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Prevalence of human tuberculosis and its correlation with abiotic parameters in the North-East of Algeria

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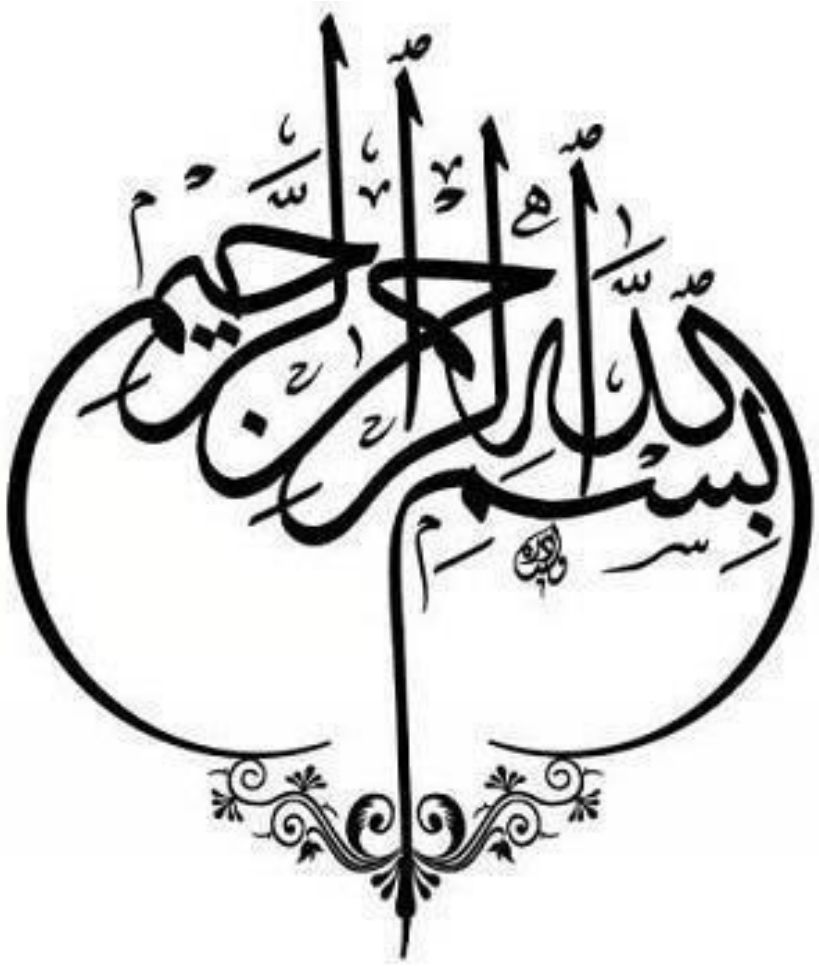
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Thanks

At the end of this work, we would like to express our thanks and our deep gratitude above all to God who gives us the strength, the courage, and the will to develop this modest work.

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Mohamed Baha Eddine and Nesrine

Dedication

Praise be to God, Lord of the worlds, and prayers and peace be upon our master Muhammad, the most honorable of the messengers, and upon his family and companions.

Years of hard work and vigil, we conclude with lines, even if they are many, they will not narrate the joy, sadness, fear, and hope we experienced... We have arrived, you who said you will not pray, so praise be to God who shamed us with His mercy, compassion, and grace. To the one who suffered from fatigue, and endured the hardships of life for us, to the one who said to me on the day that you will not be miserable as long as I live, to my support, my support, my strength and my reclining, my dear father **"Amar".**

To the warm heart and the merciful chest, to the one who gave me without question and pushed me to move forward despite the difficulties, to the one whose eyelids left sleep to comfort me, to the one who drew the slogan of success on my heart and made it a medal on my chest, to the one who owes her abundant and great credit for what she has reached, to Qara My dear mother's eyes **"Abla"** To those who are closer to me than my soul, to my support and consolation in this life to my brothers **"Houdaandimene".**

To my friends and companions, each with its own name.

To all my family and everyone who has supported and encouraged me in my life and given me a push forward.

To everyone who helped me from near or far, even with a kind word.

To all the people I met in my life and had beautiful situations with them.

To all of the breadth of my heart and did not satisfy my paper.

Finally, I dedicate this humble work to the one who supported me and took my steps with me and eased the difficulties for me, to the one who lit the lamps of knowledge and knowledge in my heart, to the one who preceded me in everything and advised me before anything happened, to the one who granted without waiting and forgave without excuses to my dear teacher.**"TayaaHakima"** To all of you... I dedicate this work.

Aziez Mohamed Baha Eddine

Dedication

Praise be to God, Lord of the worlds, and prayers and peace be upon our master Muhammad, the most honorable of the messengers, and upon his family and companions.

Years of hard work and vigil, we conclude with lines, even if they are many, they will not narrate the joy, sadness, fear, and hope we experienced... We have arrived, you who said you will not pray, so praise be to God who shamed us with His mercy, compassion, and grace.

To the one who suffered from fatigue, and endured the hardships of life for us, to the one who said to me on the day that you will not be miserable as long as I live, to my support, my support, my strength and my reclining, my dear father **"Mohamed".**

To the warm heart and the merciful chest, to the one who gave me without question and pushed me to move forward despite the difficulties, to the one whose eyelids left sleep to comfort me, to the one who drew the slogan of success on my heart and made it a medal on my chest, to the one who owes her abundant and great credit for what she has reached, to Qara My dear mother's eyes **"Linda"**To those who are closer to me than my soul, to my support and consolation in this life to my brothers **"Meriem, Hanane ,Mohsen , Ahmed".** To my sweet heart and supporter, to my warm haven my friend **"Ghada".**

To my friends and companions, each with its own name. To all my family and everyone who has supported and encouraged me in my life and given me a push forward. To everyone who helped me from near or far, even with a kind word. To all the people I met in my life and had beautiful situations with them. To all of the breadth of my heart and did not satisfy my paper.

Finally, I dedicate this humble work to the one who supported me and took my steps with me and eased the difficulties for me, to the one who lit the lamps of knowledge and knowledge in my heart, to the one who preceded me in everything and advised me before anything happened, to the one who granted without waiting and forgave without excuses to my dear teacher.**"Tayaa Hakima"** To all of you... I dedicate this work

Lalali Nesrine

Abstract

In order to determine the epidemiological and clinical characteristics of human tuberculosis in the Mila district, we developed a retrospective study during a period extending from January 2013 to December 2023, and the other prospective of three months (January-March 2024). We collected data at the level of the Directorate of Health and Population (DSP) Mila, for the retrospective descriptive analytical study we processed 90,912 examinations, 6031 were positive, with an infestation rate of 6.58%. Among the positive cases, 64.09% were women and 35.91% were men; patients aged [20-44] years are the most exposed to tuberculosis. The years 2022 and 2019 recorded the highest infection rates, 10.11% and 10.28% respectively and the spread of these bacteria was observed during the Spring season. A high rate of these bacteria was noted during the months of April, May and June.

The climatic conditions of the Mila region, such as ambient temperature, duration of insolation and wind speed increase the dissemination of the bacteria, humidity and precipitation cause a decrease in the bacterial index.

The results obtained during the three months of our prospective study (January-March 2024) confirmed what we had deduced from the results above (the retrospective study from 2013 to 2023).

Keywords: Bacteria, tuberculosis, epidemiology, prevalence, correlation, meteorological parameters, Mila.

Résumé

Afin de déterminer les caractéristiques épidémiologiques et cliniques de la tuberculose humain dans le district de Mila, nous avons élaboré une étude rétrospective durant une période s'étendant de Janvier 2013 à Décembre 2023, et l'autre prospective de trois mois (Janvier-Mars 2024). Nous avons collecté les données au niveau de la Direction de laSanté et de la population (DSP) Mila, pour l'étude analytique descriptive rétrospective nous avons traité 90.912 examens, 6031 étaient positifs, avec un taux d'infestation de 6,58 %. Parmi les cas positifs, 64,09% étaient des femmes et 35,91% étaient des hommes, les patients âgés [20-44] ans sont les plus exposés à la tuberculose. Les années 2022 et 2019 ont enregistré les taux d'infection les plus élevés, respectivement 10,11% et 10,28% et la propagation de ces bactéries a été observée durant la saison Printemps. Un taux élevé de cette bactérie a été notée durant les mois d'Avril, Mai et Juin.

Les conditions climatiques de la région de Mila, comme la température ambiante, la durée d'insolation et la vitesse du vent augmentent la dissémination de la bactérie, l'humidité et les précipitations provoquent une diminution de l'indice bactérien.

Les résultats obtenus au cours des trois mois de notre étude prospective (Janvier- Mars 2024) ont confirmé ce que nous avions déduit des résultats ci-dessus (l'étude rétrospective de 2013 à 2023).

Mots clés : Bactéries, tuberculose, épidémiologie, prévalence, corrélation, paramètres météorologiques, Mila.

ملخص

من أجل تحديد الخصائص الوبائية والسريرية لمرض السل البشري في منطقة ميلة، قمنا بتطوير دراسة استرجاعية خلال فترة تمتد من يناير 2013 إلى ديسمبر 2023، وأخرى محتملة مدتها ثلاثة أشهر (يناير – مارس 2024). قمنا بجمع المعطيات على مستوى مديرية الصحة والسكان بميلة. من أجل الدراسة التحليلية الوصفية الاسترجاعية، قمنا بإجراء 90912 فحصًا، 6031 منها كانت إيجابية، مع نسبة إصابة 6.58%. ومن بين الحالات الإيجابية، كانت 64.09% من النساء و35.91% من الرجال، والمرضى الذين تتراوح أعمارهم بين (20-44) سنة هم الأكثر عرضة للإصابة بالسل.

سجل عامي 2022 و2019 أعلى معدلات الإصابة 10.11% و10.28% على التوالي، ولوحظ انتشار هذه البكتيريا خلال أشهر أبريل ومايو ويونيو.

الظروف المناخية لمنطقة ميلة، مثل درجة الحرارة المحيطة ومدة التشميس وسرعة الرياح تزيد من انتشار البكتيريا، في حين تسبب الرطوبة وهطول الأمطار انخفاضًا في المؤشر البكتيري.

وأكدت النتائج التي تم الحصول عليها خلال الأشهر الثلاثة من دراستنا الاستطلاعية (يناير-مارس 2024) ما استنتجناه من النتائج أعلاه (الدراسة الاسترجاعية من (2013-2023).

الكلمات المفتاحية: البكتيريا، السل، علم الأوبئة، الارتباط، بارامترات العوامل المناخية، ميلة.

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Abbreviations List

ANDI	National Investment Development Agency
A.N.I.R.E.F	National Agency for Land Intermediation and Regulation
C°	Degree Celsius
TB	Tuberculosis
MTB	Mycobacterium Tuberculosis
SPSS	Statistical Package for the Social Sciences
%	Percentage
&	And
R	Correlation Coefficient
WHO	World Health Organization
PT	Pulmonary Tuberculosis
EPT	Extra Pulmonary Tuberculosis
SBI	The Simple Bacteriological Index
J.T.C.B.T.S	Joint Tuberculosis Committee of the British Thoracic Society.

Introduction

Introduction

Tuberculosis (TB) is regarded as one of the world's deadliest diseases caused by a single infectious agent, second only to acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV) . TB is caused by *Mycobacterium tuberculosis* (MTB), which can be expelled into the air when the infected people cough, talk, sneeze or sing . In most situations, MTB generally affects the lungs of infected individuals. Tuberculosis is so highly contagious that the susceptible are likely to develop TB even when they inhaled tiny particles containing MTB. The MTB is very small and can stay in the air for a long time and keep moving. The immune system is an essential defense mechanism that limits the growth and spread of MTB. If the immune system cannot suppress their growth, they will most likely spread throughout the body (Extrapulmonary TB) **(Wu et *al.*, 2020).**

The prevention and control of tuberculosis: an analysis based on a tuberculosis dynamic model derived from the cases of Americans. *BMC Public Health* . Extra-pulmonary TB can affect any part of the body and particularly the lymph, pleura, bone and joints, pericardia and the meninges. **(Agyeman et *al.*, 2017).**

One in three persons across the world representing 2–3 billion individuals are known to be infected with *Mycobacterium Tuberculosis* (M. Tuberculosis) of which 5–15% are likely to develop active TB disease during their lifetime . In 2014, an estimated 9.6 million people fell ill due to TB, around 1.5 million people died from the disease including 1.1 million HIV-negative persons and 400,000 HIV patients . While TB is present in every country majority of TB sufferers live in low income and middle income countries especially in regions such as Sub-Saharan Africa and South East Asia . Over the past decade, significant progress has been made towards TB control with most of the TB targets set as part of the Millennium Development Goals (MDGs) having been achieved . TB mortality for instance has declined by 47% since 1990, with nearly all of that happening in the era of the MDGs. In all, effective diagnosis and treatment of TB has been estimated to have saved over 40 million lives between 2000 and 2014. While these achievements are remarkable, there are calls for intensified efforts to eradicate the disease. In 2014, the World Health Assembly (WHA) adopted the End TB strategy with targets linked to the newly adopted Sustainable Development Goals (SDGs) . The End TB strategy serves as the key guide for countries to reduce TB deaths by 90% by 2030 as well as achieve an 80% reduction in TB incidence rate compared with 2015 . TB still pose as a huge threat to

economic development as over 90% of TB-related deaths occur among adults in the most productive age groups.**(Agyeman et *al.*, 2017).**

According to the WHO guideline , for new cases, a 6-month standard regimen which involves 2 months intensive phase treatment with isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) is recommended. This is followed by a 4-month continuous phase treatment involving isoniazid and rifampicin. **(Agyeman et *al.*, 2017).**

Emerging issues such as Multi-drug and extensively drug resistant TB is seen as a major challenge in effective control of the disease in many regions. Treatment outcomes for drug resistant TB are still poor and inadequate reporting remains a growing challenge. Of the 480,000 cases of multidrug-resistant TB (MDR-TB) estimated to have occurred in 2014, only about 25% were detected and reported . Moreover, just around 30% of the over 7,000 MDR-TB patients from 13 countries were successfully treated in 2007 **(Agyeman et *al.*, 2017).**

BCG is the most commonly administered vaccine in the world and has been used for TB prevention for 100 years. A meta-analysis of 1264 studies on BCG vaccination showed that on an average BCG vaccination provides 50% protection from different forms of TB across ages.Also, using a mathematical model, it has been estimated that 90% global BCG vaccination coverage prevents 117 132 TB deaths per birth cohort up to the age of 15 . In adults, BCG-induced protection against TB in different populations can range from very high (incidence rate ratio 0.22) to very low (incidence rate ratio 1.05). However, the consensus from data that has emerged from numerous trials is that BCG efficacy is variable and appears to be influenced by numerous factors such as age at vaccination , BCG strains and route of administration . .**(Agyeman et *al.*, 2017).**

Formerly, a country with a high TB prevalence, Algeria was able to join the group of countries with moderate prevalence since the 1980s. Throughout half a century, considerable efforts were made to improve the care, the detection rate of sputum smear-positive PTB cases, and treatment of TB. The incidence per 100,000 inhabitants of PTB declined by 49.1% from 1982 to 2018 and that of EPTB decreased first by 29.5% from 1982 to 1992, and then increased gradually between 1993 and 2018 by 20.8%. Between 1982 and 2000, PTB has been in the lead. In 2001, EPTB cases took over and stayed ahead since. **(Selmane and L'Hadj 2020).**

Indeed, climate change can also have an impact on the overall human health system. Fluctuations in extreme temperatures, extreme weather events such as floods or droughts, and

changes in seasonal patterns can cause social and economic instability, which in turn can affect the spread of TB. These factors can lead to human migration, food insecurity, reduced nutritional status, and vulnerability to infectious diseases, including TB. **(Tosepu et al., 2023).**

Our objective is to establish an epidemiological situation update on the evolution of tuberculosis in the Mila region at the laboratory level of the service for the fight against tuberculosis and respiratory diseases (S.C.T.M.R) of the public clinical establishment Bouaarouj – Mila during the period (2013 to 2023) , the main objectives are:
A. Identify existing cases of tuberculosis (pulmonary and extra-pulmonary) in the wilaya of Mila.

B. Determine certain parameters that may influence the proportions of affected subjects (Age, sex, type of tuberculosis, location (for extra-pulmonary tuberculosis) and year, etc.).

C. Appreciate the correlation between the spread of *Mycobacterium tuberculosis* and meteorological parameters.

Apart from the introduction and conclusion, as well as some suggestions and recommendations, this work is subdivided into four chapters:

* The first will deal with bibliographical synthesis;

* The second will deal with materials and methods;

*The third will have to present and interpret the results;

* The fourth will be devoted to the discussion of the results obtained.

Chapter I:

Presentation of Biological Model

1. PRESENTATION OF BIOLOGICAL MODEL

1.1. History of Tuberculosis

Tuberculoses a disease also historically known as consumption, wasting disease, and the white plague have affected humans for centuries. Until the mid-1800s, people thought that tuberculosis, or TB, was hereditary or attributable to an unhealthy life. They did not realize that it could be spread from person to person through the air. Also, until the 1940s and 1950s, there was no antibiotic treatment for TB. For many people, a diagnosis of TB was a slow death sentence. TB has affected humans for centuries. **(SSMOT , 2019)**

In 1865 a French surgeon, Jean-Antoine Villemin , showed that TB was contagious, and in 1882 a German scientist named Robert Koch discovered the bacterium that causes TB. Yet, half a century passed before drugs were discovered that could treat TB. Until then, many people with TB went to sanatoriums, which were special rest homes where they followed a prescribed routine every day. No one knows whether sanatoriums really helped people with TB; and even if they did, many people with TB could not afford to go to a sanatorium, and they died at home. A breakthrough came in 1943. An American scientist, Selman Waksman and one of his assistants, Albert Schatz, discovered a drug that could kill TB bacteria. Between 1943 and 1952, two more drugs were found. After these discoveries, many people with TB were treated, and the death rate for TB in the United States dropped dramatically. Each year, fewer and fewer people died from TB. **(SSMOT , 2019)**

In the 1940s and 1950s, drugs were discovered to treat TB. After this, the death rate for TB in the United States dropped dramatically, and fewer and fewer people died from TB. The funding helped health departments and other organizations successfully boost their eforts to prevent and control the disease. Since 1993, TB cases in the United States overall have been steadily declining. However, prevention and control eforts must be maintained, since TB continues to be reported in every state throughout the country. Moreover, even today, TB can be fatal if not treated in time. A timeline of major events in the history of TB is shown in Figure 1.1. In the mid-1980s, the number of TB cases started increasing again. Since 1993, due to enhanced prevention and control eforts, the number of TB cases has been declining. **(SSMOT , 2019).**

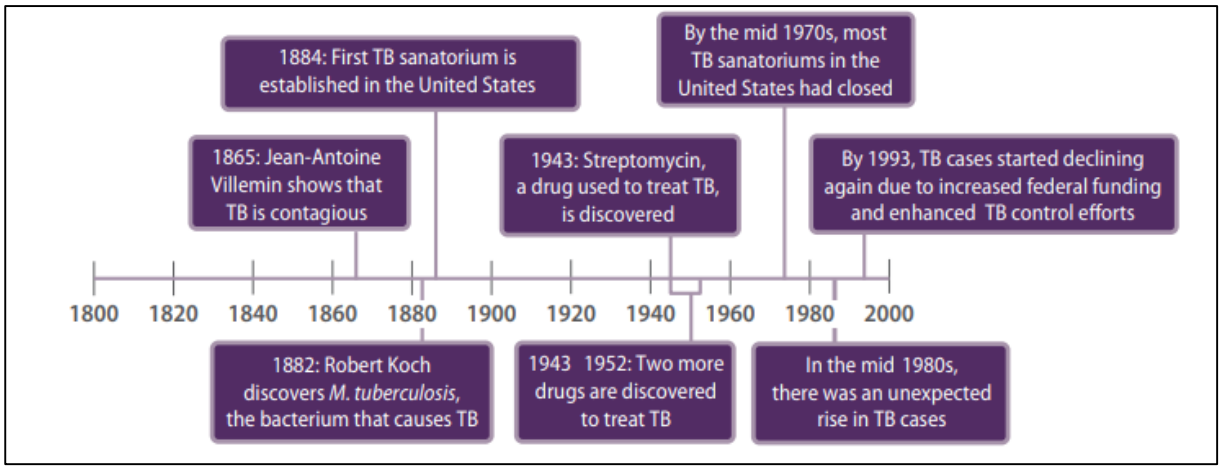

Fig. 01 : Timeline of major events in the history of TB**. (Blamed, 2012).**

The Timeline in **figure 01** illustrating the major events in the history of TB from 1800-2000. 1865: Jean-Antoine Villemin shows that TB is contagious Ÿ 1882: Robert Koch discovers M. tuberculosis, the bacterium that causes TB Ÿ 1884: First TB sanatorium is established in the United States Ÿ 1943: Streptomycin, a drug used to treat TB, is discovered Ÿ 1943–1952: Two more drugs are discovered to treat TB Ÿ By the mid-1970's most TB sanatoriums in the United States had closed Ÿ In the mid -1980's there was an unexpected rise in TB cases Ÿ By 1993, TB cases started declining again due to increased federal funding and enhanced TB control efforts . **(SSMOT , 2019)**

1.2. The study of the Path physiology of Tuberculosis

1.2.1. Characteristics of *Mycobacterium tuberculosis*

Bacillus *Mycobacterium tuberculosis* (variant tuberculosis), along with other variants (e.g. *bovis* , *africanum* , *microti*), make up the Mycobacterium tuberculosis complex, a group of bacteria that cause clinical tuberculosis (TB) in humans .

Most TB cases are caused by *M. tuberculosis* variant tuberculosis. Cases due to other variants are less prevalent. *M. tuberculosis* is a small, rod-shaped, strictly aerobic, acid-fast bacillus. Like other mycobacterium, it is slow growing, resulting in more gradual development of disease when compared with other bacterial infections. **(Kinsi and Nimao, 2019)**

Tuberculosis is an infection caused by the rod-shaped, non-spore-for ming, aerobic bacterium *Mycobacterium tuberculosis*. *Mycobacterium* commonly measure 0.5 μm by 3 μm, are classified as Acid-fast bacilli, and have a unique cell wall structure crucial to their survival. The well developed Cell wall contains a considerable amount of a fatty acid, my colic acid, covalently Attached to the underlying peptidoglycan-bound polysaccharide arabinogalactan

(Biopolymer Consisting of arabinose and galactose monosaccharide), providing an extraordinary lipid barrier. This barrier is responsible for many of the medically challenging physiological characteristics of Tuberculosis, including resistance to antibiotics and host defense mechanisms. The composition and quantity of the cell wall components affect the bacteria's virulence and growth rate**. (Kinsi and Nimao, 2019)**

The Peptidogly can polymer confers cell wall rigidity and is just external to the bacterial cell Membrane, another contributor to the permeability barrier of mycobacterium. Another important Component of the cell wall is lipoarabinomannan (Glycolipid and major virulence factor in the Bacteria genus Mycobacterium), a carbohydrate structural antigen on the outside of the organism that is immunogenic and facilitates the survival of *mycobacterium* within macrophages. The cell Wall is key to the survival of *mycobacterium*, and a more complete understanding of the Biosynthetic pathways and gene functions and the development of antibiotics to prevent formation of the cell wall are areas of great interest. **(Kinsi and Nimao, 2019).**

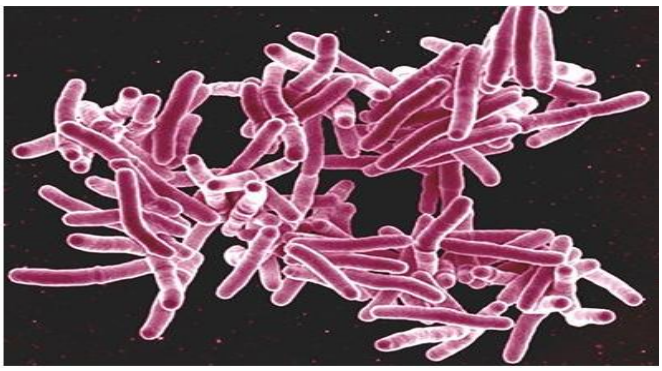

Fig. 02 : Bacterium *Mycobacterium tuberculosis* **(website 01)**

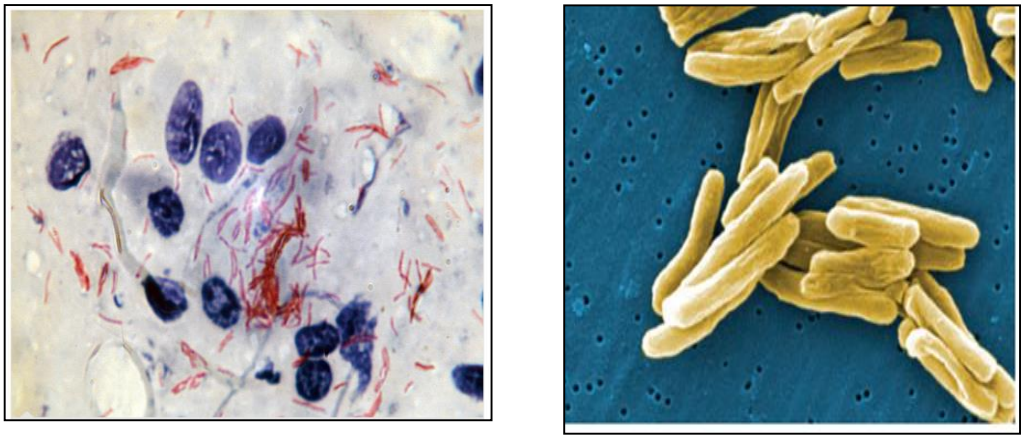

Fig.03 : Bacilli tuberculeux ***(****Mycobacterium tuberculosis****)*** **(website 02,03)**

1.2.2.Taxonomy and Classification

The causative agent of pulmonary/respiratory tuberculosis in humans is the Gram-positive bacillus, *Mycobacterium tuberculosis* (Mtb). During experimental infections, the bacterium can shift from lipid metabolism and microaerophilic mode to carbohydrate metabolism and aerobic mode. And like other Mycobacteria species, the Mtb is a facultative intracellular parasite that proliferates inside phagocytic cells namely monocytes and macrophages. Disturbingly, the bacterium can persist in humans for many decades even in the presence of a healthy immune system**. (Venus , 2021)**

a. Taxonomy

As shown in **Table.01** , the family of the bacterium is under the order Actinomycetales, which is closely related to bacteria such as Nocardia, Corynebacterium, and Rhodococcus. Mtb is a known member of the *Mycobacterium tuberculosis* complex that is composed of several species namely, *M. bovis*, *M. caprae*, *M. africanum*, *M. microti*, all of which are causative agents of tuberculosis in different hosts. Interestingly, *Mycobacterium tuberculosis*, the most clinically significant species of the family, was previously thought to have evolved from *M. bovis* due to the domestication of cattle. However, genome analyses proved otherwise. **(Venus , 2021)**

Table.01. Taxonomic classification of the pathogenic obligate aerobe, *Mycobacterium tuberculosis*

Domain	Bacteria
Phylum	Actinobacteria
Class	Actinobacteria
Order	Actinomycetales
Family	Mycobacteriaceae
Genus	*Mycobacterium*
Species	*Mycobacterium tuberculosis*

1.2.3. Cellular Morphology

A major hallmark of the Mtb is the complexity of its cell wall structure that is rich in polysaccharides and lipids, providing an exceptionally robust impermeable barrier against noxious drugs and compounds. Advancements in microscopic techniques has revealed that the bacterium possesses an outer membrane that is functionally analogous to what is observed in Gram-negative bacteria, packed in an asymmetric lipid bilayer composed of glycolipids and waxy substances on the outer layer and long fatty acid chains (C60 to C90) in the inner layer (my colic acids).

Together, the outer and inner membranes constitute the periplasmic space, with a thin peptidoglycan layer in the innermost layer covalently linked to the lipoarabinomannan and arabinogalactan, that are joined to the my colic acids **(Venus , 2021)**

Another structure that can be found in the Mtb cell envelope is its external mycobacterium capsule. Only superficially linked to the cell wall, the Mtb capsule can be ridden off the growth medium while still keeping the some physico-chemical properties.

