THYROID CANCER AMONG GOITROUS PATIENTS IN SOUTHWESTERN ETHIOPIA: A HOSPITAL BASED HISTOPATHOLOGIC REVIEW

BY: FILAGOT DEBEBE (MD)

THESIS SUBMITTED TO POST GRADUATE PROGRAMME, COLLEGE OF PUBLIC HEALTH AND MEDICAL SCIENCES IN PARTIAL FULFILLMENT OF THE REQUIREMENT OF CERTEFICATE OF GENERAL SURGERY SPECIALITY.

NOV, 2015

Jimma, Ethiopia

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BY: FILAGOT DEBEBE (MD)

Advisors : Dr Mesele Bezabhi (MD,Pathologist,Epidemiologist)

Dr Alaje Tekie (MD, Surgeon)

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Abstract

Introduction-Thyroid cancer is the most common endocrine cancer (accounts for 95% of all endocrine cancers) and its incidence has continuously and sharply increased in the last six decades all over the world. There are four histologic types of thyroid cancer: papillary, follicular, medullary and anaplastic. The distribution of the histologic type varies from country to country based on radiation exposure status and rate of goiter. Goiter is a pathological condition with epidemic dimensions in some areas because of several factors like geographical, nutritional, and genetic factors which has been linked to a higher risk of thyroid cancer, especially for the follicular histotype. Goiter is a major concern in many parts of the world, including Ethiopia and therefore taking a prevention measures may reduce the rate of progression to cancer.

Objective- The aim of this study was to describe the histopathologic pattern of thyroid cancer among goiterous patients in Jimma University spcialized Hospital, Southwestern Ethiopia, over a five years period, from 1st Sep. 2010 to 31st Aug. 2015 G.C.

Methods- retrospective study was carried out at Jimma University specialized hospital, department of pathology, over a period of five years from 1st Sep. 2010 to 31stAug.2015 G.C. All patients who proved to have cytohistopathologic features of thyroid cancer (cancerous goiter) was included in the study. All data including age, sex, fine needle aspiration cytology, type of goiter (nodularity by clinical diagnosis), and final histopathology report for non-diagnostic or suspicious malignancy results by FNA reports were documented on standard form.

Result –seventy five (75) patients with thyroid cancer were included in this study; out of this 29 (38.7%) were found to be papillary and 27 (36%) were follicular cancer followed by anaplastic and medullary ca with a rate of 20 %(15) and 2.67 %(2) respectively. Generally a female preponderance has been noted among the cancerous patients, with a female-to-male ratio of 1.6:1. From all thyroid cancer diagnosed patients 3 (2.7%) patients were found to be toxic by biochemical tests and clinically 39 (52%) of the patients appeared with discrete (solitary/dominant) nodular goiters.

Conclusion and recommendation.- Unlike the belief that thyroid cancer is a rare disease, it was seen in 75 (8.3%) of patients with goiter. Papillary ca is the most frequent cancer seen in this series. Toxicity is a negligible or a very rare event in thyroid malignancies. Clinical evaluation of goiters should be thorough, and use all means esp. histopathology study of the specimen to arrive at definitive diagnosis, as thyroid ca is not uncommon.

Acknowledgment

It is my sincere gratitude to acknowledge the invaluable contribution and support of my supervisors, Dr Messele Bezabih and Dr Alaje Tekie. Their guidance, advice, repeated corrections and revisions helped shape this study the way it is now.

I also appreciate the contributions from the Department of Surgery (JU) and the JU Research, Graduate studies and Community Based Education Coordinating office.

Many thanks go to Dr Dawit Teare,Yonas Yilma, Dr Hiwot Amare and Mr. Anteneh Kebede for their dedicated and timeless help.

Finally, thank you, too many colleagues and pathology department staffs that helped me collect to data.

Table of contents

ABBREVIATIONS

CA	CARCINOMA
FNAC	FINE NEEDLE ASPIRATION
TC	THYROID CANCER
IDD	IODINE DEFICIENCY DISORDERS
HIV	HUMAN IMMUNDEFENSENCY VIRUS
NCG	NODULAR COLLOID GOITRE
MNG	MULTINODULAR GOITER
UK	UNITED KINGDOM
USA	UNITED STATES OF AMERICA
WHO	WORLD HEALTH ORGANISATION
JU	JIMMA UNIVERSITY
JUSH	JIMMA UNIVERSITY SPECIALIZED HOSPITAL
BLH	BLACK LION HOSPITAL
APC	ANNUAL PERCENTAGE CHANGE
G.C.	GRIGORIAN CALENDER
Sep.	SEPTEMBER
Aug.	AUGEST

List of tables and Figures

Chapter One: - Introduction

1.1 Background

Thyroid cancer (TC), a malignancy with a rising incidence and a wide spectrum of clinical behavior and therapeutic responsiveness, is the most common endocrine malignancy(2,3,5).Goitrous thyroid is believed to be a precursor to the development of TC ,It may present either as a solitary nodule or as a dominant nodule in a multinodular goiter(7,8,9).

It has been estimated that the worldwide incidence of goiter in the world's population is about 4%–7% (Gaitan et al., 1991; Muller et al., 2001)(8) and the incidence of malignancy in goitrous thyroid is approximately 10 %(7,8).The World Health Organization estimated that at least 1.6 billion people are at risk of iodine deficiency disorders. Among these, 655 million are affected by goiter, 27% of whom are in Southeast Asia, followed by the Western Pacific countries (4,6,8)

Iodine deficiency is the major cause but goitrogens are incriminated as well [4,6,9].The reported incidence of both benign and malignant lesions in surgically treated thyroid swellings varies widely from one geographical area to another [8,9].Of the world's 191 countries, iodine deficiency disorders (IDD) was a public health problem in 130, and data was insufficient to categorize another 41. The prevalence of iodine deficiency disorders (IDDs) in most African countries ranges from mild in low-lying areas to severe in highlands (4).

The reported prevalence of goiter in Ethiopia varies between 18% and 30%. The prevalence of goiter in different geographic areas of Ethiopia is also high. A cross-sectional survey in Sekotta district showed the overall prevalence of goiter to be 22.8%. Similarly a study carried out to detect the prevalence of goiter in school children and household members has shown the prevalence of goiter to be 30.6% and 18.7 % respectively (9).

