CLINICOPATHOLOGY AND TREATMENT PATTERNS OF HEAD AND NECK CANCERS AT TIKUR ANBESSA SPECIALIZED HOSPITAL, RADIOTHERAPY CENTER, ADDIS ABABA, ETHIOPIA

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ACRONYMS

AACCR	Addis Ababa City Cancer Registry
AAU	Addis Ababa University
ACS	American Cancer Society
AIDS	Acquired Immune Deficiency Syndrome
AJCC	American Join Committee on Cancer
CHS	College of Health Science
CI	Confidence Interval
Co-60	Cobalt 60
CRT	Concurrent Chemo Radiotherapy
CXR	Chest X-Ray
CT	Computed Tomography
DM	Diabetes Mellitus
EBRT	External Beam Radiotherapy
ECOG	Eastern Cooperative Oncology Group
FMOH	Federal Ministry of Health
FNAC	Fine Needle Aspiration Cytology
GLOBOCAN	Global Burden of Cancer
HIV	Human Immune Virus
HNC	Head and Neck Cancer
HNSCC	Head and Neck Squamous Cell Carcinoma
HR	Hazard Ratio
HTN	Hypertension
IAEA	International Atomic Energy Agency
INCTR	International Network for Cancer Treatment and Research
MRI	Magnetic Resonance Imaging
NCD	Non-Communicable Disease

OR	Odds Ratio
RVI	Retro Viral Infection
RR	Relative Risk
RT	Radiotherapy
SPH	School of Public Health
SPSS	Statistical Package for Social Science
TASH	Tikur Anbessa Specialized Hospital
TNM	Tumor Size, Nodal involvement, Metastasis
UICC	Union of International Cancer Control
WHO	World Health Organization
5 – FU	5- Fluorouracil
Gy.	Gray

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SUMMARY

Background: Head and neck cancer (HNC) is one of the most common cancers worldwide and its incidence is reported to be increasing both in developed and developing countries. There is lack of published data on clinicopathology and treatment patterns of head and neck cancers in Ethiopia.

Objective: To assess clinicopathology and treatment patterns of head and neck cancers at Tikur Anbessa Specialized Hospital, Radiotherapy Center, Ethiopia

Methodology: A retrospective cross-sectional study design and simple random sampling technique was used to select the required sample size. Descriptive statistics (mean, SD, frequency, percentage, graph and table) and chi-square results were generated by using SPSS version 21. The level of significance was obtained at 0.05.

Results: Four hundred twenty two (422) histopathologically confirmed head and neck cancers that were treated at TASH from 2014 to 2017 G.C were analyzed in this study. The male to female ratio (M: F) was 1.98: 1. The most common primary site of head and neck cancers was pharynx 156 (37%) and the major histologic type was carcinoma which accounted 358 (84.81%). From carcinomas, squamous cell histologies were 330 (92.12%). Majority of the cases had advanced disease at diagnosis (89.29%). There was unacceptable delay between diagnosis and initiation of treatment.

Conclusion/recommendation: This study showed that head and neck cancers treated at this hospital presented at advanced stage of the disease. Only small proportion of patients took concurrent chemo radiotherapy and there was long duration between diagnosis and initiations of treatments. These all might have reduced the curability of the disease. Majority of cases were males and relatively young at diagnosis. The awareness of the society on head and neck cancers should be increased as it helps to diagnose at early stages of the disease. The government and other stakeholders should expand cancer centers to reduce the treatment delay and increase quality of care of these cancers. Further studies are very important on head and neck cancers to optimize treatment out come.

Key words*: head and neck cancer, Patterns of treatments, primary site, clinical Stage, pathology, TASH, Ethiopia*

CHAPTER ONE:

INTRODUCTION

1.1 Background

Head and neck cancers are malignancies occurring in the nasal cavities, pharynx (nasopharynx, or pharynx, hypo pharynx), larynx, paranasal sinuses, ear, scalp, oral cavity and salivary glands (1). These cancers interfere with vital functions of life such as breathing, swallowing, speech, hearing, vision, taste and smelling (2).

These cancers are among the top ten cancers in the world (3). The incidence is increasing more rapidly in developing countries (4). About 650,000 new cases are diagnosed each year and 330,000 deaths worldwide annually (5). The incidence varies from one geographic region to another and ranges from 5-50 % (6). In Europe and America, they account 5–8 % of total body cancers (7-9). In India it constitutes about 30 % of all cancers (10, 11). The report from sub-Saharan Africa from 18,099 in 2008, the top six primary sites were lip, oral cavity, nasopharynx, or pharynx and hypo pharynx, and larynx (10). Male was affected more than female from this result (11).

Excess alcohol consumption and heavy tobacco smoking are the predisposing factors for head and neck cancers (7). These predisposing factors are preventable (12). About 90% of these cancers are of epithelial origin commonly associated with smoking and alcohol consumption. Squamous cell carcinoma constitutes the greatest majority of these epithelial origin cancers (13, 14). The others histology includes adenocarcinoma, lymphomas, sarcomas, blastomas, neuroendocrine tumors (14).

The treatment of head and neck cancers are better treated with a team including radiation and medical oncologists, head and neck surgeons, radiologists, pathologists, plastic surgeons, psychologists, speech therapists, dentists, social workers and other interested expertise (15). The treatment of these malignancies vary based on primary site, stage of the tumor, the availability of facility and expertise in the treating center, the patient treatment preference (14).

The outcome of treatment and prognosis also depends on clinical stage, histological type and treatment modalities delivered (14, 15). For organ preservation, radiotherapy is an accepted alternative to surgery (16). The outcome of radical radiotherapy regimens has been further improved by the use of induction chemotherapy, concurrent chemo radiotherapy, and concurrent epidermal growth factor inhibitors for some types of head and neck cancers like nasopharyngeal and laryngeal cancers (17).

Like other centers, treatment delivered in our center was based on the histological types, stage of the disease, and primary sub-site and performance status of the patient. Because of our limited resources and long waiting list for upfront radiotherapy, majority of our patients received chemotherapy as induction or palliation therapy (18). Adjuvant chemotherapy or radiotherapy, concurrent chemo radiotherapy was also delivered based on the indications. Due to lack of awareness and scarcity of oncology centers, majority of our patients present at late stages. Even after they referred to TASH which is the only radiotherapy center in the country, they stay for months before starting radiotherapy.

To my knowledge, there is no published data on the clinicopathology and patterns of treatments of head and neck cancers in Ethiopia. This retrospective study tried to give objective evidence on demography, primary sites, and clinical stage at diagnosis and patterns of treatment delivered for head and neck cancers in this hospital. The possible associated risk factors for head and neck cancers were also analyzed.

1.2 Statement of the problem

Ethiopia is home to a growing population of more than 105 million people and is expected to become the ninth most populous country in the world by 2050 with rising cancer burden in parallel (19). Despite the increment of cancer burden, much attention is still on the communicable diseases like HIV/AIDS, malaria, and tuberculosis (20). The inadequate attention of governmental organizations, policy makers and non-governmental organizations could be due to low awareness on the scale of burden of cancer in the country.

