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DEPARTMENT OF DERMATOLOGY & VENEREOLOGY**

Magnitude and Clinical pattern of cutaneous Tuberculosis among patients attended Dermatology Clinic at ALERT center from April 2016-March 2021 GC, Addis Ababa, Ethiopia

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Abbreviations

AAU -Addis Ababa University

AIDS -Acquired Immune Deficiency Syndrome

AFB-Acid Fast Bacilli

ALERT- All Africa Leprosy and Rehabilitation Training Centre

CTB- Cutaneous Tuberculosis

DOPD-Dermatology outpatient Department

EIB-Erythema Induratum of Basin

EN-Erythema Nodosum

EPI- Expanded Program on Immunization

FNAC-Fine Needle Aspiration Cytology

HIV-Human Immunodeficiency Virus

HLA-Human leukocyte antigen

IRB-Institutional Review Board

LV-Lupus Vulgaris

MDT-Multi Drug Therapy

MT-Mantoux Test

PLHIV-people living with HIV

PNT-Papulonecrotic Tuberculid

PI -Principal Investigator

SFD-Scrofuloderma

SPSS-Statistical Package of Social science

SNNPR-southern nation and nationality people region

TB-Tuberculosis

TST-Tuberculin Skin Test

TVC- Tuberculosis verrucosa cutis

WHO-World Health Organization

ZNS-Ziehl-Neelsen Stain

Abstract

Background: - Cutaneous tuberculosis is an infection caused by *M. tuberculosis* complex, *M. bovis* and Bacillus Calmette-Guérin, which depending on individual immunity, environmental factors and type of inoculum may present varied clinical and evolutionary aspects(3). Cutaneous TB is one of the most elusive and more difficult diagnoses to make for dermatologists practicing in developing countries because of the difficulty in obtaining a microbiological confirmation(3).Cutaneous TB comprises only a small proportion (1%- 2%) of all cases of TBnevertheless, bearing in mind the high prevalence of TB in many developing countries, these numbers become significant (19).

Method: - Hospital based retrospective cross sectional study was conducted with secondary data of patients who were diagnosed to have cutaneous tuberculosis diagnosed with different diagnostic modalities. All the data were collected from the patient's chart. Socio demographic, diagnosis and diagnostic modality related to the patient were included. Data were compiled, checked, coded, entered and cleaned using Epi Data 4.4.1 and all statistical tests were done using version 26 SPSS software.

Result: - A total of 81 patients were found to have a cutaneous TB. The mean age was 32.3 (± 18.63) years. The age ranges from 2 year to 77 years. Out of 81 patients, 41(50.6%) were female and 40(49.4%) were male. The overall magnitude of Cutaneous TB was 0.13%. The most clinical pattern was scrofuloderma (n=39, 48.2%) followed by TB abscess 8/81, lupus vulgaris 7/81. Cutaneous TB clinical pattern were not specified in 14/81, 17.3%. The most commonly employed diagnostic modality was FNAC (n=32, 39.5%), AFBsmear was positive in 12/81. Commonly body site affected were neck and face (n=27, 33.3%) followed by axilla and trunks (n=26, 32.1%). Only 5/81cases of cutaneous TB and HIV identified.

Conclusion: - In this study the observed number of patients shows that cutaneous TB is still the existing medical problem despite promising achievement in reducing TB incidence annually by 9% at national level. Scrofuloderma is a form of cutaneous tuberculosis, most prevalent in children and adult age groups. For diagnosis of cutaneous TB FNAC used as the main diagnostic modality

1. Introduction

1.1. Background

Tuberculosis is a major public health problem worldwide and especially in the developing countries (2). According to the World Health Organization (WHO) global TB report for 2017, approximately 10.4 million become ill, 1.1 million deaths from TB among HIV seronegative persons and an additional 350,000 deaths from HIV-associated TB. Extra pulmonary tuberculosis constitutes approximately 10% of all cases of tuberculosis and cutaneous tuberculosis makes up only a small proportion of these cases (19). Cutaneous tuberculosis was a major public health problem in the nineteenth and early twentieth centuries in developed nations. With the improvement of hygiene habits in the general population, the improvement of living standards, the use of the BCG vaccine, and the introduction of effective chemotherapy, there was a significant decrease in the number of cases (19). From the mid twentieth century onwards, there was a resurgence of the disease with the main causes being the increased incidence of HIV-positive patients, the emergence of multidrug-resistant tuberculosis and the growing number of patients receiving immunosuppressive treatments (3).

In Ethiopia tuberculosis is a major public health problem posing significant deleterious health impacts by affecting the productive segment of the population and resulting in a serious burden to the health system and exploiting the individuals/household economy (1). According to WHO the prevalence and mortality of Tuberculosis of all forms is estimated to be 546 and 73 per 100,000 population respectively (2). In Northern Ethiopia cutaneous TB appears to be 0.7% among patients attending Dermatovenerology outpatient department (2).

Cutaneous TB comprises only a small proportion (1%-2%) of all cases of TB. Nevertheless, bearing in mind the high prevalence of TB in many developing countries, these numbers become significant (2).

The cutaneous tuberculosis classification covers a wide variety of clinical presentations. Infection can occur through exogenous routes, (tuberculous chancre, tuberculosis verrucosa cutis and some cases of lupus vulgaris) or endogenous ones (most cases of lupus vulgaris, scrofuloderma, miliary tuberculosis and orificial tuberculosis). The tuberculids include lichen

scrofulosorum, erythema induratum of Bazin, some cases of papulonecrotic tuberculid, and the recently identified nodular granulomatous phlebitis (19).

Diagnosis of cutaneous tuberculosis is challenging because the clinical picture can be so varied and the incidence of positive cultures is low. It requires the correlation of clinical findings with diagnostic testing; in addition to traditional AFB smears and cultures, there has been increased utilization of PCR because of its rapidity, sensitivity and specificity (16).