Epidemiological studies have shown that, in some areas rich in iodine, 6–7% of the adult population have a thyroid nodule that can be detected by clinical examination, and 5% of the clinically identified nodules are malignant (Hegedus, 2004). Since thyroid nodules are highly prevalent, it is a common clinical task to predict the risk of malignancy of a given nodule (6,8).

There are four main types of thyroid cancers (based on pathology observed under a microscope): papillary, follicular, medullary, and anaplastic lesions. Differentiated thyroid cancer (DTC, including papillary and follicular) accounts for 90% of all the thyroid malignancies diagnosed, with papillary thyroid cancer accounting for 80% of all thyroid cancers (2-11). Follicular thyroid carcinoma and anaplastic thyroid carcinoma have been reported to occur more frequently in endemic goiter regions than in goiter-free areas. This suggests that highly aggressive TCs are more prevalent in countries with endemic goiter (3,4,8,11). Exposure to ionizing radiation, changing levels of iodine nutrition and increased pathologic diagnosis of clinically unimportant thyroid neoplasia have all been proposed as explanations for a worldwide rise in the incidence of thyroid carcinoma over the past six decades(3,5,7,8). The objective of this study is to describe the histopathologic pattern of Thyroid cancer among goiterous patients in Jimma University specialized Hospital, Southwestern Ethiopia.

1.2 Statement of the problem

Cancer caused over 8 million deaths worldwide in 2013 and has moved from the third cause of death in 1990 to the second leading cause behind cardiovascular diseases in 2013(1). And it has poses a major threat to public health problem worldwide, and incidence rates have increased in more countries since 1990.The trend is particular to that developing countries with health systems that are ill equipped to deal with complex & expensive cancer treatment(1)

Thyroid cancer is the most common endocrine malignancy with estimated 44,670 new cases (1-1.5%) diagnosed in USA in 2010 and it accounts for approximately 10 % of malignancies diagnosed in person aged between 15-29 years(2,3).Currently, thyroid cancer is the fifth most common cancer in women and in Italy; it is the second most frequent cancer in women below 45 years of age(3).Since the last five decades its incidence has been increasing at alarming rate all over the world except Africa where detection is possibly insufficient (2,3,5)

By 2019, thyroid cancer (papillary type) will double in incidence and become the third most common cancer in women of all age at a cost of $ 18 to $ 21 billion dollars in USA(5). The increased incidence is indicated by annual percent change (APC) that in USA was 2.4% from 1980 to 1997 and 6.6 % from 1997 to 2009 (both genders). At variance ,with most tumors (including breast ca, colorectal ca, lung ca & prostate ca whose mortality has decreased in the last two decades, thyroid cancer mortality is not decreased but rather slightly increased (+0.8 % APC ,primary in males)(3). Other studies showed a 50.2% increment of mortality from 1990 (24,000 (95% uncertainly interval: 18,000-29,000) to 2010 (36,000: 26,000-43200)). Globally it ranks 92nd and in south Asia 94th disease in terms of contribution of death (4).

Goiter is believed to be a precursor to the development of thyroid cancer especially in iodine deficient (endemic goiter) areas unlike to iodine replete regions where radiation exposure to the head and neck region claimed to be the major factor(2,3,5). These environmental factors are known to influence the thyroid ca histologic distribution. Papillary cancers tend to be the commonest type in developed countries, follicular & anaplastic cancers are the commonest histological types in sub-Saharan Africa where goiter is endemic due to iodine deficiency. This suggests that highly aggressive types are more prevalent in countries with endemic goiter(6,9,10) thus, prevention measures in iodine deficient areas may alleviate the progressive risk to cancer.

It has been estimated that the worldwide prevalence of goitre among the general population is about 4%–7%, and the incidence of malignancy in goitrous thyroid is approximately 10% (8,9,10). It may present either as a solitary nodule or as a dominant nodule in a multinodular goiter, although its prevalence in the two conditions remain uncertain(3). But different studies showed that multinodular goiter has a tendency to progress to cancer in 8-15% of cases & it is the commonest indication for thyroidectomy in endemic areas where the health facility is poor (7,10) and also patients normally present with advanced disease or after progression to cancer. In Ethiopia the estimated prevalence of endemic goiter is between 18% & 30% (9). A cross-sectional survey in Sekotta district showed the overall prevalence of goiter to be 22.8%(9). Similary a study carried out to detect the prevalance of goiter in school children and household members has shown the prevalence of goiter to be 30.6% and 18.7 % respectively (9).

Though, the high prevalence of thyroid nodules ,affecting upto 30-50% of the population in late adulthood ,constitutes an enormous reservoir of potential cancer lesion and most thyroid ca (over 80%) are smaller than 2 cm at the time of diagnosis is consistent with the need of more sensitive diagnostic tools(i.e., scintigraphy, cytology and histology) (3),it is impractical in our set up due to the immense resources & high cost of follow up. Besides, knowing that pre-operative evaluation for thyroid cancer by means of fine needle aspiration biopsy is difficult in multinodular goiter owing to the presence of multiple nodules and thyroid cancer is frequently an unexpected post operative finding (3,18)

Despite problems in obtaining valid epidemiological data, the following trends are obvious in the majority of countries (2,3,5)

- The overall incidence of thyroid cancer has increased in both sexes during the past decades, but the latest available data do not indicate whether this trend will further continue.
- Even though increament is mainly due to papillary thyroid cancer,follicular ca also becoming high in endemic goiter areas
- Especially in countries where preexisting iodine deficiency has been supplemented,the above-mentioned current trend can be observed: not only the relative contribution, but also the incidence of papillary carcinoma has increased markedly.

- Moreover, thyroid cancer mortality, despite earlier diagnosis and better management has not decreased but is rather increasing
- Since women are affected earlier and predominantly than men it will therefore suffer greater price in terms of economic and social impacts.

1.3 Significance of the study

Although the global incidence of thyroid cancer is increasing significantly, the lack of attention paid to the problem is being highlighted by different studies. The limited fund for researches & the non advanced diagnostic tools which stayed for the last three decades are evidences. Furthermore, there is a scarcity of epidemiologic data to show the clinical & economic burden of the cancer, especially in Africa where the health facility recourse is limited to cope up with the overall increasing incidence of cancer in general and thyroid cancer in particular. Recent studies suggest that thyroid cancer is increasingly a major health issue, particularly for women (6). According to the studies thyroid cancer should receive a higher priority in funding so that more research on etiology, prevention, innovation of more sensitive diagnostic tools improved treatment might take place. But in our context the major focus should be to have a base line data on the issue, pave the way for further studies and take preventing measures on the anticipated etiologic factors.