From our daily observation, most of our head and neck cancer patients have locally advance disease at diagnosis. There is diversity on primary site and histological types of these cancers. The suggested causes for late stages of the disease are: lack of adequate awareness of our society on cancer, social stigma on cancer patients, economic problems, lack of cancer centers in the nearby to the society. Patients also go to local healers and holy sprits than to modern medicine especially in rural areas.

So far, there are only two institutions based studies done showing the pattern of cancer; one at Tikur Anbessa Specialized hospital and the other at Gondar hospital (21, 22). A study done at Tikur Anbessa Specialized hospital on pattern of cancer disease from 1998 to 2010 showed a sharp increase yearly new cancer diagnosis and head and neck cancer was the leading cancer in males accounting 22% (21). There is however no other analysis done since then to see any change in the pattern of disease and stage of diagnosis of head and neck cancers. Hence this study helped to determine the clinical stage at presentation, primary sites, and histopathological types and the differentiation of head and neck cancer among patients treated in TASH hospital. This study also described the sex, age, geographic distribution of head and neck cancer patients treated at TASH. It also analyzed patterns of care given in this center and possible associated risk factors for these cancers.

1.3 Significances of the Study

The result of this study showed that head and neck cancer patients present at advanced stage and at young age. The treatment pattern delivered showed there was an acceptable delay before initiation of therapy. So this study can be used as an input for policy makers and other concerned body to give attention on these cancers. These concerned bodies will work to increase awareness of our societies on cancers and try to increase cancer centers to decrease treatment delay. The study will also stimulate other researchers to do further studies on head and neck cancers in Ethiopia

CHAPTER TWO: LITERATURE REVIEW

Head and neck cancers are diverse group of malignancies originating in the nasal cavity, pharynx, larynx, cheek, mandible, ear, gingival, orbit, scalp, oral cavity, neck lymph nodes and salivary glands (1). They constitute a major health burden in the world being an important cause of morbidity and mortality (1-3). The GLOBOCAN data showed the incidence and prevalence of cancer is increasing. In 2012 the estimated new cancer cases was 14.1million of which 8.2 million cancer deaths. There were estimated 32.6 million people living with cancer worldwide (23).

The overall age standardized cancer incidence rate is almost 25% higher in men than in women, with rates of 205 and 165 per 100,000 respectively (23). Head and neck cancers vary from one geographic region to another constituting from 5-50% of all cancers (6). In Europe and America, they account 5–8 % of total body cancers (7). In black American, head and neck cancers occur at younger ages than Caucasians (24). The report from sub-Saharan Africa from 18,099 cases in 2008, the top six primary sites was lip, oral cavity, nasopharynx, oropharynx and hypo pharynx, and larynx (10). Male was affected more than female from this result (24, 25).

In addition to infectious disease, cancer is also an emerging public health problem in Africa (4). The incidence is increasing rapidly due to adoption of western life style and dietary practices (7). Both new cases and number of deaths is high in this continent (26). For many reasons, cancers in Africa are diagnosed at late stages. Study shows that about 95% of cases present at late and end-stage of the disease (27). Delayed diagnosis of these patients are due to low level of awareness of population and health workers, culture and constraints on access to specialized care and absent in these countries (28).

Ethiopia is one of the east African countries with an estimated population of 106,255,051 as of January 3, 2018, based on the latest United Nations estimates (18). Ethiopia is also one of the countries where the proportion of cancer burden outweighs the control programs. It is among the leading cause of morbidity and mortality (26). It is estimated that the annual incidence of cancer is around 60,960 cases and the annual mortality is over 44,000 (21).

There was one study done at TASH on patterns of cancer from 1998 to 2010. A total of 13,451 patients are recorded as cancer cases over this study period and 12,671 of them were analyzed. The study showed, the prevalence of cancer is more common in females (72.8%) than males (27.2 %) and study showed only 10% of patients did come to the center in early stage I and II (21).

TASH is the only oncology center with radiotherapy and chemotherapy services, it has the power to represent cancer statics in the country referred from other health care centers or those who came for care by themselves. So this report can be considered strong evidence in this regard. It however, did not included cancer statics from pediatric oncology and hematology departments which limit completeness to represent inclusive cancer pattern in the country.

The head and neck cancers should be treated in multidisciplinary approach. Before deciding the choice of treatment, the primary site of the tumor, extension of the disease, the intent of treatment and aim of organ preservation should be considered. The AJCC stage I and II is treated with single modality such as radiotherapy or surgery with similar outcome (29). The advanced stages (stage III and IV) are treated with multimodality (29). Targeted therapies are being used for squamous cell carcinoma of head and neck cancer (30). There is different chemotherapy regimen but the most commonly used are platinum based (31). Combination of chemotherapy into treatment of loco regionally advanced HNC has been shown to be useful for organ preservation for larynx and hypo pharyngeal cancer (32–34) and to improve survival in unrespectable HNC patients treated with concurrent chemo radiation (CRT) (35, 36). Surgery is the primary treatment method for some head and neck cancers. Postoperative radiotherapy (RT) with or without chemotherapy for high-risk patients may improve loco regional control and survival (35, 36)

CHAPTER THREE: OBJECTIVES

3.1 General objective

- To assess clinicopathology and treatment patterns of head and neck cancers at Tikur Anbessa Specialized Hospital, Radiotherapy Center.

3.2 Specific objectives:

- To describe the distribution of head and neck cancer in sex, age, and region.
- To determine the clinical stages of head and neck cancers at diagnosis
- To assess the primary sites and histopathological types of head and neck cancers among patients treated in TASH.
- To identify risk factors of head and neck cancers.
- To describe the patterns of treatment delivered to head and neck cancers.

CHAPTER FOUR: METHODOLOGY

4.1 Study area:

The study area was AAU, Tikur Anbessa Hospital, oncology department, which is found in Addis Ababa city administration, Addis Ababa, Ethiopia. The department was established in 1990 G.C and has OPD, 18 beds for inpatient, day care chemotherapy, and radiotherapy facility. It has two cobalt-60 External beam radiotherapy machines and one brachytherapy machine which are in use. Linear accelerator machine is installed and CT scan simulation is being used in this center.

Black Lion Hospital, Addis Ababa, houses Ethiopia's only cancer referral centre

Figure 4.1: Study area (Black lion hospital, Addis Ababa, houses of Ethiopia's only cancer referral center)

4.2 Study design

An institution based cross sectional study design was used.

4.3 sources of data

Data was collected from patient charts and log books.

4.4 Source population

Source population were all cancer cases treated at TASH, Radiotherapy Center from January, 2014 to December, 2017 (4years)

4.5 Study population

Histopathologically confirmed cases of head and neck cancer treated at TASH, Radiotherapy Center from January, 2014 to December, 2017

4.6 Inclusion criteria

Histopathologically confirmed head and neck cancer cases registered TASH radiotherapy center from January, 2014 to December, 2017 and with complete demographic data.

