

Studying cases of extrapulmonary tuberculosis in the National Center for Tuberculosis Control in Damascus

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Case Report

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Abstract

Background :

Tuberculosis (TB) is a major public health concern worldwide and is the 13th leading cause of death and the second deadliest infectious disease after COVID-19. ¹ Extrapulmonary tuberculosis (EPTB) cases accounted for 16% of the 7.5 million cases of TB worldwide in 2019. ² global statistics indicate that Tuberculosis kills about 4,500 patient every day¹.

Aims :

1. To know the epidemiology of extrapulmonary tuberculosis in Syria.
2. To know the effect of pulmonary tuberculosis risk factors on extrapulmonary tuberculosis.
3. To know the percentage of TB recurrence .
4. To know the percentage of non-adherence to tuberculosis treatment.
5. The comparison of the incidence of extrapulmonary tuberculosis over an 18-year period.

Methods :

A retrospective study conducted at the National Center for Tuberculosis Control in Damascus and its countryside for the year of 2020 to analyze the patients with extrapulmonary tuberculosis .

Results :

205 patients were diagnosed with extrapulmonary tuberculosis in Damascus and its countryside in the year of 2020 and the sites of extrapulmonary tuberculosis were distributed as follows :

Lymph Nodes TB (102) 49.75% , peritoneal TB (28) 13.66% , pleural TB (26) 12.68% , spine TB (Pott's disease) (11) 5.36% , meningeal TB (8) 3.90% , skeletal TB (7) 3.41% , skin and soft tissue TB (5) 2.44% , genitourinary TB (5) 2.44% , gastrointestinal tuberculosis (5) 2.44% , pericardial TB (3) 1.46% , eye Tb (3) 1.46% , ENT Tb (1) 0.49% , breast TB (1) 0.49%

In diagnosing tuberculosis of the lymph nodes by biopsy the affected nodes were distributed as follows :

Cervical lymph nodes 80.40% , Axillary lymph nodes 6.86% . , Supraclavicular lymph nodes 4.90% , Submandibular lymph nodes 2.94% , Mesenteric nodes 2.94% , Mediastinal nodes 1.96%.

Most incidence rate was in patients between 25 and 34 years old , while the least incidence rate was in patients older than 65 years old . The percentage of infected females was approximately 66%, while the percentage of infected males was approximately 34% . The majority of infected patients were residents in the city (78.68%) compared to infected patients from the countryside (21.31%). The most common comorbidities among patients with extrapulmonary tuberculosis were:

Hypertension: 23.41% of cases , Diabetes Mellitus : 15.12% cases , Chronic obstructive pulmonary disease: 2.4% , Covid-19: 9.75% were diagnosed with COVID-19, 9 of which were confirmed by PCR testing, and 11 cases were diagnosed clinically . 17 of those infected with Covid-19 had lymph nodes tuberculosis, two had urogenital tuberculosis, and one case was with pleural tuberculosis . Possible risk factors were : Smoking: (cigarettes and hookah) 38.53% of extrapulmonary tuberculosis patients were smokers of cigarettes and waterpipes in addition to passive smokers, while 61.46% were non-smokers , Unhealthy housing: 23.41% of patients live in an unventilated or unsunny houses , Forced displacement: 20.97% of all patients which forced them to live in crowded and unhealthy places , cases of relapse: 12 cases of recurrence (5.85%) , cases of non-adherence to tuberculosis treatment: 9 cases (4.39%) , Prisoners : 6 cases (2.92%). The most common general symptom associated with extrapulmonary tuberculosis was fever 55.60%, while night sweats was the least common symptom 14.63% .

Conclusion :

Tuberculosis is a major public health concern worldwide that can cause death or cause long-lasting complications but still is a preventable and treatable disease that's why disease prevention , early diagnosis and early treatment are vital.

Introduction

Tuberculosis is a major public health concern worldwide.