1.2. Statement of the problem

Tuberculosis is a major public health problem throughout the world by infecting an estimated one-third of the world's population and putting them at risk of developing active disease during their lifetime. Tuberculosis is the leading cause of deaths every year among the infectious disease worldwide alongside HIV. It kills more than five thousand children, women and men each day (1). Ethiopia is among the 30 High TB, HIV and MDR-TB Burden Countries, with annual estimated TB incidence of 177/100,000 populations and death rate of 25 per 100,000 populations for 2016 (4). Among the notified TB cases in 2016, 2.7% of new TB cases and 14% among previously treated TB cases were also estimated to harbor drug resistant TB (1). Cutaneous TB comprises only a small proportion (1%-2%) of all cases of TB. If one assumes that 1% of all TB cases will have cutaneous involvement, Ethiopia annual estimated cutaneous TB incidence will be 2/100,000 populations. HIV has led to a 20% increase in the incidence of extra-pulmonary tuberculosis in developed nation. As cutaneous tuberculosis constitutes 1.5% of all cases of extra-pulmonary tuberculosis in this area, it is natural that its incidence will increase proportionately. In Ethiopia HIV co-infection impedes the TB control efforts contributing to around 8% of annually notified TB cases with likely proportional cases of cutaneous TB.

1.3. Significance of the study

Even though; TB is a major public health problem throughout the world the burden of cutaneous TB is not well studied and remains one of the least studied form of cutaneous TB (20).

In Ethiopia, cases of TB are seen at different clinical service point with trained and qualified clinicians focusing mainly on pulmonary TB. A few cases of cutaneous TB identified and treated in most settings including Dermatology clinics at ALERT center. However, so far there are limited researches done describing the epidemiology and clinical characteristics of cutaneous TB in Ethiopia.

Therefore, this study may provide some insight into the magnitude of the problem at ALERT center which is the largest dermatology referral center in the country and serves as a basis for the future studies on the subject matter. It may also be help to improve the practice in diagnosis of these form of TB at the hospital level by identifying gaps in this area.

2. Literature review

Tuberculosis, which is known to have existed since 3000 BC, continues to pose a significant public health problem even today, and kills around 3 million people annually. The emergence of the human immunodeficiency virus (HIV) has led to a 20% increase in the incidence of extra-pulmonary tuberculosis in the US. As cutaneous tuberculosis constitutes 1.5% of all cases of extra-pulmonary tuberculosis, it is natural that its incidence will increase proportionately (9).

The prevalence of cutaneous tuberculosis among patients attending various dermatology OPDs in India has hovered at 0.1–0.5% over the last few decades. Study done at Chandigarh, India Dermatology Department of the Postgraduate Institute of Medical Education and Research (PGIMER) shows, of the 267420 patients who attended the Dermatology Out-Patient Department (OPD) between 1975 and 1995, 280 had cutaneous tuberculosis, giving a prevalence rate of 0.1% among dermatology patients. With the exception of tuberculous chancre, all forms of cutaneous tuberculosis were seen. Lupus vulgaris was the commonest form seen in 154 patients (55%), followed by scrofuloderma (SFD), in 75 (26.8%), tuberculosis verrucosa cutis (TVC) in 17 (6. %), tuberculous gumma(s) in 15 (5.4%) and tuberculids in 19 (6.8%)(9).

On a description of 75 CTB case series in Brazil Rio de Janeiro, different clinical patterns were identified as scrofuloderma represented 50.7% of the cases, followed by erythema induratum of Bazin (EIB) (18.7%), tuberculous gumma (13.3%), lupus vulgaris (8%), TB verrucosa cutis (4%), orificial TB (2.7%) and associated forms (2.7%). All patients who completed anti-TB treatment (97.3%) had their lesions healed. Fifty percent of EIB patients presented with recurrence (4).

Study done in tertiary care hospital in coastal Karnataka India identified 62 total cases of CTB attending skin and STD outpatient department during the period 2005 – 2014. The common age group affected was 50 years and above. Males were most commonly affected than females with M: F ratio of 1.2:1. The most common affected sites were lower limb (37.10%) followed by face and neck (24.19%). Clinically majority of the cases presented as plaque lesion (46.77%) followed by sinus (22.58%), ulcer (16.13%), verrucous lesion (11.29%) and papule (3.23%). The most common type of CTB encountered were Lupus vulgaris (35.48%) followed by scrofuloderma (33.8%). Systemic involvement was seen in 29 cases. Mantoux test was positive

in 80% of cases and tubercular bacillus was isolated in only 3% of cases. HIV test was positive in 4% of cases. All the clinically diagnosed cases of Cutaneous TB were confirmed on histopathology and responded well to anti-tubercular therapy (12).

All cases of cutaneous tuberculosis seen in the Dermatology Department of Ibn Rochd Hospital Center in Casablanca, Morocco, from January 1981 through December 2004 were 216 out of 11 073 patients hospitalized in the department. Represented 2% of all cases of skin diseases seen. Men and women were equally affected. The mean patient age was 29 years. Major clinical types of cutaneous tuberculosis were scrofuloderma and gumma (72%), lupus vulgaris (12%), tuberculosis verrucosa cutis (7%), tuberculids (6%), orofacial tuberculosis (1%), and tuberculous chancre (1%). Systemic involvement was seen in 35%. Mantoux skin tests were performed in (66%), 81% of subjects had positive. Lesion biopsy for histopathologic study was performed in 81% of patients and showed classical tuberculous findings in 57%. Mycobacterium tuberculosis was isolated in culture from 9% of patients. Only a minority of these patients were tested for HIV and all were seronegative (20).

Study in Brazil Rio de Janeiro shows 15 cases of CTB represented 2.5% of TB/HIV cases in the National Institute of Infectious Diseases, attended over a period of 17 years. Different from other opportunistic illnesses, TB can occur in patients with HIV who have widely varying CD4 counts, from those with preserved immunity to different degrees of cellular immunity impairment (11).

A 10 year (1983-1992) retrospective survey in public sector of Hong Kong included total of 176 recorded confirmed cases. This represents 0.066% of all new skin cases seen during the 10-year period. Among these, 79.5% are erythema induratum, 6.3% lupus vulgaris, and 4.5% tuberculosis verrucosa cutis. They are further divided into true cutaneous tuberculosis (14.8%, n=26) and the tuberculide (85.2%, n=150). Among the patients with true tuberculosis, 42.3% had lupus vulgaris, 30.8% had tuberculosis verrucosa cutis, and 26.9% had scrofuloderma. Among the tuberculides, erythema induratum accounted for 93.3 % (21).