4.7 Exclusion criteria:

1. Diagnosis not confirmed by histopathologically
2. Incomplete charts (if no age, sex, region, residency, card number)
3. Thyroid and parathyroid cancers
4. Cancers of two or more primary sites

4.8. Variables

4.8.1 Dependent variable

- Clinical stage of cancers at diagnosis (Both TNM and Group stage).
- Primary sites of head and neck cancers
- Histopathological types of head and neck cancers
- Histological grade
- Treatment pattern (chemotherapy, radiotherapy, surgery or their combinations)

4.8.2 Independent variable

- Age of patient at diagnosis
- Sex of patient
- Place of residency
- Risk factors (drinking alcohol and smoking cigarette)
- Presence of Co-morbid illness (HIV/AIDS, DM, hypertension)
- Performance status (ECOG 0-IV)

4.9 Sample size determination and sampling procedure

4.9.1 Sample size determination

The sample size required for this study was determined by using single population proportion formula considering the following assumptions.

$$n = \frac{(Z\alpha/2)^2 P(1-P)}{d^2}$$

When:

n = minimum sample size required for the study

Z= standard normal distribution with confidence interval of 95%, Z=1.96

d = Absolute precision or tolerable margin of error (d=0.05)

P= is the anticipated population proportion

Since there was no enough similar study conducted previously in Ethiopia, the prevalence of head and neck cancer patients was considered as 50% which will give the maximum sample size. Therefore, 50% was used to anticipate the proportion of the population of cancer patients who experience head and neck cancer

Therefore, the sample size required for the study was calculated as follow

$$n = \frac{0.5(1-0.5)1.96^2}{(0.05)^2} = 384$$

The calculated sample size became 384. However, 10% of the calculated sample size was added for contingency that might happen due lost charts or incomplete reports and finally got a sample size of 422.

4.9.2 Sampling procedure

Patient chart numbers and names registered from January 2014 to December 2017 were identified from log books. Head and neck cancers were identified from this list and collected from chart room. The eligible charts were selected for data source after all charts reviewed.

As the total number of eligible chart was larger than the required sample size, simple random sampling technique was used to select patient chart included in the study. For patients who took radiotherapy, treatment sheet was identified and additional data was collected from it.

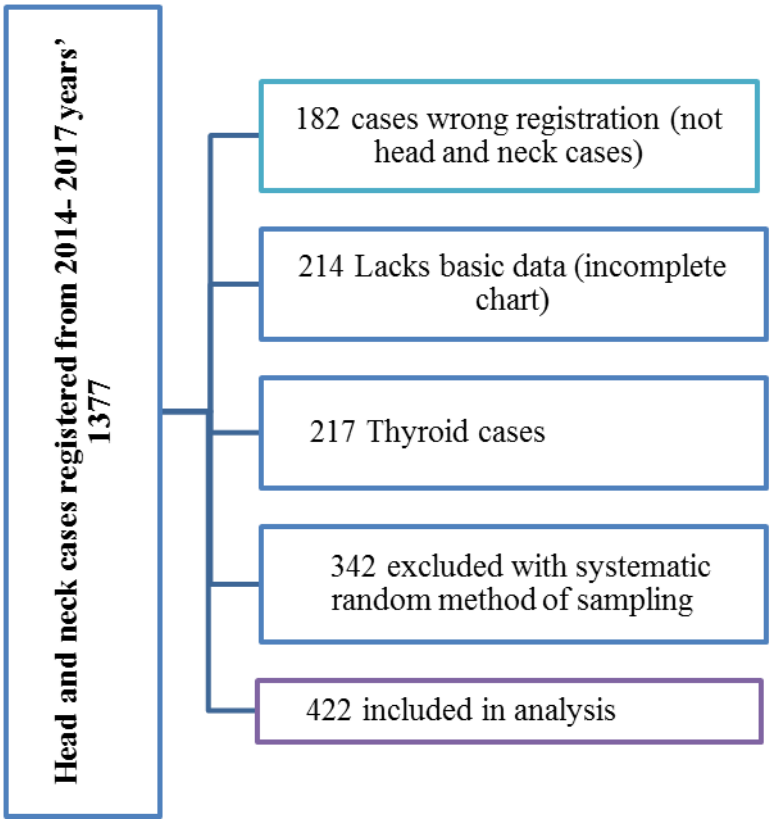

Figure 4.2 sample procedure

4.10 Data collection tool and procedure

Training was given on the purpose of the study, data extraction techniques for data collectors, chart finders and others who were involved in the data collection team. The collecting team consisted of two chart finders from chart room; two oncology residents and one supervisor.

Pretesting of the data extraction format was given by the principal investigator prior to the actual study on 10% of the head and neck patient's chart which was not included in the study. Appropriate modifications were made based on the pre-test result. Patient chart numbers and names was identified from log books and collected from the chart room. Review checklist filled was collected in daily basis and checked for completeness by the principal investigator and supervisors closely. The supervisor ensured that each form is filled correctly, and data entry as planned by the data clerk and principal investigator.

4.11 Data processing and Analysis

Data was coded, cleaned and entered into SPSS version 21 for analysis. Basic descriptive analyses like frequency, proportion mean and median was done. Chi-square test was done for test of association using level of significance set at 5%.

4.12 Ethical Consideration

An ethical clearance for the proposed study was obtained from the research ethical committee of school of public health, Addis Ababa University. Consent from medical director and cancer treatment center focal person of Black Lion Hospital was obtained. Confidentiality of the information was maintained throughout the study by excluding names as identification in the data extraction form and the data was used only for the purpose of the proposed study. In addition, health care professionals from the cancer treatment center extract the data from medical records respecting the confidentiality.

4.13 Dissemination of Result

This thesis was submitted to oncology department, Addis Ababa University College of Health Science**.** The findings will be presented at different seminars and conference. It may be sent for possible publication in peer-reviewed national and international medical journals. In addition, it will be presented to SPH cancer research groups and FMOH NCDs department through presentation and hard copy.

4.14 Operational definitions

Head and neck cancers (HNC): cancers arising in head and neck region including pharynx, nasal cavity, sinuses, lips, mouth, salivary glands, throat, and larynx.

Clinical stage: staging with physical examination and imaging like CT scan, ultrasound, endoscopy, MRI, X-ray.

Histopathology: refers to microscopic study of tissue from biopsy or surgical specimen.

ECOG Performance Status: it is scale used to assess how patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis and is developed by Eastern Cooperative Oncology Group.

Histology grade: is a description of a tumor based on how abnormal cancer cell and tissue look under a microscope and how quickly the cancer cells are likely to grow and spread.

TNM stage: T describes size of the tumor and spread to nearby tissue, N describes spread of cancer to nearby lymph nodes, M explains the distant spread to other parts of the body

Group stage: this explains the combined score of T, N & M stages

Treatment patterns: treatment types given including surgery, radiotherapy, chemotherapy or combination of two or more of these treatment options.

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CHAPTER FIVE: RESULTS

5.1 Socio demographic characteristics of the patients

Head and neck cancers cases those fulfill criteria of inclusion included in this analysis. From those registered from January, 2014 to December, 2017 four hundred twenty-two cases analyzed. This study showed 276 (65.4%) were males, the rest 146 (34.6%) were females with male to female ratio (M: F) of 1.9:1. The mean age of these patients was 42.8±18.8SD. Majority of them were from rural areas 230 (54.5%) and 185 (43.83%) of them were from urban. The region, occupation, marital status, smoking, alcohol consumption profiles are displayed below (Table 5.1.1).

