Libyan Journal of Science & Technology 15:1 (2024) 176-180

Faculty of Science - University of Benghazi

Libyan Journal of Science & Technology

journal home page: https://journals.uob.edu.ly/LJST

The Frequency of Ear, Nose, Throat, Head and Neck Lesions of Tuberculosis in the Eastern District of Libya.

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Highlights

- **This study of ear, nose, and throat lesions of tuberculosis. cervical lymphadenitis is the most common presentation.**
- **The lesion can mimic many conditions such as malignancy and chronic granulomatous diseases making the diagnosis difficult.**

ARTICLE INFO

Article history:

Received 16 December 2023
Revised 05 January 2024
Accepted 20 January 2024

Keywords:

Extra-pulmonary Tuberculosis, Cervical lymphadenopathy, tuberculous laryngitis, tuberculous otitis media, Nasal tuberculosis, Tuberculosis deep neck spaces.

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ABSTRACT

Tuberculosis (TB) in the head and neck region represents a diagnostic challenge as it can mimic many conditions, such as malignancy and chronic granulomatous diseases. Therefore, the clinician must have a high index of suspicion for head and neck TB increasing the awareness of health workers in Libya of how TB affects the head and neck areas and its common presenting features may prevent unnecessary delays in the diagnosis and treatment of these cases and improve their outcomes. Objective: Assess the frequency of ENT manifestations of tuberculosis. A cross-sectional observational study was conducted, and the cases were subjected to a detailed history and a head and neck examination. The data were analyzed to assess any association existing between the study variables and the prevalence of ENT, head, and neck manifestations of tuberculosis. The results of this study showed that, out of 168 cases of TB included in the study, 49 were positive for ENT, head, and neck tuberculosis. Tuberculous lymphadenitis was the most common TB manifestation in the head and neck region, accounting for 87.8% of positive cases. Laryngeal TB and TB abscesses of the deep neck spaces account for 4.1% and 4.1% of positive cases, respectively. TB otitis and nasal TB account for 2% and 2% of positive cases, respectively. Conclusion: TB in the head and neck region represents a diagnostic challenge, and a high index of suspicion is needed. All suspected cases should be investigated appropriately. Close cooperation between TB-related medical specialists is needed.

1. Introduction

Tuberculosis (TB) is a chronic infectious disease that can affect various parts of the body. Tuberculosis has affected humankind for thousands of years, but a deeper understanding of its cause and transmission only arose after Robert Koch discovered *Mycobacterium tuberculosis* in 1882. Valuable insight has been gained since, but the accumulation of knowledge has been frustratingly slow and incomplete for a pathogen that remains the number one infectious disease killer on the planet (Coleman *et al*., 2022).

1.1 The burden of disease worldwide

By the 1980s of the last centuries, tuberculosis had become very rare in the developed world because of the development of anti-tuberculosis drugs, vaccines, and improved socioeconomic conditions (Cleary and Batsakis, 1995; Kandiloros *et al*. 1997). However, since 1980, the global incidence of tuberculosis has been rising as a consequence of the spread of HIV infection, low living standards with malnutrition, the development of drug-resistant mycobacteria, and immigration from tuberculosis-endemic countries. These changes made the WHO declare tuberculosis a global emergency (Richter *et al*., 2001; Rizzo *et al*., 2003). In 2021, up to 10.6 million people got infected with tuberculosis an increase of 4.5% from 2020, and 1.6 million people died from tuberculosis. The TB incidence rate (new cases per 100.000 population per year) is estimated to have increased by 3.6% between 2020 and 2021, following declines of about 2% per year for most of the past two decades (Global Tuberculosis Control Report, 2022).