Retrospective study of all cases of CTB diagnosed from October 2007 to November 2009 at an outpatient clinic of a tertiary-care hospital in Northern India shows overall incidence 0.7% (131 of 18720 outpatients). HIV concurrence was 9.1% (12 cases) of all cutaneous tuberculosis cases. Most common variants seen were scrofuloderma (36.5%), lupus vulgaris (31%), tuberculosis verruca cutis (12.9%), lichen scrofulosorum (11.4%), papulonecrotic tuberculids (3.8%), erythema nodosum (2.2%) and erythema induratum of Bazin (1.5%) (17).

Data of patients analyzed retrospectively from 2000 to 2009 in Southeast of Turkey identified 40 patients with CTB. The mean age was 35.2 ± 18.4 years (range 7-95 years). Sixteen were men (40%) and 24 were women (60%). The male / female ratio was 0.66. Lupus vulgaris (LV) was diagnosed in 30 of the all 40 cutaneous TB patients. The diagnosis of the scrofuloderma (SFD) was made in 10 patients (13).

Prospective study in patient who attended department of Dermatology community based college from July 2006 to June 2010 in Bangladesh shows the overall incidence of CTB to be 0.81%. The male to female ratio 15:7. Economically productive age group 16 to 30 account 44.55%. Only 3 morphological variant of CTB was presented lupus vulgaris (49%), tuberculosis verrucosa cutis (29%), and scrofuloderma (21%) (10).

A retrospective study done between January 1991 and December 2011 which included all cases of cutaneous TB observed at the infectious diseases and Dermatology Units of the Tunis la Rabta Hospital showed 137 patients had cutaneous TB. The most frequent clinical presentations in the series were scrofuloderma in 93 cases (65%), tuberculous gumma and abscesses in 23 cases (16%), and lupus vulgaris (LV) in 17 cases (11.8%). Seven patients presented with tuberculids (4.8%) and three patients (2%) with a tuberculous chancre (5).

On the study in South Africa total of 37 cases of cutaneous tuberculosis, were observed in a patient population of 152,000 (0.024%) over a period of five years from 1999 to 2004. Giving a prevalence of 0.02% among patient attending the dermatology center. The spectrum of infection included 19 (51%) cases of lupus vulgaris, 7 (19%) cases of papulonecrotic tuberculids, six cases each of tuberculosis verrucosa cutis and scrofuloderma. One case had scrofuloderma and lupus vulgaris and another both scrofuloderma and papulonecrotic tuberculide. One case of lichen scrofulosorum was seen in a seven year old boy.

11 cases revealed evidence of systemic tuberculosis. Seven cases of HIV with CD4 counts between 50-500 cells/ μ l were observed in the study

Prospective study done in Northern region of Ethiopia Mekele Italian Dermatological Centre (IDC) report 202 cases of CTB in the 34- month period between January 2005 and October 2007. A diagnosis of CTB was based upon a combination of clinical features, fine-needle aspiration

cytology (FNAC) and Ziehl-Neelsen (ZN) staining and/or biopsy for histopathological evidence. Scrofuloderma (SFD) was the commonest form seen in 143 patients (70.8%), followed by lupus vulgaris (LV) in 22 (10.9%), gumma in 18 (8.9%), lichen scrofulosorum (LS) in 11 (5.4%), tuberculosis verrucosa cutis (TBVC) in 6 (3%) and erythema induratum of Bazin in 2(1). HIV-positive patients numbered 45 (22%); lung involvement was present in 20 over 45 (44.4%). Among 49 pediatric patients, 12 (24.5%) had the HIV-TB co-infection. All HIV patients clinically presented with SFD and 5 of them had gumma. Three patients affected by HIV and on MDT for pulmonary TB developed SFD of the axilla or of the submandibular area during the continuation phase of treatment (2).

3. Objective

3.1. General Objectives

- To assess the magnitude and clinical patterns of cutaneous TB at ALERT dermatology OPD from April 2016-March 2021, Addis Ababa, Ethiopia

3.2. Specific objectives

- To assess the frequency of cutaneous TB
- To assess the frequency of different patterns of cutaneous TB
- To determine the concurrency rate of HIV and cutaneous TB
- To assess how the diagnosis was established
- To assess body sites frequently affected and co-involvement of other systems

4. Methods and Materials

4.1. Study area and period

The study was conducted from June 2021- August 2021 in ALERT center which is located in the South West aspect of Addis Ababa, Ethiopia, Africa, and it is specialized center in Leprosy. It was originally focused on rehabilitating and teaching Leprosy and Leprosy patients, but now it has expanded to include tuberculosis and changed the previous name which was All Africa Leprosy Rehabilitation and Training Center to All Africa Leprosy and Tuberculosis Rehabilitation and Training Center. ALERT's activities majorly focus on diagnosing, treating and rehabilitation of Leprosy patients. In addition to that, it also has training programs for leprosy personnel from around the world and leprosy control program. It currently provides a multidisciplinary department that gives services in Dermatovenereology, ART, Pediatrics, Obstetrics and Gynecology, Emergency, Orthopedics, Neurosurgery, trauma center, Plastic surgery and Dentistry. The center receives patients who are referred from across the country to dermatology cases. It was selected because it is the largest tertiary referral hospital for Dermatovenereology cases and it is possible to obtain a sufficient number of patients who came from different parts of Ethiopia.

4.2. Study design

Hospital based retrospective cross sectional study was employed among adult and pediatric unit of ALERT dermatology OPD using patients' chart of the aforementioned period.

4.3. Source population

All medical records of patients who attended ALERT dermatology clinic from the year April 2016-March 2021 were included.

4.4. Study population

All medical records of patients attending ALERT dermatology clinic who was diagnosed to have cutaneous TB within the time frame of April 2016-March 2021 were included in the study.

4.5. Eligibility

4.5.1. Inclusion criteria

All patients who were diagnosed to have cutaneous TB with different clinical type and linked to initiate ant-TB at ALERT center, Dermatology and TB clinics from April 2016-March 2021 were included in the study.’

4.5.2 Exclusion criteria

Cases that were diagnosed as CTB, but re-evaluated after completion of anti-TB and alternative diagnosis is established. Incomplete data, especially in the outcome variable.

4.6. Sampling techniques

We have seen charts of patients seen in Dermatological clinic for the last five years from April 2016-March 2021. Of these, 81 of them were cutaneous TB patients. All charts were reviewed using data extraction sheet and included in the study.