Under laboratory conditions, the components of the capsule include polysaccharides (neutral), proteins, and lipids. The overall thick cell wall architecture of Mtb and other Mycobacterium renders them resistant to Gram-staining. This is for the reason that when stained with Gram stain dyes, the cell wall can resist the acid alcohol decolourizer and gives the nickname, “acid-fast”. This property served as the basis for the development of novel staining methods and the foundation for diagnosing tuberculosis. **(Venus , 2021)**

Interestingly, the actively-replicating acid-fast-positive Mtb can sometimes become a dormant acid-fast-negative bacteria, and this loss of property is called the Koch’s paradox. This usually happens during an infection where the cell wall composition is changed and physiological metabolism is altered due to the entry to dormancy. This phenomenon is believed to harbour significant consequences for the epidemiology and diagnosis of tuberculosis**. (Venus , 2021)**

Mycobacterium bovis is a member of the *M. tuberculosis* complex (MTBC), a very closely related phylogenetic group which includes M. tuberculosis, M. microti and M. africanum and along with other *Mycobacterium* causes disease among animals and humans . The latest phylogenetic analyses suggest that all members of the MTBC should be regarded as subspecies or host-adapted strains of a single bacterial species *(M. tuberculosis)*. Therefore,

according to strict molecular criteria, these organisms should be named *M. tuberculosis* ssp. *tuberculosis, M. tuberculosis* ssp. bovis and so on. This, however, has not been widely accepted by the scientific community (De la Rua-Domenech 2006) and hence the names *M. tuberculosis*, *M. Bovis* **,** etc. as first proposed by Karlson and Lessel (1970) have been used in this review. *Mycobacterium bovis* has one of the broadest host ranges of all known pathogens and has been shown to be the principal agent of tuberculosis in a wide range of domestic and wild animals (O'Reilly and Daborn 1995). *Mycobacterium bovis* infection of humans is indistinguishable clinically and pathologically from M. tuberculosis, with differentiation only being achieved by sophisticated laboratory methods involving bacteriological culture followed by typing of isolates according to growth characteristics and biochemical properties .**(Rowe and Donagh, 2008)**

1.3. The study of disease

1.3.1.Tuberculosis Definition

Tuberculosis, a deadly disease of the pulmonary system, is caused by a group of closely related, slowly growing mycobacteria collectively named the M. tuberculosis complex (MTC). The name "tuberculosis" comes from the nodules, called "tubercles", which form in the lymph nodes of affected animals. The members of the MTC include M. tuberculosis, M. bovis, Mycobacterium bovis bacille Calmette-Guérin (BCG), Mycobacterium caprae, M. africanum, Mycobacterium pinnipedii, Mycobacterium microti, Mycobacterium mungi, and M. canettii. With the exception of strain BCG, all MTC members are pathogenic and capable of causing tuberculosis in a variety of mammalian hosts. MTC strains are approximately 99.9% similar at the genetic level, but there are distinct differences phenotypically with regard to the level of their pathogenicity. Among all of these pathogenic mycobacteria, M. tuberculosis sensu stricto has emerged as the most prevalent mycobacterial species and one of the most historically successful human pathogens. Approximately one-third of the world's population is infected with mycobacteria capable of causing tuberculosis.**(website 4) .**

Tuberculosis (TB) is an infectious disease caused by a bacterium of the Mycobacterium (M. tuberculosis) complex **(Raviglione & Gori, 2022).** TB is primarily a respiratory disease that is transmitted by inhalation of airborne infected droplets. However, other organ systems can also be affected **(Raviglione & Gori, 2022)**; these conditions are called extrapulmonary TB and miliary TB.

Tuberculosis is usually spread from one person to another through droplet infection. This means that if an individual is carrying the tuberculosis bacteria in their lungs, by coughing up phlegm that carries the tuberculosis bacteria, they can spread it from one individual to another. In other words, tuberculosis spreads only on close contact.

Tuberculosis generally affects people of the lower socio-economic classes because of a lack of sanitary conditions and closed living spaces.The presence of the human immunodeficiency virus i.e. HIV is a strong risk factor for tuberculosis as well.Those who suffer from diabetes also have altered immunity and may have an inability to fight the tuberculosis bacteria. Finally, individuals who are taking certain medications that suppress their immunity are also prone to picking up tuberculosis infection. **(website 5)**

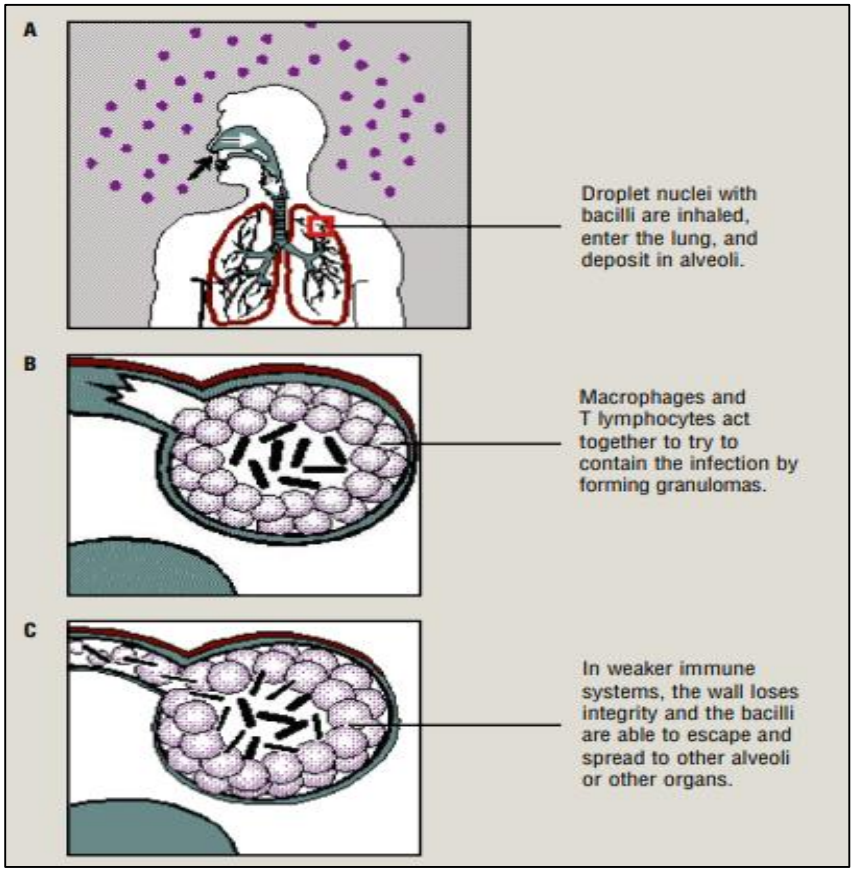

Fig. 04 : Pathophysiology of tuberculosis. **(Knechel, 2009).**

Pathophysiology of tuberculosis : inhalation of bacilli (A), containment in a granuloma (B), and breakdown of the granuloma in less immunocompetent individuals (C). **(Knechel, 2009).**

1.3.2. Pathogenesis and Morphology of Tuberculosis

The sequence of events/pattern of host response following an infection depends on the state of host immunity and whether the infection represents a primary exposure to the organism or secondary reaction in an already sensitized host. **(UDOH ,2009)**

- **Primary infection**

With *M. Tuberculosis* begins with inhalation of the organism and ends with a T-cell mediated immune response that controls the infection in 95% of cases. Inhaled *M. Tuberculosis* is endocytosed by alveolar macrophages by binding lipoarabinomannam on the bacterial cell wall through mannose receptors and binding opsonized mycobacteria through complement receptors. At this point the macrophages are naïve and unable to kill mycobacteria which multiply, lyses the host cell, infect more macrophages and through them reach the hilar lymph nodes. **(UDOH ,2009)**

Live bacteria prevent phagolysosome fusion by mechanisms including inhibition of Ca2+ signals and blockage of recruitment and assembly of proteins mediating phagolysosome fusion. Dissemination through the blood to other parts of the lungs and body may occur at this stage. A T-cell mediated immunity demonstrable by a positive purified protein derivative test reaction usually develops at about 3wk post infection This T helper 1 (THI) response activates macrophages to become bactericidal. **(UDOH ,2009)**

This THI response is stimulated by mycobacterial antigenes draining to Lymph Nodes and presented by Antigen Presenting Cells which produce IL-12 that causes the differentiation of THI cells. Activation of T-cells leads to the following • CD4+ T cells secrete INγ to activate macrophages leading to epitheloid cell and granuloma formation and killing of intracellular mycobacterium through reactive Nitrogen Intermediates (NO,NO2,HNO3) • CD8+ T cell lysis of infected macrophages with killing of mycobacterium this process is Fas independent, granule dependent • CD4- CD8- T cells lyse macrophages without killing bacteria (Fas dependent). Lyses of the macrophages results in the formation of caseating granulomas. mycobacteria being unable to grow in this acidic excracellular anaerobic environment are thus contained. **(UDOH ,2009)**

- **Morphology**

Generally the only evidence of infection that remains if any is a tiny fibrocalagic scar at the site of healed infection. Active lesions are seen as characteristic granulomatous inflammatory reaction that form caseating [**Fig. 5 and 6]** and non cassation tubercles [**Fig.7] .** Individual tubercles are microscopic but may coalesce to become macroscopically visible **(UDOH ,2009)**

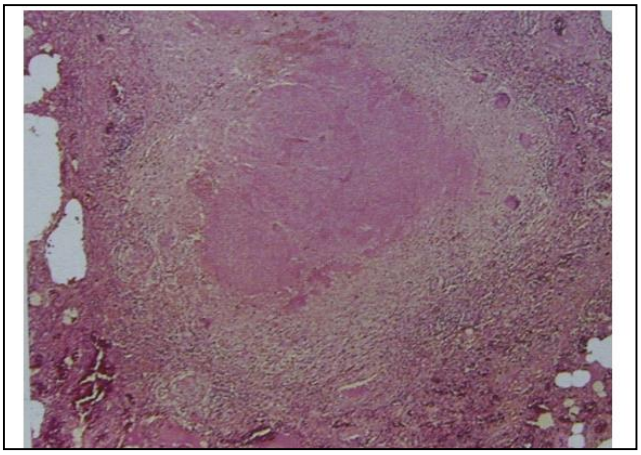

Fig. 5 : Caseating Tubercle **(UDOH ,2009).**

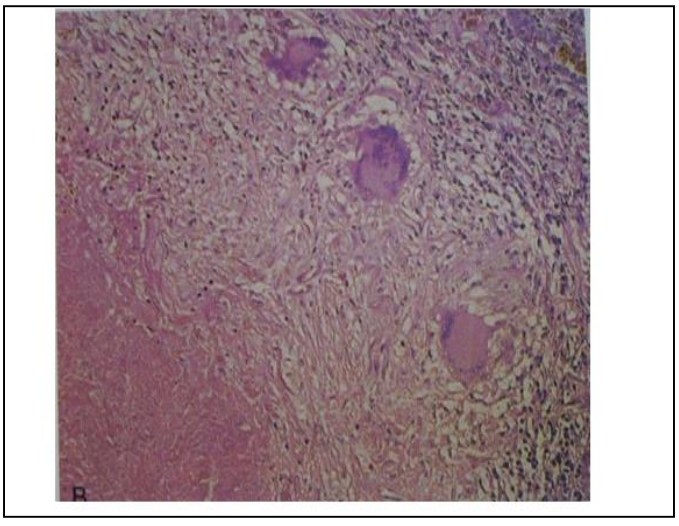

Figure.6 : Caseating Tubercle . **(UDOH ,2009).**

Granulomas are an accumulation and epitheloid macrophages arranged in small clusters or nodular collections surrounded by a fibroblastic rim punctuated by lymphocytes. some the macrophages form giants cells and in TB a central area of caseating necrosis is characteristically seen [**Fig.7]. (UDOH ,2009)**

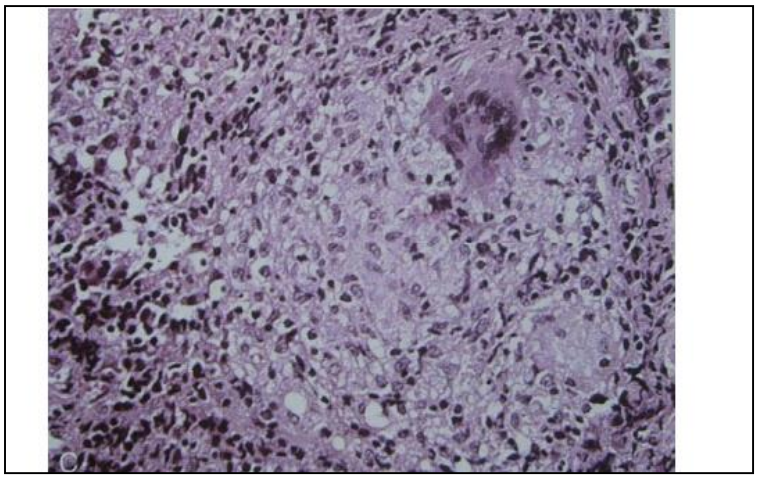

Figure 7 : Non-Caseating Tubercle. **(UDOH ,2009)**

- **Secondary and Disseminated TB**

This occurs as a result of a reinfection, reactivation of dormant disease or direct progression of a primary TB into disseminated disease. This may be due to increased susceptibility of the host to disease or to a particularly virulent strain of mycobacterium**. (UDOH ,2009)**

Granulomas of secondary TB are found most often in the lung apices or may be disseminated in the lungs, kidneys, meanings, marrow and other organs. These granulomas that fail to contain mycobacterium infection are the major cause of tissue damage in secondary TB. Cavities are a common feature of 20 TB. Necrosis may rupture into vessels or airways spreading mycobacterium throughout the body or releasing them in aerosols.(UDOH ,2009)

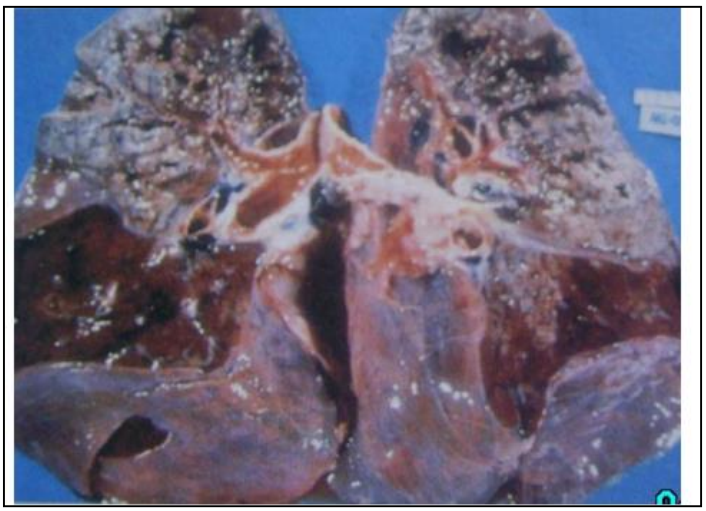

Fig. 08 : Secondary Pulmonary TB **(UDOH ,2009)**

- **Morphology of Secondary TB**

Secondary TB may take any of many forms. In all, granulomas are seen in the organs or at sites involved. Initial lesion is usually a small area of consolidation at the lung apex. Progressive pulmonary TB, common in elderly or immunocompromised , occurs as an expansion of apical lesion [**Fig.08]** with expansion of area of caseation erosion into bronchus evacuates the caseous center leaving a cavity. **(UDOH ,2009)**

- ✓ miliary pulmorary TB occurs as a consequence of lymphatic drainage ultimately to the right heart, then to pulmonary arterial circulation producing microscopic or milet seed lesions throughout the lungs. Pleural effusion, tuberculous empyema and tuberculous fibrous pleuritis may develop.
- ✓ Endobronchial, endotracheal, laryngeal TB
- ✓ Systemic miliary TB- liver, bone, adrenals, spleen , kidneys, meninges
- ✓ Isolated organ TB
- ✓ Lymphadenitis –usully unifocal
- ✓ Intestinal TB – mucosal ulceration. **(UDOH ,2009).**

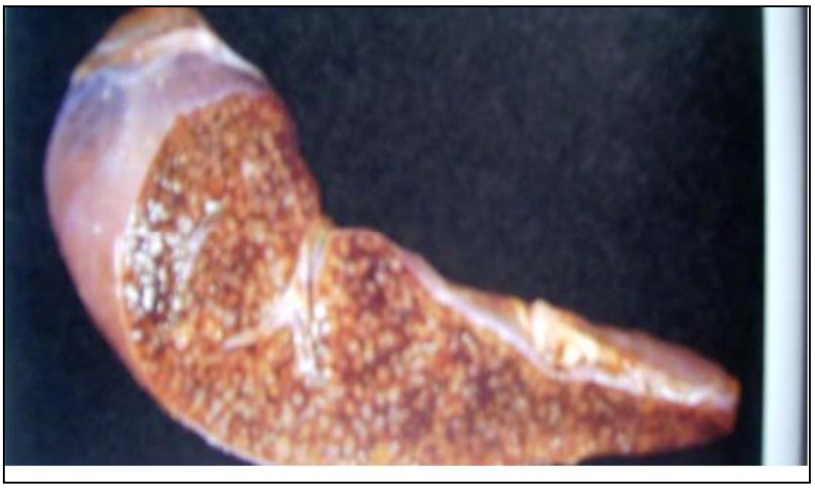

Figure .09 : Miliary TB of The Spleen. **(UDOH ,2009).**

- **Mycobacterium Avium Intracellulare Complex**

The 3 subspecies or *Mycobacterium Avium and Mycobacterium Intracellular* cause similar infections and are simply referred to as *Mycobacterium Avium* Intracellular Complex or MAC. Clinically significant infection is only common among people with AIDS and low CD4+ *T LYMPHOCYTES* (<60CELLS/mm3) Disseminated disease with high levels of organisms is seen in AIDS. Patients are feverish, lose weight and have drenching night sweats. Rarely in

patients without HIV, MAC infection occurs and presents primarily as a pulmonary infection with productive cough and weight loss. **(UDOH ,2009).**

- **Morphology**

Widely disseminated infection affecting lymph nodes, liver and spleen . Organ may have a yellow tinge due to abundant organisms in tissue macrophages. Microscopically abundant acid-fast bacilli are seen within macrophages (Fig. 10). Granulomes, lymphocytes and tissue destruction are rare**. (UDOH ,2009).**

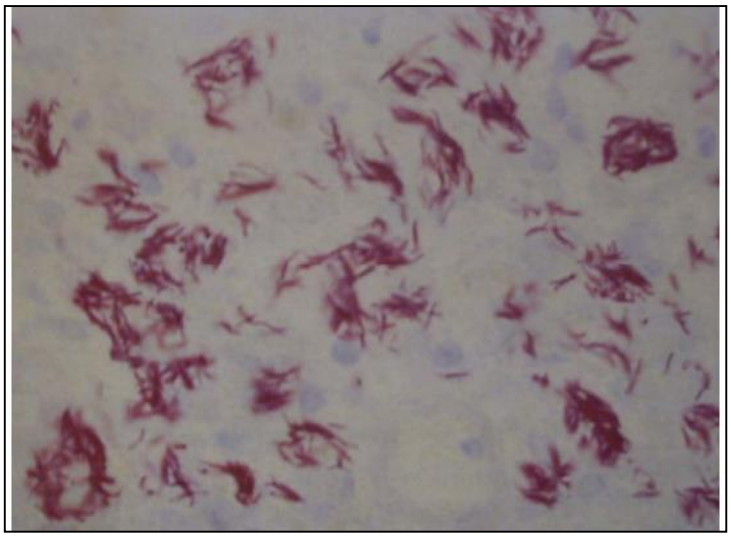

Figure 10 : Abundant Acid-Fast Bacillin Macrophages**. (UDOH ,2009).**

1.3.3. Tuberculosis Types

1.3.3.1. Pulmonary Tuberculosis

Pulmonary tuberculosis (TB) is a common worldwide lung infection. Classically, tuberculosis is divided into primary, common in childhood, and postprimary, usually presenting in adults. Several complications are associated with tuberculous infection, such as hematogenous dissemination (miliary tuberculosis) or extension to the pleura, resulting in pleural effusion. **(Andreu *et al.*, (2004).**

1.3.3.1.1. Primary Disease

Primary pulmonary tuberculosis is often asymptomatic, so that the results of diagnostic tests are the only evidence of the disease. Associated paratracheal lymphadenopathy may occur because the bacilli spread from the lungs through the lymphatic system. If the primary lesion enlarges, pleural effusion is a distinguishing finding. This effusion develops because the bacilli

infiltrate the pleural space from an adjacent area. The effusion may remain small and resolve spontaneously, or it may become large enough to induce symptoms such as fever, pleuritic chest pain, and dyspnea. Dyspnea is due to poor gas exchange in the areas of affected lung tissue. (Knechel, (2009).Dullness to percussion and a lack of breath sounds are physical findings indicative of a pleural effusion because excess fluid has entered the pleural space. **(Knechel, 2009).**

A. Latent Tuberculosis

Persons with latent tuberculosis have no signs or symptoms of the disease, do not feel sick, and are not infectious. and if the immune system later becomes compromised, as it does in many critically ill patients, the disease can be reactivated. Although coinfection with human immunodeficiency virus is the most notable cause for progression to active disease, other factors, such as uncontrolled diabetes mellitus, sepsis, renal failure, malnutrition, smoking, chemotherapy, organ transplantation . Additionally, persons 65 years or older have a disproportionately higher rate of disease than any does other age group, often because of diminishing immunity and reactivation of disease. **(Knechel, 2009).**

Immune reactivity to *Mycobacterium tuberculosis* is assessed by either tuberculin skin testing (TST) or interferon-gamma release assay (IGRA), with a positive result by either method indicating LTBI. **(Salgame *et al.*, 2015).**

Fig. 11 : This is a primary form of tuberculosis f, later accompanied by necrosis and formation of fistulae. **(Kumar *et al.*, 2010)**

B. Primary Progressive Tuberculosis

Active tuberculosis develops in only 5% to 10% of persons exposed to M tuberculosis. . Manifestations often include progressive fatigue, malaise, weight loss, and a low-grade fever accompanied by chills and night sweats. Wasting, a classic feature of tuberculosis, is due to the lack of appetite and the altered metabolism associated with the inflammatory and immune responses. Wasting involves the loss of both fat and lean tissue; the decreased muscle mass contributes to the fatigue. Finger clubbing, a late sign of poor oxygenation, may occur . A cough eventually develops in most patients. Although the cough may initially be nonproductive, it advances to a productive cough of purulent sputum. The sputum may also be streaked with blood. Hemopty sis can be due to destruction of a patent vessel located in the wall of the cavity, the rupture of a dilated vessel in a cavity, or the formation of an aspergilloma in an old cavity. The inflamed parenchyma may cause pleuritic chest pain. Extensive disease may lead to dyspnea or orthopnea because the increased interstitial volume leads to a decrease in lung diffusion capacity. Hematologic studies might reveal anemia, which is the cause of the weakness and fatigue. Leukocytosis may also occur because of the large increase in the number of leukocytes, or white blood cells, in response to the infection. **(Knechel, 2009).**

C. Reactivation

Approximately 90% of all cases of TB in adults are a reactivation of latent infection. Reactivation typically occurs several years after the infection . The clinical presentation of primary progressive TB and reactivation of latent TB are indistinguishable .

1.3.3.2. Extrapulmonary tuberculosis

extrapulmonary tuberculosis is defined according to WHO classification criteria as an infection by M.tuberculosis which affects tissues and organs outside the pulmonary parenchyma. It represents between 20 and 25% of all TB cases .Extrapulmonary TB (EPTB) results from the hematogenous and lymphatic spread of M.tuberculosis bacilli. **(Ramirez *et al.*, 2015).**

A. Miliary tuberculosis

The term “miliary” refers to innumerable small pulmonary nodules scattered through the lung like millet seeds in the pathology sample. However, today it also refers to progressive and widely spread forms of TB. It entails a hematogenous spread of the disease to several organs and it can be a result of primary infection (especially in children) or of the reactivation of a

latent focus. It is a severe manifestation of the disease mainly involving elderly, malnourished patients and individuals with altered cell-mediated immunity such as HIV infected patients, people suffering from chronic kidney disease, solid organ transplant recipients and individuals undergoing antiTNF therapies. The most frequently affected organs are the liver, the spleen, the lung, the lymph nodes, the meninges, the bone marrow and the adrenal glands. **(Ramirez *et al.*, 2015).**

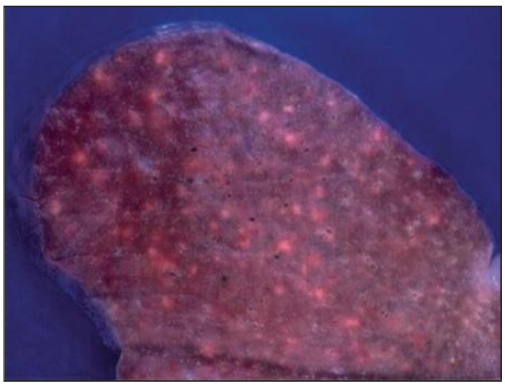

Fig. 12 : Miliary tuberculosis . **(Kumar *et al.*, 2010)**

B. Osteoarticular tuberculosis

It accounts for 11% of EPTB forms according to published series . Although it can affect any bone, spondylitis or Pott disease, represents 50% of all cases . **(Ramirez *et al.*, 2015).**

Infection generally begins with inflammation of the anterior aspect of vertebral bodies, typically, it spreads behind the anterior ligament to the disc and to adjacent bodies. Eventually the infection can spread to adjacent soft tissues with the formation of paravertebral abscesses and affecting the posterior aspect of vertebral bodies eventually involving the spinal cord which is then at risk of compression. Pott disease most commonly affects the lower thoracic region in younger patients and the upper lumbar region in elder patients. **(Ramirez *et al.*, 2015).**

Tuberculous arthritis can occur in virtually any joint, but it tends to occur in the hip or in the knee. **(Ramirez *et al.*, 2015).**

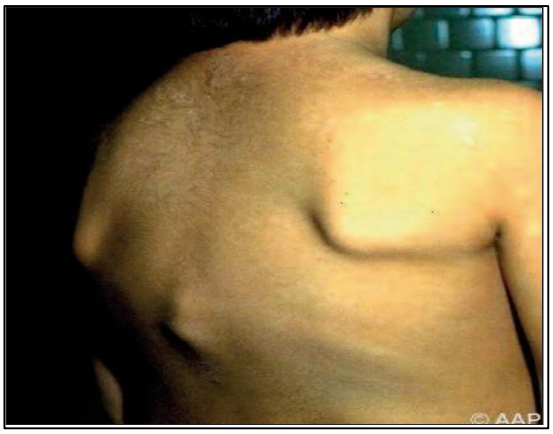

Fig. 13 : Spinal tuberculosis. **(Kumar *et al.*, 2010).**

C. Lymph node tuberculosis

It is one of the most common forms of extrapulmonary tuberculosis and it most frequently affects children and young adults. It accounts for between 30 and 40% of all EPTB cases . It can be due to a primary form or to the reactivation of a focus. The most common location is cervical lymphadenopathy (63-77%) although it can also affect other areas such as supraclavicular, axillary, thoracic and abdominal nodes **(Ramirez *et al.*, 2015).**

D. Genital tuberculosis

In men, the involvement of the prostate, epididymis and testicles is common with the development of subacute prostatism and epididymoorchitis. Microbiological testing of urine, prostatic fluid samples or FNAB or open biopsy samples is necessary for the establishment of the diagnosis. In women, the Fallopian tubes are bilaterally involved in up to 80% of cases. This is a common cause of abdominal pelvic pain and in developing countries it is a common cause of infertility. Diagnosis requires the realization of hysterosalpingography and culture of menstrual fluid, endometrial biopsy and sampling of other affected tissues by means of laparoscopy **(Ramirez *et al.*, 2015).**

E. Urinary tuberculosis

Genitourinary tuberculosis is a common form of extrapulmonary disease, it has been estimated to account for 6.5% of all cases. It is more common in men than in women. Hematogenous seeding at the time of primary pulmonary infection can lead to renal involvement; infection can also occur in the setting of late reactivation disease or miliary disease. **(Ramirez *et al.*, 2015).**

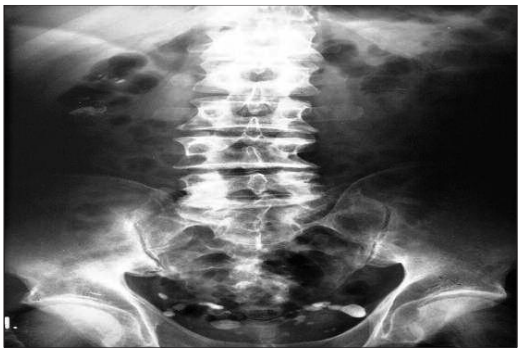

Fig. 14 : Plain abdominal radiograph in a male patient with genitourinary tuberculosis . **(Kumar *et al.*, 2010).**

F. Pleural tuberculosis

It is a common form of EPTB, accounting for almost 20% of all cases. It is caused by a set of hypersensitivity reactions against mycobacterial antigens in the pleural space. These organisms and/ or their antigens probably enter the pleural space due to leakage or rupture of a subpleural focus of disease.**(Ramirez *et al.*, 2015).**

G. Tuberculous pericarditis

Pericardial infection with *Mycobacterium tuberculosis* may occur via extension of infection from the lung or tracheobronchial tree, adjacent lymph nodes, spine, sternum, or via miliary spread. It is usually associated to concomitant infection in other locations. **(Ramirez *et al.*,2015).**

Ecocardiography can be useful in the establishment of the diagnosis as well as in the assessment of potential complications such as constrictive pericarditis and cardiac tamponade. Tuberculous pericardial effusions are typically exudative and characterized by high protein content and increased leukocyte count, with a predominance of lymphocytes and monocytes.. **(Ramirez *et al.*, 2015).**

