined the Distant Metastasis Free Survival (DMFS) (censored). All potential prognostic indicators were used to stratify OS and RFS. Kaplan-Meier was used to estimate these time-to-event distributions, and two-sided exact stratified log-rank tests were used to compare them. Independent prognostic factors were identified and their effects on OS and RFS were estimated using the Cox proportional hazards regression model.

RESULTS

We found that the mean age of the studied cases was 55.58 years and 63.5% of the cases were more than 50 years old. Males represented 68.3% of the cases and also 66.4% of the cases were from urban areas and 52.8% were current smokers (Table 1).

We found that 79.9% of the studied cases had radical surgery. The frequency of chemotherapy was as follows: definitive (5.5%), induction (4.1%), concurrent (43.5%), adjuvant (22.2%) and palliative (1.1%). Regarding radiotherapy, 93% of the cases had radiotherapy most frequent was postoperative (56%), 93.4% of the cases had A/Es but only 19.2% were serious and 22.1% were grade III (Table 2).

Complete response (CR) was reported in 19.6% of the cases and OAR in 53.1% of the cases. Local recurrence was found in 62.4% of the 133 cases and regional in 62.4% of them. Distant metastasis was found in 19.5% and relapse in 77.8% of 135 cases while regression in 83.8% of 136 cases. Finally, the mortality rate was 52%, the median of different free survival and overall survival were shown in (Tables 3& 4)

Statistically significant increases were found in cases > 50 years old among the dead compared to lived cases, and current smokers among the dead compared to lived cases ($p<0.01$). Also, statistically significant increases were found in adenoid cyst carcinoma, adenocarcinoma pathological type, and AJCC grade IV A & B among dead compared to lived cases ($p<0.004$) (Table 5).

There were statistically significant increases in NR, local recurrence, distant metastasis, relapse, and progression response among dead compared to lived cases ($p<0.001$) (Table 6).

Table (1): Demographic data of the studied cases

Variable		(*n*=271)	
Age: (years)	*Mean ± Sd* *Range*	55.58 ± 11.64 18-81	
Variable		**No**	**%**
Age group:	*≤ 50 years* *> 50 years*	99 172	36.5 63.5
Sex:	*Male* *Female*	185 86	68.3 31.7
Residence:	*Rural* *Urban*	91 180	33.6 66.4
Smoking:	*Non-smoker* *Ex-smoker* *Current smoker*	93 35 143	34.3 12.9 52.8

SD: Standard deviation

Table (2): Treatment data and Adverse events (A/Es) among the studied cases

Variable		(n=271)	
		No	**%**
Radical surgery:	No Yes	82 189	30.3 69.7
LN dissection:	No Yes	92 179	33.9 66.1
Surgical margin:	 -ve +ve	(n=189) 129 60	 68.3 31.7
Definitive chemotherapy:	No 5FU+Platinol Taxoter+Platinol+5FU Gemcitabine + Platinol	256 1 11 3	94.5 0.4 4.1 1.1
Induction chemotherapy:	No 5FU+Carboplatin Taxoter+Platinol+5FU Taxol+Platinol+5FU Gemcitabine + Platinol	260 3 6 1 1	95.9 1.1 2.2 0.4 0.4
Concurrent chemotherapy:	No 5FU Cisplatin Carboplatin	179 1 87 4	66 0.4 32.1 1.5
Adjuvant chemotherapy:	No 5FU+Platinol 5FU+Carboplatin	238 30 3	87.8 11.1 1.1
Palliative chemotherapy:	No 5FU+Carboplatin Taxoter+Platinol+5FU Gemcitabine + Platinol	268 1 1 1	98.9 0.4 0.4 0.4
Radiotherapy:	No RT Preoperative Postoperative Definitive Palliative	19 18 152 79 3	7 6.6 56 29.2 1.1
Any A/Es:	Absent Present	18 253	6.6 93.4
A/Es serious:	Absent Present	219 52	80.8 19.2
A/Es grade III:	Absent Present	211 60	77.9 22.1

Table (3): Outcome among the studied cases

Variable		(n=271)	
		No	%
Response to treatment:	CR	53	19.6
	PR	91	33.6
	SD	24	8.9
	PD	20	7.4
	Not applied	83	30.6
Response:	OAR	144	53.1
	NR	43	15.9
	N/A	84	31
Recurrence:		(n=133)	
	Local	96	72.2
	Regional	83	62.4
Distant metastasis:		(n=266)	
	Absent	214	80.5
	Present	52	19.5
Relapse:		(n=135)	
	No	30	22.2
	Yes	105	77.8
Progression:		(n=136)	
	No	22	16.2
	Yes	114	83.8
Mortality:	Alive	130	48
	Dead	141	52