4.7. Data collection

This study was a hospital-based retrospective record review of patients registered in the study period and units. All five years’ medical records of all patients who received dermatological treatment were included in the review and screened from the registry log book. Data abstracted using a uniform data abstraction format prepared to gather relevant data from the medical records both paper copy file and e-file/smart care/after the data abstraction format pretested. BSc Nurses were recruited for data abstraction. Data collectors and supervisors were trained for one day on how to retrieve, abstract relevant data from the medical records, and keep records back in the original location. The data abstraction format pretested in 10 medical records two weeks before the actual data abstraction period for fitness and consistency. Moreover, clinical data were collected from the patient’s chart.

4.8. Data quality management

The questionnaire was prepared in English. During data collection the principal investigator actively participated and personally involved in all activities during the data collection. Data completeness and consistency was checked on spot questionnaires with missed variables were checked and refilled again.

4.9. Data Analysis

Data entered in Epi data manager 4.3 and analyzed using SPSS Version 26.0 software. We calculated Mean and Standard Deviation (SD), and proportions for continuous variables and categorical variables, respectively. The findings presented in text, tables, and figures.

5. RESULT

Of the 62574 patients who attended the Dermatology Out-Patient Department (OPD) between April 2016 and March 2021, 81 had cutaneous tuberculosis, giving a magnitude rate of 0.13% among dermatology out patients. Patient ages ranged from 2 years to 77 years with a mean of 32.29 ± 18.63 years. Majority (27.2 %, n=22) belonged to the age group 30-40 years. Those between 0-9 years of age consisted of 8.6% (7/81) of the total. Regarding the sex distribution, 50.6% (41/81) were females and 49.4 % (40/81) were males with female to male ratio of 1.03:1. Majority, thirty four (42 %) were from Addis Ababa followed by twenty seven (33.3%) from Oromia and ten (12.3%) from SNNPR.

The distribution of patients according to their age group, sex and region is depicted on Table 1-3

Table 1: distribution of patients according to sex, age-range and region

Sex	Frequency	Percent	Cumulative Percent
Female	41	50.6	50.6
Male	40	49.4	100.0
Total	81	100.0	
Age			
0-9	7	8.6	8.6
10-19	15	18.5	27.2
20-29	15	18.5	45.7
30-39	22	27.2	72.8
40-49	5	6.2	79.0
>50	17	21.0	100.0
Total	81	100.0	

Region			
Addis Ababa	34	42.0	42.0
Oromia	27	33.3	75.3
Amhara	7	8.6	84.0
SNNPR	10	12.3	96.3
Other region	3	3.7	100.0
Total	81	100.0	

25 (30.9%) cases of cutaneous TB seen during the first year of the study period followed by 21 (25.9%) on the next year, 9 (11%) on third year 15 (18.5%) on fourth and 11 (13.6) on the last years

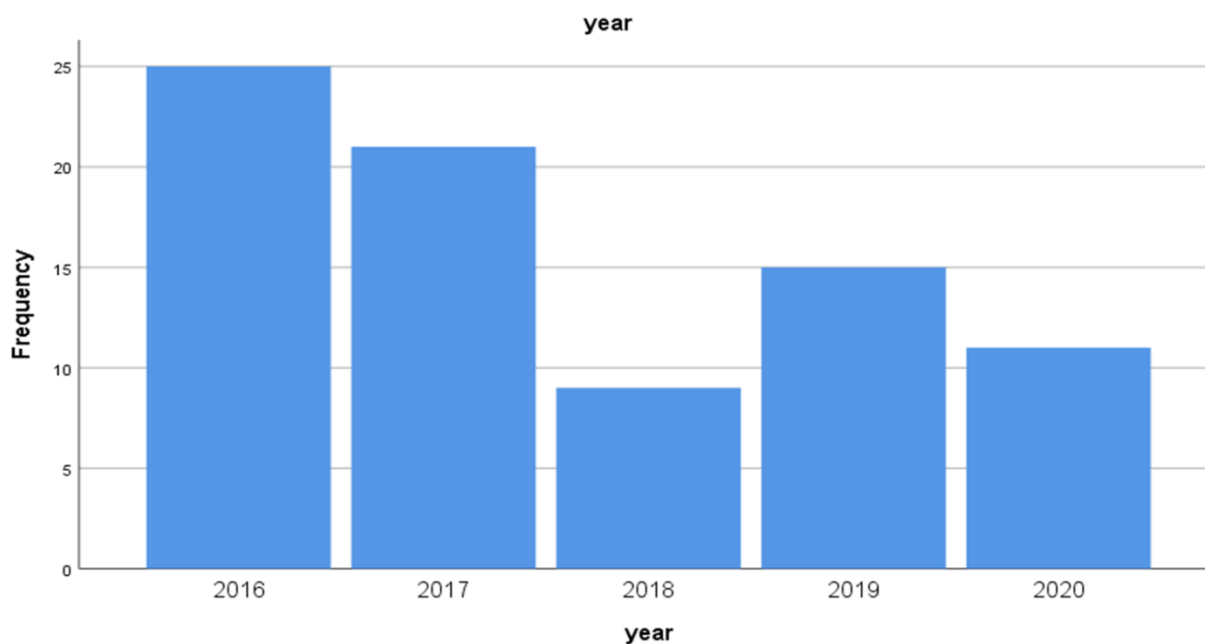


Figure 1: Trend of cutaneous tuberculosis over the studied period

The most frequent clinical presentations in this series were scrofuloderma in 39 cases (48.1%), tuberculous gumma and abscesses in 8 (9.9), and lupus vulgaris in seven cases (8.6%). Six (7.4%) patients had two clinical pattern like TB abscess and scrofuloderma, lupus vulgaris and scrofuloderma, papulonecrotic tuberclid and scrofuloderma. Other patterns were papulonecrotic tuberclid 3(3.7%),miliary TB 2(2.5%), tuberculosis verrucosa cutis 1(1.2%) and erythema induratum of basin in the setting of clinical, microbiological and/or histopathological evidence of TB(1.2%). Fourteen patients (17.3%) were diagnosed as cutaneous TB without determining the clinical type. See table-2 and figure 1