H. Central nervous system tuberculosis

CNS tuberculosis occurs due to hematogenous spread from distal foci or during a disseminated form of the infection. It is a severe form of the disease which entails high morbidity and mortality: 25% of patients can suffer some type of sequelae and between 15 and 40% can pass away despite the initiation of treatment. Tuberculous meningitis is the most common form of the disease, yet the infection can also entail intracranial tuberculoma and

periarteritis and vascular thrombosis with the development of ischemic stroke and proliferative arachnoiditis which can eventually produce obstructive hydrocephalus with intracranial hypertension. Tuberculous meningitis typically presents a subacute insidious course. Initially it can present headache, malaise, lassitude and progressively lethargy, coma and for the majority of untreated patients, death ensues within five to eight weeks of the onset of illness. Intracranial tuberculoma can be asymptomatic or produce headache, seizure or some type of neurological impairment. Early treatment is of paramount importance to avoid complications. **(Ramirez *et al.*, 2015).**

I. Gastrointestinal and peritoneal tuberculosis

Tuberculous enteritis can involve any aspect of the gastrointestinal tract although the ileocecal region is the most common site of intestinal involvement. The pathogenesis of tuberculous enteritis can be attributed to four mechanisms: ingestion of contaminated milk or food in the case of infection by *Mycobacterium bovis,* swallowing of infected sputum, hematogenous spread from active pulmonary or miliary TB or contiguous spread from adjacent organs. **(Ramirez *et al.*, 2015).**

The organism penetrates the mucosa and localizes in the submucosal lymphoid tissue, where it initiates an inflammatory reaction with subsequent lymphangitis, endarteritis, granuloma formation, caseation necrosis, mucosal ulceration, and scarring. The symptoms and signs of tuberculous enteritis are relatively vague and nonspecific. Nonspecific chronic abdominal pain is the most common symptom occurring in 80 to 90 percent of patients. A palpable abdominal mass is present in some patients. Anorexia, fatigue, fever, night sweats, weight loss, diarrhea, constipation, or blood in the stool may be present. Fistula and intestinal stricture may occur. **(Ramirez *et al.*, 2015).**

Tuberculous peritonitis usually occurs as a consequence of the reactivation of latent foci in the peritoneum following hematogenous spread of the infection or from the contiguous spread from adjacent foci such as genitourinary or intestinal TB. As the disease progresses, the visceral and parietal peritoneum become increasingly studded with tubercles. Ascites develops secondary to "exudation" of proteinaceous fluid from the tubercles. More than 90 percent of patients with tuberculous peritonitis have ascites at the time of presentation, while the remainder present with a more advanced "dry" phase, representing a fibroadhesive form of the disease . **(Ramirez *et al.*, 2015).**

J. Abdominal Tuberculosis

It has seen more commonly between 25 to 45 years of age. The modes of infection of the GI include hematogenous spread from a primary lung focus that reactivates later or miliary tuberculosis, spread via lymphatics from infected sources such as milk products of by direct spread from adjacent organs. Involvement of the abdominal lymph nodes and the peritoneum may occur without other organ involvement. The most common site for abdominal TB is the ileocecal area. Infection often results in granuloma formation, caseation, mucosal ulceration, fibrosis, and scarring . **(Kumar *et al.*, 2010).**

K. Ocular Tuberculosis

Tuberculosis affecting the eyelid is most often found in children. The most common form of cutaneous tuberculosis, lupus vulgaris, is charac- terized by reddish-brown nodules that blanch to an "apple-jelly" color when pressure is applied and may appear on the skin of the eyelids. Tuberculosis can also manifest as a "cold abscess," a soft, fluctuant mass without acute inflammation, or simulate a chalazion. Primary infection of the conjunctiva is unusual and more commonly affects children. Tuberculous conjunctivitis is often a chronic disease that may lead to scarring of the involved tissue. Patients with tuberculous conjunctivitis have nonspecific complaints such as ocular redness and discomfort. Examination may reveal mucopurulent discharge and lid edema, often with an accompanying marked lym- phadenitis such as in Paranoid oculoglandular syndrome, which is absent in most other forms of bacterial and allergic conjunctivitis and less prominent in viral conjunctivitis. In cases of primary conjunctival tuberculosis, M. tuberculosis can be detected via traditional acid-fast stains on either a conjunctival smear or a bioptical specimen . **(Kumar *et al.*, 2010).**

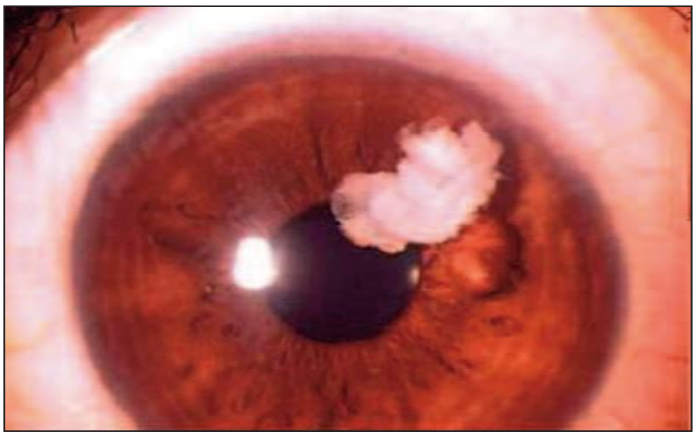

Fig. 15 : Ocular tuberculosis **(Kumar *et al.*, 2010).**

1.3.4. Epidemiological Aspects

1.3.4.1. *Mycobacterium tuberculosis* life cycle

we consider the Mtb life cycle initiated when it reaches the airway and lung . This first encounter between the airway and bacillus is also called primary infection. Mtb first enters through the nose or mouth, encounters cells in the upper airway, and in most cases passes into the distal lung to arrive in the alveolar space. To survive and establish infection, Mtb then invades beyond the mucosal or alveolar epithelium. As it flows through the upper and lower airways, Mtb can infect epithelial cells and microfold cells encountered in nasal associated mucosal tissue or bronchusassociated mucosal tissue as an initial route to transit from the airway. Once the upper and larger distal airways are passed, the next site of interaction with the host occurs within the alveolus. **(Rahlwes *et al.*, 2023).**

Because alveoli are continuously exposed to airborne particulates and pathogens, they also contain specialized innate immune cells known as alveolar macrophages that sample and engage with airborne antigens. In addition to alveolar macrophages, dendritic cells found within the interstitial space can also interact with airborne particles. Thus, during primary infection, Mtb that reaches the alveolus infects alveolar macrophages that reside in the alveolar space, as well as interstitial dendritic cells . As an alternative route of entry, type II alveolar epithelial cells can also be infected by Mtb . These cells fail to control infection with associated high rates of cell death . Since alveolar epithelial cells vastly outnumber alveolar macrophages, this route may represent an important mechanism through which Mtb traverses the mucosa. **(Rahlwes *et al.*, 2023).**

Mtb-infected alveolar macrophages and dendritic cells both serve as early reservoirs of infection and function to activate an adaptive immune response. Infected alveolar macrophages migrate from the alveolar sac into the interstitial space . In some circumstances, the infected macrophages will then reside within the interstitium , and in other circumstances, infected macrophages in addition to infected dendritic cells migrate from the lung to draining lymph nodes to prime and activate T and B cells that function to limit progression of infection . Within the interstitium, resident interstitial macrophages engulf extracellular bacteria that escape initial phagocytosis or after their release from dying cells. Both types of infected macrophages – alveolar and interstitial – along with non-infected macrophages, inflammatory monocytes, neutrophils, and T cells recruited by the inflammation and tissue damage then form the characteristic TB granuloma . However, in most primary infections, infection is controlled,

either through complete eradication of the bacteria leaving behind only immunologic memory of the interaction or through formation of a stable granuloma. **(Rahlwes *et al.*, 2023).**

From the host's perspective, a well-formed and stable granuloma limits the progression of infection and constrains any tissue damage to a small, wellcircumscribed region. Most Mtb-infected individuals will contain the disease at this step and be asymptomatic. From the bacterial perspective, the granuloma permits the bacteria to maintain a state of dormancy and thus avoid clearance by the immune system . Thus, contained, Mtb may persist indefinitely. this condition can currently only be diagnosed with TST or IGRA. Recently, some have questioned whether the vast numbers of individuals with LTBI , ~1/4 to 1/3 of the world's population as estimated by the WHO, truly coexist with viable organisms versus having cleared the infection and demonstrating an appropriate amnestic cell mediated immune response . **(Rahlwes *et al.*, 2023).**

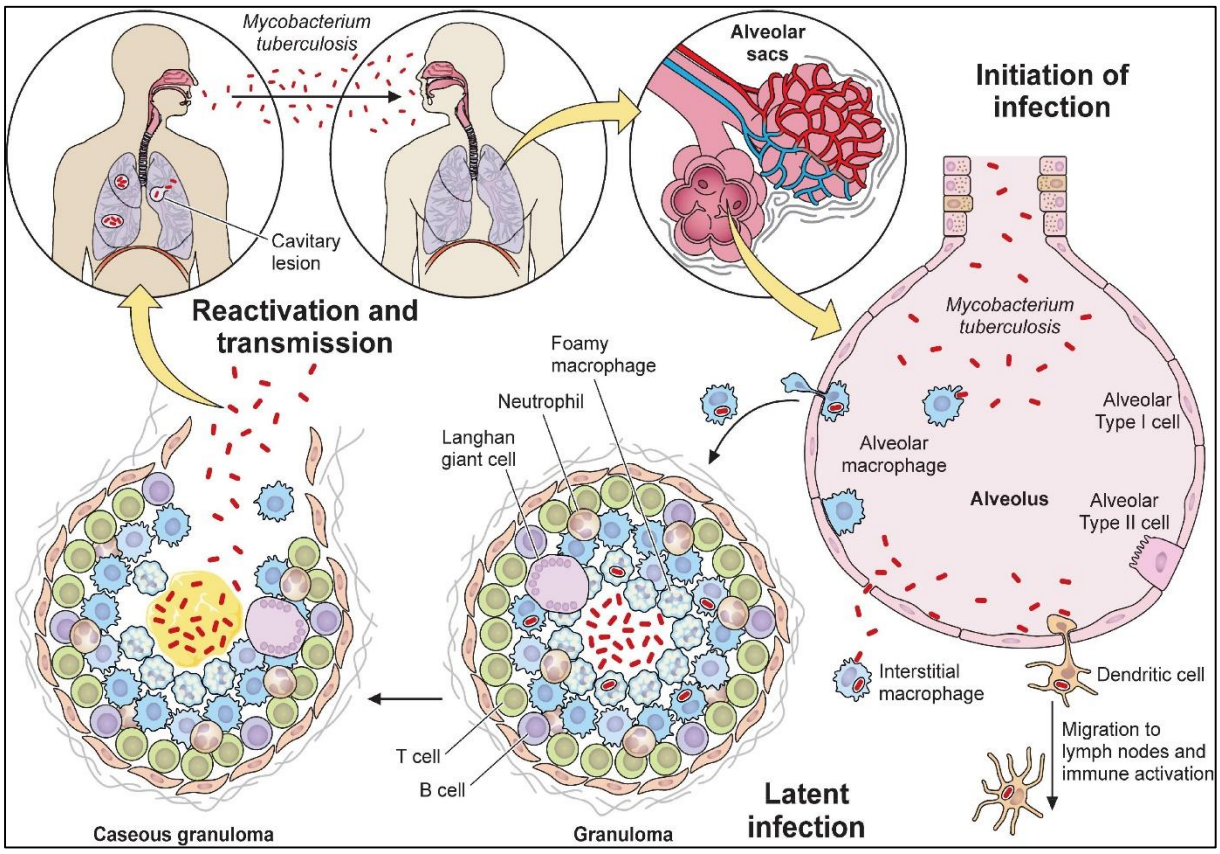

Fig. 16 : Mycobacterium tuberculosis life cycle **(Rahlwes *et al.*, 2023).**

Notwithstanding the question of prevalence of "true" LTBI, some infected individuals proceed to active infection, either directly after the primary infection or after "reactivation" from latent infection, generally in the setting of immunosuppression. Often when this occurs, the structure of the granuloma changes and is associated with the presence of a material known

as caseum which can facilitate more rapid Mtb growth. The central region of caseum can liquify, creating an even more favorable growth environment. Mtb can then spread beyond the lung to other parts of the body either via lymphatics or blood vessels . Ultimately, granuloma liquefaction, which is also associated with tissue destruction , can facilitate the spread of tuberculosis to naive hosts through airborne transmission .In the absence of treatment, ATB has a high mortality rate . During this phase, Mtb stimulates airway nociceptive neurons to produce a chronic, bloody cough that is one of the most characteristic symptoms of ATB disease. This persistent cough is also one vector of transmission that allows Mtb to escape and propagate infection . in this was , Mtb may renew its life cycle in a naive host . **(Rahlwes *et al.*, 2023).**

1.3.4.2. Modes of Transmission of *Mycobacterium tuberculosis*

M. tuberculosis is transmitted from human-to-human and spread is mainly airborne. The source of infection is usually a person with pulmonary TB (PTB) or laryngeal TB. During coughing, speaking, or sneezing, the person produces tiny infectious droplets. These particles, called droplet nuclei, are about 1 to 5 microns in diameter. Depending on the environment, they can remain suspended in the air for several hours. Transmission may occur when these infectious droplets are inhaled. Containing *M. tuberculosis* and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs. UV light (sunshine or artificial sources) and ventilation reduce the probability of transmission Other modes of transmission are far less common. or via solid organ or hematopoietic stem cell transplantation.(Citation The reservoir for *M. tuberculosis* is humans. Bovine TB, which in the past was caused by ingestion of milk heavily infected by *Mycobacterium bovid* that then penetrated the mucosa of the or pharynx or the gastrointestinal tract, has been much reduced globally and almost completely eliminated as a result of the pasteurization of milk and tuberculin. **(Long *et al* , *2022*).**

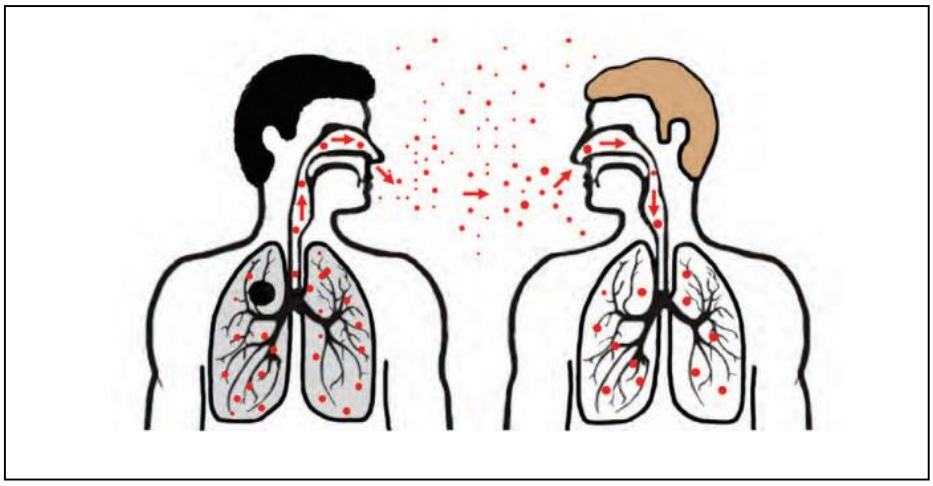

Fig.17 : Transmission of TB TB is spread from person to person through the air. The dots in the air represent droplet nuclei containing tubercle bacilli **(website 03)**

Inoculation of coetaneous or mucous membranes rarely occurs, although such cases have been observed in laboratory personnel. Congenital infection (by transplacental transmission or via aspiration or swallowing of infected amniotic fluid at birth) has been reported, but is very rare. Transmission through breast milk does not occur. The infectiousness of a person is associated with the quantity of bacilli contained in their sputum. Patients with smear-positive sputum on microscopy are by far the most infectious. Those with smear-negative/culture-positive results are less infectious, but still contribute to TB transmission due to more frequent delays in diagnosis. Persons infected with *M. tuberculosis*, but who have not developed active TB (latent tuberculosis infection), are not infectious. Persons with extra pulmonary TB (EPTB) are only infectious in exceptional circumstances. Children are generally much less infectious than adults. This may be due to weaker cough mechanics, less sputum production and lower bacillary load. Not everyone who is exposed to an infectious TB patient becomes infected with M. tuberculosis. The probability that TB will be transmitted depends on several factors. **(Francis *et al.,2023*)**

✓ **infectiousness of the source** (the most important factor)

• Bacteriological status: smear-positive patients are the most infectious.

• Virulence of the bacilli: some strains are highly transmissible (and/or more likely to cause active TB).

✓ **Environment where the exposure occurred**

• Outdoor environments or those with good ventilation and sunlight are less likely to lead to transmission. Small rooms or rooms with no ventilation are conditions most likely to lead to transmission.

• The proximity of the contact person to the patient is also important (e.g. the risk is higher if the person sleeps next to the patient than if they sleep 20 metres away from the patient). **(Francis *et al.,2023*)**

Duration of exposure

People in close and prolonged contact with a person with TB are at highest risk of becoming infected with *M. tuberculosis*. They may be family members, roommates, friends, co-workers or other people who spend several hours a day with the infectious patient.

The best way to stop transmission is to start effective TB treatment as soon as possible. It is estimated that a person with untreated smear-positive TB transmits the bacillus to 10 to 20 people a year (with variations according to living conditions and environment). **(Francis *et al., 2023*)**

Variable 5% of infected individuals develop primary or progressive primary active disease within 18 to 24 months after infection, and 5% develop post primary disease over the remainder of their lifetime. While the subsequent risk of active pulmonary or extra pulmonary TB is greatest within the first 2 years after infection, without treatment, LTBI will persist for a lifetime**. (DHU, 2017)**

- **Incubation Period**

5% of infected people develop active disease within 24 months and 5% will develop over the remainder of their lifetime. Latent TB will persist for a lifetime**. (DHU, 2017)**

- **Period of Communicability**

Communicable as long as viable tubercle bacilli are discharged in the sputum. The degree of communicability depends on the number of bacilli discharged, virulence of the bacilli, and adequacy of ventilation, and opportunities for aerosolization through coughing, sneezing or procedures such as intubations, bronchoscopes. For smear positive or symptomatic infections the period of communicability may be 3 months before symptom onset, asymptomatic smear

negative with no evidence of cavities may be infectious 4 weeks prior to date of diagnosis. Effective antibiotic treatment eliminates communicability within 2-4 weeks**. (DHU, 2017)**

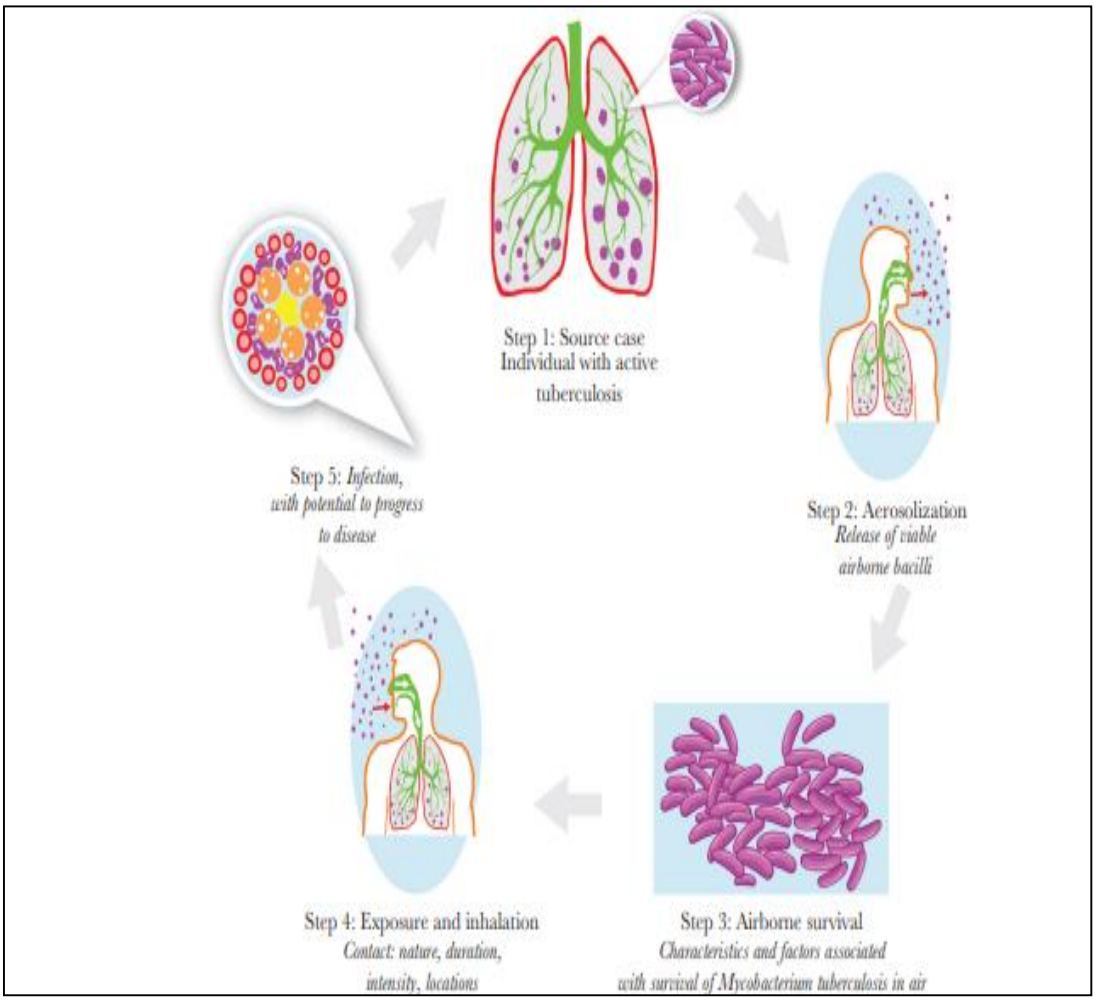

Fig.18: Cascade of tuberculosis transmission. **(JID,2017)**

A. Evolution of tuberculosis infection and disease in humans

When a person inhales infectious droplets containing *M. tuberculosis*, most of the larger droplets become lodged in the upper respiratory tract (nose and throat) where infection is unlikely to develop. However, smaller droplet nuclei may reach the small air sacs of the lung (the alveoli) where infection can occur. **(Francis *et al., 2023*)**

B. Primary infection and latent tuberculosis infection

After transmission, M. tuberculosis multiplies slowly, in most cases in the terminal alveoli of the lungs (primary focus) and in the lymph nodes of corresponding drainage areas: this is the primary infection. The primary focus and related Hilary lymphadenopathy form the

primary complex. In one to two months, due to the action of lymphocytes and macrophages (cellular immunity), the primary focus is contained and encapsulated, with a central zone of parenchyma necrosis (caseous lesions). It is not usually detectable on chest x-ray, unless it calcifies or grows substantially. Primary infection is usually asymptomatic. In most cases (90 to 95% of non-HIV infected patients), the pulmonary lesions gradually heal. During the primary infection, specific immunity develops and a positive skin reaction to tuberculin is observed. This immune response may persist without clinical signs of TB.

The patient is infected by *M. Tuberculosis*, but does not develop the disease. This is referred to as latent tuberculosis infection (LTBI).

In 5 to 10% of infected people, primary infection and/or LTBI progresses to active TB over their lifetime. For HIV co-infected patients, this risk is much higher. **(Francis *et al.,2023)***

C. Active tuberculosis

Before immunity is established, bacilli from the primary infectious focus or from a near-by lymph node can be transported and disseminated throughout the body via the lymph system or the bloodstream. **(Francis *et al.,2023*)**

Secondary foci can develop this way, particularly in the lungs, lymph nodes, serous membranes, meanings, bones and kidneys. As soon as an immune response is mounted, most of these foci resolve spontaneously. However, some bacilli may remain dormant in the secondary foci for months and sometimes years. Different factors can reduce the immune response (e.g. HIV infection) and lead to reactivation of the bacilli and their multiplication in one or more of these foci.

This reactivation or progression of the primary or secondary foci results in active TB .

An active TB lesion contains actively, slowly or sporadically multiplying bacilli as well as dormant bacilli.

While active TB may occur months or years following primary infection, half of TB cases appear in the year following infection. **(Francis *et al.,2023*)**

1.4.3.4. Symptoms

- **Latent TB**

A person with latent TB will have no symptoms, and no damage will show on a chest X-ray. However, a blood test or skin prick test will indicate that they have TB infection.

- **Active TB**

An individual with TB disease may experience a cough that produces phlegm, fatigue, a fever, chills, and a loss of appetite and weight. Symptoms typically worsen over time, but they can also spontaneously go away and return.

- **Early warning signs**

A person should see a doctor if they experience Trusted Source:

- a persistent cough, lasting at least 3 weeks
- phlegm, which may have blood in it, when they cough
- a loss of appetite and weight
- a general feeling of fatigue and being unwell
- swelling in the neck
- a fever
- night sweats
- chest pain

- **Beyond the lungs**

TB usually affects the lungs, though symptoms can develop in other parts of the body. This is more common in people with weakened immune systems.

- **TB can cause**
  - persistently swollen lymph nodes, or "swollen glands"
  - abdominal pain
  - joint or bone pain
  - confusion
  - a persistent headache
  - seizures. **(website 6).**

The classic symptom of pulmonary TB disease is a chronic cough of at least 2-3 weeks' duration. This cough is initially dry but after several weeks to months will become productive. Cough of 2 weeks duration is a more sensitive criterion, but cough of 3 weeks duration will be more specific. Selection of 2 or 3 weeks as the criterion depends on the local experience and

epidemiology of TB. Fever and night sweats are common but may be absent in the very young and the elderly. Hemoptysis, anorexia, weight loss, chest pain and other symptoms are generally manifestations of more advanced disease.1,2 SIGNS The most common physical finding in pulmonary TB is a totally normal examination, even in relatively advanced cases. Bronchial breathing, rales or crepitations will be found in more advanced cases. It is important to examine for signs of extra pulmonary disease, such as lymphadenopathy , pleural effusion and abdominal or bone and joint involvement, as these may be present concomitantly, particularly in HIV-infected individuals. **(PHAC, 2014)**

1.3.4.4. Risk Factors

The development of TB in an exposed individual is a two-stage process following infection. In most infected persons, infection is contained by the immune system and bacteria become walled off in caseous granulomas or tubercles. In about 5% of infected cases, rapid progression to tuberculosis will occur within the first two years after infection . About 10% of people with latent infection will reactivate, half within the first year, the remainder over their lifetime mostly by reactivation of the dormant tubercle bacilli acquired from primary infection or less frequently by reinfection. Overall, about 10–15% of those infected go on to develop active disease at some stage later in life , but the risk of progression is much higher at about 10% per year in HIV-positive and other immunocompromized individuals.

The risk of progression to infection and disease is two different aspects and proper understanding of these factors is essential for planning TB control strategies . the risk of infection following TB exposure is governed by factors :

(Narasimhanet *al.*, 2013)

A. Factors Related to the Individual

A.1. Age :

The year in which a person was born, and therefore the age of the person plays a crucial factor in the risk of being infected. **(Davies, 2005).**

Work from South Africa suggests that rates in children aged 0-5 is 3.5 times higher than in adults . young children are very much more likely to develop disease from infection than other groups . Mortality is also highest in these groups. The lifetime risk of developing disease

after infection is 43% in the first year of life, 24% between 1 and 5 years and 15% in adolescents compared to immunocompetent adults with a lifetime risk of 5-10% . **(Davies, 2005).**

Most tuberculosis in adults arises many years after primary infection because of exogenous reinfection or endogenous reactivation of a latent focus of infection (30) **(Lienhardt, 2001).**

A more recent study suggests that rates may increase again in older age groups, those over 65. This may indicate a natural decline in host defence with the ageing process **.(Davies, 2005).**

A.2. Gender

Contemporary evidence from the UK suggests that in the older age groups of the white population rates of disease in males exceed that of females by threefold . (Davies, (2005). All evidence points to there being no gender difference in tuberculosis rates in the 1-14 age group. This suggests that if there is a genuine difference between the genders susceptibility it is not apparent until after puberty implying that hormonal differences may play a part. **(Davies, 2005).**

This difference after adolescence may reflect greater exposure among adult males because of differentiated social roles and economic activities (92), but it also may reflect a genuine sex difference in susceptibility to tuberculosis infection related to a different predisposition to responsiveness to delayed-type hypersensitivity . **(Lienhardt, 2001).**

A.3. Poverty

That there is a very strong correlation between poverty and tuberculosis is not in doubt. Recent studies from the UK have shown a close correlation even in a Western city at the end of the 20th century . What is less clear is the various aspects of poverty which may constitute the increased risk. It is likely that poor housing in terms of crowding leading to increased transmission and poor nutrition leading to diminished immunity are the two most important factors. **(Davies, 2005).**

A.4. Malnutrition

Studies have shown that malnutrition (both micro- and macro-deficiency) increases the risk of TB because of an impaired immune response . TB disease can itself lead to

malnourishment because of decreasing appetite and changes in metabolic processes . The association between malnutrition and TB has been shown with BCG vaccine trials performed in USA during the late 1960s estimating that malnourished children are twice as likely to contract TB disease as their appropriately nourished peers . The first National Health and Nutrition Examination (NHANES-1) and the NHANES-1 Epidemiological Followup Study (NHEFS) conducted during 1982–84 from the USA among adults reported an increased adjusted hazard of TB from six- to ten-fold in malnourished individuals. **(Narasimhanet *al.*, (2013).**

A.5. Diet

It is often difficult to control for factors related to poverty in order to study just one. A study of life-style factors of over 100 patients in Liverpool and over twice as many controls showed that controls tended to eat more salads and dairy products than patients . It was also of interest that being on treatment for blood pressure seemed to be protective against tuberculosis. Body build was not assessed in this particular study but the tendency for raised blood pressure to be associated with obesity may have a compounding effect on relative protection from tuberculosis. **(Davies, 2005).**

A.6. Healthcare Workers

Healthcare workers (HCWs) are at increased risk of exposure to TB. A review by Seidler et al. showed that, among HCWs in high-income countries, the overall incidence of TB disease in the general population and native born HCWs was less than 10 and 25 per 100 000 per year . Joshi and colleagues summarized evidence on the incidence and prevalence of latent TB infection (LTBI) and disease among HCWs in low- and middle-income countries. In their review of 51 studies the authors found that the prevalence of LTBI among HCWs was on 55%, the estimates of the annual risk of LTBI ranged from 0.5 to 14.3%, and the annual incidence of TB disease ranged from 69 to 5780 per 100000. **(Narasimhanet *al.*, 2013).**

B. Socioeconomic and Behavioural Factors

Rapid urbanization witnessed in developing countries and socioeconomic status (SES) of individuals has also been shown to have influence on a person's susceptibility to infection. The TB burden follows a strong socioeconomic gradient between and within countries with the poorest having the highest risk . People with low SES are exposed to several risk factors (including malnutrition, indoor air pollution, alcohol, etc.) which increases their risk for TB.