Table 5.1.1: Demographic characteristics of head and neck cancer among patients treated at Tikur Anbessa Specialized Hospital, Radiotherapy Center (n = 422)

Variables	**Frequency**	**Percent**
Sex		
Male	276	65.4
Female	146	34.6
Region		
Oromia	124	29.4
Addis Ababa	114	27
SNNPR	71	16.8
Amhara	62	14.68
Tigray	21	4.97
Somali	18	4.26
Others	12	2.84
Residence		
Urban	185	43.8
Rural	230	54.5
Not documented	7	1.65
Marital status		
Married	238	56.39

Single	75	17.77
Divorced	25	5.9
Widowed	21	4.97
Not documented	63	14.92
Job		
Farmer	149	35.3
Merchant	59	13.98
Employee	83	19.66
Student	38	9
Not documented	93	22.03
Drinking Alcohol		
Yes	124	29.38
No	221	52.36
Not documented	77	18.24
Cigar ate smoking		
Yes	70	16.58
No	222	52.58
Not documented	130	30.8

Clinical staging determines options of treatment and prognosis of patients. The following tables show the TNM staging and group staging according to AJCC staging of 7th edition.

Table 5.1.2: Clinical factors of head and neck cancer among patients treated at Tikur Anbessa Specialized Hospital (n = 422)

Variables	Frequency	Percent
TNM (T) stage of disease		
T1	18	4.26
T2	36	8.53
T3	70	16.58
T4	155	36.72
Tx	110	26.1
Not documented	33	7.81
TNM (N) stage of disease		
N0	47	11.13
N1	81	19.19
N2	82	19.43
N3	48	11.37
Nx	131	31
Not documented	33	7.81
TNM (M) stage of disease		
M0	310	73.45
M1	37	8.76
Mx	47	11.13
Not staged	28	6.63

The clinical TNM staging showed majority of the cases had locally advanced (stage III to IVb) accounting 241 (77.49%) at diagnosis. The detail is put in the tables below (5.2.1 and 5.1.3)
Group staging depends on proper TNM staging. In this result group staging couldn't be made in 112 (26.54%) cases due to lack of proper T, N or M records.

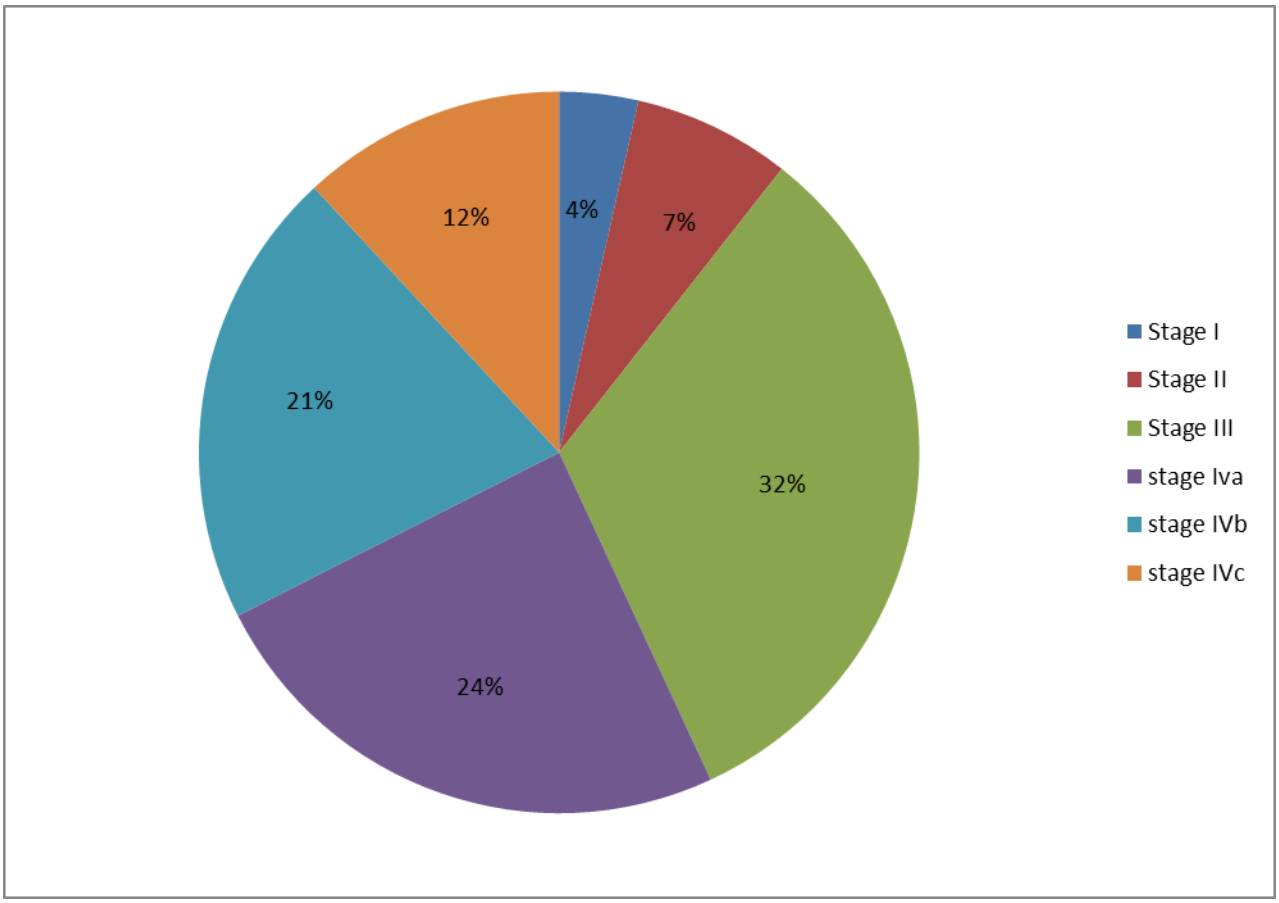

Figure 5.1.1: Clinical group staging of head and neck cancers treated at TASH (n=422)
The primary sites and sub-sites of head and neck cancers showed that the most common site was pharynx 156 (37%). From these, nasopharynx accounted 132 (31.3%) and oropharynx and hypo pharynx comprised the rest 24 (5.7%). The next common sites were oral cavity 59 (14%), larynx 52 (12.32%), cervical lymph nodes 37 (8.76%), face and scalp 37 (8.76%), the nasal and paranasal cancers 31 (7.34%), major and minor salivary gland 30 (7.1%), cancer of unknown primary 20 (4.7%).