Clinical patterns	Frequency	Percent	Cumulative Percent
Scrofuloderma	39	48.1	48.1
Non-determined clinica type	14	17.3	65.4
TB abscess	8	9.9	75.3
Lupus vulgaris	7	8.6	84.0
Papulonecrotic tuberclid	3	3.7	87.7
Srofuloderma and TB abscess	3	3.7	91.4
Miliary TB	2	2.5	93.8
Scrofuloderma and TVC	1	1.2	95.1
Lupus vulgaris and scrofuloderma	1	1.2	96.3
Scrofuloderma and Papulonecrotic tuberclid	1	1.2	97.5
TVC	1	1.2	98.8
Erythema induratum of basin	1	1.2	100.0
Total	81	100.0	

Table 2: stratification of cutaneous tuberculosis by clinical pattern

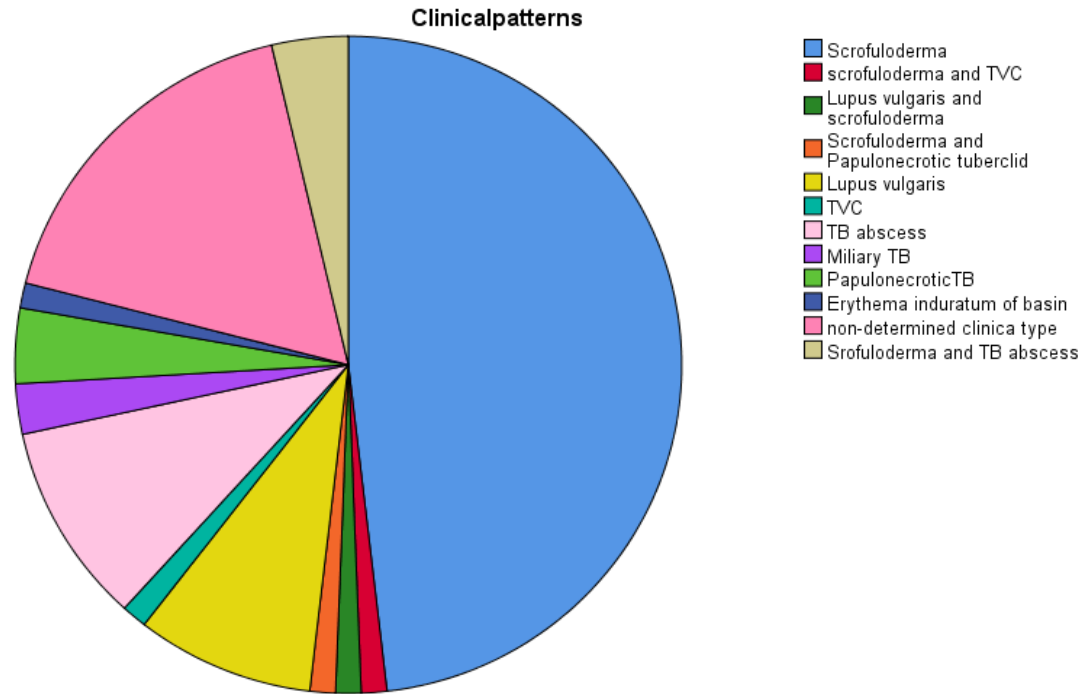


Figure 1: Clinical patterns of cutaneous tuberculosis

Twenty two (27.2%) females and seventeen (20.98%) males had scrofuloderma, 5/7 lupus vulgaris were identified in females and 5/8 TB abscess in males. More than one clinical type were (n=4/6 males and 2/6 females), non-determined clinical types were proportional in both sex. In age < 20, nine cases of scrofuloderma and 2 tuberculosis gumma were seen, 4/7 lupus vulgaris identified in 20-40 years age group. Scrofuloderma was the commonest cutaneous TB pattern seen in all age group.

See figure 2, 3 and 4: Stratification of sex, age range and site affected for types of cutaneous TB