Marginalized populations including prisoners have a higher chance of getting infected with TB mostly because of crowded living conditions and coinfection with HIV and injection drug abuse **.(Narasimhanet *al.*, 2013).**

B.1 Migration

If migration occurs from an area of low incidence to an area of higher incidence of tuberculosis, then a number of people are likely to undergo primary infection in the new environment, so that tuberculosis develops within the first few years after entry . Conversely, groups of people moving from an area of high incidence of tuberculosis to an area of lower incidence include a number of tuberculosis cases whose disease will become manifest any time after migration.

Similarly, in Massachusetts, it was recently found that the foreign-born population in the United States was considerably more resource-poor than its US counterparts (114). The higher incidence of tuberculosis in migrants as compared with the indigenous population thus could be explained by the combined effects of a higher risk of infection in the country of origin and differences in SES in the host country . **(Lienhardt , 2001).**

B.2. Smoking

The association between smoking and tuberculosis has been established for at least a decade. Original observations suggested that the change in the pattern of tuberculosis between men and women was due to the fact that men took up smoking after the First World War in large numbers whereas women did not . More accurate studies by Doll and the life-style survey in Liverpool showed that those who smoked more than 20 cigarettes a day were between two and three times more likely to develop tuberculosis compared with never smokers . The same observation has been made in China and India . Here tuberculosis has been shown to be the commonest cause of death in smokers . **(Davies, 2005).**

B.3. Alcohol

Alcohol has been recognized as a strong risk factor for TB disease , A systematic review of 3 cohort and 18 case control studies concluded that the risk of active tuberculosis is substantially elevated among people who drink more than 40 g alcohol per day and/or have an alcohol use disorder . Reasons for increased risk include alteration in the immune system. **(Narasimhanet *al.*, 2013).**

C. Weakened immune system

A healthy immune system often successfully fights TB bacteria, but body can't mount an effective defense if resistance is low. A number of diseases and medications can weaken immune system, including:

- HIV infection (the virus that causes AIDS)

- Diabetes

- Severe kidney disease

- Cancer treatment, such as chemotherapy

- Drugs to prevent rejection of transplanted organs

- Some drugs used to treat rheumatoid arthritis,

- Crohn's disease and psoriasis

- Malnutrition

- Very young or advanced age

- Low body weight (10% below ideal)

- Certain cancers (Head and neck cancer). **(Mohamoud, 2019).**

D. Geographical factor

By far the greatest risk factor for infection across the globe is the incidence of tuberculosis in the community in which an individual was born and spent their early years . Individuals born in a part of the world with a very high incidence of disease such as Southern Asia or sub-Saharan Africa will have a very high risk of infection. Annual rates of infection can be calculated from sequential tuberculin skin test surveys or by testing different age groups of children and young people . These have been shown to be especially high in Southern Africa . The incidence of disease in a country of origin is reflected in the incidence of disease in these individuals on immigration to a developed country . This can be seen very clearly in rates of disease by ethnic origin in the UK and in the USA . Thus those immigrating from China to the UK have rates of disease about 10 times the rate in the indigenous white population , those from South Asia have rates about 20-30 times the white rate and those from Africa rates 80 times as

great. The sooner disease presents after arrival in the adopted country, the higher the rate of disease appears to be . **(Davies, 2005).**

Conversely areas of the world where tuberculosis has been allowed to decline over more than a century where living conditions have steadily improved and where little or no migration from developing countries has taken place, such as the northern Scandinavian countries have all but eliminated the disease . **(Davies, 2005).**

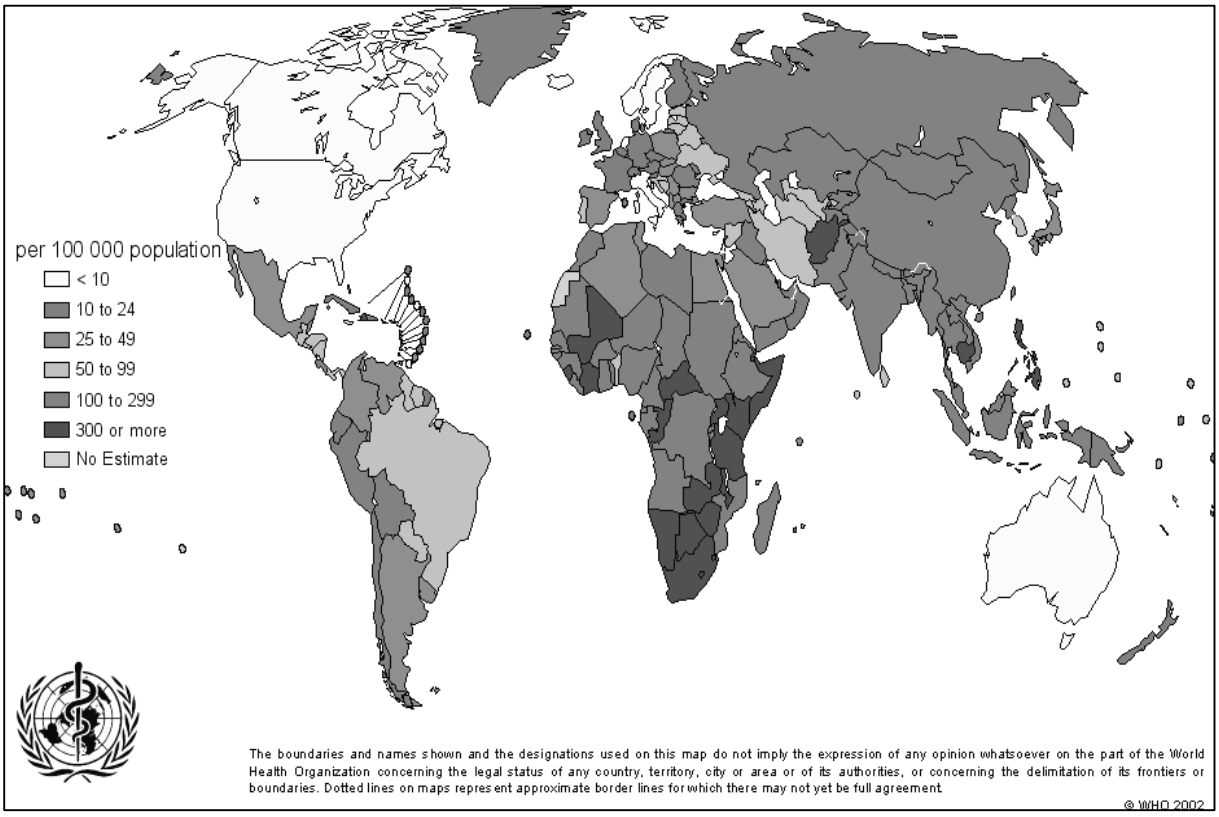

Fig.19: Estimated TB Incidence Rates, 2000. **(Davies, 2005).**

1.3.4.5. Epidemiology of tuberculosis

1.3.4.5.1. Tuberculosis in the world

Worldwide, tuberculosis (TB) is the leading cause of death from a single infectious disease agent and the leading cause of death among persons living with human immunodeficiency virus (HIV) infection, accounting for approximately 40% of deaths in this population. The United Nations' (UN) Sustainable Development Goals and the World Health Organization's (WHO's) End TB Strategy have defined ambitious targets for 2020–2035, including a 35% reduction in the absolute number of TB deaths and a 20% reduction in TB incidence by 2020, compared with 2015 . Since 2000, WHO has produced annual TB estimates for all countries . Global and regional disease estimates were evaluated for 2017 to determine

progress toward meeting targets. In 2017, an estimated 10 million incident cases of TB and 1.57 million TB deaths occurred, representing 1.8% and 3.9% declines, respectively, from 2016. Numbers of TB cases and disease incidence were highest in the WHO South-East Asia and Africa regions, Overall progress in global TB elimination was modest in 2017, consistent with that in recent years ,intensified efforts to improve TB diagnosis, treatment, and prevention are required to meet global targets for 2020–2035**. (Adam *et al., 2019*)**

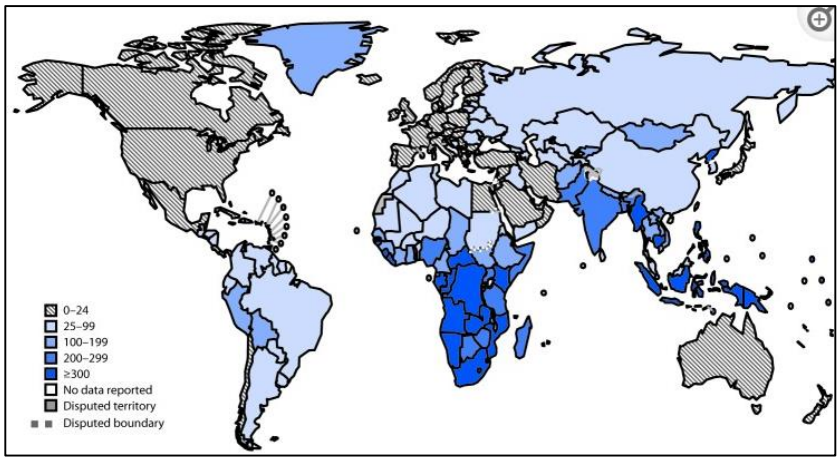

Fig.20: Annual tuberculosis incidence by region worldwide **(Adam et al., 2019)**

1.3.4.5.2. Tuberculosis in the African Region

An estimated 2.5 million people fell ill with tuberculosis in the African Region in 2021, and as many as half-a-million people died due to the disease in the same year. Tuberculosis (TB) is an infectious disease that primarily affects adults in their most productive years. While commonly affecting the lungs, TB also affects the kidneys, brain, spine, and skin. As shown in Figure 1, geographically, most TB cases in 2021 were in the WHO regions of SouthEast Asia, Africa, and the Western Pacific, with smaller shares in the Eastern Mediterranean, the Americas, and Europe. Despite being preventable and curable, tuberculosis was the second leading infectious disease killer (after COVID-19) and the 13th leading cause of death worldwide during 2020–2021.1 It remains a leading cause of death for people living with HIV/ AIDS**. (WHO ROAB, 2023)**

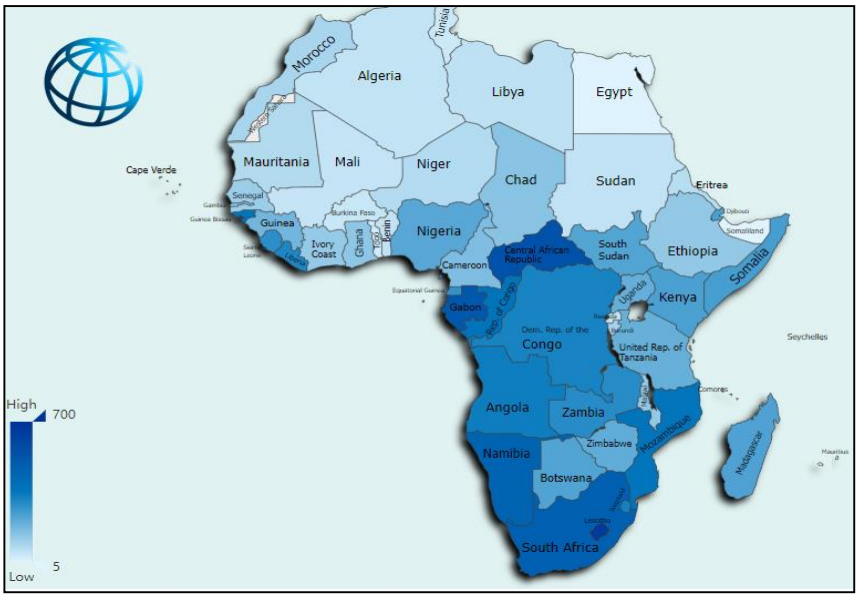

Fig.21: Estimated TB Incidence of tuberculosis (per 100,000 people) the in African Region - 2022. **(website 7).**

TB continues to be a significant public health problem in the WHO African Region, with a high number of cases and deaths. Despite making up only 15% of the world's population, the region accounted for 23% of new TB cases and 31% of TB-related deaths in 2021.2 This is the equivalent of 2.5 million people falling ill with tuberculosis and an estimated 500 000 deaths. Approximately 20% of the new TB cases were reported among people living with HIV/AIDS. TB mortality in the region remains high, with a small number of countries carrying large disease burdens. The estimated number of deaths in 2021 in the Democratic Republic of Congo, Nigeria, and South Africa, for instance, accounted for 48% of all TB deaths in the African Region. The global burden of drug-resistant TB is increasing, including an increasing number of deaths. In 2021, there were an estimated 450 000 new cases of rifampicin-resistant TB (RR-TB) at the global level and an estimated 77 000 multidrug-resistant TB (MDR-TB) cases in the African Region (Figure 2).3 Of these cases, 53% were from Nigeria and South Africa. **(WHO ROAB, 2023).**

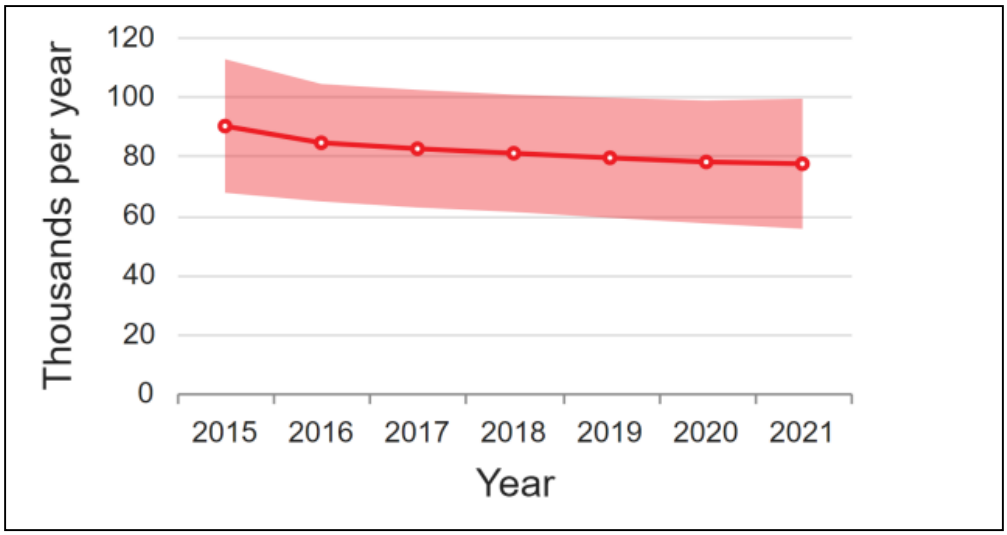

Fig.22: Estimated number of incident cases of MDR/RR-TB, WHO African Region, 2015–2021 **(WHO ROAB, 2023).**

Remains large, despite an overall narrowing trend. There is substantial variation by region, with the African Region recording the largest gaps. Gaps in recording the actual number of drug-resistant TB cases are even larger. While case detection has improved for RR-TB and MDR-TB thanks to improved diagnostics, an estimated 1 million cases of isoniazid-resistant TB were missed in the region in 2021. Additionally, TB prevention and control programmes also face challenges in the identification of cases among children. With an estimated 322 000 children and young adolescents aged 0–15 years (one third of cases among children under 15 years worldwide), increased measures are required to improve detection, bacterial confirmation, and treatment of paediatric TB. **(WHO ROAB, 2023).**

1.3.4.5.3. Tuberculosis in the Algiers

Demonstrates that TB poses a threat to human health and has a detrimental impact on social and economic life. Although Algeria may not be among the top eight countries with the highest concentration of TB cases globally, it is still a significant concern in Algeria. Thus, it is imperative.

That government agencies and scientists work together to manage and combat the spread of TB epidemics. Vaccination is one of the most vital factors in stopping and controlling the spread.

of TB. The tuberculosis vaccination against Bacillus Calmette–Guérin (BCG) was first given to a human in 1921. To address the prevailing epidemiological situation, the Algerian

Health Care Administration implemented a dedicated vaccination schedule and mandatory vaccination campaigns for children. As a result, the BCG vaccination coverage reached a remarkable rate of over 98% across newborns. However, BCG vaccination is not typically recommended for adults, as its effectiveness in this age group is limited. Therefore, this paper neglects it.The mathematical modeling of tuberculosis relies on vaccination for its importance in giving predictions to eradicate the disease. There are many previous studies concerned with this topic; for example, in developed a mathematical model that includes immunization of newborn children and older susceptible people in the dynamics of TB transmission in a population, with the goal of providing protection to older susceptible people. Revelle et al. formulated models for the economic allocation of activities to control tuberculosis in developing countries. To the best of our knowledge, the proposed model is not considered elsewhere in its present form and there is no research on modeling the dynamic transmission of tuberculosis in Algeria using a compartmental model while simultaneously estimating the relevant biological parameters specific to the country. Therefore, conducting research in this domain would make a valuable contribution to the field of TB modeling and control in Algeria. In this study, we propose a VSEIT epidemiological model to investigate the dynamics of TB disease in Algeria. To confirm its performance we estimated the biological model's parameters using specific TB data, including disease incidence, prevalence, and other relevant epidemiological information from 1990 to 2020 from the WHO Global TB Report . ***(*Chennaf Bouchra *et al.,2023).***

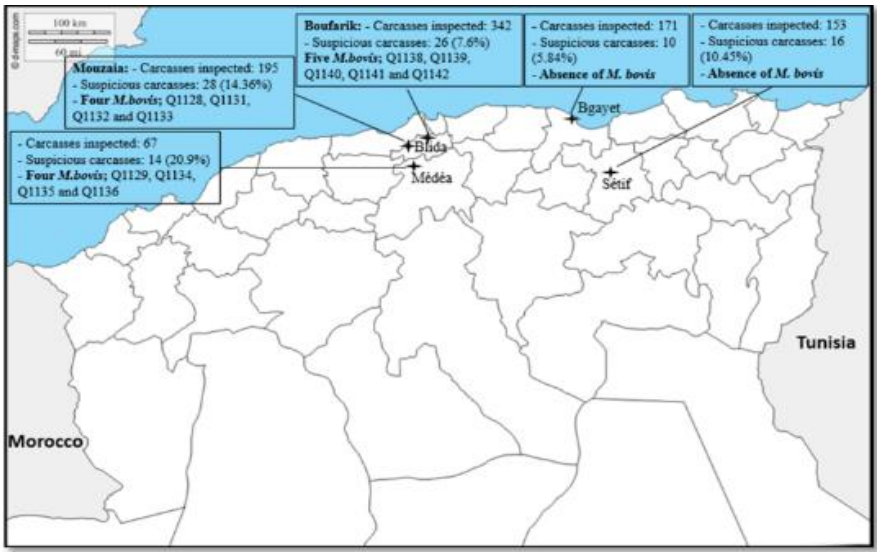

Fig.23: Location of the five slaughterhouses in four departments in northern Algeria **(website 08).**

1.4. Diagnosis of tuberculosis

Active TB disease can affect nearly any organ of the body. Thus, there are diverse disease presentations that make it difficult to outline a single approach to its diagnosis. The majority of persons diagnosed with active TB disease have pulmonary disease (and are potentially infectious). Nonetheless, a substantial minority of persons have extra pulmonary disease, either with or without pulmonary involvement. A diagnosis of TB disease is established through a medical history, physical examination, chest radiograph (CXR), and laboratory test results. While a definitive diagnosis of TB disease depends upon a positive culture or nucleic acid amplification (NAA) test result for *Mycobacterium tuberculosis (M. tuberculosis)* complex, a high degree of clinical suspicion can be established based on epidemiologic findings, medical history, radiographic findings, and physical examination. Increased clinical suspicion for active TB is warranted for persons with TB risk factors when they fail to improve after initial empiric treatment for conditions such as community acquired pneumonia. Clinicians should consider factors that may affect the typical presentation of TB disease, such as the patient's age and coexisting diseases. TB may present in atypical ways in immunosuppressed patients as well as in young children. Symptoms of TB disease in extrapulmonary sites may not include cough, but instead reflect the site of disease. For example, individuals with meningeal TB may present with new onset seizures, worsening headache, or meningeal signs. During an encounter with an individual for whom clinical suspicion for TB disease is high, a complete medical evaluation is performed, including medical history, physical examination, human immunodeficiency virus (HIV) testing, interferon gamma release assay (IGRA) or tuberculin skin test (TST), radiological imaging, and mycobacteriological evaluation (acid-fast bacilli [AFB] smear and culture). **(DTC, 2022).**

1.4.1. Physical Examination

A physical exam can provide valuable information about the patient's overall condition and other factors that may affect how TB is treated, such as HIV infection or other illnesses. **(CDC, 2011).**

1.4.2. Test for TB Infection

The Mantoux tuberculin skin test (TST) or the TB blood test can be used to test for M. tuberculosis infection. Additional tests are required to confirm TB disease. The Mantoux tuberculin skin test is performed by injecting a small amount of fluid called tuberculin into the skin in the lower part of the arm. The test is read within 48 to 72 hours by a trained health care

worker, who looks for a reaction (induration) on the arm.The TB blood test measures the patient's immune system reaction to M. Tuberculosis. **(CDC, 2011).**

A baseline physical exam is conducted for each patient, including a general assessment to detect signs of TB, a directed examination as per symptoms or signs, and an assessment of vital signs (including weight, blood pressure, temperature, and pulse). Although the physical examination cannot be used to confirm or rule out TB disease, it can provide valuable information about the patient's overall condition. Sites of assessment include: • Head (including ears, eyes, and throat)

• Neck

• Lungs

• Heart

• Abdomen

• Extremities

• Skin. **(DTC,2022).**

3.Chest radiograph

Chest Radiograph A posterior-anterior chest radiograph is used to detect chest abnormalities. Lesions may appear anywhere in the lungs and may differ in size, shape, density, and cavitation. These abnormalities may suggest TB, but cannot be used to definitively diagnose TB. However, a chest radiograph may be used to rule out the possibility of pulmonary TB in a person who has had a positive reaction to a TST or TB blood test and no symptoms of disease. **(CDC, 2011).**

CXRs are obtained for all persons with confirmed TB disease or signs and symptoms consistent with TB disease, including those with only extra pulmonary sites of disease. A baseline posterior-anterior CXR is obtained for all adult patients. Other views (e.g., lateral, lordotic) or additional studies (e.g., computed tomography [CT] scans) are obtained when necessary. A lead shield is used when obtaining a CXR in a pregnant patient or a patient who could be pregnant. Pregnant patients who are being evaluated for TB disease undergo CXR without delay, even during the first trimester. Pulmonary TB disease has a myriad of presentations on the CXR that manifest in the parenchyma and pleura, or that can suggest hilar

or mediastinal lymphadenopathy. Classic TB disease findings are seen in the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe. **(CDC, 2000).**

However, abnormalities may appear anywhere in the lungs and may differ in size, shape, and density. Cavitary lesions, when present, are associated with a higher degree of infectiousness and may influence treatment length. Hematogenous spread of TB causes a miliary pattern (one to five millimeter millet seed-like densities) and when seen, prompts the consideration of additional sites of disease. Finally, the CXR may be entirely normal in persons with HIV infection or other immunosuppressive conditions who have culture-positive pulmonary TB disease. **(DTC, 2022)**

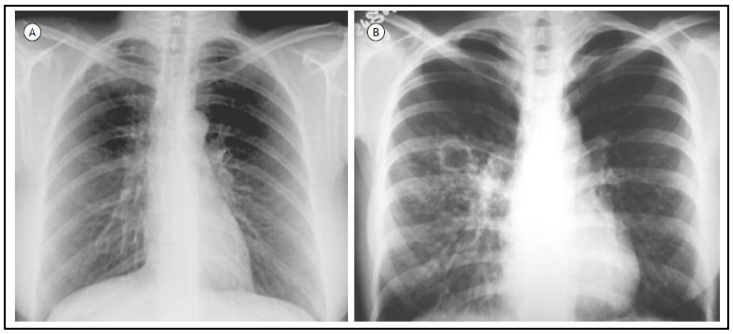

Fig.24: Chest X-ray findings of tuberculosis**. [** In A, small clustered opacities in the right infraclavicular area. In B, a thick-walled cavity located in the middle third of the right lung, accompanied by small airspace nodules, also known as satellite lesions, which are classically representative of bronchial dissemination of the disease.**] (Denise et al., 2021)**

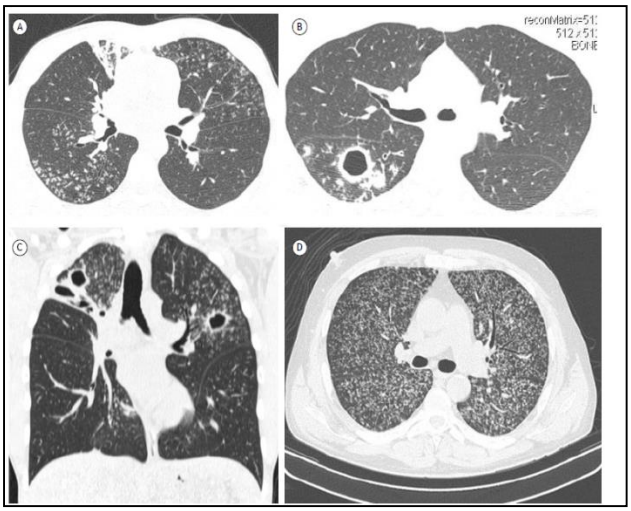

Fig.25: CT findings of tuberculosis.[In A, diffuse airspace nodules, some of which are dichotomous, resulting in a tree-in-bud pattern. In B (same case as), a thick-walled cavity, accompanied by satellite nodules and marked bronchial wall thickening, in the apical segment of the right lower lobe. In C, coronal reconstruction showing thick-walled cavities and satellite nodules, bilaterally. In D, a miliary pattern of diffuse micronodules]. **(Denise et al., 2021).**

1.4.4. Diagnostic Microbiology

The presence of acid-fast-bacilli (AFB) on a sputum smear or other specimen often indicate TB disease. Acid-fast microscopy is easy and quick, but it does not confirm a diagnosis of TB because some acid-fast-bacilli are not M. tuberculosis. Therefore, a culture is done on all initial samples to confirm the diagnosis. (However, a positive culture is not always necessary to begin or continue treatment for TB.) A positive culture for M. tuberculosis confirms the diagnosis of TB disease. Culture examinations should be completed on all specimens, regardless of AFB smear results. **(CDC, 2011).**