Table (4): Survival rates among the studied cases

Variable	N	Events	Median	95% CI
Local recurrence free survival	133	96	26	21.38-30.62
Regional recurrence free survival	133	83	26	20.96-31.04
Distant metastasis free survival	266	52	69	65.65-72.63
Disease free survival	133	105	25	20.47-29.54
Progression free survival	136	114	17	14.61-19.39
Overall survival	271	141	56	50.82-61.18

Table (5): Relationship between clinicopathological characteristics and survival among the studied cases

Variable		N	Alive (n=130)		Dead (n=141)		χ^2	P
			No	%	No	%		
Age group:	≤ 50 years	99	66	66.7	33	33.3	21.85	**<0.001**
	> 50 years	172	64	37.2	108	62.8		**
Sex:	Male	185	86	46.5	99	53.5	0.51	0.47
	Female	86	44	51.2	42	48.8		NS
Residence	Rural	91	47	51.6	44	48.4	0.74	0.39
	Urban	180	83	46.1	97	53.9		NS
Smoking:	Current smoker	143	59	41.3	84	58.7		
	Non-smoker	93	56	60.2	37	39.8	**8.35**	**0.01***
	Ex-smoker	35	15	42.9	20	57.1		
Site:	Oral cavity	81	44	54.3	37	45.7		
	Nasopharynx	41	20	48.8	21	51.2		
	Oropharynx	13	4	30.8	9	69.2		
	Hypopharynx	19	5	26.3	14	73.7		
	Larynx	64	35	54.7	29	45.3	15.73	0.07
	Nose & Nasal cavity	10	6	60	4	40		NS
	Paranasal sinus	9	1	11.1	8	88.9		
	Salivary glands	20	10	50	10	50		
	Ear	13	4	30.8	9	69.2		
	Unknown primary	1	1	100	0	0		
Subsite:	Lip	29	15	51.7	14	48.3		
	Buccal mucosa	15	6	40	9	60		
	Gingiva	2	2	100	0	0		
	Hard palate	4	3	75	1	25		
	Floor of mouth	2	1	50	1	50		
	Oral Tongue	28	17	60.7	11	39.3		
	Retromolar trigone	1	0	0	1	100	30.16	0.23
	Nasopharynx	41	20	48.8	21	51.2	NS	NS
	Soft palate	2	1	50	1	50		
	Anterior tonsillar pillar	1	1	100	0	0		
	Tonsillar fossa	2	0	0	2	100		
	Posterior tonsillar pillar	7	2	28.6	5	71.4		
	Vallecula	1	0	0	1	100		
	Supraglottic	18	10	55.6	8	44.4		
	Glottic	24	17	70.8	7	29.2		
	Subglottic	22	8	36.4	14	63.6		
	Nose	7	4	57.1	3	42.9		
	Nasal cavity	3	2	66.7	1	33.3		
	Maxillary sinus	7	1	14.3	6	85.7		
	Ethmoidal sinus	2	0	0	2	100		
	Parotid	18	9	50	9	50		
	Submandibular	2	1	50	1	50		
	External ear	13	4	30.8	9	69.2		
	Unknown primary	1	1	100	0	0		
	Postcricoid	3	1	33.3	2	66.7		
	Pyriform fossa	16	4	25	12	75		
Pathology:	Squamous cell carcinoma	251	121	48.2	130	51.8		
	Adenoid cystic carcinoma	4	0	0	4	100		
	Mucoepidermoid carcinoma	4	4	100	0	0	**11.56**	**0.04***
	Undifferentiated carcinoma	2	1	50	1	50		
	Adenocarcinoma	6	1	16.7	5	83.3		
	Epithelial Myoepithelial carcinoma	4	3	75	1	25		
AJCC pathological:	II	105	59	56.2	46	43.8		
	III	61	21	34.4	40	65.6		
	IV A	22	5	22.8	17	81.8	**13.3**	**0.004***
	IV B	1	0	0	1	100		
	N/A	82	45	54.9	37	45.1		

χ^2: Chi square test
NS: Non significant (P>0.05)
*: Significant (P<0.05) **: Highly significant (P<0.001)