Therefore, the study on pattern of thyroid cancer will be help full in multidirectional ways:

- In future, to be a base line study for further researches to be done, because the study area is a university teaching hospital where a vast number of researchers are available to be interested on the topic.
- To create at least a coarse understanding on the clinical & economic burden of the cancer & overall surgical management & follow up of patients with thyroid swellings.
- To help in outlining prevention plans by drawing the attention of public health bodies because of wide catchment area of the hospital & representing a big segment of the country (south western Ethiopia) for its cytology/histology services.
- To be an objective data for the hospital management bodies to improve the diagnostic tools in the pathology unit, radiology units & surgical department including the operation theater.
- Overall, it contributes a concrete figure to assimilate the worldwide concern of TC for the academicians & students in the university teaching hospital.

Chapter Two: - Literature review

Globally, Thyroid cancer is the most common malignancy of the endocrine system (95%) and is responsible for more deaths than any other endocrine cancers combined. Clinically recognized thyroid cancer represents approximately 0.5–1% of all human malignancies. Recent data suggests there were more than 213,000 new cases worldwide. In both sexes it ranges with less than 0.5% behind the 20 most frequent causes of cancer deaths. In geographical areas of low iodine intake and in areas exposed to nuclear disasters the incidence of thyroid cancer is higher. Yet considerable difference exists in the incidence; in M:F ratio; in the histologic subtypes for some countries and for individual regions ,ethnic population and age group within the same country(1-5).

In most countries data for the annual incidence of TC per 100,000 individuals ranges from 0.5-10 cases per 100,000(from 0.9 to 2.6 in men and from 2.00 to 5.9 in females). Countries of which the incidence rate exceeds 3.00 in males or 4.00 in females (i.e approximately twice the average) are as follows: Iceland (6.2 in males and 8.3 in females), the Jewish population in Israel, Colombia, few regions in USA, Canada, Japan, Norway and Finland. In USA, exceptionally high incidence rates were seen in Hawaii particularly in Chinese (8.1 in males and 11.3 in females) and Filipino (6.6 in males and 24.2 in females) populations. And worldwide the lowest rate was reported in Barshi, India, where the rate was 0.2 per 100,000 for females. Likewise TC is a among the commonest malignancies in some countries (e.g. In Italy and Saudi Arabia, thyroid cancer was the 2nd most common malignancy after breast cancer, while it was reported as the 3rd most common in the United Arab Emirates and 4th most common cancer in Filipino women, in USA also it was the 6th most common ca in women in 2010).For reasons that are unclear TC is 2 to 3 fold more common in females than males. Although the peak incidence of TC diagnosis is 45-49 years in women and 65-69 years in males, it does affect young people. It accounts for about 10% of malignancy diagnosed in person aged 15-29 years. In adults ,the incidence of TC in general tends to increase with age. Concerning the population of histologic subtypes of TC, remarkable difference exists between different countries with follicular dominance in iodine deficient areas and papillary predominance in iodine sufficient areas but radiation exposure risk areas. According to WHO classification which does not recognize Hurtle cell ca as a separate type, most literatures reports ranges of 40-80% for papillary , 10-40 % for follicular, 1-10% for medullary and 2-14 % for anaplastic types.(1-4,7,8)

In USA, the overall the incidence was 8.7/100,000 person-year (12.7 in females and 4.5 in males) according to SEERS data base,1992-2007, of total 59,611 cases, from which 50,453(84.6%) were papillary, 5,824(9.8%) follicular,1241(2.1%) were medullary ,559 cases anaplastic (0.94%) and 1,535 unspecified(3). The data from National Cancer data base (53,856 cases during the period of 1988-95) revealed 79% papillary, 13%follicular, 2.9%hurtle, 3.6%medullary & 1.7% undifferentiated or Anaplastic. Also the age at diagnosis has been reported as 30-39 years for papillary, 30-49 years for follicular and over 70 years for Anaplastic type. Based on the incidence data from 1992 through 2009, the APC projections showed the incidence of papillary thyroid cancer in females will be 37.0/100,000 women-years, surpassing ovarian (10.8) and colorectal ca (30.4) in incidence by 2019 to become the 3rd most common cancer in women of all age after breast (75.0) and lung cancer (42.1). At that time, TC also become the 2nd most common cancer in women under age 45 with an incidence (19.3/100,000 years) second only to breast cancer. In the United States, which is an iodine sufficient environment, 4 to 7% of the adult population has a palpable thyroid nodule [2,3.5]. However, only 1 of 20 clinically identified nodules is malignant(3,5).

In Europe where the incidence of TC reported as 2-3 per 100,000 populations in UK and the mean age of patients TC in general at diagnosis ranged from 44 to 58 years. According to data analyzed from 1,017 patients whose primary therapy took place in department of nuclear medicine (University Hospital Essen, Germany) from 1978 to 1998, the peak age was the 3rd to the 5th decade for papillary, the 4th to the 5th decade for follicular, and the 5th decade for Hurtle cell. This study of endemic goiter region where papillary micro adenomas are excluded revealed that 61% papillary,24% follicular,7% hurtle cell,5% medullary and 3% anaplastic. Another Swedish autopsy study of 500 complete thyroid gland tissue showed a prevalence of 8.6 % carcinomas from which 74% were papillary, 16% follicular & 9% medullary with M:F ratio of 1:3 in papillary and 1:2 in follicular ca(3-5)

Asian literatures revealed wide range of results according to the geographic variation, developmental status of the specific country and environmental precursor conditions for the cancer. In Japan ,where the age adjusted rates of TC in the year 1985 were 1.1/100,000 for male and 3.1/100,000 for women (high in Hiroshima and Nagasaki),the male to female ratio was 1:6 in papillary & 1:2 in medullary and anaplastic. The histological type (Ezaki et al.) showed papillary in 78.4%, follicular in 17.2%, medullary in 1.4%, anaplastic in 2.7% . Chinese study also showed a rate of 13.18% (222/1685) TC

with a papillary predominance (89.64%) followed by follicular (13/222), medulary (6/222), lymphoma (3/222) & undifferentiated (1/222) with a M:F ratio of 1:6.66. From patients with TC 60.81 % were in range of 31-50 years (M:F ratio of 1:8.00) with lowest frequency for aged below 20 years. This study also described rate of TC as 27.78 & 13.18% from nodular & solitary goiters respectively(23).