Globally, tuberculosis is the 13th leading cause of death and the second deadliest infectious disease after COVID-19. ¹

Although tuberculosis most commonly affects the lungs, it can also affect other sites and is known as extrapulmonary tuberculosis.

In 2020, an estimated 10 million people got infected with tuberculosis (TB) worldwide. 5.6 million men, 3.3 million women and 1.1 million children. TB is present in all countries and age groups but 98% of cases occur in developing countries¹. Extrapulmonary tuberculosis (EPTB) cases accounted for 16% of the

7.5 million cases of TB worldwide in 2019. ² Although it is a preventable and treatable disease, global statistics indicate that this disease kills about 4,500 patient every day¹.

Methods

A retrospective study conducted at the National Center for Tuberculosis Control in Damascus and its countryside for the year of 2020 to analyze the patients with extrapulmonary tuberculosis. The authors collected clinical data from medical records and contacted patients by phone as the medical records was missing some data. The data included sociodemographic information, information related to extrapulmonary tuberculosis.

Inclusion and exclusion criteria :

Inclusion criteria: All patients with confirmed extrapulmonary tuberculosis according to the criteria of the World Health Organization (WHO).

Exclusion criteria: cases of pulmonary tuberculosis, suspected and probable cases that have not been confirmed with EPTB, in addition to cases of insufficient data and patients who did not return to the center after diagnosis .

This study was approved by the Ethics Committee of the National Center for Tuberculosis Control of the Syrian Directorate of Health.

Results

205 patients were diagnosed with extrapulmonary tuberculosis in Damascus and its countryside in the year of 2020 and the sites of extrapulmonary tuberculosis were distributed as follows :

• Lymph Nodes TB (102) 49.75%	• Peritoneal TB (28) 13.66%
• Pleural TB (26) 12.68%	• Spine TB (Pott's disease) (11) 5.36%
• Meningeal TB (8) 3.90%	• Skeletal TB (7) 3.41%
• Skin and Soft tissue TB (5) 2.44%	• Genitourinary TB (5) 2.44%
• gastrointestinal TB (5) 2.44%	• Pericardial TB (3) 1.46%
• Eye Tb (3) 1.46%	• ENT Tb (1) 0.49%
• Breast TB (1) 0.49%	

According to this distribution, the most common type of extrapulmonary TB is lymph node TB followed by peritoneal TB, while the least common type of extrapulmonary TB is ENT TB and breast TB. **Figure1**

In diagnosing tuberculosis of the lymph nodes by biopsy the affected nodes were distributed as follows:

- Cervical nodes: 82/102 cases (80.40%).
- Axillary nodes: 7/102 cases (6.86%).
- Supraclavicular nodes: 5/102 cases (4.90%).
- Submandibular nodes: 3/102 cases (2.94%).
- Mesenteric nodes: 3/102 cases (2.94%).
- Mediastinal nodes: 2/102 cases (1.96%).

Prevalence of extrapulmonary tuberculosis by age and gender :

Most incidence rate was in patients between 25 and 34 years old , while the least incidence rate was in patients older than 65 years old . The percentage of infected females was approximately 66%, while the percentage of infected males was approximately 34% . **Table 1** shows the prevalence of extrapulmonary tuberculosis by age and gender .

Table 1.

Age	Male [n = 70]	Female [n = 135]	Total [n = 205]
0-4 years	(7/70) 10.00%	(6/135) 4.44%	(13/205) 6.34%
5-14 years	(11/70) 15.27%	(16/135) 11.85%	(27/205) 13.17%
15-24 years	(9/70) 12.85%	(28/135) 20.74%	(37/205) 18.04%
25-34 years	(16/70) 22.85%	(30/135) 22.22%	(46/205) 22.43%
35-44 years	(10/70) 14.28%	(18/135) 13.33%	(28/205) 13.65%
45-54 years	(11/70) 15.27%	(21/135) 15.55%	(33/205) 16.09%
55-64 years	(3/70) 4.28%	(10/135) 7.40%	(13/205) 6.43%
older than 65 years	(3/70) 4.28%	(6/135) 4.44%	(9/205) 4.39%

Distribution of Extrapulmonary tuberculosis types among males and females : Table 2 .