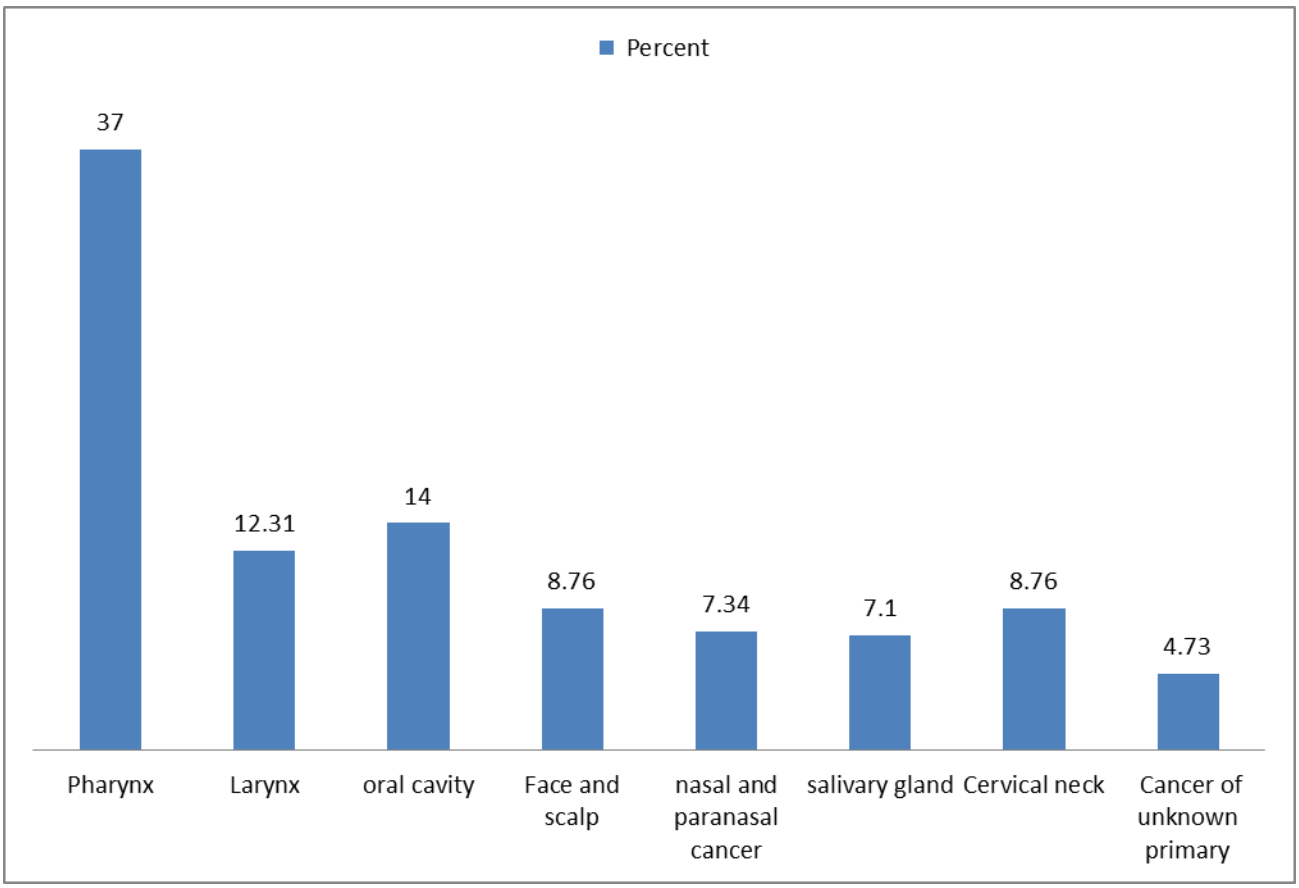

Figure 5.1.2 Primary sites of head and neck cancers treated at TASH (n=422)

The histopathology analysis showed squamous cell carcinoma was the most common histological type of head and neck cancer accounting 330 (78.2%).

Lymphoma, adenocarcinoma, sarcoma, mucoepidermoid carcinoma were 42 (10%), 28 (6.63%), 8 (1.9), and 7 (1.65%) respectively.

The rest like clear cell carcinoma, adenocystic, blastoma and others accounted less than 2 percent.

Table 5.1.3: Histological types of head and neck cancers among patients treated at TASH (n=422)

Histological Type	Number	Percent
SCC	330	78.2
Adenocarcinoma	28	6.6
Lymphoma	42	10
Adeno cystic carcinoma	6	1.4
Blastoma	1	0.2
Sarcoma	8	1.9
Others (clear cell,maltoma)	7	1.7

The histological grades of carcinomas showed that 119 (28.19%) were well differentiated, 99 (27.65%) undifferentiated, 44 (12.29%) were poorly differentiated, 27 (7.54%) are moderately differentiated, and for 69 (19.27%) carcinomas grade was not mentioned.

Table 5.1.4: Histological grades of head and neck cancers treated at TASH (n=358)

Histological grade	Number	Percent
Well differentiated	119	28.19
Moderately differentiated	27	7.54
Poorly differentiated	44	12.29
Undifferentiated	99	27.65
Not mentioned	69	19.27

The performance status result showed majority of the cases 282 (66.8%) had ECOG I.

The rest cases 82 (19.4%), 40 (9.5%), 11 (2%), 2 (0.5%) were ECOG II, 0, III, IV respectively

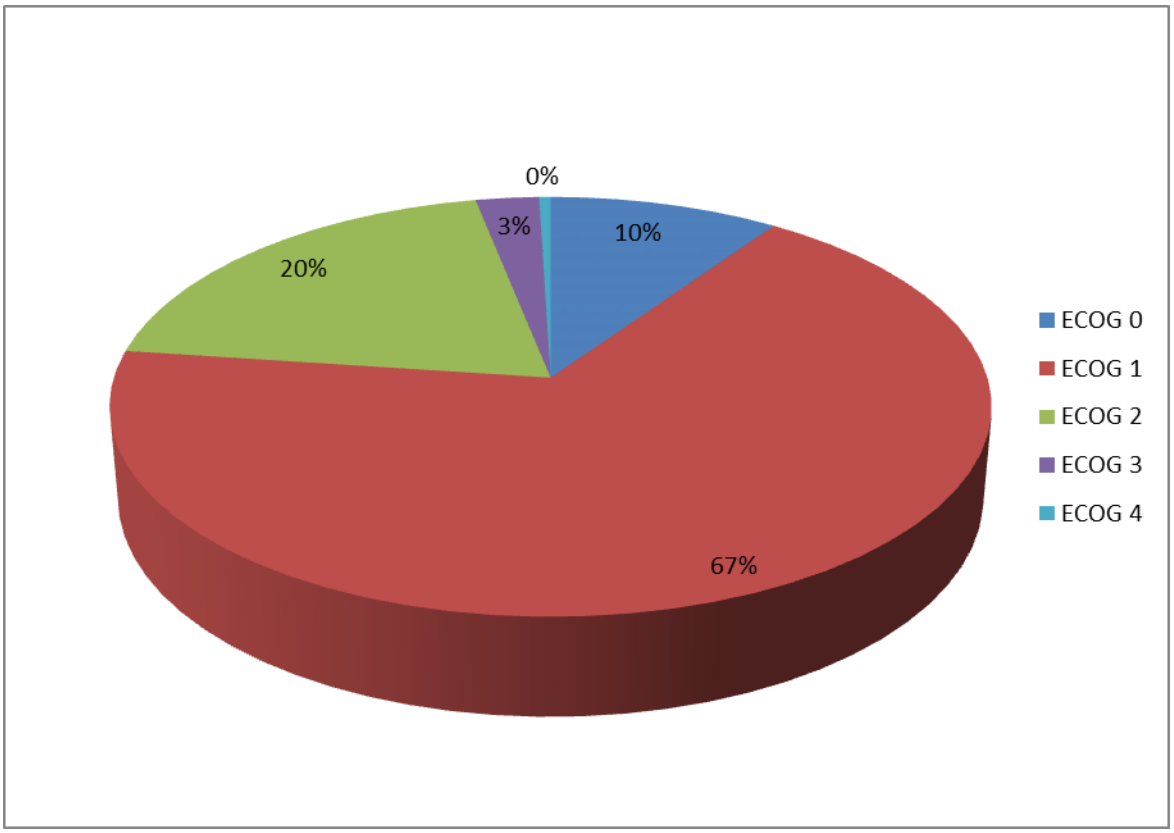

Figure 5.1.3: Functional status of the patients at start of treatment (n=422)