In Pakistan where TC is claimed to be responsible for 1.2% cases of all malignant tumors, the overall incidence of malignancy was reported to be 11% with a M:F ratio of 1:7 on a study of incidence of TC in MNG, Isra university. The rate of malignancy in MNG has been found to vary from 7.5% to 13%(There are no statically significant differences between incidence of TC in patients with a solitary nodule & those with MNG). Papillary ca constitutes the majority (57% to 89%) of all thyroid malignancy followed by follicular (12.5%) and anaplastic (12.5%).This study reported the mean age at diagnosis as 52 years (from 42-68 years). Another retrospective study which was done in Karachi, Pakistan to evaluate the histologic spectrum of surgically treated thyroid disease shown over all malignancy rate of 14.35 %, Whereas in USA it was 5.8%, in Libya 9.7% and in South Africa 5.4% (3,5,8,).Papillary carcinoma was found to have higher rate (77.89%) than follicular carcinoma (14.74%),medullary (4.21%) & anaplastic(3.16%)(18-21).

A high incidence of malignancy in multinodulargoitres has been reported from sub-Saharan Africa with rates varying from 13 to 20%(13-15].Recent reports on thyroid malignancies(ca) in Africa abound and differentiated TCs are noted to occur more commonly than the other forms of TC. The documented TC in the African continent are as follows (papillary: 6.7-72.1%,follicular: 4.9-68% ,anaplastic and medullary :2.6-13.8%). For differentiated TC, there is a changing trend toward the more occurrence of papillary ca compared to follicular ca(12,14).A study at the University Teaching Hospital , Lusaka during the period January 1981 to December 1990 showed doubling of the incidence of adenoma and carcinoma when compared to the study done at the Central Hospital, Kitwe in the late sixtie which showed 76.6% papillary, 15.6% follicular,6.3% anaplastic, and 1.5% medullary carcinoma (10,13). In the Lusaka study Follicular cancer was the most common malignancy 68% followed by Papillary 14% Anaplastic carcinoma 9% and Undifferentiated carcinoma 9%(10,13).In this study the incidence of TC was 10.8% with a M:F ratio of 1:2.25.

Another study in lusaka (Desai et al) showed that overall incidence malignancies 16.4%.Follicular carcinoma was commonest 42%, followed by Anaplastic 30% and Papillary carcinoma 10 %(13)

Studies from Nigeria and in Leo/Burkina Faso have reported follicular carcinoma as the commonest thyroid cancer.In Nigeria study showed overall incidence of malignancies 11% and commonest was follicular carcinoma. The study revealed as Follicular 68%, papillary 14%, anaplastic 9% & undifferentiated 14%. The latter retrospective study on 253 patients who underwent operation for thyroid diseases during a 7-year period from 2001 to 2008, Follicular cancer was found in 15 cases, and anaplastic carcinoma was found in 1case [6.].Recent review of trends of differentiated CA from some west Africa tertiary centres, the results in the 1980s, there was a predominance of follicular ca over papillary ca (35.8% vs 27.3%); However , in years from 1990 to 2004 ,there was a documented predominance of papillary over follicular ca(14,15)

In Ethiopia, according to a study done in Addis Ababa University (BLH), 21% (164/780) were neoplastic from which TC accounted for 8.2% (64) and adenoma 12.8% (100). Nodular colloid goitre (NCG) was found in 600 (76.9%) cases. The morphological subdivision of the 64 thyroid carcinomas showed 76.6% of papillary, 15.6% follicular, 6.3% anaplastic, and 1.5% medullary carcinom [10]. Studies have also proved colloid goiter to be a result of iodine deficiency and iodine supplement was found to decrease the prevalence of goiter and the subsequent risk of cancer in endemic goiter areas(9).

Chapter Three: - Objectives

3.1 General Objectives

- ✓ To describe the histopathological pattern of thyroid cancer among goitrous patients in Jimma University Specialized Hospital, Southwestern Ethiopia, over a 5 years period , from 1st Sep.2010 to 31st Aug., 2015 G.C.

3.2 Specific objectives

- ✓ To determine the proportion of histological types of thyroid cancer.
- ✓ To describe the distribution of thyroid cancer histological types with respect to age and sex.
- ✓ To illustrate thyroid cancer in relation to the clinical nodularity of the goiter and biochemical toxicity of thyroid ca.
- ✓ To depict the trend of thyroid cancer by its histological types,over the five years.

Chapter Four: - Methodology

4.1Study area

The study was conducted at Jimma University (JU).JU is one of the higher institutions in Ethiopia. It is located in Jimma town which is about 335 kms southwest of Addis Ababa. And the main campus is situated to the east of the town at about 3kms from the down town, Jimma municipality

Jimma university teaching hospital which is part of JU, established in 1930, is located in the main campus. It is a referral hospital which provides services for approximately 9000 in patient and 80,000 outpatient attendances a year with a very wide catchment population of about 15 million people in southwest Ethiopia. Thus, is attended by patients of different socio demographic characteristics.

The services given by the hospital includes clinical, pathology & laboratory, pharmacy & other services. The main diagnostic modalities in the hospital are routine laboratory, radiology & pathologic services. The department of Pathology, having two pathologists, eight residents & four supporting staffs, is actively involved in biopsy services and FNA cytology. Despite the presence of several health institutions in the area, it is the only hospital that provides FNAC and histopathological services to this segment of the country.

4.2 Study period

Retrospective desk was reviewed of the histopathology register in pathology department within a period of one month (Aug. 1-31, 2015 G.C)

4.3 Study design

A cross-sectional retrospective study

4.4 Population

4.4.1 Source population

All cases of thyroid swellings (goiters) whose sample materials were taken for cytohistopathologic analysis (diagnosis) in pathology department, JUSH, from 1st Sep.2010 to 31st Aug, 2015 G.C.

4.4.2 Study population

All cases of goiter that were proven to have cytohistopathologic features of malignant neoplasm of the thyroid gland in pathology department ,JUSH ,over five years period ,from 1st Sep.2010 to 31st Aug. 2015 G.C.