TB Type	Males [n=70]	Females [n=135]	Total [n=205]
Lymph Nodes TB	25/70 (35.71%)	77/135 (57.03%)	102/205 (49.75%)
Pleural TB	15/70 (21.42%)	11/70 (8.14%)	26/205 (12.68%)
Meningeal TB	5/70 (7.14)	3/135 (2.22%)	8/205 (3.90%)
Skin and Soft tissue TB	2/70 (2.85%)	3/135 (2.22%)	5/205 (2.44%)
gastrointestinal TB	0/70 (0.00%)	5/135 (3.70%)	5/205 (2.44%)
Eye Tb	1/70 (1.43%)	2/135 (1.48%)	3/135 (1.46%)
Breast TB	0/70 (0.00%)	1/135 (0.74%)	1/205 (0.49%)
Peritoneal TB	6/70 (8.57%)	22/135 (16.29%)	28/205 (13.66%)
Pott's disease	5/70 (7.14%)	6/135 (4.44%)	11/205 (5.36%)
Skeletal TB	5/70 (7.14%)	2/135 (1.48%)	7/205 (3.41%)
Genitourinary TB	2/70 (2.85%)	3/135 (2.22%)	5/205 (2.44%)
Pericardial TB	3/70 (4.28%)	0/135 (0.00%)	3/205 (1.46%)
ENT Tb	1/70 (1.43%)	0/135 (0.00%)	1/205 (0,49%)

Table 2. Distribution of Extrapulmonary tuberculosis types among males and females

Distribution of Extrapulmonary tuberculosis cases between rural and urban areas :

The majority of infected patients were residents in the city (78.68%) compared to infected patients from the countryside (21.31%).

Diseases associated with extrapulmonary tuberculosis :

The most common comorbidities among patients with extrapulmonary tuberculosis in the study were :

1. **Hypertension:** (48/205) 23.41% of cases.
2. **Diabetes Mellitus:** (31/205) 15.12% of cases.
3. **Chronic obstructive pulmonary disease (COPD) :** (5/205) 2.4% of cases .
4. **COVID-19:** (20/205) 9.75% were diagnosed with COVID-19, 9 of which were confirmed by PCR testing, and 11 cases were diagnosed clinically . 17 of those infected with Covid-19 had lymph nodes tuberculosis, two had urogenital tuberculosis, and one case was with pleural tuberculosis .

Possible risk factors for extrapulmonary tuberculosis :

1- Smoking (cigarettes and hookah) :

79/205 (38.53%) patients who smoked cigarettes and waterpipe in addition to passive smokers, and in contrast 126/205 (61.46%) were non-smokers.

2- Unhealthy housing: 48 cases (23.41%) live in an unventilated or sunny environment.

3- Forced displacement: 43 cases (20.97%) were displaced, which forced them to live in crowded and unhealthy places .

3- Relapse Cases:

There were 12 cases of relapse of 5.85% distributed as following :

1. 7/102 (6.86%) of Lymphocytic TB cases in the study.

2. 2/28 (7.14%) of Peritoneal TB cases in the study.

3. 2/11 (18.18%) of Pott's disease cases in the study.

4. 1/8 (12.50%) of Meningeal TB cases in the study.

4- Non-adherence to tuberculosis treatment: 9 cases were recorded (4.39%)

5- Prisoners: 6 (2.92%).

Types of extrapulmonary tuberculosis with its associated general symptoms :

The most common general symptom associated with extrapulmonary tuberculosis was fever 55.60%, while night sweats was the least common symptom 14.63% . **Table 3** shows types of extrapulmonary tuberculosis with its associated general symptoms .