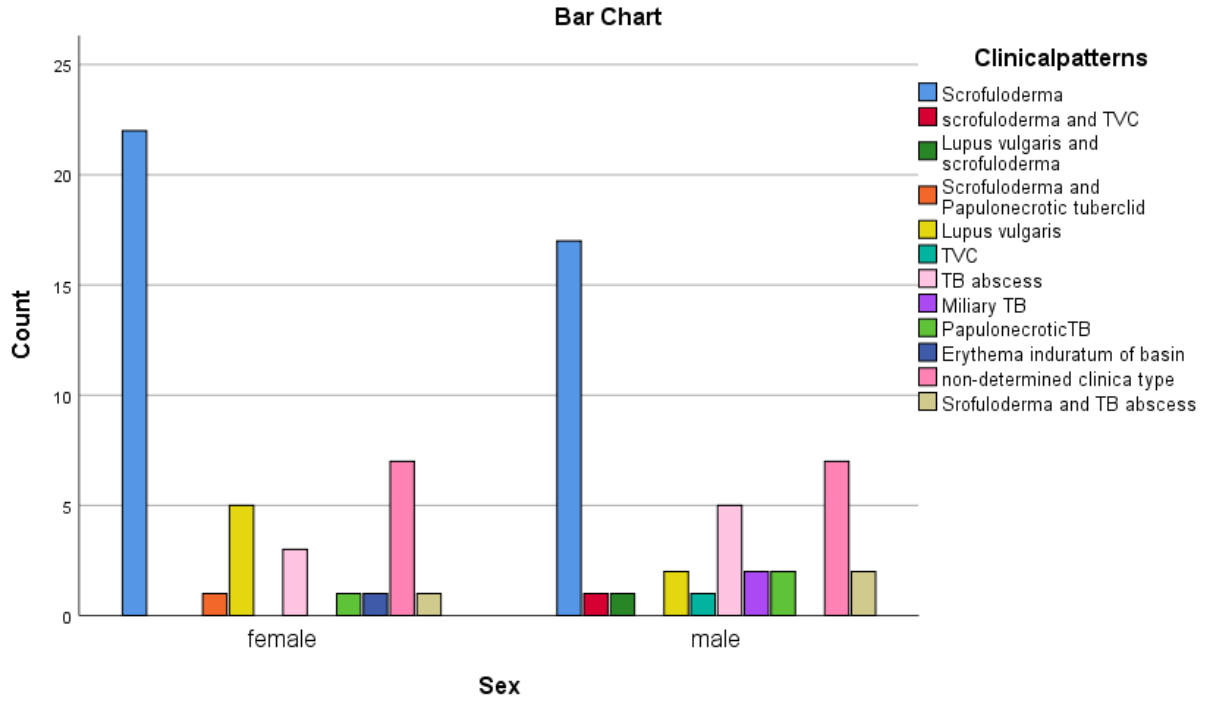


Fig 2: sex of the patients and clinical type of cutaneous TB

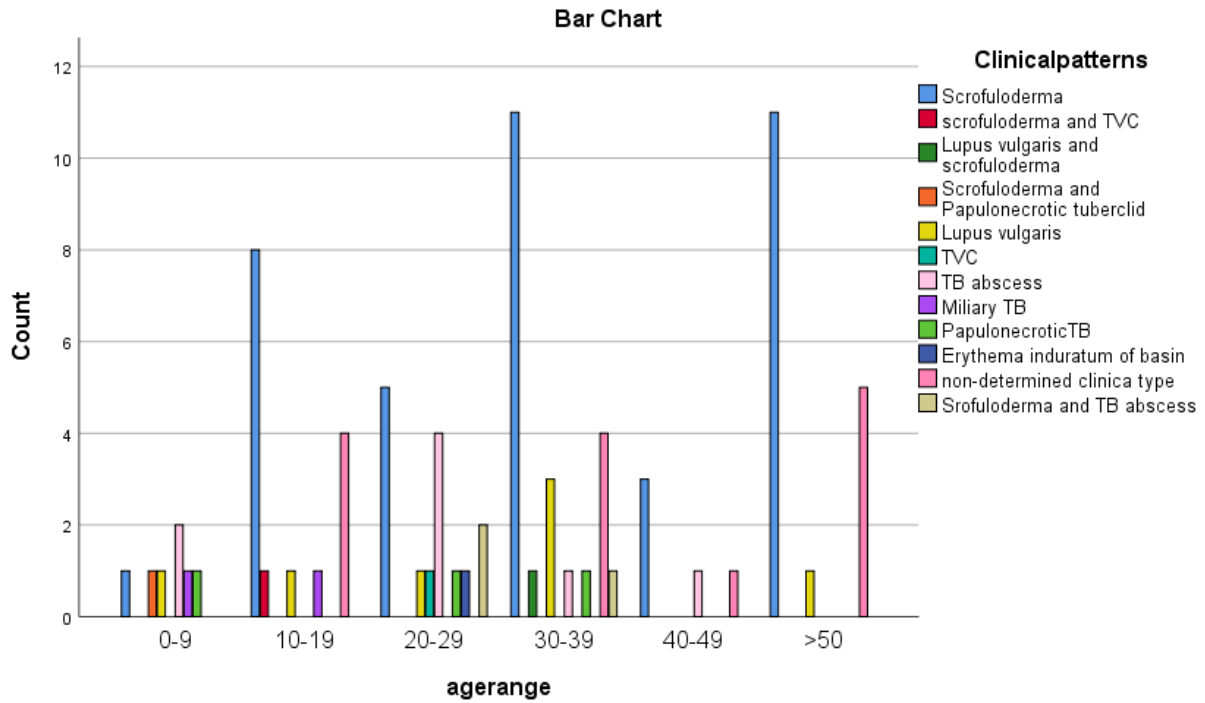


Fig 3: Age range and clinical type of cutaneous tuberculosis

Regarding anatomic site affected: Lupus vulgaris (n= 6/7) identified on face and neck, scrofuloderma seen frequently on face and neck (n=17/39) and trunk alone or with contagious extension (n=9/39). Of ten cutaneous TB diagnosed on extremity in 5 cases clinical type were not specified. Multiple anatomic sites are affected in (n=17/81) primarily face, neck and trunks, anogenita and trunks or diffusely many regions of the body.