1.2 The burden of disease in Libya

In 2021, the total number of TB cases in Libya was 4000, with an increase of 47% from 2015. 1500 (37.5%) cases were females, and 2400 (60%) cases were males. The influx of immigrants from tuberculosis-endemic countries including Niger, Sudan, and Chad, into Libya, tuberculosis relapse in the host population and chronic low governmental spending on TB control programs caused a rise in tuberculosis incidence from forty per 100.000 population in 2013 to fifty-nine per 100.000 in 2015, and it remained at fifty-nine per 100.000 in 2021 (Balakrishnan, 2022). The host population makes up 70% of those who have been diagnosed with tuberculosis in Libya. The mortality rate of tuberculosis in Libya is thirteen per 100.000 per year. Only 40% of TB cases in Libya get effective treatment. The Libyan government needs to raise finances to handle the tuberculosis problem and to strengthen the national tuberculosis program's abilities to protect both the migrant communities and the host population in Libya (Balakrishnan, 2022). Tuberculosis usually affects the lungs, however, any part of the body including the head and neck regions can be affected. 20% of TB cases present as extra pulmonary lesions, among which the most common sites include the lymph nodes, peritoneum, ileocecal, hepatosplenic,

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genitourinary, central nervous system, and musculoskeletal regions (Ramzan *et al*., 2009 and Rastogi *et al*., 2007). Head and neck tuberculosis (HNTB) accounts for 10% of TB patients. Head and neck tuberculosis can affect most organs in the head and neck region, such as the lymph nodes, larynx, middle ear, oral cavity, and pharynx (Gambhir *et al.*, 2017). In general, the entrance of *Mycobacterium tuberculosis* into these regions is covered with epithelium mucosa; therefore, immunosuppression or a break in this natural barrier caused by trauma, inflammation, poor oral hygiene, or pre-existing lesions, such as leukoplakia, periapical granuloma, cysts, and abscesses, could induce the occurrence of tuberculosis (Kumar, 2011 and Andrade and Mhatre, 2012). Because the early manifestations of head and neck tuberculosis are often similar to neoplasm or inflammation, clinical consideration of head, and neck tuberculosis usually occurs only after ineffective anti-inflammatory treatment, a biopsy, or even surgical resection (Sheikh *et al.*, 2012; Bruzgielewicz *et al.*, 2014). To the best of our knowledge, no study so far has evaluated the prevalence of ENT, and head, and neck manifestations of TB in Libya. Increasing the awareness of health workers in Libya of how TB affects the head and neck areas and its common presenting features may prevent unnecessary delays in the diagnosis and treatment of these cases and improve their outcomes (Khateeb *et al*., 2016 and Tellez- Rodriguez *et al*., 2016). The cross-sectional study aimed to answer this question and determine any socio-demographic risk factors for TB in the head and neck regions.

2. Materials and methods

(a) Study Participants

Selected cases from TB Patients who attended at the National Center for Disease Control in Benghazi, the National Center for Disease Control in Ajdabiya and Alkwifia Chest Hospital between April 2021 and March 2023 were enrolled in this cross-sectional observational study. The patients were diagnosed based on chest radiograph findings, culture, microscopic examination histopathology and molecular testing of the patient's Sputum and other specimens based on the site of disease. Inclusion criteria include Libyan and non-Libyan cases, adult patients aged 18 and older, Both male and female and residents in the eastern region of Libya (Benghazi and surrounding cities). Exclusion criteria include Patients aged less than 18 years, residents outside the eastern district of Libya, and Multidrug-resistant TB cases.

(b) Ethical issue justification

The study was aimed at addressing a pure scientific theory using an observational design, The issue of confidentiality and the patient`s privacy and safety have been guaranteed by the researcher. The patient was not exposed to any sort of risk. No personal identification was used.

(c) Study Design, Setting, and Study Period

A cross-sectional study design was applied. The study was conducted between April 2021 and March 2023 at the National Centre for Disease Control (NCDC) in Benghazi, the National Center for Disease Control in Ajdabiya, and Alkwifia Chest Hospital.