1.4.5. Bacteriological Diagnosis

1.4.5.1. Smear microscopy

Sputum smear microscopy is important for the diagnosis of tuberculosis because it identifies patients with active tuberculosis, who feed the chain of disease transmission. Smear testing for AFB is a rapid, inexpensive method. However, although the sensitivity of direct smear microscopy examination of spontaneous sputum is as high as 80% in the presence of extensive cavitary lesions, it ranges, on average, from 40-60% in patients with minimal lesions, and smears are positive in only 20% of those patients. In addition, smear microscopy has lower sensitivity (ranging from 20-60%) in patients coinfected with HIV.Two to three sputum

samples, at least one being collected in the early morning to optimize results, should be sent for smear microscopy.the sputum volume should be greater than 3 mL, the optimal volume being 5-10 mL.Fluorescence microscopy can increase the capacity to detect *mycobacteria* by 10%, compared with conventional light microscopy. A 10-20% increase in the sensitivity of smear microscopy can also be achieved by using sputum centrifugation or sedimentation.Sputum induction with hypertonic saline solution is a useful technique in individuals who have negative sputum smears or who are unable to produce sputum, because it increases the yield of smear microscopy and culture. Sputum induction with hypertonic saline solution has a diagnostic yield similar to that of bronchoscopy with BAL and is more cost-effective. If a diagnosis is not possible on the basis of spontaneous or induced sputum collection and suspicion of pulmonary tuberculosis persists, bronchoscopy and BAL fluid collection can be performed for smear microscopy and culture. Bronchoscopy also plays a role in the diagnosis of smear-negative pulmonary tuberculosis, in cases of hemoptysis caused by tuberculosis, and in the exclusion of alternative diagnoses. **(Denise *et al*., 2021).**

In cases of suspected extrapulmonary tuberculosis, smear microscopy examination of the material collected is also indicated, although its sensitivity is lower. In cases of lymph node tuberculosis, the diagnosis is made by needle puncture-aspiration or lymph node resection. In pleural tuberculosis, the pleural fluid presents as an exudate with a predominance of lymphocytes but with a low yield for the detection of AFB (< 5%). Conversely, the yield of smear microscopy is high in tuberculous empyema. Increased adenosine deaminase levels (> 40 U/L) in the pleural fluid are considered highly suggestive of the diagnosis of pleural tuberculosis. **(Denise *et al., 2021)*.**

1.4.5.2. Histopathological Diagnosis

Histopathology is an important method for diagnosing pulmonary and extra pulmonary tuberculosis on the basis of specimens of tissue infected with M. tuberculosis. The typical histopathological lesion in pulmonary tuberculosis is a granuloma with caseous necrosis, composed of epithelioid histiocytes around a necrotic center, usually accompanied by a variable number of multinucleated giant cells and lymphocytes, which are found in up to 80% of cases. Non-necrotic granulomas may also be present, especially in immunocompromised patients when there is an incomplete inflammatory reaction. Granulomas without caseous necrosis should be interpreted with caution and in conjunction with clinical and epidemiological findings, given that they can be found in other pulmonary and systemic granulomatous diseases, such as silicosis, mycoses, and sarcoidosis.4,35 In immunocompetent patients with

tuberculosis, smear microscopy of lung tissue is usually negative, whereas it is typically positive in immunocompromised patients. However, the only definitive diagnostic method is culture followed by biochemical or molecular confirmation of M. tuberculosis. The diagnosis of extrapulmonary forms of tuberculosis is more difficult because of the paucibacillary nature of samples, the lack of sufficient sample quantities or volumes, and the fact that samples are fractionated in order to perform several diagnostic tests, such as histology/cytology, biochemical analysis, microbiology, and molecular biology methods. **(Denise *et al., 2021*).**

1.4.6. Diagnosis of Tuberculosis in Children

The WHO estimates that each year more than one million children become ill with tuberculosis worldwide-approximately 10% of the total number of cases-and that the incidence of childhood tuberculosis is underestimated because of the difficulty in diagnosing the disease in children. There are approximately 200,000 tuberculosis deaths per year among children and adolescents aged 0-14 years. Approximately 80% of those deaths occur among children under 5 years of age, and 17% occur in HIV-infected patients. Twenty-five thousand children under 14 years of age develop MDR-TB each year, although only approximately 5% receive treatment. The difficulties in diagnosis, contact tracing, and access to health care facilities would explain this challenge from a public health standpoint. **(Denise *et al., 2021*).**

Children under 10 years of age typically have paucibacillary disease, which makes it difficult to detect M. tuberculosis in clinical specimens. Antituberculosis treatment is almost always started on the basis of clinical history, symptoms, and signs, as well as, when possible, on the basis of radiological findings and tuberculin skin test (TST) results.4,44 Figures 5 and 6 show radiological features of tuberculosis in children**. (Denise *et al., 2021*).**

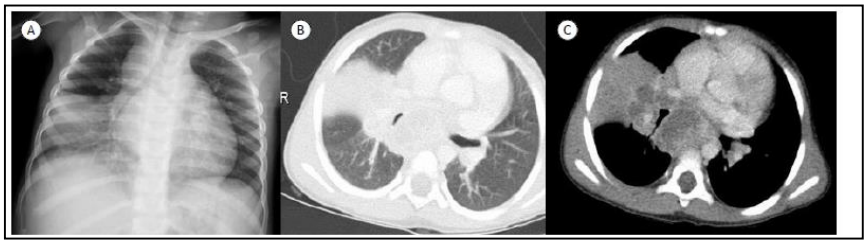

Fig.26: Primary tuberculosis in a child aged four years and nine months. **[**In A, chest X-ray showing opacity in the right middle lower third accompanied by widening of the right paratracheal stripe, consistent with enlarged lymph nodes. In B, chest CT (lung window) showing opacity and extrinsic obstruction of the intermediate bronchus by enlarged lymph nodes, which are indicative of middle lobe syndrome . In C, chest CT (mediastinal window

settings) showing enlarged lymph nodes of varying density in the right hilum and posterior mediastinum**]**. *(*Denise *et al., 2021).*

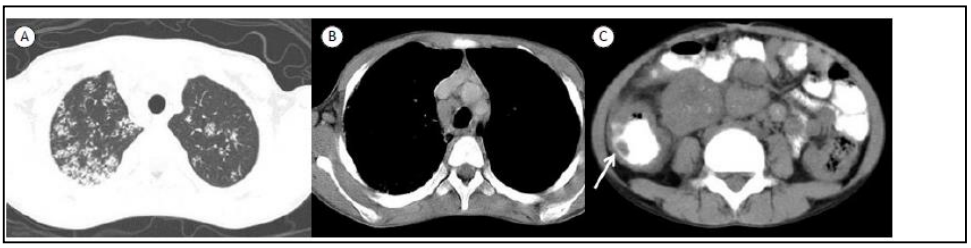

Fig.27: Chest CT scans showing disseminated tuberculosis in a nine-year-old child. **[** In A, airspace nodules exhibiting a tree-in-bud pattern. In B, enlarged right paratracheal lymph nodes. In C, marked thickening of the cecum (arrow) **]** . **(Denise *et al., 2021*)**

1.5. Tuberculosis Treatement

1.5.1 Management of tb

The American Thoracic Society (ATS) and Centers for Disease Control (CDC) have classified persons, exposed to and /or infected with M. tuberculosis.The classification is based on the broad host–parasite relationship as described by exposure history, infection and disease. The suggested intervention required in each of the categories is shown in **Table 2.** This classification helps us to understand the natural history of TB infection in man and the rationale for intervention required at each stage.(Joshin,(2011). .

Table 02: categories of persons exposed to and/or infected with *M.tuberculosis* and appropriate intervention for each category **(Joshin , 2011).**

Category	Appropriate intervention
No tuberculosis exposure, no infection	None
Tuberculosis exposure, no evidence of infection Negative TT	Environmental control / BCG
Tuberculosis infection, no disease Positive TT	Chemoprophylaxis
Tuberculosis, clinically active Diagnostic Test Positive	Recommended chemotherapy
Tuberculosis, not clinically active Diagnostic testes negative	None / Chemoprophylaxis
Tuberculosis suspect (Diagnosis pending)	Treat empirically and diagnose or diagnose and treat.

1.5.2. THE ANTI-TUBERCULOSIS DRUGS

Isoniazid (H), rifampin (R), ethambutol (E), pyrazinamide(Z) and streptomycin (S) are the essential first-line anti-tuberculosis drugs. Aminoglycosides (kanamycin, amikacin), quinolones (ciprofloxacin, ofloxacin, levofloxacin), ethionamide or prothionamide, cycloserine, para-aminosalicylic acid (PAS) and polypeptide (capreomycin) are the second-line anti-tuberculosis drugs. The recommended doses of the anti-tuberculosis drugs are as shown in **Tables 03, 04** . **Table 05** shows drugs which may be used as salvage therapy for XDR TB.

Table 03 : WHO recommended doses of the first-line anti-tuberculosis drugs **(Joshin , 2011).**

Drugs	Daily doses (mg/kg)	Route	Thrice weekly dosage (mg/kg/dose)
Isoniazid (H)	5 (4–6)	Oral	10 (8–12)
Rifampin (R)	10 (8–12)	Oral	10 (8–12)
Ethambutol (E)	15 (15–20)	Oral	30 (25–35)
Pyrazinamide (Z)	25 (25–30)	Oral	35 (30–40)
Streptomycin (S)	15 (12–18)	Oral	15 (12–18)

Table 04: Recommended doses of second-line anti-TB drugs **(Joshin , 2011).**

Drugs	Daily doses (mg/kg)	Route	Maximum daily dose
Kanamycin (K)	15	IM	Up to 1 g
Amikacin (A)	15	IM	Up to 1 g
Ethionamide (Eto)	10–15	Oral	Up to 1 g
Cycloserine (Cs)	10	Oral	Up to 1 g
Para amino salicylic acid (PAS)	250	Oral	Up to 1 g
Ofloxacin (Ofx)	15–20	Oral	800–10000 mg
Levofloxacin	7.5–10	Oral	750-1000 mg
Moxifloxacin	7.5–10	Oral	400 mg

Table 05 : shows drugs which may be used as salvage therapy for XDR TB. **(Joshin , 2011).**

Clofazimine (Cfz)
Amoxicillin/clavulanate (Amx-clv)
Linezolid
Thioacetazone
Imipenem/cilastatin
Clarithromycin
High-dose isoniazid (16–20 mg/kg per day)

1.5.3. PRINCIPLES OF ANTI-TUBERCULOSIS CHEMOTHERAPY

The anti-tuberculosis therapy is a unique, two-phased chemotherapy consisting of initial intensive phase with multiple drugs (three or more) and continuation phase with two or three drugs. The multidrug initial intensive phase is given to take care of the drug-resistant organisms and to achieve 'a quick kill' to reduce the bacillary load, which in turn reduces the number of "persisters' in the lesions. "Persisters" are drug-sensitive organisms, which become dormant and are later responsible for relapses. The continuation phase of chemotherapy, consisting of two drugs is therefore given to kill the "persisters," which show intermittent activity. The role of individual drugs in first-line chemotherapy of TB is unique. Isoniazid is responsible for the initial kill of about 95% organisms during the first two days of treatment. Its bactericidal role is then replaced by rifampicin and pyrazinamide during the intensive phase. In the continuation phase, rifampin is the most effective drug against dormant bacilli (persisters), . When either rifampin or isoniazid is not used, the duration of chemotherapy is 12 to 18 months. When both isoniazid and rifampin are used in treatment, the optimum duration of chemotherapy is 9 months. Addition of pyrazinamide, but not neither streptomycin nor ethambutol reduces the duration to six months. Prolongation of chemotherapy beyond these periods increases the risk of toxicity while providing no additional benefit. Second-line therapy duration ranges from 18 to 24 months. **(Joshin , 2011).**

1.5.4. TREATMENT GUIDELINES: PAST, PRESENT AND FUTURE

Public health programs in many countries follow guidelines for treatment of TB developed by the World Health Organization (WHO). These guidelines were practiced till 2009 in which the treatment regimes were categorized into four categories **[Table 06].** Categories 1–3 used a combination of first-line drugs for the shortest acceptable period. **(Joshin , 2011)**.

Category 1 is for treatment of new cases (an initial intensive phase (IIP) of four drugs ethambutol, isoniazid, rifampicin, pyrazinamide for 2 months and 4 months of continuation phase (CP) of two drugs isoniazid and rifampicin -2EHRZ/4HR). **(Joshin , 2011).**

Category 2 is ‘‘retreatment’’ regimen (8 months of isoniazid, rifampin, ethambutol, with pyrazinamide, and streptomycin added for the first 2 months—2SHRZE/1HRZE/5HRE) was recommended for relapse and retreatment cases. **(Joshin , 2011).**

Category 3 recommended omission of ethambutol for children, patients, with smear-negative pulmonary or extra-pulmonary TB that is fully drug-susceptible and patients negative for Human immunodeficiency virus (HIV). **(Joshin , 2011).**

Category 4 was for treatment of drug-resistant TB using a standard treatment regimen (STR) using combination of second-line drugs; the initial phase five drugs, pyrazinamide (Z), kanamycin (Km), ofloxacin (Ofx), ethionamide (Eto) and cycloserine (CS) for 6–8 months and the continuation phase of three drugs, ofloxacin (Ofx), ethionamide (Eto) and cycloserine (CS) for 12 months. For treatment of XDR-TB, salvage chemotherapy may be considered29,30 using capreomycin (Cm), moxifloxacin (Mfx), para amino salicylic acid (PAS) +/– cycloserine (Cs) . **(Joshin , 2011).**

The category 1 treatment regimen was recommended based on the results of randomized trials. This regimen was found to have good bactericidal property (infectious patients quickly become non-infectious and sputum conversion occurs at two months in more than 90% cases) and good sterilizing property (low relapse rates of 0–2%), is equally efficacious in primary isoniazid resistant cases and has high cure rates even after premature discontinuation. Further it was found suitable for adults and children, for pregnant and lactating women, for cases associated with diabetes mellitus (DM) and HIV infection, for cases with pre-existing liver diseases (but normal liver functions) and mild renal failure. Unlike the category 1, the category 2 retreatment regimen was a product of expert opinion. It was originally designed for resource-poor settings with low prevalence of initial drug resistance, and for patients previously treated with a regimen that used rifampin only for the first two months of therapy. However, this regimen was increasingly criticized because of poor results, particularly in settings where rifampin was used throughout initial therapy or prevalence of initial drug resistance was high. When used after failure of category 1 treatment, this regimen effectively allowed addition of SM , addition of one drug to a failing regimen, which was against the basic principle of TB chemotherapy. Similarly, in category 3 ethambutol omission was recommended based on the

assumption that lesions in some cases like those negative for HIV, smear-negative pulmonary or extra-pulmonary TB harbour fewer bacilli and hence have little risk of selecting resistant bacilli. However, as initial resistance to isoniazid Is common in many areas; a revised guideline in 2004 recommended that ethambutol be included as a fourth drug during the initial phase of treatment even for smearnegative pulmonary or extra-pulmonary TB patients and effectively eliminated category 3. **(Joshin , 2011).**

These treatment categories were not only controversial but also created confusion for the treating physician. Therefore the WHO guidelines were revised and updated in 2009 **[Table 07].** It remains to be seen if the revised guidelines address deficiencies of the previous guidelines. However, the recommendation to start empiric second-line therapy in previously treated cases with high likelihood of MDR may result in hasty and casual initiation of secondline therapy and create further drug resistance resulting in XDR/XXDR/TDR. It would be reasonable to allocate treatment groups into more definitive categories **[Table 08] .** While standard 2EHRZ/4HR should be used for all new cases, in cases where retreatment is required for relapse after first-line therapy, it is prudent to start first-line therapy and order drug susceptibility testing (DST). If DST is not available and the patient shows good response in 2–3 months or DST shows drug-sensitive disease, CP may be commenced and given for 7 months. Cases that show failure of fully supervised first-line therapy or show MDR-TB on DST should be treated with second-line drugs. Cases failed on MDR treatment or showing XDR on DST may be treated with salvage regimens. **(Joshin , 2011).**

Table 06: Previous World Health Organization (WHO) treatment categories **(Joshin , 2011).**

Category	Treatment regimen
New sputum smear positive, Severely ill sputum smear negative Seriously ill extra pulmonary	2EHRZ+4HR
Relapse Retreatment Defaulter	2SHERZ+HERZ+5HRE
New sputum smear negative Not seriously ill extra pulmonary	2(E)HRZ/+4HR
Treatment failure	8Km-Ofx-Eto-Cs-E-Z+12Ofx-Eto-Cs-E

Table 07: World health organization (WHO) treatment categories **(Joshin , 2011).**

Category	Treatment regimen
Treatment of new cases	2EHRZ+4HR
Treatment of previously treated cases	
a) low to medium likelihood of MDR	2SHERZ+HERZ+5HRE
b) high likelihood of MDR	Treat as MDR

Table 08: Proposed treatment categories **(Joshin , 2011).**

Category	Treatment regimen
Treatment of new cases	2EHRZ+4HR
Treatment of relapse cases	2HERZ+7HRE
i) Previous cure with supervised standard first line therapy	
ii) HR sensitive on DST	
Treatment of MDR cases	6/8Km-Ofx-Eto-Cs+12/18Ofx-Eto-Cs
i) Failure of supervised standard first-line therapy	
ii) MDR on DST	
Treatment of XDR cases	CM-Mfx-PAS-2 or 3 Group 5 agents +/– Cs
i) Failure of standard second-line therapy	
ii) XDR on DST	

1.5.5. CHEMOTHERAPY OF TB IN SPECIAL SITUATIONS

A. Pregnancy

Rifampin, isoniazid, ethambutol, and pyrazinamide can be used safely during pregnancy. Streptomycin is not given as it can cause ototoxicity to the fetus. Addition of pyridoxine in the dose of 10 mg/day is recommended to prevent isoniazid peripheral neuropathy. **(Joshin ,2011).**

B. Diabetes mellitus

Standard recommended chemotherapy must be used. Tight glycemic control is desirable. Doses of oral hypoglycemic agents may have to be increased due to drug interaction with rifampin. Prophylactic pyridoxine in the dose of 10 mg/day is recommended to prevent isoniazid peripheral neuropathy. **(Joshin , 2011).**

C. Renal failure

Dosages may have to be adjusted according to the creatinine clearance especially for streptomycin, ethambutol and isoniazid. In acute renal failure, ethambutol should be given 8 hours before hemodialysis. Creatinine clearance should be estimated for adjustment of some of the antituberculosis drugs. The formula, creatinine clearance = (140 - Age) Weight / 72 × serum creatinine, gives a rough estimate of the glomerular filtration rate. According to the creatinine clearance, either the dosage interval is changed or the dose is reduced as a percentage of the normal daily dose **[Table 09] .**

Table 09: Dose adjustment based on glomerular filtration rate **(Joshin , 2011).**

Drugs	**Glomerular filtration rate**		
	>50 ml/min	**10–50 ml/min**	**<10 ml/min**
Kanamycin	60–90%	30–70%	20–30%
Streptomycin	24 h	24–72 h	72–96 h
Ethambutol	24 h	24–36 h	48 h
Isoniazid	100%	100%	66–75%

D. Post transplant patients and other special situations

Rifampin-containing regimens are avoided as rifampin causes increased clearance of cyclosporin. **(Joshin , 2011).**

E. Pre-existing liver disease

In stable disease with normal liver enzymes, all antituberculous drugs may be used but frequent monitoring of liver function tests is required. **(Joshin , 2011).**

Baseline and regular monitoring of liver function is required in patients with known chronic liver disease such as alcoholism, chronic active hepatitis, cirrhosis, and in those known to be hepatitis B or C antigen positive. In such patients surveillance should be particularly frequent in the first two months of treatment (weekly liver function tests for the first two weeks, and then at two weekly intervals). **(J.T.C.B.T.S , 1998).**

F. Treatment in unconscious patient/patients unable to swallow

If patients are fed by nasogastric tube or gastrostomy tube, usual doses and drugs may be powdered and administered avoiding feeds 2–3 hours before and after the dose. In cases where enterostomy has been performed or parenteral nutrition is being used, intramuscular streptomycin and intravenous quinolones may be used and switch to oral therapy once oral feed resume. **(Joshin , 2011).**

G. Tuberculosis with hiv co-infection

In early stages, the presentations of TB in TB-HIV coinfection is the same as HIV negative but in late stages extra-pulmonary and dissemination are common. Diagnostic problems arise as other respiratory diseases occur frequently and tuberculin test may be negative. The usual short course chemotherapy as per treatment categories is indicated in HIV-positive patients. The response is usually good but relapse is more frequent. **(Joshin , 2011).**

H. Seriously Ill patients with Suspected tb

Use of specific empiric anti-tuberculosis therapy (SEATT) with isoniazid, ethambutol, pyrazinamide can be used as a method for rapid presumptive diagnosis and treatment of febrile patients with clinical and radiological suspicion of TB, who are seriously ill and where no bacteriological or histologicalproofisavailable. Fever is used as guide for response to therapy. Rifampicin and aminoglycosides or quinolones are not used, to ensure that defervescence of fever is due to action of specific anti-TB drugs i.e. isoniazid, ethambutol and pyrazinamide. Rifampicin may be added as soon as the patient is afebrile. **(Joshin , 2011).**

I. Corticosteroids

Because of enzyme induction the maintenance dose of corticosteroid taken for other conditions should be doubled if rifampicin is used. Corticosteroids should be given, in addition to antituberculosis treatment, for pericarditis, for stage II and III meningitis, and for endobronchial disease in children. Corticosteroids may be indicated in tuberculosis aVecting the ureter, in pleural eVusions, in patients with extensive pulmonary disease, and to suppress hypersensitivity reactions to antituberculosis drugs. **(J.T.C.B.T.S , 1998).**

Fig. 28 : Different drugs for tuberculosis traitement **(website 9)** .

1.5.6. Preventive treatment

1.5.6.1. Chemoprophylaxis

It is important to di Verentiate between infection and disease. In tuberculous infection the tuberculin skin test is positive, the chest radiograph is normal, and the patient asymptomatic. In tuberculous disease the skin test is usually positive and there are clinical signs and symptoms or radiographic changes present. Asymptomatic, tuberculin positive patients with normal chest radiographs (infection) are usually treated (chemoprophylaxis) with either one drug for six months or, alternatively, with two drugs for three months. Infection, in contrast to disease, implies the presence of small numbers of tubercle bacilli in the body . The administration of one or two antituberculosis drugs for a shorter period of time than for disease (chemoprophylaxis) is likely to kill these organisms, preventing possible progression to disease at a later date. Many studies have shown that chemoprophylaxis with isoniazid for 12 months is highly effective and that six months is probably as effective .

Regimens of rifampicin and isoniazid lasting only three months have been used in clinical practice in some areas of the United Kingdom with good effect and no increased adverse reactions, and have been shown to be as good as six months of treatment with isoniazid in a randomised controlled trial in Hong Kong . In contacts of an isoniazid resistant patient, rifampicin for six months has been shown to be effective . **(J.T.C.B.T.S , 1998).**

1.5.6.2. BCG vaccine

A. Status of Current TB Vaccine (BCG)

The only currently licensed vaccine against pulmonary and extrapulmonary TB is the live attenuated BCG vaccine. It was originally derived from the pathogenic *Mycobacterium bovis* that causes TB primarily in cows . To attenuate its pathogenicity, two French scientists, Calmette and Guerin, cultured M. bovis on an artificial medium in vitro for 13 years (1908–1921) and a total of 231 passages. The resulting organism, BCG, did not cause TB lesions in various animal models but was immunogenic and protected the immunized animals against challenges with M. bovis . Since 1921, the BCG vaccine has been used in infants and children and is effective in providing protection against childhood TB, avoiding 120,000 childhood deaths per year . However, it fails to protect against adult pulmonary TB, the major manifestation of the disease . For example, although high-incidence nation China has an overwhelming BCG vaccine coverage, three-quarters of TB is estimated to occur in the 45-year-old or older population . BCG's decline in efficacy after 10 years is an additional problem for countries with a high incidence of TB, as BCG vaccination occurs at birth, leaving people at risk later in life when they are most vulnerable . In fact, the elderly have been shown to have a higher prevalence of TB across all age groups . **(Whitlow *et al.*, 2020).**

The BCG vaccine also poses a risk to immunocompromised individuals [18,19]. Those with primary immunodeficiencies are prone to develop severe vaccine-derived complications . Additionally, BCG vaccination of HIV-exposed but uninfected infants resulted in reduced BCG-specific T-cell proliferation and production of lower concentrations of protective cytokines IFN-γ and TNF-α, compared to healthy infants . The results further showed a delay in immune system maturation of HIV-exposed uninfected infants and hence resulted in a higher risk for developing TB . Furthermore, BCG vaccination of HIV-infected infants and children has the risk of causing a TB-like disseminated disease known as BCG-osis . In addition, BCG is a preventative pre-exposure or prophylaxis vaccine and is not effective as a therapeutic vaccine against post-exposure active and latent TB . **(Whitlow *et al.*, 2020).**

Fig. 29 : BCG vaccine **(website 10).**

B. Is BCG effective ?

BCG is derived from an attenuated strain of *Mycobacterium bovis,* and since its introduction in 1921 over 3 billion doses of the vaccine have been given worldwide.1 Although BCG remains the world's most popular vaccine with over 80% coverage of the world's population, there is considerable debate with respect to its eVectiveness in the control of TB. A metaanalysis of over 1200 articles from international publications has concluded that the overall protective value of BCG against all forms of TB was of the order of just 50%, but that protection against more serious infection was greater, being 64% and 78% against tuberculous meningitis and disseminated infection, respectively. It was also found that the reported efficacy of BCG varies considerably in different studies. This may result from various possible factors: variation in study validity; use of differing BCG preparations (several substrains of the vaccine are in current use); diverse population genetics and levels of nutrition; and environmental factors such as exposure to environmental (atypical) mycobacteria, climate, socioeconomic issues, and sunlight. For example, the reported efficacy of BCG in the prevention of pulmonary TB varies from 0% in South India to 77% in the UK Medical Research Council trial. Evidence for the protective value of BCG in the UK is encouraging, with a reported overall value of 75% with greater levels of protection provided against TB meningitis and miliary infection. **(Bannon, 1999).**

C. Who should receive BCG and when should it be given?

Recommendations for BCG immunisation of children in the UK are to be found within Immunisation against infectious disease. BCG is generally recommended for children who have not previously received the vaccine and who are found to have negative tuberculoprotein hypersensitivity on skin testing. Most districts implement an immunisation programme that is

specifically directed towards high risk newborns, children who are recent immigrants from high risk areas, and schoolchildren aged 10–14 years. The value of neonatal BCG immunisation is accepted and tuberculin reactivity after neonatal intradermal BCG immunisation remains high and sustained at least until 4 years of age. A selective rather than universal BCG immunisation policy is currently advised by the Department of Health, whereby BCG is offered to newborn infants whose parents are from areas with a high prevalence of TB— mainly Asia, Africa, Central and South America. . It has been suggested that universal BCG immunisation should be undertaken in districts where the prevalence of TB is relatively high (that is, greater than 40 notifications/100 000 resident population each year). This approach may be more practical to implement and be more acceptable politically to local populations. **(Bannon, 1999).**

With regard to the optimal time for giving BCG to infants, there is some evidence to suggest that later immunisation during infancy may confer a higher degree of immunity. BCG immunisation at 3 months of age was found in one study to provide a higher rate of tuberculin protein skin responses with fewer complications than when given during the first three days of life. **(Bannon, 1999).**

1.6. Prophylaxie

A. Ventilation

- ✓ The exchange of indoor air with outdoor air reduces the risk of infection by diluting the concentration of airborne pathogens. Theoretically, the risk of transmission should decrease with increasing fresh-air ventilation.
- ✓ -A medical mask should be used by individuals with, or being evaluated for, respiratory tuberculosis when in the healthcare setting and outside an airborne infection isolation room.
- ✓ Baseline tuberculin skin testing is recommended for all health care workers in all healthcare settings. Recommendations for periodic and serial (repeated) tuberculin skin testing for health care workers vary with the setting, but periodic (repeated) testing is no longer routinely recommended for all health care workers. **(Johnston *et al., 2022*)**

B. Ultraviolet germicidal irradiation

- ✓ Ultraviolet germicidal irradiation (UVGI) is effective at inactivating airborne bacteria and in reducing the risk of M. tuberculosis transmission. UV light kills off TB bacteria

- ✓ -Healthcare settings should have policies in place regarding requirements for cleaning, disinfection and sterilization of medical equipment based on its intended use.
- ✓ BCG is a safe and effective vaccine for the prevention of childhood TB. (Johnston *et al., 2022*)
- ✓ Good hygiene, covering the mouth and nose when coughing or sneezing reduces the spread of TB bacteria.
- ✓ Wash your hands after coughing or sneezing. **(website 11).**

1.7. Prévention

1.7.1. What to Know

This can be done through raising awareness of TB, so people with TB symptoms know to seek help. Outreach workers and volunteers also work within communities with high rates of TB to find people with symptoms and refer them for testing. When someone is diagnosed with infectious TB, their close contacts are screened for the illness this is known as contact tracing. and the regular screening of healthcare workers for TB. **(website 11) .**

- ✓ Doing physical exercises contributes to exposure to a state of chronic stress**.(website 12)**

To prevent TB infections through guidance and implementation of infection prevention and control measures. These measures are critical in situations where the risk of TB transmission is high, such as health-care facilities, congregate settings and TB-affected households. WHO also promotes preventive action through early screening and treatment for active TB, by addressing co-morbidities and health risks as well as social determinants of the disease, and by promoting access to universal health care. **(website13).**

1.7.2. Tips to prevent TB infection

Here are some tips for preventing TB infection

- Avoid close contact with people who have active TB disease.
- Wash your hands often and cover your mouth when coughing or sneezing.
- Eat a nutritious diet and exercise regularly to keep your immune system strong.
- If you work in a healthcare setting abroad, follow protocols for wearing protective gear such as masks and gowns.
- If you have a latent TB infection, follow the entire treatment protocol.