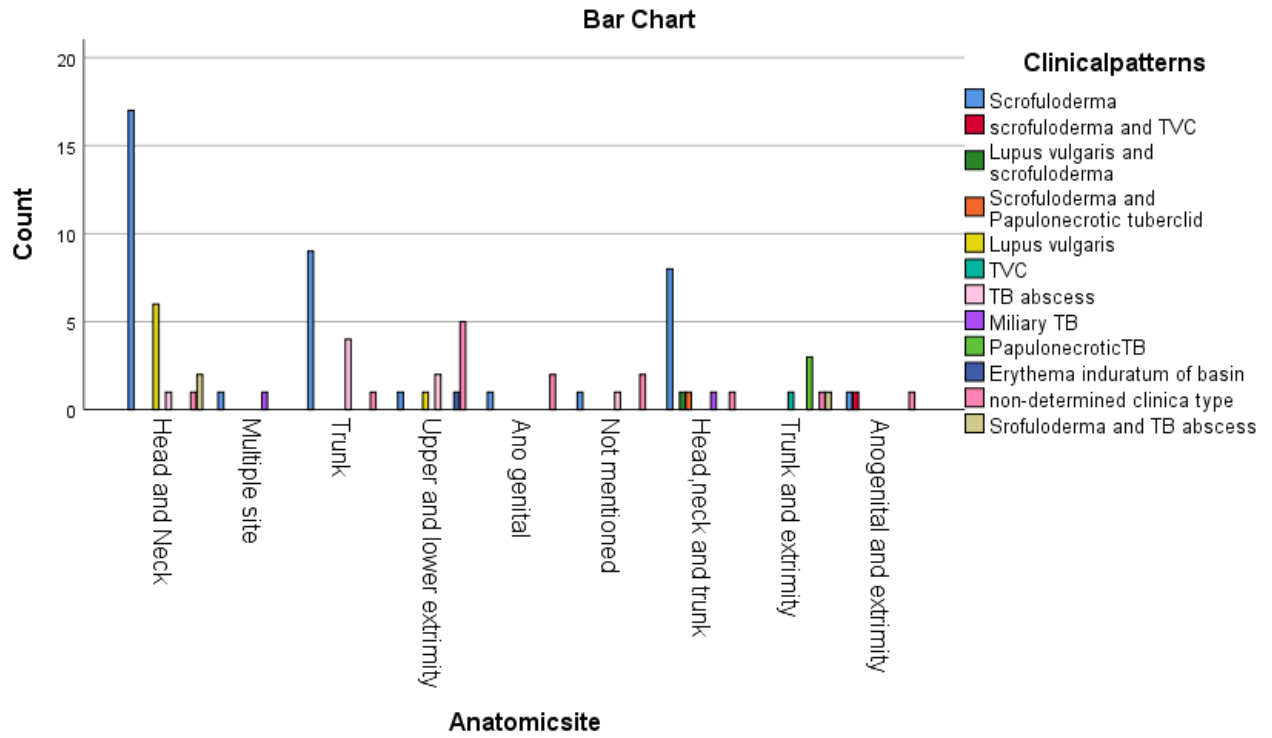


Fig: 4 Anatomic site involved and types of cutaneous tuberculosis

Different diagnostic test were done for single patients, test with confirmatory results were selected as diagnostic test in this study. In twelve (14.8%) case smear with Zeihl-Neelsen stain test identified AFB from lesion fluid/discharge, Xpert MTB/RIF assay detected 5(6.2%) of cases. Majority 46 (56.79%) had FNAC and histopathology as confirmatory diagnostic cutaneous TB test. Five patients had both FNAC and histopathology mentioned cutaneous TB as differential diagnosis, in four patients the results of the attached diagnostic test to the patients charts were nonspecific but in both scenario patients were started ant TB. In seven patients FNAC and histopathology report were considered as consistent with cutaneous TB. In the remaining patients the diagnostic test were not clear even though patients started ant TB. Complete blood count, ESR and chest X-Ray were done in addition to specific diagnostic test for cutaneous TB for majority of patients

Diagnostic test			
	Frequency	Percent	Cumulative Percent
FNAC	32	39.5	39.5
Histopathology	14	17.3	56.8
AFB	12	14.8	71.6
GenExpert	5	6.2	77.8
FNAC and Histopathology	5	6.2	84.0
Clinical desicion	4	4.9	88.9
Histopathology and clinical decision	4	4.9	93.8
FNAC and clinical decision	3	3.7	97.5
	1	1.2	98.8
Culture	1	1.2	100.0
Total	81	100.0	

Table 3: diagnostic tests of cutaneous tuberculosis

Among patients with known HIV Serostatus (27.2%, 22/81) either historically or based on the PICT results attached on the chart, 5 were reactive and 17 were nonreactive. HIV Serostatus in 72.8% (59/81) of patients were not determined. Over the study period 1028 patients from different department with different form of TB were linked to the study center TB unit to start anti-TB. Out of this 81 were cutaneous TB giving a prevalence of 7.8% among TB patients in the study center. Eighteen (23.5%) cases had lung involvement or history of pulmonary TB. Lymph node involvement with cutaneous extension was described in 19(23.5%) cases. Twelve (14.8%) patient had disseminated TB with cutaneous and other organ involvement, nine (11.1%) has no pulmonary or lymph node TB. Evidence is not recorded on extra cutaneous involvement in forty(49.4%) patients. See table 4.

Table 4:HIV status, pulmonary, lymph node and disseminated TB presence of studied patients

HIV status	Frequency	Percent	Cumulative Percent
Positive	5	6.2	6.2
Negative	17	21.0	27.2
Unknown	59	72.8	100.0
Total	81	100.0	

Pulmonary TB			
Yes	18	22.2	22.2
No	30	37.0	59.3
Not mentioned	33	40.7	100.0
Total	81	100.0	

TB lymphadenitis			
Yes	19	23.5	23.5
No	9	11.1	34.6
Not mentioned	53	65.4	100.0
Total	81	100.0	

Disseminated TB			
Disseminated TB	12	14.8	14.8
No history of disseminated TB	69	85.2	100.0
Total	81	100.0	

6. Discussion

The epidemiology of cutaneous TB in much of the world is highly variable like other preventable infectious disease. Scrofuloderma is the most common form of cutaneous TB seen in many developing countries. It is caused by the continuous propagation of infection from an underlying structure, most commonly lymph node or bone. Lupus vulgaris is the most common form of cutaneous TB in India, Pakistan, and Tunisia and used to be the predominant form seen in Europe. Females seem to be more commonly affected (19).

In this study cutaneous TB accounts for 0.13% of the total dermatology outpatients in the study center. This finding is lower than the prospective study done at northern Ethiopia Italian Dermatology center Mekelle that indicates cutaneous TB representing 0.7% of Dermatology outpatients. Terrnova et al. which may be explained by the study time (2005-2007) when the national TB control program is not as effective as this study period. However this magnitude is comparable with several reports from Asia countries indicating that cutaneous tuberculosis represents approximately 0.2% of all cases seen in dermatology outpatient clinics. Abdul et al. In India cutaneous TB accounts for 0.1-0.9% of the total Dermatology outpatients. The range in which our study is found. Study of Ibn Rochd Hospital Center in Casablanca Morocco shows cutaneous TB prevalence in DOPD is 2%. Zouhair et al. that is much higher than this study findings.

Mean age of patients diagnosed with cutaneous TB was 32.29 ± 18.63 that is comparable with study done at northern Ethiopia Italian dermatological Centre, Mekelle that shows 27 year mean age. Terrnova et al. On retrospective study done in Morocco mean patient age was 29 years. Zouhair et al. Children aged under 10 years were 7(8.6%) similar with retrospective study of cutaneous TB in Tunisia (5.1%) (5). Under 10 years are the age group mainly affected in Pakistan Dermatology department study which is sixty-nine (45.1%) cases. There was no considerable ratio difference of the disease between male and female patients. Similar with an epidemiological observations of cutaneous tuberculosis in Larkana, Pakistan (8) and many other studies unlike retrospective study of Tunisia were 72.3% of the patients are female (5).

The different clinical types of cutaneous TB are reported in the literature with very variable incidence from different countries. Scrofuloderma and lupus vulgaris appear to be the most common forms. In this study scrofuloderma was the commonest form seen in 39 patients

(48.1%), followed by gumma in 8 (9.9%), lupus vulgaris in 7 (8.6%), in 14 patients (17.3%) unlike many other previous studies the clinical type of cutaneous TB was not specified on patient charts. This may hinder the true pattern of clinical type of cutaneous TB in this study.