4.5 Exclusion criteria

All cases with incomplete documentation as well as, diagnoses beyond the stated period of time was excluded. Patients with inconclusive FNA examination which hasn't been confirmed by histopathology biopsy result. The results of recurrent presentation and repeated samples for unconfirmed results were excluded, so that every subject was counted once only.

4.6 Variables

4.6.1 Independent variables

- ✓ Age
- ✓ Sex
- ✓ Duration of the goiter

4.6.2 Dependent variables

- ✓ Histological diagnosis
- ✓ Clinical diagnosis

4.7 Data collection

4.7.1 Data collection instruments & process

A structured instrument was developed by English language to extract relevant information based on the study from logbook in pathology department. The logbook is regularly registered and it contains the date, patients name, sex, age and the biopsy/cytology serial number and result, relevant clinical information. The questionnaire was also prepared in a way to retrieve the relevant information for the study like; demography (sex,age) of the patient, clinical &cytohistopathologic diagnosis ,duration of the goiter and others. Therefore, the datum was collected by isolating the histlologic diagnoses of thyroid malignacies in relative to the benign ones by avoiding duplications.

4.7.2 Data collectors

The data was collected by data collectors. For the quality and welfare of the data, the data clerks in the pathology department was negotiated with attractive incentives to do the data collection. Three data clerks was selected based on their motivation and oriented on the objectives of the study and the information needed by the principal investigator. The questionnaires was given to them and planned to complete the data collection based on the study period. The principal investigator provides mentoring for the collectors in a daily basis.

4.8 Data quality control

The collected data was first checked for completeness and edited every day after data collection by the primary investigator.

4.9 Data analysis, interpretation and dissemination

Data was refined by using prepared format and then data was cleared, entered and analyzed for descriptive statics using SPSS version 20 software package and the results was presented by using tables and figures. Frequency distributions by percentage, mean and median and statistical associations by using chi-square test was made for selected variables.

4.10Ethical considerations

Ethical clearance was obtained from Jimma University ethical committee and a supporting letter to be delivered to pathology department was requested from surgery department for retrieval of individual records of cytohistopathologic result.

All the information obtained from the records was anonymous.

Honesty was maintained during data collection, analysis and interpretation

4.11 Limitations

Shortage of research done on the topic (especially in the local area)

The data might not be representative of the whole population as the histopathogy result is only for ones who came to this hospital

In addition, regarding to Goiterous patients who visited the surgical outpatient department even though the routine trend is to send all of them for pathologic analysis, few patients may escape from the trend practice.

4.12 Definition of terms and operational definitions

4.12.2 Definition of terms

- ✓ Malignant lesion: A lesion that invades and destroys the tissue in which it originates and can spread to other sites in the body via blood steam and lymphatic system.
- ✓ Goiter- Any enlargement of thyroid gland (normal thyroid gland is impalpable)
- ✓ Thyroid nodule: descrete swelling in one lobe with no palpable abnormality elsewhere (solitary nodule) or with evidence of abnormality elsewhere in the gland(dominant nodule).
- ✓ Multinodular goiter: multiple nodules arises from the thyroid gland (>2)
- ✓ Biopsy: Removal and examination of a small piece of living tissue from any organ or part of the body.
- ✓ Fine needle aspiration cytology (FNAC):Type of diagnostic approach through which needle is inserted to the diseased organ and tissue aspirated inorder to examine through microscope.
- ✓ Pathology : The study of disease process with the aim of understanding their nature and cause.
- ✓ Diagnosis: The skill of distinguishing one disease from the other by using symptom , signs and tests.

4.12.2 Operational definition

- ✓ Incidence –The Number of thyroid cancer patients newly diagnosed over the past five years (1st Sep.2010-31st Aug.2015 G.C)
- ✓ Pattern : the distribution of the specimens in terms of person and time.
- ✓ Histopathology: the study refers to both FNAC and tissue biopsy analysis
- ✓ Nodularity of goiter: the type of goiter diagnosed and documented by the physician as either thyroid nodule (solitary& dominant) or multinodular.

Chapter Five: - Result

A total of 906 thyroid gland specimens were submitted for cyto-histopathologic analysis in 5 years period from 2010-2015 G.C. in JUSH at department of Pathology. The information was obtained from histocytological reports and other information sources like clinical reports. The overall number of cases of thyroid cancer registered was 75 (8.3%). Table 1 shows the distribution and proportion of thyroid cancer with respect to the total goiter sample analysis in the 5 years period.

Table 1-Distribution and proportion of thyroid cancer diagnosis in respect to total goiter specimens over 5 years, Sept.2010-Aug.2015 at JUSH.

Year	Collected & analyzed Goiter specimens	Thyroid cancer diagnosed specimens	% of thyroid cancer
2003 E.C (2010-2011 G.C)	250	11	4.4%
2004 E.C (2011-2012 G.C)	138	12	8.7%
2005 E.C (2012-2013 G.C)	189	17	9.0%
2006 E.C (2013-2014 G.C)	133	14	10.5%
2007 E.C (2014-2015 G.C)	196	21	10.71%
Total	906	75	8.3%

Among the 75 individuals registered 46(61.3%) were females and 29(38.7%) males, with a male-to-female ratio of 1:1.6. The mean age was 42.4 (range 17-80) years for females and ---- years for males. Majorities (65.3%) of the patients were below 50 years old and females accounted for 62.2% of the cases below the mentioned age level. Figure 1 and Table 2 shows the distribution of thyroid ca in relation to age and sex at diagnosis.

Figure 1: A bar showing the distribution of thyroid ca in relation to age and sex over 5 years, Sept.2010-Aug.2015 at JUSH.