TB Type	Symptoms associated General					
Lymph Nodes TB	Fever	Nodes Swelling	Single Lymphadenopathy	Multiple Lymphadenopathy	Tenderness	
	(47/102) 46.07%	(92/102) 90.19%	(90/102) 88.23%	(12/102) 11.76%	(35/102) 34.31%	
Pleural TB	Fever	Coughing	Chest Pain	Dyspnea		
	(17/26) 65.38%	(21/26) 80.76%	(19/26) 73.07	(12/26) 46.15%		
Peritoneal TB	Fever	Abdominal Pain	Ascites	Nausea and Vomiting	Diarrhea	Jaundice
	(23/28) 82.14%	(23/28) 82.14%	(28/28) 100%	(23/28) 82.14%	(6/28) 21.42%	(11/28) 39.28%
Meningeal TB	Fever	Headache	Nausea and Vomiting	Mental Confusion	Neck Stiffness	
	(5/8) 62.50%	(5/8) 62.50%	(3/8) 37.50%	(3/8) 37.50%	(5/8) 62.50%	
Pott's disease	Fever	Back Pain	Abnormalities Morphological	Abscesses	Nerve (hemiplegia) injury	
	(6/11) 54.54%	(10/11) 90.90%	(4/11) 36.36%	(7/11) 63.63%	(2/11) 18.18%	
Skeletal TB	Localized warmth	Skeletal Pain	Swellings	Movement Limitations		
	(4/7) 57.15%	(6/7) 85.72%	(5/7) 71.50%	(7/7) 100%		
Skin and tissue TB Soft	Fever	Painful Areas Erythematous	Hard Painless Ulcer			
	(3/5) 60%	(1/5) 20%	(4/5) 80%			
Genitourinary TB	Fever	Lower Abdominal Pain	Urinary Symptoms	Menstrual Changes	Sterility	
	(1/5) 20%	(2/5) 40%	(1/5) 20%	(2/5) 40%	(3/5) 60%	
TB gastrointestinal	Fever	Abdominal Pain	Bowel Habits Changes	Weight Loss	Right Iliac Fossa Mass	Nausea and Vomiting
	(2/5) 40%	(4/5) 80%	(1/5) 20%	(3/5) 60%	(1/5) 20%	(2/5) 40%
Pericardial TB	Fever	Coughing	Chest Pain	Dyspnea		
	(3/3) 100%	(2/3) 66.66%	(2/3) 66.66%	(3/3) 100%		
Eye Tb	Redness Eye	Gradual Vision Loss				
	(3/3) 100%	(3/3) 100%				

Table 3. Types of extrapulmonary tuberculosis with its associated general symptoms

Discussion

The data show that lymph node tuberculosis is the dominant type of extrapulmonary tuberculosis in Damascus city and its countryside, accounting for 49.75% of all EPTB cases. Several studies in different countries have shown that the type of extrapulmonary tuberculosis differs with different geographical location. For example, lymph nodes were the most common type of extrapulmonary tuberculosis in the Netherlands (39%), the United States (40%), and the United Kingdom (37%)^{4 5 6}, while pleural tuberculosis was the most common type of extrapulmonary tuberculosis in Poland (36%) and Romania (58%).⁷

There could be a possible reason for the difference in the most common site of EPTB infection between Syria and other countries, which is that the BCG vaccine is used in Syria which provides immunity to various forms of TB, but it is not given in many countries of the world, may cause the absence or decrease in the appearance of certain types of Extrapulmonary TB, while in countries where this vaccine is not given, the rates of emergence of the types that the vaccine decreases may be higher this was also seen in two studies about the BCG vaccine.^{8 9}

Although extrapulmonary tuberculosis primarily affects adults, 19.51% of cases occurred in children under the age of 15 years, and this may be due to the lack of vaccination due to the war in Syria and due to displacement cases, which amounted to 20.97%.