(d) Data Collection

The data was collected using a history sheet, clinical examination, and reviewing patient files for important investigations. To avoid selection bias, questions such as age and original residency were asked. Additional questions on employment, marital status, smoking habits, last level of education, any contact with tuberculosis cases, and past medical and surgical history were asked. The cases were questioned on the symptoms of tuberculosis in general, such as fever, night sweats, weight loss, and any symptoms suggestive of Ear Nose and Throat (ENT), head, and neck involvement, such as nasal obstruction, nosebleed, ear discharge, nasal mass, hearing loss, hoarseness, dysphagia, and odynophagia. The clinical examination was guided by the history's findings. Anterior rhinoscopy, otoscopy, indirect laryngoscopy, and head and neck examination were done, and patients with hoarseness were subjected to flexible nasopharyngoscopy and/or rigid laryngoscopy. The findings in the chest radiographs, neck computerized tomography (CT) scan, ultrasonography, and histopathology reports were documented. The results of lab investigations such as hemoglobin level, white blood cell (WBC), Erythrocyte Sedimentation Rate (ESR), and microscopic sputum examination at admission time were documented.

(e) Sampling technique and sample size

A purposive sampling technique was used to get the required sample. The study population is the number of TB cases in the eastern district of Libya. Based on the global report of the World Health Organization (WHO) published in 2022, there are up to 4000 cases of tuberculosis in Libya and up to 1500 cases in the eastern district (Global Tuberculosis Control Report, 2022). Based on previous studies (Srivanitchapoom and Sittitrai, 2016 and Kulchavenya, 2014). The expected proportion of patients with TB in the head and neck regions is 10%. Taking into consideration, an accepted margin error of 5%, and a confidence level of 95%, with the above-mentioned data, the sample size was calculated using epidemiology information (Epi-Info.), a software suite built and maintained by the Centre for Disease Control and Prevention (CDC). The calculated sample size was 127 cases.

(f) Statistical analysis

Data was entered, reviewed, and analyzed using SPSS version 26 for Windows. For continuous data, the mean and standard deviation were used for normally distributed data, while the median and interquartile range were used for non-normally distributed data. The Chi-square test was used to assess any association existing between the study variables and the prevalence of ENT, head, and neck manifestations of tuberculosis. A significance level of 0.05 was used as the cut-off limit to judge any statistical relevance.

3. Results

Out of 175 cases recruited in the survey, 168 cases were eligible for the final analysis. Seven cases were excluded because of their age and address. The results from 119 (70.8%) cases were negative. Forty-nine (29.2%) cases were positive for ENT, head, and neck manifestations. Out of forty-nine positive cases, there were 43 (87.8%) cases of cervical TB lymphadenitis, two (4.1%) cases of laryngeal TB, two (4.1%) cases of TB parapharyngeal abscess, one (2%) case of tuberculosis otitis media, and one (2%) case of nasal TB. Two positive cases of cervical lymphadenopathy have concomitant pulmonary tuberculosis. The distribution of positive cases depending on their TB head and neck manifestations is described in Fig. 1.

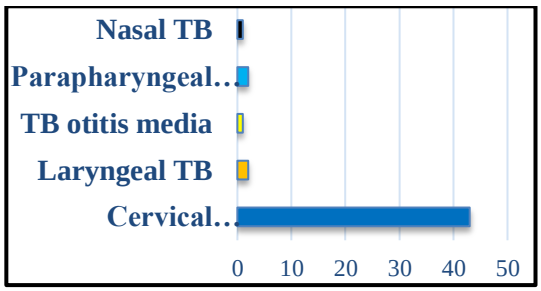

Fig 1. Distribution of positive cases according to their TB head and neck manifestations

The mean age of positive cases is 37.59±14.24 years. Thirty-two (65.3%) of the positive cases were less than forty years of age. There were twenty-seven (55.1%) positive males and twenty-two (44.9%) positive females. The distribution of positive cases based on their gender and smoking habit is shown in Fig. 2**.** The distribution of positive cases based on their nationality is shown in Fig. 3.