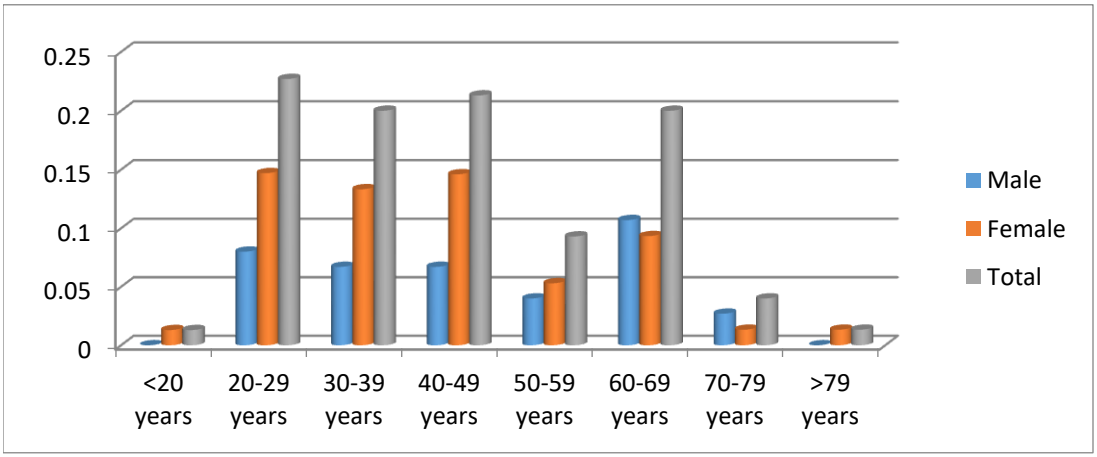


Table 2- Distribution of thyroid cancer in relation to age and sex over 5 years, Sept.2010-Aug.2015 at JUSH.

		Sex		Total(%)
		Male (%)	Female (%)	
Age in year	10-19	0(0.0%)	1(1.3%)	1(1.3%)
	20-29	6(8.0%)	11(14.7%)	17(22.7%)
	30-39	5(6.7%)	10(13.3%)	15(20.0%)
	40-49	5(6.7%)	11(14.6%)	16(21.3%)
	50-59	3(4.0%)	4(5.3%)	7(9.3%)
	60-69	8(10.7%)	7(9.3%)	15(20.0%)
	70-79	2(2.7%)	1(1.3%)	3(4.0%)
	80-89	0(0.0%)	1(1.3%)	1(1.3%)
Total		29(38.7%)	46(61.3%)	75(100.0%)

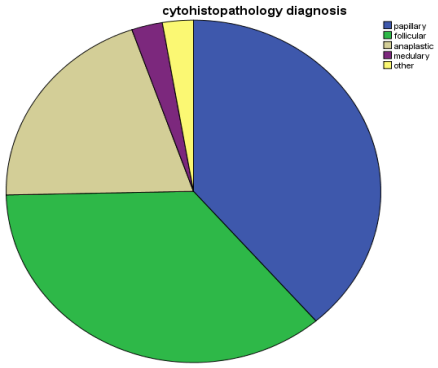
Concerning the clinical diagnosis upon presentation, about 51.9 % of the patients with goiter were diagnosed to have discrete nodular goiter (solitary and dominant nodules) clinically. In addition toxicity is confirmed in 2(2.7%) follicular ca patients by thyroid function tests. Table 3 shows the distribution of thyroid ca histologic types in relation to clinical nodularity of the goiter.

Table 3- The distribution of thyroid cancer histological types in relation to the clinical nodularity of the goiter over 5 years, Sept.2010-Aug.2015 at JUSH.

		Clinical diagnosis			Total(%)
		MNG(%)	Diffuse goiter(%)	Discrete(%)	
Cyto-histopathology diagnosis	papillary	10(13.3%)	3(3.9%)	16(21.3%)	29(38.6%)
	Follicular	11(14.7%)	2(2.7%)	14(18.7%)	27(36.0%)
	Anaplastic	6(8.0%)	2(2.7%)	7(9.3%)	15(20.0%)
	Medullary	1(1.3%)	0(0.0%)	1(1.3%)	2(2.7%)
	Other	1(1.3%)	0(0.0%)	1(1.3%)	2(2.7%)
Total		29(38.7%)	7(9.3%)	39(51.9%)	75(100%)

About the histology of thyroid cancer, 29(38.7%) were papillary ca, 27(36.0) follicular ca, 15(20.0%) anaplastic ca and 2(2.6%) medullary ca. As the study showed papillary carcinoma was the commonest. Figure 2 shows the distribution of the histological types.

Figure 2-Pie chart showing histological types of thyroid cancer over 5 years, Sept.2010-Aug.2015 at JUSH



Thyroid ca predominates in females; the ratio of female to male ratio for papillary, follicular & medullary was 1.9:1, 2.85:1 and 2:0 respectively. Exceptionally the anaplastic type mainly occurred in males with a female to male ratio of 1:2.75.Table 4 and figure 3 shows the distribution of histological types of thyroid cancer by sex.

Table 4-Distribution of thyroid cancer histology by sex over 5 years, Sept.2010-Aug.2015 at JUSH.

		Sex		Total (%)
		Male (%)	Female (%)	
Cyto-histopathology diagnosis	Papillary	10(13.3%)	19(25.4%)	29(38.7%)
	Follicular	7(9.3%)	20(26.7%)	27(36.0%)
	Anaplastic	11(14.7)	4(5.3%)	15(20.0%)
	Medullary	0(0.0%)	2(2.7%)	2(2.7%)
	Other	1(1.3%)	1(1.3%)	2(2.7%)
Total		29(38.7)	46(61.3%)	75(100.0%)