As mentioned previously, the percentage of patients infected with extrapulmonary tuberculosis was higher in the city of Damascus compared to its countryside, at a rate of 78.68%, This may have been contributed by the far distance between the tuberculosis center and the countryside, and thus the

decrease in the number of patients coming from the countryside, in addition to the movement of most of the rural population to the city, especially during the war years.

In cases that were associated with chronic diseases, the study showed that Hypertension was the most common accompanying disease with a rate of 23.41%, as well as in a Taiwanese and an Indian study.¹⁴

This study didn't show a close association between diabetes and the increase in the incidence of extrapulmonary tuberculosis (EPTB), this was also the case in a Brazilian and Taiwanese study.

As for the relation between AIDS and extrapulmonary tuberculosis, the National Center for Tuberculosis Control in Damascus and its countryside stopped conducting all HIV-related tests from 2011 due to the war's circumstances.

On the other hand, extrapulmonary tuberculosis (EPTB) was not associated with Pulmonary TB risk factors (smoking, prisons and unsanitary housing). Although smoking is considered a common social habit in Syria, according to World Bank statistics 2020, where about 4.5 million smokers were registered, only 73 cases were recorded of smoking between active and passive smoking.¹⁵ Perhaps this is due to the small sample size or the absence of an actual connection between smoking as a risk factor and between infection with extrapulmonary tuberculosis

With regard to cases of recurrence, the rate of recurrence in Pott's disease was the highest compared to the number of infections of the same type, 18.18%.

According to the records of the National Center for the city of Damascus over the course of 18 years (2003-2020), it was found that the rate of extrapulmonary tuberculosis was almost stable from 2003 to 2010, but in 2011 and 2015 we noticed a significant increase in infection numbers before they returned to their usual range between the years 2016 to 2020, this increase may be strongly attributed to the war that took place in Syria, where not all children were able to obtain the national vaccination program, which led to an increase in the incidence of many diseases, including tuberculosis, in addition to the re-emergence of other diseases such as polio. for example. **Table4**

Table 4. Number of Extrapulmonary TB cases from 2003 to 2020 :

Year	Number of Cases
2003	315 Case
2004	295 Case
2005	330 Case
2006	326 Case
2007	375 Case
2008	330 Case
2009	339 Case
2010	272 Case
2011	410 Case
2012	701 Case
2013	772 Case
2014	800 Case
2015	611 Case
2016	391 Case
2017	303 Case
2018	254 Case
2019	231 Case
2020	205 Case

References

- <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>
- <https://www.who.int/publications-detail-redirect/9789241565714>
- te Beek LA, van der Werf MJ, Richter C, Borgdorff MW Extrapulmonary tuberculosis by nationality, The Netherlands .1993-2001Emerg Infect Dis. 2006;12:1375–82 <http://dx.doi.org/10.3201/eid1209.050553>
- Peto HM, Pratt RH, Harrington TA, LoBue PA, Armstrong LR.Epidemiology of extrapulmonary tuberculosis in the United States, 1993–2006. Clin Infect Dis. 2009;49:1350–7 .<http://dx.doi.org/10.1086/605559>
- Kruijshaar ME, Abubakar I. Increase in extrapulmonary tuberculosis in England and Wales 1999–2006. Thorax64;2009 .:1090–
.5<http://dx.doi.org/10.1136/thx.2009.118133>