Prospective study done in Northern Ethiopia also indicates scrofuloderma as the commonest form seen in 70.8% of studied cases relatively higher than this study followed by lupus vulgaris 10.9% and gumma 8.9%(2). In Morocco scrofuloderma and gumma are major cutaneous TB clinical type (72%) followed by lupus vulgaris (12%) and tuberculosis verrucosa cutis (7%) (2). But retrospective studies in India shows that lupus vulgaris was the commonest form, seen in (55%) of cases, followed by scrofuloderma in (26.8%), tuberculosis verrucosa cutis in (6%), tuberculous gumma(s) in (5.4%) and tuberculids in 19 (6.8%) (9). Unlike many various clinical studies in which either scrofuloderma or lupus vulgaris is the commonest pattern in Hong Kong Erythema induratum of basin is markedly the commonest pattern (79.5%) (21). It is difficult to find a satisfactory explanation for these differences in clinical subtype in different study.

Primary inoculation TB, orofacial cutaneous TB and lichen scrofulosorum are clinical type of cutaneous TB not identified in the study.

Table 5: Comparison of clinical type of TB of previous studies with the current study

Authors	Kumar.et.a 1.1999	Mann.et. al.2019	Abdelmalek.e t.al.2013	Zouhair.et .al.2006	Terranova.e t.al.2008	Present study
Total cases seen	280	75	137	216	202	81
Clinical patterns						
Scrofuloderma	26.8%	50.7%	65%	72%	70.3%	48.1%
Lupus vulgaris	55%	8%	11.8%	12%	10.9%	8.6%
Gumma(s)	5.4%	13.3	16%		8.9%	9.9%
TVC	6%	4%		7	3%	1.2%
PNT			4.8%	6%		3.7%
Erythema induratum of basin (tuberculid)		18.7%			1%	1.2

The different clinical type of cutaneous type have different preferential sites. Because scrofuloderma is the predominant clinical type in this study the most common sites involved were neck and face, 17(20.99%) cases of scrofuloderma and 6 (7.4%) lupus vulgaris, frequent on cervical and submandibular area with possible underlying TB lymphadenitis. Axilla and trunk affected with scrofuloderma in (11.1%) and gumma (4.9%), 9.9% cases of scrofuloderma diffusely involved neck and upper trunks. Study on children and adolescent in Bangladesh reveals scrofuloderma was mostly common on neck that is similar with this finding, followed by groin and lupus vulgaris is more common on lower extremity followed by face (2) which is different patterns from this study. Prospective study in India also indicated face and neck was the second commonest site after lower extremity(12).

Because of difficulty in identifying the bacilli and broad differential diagnosis, diagnosis of cutaneous TB is challenging. Studied patients had multiple diagnostic tests. Results that identified AFB or reported TB as diagnosis was accepted as the diagnostic test. Out of 81 cases of cutaneous TB in the study FNAC was diagnostic in 32(39.51%) with the report of cutaneous TB as the diagnosis. Both FNAC and histopathology was diagnostic in 6.2%. On study done in northern Ethiopia FNAC was the diagnostic modality, AFB seen on Ziehl-Neelsen stain 5 in cases. In this study histopathologic examination from skin biopsy was done in 28.4%, diagnostic in 17.3% cases, aid in clinical decision in 11.1% cases with other results. This is relatively low in comparison to studies done Tunisia in which histopathology is diagnostic in 65% of cases (5). Generally in this study diagnosis was based on the combination of clinical, histopathologic, laboratory features and response to ant tuberculous therapy.

In this study cutaneous TB represented 7% of all cases of TB seen in the center relatively higher than 1-2% in many literatures which may be explained by the study center being perceived as the only dermatology center in the country and high load of dermatology cases in the center. Even though infection of cutaneous TB was not usually associated with a cases of pulmonary TB (10) pulmonary involvement was identified in 22.2% cases, 23.2% had underlying TB lymphadenitis, and 14.8% disseminated TB that involved the skin. Only 6.2% were cutaneous TB and HIV, out of 27.2% who had documented HIV seroreactivity.

7. Conclusion

In this study the magnitude of cutaneous TB was 0.13%. This result showed that cutaneous TB continued to be a significant medical problem even with advent of highly effective anti-TB therapy. There are varied clinical presentation of cutaneous TB with scrofuloderma the commonest pattern so very important to be aware of this to diagnosis cutaneous TB as early as possible to avoid late complication. Almost all of the investigative method confer lesser sensitivity and specificity for cutaneous TB but FNAC and histopathology offer better positive result practitioner should remember this and investigate with all available tests. The study was done to create some awareness amongst the primary physician or non-Dermatologist

8. Limitation of the study

- Lost charts, Incomplete or illegible patient medical records
- Absence of important clinical information from patients chart
- Not determining clinical type of cutaneous TB
- Not testing or documenting the HIV status of studied patients
- The study is conducted in ALERT, it might not be representative all cutaneous TB patients

9. Recommendations

- At ALERT center level:
 - Needs to Specifying clinical type of cutaneous TB
 - Evaluate for co-involvement of systemic tuberculosis
 - Determine HIV Serostatus of cutaneous TB patients
 - Important to recognize the myriad clinical presentations of CTB and low yield of tests to prevent missed or delayed diagnosis
- Making general practitioner to be familiar with scrofuloderma enable to diagnosis around 50% of cutaneous TB
- To make available FNAC with Ziehl neelsen stain test at different level will help diagnosis of cutaneous TB

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10. Annex's

Data extraction sheet

Part I: Socio demographic data

Table 1

Medical record number	
Year of treatment (E.C)	
Age	
Sex	
Address/region	

Part II: Clinical characteristics

Table 2

Clinical patterns of cutaneous TB	Scrolofuloderma	Tuberculosis verrucosa cutis	Lupus vulgaris	Orofacial TB	Gumma
	Papulonecrotic tuberculid	Lichen scrofulurum	EIB of TB	Others if specified	

Table 3

HIV status	HIV positive	HIV negative		Unknown
Pulmonary or other extra pulmonary TB	Has pulmonary TB	No pulmonary TB	Other extra pulmonary TB	Not mentioned

Table 4

How diagnosis reached (more than one answer possible)	
AFB	
Gene expert	
Culture	
FNACs	
Histopathology	
PCR genetics	
Clinical decision	
Other methods (specify)	

Table 5

Anatomic site affected by the TB(specify)	Head and neck	Trunk	Upper extremity	Lower extremity	Anogenital