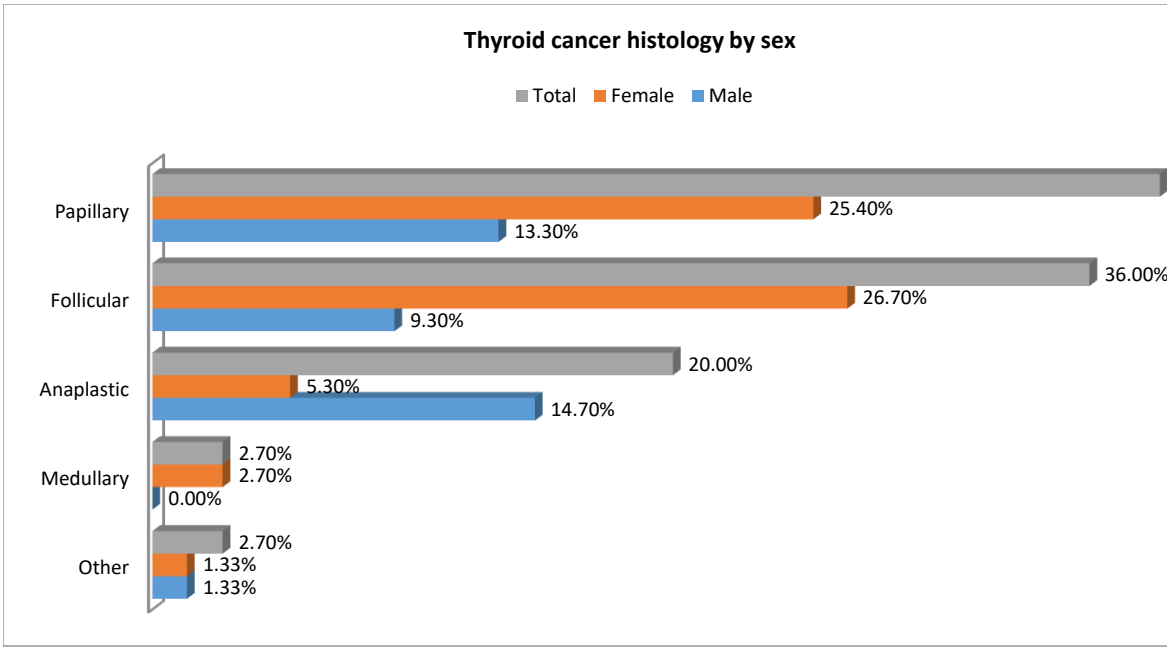


Figure 3- A bar graph showing histology of thyroid cancer in relation to sex over 5 years, Sept.2010-Aug.2015 at JUSH.

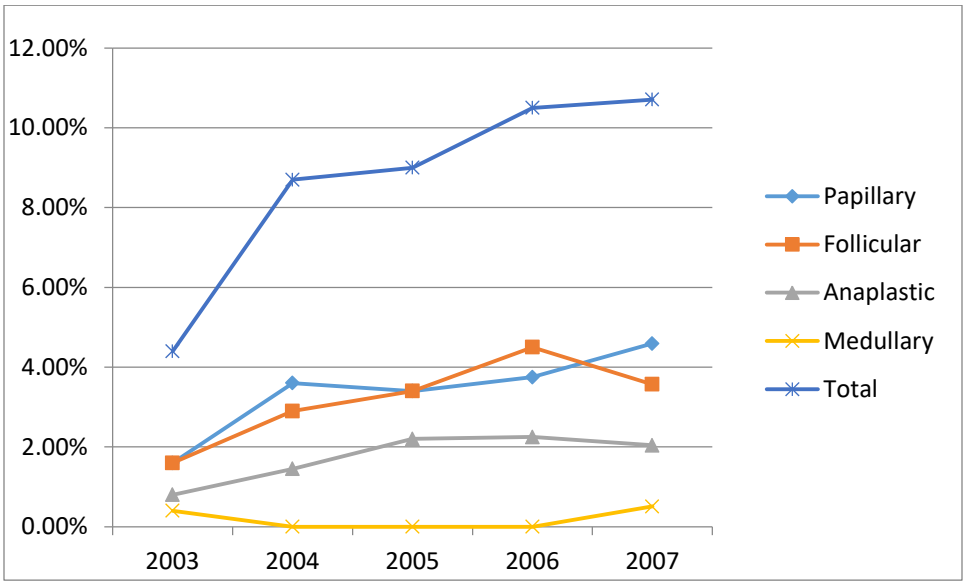
Relating to the age of the patients with the histology, papillary ca occurred relatively in the earlier ages than the other histologic types. The average age of occurrence for papillary is 42.4 years, for follicular 41.3 years, for anaplastic 51 years, for medullary 65 years. Table 5 depicts the distribution of the histology in relation to the age groups of the patients.

Table 5- Distribution of thyroid cancer histology by age over 5 years, Sept.2010-Aug.2015 at JUSH.

		Cyto-histopathology diagnosis					Total (%)
		Papillary (%)	Follicular (%)	Anaplastic (%)	Medullary (%)	Other (%)	
Age in years	10-19	0(0.0%)	1(1.3%)	0(0.0%)	0(0.0%)	0(0.0%)	1(1.3%)
	20-29	7(9.3%)	6(7.9%)	3(4.0%)	0(0.0%)	1(1.3%)	17(22.7%)
	30-39	7(9.3%)	7(9.3%)	1(1.3%)	0(0.0%)	0(0.0%)	15(20.0%)
	40-49	6(7.9%)	6(7.9%)	3(3.9)	0(0.0%)	1(1.3%)	16(21.3%)
	50-59	3(4.0%)	2(2.7%)	1(1.3%)	1(1.3%)	0(0.0%)	7(9.3%)
	60-69	4(5.4%)	5(6.8%)	6(8.1%)	0(0.0%)	0(0.0%)	15(20.3%)
	70-79	1(1.3%)	0(0.0%)	1(1.3%)	1(1.3%)	0(0.0%)	3(4.0%)
	80-89	1(1.3%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	1(1.3%)
Total		29(38.7%)	27(36.0)	15(20.0%)	2(2.6%)	2(2.6%)	75(100%)

As to the trends of the thyroid cancer over the five years, the study revealed an overall increased pattern, and papillary ca showed a persistent increment in rates while the medullary and anaplastic showed a relatively stable pattern. Figure 4 shows the trend of thyroid cancer over the five years.

Figure 4- A graph showing the trend of thyroid cancer over 5 years, Sept.2010-Aug.2015 at JUSH.



Chapter six: - Discussion

Thyroid cancer accounts for approximately the 2% of all cancers diagnosed worldwide and 95% of all endocrine cancers. The global incidence of thyroid cancer has increased by up to five-fold during the past 60 Years . The annual incidence of thyroid cancer varies considerably in different registries and is increasing in some European countries, USA and Canada(13). There are several possible reasons for the increase in thyroid cancer and include ionizing radiation, sex hormones, iodine deficiency and other factors but the findings are inconsistent. Recent data suggest there were more than 213,000 new cases of thyroid cancer worldwide with a crude incidence rate of 3.1/100,000 and a cumulative risk of developing the disease of 0.31. The male to female ratio was approximately 1:3.3, while the crude incidence for men was 1.4/100,000 and that of women was 4.9/100,000(1-5).