- If you’re traveling to a high risk area and you have a compromised immune system, talk with a doctor about preventive treatments.

Takeaway

TB prevention measures include avoiding close contact with people with active TB disease and treating latent TB infections.

Vaccinations:

A TB vaccine, called the bacillus Calmette-Guérin (BCG) vaccine, is mostly usedi. **(website 14).**

Fig.30: The actions of Prophylaxis Tuberculosis **(Websites 15 , 16 , 17).**

Chapter II :

Presentation of The Study Area

2. Presentation f The Study Area

2.1. Geographic location

The wilaya of Mila is located in north-eastern Algeria at an altitude of 464 m, and 70 km from the Mediterranean Sea. It is also in the eastern part of the Tell Atlas, a mountain range that extends from west to east across the northern territory of the country **(A.N.D.I., 2013).**

The wilaya of Mila is limited:

- To the northwest by the wilaya of Jijel.
- In the North East by the wilaya of Constantine.
- In the West by the wilaya of Sétif.
- In the East by the wilayas of Constantine and Skikda.
- In the South East by the wilaya of Oum El Bouaghi.
- In the South by the wilaya of Batna.
- The wilaya of Mila covers an area of 9373km² **(A.N.I.R.E.F., 2011).**

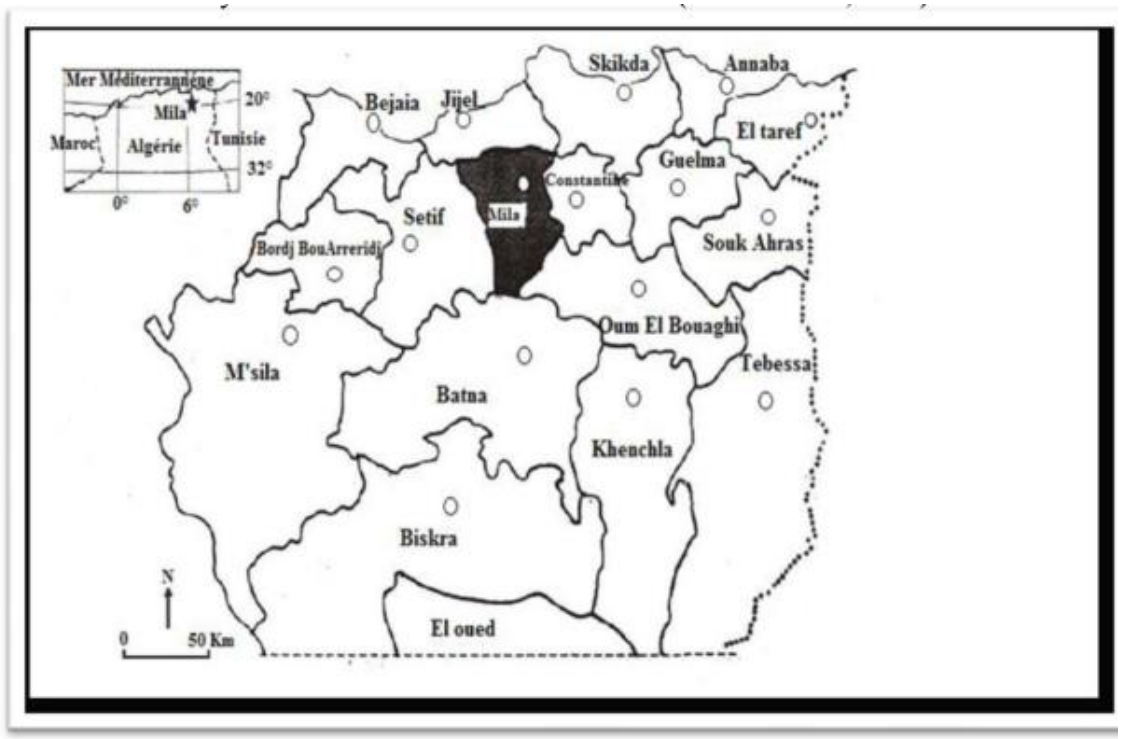

Fig. 31: Geographic location of the Mila region **(Doula and Ferhat, 2014).**

2.2. Demographic situation

The wilaya of Mila is divided into 13 daïras. It covers an area of 3,480 km² with a population of 865,370 inhabitants, i.e. a density of 248.7 inhabitants/Km2 . This density varies from one commune to another due to multiple regional specificities of an economic (agriculture, industry and trade), geomorphologicl (nature and relief of the land) and administrative (area allocated to each commune during the administrative division) nature. (Abid, 2014). Number of women is slightly higher than that of men, 408604 for 401766. The population of the wilaya is relatively young, more than 50% is located in the age range of 1 to 24 years, or 420887 inhabitants, for a total of 810370 inhabitants. The population is largely rural and suburban. It is generally made up of workers on the land, both on the high plains and in the mountainous regions. The urban population, concentrated in the large cities, is still imbued with the values of rurality **(Seddiki et al., 2013).**

2.3. Administrative Aspects

The wilaya of Mila was created during the last Algerian administrative division of 1984, with the city of Mila as the capital of wilaya 43 (A.N.D.I, 2013).The wilaya of Mila has 13 daïras comprising 32 municipalities **(table 11).**

Table. 10 : The administrative division of the Mila region **(Boularas and Kadjoudj, 2016).**

Dairas	Municipalities
Mila	Mila- Ain Tine- Sidi Kkhlifa
Grarem Gouga	Grarem Gouga- Hamala
Sidi Merouan	Sidi. Mérouane- Chigara
Oued Endja	Oued Endja- Zeghaia- A. Rachdi
Rouached	Rouached- Tiberguent
Terrai Beinen	Terrai Beinen- AmiraArres- Tassala Lamtai
Ferdjioua	Ferdjioua- Y. B. Guecha
Tassadane.H	ZarzaTassadane Hadda- Minar
Bouhatem	Bouhatem- D. Bousselah
Ain Baidah H	Ain B.Ahrich- AyadiBerbes
Teleghma	Telaghma- OuedSeguen - El M'chira
Chelghoum Laid	Chelgoum El Aid- O. Atmania- AinMelouk
Tadjenanet	Tadjnanet- Ben Yahia A- OuledKhlouf

2.4. Vegetation

The plant cover is not very important; it consists mainly of cereal crops and wild grasses **(Remmache, 2006).**

2.4.1. Agricultural activities

The total agricultural area is important in the wilaya of Mila, it covers more than 90% of the territory of the wilaya (about 315,745 ha). It also evolved positively between 1999 and 2010 (+12.8%). The usable agricultural area is also important, it has certainly changed little over the last ten years, but it has remained quite significant, of the order of 2370557 ha. This shows that we are in an essentially agricultural region. On the other hand, the irrigated areaeven if it has increased slightly in 10 years (+5.8%)-is considered to be very low, and this is explained by the ban on the use of water from the two dams (Beni Haroun and Grouz). The rest of the land is made up of rangeland, maquis forest and unproductive land **(Metaai and Beldi, 2011).**

2.4.2. Forest heritage

The forest area in the wilaya of Mila covers 33870 ha or 9.7% of the total area of the wilaya. The Aleppo pine represents the dominant species of the forests of the wilaya, it occupies about 48.57% of the total forest area it is generally found in the forests of Ferdjioua, Ain Beida, Bouhatem, Mila, Chelghoum-Laid and Tadjnanet . **(Fig. 32) .**

✓ The cork oak occupies about 16.73% which are generally found in the forests of Grarem, Sid-Merouane, Tassadane and Tarai-Beinen. Other forest species such as oak zeen, pinion pine, ash and eucalyptus occupy small areas respectively about: 1.29%, 1.77%, 0.59%, 0.29% of the total forest area (Metaai and Beldi, 2011).

Fig. 32: Map of the forest cover of the wilaya of Mila (Doula and Ferhat, 2014).

2.5. Geology

The study region in the Alpine chain of North Africa whose complex geological framework is characterized by the presence of thrust sheets. These aquifers constitute vast sets of terrains from the Antecambrian to Lower Miocene age which moved (in the form of "thick" scales) horizontally over distances of several kilometers and were deposited according to varied and complex methods **(Boularas and Kadjoudj, 2016).**

2.6. Pedology

In general, the Mila region is covered by vertic light brown soils (Berkal and Elouaere, 2014). These soils are characterized by a clayey structure, medium to fine on the surface and finer in depth. They are rich in exchangeable potassium, calcareous and poor in assimilable phosphorus. As well as this type of soil has high water retention and is characterized by the appearance of shrinkage cracks in dry periods **(Berkal and Elouaere, 2014).**

2.7. Relief

The wilaya of Mila is entirely surrounded by mountain ranges belonging to different paleogeographic domains:

-In the north, a set of high mountains, characterized by very high altitudes and excessively marked slopes, such as: M'Cid Aicha and Sidi Driss.

-In the south, a set of high plains (plains and hills), such as: Djebel Osman and Grouz. Djebel Lakhal, Chettaba and Kheneg from the east, and Djebel Boucherf and Oukissene by the west **(A.N.D.I, 2013; Merghadi et al., 2018)**

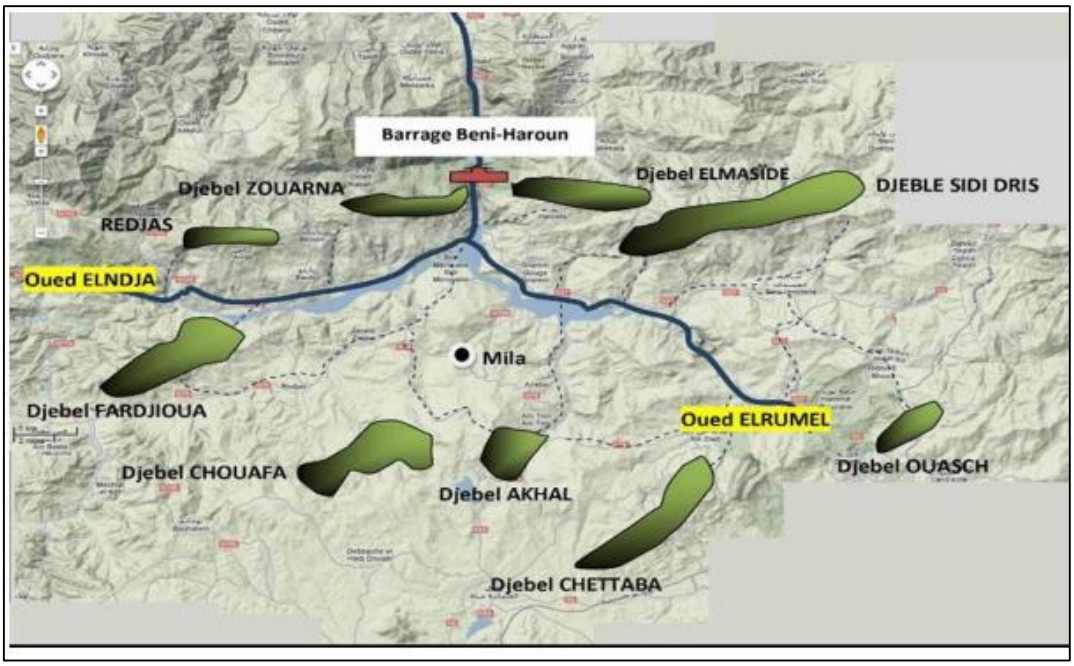

Fig. 33: Map of the major relief features of the Mila basin **(Barik, 2012)**

2.8. Hydrographic network

the wilaya is home to an important hydrographic network composed of rivers and dams: the largest water dam at the national level, the Beni Haroun dam, which supplies a large part of eastern Algeria with drinking water and irrigation water, as well as the Oued Athmania dam, and the Oued Seguène dam. The Oueds Rhumel and Oued Endja (Oued El Kebir) are the main sources of supply for the Beni Haroun dam **(Abid, 2014).**

There are 415 water sources in the wilaya; 57 wells and 87 boreholes located in the southern part of the wilaya **(Soukehal and Cherrad , 2011).**

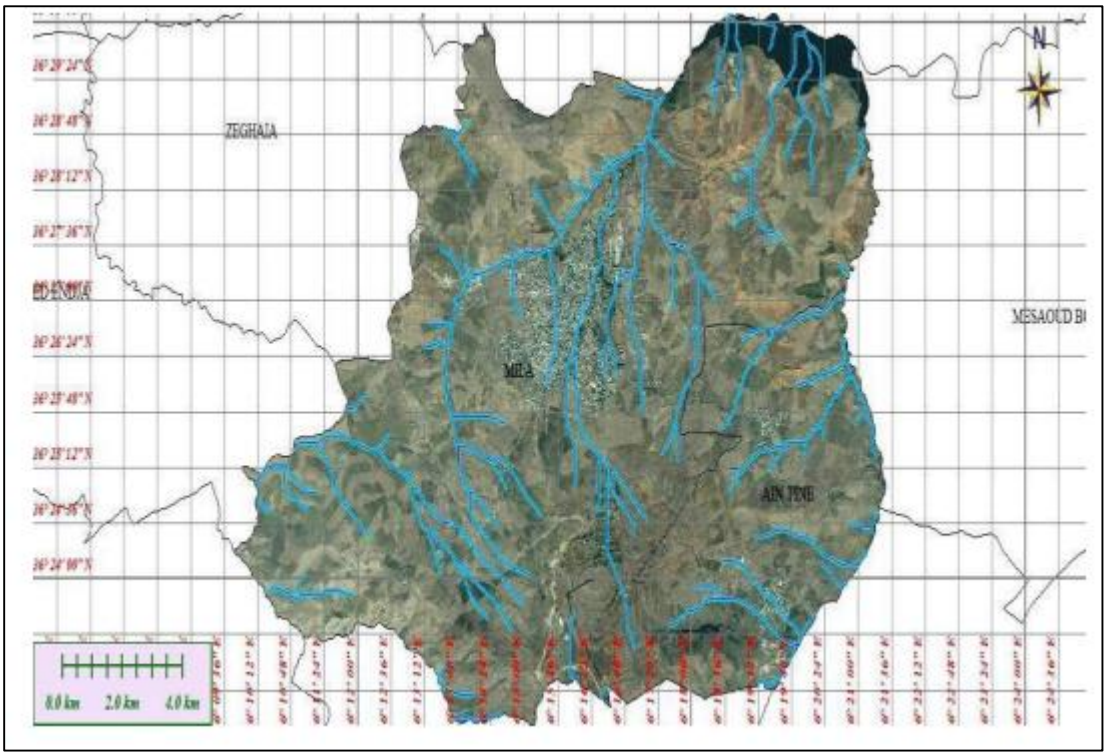

Fig. 34: Hydrographic network of the Mila region **(Soukehal and Cherrad ,2011)**

The Beni Haroun dam located at the heart of a huge hydraulic complex, with a storage capacity of 960 million cubic meters, and a height of 120 meters **(Seddiki et al., 2013).** It is the largest Artificial Reservoir in Algeria and the second largest on the African continent (after the Al Sad El Alli dam in Egypt) with a reserve of 1 billion m3 of water reached in February 2012 (i.e. 40 Million m3 beyond its target capacity), distributed over 3,900 hectares. Located on Wadi el Kebir, it is fed by two main branches, with the wadis Rhumel and Endja **(Seddiki et al., 2013).**

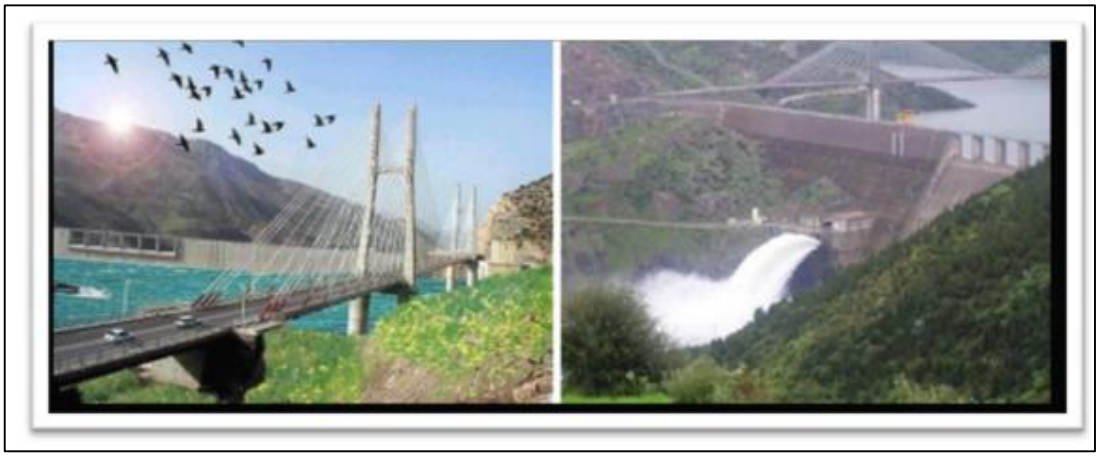

Fig. 35: The Beni Haroun dam **(Abid, 2014).**

2.9. Climatology

Climatology is the set of meteorological characteristics of a given region. However that, climate is the set of meteorological phenomena that characterize the average state of the atmosphere at a point on the earth's surface (Soukehal, 2009). The most important environmental factor is certainly the climate. It has a direct influence on the fauna and flora. It demonstrates an impact on migratory birds: shifting of migration periods, modification in the reproduction and survival of species, displacement of breeding and wintering areas. The climate of the wilaya of Mila is a typical Mediterranean climate. It is characterized by :

- A wet and rainy season (winter) extending from November to April.
- And a long hot and dry summer period from May to October **(Zouaidia, 2006).**

➢ **Temperature**

Temperature is an essential and fundamental ecological climatic factor for the life of living beings. Temperature can affect organisms directly or indirectly because thermal conditions affect other organisms to which an individual is ecologically related, although these relationships could be complex. It acts directly on the reaction rate of individuals, on their abundance and their growth (Faurie et al., 1980) and it explains that living beings can only carry out their activities in a range of temperatures ranging from 0 at 35°C. A moderate Mediterranean temperature during the months of autumn, winter and spring. During the summer, the temperature increases rapidly, especially inside the wilaya. In any case, the temperature is favorable for crops both in summer and winter **(Soukehal, 2011).**

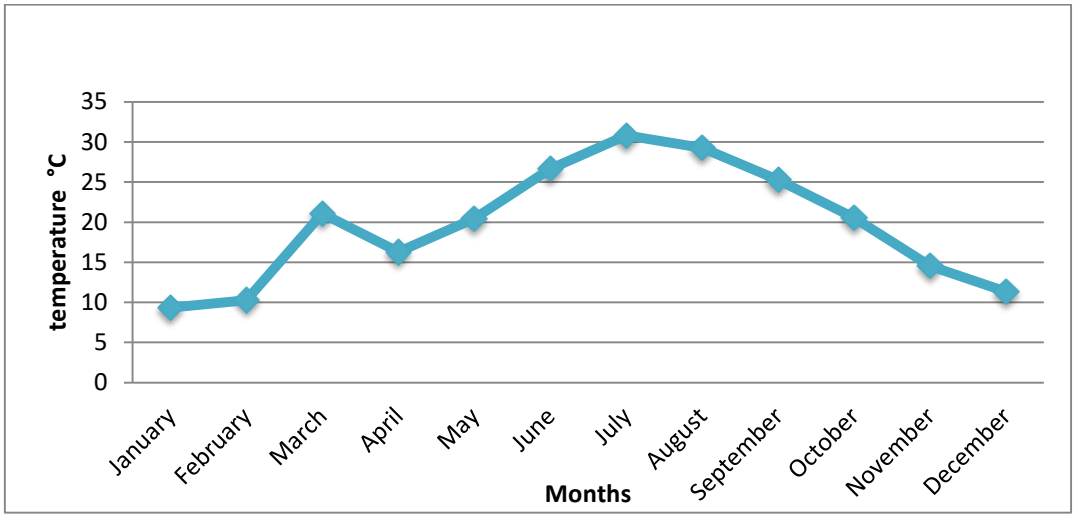

Fig. 36: Average monthly temperature of the Mila region **(Mila meteorological station, 2013 to 2023).**

According to **(fig. 36)**which gives the average monthly temperature changes for our region, we note that the maximum temperature is recorded during the month of July when it reaches 30.81 degrees Celsius, while the month of January is characterized by cold degrees, with a temperature not less than 9.36 Celsius.

- **Precipitation**

Precipitation refers to any type of water that falls from the sky, in liquid or solid form (Dajoz, 2000). It represents an essential climatic factor with regard to the ecological cycle, the hydrographic regime and agricultural activity. The variation of annual precipitation is the striking fact in this wilaya. Rainfall in Mila is unevenly distributed across the months of the year and precipitation is, naturally, confined to the cool semester which begins in November and ends in March. The lack or abundance of precipitation has a significant effect on water reserves; quantities mobilized and quantities exploited. The drought acts directly on the behavior of the population in this area **(Soukehal, 2011).**

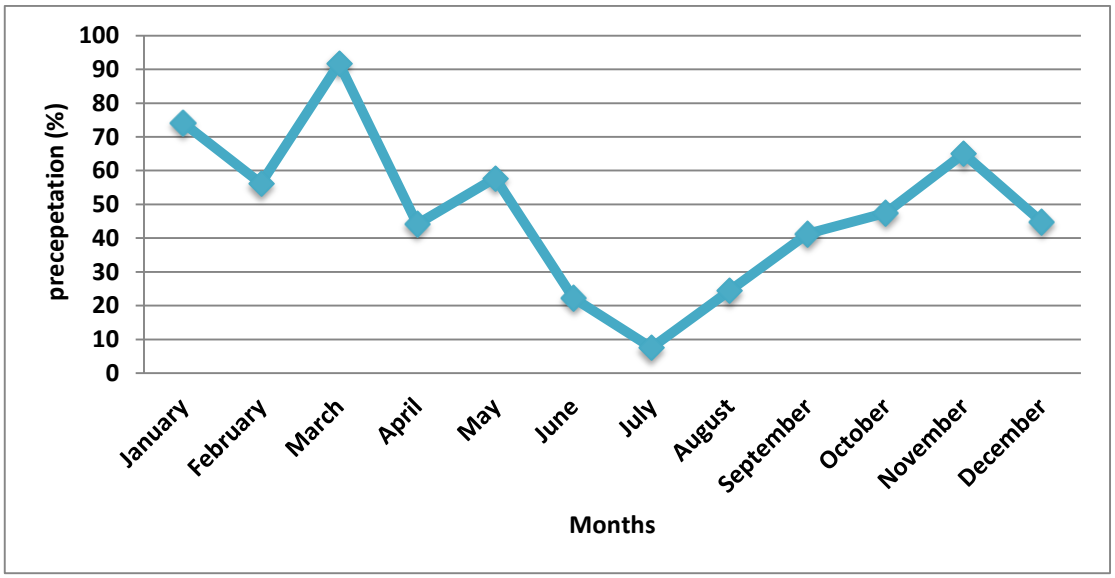

Fig. 37: Average monthly precipitation in the Mila region **(Mila meteorological station, 2013 to 2023).**

The study area is considered one of the wettest areas. From the (**fig. 37)** above, we see that March is the month with the most rain, as it experienced an excess of 91.81 mm, and on the contrary, July experienced a deficit of 10.36 mm, which is the driest month and the annual average of precipitation.

***Seasonal pattern of precipitation**

The rainfall year has been divided into four conventional seasons. The seasonal regime of our study region during the period (2013 - 2023) is of the S. W. A. S type (Spring, Winter, Autumn, Summer). The existence of a summer drought period is one of the essential factors that explain the characteristics of Mediterranean forests.

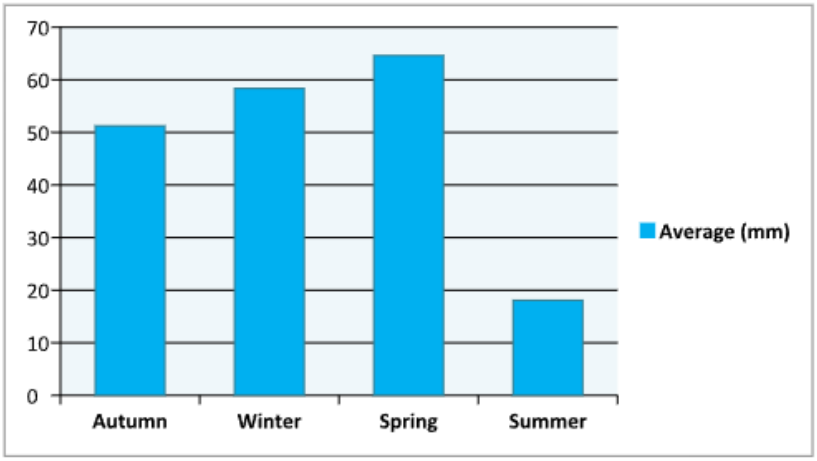

Fig. 38 : Seasonal rainfall diagram of the Mila region (2013 - 2023)

This diagram **(Fig. 38)** shows that the spring season is the wettest with an average of (65.5 mm/month), which produces groundwater recharge, while summer is dry with a low recharge of (19 mm/month), which produces evaporation.

- **Humidity**

It is the ratio between the quantity of water vapor in a given volume of air and the quantity possible in the same volume at the same temperature (Villemeuve, 1974)**.** It depends on several climatic factors such as rainfall, temperature and wind **(Faurie et al., 1980).**

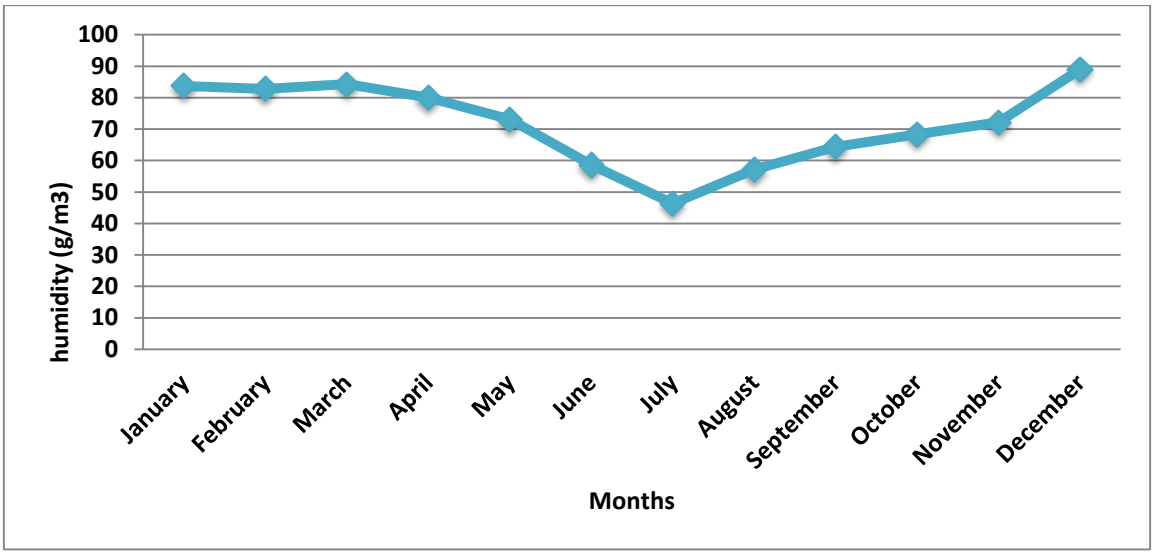

Fig. 39: Average monthly humidity variations in the Mila region **(Mila Meteorological Station, 2013 to 2023).**

According to **Fig. 39,** the month with the highest humidity is December with 89% and the month with the lowest value is July with 46.36%.

- **Wind speed :**

The wind is one of the most characteristic elements of the climate. It acts by activating the precipitation which can induce a drought **(Seltzer, 1946).**

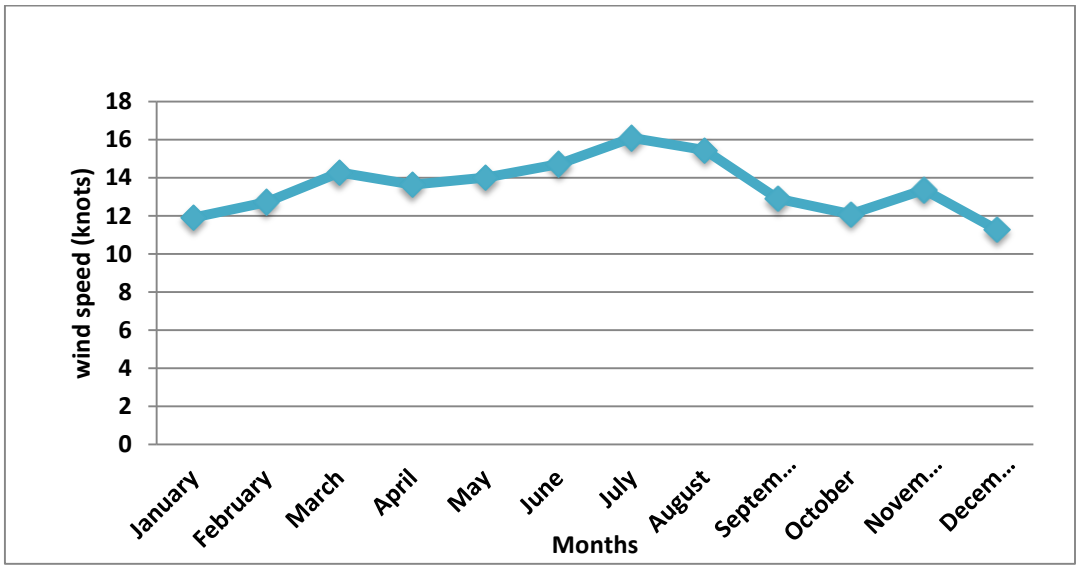

Fig. 40: Average monthly wind speed variations in the Mila region **(Mila meteorological station, 2013 to 2023).**

Fig.40 shows that the maximum wind speed is recorded in the month of July with a maximum value of 16.09 knots, and the minimum speed is in the month of December with a value of 11.27 knots.