Table 5.1.5 Co morbidity associated with head and neck cancers treated at TASH (n=422)

Co morbidities	**Number**	**Percent**
HIV	26	6.16
DM	16	3.8
HTN	69	16.35
Cardiac disease	6	1.42
Others (bronchial asthma, COPD)	13	3.1
No Co Morbidity	292	69.12

The basic investigations like LFT, RFT were done for 398 (94.31%) of them and in normal range in 383 (96.23%) of the cases. Complete blood count was done for 411 (97.39%) and white blood cell count and platelet were in normal range for 392 (95.37%) of the cases. Hemoglobin level

before start of treatment (chemotherapy or radiotherapy) was 10gm/dl and above in 315 (76.64%) of patients. It was below 10gm/dl in 86 (20.92%) cases and not documented in 13 (3.08%). Base line chest x-ray (CXR) and abdominal pelvic ultrasound was done for 396 (93.83%) and 378 (89.57%) of the cases respectively. Head and neck CT scan was done for 278 (65.87%) and head and neck MRI was done for 43 (10.18%) of cases.

5.2 Patterns of treatment delivered for head and neck cancer patients at TASH, Radiotherapy Center.

The patterns of treatment delivered for head and neck cancers in TASH were induction chemotherapy followed by radiotherapy 86 (20.37%), surgery alone 46 (10.9%), surgery followed by chemotherapy 18 (4.26%), concurrent chemo radiotherapy 29 (6.87%), surgery followed by radiotherapy 30 (7.1%), chemotherapy alone 83 (19.66%), radiotherapy alone 31 (7.34%). The rest patients 92 (21.8%) didn't take any form of treatment. These patients disappeared for unknown reason after the diagnosis settled and treatment plan made.

Table 5.2.1 Patterns of treatment given for head and neck cancers in TASH (n=422)

Patterns of treatment	Frequency	Percent
Induction CT then RT	86	20.37
Surgery followed by induction CT	18	4.26
CCRT	29	6.87
Surgery then RT	30	7.1
CT alone	83	19.66
RT alone	31	7.34
Surgery alone	46	10.9
Other treatment(analgesics)	7	1.66
No any form of treatment given	92	21.8
Total	422	100.0

Chemotherapy: The chemotherapy regimens given were cisplatin and 5-Fu 120 (28.43%), cisplatin and paclitaxel 50 (11.84%), other regimens 58 (13.74%). These chemotherapy regimens were given as induction, adjuvant, concurrent and palliation of metastatic disease.

The number of cycles of chemotherapy ranges from 1 to greater than 6. Majority of the cases 112 (26.54%) took 6 cycles of chemotherapy, 50 (11.8%) took 1-3 cycles, 17 (4%) took greater than 6 cycles. For rest 49 (11.61%) cases the number of cycles given was not mentioned.

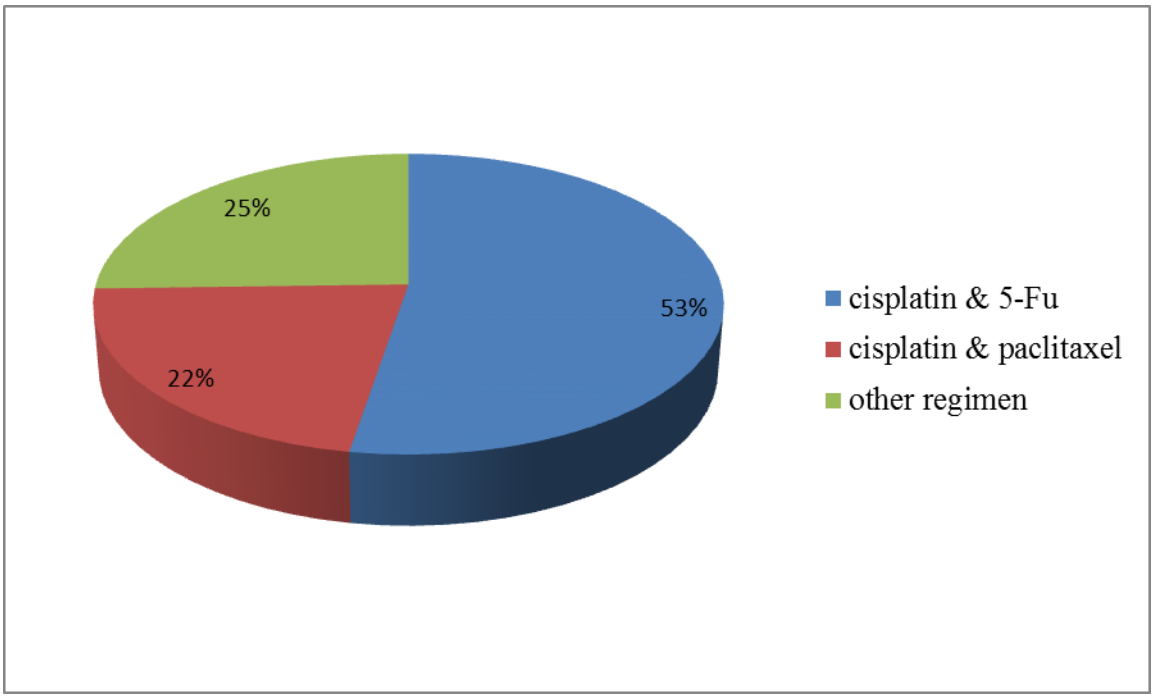

Figure 5.2.1 Induction chemotherapy regimen given for head and neck cancers at TASH (n=288)

The dose of radiotherapy delivered varied based on the intent of treatment. Majority of the case took curative dose of radiotherapy greater than 54Gy in 97 (22.98%), 43 (10.18%) took 20-30Gy, 16 (3.79%) took 31-54Gy and 10 (2.36%) took less than 20Gy. For the rest ten cases dose of radiation delivered was not mentioned.