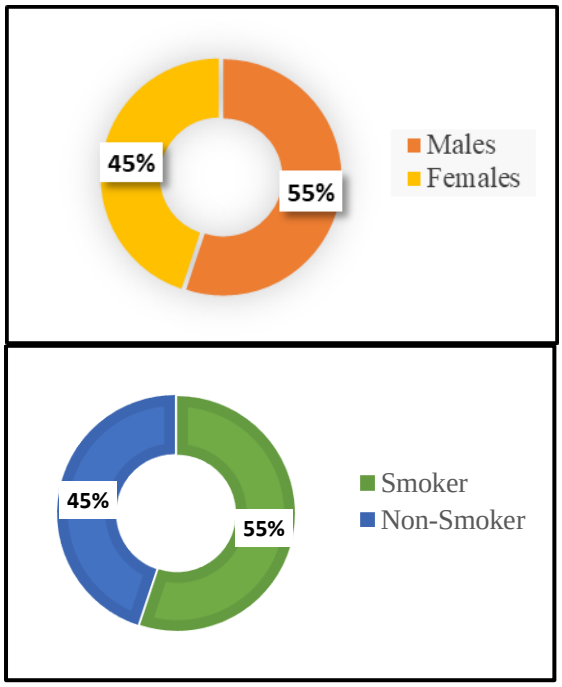

Fig. 2. Distribution of positive cases based on their gender and smoking habit

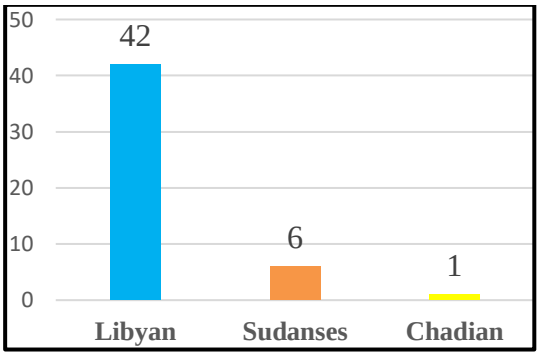

Fig. 3. Distribution of positive cases based on their nationality.

On the past medical history of positive cases, twenty-eight (57.1%) cases were known to be diabetics, and twenty-one (42.9%) cases were non-diabetic. Additionally, four (8.2%) cases were hypertensive. A history of contact with TB cases was positive in seven cases (14.3%). Regarding the education level of positive cases, twenty-five (51%) of cases have an education level below a bachelor's degree, and twenty-four (49%) cases have a bachelor's degree. A Chi-square test was conducted to assess any association between the participants 'age, gender, marital status, smoking, and past medical history of diabetes mellitus or hypertension and the prevalence of tuberculosis in the ENT, head, and neck regions. There was no statistically significant relationship between the frequency of ENT, head & neck involvement in patients with tuberculosis and their ages (P=0.810), smoking habits, or hypertension (P=0.715). There was a statistically significant relationship between the level of education of patients with TB and the frequency of TB in the ENT, head, and neck regions, $\chi2(3)=16.507$, p=0.001. Diabetes mellitus has a significant impact on the frequency of tuberculosis in the ENT, head, and neck regions, $\chi2(1)=8.597$, p=0.003. Smoking has a significant impact on the frequency of tuberculosis in the ENT, head, and neck regions, $\chi2(1)=6.685$, p=0.010. The female was associated with a higher prevalence of ENT, and head, and neck involvement in patients with tuberculosis. $\chi2(1)=7.581$, p=0.006. Married participants have a higher rate of ENT, head, and neck involvement as compared with unmarried participants. This association was significant. $\chi2(1)=7.136$, p=0.006.

4. Discussion

This cross-sectional study aimed to assess the prevalence of tuberculosis ENT, head, and neck manifestations in patients with tuberculosis and to determine any socio-demographic risk factors. Despite the efforts of Libyan governments to control tuberculosis, the TB incidence rate has increased by 47% between 2015 and 2021. This may be attributed to the increase in the number of immigrants moving from tuberculosis-endemic countries such as Sudan, Chad, Niger, and Mali into Libya. However, according to the data from the National Centre of Disease Control, the burden of disease among the Libyan population has also increased (Balakrishnan, 2022).