- **sunshine duration :**

Sunshine duration is the length of time that the ground surface is irradiated by direct solar radiation (i.e., sunlight reaching the earth's surface directly from the sun). **(Iqbal, M. 2012)**

As the threshold value for the occurrence of sunshine is defined in terms of direct solar irradiance, it is also possible to observe sunshine duration with a pyrheliometer. **(Iqbal, M. 2012)**

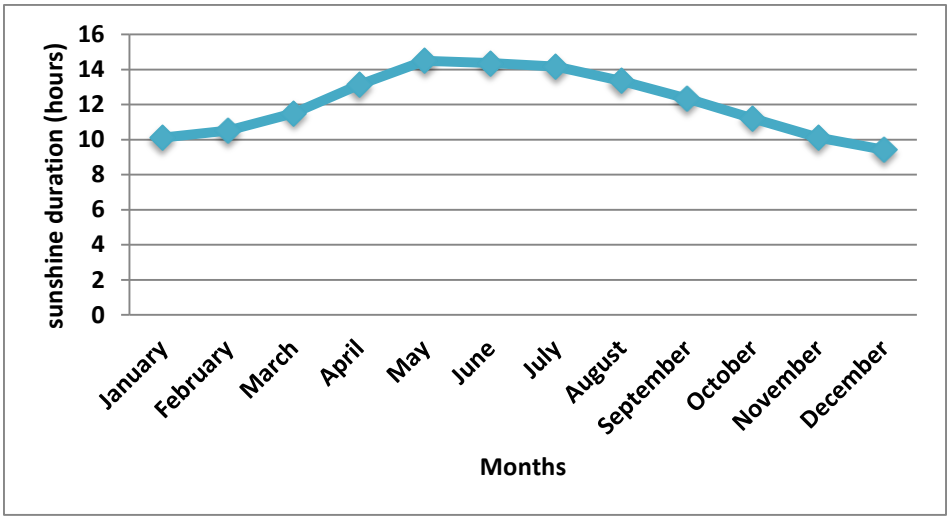

Fig. 41: Average monthly sunshine duration variations in the Mila region **(Mila Meteorological Station, 2013 to 2023).**

According to **fig. 41**, the month with the highest Sunshine duration is May with 14.50% and the month with the lowest value is December with 9.42%.

According to the climatic data and the value of Q index of Emberger's climagram, we deduce that the region of Mila where the perimeter of our study is located is classified in the bioclimatic stage of subhumid vegetation with warm winter. **(Fig. 42)**

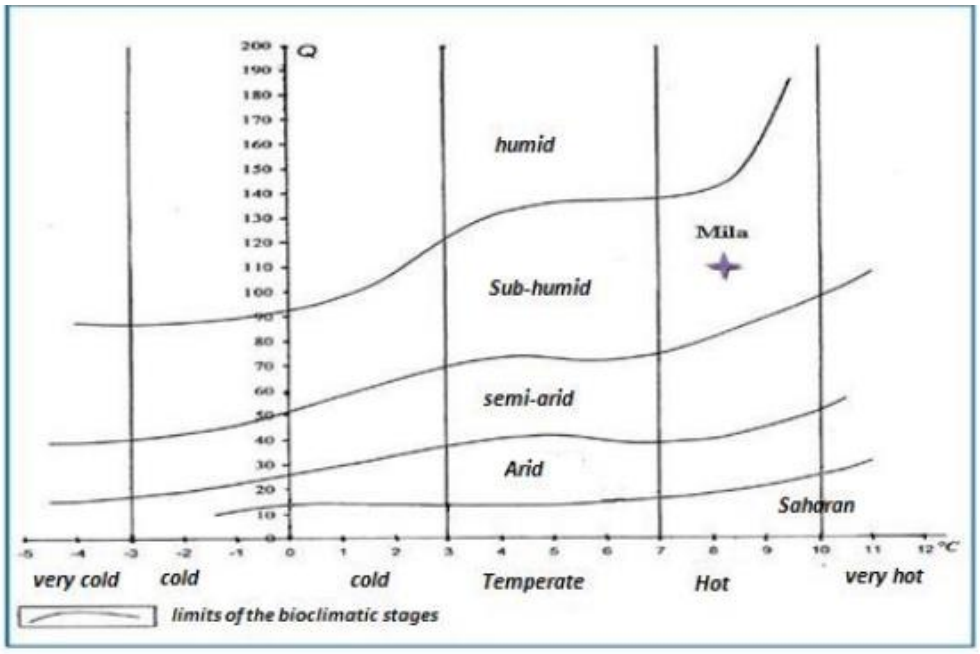

Fig. 42: Situation of the Mila region in the Emberger climagram (Chahlet and Kerdoud, 2018).

2.10. Health structure

Epidemiologically, the wilaya records several hundred cases of notifiable diseases each year, with tuberculosis occupying 1st place followed by meningitis and a few dozen cases of zoonoses (leishmaniasis and brucellosis) as well as some cases of viral hepatitis B and C (Abid , 2014). The wilaya of Mila is organized around five (05) Public Hospitals Establishments (DSPM, 2014).

Table 11: Public Hospital Establishments (EPH) **(DSPM, 2014).**

Denomination	Number of services
Public Hospital Establishments Brothers Maghlaoui Mila.	7
Public Establishments Hospitaliers Brothers Tobal Mila.	9
Public Hospital Establishments Brothers Boukchem Oued El Athmania.	8
Public Hospital Establishments Ferdjioua.	11
Public Hospital Establishments Chelghoum Laid	12

Table 12: Local public health establishments **(DSPM, 2014)**

Denomination	Number of polyclinics	Number of treatment rooms	Communes covered
Mila	14	34	08
Ferdjioua	10	46	09
Chelghoum laid	09	29	06
Ain Beida ahrich	06	29	06
Tadjnanet	02	19	03
Total	40	157	32

With a specialized hospital establishment, the EHS in psychiatry of Oued Athmania, 38 polyclinics, 145 treatment rooms and 02 private clinics **(DSPM, 2014).**

Chapter III :

Material and Methods

3. Material and Methods

3.1. Epidemiological investigation

3.1.1. Location, Type and Duration of the Study

This epidemiological study of human tuberculosis takes place at the level of the tuberculosis and respiratory diseases control service (S.C.T.M.R) of the public clinical establishment Bouaaroudj – Mila.

This study was carried out following the retrospective analytical descriptive method based on the documentary analysis of registers during the study period which was carried out from January 2013 to December 2023 over a period of 10 years.

3.1.2. The patients

This epidemiological study focused on all direct bacteriological examinations of patients sent to the tuberculosis laboratory.

The patients in our study bring together adults and children hospitalized or consulting in the different departments of the Hospital, from very diverse origins both geographically (different municipalities in the Mila region) and socially (patients from the public and private sectors).

During this investigation we collected the statistics of subjects who presented pulmonary and/or extrapulmonary tuberculosis which were recorded at the health program office level in the health department of the wilaya of Mila from the beginning of 2013 at the end of 2023, which was interested in 91700 sick subjects.

Our prospective study focused on 315 patients referred to the bacteriology laboratory during the first three months of 2024.

3.1.3. Bacteriological analysis (January-March 2020)

3.1.3.1. The materials used

→ Sputum bottles .

→ Gloves.

→ Slide.

→ Optical microscope .

→ Bunsen burner.

→ The platinum handle .

→ Cotton mounted on a stem .

Fig. 43 : Laboratory equipment used for the diagnosis of human tuberculosis **(Personal Photo, 2024).**

3.1.3.2. Reagents

√ Basic fuchsin.

√ Sulfuric acid.

√ Alcohol 90°.

√ Methylene Blue.

√ Immersion oil.

Fig . 44: Reagents used in the laboratory for the diagnosis of human tuberculosis **(Personal Photo, 2024).**

3.1.3.3. Bacteriological diagnosis

A- Diagnostic objectives

Permanently identify cases of smear-positive pulmonary tuberculosis present in the community with a view to treating them with anti-tuberculosis chemotherapy and thus sterilizing the sources of infection. This helps protect the community by breaking the chain of transmission of *Mycobacterium tuberculosis.* Identify cases of microscopy-negative pulmonary tuberculosis and cases of extrapulmonary tuberculosis that should also be treated with chemotherapy.

B- Diagnosis of pulmonary tuberculosis

The diagnosis of pulmonary tuberculosis is based on orientation criteria (clinical and radiological) and certainty criteria (bacteriological).

B-1. Orientation criteria

Are elements of suspicion. The most commonly observed are:

- Respiratory functional signs: persistent cough for three weeks or more, sputum sometimes streaked with blood and small amounts of hemoptysis.

- General signs: anorexia, weight loss, asthenia, persistent fever and night sweats.

- Radiological signs: radiology or x-ray photography provides elements of presumption by showing suspicious images of tuberculosis.

B-2. Certainty criteria

- Only the microscopic examination of three sputum samples taken over two days: two spot specimens (samples collected on site) and one overnight specimen (morning sample collected at home), allows the definitive diagnosis of the most contagious forms of tuberculosis in highlighting the tuberculosis.

- Culture on Lowenstein-Jensen medium of the sputum of patients for whom several microscopic examinations (three, six or more) are negative makes it possible to prove the diagnosis of forms of pulmonary tuberculosis with negative microscopy.

B-3. Expectoration

Sputum is the most frequently received sample in the laboratory. In a patient suspected of pulmonary tuberculosis, it is appropriate, whenever possible, to take three (3) samples according to the following methods:

After the consultation, the first sample (called spot specimen) is collected under the supervision of the nurse in a rigid cuspidor, with a wide opening, with a screw lid, closes tightly. The nurse must explain to the patient that expectoration must be done after a deep and vigorous cough in order to bring back bronchial mucus.

He must give the patient a second spittoon and ask him to collect a second sample during the night or in the morning upon waking (overnight or specimen collection) and bring it back to the laboratory as quickly as possible.

When the patient returns, a third sample can be taken on site (spot specimen).

The risk of contamination is considerable when the patient coughs, so the sample must be taken outside or in an isolated room, in front of an open window and far from any other person.

Fig.45 : Sputum Bottles for sampling
(Personal Photo, 2024).

B-4. Microscopic examination technique

Making a smear from sputum

The smear must be done on a new slide, previously degreased and dried. The number assigned to the patient in the laboratory register must be written at one end of the slide.

From the sample, we choose a mucopurulent or hemorrhagic patch which we spread on the slide, using a platinum loop.

Spreading is done in circular movements about 3 cm long and 2 cm wide. The smear should be air dried.

Fig 46: Numbered Slides
(Personal Photo, 2024).

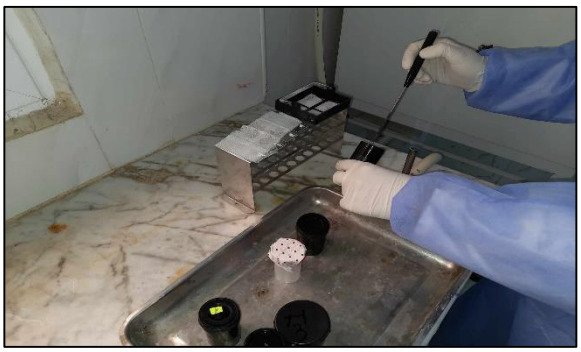

Fig 47: Sampling
(Personal Photo, 2024).

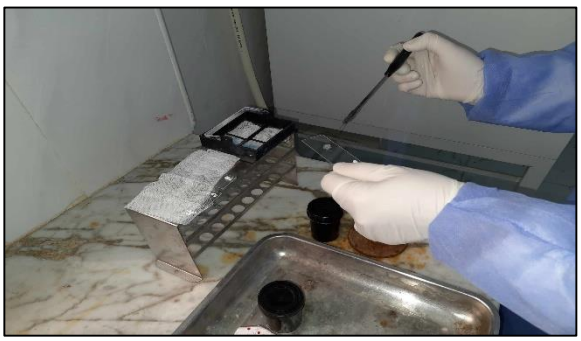

Fig. 48: Spreading The Slide
(Personal Photo, 2024).

Fixation of the smear

The smear is fixed using heat, by 3 to 4 rapid passes of the blade over a Bunsen burner flame or an alcohol lamp.

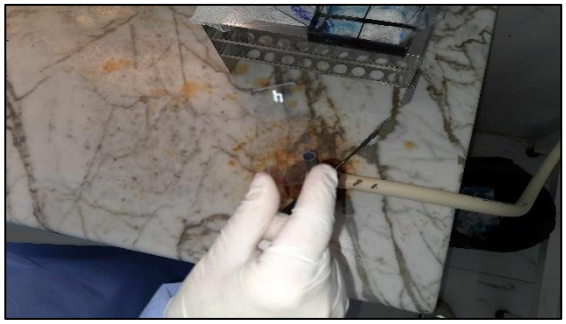

Fig. 49: Heat fixation of the smear
(Personal Photo, 2024).

Coloring by Ziehl Nelson

Place the slide on a glass or metal holder and cover it with filtered Ziehl's carbol fuchsin.

Using a cotton ball mounted on a stick, dipped in alcohol and flambé, pass the flame under the blade covered with fuchsin and stop heating immediately as soon as vapors are emitted. Leave to act for three minutes.

Heat a second time, then a third time, until steam is emitted, leaving to act for three minutes each time.

Avoid boiling and drying out of the dye, discard the fuchsin and rinse the slide with tap water, taking care not to loosen the smear (using too strong a tap from the tap, for example).

Fig.50: Carbol Fuchsin Staining
(Personal Photo, 2024).

Fig .51 : The Flambage
(Personal Photo, 2024).

Discoloration

Cover the slide with quarter-diluted sulfuric acid.

Leave to act for three minutes.

Rinse the blade in the same way as before.

Cover the slide with rubbing alcohol for 5 minutes.

Rinse again. The smear is then slightly tinted pink or colorless.

Fig. 52: Discoloration with alcohol and sulfuric acid
(Personal Photo, 2024).

Counter coloring

Cover the slide with methylene blue. Leave on for 30 seconds to 1 minute then rinse and air dry.

Fig. 53: Counter Coloring with Methylene Blue .
(Personal Photo, 2024).

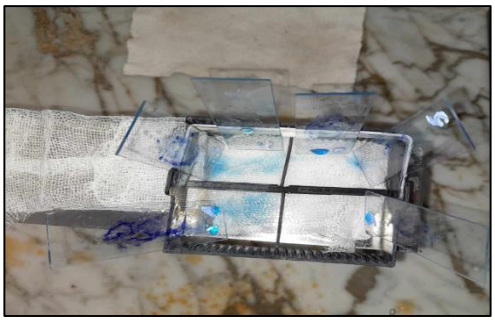

Fig. 54: Rinse the slides and air dry
(Personal Photo, 2024).

Reading and interpretation of results

Reading is done under an ordinary white light microscope, using an immersion objective (x100). Acid-fast bacilli (AFR) will appear pink-red on a slightly bluish background.

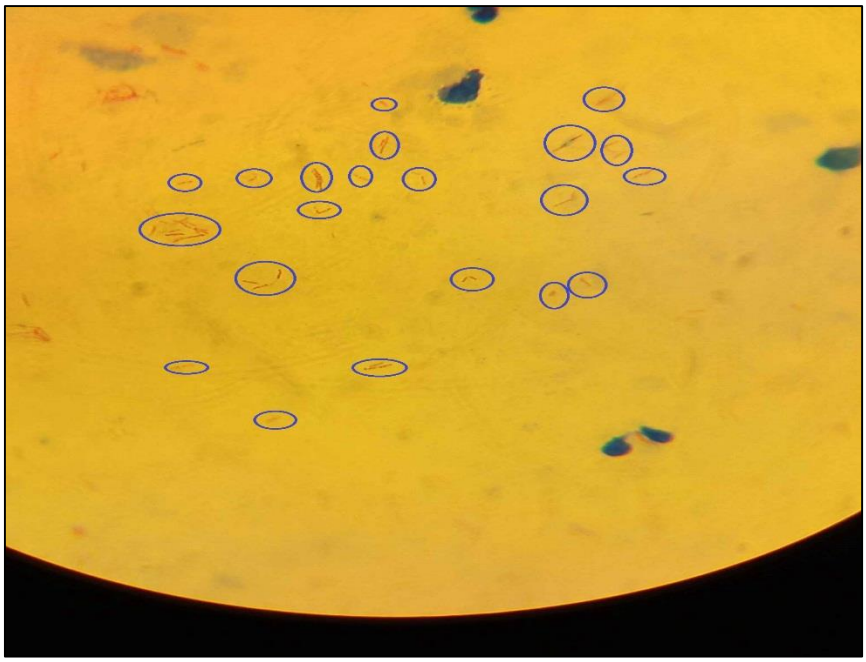

Fig. 55: *Mycobacterium Tuberculosis Bacilli*
(Personal Photo, 2024).

Focus

Before focusing, place a drop of immersion oil on the preparation.

Bring the objective into contact with the drop of oil so as to obtain a sharp image. The surface observed then represents a microscopic field.

Slot reading

- The smear must be read over its entire length, which corresponds to 100 microscopic fields. We note the number of bacilli (red sticks) that are detected.

- If no bacillus is discovered on 100 fields, the microscope carriage is shifted one notch forward or backward to read the next line in the opposite direction (slot reading) and so on until to cover 3 slide lengths or 300 microscopic fields.

- If 1 to 9 bacilli are discovered on 300 fields, we note the exact number of bacilli discovered and we declare the doubtful result (±), Examination to be repeated.

- If 1 to 99 bacilli are discovered on 100 fields, we note the exact number of bacilli discovered and we declare the positive result at (1 +). If we discover less than 10 AFB in the first 100 fields, we continue reading up to 300 fields.

- If more than 1 bacillus is discovered on 1 field, we continue reading 10 fields and note the average number of bacilli discovered per microscopic field (2 +).

- If more than 10 bacilli are discovered on 1 field, we continue reading 10 fields and note the average number of bacilli discovered per field (3 +).

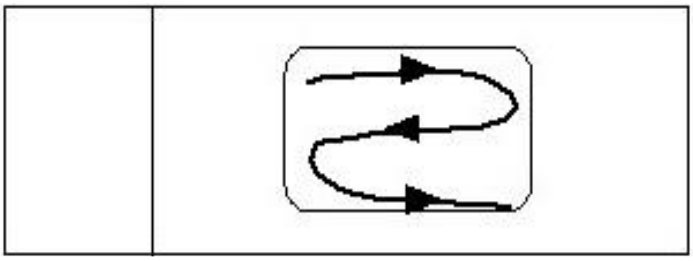

Fig.56 : procedure for microscopic examination of the slide
(website 18)

Expression of results

Four possibilities may arise when reading the slides:

Negative Slide:

0 bacilli on 300 fields:

Enter: 0 BAAR /300 fields (0).

Questionable Slide:

1 to 9 bacilli on 300 fields;

Example: 4 BAAR /300 FIELD (±) Repeat the examination.

Weakly positive Slide :

10 to 99 bacilli per field (average over 10 fields).

Example: 25 BAAR / 1 field (2 +), or (++).

Strongly positive Slide :

> 10 bacilli per field, (average 10 fields (3 +), or (++).

C- Extra-pulmonary tuberculosis includes

Extra-pulmonary tuberculosis includes respiratory locations other than pulmonary of the disease:

- Serofibrinous, serohemorrhagic or purulent pleurisy and mediatisnal lymphadenopathy.

- Other serious locations of the disease: meningitis, pericarditis, peritonitis.

- Lymph node locations, either peripheral: cervical, axillary, inguinal, or deep: mesenteric.

- Bone and osteoarticular locations: vertebral or limbs.

- Visceral locations: renal; hepatic, splenic, cerebral, genital.

- Skin or mucous membrane locations.

These criteria are based on clinical signs; radiological; biological; and immunological.

3.1.4. Collection of data

The collection of information in a first part is made from the registers of the service for the fight against tuberculosis and respiratory diseases (S.C.T.M.R), where the samples were taken, as well as the collection of clinical information, operating records including: the identity of the patients (surname, first name, sex and age), the date of sampling, the services and the results of macroscopic and microscopic examinations of EBD. The data collected over a period of 10 years, from January 2013 to December 2023, were recorded on a Windows Excel file.

3.1.5. Weather data

The data necessary for carrying out this study were provided from the Ain Tine meteorological station. These are meteorological data relating to the wilaya of Mila concerning five climatic parameters which are:

→ The average annual temperature.

→ Average annual insolation.

→ Average annual humidity.

→ The average annual wind speed.

→ Average annual evaporation.

3.1.6. Statistical analysis of data

Data were entered into Excel software and processed using SPSS [(Statistical Package for the Social Sciences) V 26] . The variation each parameter following sex , age slices,months seasens years and the interaction (sex × ages slices) was tested usingone way and two-way analysis of variance (ANOVA).

Chapter IV :

Results

4. Results

This survey reveals cases diagnosed at the bacteriological analysis laboratory level in the wilaya of Mila during the period 2013-2023. According to the prescription of the attending physician, patients with respiratory disorders are referred for a direct bacteriological examination (DBE), During this period 90,912 patients are tested . Where we found 6031 patients are positive for Tuberculosis . the epidemiological study covers four areas within the wilaya : Tadjenanet , Mila, Chelgoum laid , Ferdjioua , Ain beida aheriche .

* The Simple Bacteriological Index (SBI)

The simple bacteriological index is the percentage of subjects carried out in relation to the total number of subjects examined.

SBI = (Number of positive cases / Total number of subjects examined) X 100

4.1. Global performance of human tuberculosis during the period (2013-2023)

4.1.1. Descriptive analysis of the population during the period (2013-2023)

4.1.1.1 The distribution of patients according to the infestation rate during the study period (2013-2023)

Figure 57 and **Table 13** have show that from 91700 subjects screened for M.Tuberculosis , 6031 are infected , the infection rate is (6.63%) during the study period.

Table 13 : Distribution of patients according to infestation rate during the period (2013-2023).

	Effectives	**Frequency**
Positive cases	6031	6.58 %
Negative cases	85669	93.42%

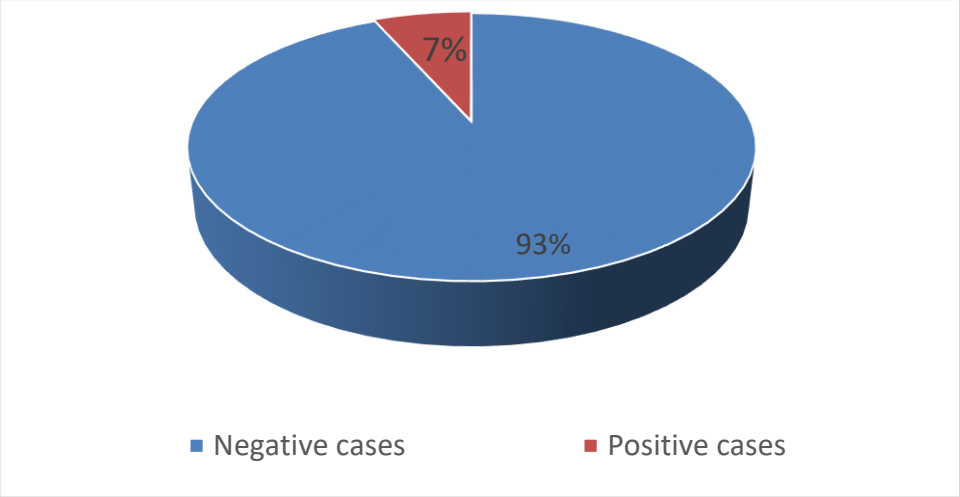

Fig .57: The distribution of patients according to the infestation rate during the study period (2013-2023).

4.1.1.2. Distribution of infected patients according to sex ratio during the study period

Our study showed those women are more exposed to *mycobacterium tuberculosis* by 64% in the state of Mila **(Table 14. Figure 58**), the graphs represented in the **Figures 59 , 61 , 62, 64** shows that women and men were more infected during the years (2019, 2022). Significantly higher rates of infection were recorded in the summer and spring seasons for both sexes. Also, the months of April and May have seen an increase in the number of cases for both sexes . The results demonstrated statistically significant differencees in the infection rates between genders.

Table 14 : Distribution of infected patients according to the sex ratio during the study period (2013-2023).

Sex	Effectives	SBI %
Males	2166	35.91%
Females	3865	64.09%

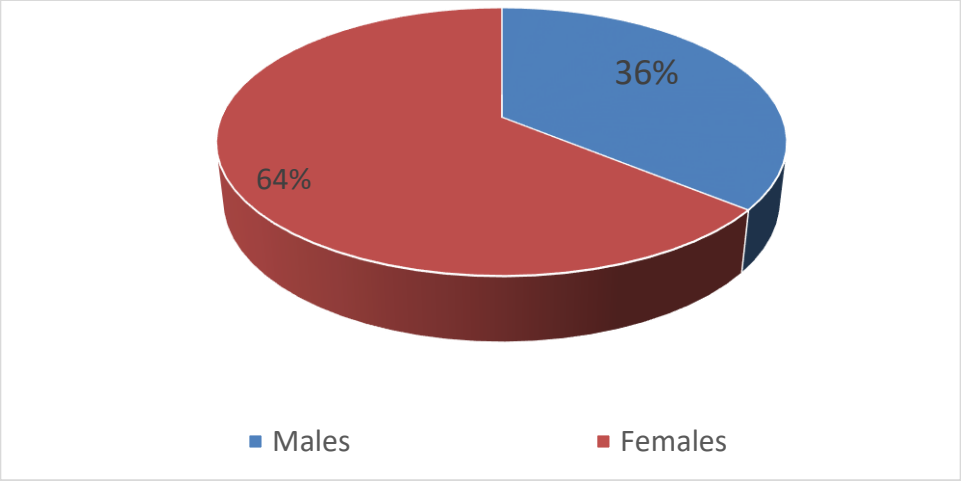

Fig 58 : Distribution of infected patients according to the sex ratio during the study period (2013-2023).

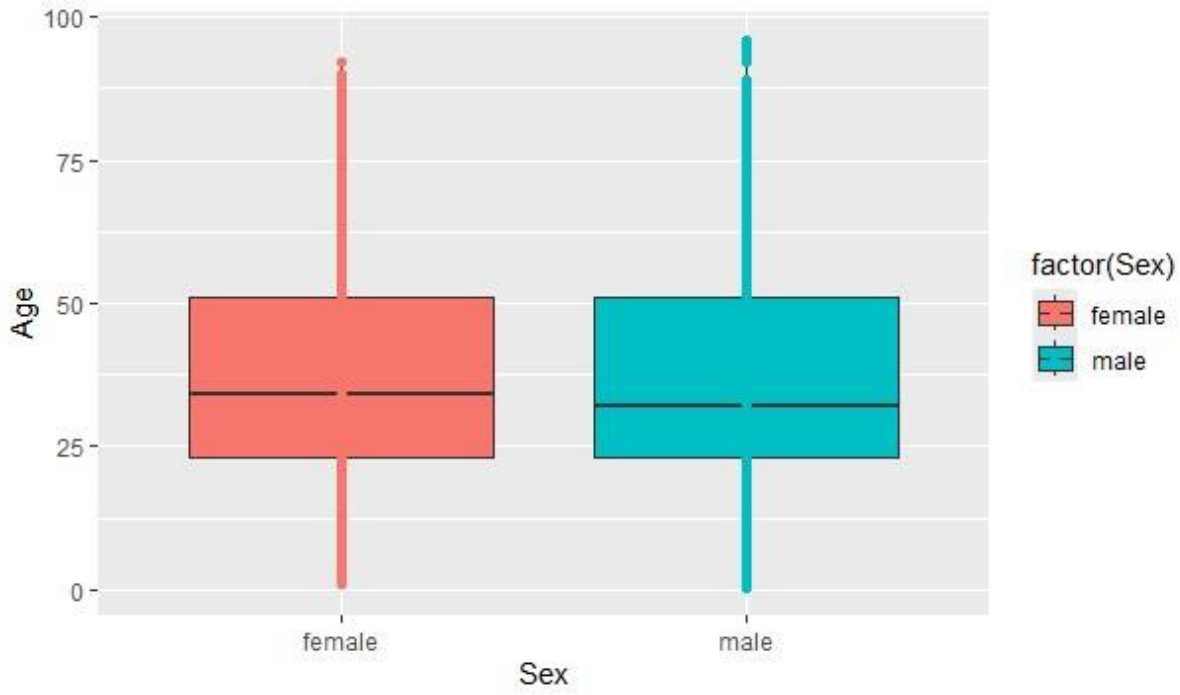

Fig. 59 Boxplots displaying the distribution of infected patients according to sex ratio during the period (2013-2023).