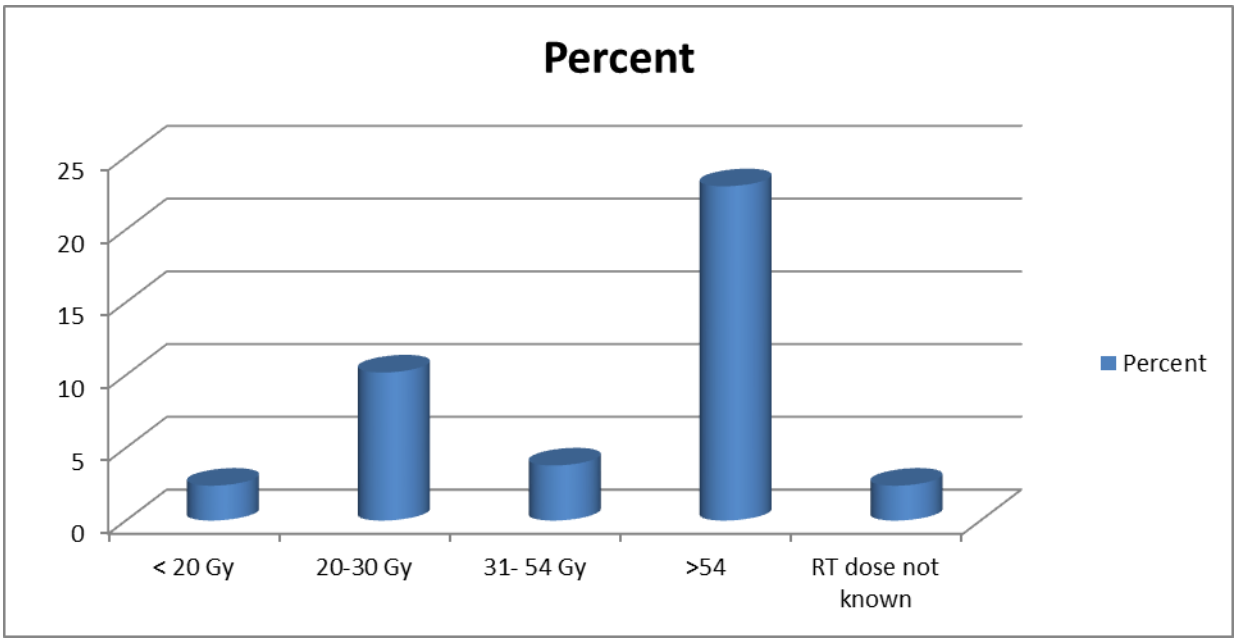

Figure 5.2.2 Doses of radiotherapy delivered for head and neck cancers at TASH (n=182)

Duration between diagnosis and initiation of treatment: the duration between the diagnosis and start of treatment varied from few days to many months.

This study showed 109 (25.82%) started their treatment chemotherapy, radiotherapy or combination of these within 3 months of diagnosis. The others 82 (19.43%), 71 (16.8%) began their treatment between 3 to 6 months and 6 to 12 months respectively.

Sixty-one cases (14.45%) of patients waited for greater than 12 months to take their first dose of chemotherapy or radiotherapy. The duration of initiation of radiotherapy was longer than for chemotherapy.

5.3 Association Analyses

5.3.1 Factors associated with clinical stages

This study indicated that cigarette smoking and alcohol consumption were significantly associated with clinical stages (P= 0.01, CI: -0.94: -0.10) and (P= 0.01, CI: 0.16: 1.00) respectively. Patients with history of cigarette smoking and alcohol consumption had locally advanced disease.

The primary site of head and neck cancer was significantly affecting clinical stages showing that pharynx was the most likely to be in the higher clinical stage.

Age, residence, sex, co morbid illness and histological type were not significantly associated with clinical stage.

5.3.2 Factors associated with primary sites head and neck cancer

Age was found to be significantly associated with primary sites of head and neck cancer. Patients with nasopharyngeal cancer were younger at diagnosis ($Chi\ square\ (x^2) = 28.53, p = 0.00$). Likewise the distributions of clinical stages in the region were significantly different. Pharyngeal cancers presented at advanced stage ($Chi\ square\ (x^2) = 58.7, p = 0.045$). In the current study using co morbid illness, alcohol and smoking cigarettes were not significantly associated with primary sites of the disease.

5.4.3 Factors associated with histology types of head and neck cancer

This study showed both alcohol consumption and primary sites were associated with histology type. Those who used to drink alcohol and tumors arising from pharynx were squamous type with value of $(x^2 = 29.6, p\ 0.003), (x^2 = 381.9,\ p = 0.00)$ respectively. Cigarette smoking was found to be statistically insignificant factor for affecting histology type.

CHAPTER SIX: DISCUSSIONS

Head and neck cancers are among the most common malignancies worldwide with half a million new case per year (5). Their incidence is also increasing in developing countries too (4). From this study we saw head and neck cancers are among common malignancies treated at Tikur Anbessa Specialized Hospital.

The mean age of these patients was 42.8±18.8SD which is similar with other results done in Africa on head and neck cancers (37, 38). There is no clear reason why head and neck cancers in Africa including Ethiopia occur in younger age than Caucasians. It could be variation in behavioral practices, socio-economic status or genetics and race. The other reason could be that the majority of Ethiopian population (49.69%) age distribution ranges from 15 to 54 years (39).

The ratio of male to female in this study was (1.9:1). The study done by Lilly-Tariah et al of male to female ratio of head and neck cancer was (2.3:1) (37) which approaches to our result. Another study done in Nigeria from 1968 to 2008 on head and neck cancers indicated that male to female ratio was (1: 1.02).

The proportion of smokers and alcohol consumers were 14.6% and 29.4% respectively in this study and evidences show that males use cigarette and alcohol more than females (39). This could be the reason that head and neck cancers were more common in our result. Alcohol and tobacco are among the proved carcinogens for head and neck cancers (39, and 40). In our study the amount of alcohol and cigarette smoking in pack-year were not documented. This made difficult to put these as risk factor of head and neck cancers. The amount of alcohol consumption and the smoke pack year helps to assess risk for these cancers.

Majority of head and neck cancer patients in our study came from rural (54.5%) and were farmers (35.3%). Studies on head and neck cancers report that these cancers are more common in low socio-economic status (37, 38) which supports our result. The clinical staging of our result showed majority of our patients had locally advanced disease at diagnosis (77.49%).

This result was similar with other developing countries of head and neck cancer regarding stage at presentation (38). From Ghana Donkor and Boating also found similar late stages of presentation of head and neck cancers (41). The reason why our patients present at locally advanced stage is not clear. The possible causes of late presentation could be lack of health facilities in far rural areas, lack of awareness on cancer, the behavior of consulting local healers than modern medicine, the lengthy process of referral to cancer center from other health facilities, financial reasons and cultural beliefs in the society. For this reason, prospective study is needed to justify this issue. The other result regarding clinical stage is, significant number of cases 112 (26.54%) didn't have proper staging. The proportion of advanced diseases could be larger than the mentioned result.

The first three common primary sites of head and neck cancers in this study were pharynx (37%), oral cavity (14%), and larynx (12.30%). This result was similar with Nigerian study in which nasopharyngeal carcinoma was the most common (42). The other study from Yemen on head and neck primary site showed oral cavity was the most common (43). The anatomical differences of the primary cancers could be due to geographic variation, risk factor exposures and socio-cultural practice in different regions.

From this study, we found that carcinoma was the most common histology type (84.80%) of which squamous cell carcinoma accounted (78.20%). Similarly, carcinoma is the most common worldwide (44-46). However, Amusa et al found that lymphoma was the most common histology in Nigeria (47)

Differentiation: The histology grade of these cancers showed 119 (33.24%) were well differentiated and 99 (27.65%) were undifferentiated. For 56 (15.64%) the grade was not mentioned. This could be due to lack of pathology services like immunohistochemistry in our country.

In addition to history and physical examination, pretreatment workup is very important to make diagnosis, stage and treat head and neck cancers (48). Basic investigations like CBC, LFT, LFT was done for majority of them. Majority (>90%) cases had chest-x-ray and abdominopelvic ultrasound.

Head and neck CT scan and MRI was done only for 65.87% and 10.58% of head and neck cases. This showed lack of adequate imaging in the center which could affect proper diagnosis, staging and treatment.