Table (6): Relation between site and outcome data of the studied cases

Variable		N	Alive (n=130)		Dead (n=141)		χ^2	P
			No	%	No	%		
Response:	OAR	144	84	58.3	60	41.7	**12.27**	**<0.001**
	NR	43	12	27.6	31	72.1		**
	N/A	83	34	40.5	50	59.5		
Local Recurrence:		(n=133)	(n=70)		(n=63)			
	Absent	37	31	83.8	6	16.2	**19.95**	**<0.001**
	Present	96	39	40.6	57	59.4		**
Distant metastasis:		(n=266)	(n=129)		(n=137)			
	Absent	214	119	55.6	95	44.4	**22.16**	**<0.001**
	Present	52	10	19.2	42	80.8		**
Relapse:		(n=135)	(n=71)		(n=64)			
	No	30	25	83.3	5	16.7	**14.62**	**<0.001**
	Yes	105	46	43.8	59	56.2		**
Progression:		(n=136)	(n=59)		(n=77)			
	No	22	18	81.8	4	18.2	**Fisher**	**<0.001**
	Yes	114	41	36	73	64		**

χ^2: Chi square test
*: Significant (P<0.05)
**: Highly significant (P<0.001).

DISCUSSION

Over 900,000 new cases and 400,000 deaths every year make head and neck cancer one of the worst forms of the disease. They represent a diverse collection of cancers, the epidemiology of which varies greatly among regions based on factors such as the prevalence of risky behaviors and the genetic makeup of the local population. Sixty-seven percent of all cases and eighty-two percent of all deaths occur in low- and middle-income countries [8].

Surgery, radiation therapy, and chemotherapy are the tried-and-true methods for curing head and neck cancer. However, radiation is the current gold standard, and other targeted therapies are being investigated and used more frequently. Surgery, radiation therapy, and chemotherapy are the tried and true methods of treating curable head and neck cancer. Radiation therapy is the gold standard right now, but other targeted therapies are getting a lot of attention and may one day replace it [8].

With rare exceptions, palliative therapy and supportive care are recommended for patients with locally recurrent or metastatic illness [9]. Chemoradiation is the mainstay of treatment due to the cancer's radiosensitivity, and it has a 75%-83% 5-year survival rate. However, a poor result is seen in about 10-15% of patients due to distant metastases and recurrent disease after final chemo-radiation [10].

Our results regarding demographic data showed that the mean age of the studied cases was 55.58 years and 63.5% of the cases were more than 50 years old. Males represented 68.3% of the cases and also 66.4% of the cases were from urban areas and 52.8% were current smokers.

In their analysis of data from 1999 to 2006, Attar et al. [11] estimated incidence, incidence rate ratios (IRRs), and 95 percent confidence intervals (CIs) broken down by age, district, and subsite. The current study was consistent with these findings. There were 1,140 confirmed cases of HNC in Gharbiah, with men accounting for 64.3% of

the total. The age range of 50-69 accounted for the majority of the reported cases (50.71 percent). About 50.79% were urban residents, and 49.21% were rural residents. 13.25 % were current smokers, 23.95% were non-smokers, 10.79% were former smokers, and 52.02% were unknown.

The present study respecting treatment options showed that 30.3% of the studied cases had radical surgery. The frequency of chemotherapy was as follows: definitive (5.5%), induction (4.1%), concurrent (43.5%), adjuvant (22.2%) and palliative (1.1%). Regarding radiotherapy, 93% of the cases had radiotherapy most frequent was definitive (64.9%).

Also, Adoga et al. [12] revealed that treatment included tracheostomy, surgical excisions with aesthetic repair, and postoperative radiation or chemotherapy, as well as an examination under anesthesia and biopsy for histological diagnosis. Patients with stage IVC illness were given palliative care. The most common surgical procedure performed on these patients was a maxillectomy (total or medial), and 102 (83.6%) underwent some form of surgery. Of these patients, 21 (17.2%) required an emergency tracheostomy due to upper airway obstruction, and 5 (4.1%) underwent an elective tracheostomy for airway access intraoperatively and to prevent upper airway obstruction before beginning radiotherapy.

Ng et al. [13] reported that concerning radiotherapy technique, 11.4% had 3D conformal, and 88.6% had intensity-modulated radiation therapy (IMRT). 29.5% received induction radiotherapy, and 66.5% had concurrent radiotherapy.

In agreement with the current study, Refaat et al. [14] reported that regarding treatment, 75.73% received chemoradiation, 0.97% had radiotherapy, 2.91% had surgery and postoperative radiation, and 20.39% had surgery and postoperative chemoradiation.