Concerning our population, this study obtained information using pathology results of thyroid gland specimens in JUSH, a tertiary teaching hospital, which provides large health coverage for the southwestern segment of the country; 75 new cases (44 males and 33 females) were detected, that means a malignancy rate of 8.3% (75/906) showed. The rate of thyroid cancer in this study population was similar to that estimated for our country and comparable to other worldwide figures. According to a study done in Addis Ababa University (BLH), 21% (164/780) were neoplastic from which TC accounted for 8.2 %(9). Another retrospective study which was done in Karachi, Pakistan to evaluate the histologic spectrum of surgically treated thyroid disease shown over all malignancy rate of 14.35 %, Whereas in USA it was 5.8%, in Libya 9.7% and in South Africa 5.4% (3,5,8,). Literatures showed that thyroid malignancy is common in females than males almost double times, and also this study identified that the problem is more common in females than males (M:F ratio is 1:1.6).

Concerning the distribution of the disease in relation to age, only approximately 1.3% and 5.3 % of the cases occurred in individuals younger than 20 years and older than 70 years respectively. Almost three fourth (64%) of the cases were observed in individuals aged 20-49 years, with a predominance of women (36%) over men (28%). It is interesting to observe that in women it occurred relatively earlier than men (Table 2). This has relevant clinical, prognostic, and social impact. While women generally develop the disease earlier in their lives, when they are professionally active and have long

life expectancy, men develop the disease later, probably after their retirement from work and have short life expectancy and probability of dying from the disease are lower. Although different studies suggested the correlation of advanced age and elevated incidence of thyroid cancer……

Regarding to the histologic types the study revealed that papillary cancer accounted for 38.7% forming the most common histological type followed by follicular (36%) and anaplastic (20%)(Figure 2).The majority (up to 90 %) of thyroid cancers occurring worldwide are differentiated types, this include follicular and papillary cancers. Follicular ca represents an increased portion of thyroid cancers in regions where dietary iodine is low. Recent review of trends of differentiated ca from some west Africa tertiary centers also Nigerian studies compared the results in years before the 1980s, there was a predominance of follicular ca over papillary ca (35.8% vs 27.3%); However , in years from 1990 to 2004 ,there was a documented predominance of papillary over follicular ca(14,15). This scenario may be reflective of the changing iodine status of the continent as a result of widespread iodine supplementation program. In addition, the tendency to develop papillary ca after iodine supplementation for simple goiter and the modified WHO histologic diagnostic criterion may contribute for the predominance of papillary ca in later decades. Although follicular ca is being supervening by papillary type, old studies had showed its predominance in sub-Saharan African iodine deficient areas. Anaplastic cancer ranges from 4% to 21.4 % according to recent studies and its high prevalence rate in some regions is due to with high prevalence of follicular ca. A study by Desai et al showed that follicular cancer was commonest 42.2% followed by anaplastic 30% and papillary(10%).According to a study in BLH the morphological subdivision of thyroid carcinomas showed 76.6% of papillary, 15.6% follicular, 6.3% anaplastic, and 1.5% medullary carcinoma(10). Pakistan study shows Papillary ca constitutes the majority (57% to 89%) of all thyroid malignancy followed by follicular (12.5%) and anaplastic (12.5%). Over all the result of this study was consistent with the current worldwide studies which showed the predominance of papillary carcinoma over the follicular types

This study showed the higher proportion of thyroid cancers diagnosed in patients with clinically solitary nodular goiters than multinodular goiters(52% vs 38.7%). Papillary (55%) and follicular (51%) cancers appeared with more of solitary nodule than MNG(Table 3). One study found that the

frequency of differentiated (papillary and follicular) thyroid cancer was significantly lower in patients with multiple nodules than in patients with single nodules (Christensen et al, 1984), and that male patients were at risk than female patients (Rago et al,2010). However, in this study the relation between gender and type of nodule is not studied. According to Pakistan study,the rate of malignancy in MNG has been found to vary from 7.5% to 13% (There are no statically significant differences between incidence of TC in patients with a solitary nodule & those with MNG).Another study in the same country(Pakistan) revealed that the majority of the patients with thyroid cancer present as multinodular goiter rather than solitary thyroid nodule. Despite this different study results, the teachings on thyroid ca blame discrete swelling a major risk.

The time trends analysis showed a relative increase in incidence of thyroid cancer during the progressive study periods (Figure 4). This trend is showed in numerous international geographic areas, which have contributed to the global increase number of thyroid cancer cases reported in several publications. As mentioned in literatures, in certain geographic areas such increase are greater than 100% and as high as 250% in some cases. It is not clear whether this is a real increase in incidence, as was demonstrated in some areas after nuclear incidents, or it reflects a general improvement in the technological means and expertise employed to detect small thyroid malignancies, which in the past have remained undiscovered.

Chapter Seven- Conclusion and Recommendation

7.1: Conclusion

The study showed that the frequencies of the different histological types were similar to those reported in numerous national and international reports. Women are affected earlier than men and therefore suffer greater personal, economic and social impacts.

Papillary cancer the major histologic type followed by follicular cancer

Toxicity in malignant thyroid swelling (goiter) is negligible or very rare.

Majority of the thyroid malignancies appeared with clinically discrete swellings /nodule goiters

7:2 Recommendations

Clinical evaluation of goiters should be thorough, and use all means esp. histopathology study of the specimen to arrive at definitive diagnosis, as thyroid ca is not uncommon

Documentation system of the hospital should be improved and if possible it is recommended to have a cancer registry for further researches on the area.

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Questionnaire

A structured questionnaire: A study on patterns of thyroid cancer histological types in pathology department, JUSH, Southwestern Ethiopia, from Aug.1-31,2015 G.C

Study no……

Card No,…… Date…….

1. Demographic information

Age. _____

Sex. M. ☐ F. ☐

2. Clinical diagnosis

Nodular Goiter:

If Nodular; To☐ ☐ Simple

Mu☐e Iso☐☐ Domi☐

Diffuse Goiter:

If Diffuse; Toxic ☐ Simple ☐

Thyroid Cancer: ☐pecify if there is associated diagnosis_____

Thyroiditis:

If thyroiditis; Acute ☐ Sub acute☐ Chroni☐

To☐ Non Toxi☐

3. Cytology Diagnosis(FNA)

Benign lesion: ☐ Colloid, ☐Cystic, ☐Thyroiditis, ☐

Malignant lesions: ☐illary, ☐aplastic, ☐dullary, ☐mphoma, ☐

Intermediate : Ce☐ar follicular lesions, ☐llicular neoplasms ☐

Non-diagnostic/Unsatisfactory: ☐

4. Specific type of operation done:_____
5. Histological diagnosis after operation(if done)_____