6. Solovic I, Jonsson J, Korzeniewska-Koseła M, Chiotan DI ,Pace-Asciak A, Slump E, et al. Challenges in diagnosing extrapulmonary tuberculosis in the European Union, 2011. *Euro Surveill.* 2013;18:20432.
7. Roy A, Eisenhut M, Harris RJ, Rodrigues LC, Sridhar S, Habermann S ,et al. Effect of BCG vaccination against Mycobacterium tuberculosis infection in children: systematic review and meta-analysis. *BMJ*:349;2014 .g4643. [http://dx.doi.org/ 10.1136/bmj.g4643](http://dx.doi.org/10.1136/bmj.g4643)
8. Pang Y, Zhao A, Cohen C, Kang W, Lu J, Wang G, et al. Current status of new tuberculosis vaccine in children. *Hum Vaccin Immunother.* 2016;12:960–70. <http://dx.doi.org/10.1080/216455152015.1120393>.
9. <https://doi.org/10.22271/27069567.2021.v3.i1i.194>
10. <https://www.ingentaconnect.com/content/iuatld/ijtld/2009/00000013/00000005/art00016#>
11. Gomes T, Reis-Santos B, Bertolde A, Johnson JL, Riley LW ,Maciel EL. Epidemiology of extrapulmonary tuberculosis in Brazil: a hierarchical model. *BMC Infect Dis.* 2014;14:9. <http://dx.doi.org/10.1186/1471-2334-14-9>
12. Lin JN, Lai CH, Chen YH, Lee SS, Tsai SS, Huang CK, et al. Risk factors for extra-pulmonary tuberculosis compared to pulmonary tuberculosis. *Int J Tuberc Lung Dis.* 2009;13:620–5.
13. https://www.google.com/publicdata/explore?ds=d5bncppjof8f9_&met_y=sp_pop_totl&idim=country:SYR:IRQ:ISR&hl=en&dl=en#!ctype=l&strail=false&bcs=d&nselm=h&met_y=sp_pop_totl&scale_y=lin

Declarations

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Availability of data and materials:

All data related to this paper’s conclusion are available and stored by the authors. All data are available from the corresponding author on a reasonable request.

Conflict of interest:

The authors declare that they have no conflict of interest.

Figures

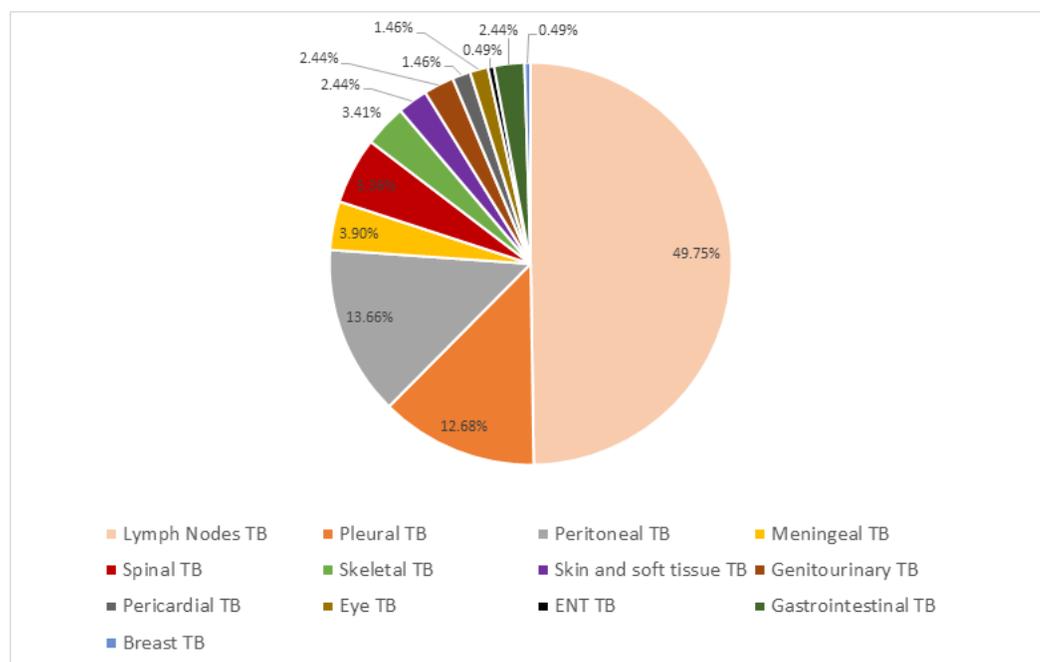


Figure 1

Prevalence of Extrapulmonary TB