Our study showed that 93.4% of the cases had A/Es but only 19.2% were serious and 22.1% were grade III. Regarding the outcome of this study, CR was reported in 19.6% of the cases and OAR in 53.1% of the cases. Local recurrence was found in 62.4% of the 133 cases and regional in 62.4% of them. Distant metastasis was found in 19.5% and relapse in 77.8% of 135 cases while regression in 83.8% of 136 cases. Finally, the mortality rate was 52%.

Refaat et al. [14] reported that relapse was reported in 84% of cases. El Din et al. [15] reported that concerning response, the complete response rate was 25.8% and the partial response rate was 13.3%.

Concerning survival rates, local recurrence-free survival regional recurrence-free survival, and distant metastasis-free survival were found in 133 cases 266 cases had distant metastasis-free survival, 136 cases had progression-free survival, and 271 had overall survival.

In agreement with the current study, Refaat et al. [14] reported that the overall survival was 77% after 5 years. Distant metastasis-free survival was reported in 89%.

The relation between the site and some of the demographic and pathological data of the studied cases showed that there was a statistically significant increase in Epithelial Myoepithelial carcinoma among NPC compared to Non-NPC, there was a statistically significant increase in Clinical AJCC Stage IVA among NPC compared to Non-NPC and NA pathological AJCC grade among NPC compare to non-NPC, In agreement with the current study, Mak et al. [10] reported that concerning NPC group, 77.3% of cases were <59 years and 22.7% were >59 years. 73.3% were males, and 26.7% were females. Concerning nodal stage, N0, N1, and N3 were represented in 21.7, 31, 33.9, and 13.4% respectively. T classification showed that T1, T2, T3, and T4 were represented in 38, 23.7, 16.5, and 21.9% respectively. 90.5% of cases had M0, and 9.5% had M1 metastasis. Concerning AJCC staging, stages I, II, III, IVA, IVB, and IVC

were represented in 9.3, 24.6, 30.6, 16.1, 9.9, and 9.5% respectively.

The relation between site and outcome data of the studied cases showed that there was a statistically significant increase in N/A response among non-NPC compared to NPC cases. The survival rates among the studied cases according to the site table showed that there was a statistically significant increase in the median of regional recurrence-free survival among non-NPC compared to NPC cases. In accordance with the present findings, Refaat et al. [14] revealed that regarding the NPC group, the overall survival was 88% after 5 years. The relapse-free survival was 87%, and distant metastasis-free survival was reported in 100%.

There were statistically significant differences between alive and dead cases (survival) regarding age, histopathological diagnosis, AJCC staging, response to treatment, response to treatment, local and regional recurrence, distant metastasis, relapse, and progression ($p<0.05$).

El Din et al. [15] reported that Response emerged as a strong indicator of survival, as There was a highly significant correlation between how quickly a patient responded and how long they lived (P 0.001). Patients with stage I and II (early stage) cancer had a CR rate of 79.3 percent, but those with stage III and IV disease only had a CR rate of 16 percent, indicating a statistically significant connection between response and disease stage. Patients who had hypofractionated radiation (RT) had the best response, and there was a statistically significant connection between response and RT fractionation (CR rate is 100 percent). This is explained as all patients who received hypofractionated RT were early-stage laryngeal cancer (T1 and T2). Another study reported that a higher T stage is correlated with a poorer prognosis [16].

In agreement with the current study, Mak et al. [10] reported that Overall survival was significantly lower in patients with more advanced age, a higher T classification, a higher N classification, and metastatic disease at presentation ($p<0.001$ for each), Poor disease-specific survival was also seen in patients with higher T and N disease ($p = 0.015$ and p 0.001, respectively), as well as those who were older ($p = 0.009$), had metastatic disease at presentation (p 0.001), and had a higher T and N disease stage at diagnosis. Similarly, Han et al. [17] found that advanced N disease was the most important predictor of poor prognosis.

The study limitations include a relatively small sample size and being a retrospective cross-sectional. Further studies are needed on larger sample sizes, and longer follow-up periods, which may elucidate epidemiological characteristics of (HNC) in the Clinical Oncology and Nuclear Medicine Department at Zagazig University Hospitals.

Conclusions:

Cancer of the head and neck has become an urgent public health issue in Zagazig. Due to the high rates of tobacco use and HPV infection, screening programs and patient monitoring of various treatment modalities are crucial for the early diagnosis of HNC..

Conflicts of interest: None

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