Table 1

Baseline characteristics of the positive cases and their associations with the prevalence of ENT, head and neck manifestations of TB

Character	Total	Positive cases	χ2	P value
Education Non -Primary -Secondary -Bachelor	 16 (9.5%) 32 (19%) 68 (40.5%) 52 (31%)	 6 (12.2%) 2 (4.1%) 17 (34.7%) 24 (49%)	16.507	.001*
DM -Positive -Negative	 67 (39.9%) 101 (60.1%)	 28 (57.1%) 21 (42.9%)	8.795	.003*
HTN -Positive -Negative	 12 (7.2%) 155 (92.8%)	 4 (8.3%) 44 (91.7%)	133	..715
Marital status -Married -Unmarried	 76 (45.2%) 92 (54.8%)	 30 (61.2%) 19 (83.3%)	206	0.008*
Age -≤ 40 ->40	 122(66.7%) 56(33.3%)	 32(65.3%) 17(34.7%)	0.58	0.810
Smoking -Smoker -Non-Smoker	 67 (39.9%) 101 (60.1%)	 27 (55.1%) 22 (44.9 %)	6.685	0.010*
Gender -Male -Female	 118 (70.2%) 50 (29.8%)	 27 (55.1%) 22 (44.9%)	7.136	0.006*

***Statistically significant at P < 0.05**

Our survey was conducted in the period between April 2021 and March 2023 in three centers for disease control in the eastern district of Libya. The researcher has found that 29.2% of TB patients in the eastern district of Libya have tuberculosis in the ENT, head, and neck regions. The most common head and neck manifestation of tuberculosis was cervical lymphadenopathy (87.7%), followed by laryngeal tuberculosis (4.1%). A tuberculosis parapharyngeal abscess was diagnosed in 4.1% of the cases. Nasal tuberculosis and tuberculous otitis media accounted for 2% and 2% of the cases, respectively. Monga *et al.* (2017) found that the most common site of TB in the head and neck regions was the cervical lymph nodes (81.25%). The nose and paranasal sinus were the second most commonly involved subsites (6.2%). The oral cavity was involved in 4.1% of cases. The larynx, retropharyngeal region, buccal space, and skin of the head, and neck regions were involved in 2.05% of cases. According to Akkara *et al.*, (2014), the cervical lymph nodes were the most commonly involved subsite in patients with TB in the ENT, head, and neck regions (95.3%). The middle ear was the second most common site (2.8%). The larynx was involved in 1.4% of cases, and the nasal cavity was involved in 0.5% of cases. In the present survey, females accounted for 44.9% and males accounted for 55.1% of cases with TB in the ENT, head, and neck regions. These findings are comparable with those of other studies done by Akkara *et al.*, (2014) and Monga *et al.*, (2017) where males accounted for 67.7% and 64.5% of cases, respectively. In contrary to our study, Female predilections were reported by Stelianides *et al.*, (1997) and Mazza-Stalder *et al.*, (2012). In the present survey, the mean age of patients with TB of the ENT, head, and neck regions was 37.5 years, and 65.3% of cases were more than forty years of age. According to Monga *et al.*, (2017), the mean age of cases of TB in the head, and neck regions was 23.4 years, and most of the cases had an age between twenty-one and thirty years. Das *et al.*, (2016) reported that most of the cases (57.1%) have an age between 15 and 24 years.

5. Conclusions

Ear, nose, and throat regions are not immune against TB. Cervical lymphadenitis is the most common presentation of TB in the head and neck regions. The larynx, oral cavity, ear, nasal cavity, salivary glands, and Deep neck spaces can also be involved in TB with less frequency. The TB in the head and neck regions can mimic many conditions such as malignancy and chronic granulomatous diseases, this makes the diagnosis more difficult and a high index of suspicion for the diagnosis is needed.

6. Recommendations

Any suspicious cases especially those with chronic symptoms not responding to treatment should alert the physician to investigate them properly keeping in mind TB as a differential diagnosis. This can prevent unnecessary delay of treatment and guarantee better outcomes. Close cooperation between ENT surgeons, physicians, microbiologists, and Histopathologists in the treatment and follow-up of TB cases is recommended. The treatment with standard anti-TB drug regimens developed by WHO is effective for most cases of head and neck TB. The study has been carried out in the eastern district of Libya. Therefore, the results should be interpreted with caution when considering the projection of the results on a wider area with different disease burdens.

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