Studies showed that surgery, radiotherapy and chemotherapy are treatment modalities for head and neck cancers (49). The order of treatment and preference of these modalities depends on stage, primary site and histology types. For the advanced stages combined modality treatment is preferred (50). Radiotherapy improves local control for locally advanced head and neck cancers (49, 50). In this study the proportion of patients who received concurrent chemo radiotherapy were small 69 (6.9%). This again indicated that only few cases took concurrent chemo radiotherapy despite the majority of them were at locally advanced stages. So the outcome of these patients might be affected though we didn't assess treatment outcome in this study. The reason for only small proportion of patients took concurrent chemo radiotherapy could be scarcity of radiotherapy centers in Ethiopia. Due to lack of adequate cancer centers, majority of patients waited for 3 months and above to start radiotherapy or chemotherapy.

Only 97(22.98%) of cases took curative dose of radiotherapy greater than 54Gy. The rest received palliative radiotherapy. Palliative radiotherapy was given for emergency conditions like bleeding, air way obstruction, dysphagia and cord compression.

The majority of chemotherapy regimen used for induction was doublet with cisplatin and 5-fu or cisplatin with paclitaxel. But the regimens recommended for head and neck cancers especially nasopharyngeal carcinoma is triplet drugs with docetaxel, cisplatin and 5-Fu (50). This could also affect the response rate for head and neck cancer treatment which was not assessed in this particular study.

Associations: This study showed clinical stages of head and neck cancer is significantly associated with cigarette smoking and alcohol consumption. Patients with history of smoking cigarette and alcohol consumption had advanced disease. But the amount of alcohol consumption and cigarette was not mentioned on the charts of our patients. High alcohol consumption and cigarette smoking are the two known risks and also affects clinical stages (7).

This result also indicated that there are significant associations between clinical stage and primary sites. It showed that pharynx is the most likely to be in the higher clinical stage. The primary site of head and neck cancer is significantly associated with age, but no significant association between co morbid illnesses (DM, HTN, and RVI).

CHAPTER SEVEN:

7.1 Strength of the Study

This is the first study to analysis clinic pathology of head and neck cancers and their treatment patterns in Ethiopia

This study is done at Tikur Anbessa Specialized Hospital Radiotherapy Center which is the only radiotherapy center for our country and may represent the society of the country at large.

The sample size is not small.

7. 2 Limitations of the study

- ✓ There was a challenge during on data collection due to poor documentation and there could be individual variation on filling patient profiles on the charts.
- ✓ The cases registered on log books and patient charts were discordant for some patients.
- ✓ Incomplete data on stages, smoking history, alcohol history, histopathology grades, and treatment delivered.
- ✓ This is retrospective study which is less powerful than prospective study

7.3 CONCLUSIONS AND RECOMMENDATIONS

This study showed that head and neck cancers at this hospital presented at advanced stage of the disease. Only small proportion of patients took concurrent chemo radiotherapy and there was long duration between diagnosis initiations of treatments. These all might have reduced the curability of the disease. Majority of cases were males and relatively young at diagnosis. The awareness of the society on head and neck cancers should be increased as it helps to diagnose at early stages of the disease. There were problems on documentation of patient files. It is highly recommended to appropriately document patient files as it helps to improve disease staging and to deliver proper treatment. Detail registration of patient data also encourages researchers to do further studies. The government and other stakeholders should expand cancer centers to reduce the treatment delay and increase quality of care of cancers. Head and neck cancers are diversified cancers in their primary sites, histologies and treatment options. For this reason, more detailed and specific studies are recommended on these cancers.

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ANNEXES

ANNEX I. DATA EXTRACTION TOOLS

Serial.No	Variable	Category
1	MRN	----------
2	Sex of patient	1. Male 2. Female
3	Age (in years)	
4	Region	1. Oromia 2. Amhara 3. Somalia 4. Tigray 5. SNNPR 6. Gambela 7. BenishangulGumuz 8. Addis Abeba 9. Harar 10. Diredawa 11. Afar
5	Residence	1. Urban 2. Rural 3. Not documented
8	Primary site of disease (write	

	specific subsite)	
9	Investigation modalities used for diagnosis and staging (write laboratory and imaging)	
9	T stage of disease	1. T1 2. T2 3. T3 4. T4 5. Tx
10	N stage	1. N0 2. N1 3. N2 4. N3 5. Nx
11	M	1. M0 2. M1 3. Mx
12	Group staging	1. Stage I 2. Stage II 3. Stage III 4. Stage IV

		5. Unknown
13	Histological grades of cancer	1. Well differentiated 2. Moderately differentiated 3. Poorly differentiated 4. Undifferentiated 5. Not mentioned
14	Histological types cancers	1. Squamous cell cancer 2. Adeno carcinoma 3. Lymphoma 4. Adenocystic carcinoma 5. Blastoma 6. Mucoepidermoid 7. Others (mention)
15	Comorbid illness	1. RVI 2. DM 3. HTN 4. Other disease(mention) 5. None

16	Functional status	1. ECOG 0 2. ECOG I 3. ECOG II 4. ECOG III 5. ECOG IV
17	Alcohol use	1. Yes 2. no 3. not documented
19	Cigarette smoking	1. yes 2. no 3. not documented
20	Treatment delivered	1. chemotherapy 2. radiotherapy 3. surgery 4. combination of these(mention) 5. no treatment given
21.	Chemotherapy regimen given (drug names)	
22	Number of chemotherapy cycles given	
23	Total dose of	

	radiotherapy delivered (in Gy)	
24	Duration between diagnosis and initiation of treatment (in months)	

ANNEX-II PATIENT INFORMATION SHEET (ENGLISH VERSION)

This patient information collection sheet is intended to assess clinicopathology and treatment patterns at Tikur Anbessa Hospital, Radiotherapy Center, Ethiopia. The study will be conducted through reviewing secondary data. The study will give some evidence and information for governmental and non -governmental organizations which work in the area of non-communicable disease specifically on HNCs at national, regional and district level by providing basic information on the mentioned title. Information which is necessary for the study will be taken from medical outpatient log book and treatment sheets. As the study will be conducted through review of medical records alone, the individual patients will not be subjected to any harm as far as the confidentiality is kept. To preserve the confidentiality, residents working in cancer treatment center of Tikur Anbessa specialized hospital will extract the data from the medical records. Moreover, no personal identifiers will be used on data collection form.

Date of review----------

Day---------- month---------- year----------

Name of reviewer---------- Signature----------

Time started---------- Time ended----------

Total number of records reviewed----------

Result; (A) complete (B) incomplete (C) excluded

Action taken for incomplete data----------

Name of supervisor----------

Signature----------

Principal investigator address: 0912496003

ANNEX – III ASSURANCE OF INVESTIGATOR

I, the undersigned Clinical Oncology Resident agree to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research and publications office of the Addis Ababa University.

Name of the Investigator: Dr. AdugnaFekadu (4th Year Clinical Oncology Resident)

Signature_____ Date_____/_____/_____

APPROVAL OF THE PRIMARY ADVISOR

Advisor Name: Dr. WondimagegnewuTigeneh (MD, MPH, Consultant Oncologist)

Signature_____ Date _____/_____/_____