4.1.1.3. Distribution of infected patients according to age slices during the period (2013-2023)

According to the data presented in **the Figure 60** we note that the most affected age group is [20-44] years with 3132 cases and a rate of 51.93%, followed by the category [45-65] years by 1176 cases and a rate of 19.49%. The category [0-1] years are the less representative group by 9 cases and a rate of 0.149 % over the study period.

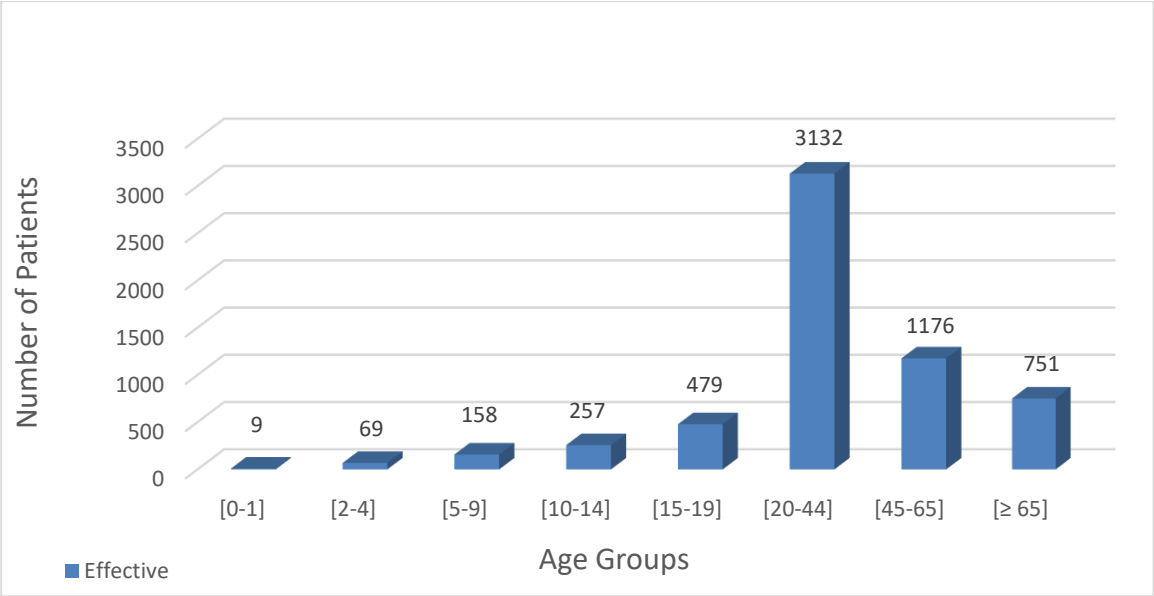

Fig. 60 : Distribution of infected patients according to age slices during the period (2013-2023).

4.1.1.4. Distribution of infected patients according to the months during the study period

The Figure 61 shows that the highest number of effected cases was recorded during the Month of April , may recorded at 9.79%, 9.71%, the lowest percentage was detected in the months of Junuary and February at a rate of 7.46%, 7.14% over the study period. The results obtained showed statistically significant differences.

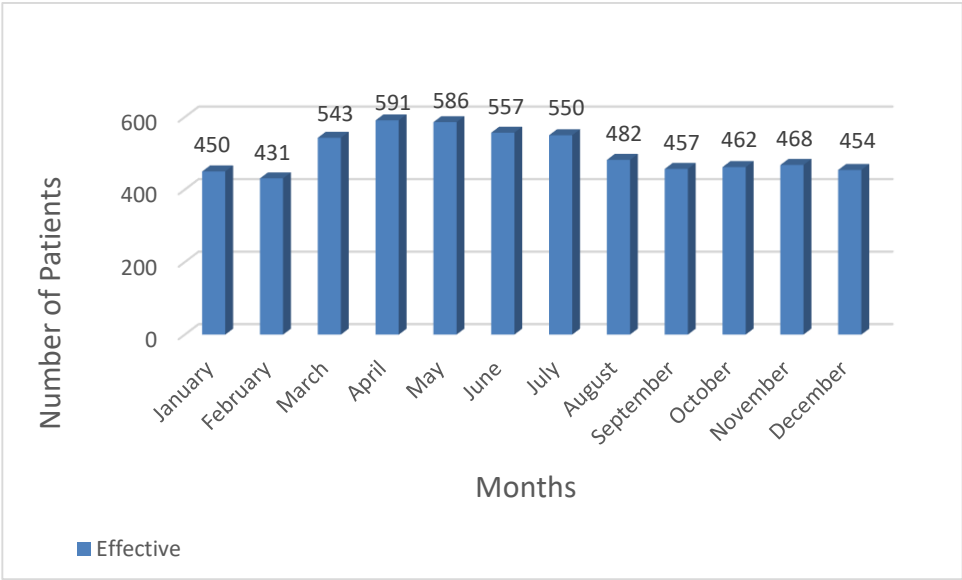

Fig.61 : Distribution of infected patients according to the months during the study period (2013-2023)

4.1.1.5. Distribution of infected patients according to the seasons during the period (2013-2023)

The Figures 62,63 shows that the highest number of infected cases was observed during Spring, followed by the Summer season especially , while the lowest cases were recorded during the Winter season. The results obtained showed statistically significant differences.

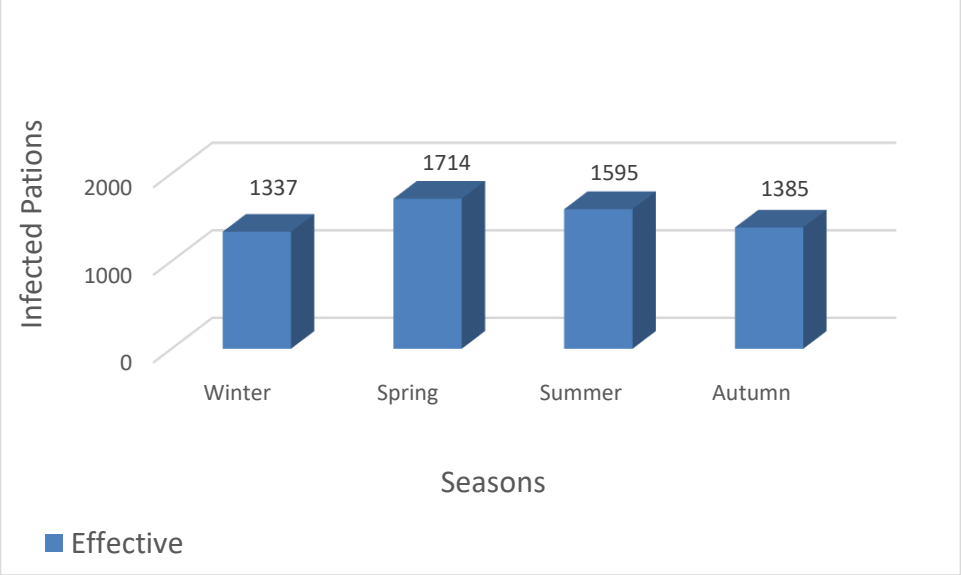

Fig.62: Distribution of infected patients according to the seasons during the period (2013-2023).

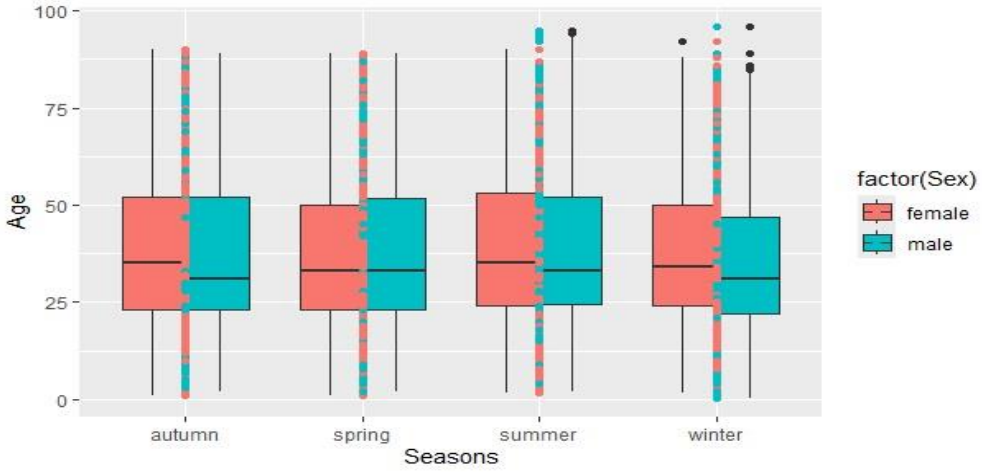

Fig. 63: Boxplots displaying the distribution of age slices of infected patients according to seasons during the period (2013-2023).

4.1.1.6. Distribution of infected patients according to the years during the period (2013-2023)

The years 2015, 2019 and 2022 recorded the highest rates of Tuberculosis infection, 9.99%, 10.11% and 10.28%, respectively, compared to other years **(Figure 64)** , the rate of Tuberculosis ranged from 7.92% to 10.28% over the period (2013-2023). The results obtained showed statistically significant differences.

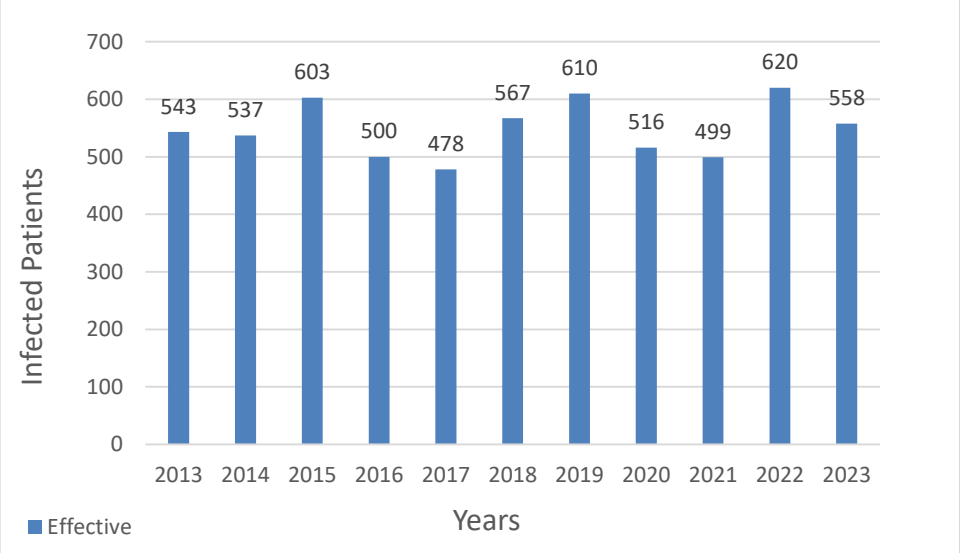

Fig.64 : Distribution of infected patients according to the years during the period (2013-2023).

4.1.1.7. Distribution of patients according to the Region during the period (2013-2023)

the **Figures 65 , 66** ,**Table 15** shows that the highest number of patients was recorded in the Ferdjioua region with a rate of 29.86% . followed by the Chelgoum laid , Mila Region and Ain beida aheriche respectively , with a rate of 25.07% , 20.56 % and 12.96% respectively during the study period (2013-2023).

Table 15: Number of infected patients according to each region of the porvince Mila .

Regions	Number of Positive Cases	SBI%
Tadjenanet	690	11.44%
Mila	1246	20.56 %
Chelgoum laid	1512	25.07%
Ferdjioua	1801	29.86%
Ain beida aheriche	782	12.96%

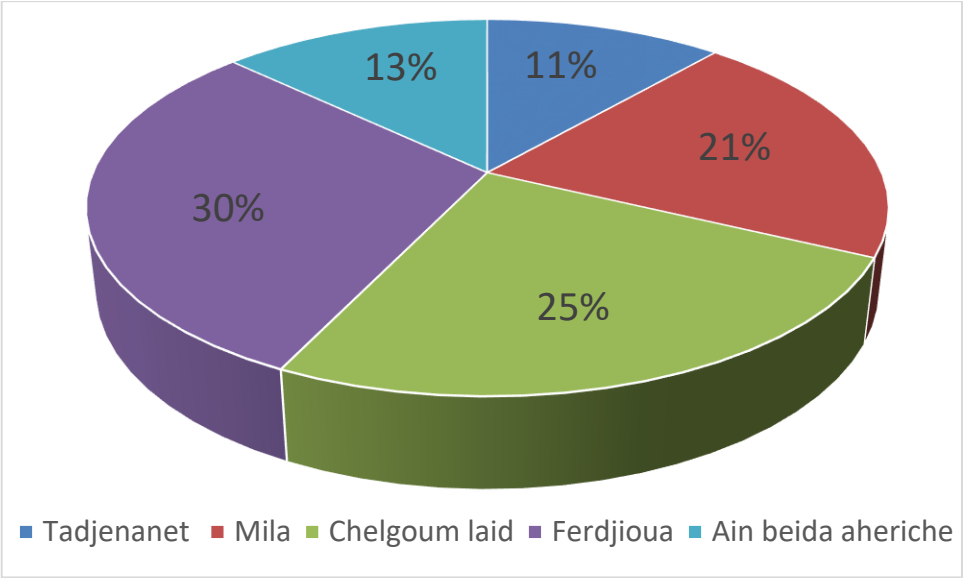

Fig .65: Distribution of patients according to the Region during the period (2013-2023).

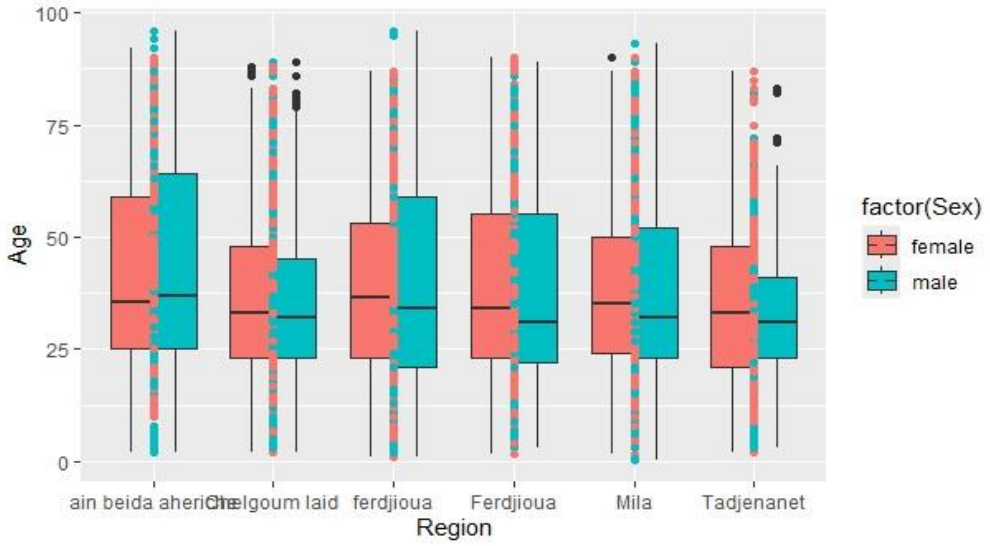

Fig. 66: Boxplots displaying the distribution of age slices of infected patients according to Regions during the period (2013-2023).

4.2. Prevalence of the population suffering from Extra pulmonary tuberculosis (EPT) during the period (2013 - 2023):

4.2.1. Descriptive analysis of the population during the period (2013-2023)

4.2.1.1. The distribution of EPT patients according to the infestation rate during the study period (2013-2023)

Figure 67 and **Table 16** have show that from 5003 subjects screened for M.Tuberculosis , 4215 are infected , the infection rate is (84.25%) during the study period.

Table 16 : Distribution of EPT patients according to infestation rate during the period (2013-2023).

	Effectives	Frequency
Positive cases	4215	84.25%
Negative cases	788	15.75%

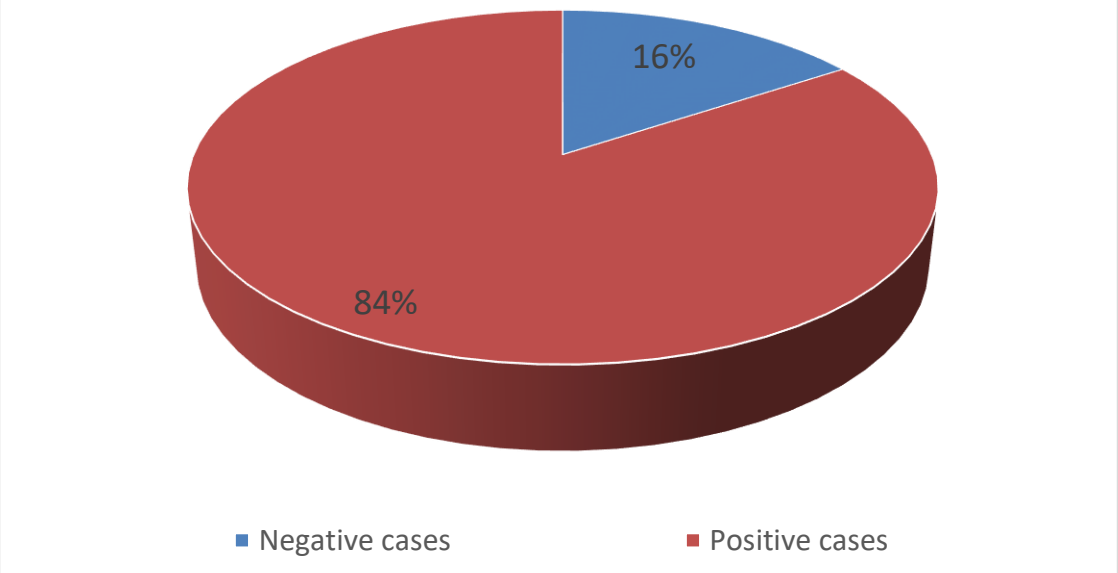

Fig.64 : The distribution of EPT patients according to the infestation rate during the study

Fig.67 : Distribution of EPT infected patients according to the sex ratio during the study period (2013-2023).

4.2.1.2. Distribution of EPT infected patients according to sex ratio during the study period (2013-2023)

Our study showed those women are more exposed to *mycobacterium tuberculosis* by 70.58% in the state of Mila (**Table 17**, **Figure 68**), the graphs represented in the **Figures 70 ,71, 72** shows that women and men were more infected during the years (2019, 2022). Significantly higher rates of infection were recorded in the summer and spring seasons for both sexes. Also, the months of April and May have seen an increase in the number of cases for both sexes . The results demonstrated statistically significant differencees in the infection rates between genders.

Table 17: Distribution of EPT infected patients according to the sex ratio during the study period (2013-2023).

Sex	Effectives	SBI %
Males	1240	29.42%
Females	2975	70.58%

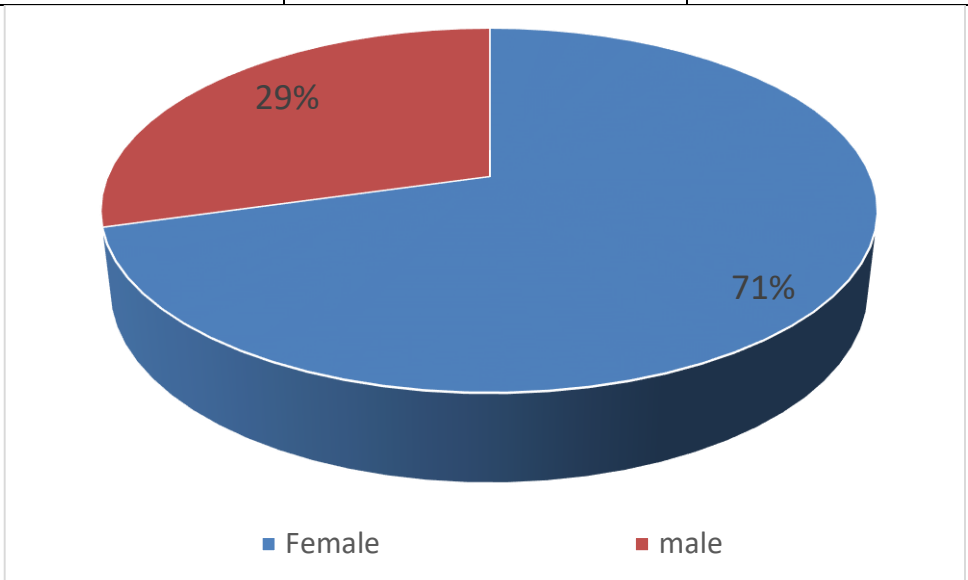

Fig.68 : Distribution of EPT infected patients according to the sex ratio during the study period (2013-2023).

4.2.1.3. Distribution of EPT infected patients according to age slices during the period (2013-2023)

According to the data presented in the **Figure 69** we note that the most affected age group is [20-44] years with 2355 cases and a rate of 55.87%, followed by the category [45-65] years

by 820 cases and a rate of 19.45%. The category [0-1] years are the less representative group by 3 cases and a rate of 0.07 % over the study period.

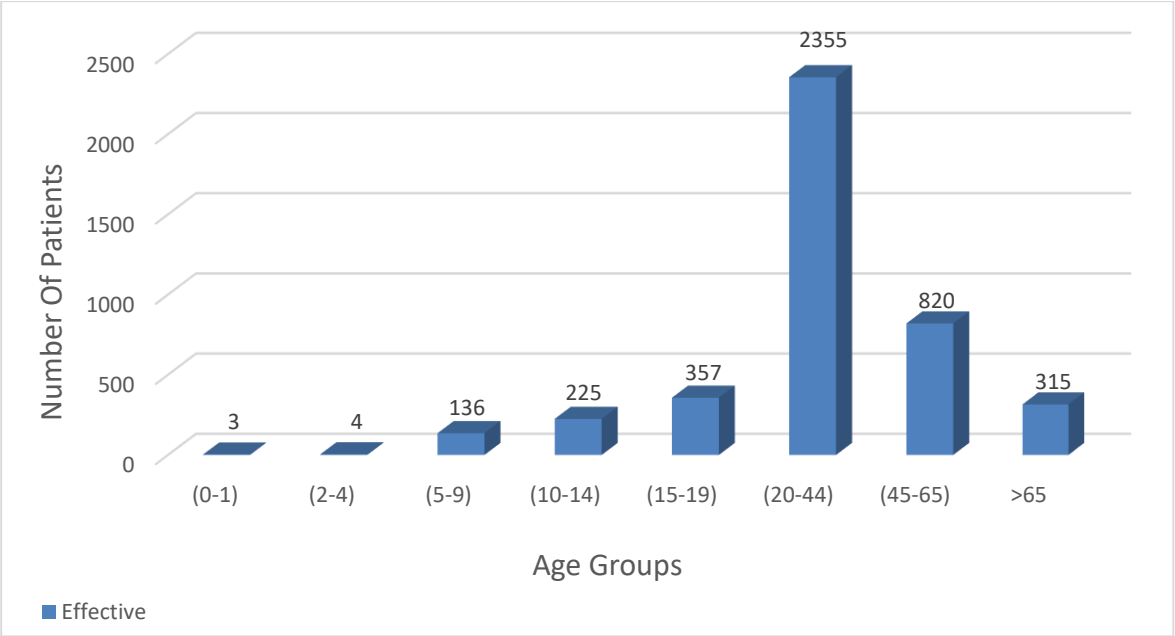

Fig. 69: Distribution of EPT infected patients according to age slices during the period (2013-2023).

4.2.1.4. Distribution of EPT infected patients according to the months during the study period

The **Figure 70** shows that the highest number of effected cases was recorded during the Month of April , May recorded at 9.56%, 9.86%, the lowest percentage was detected in the months of Junuary and February at a rate of 7.12%, 7.24% over the study period. The results obtained showed statistically significant differences.

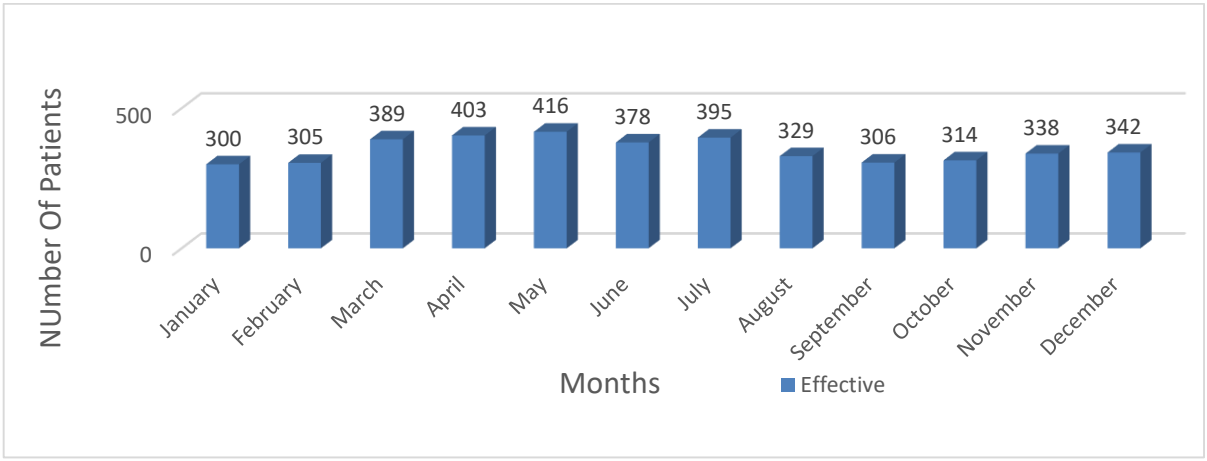

Fig.70: Distribution of EPT infected patients according to the months during the study period (2013-2023)

4.2.1.5. Distribution of EPT infected patients according to the seasons during the period (2013-2023)

The **Figure 71** shows that the highest number of infected cases was observed during Spring , followed by the Summer season especially , while the lowest cases were recorded during the Winter season. The results obtained showed statistically significant differences .

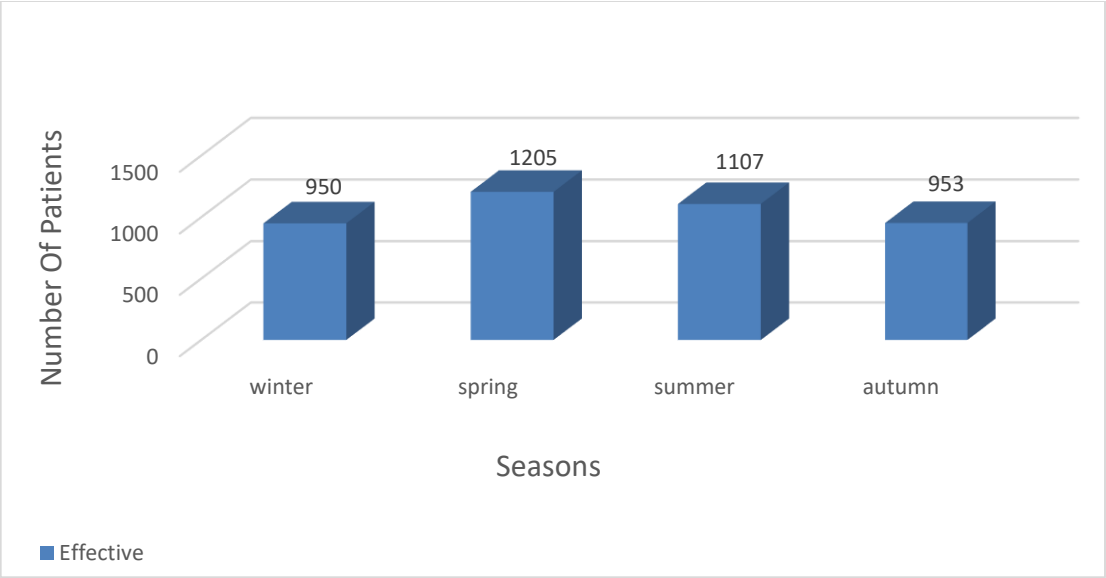

Fig.71 : Distribution of EPT infected patients according to the seasons during the period (2013-2023).

4.2.1.6. Distribution of EPT infected patients according to the years during the period (2013-2023)

The years 2019, 2022 and 2018 recorded the highest rates of Tuberculosis infection, 10.4%, 10.39% and 9.87%, respectively, compared to other years (**Figure 72**), the rate of Tuberculosis ranged from 7.97 to %10.4% over the period (2013-2023). The results obtained showedstatistically significant differences.

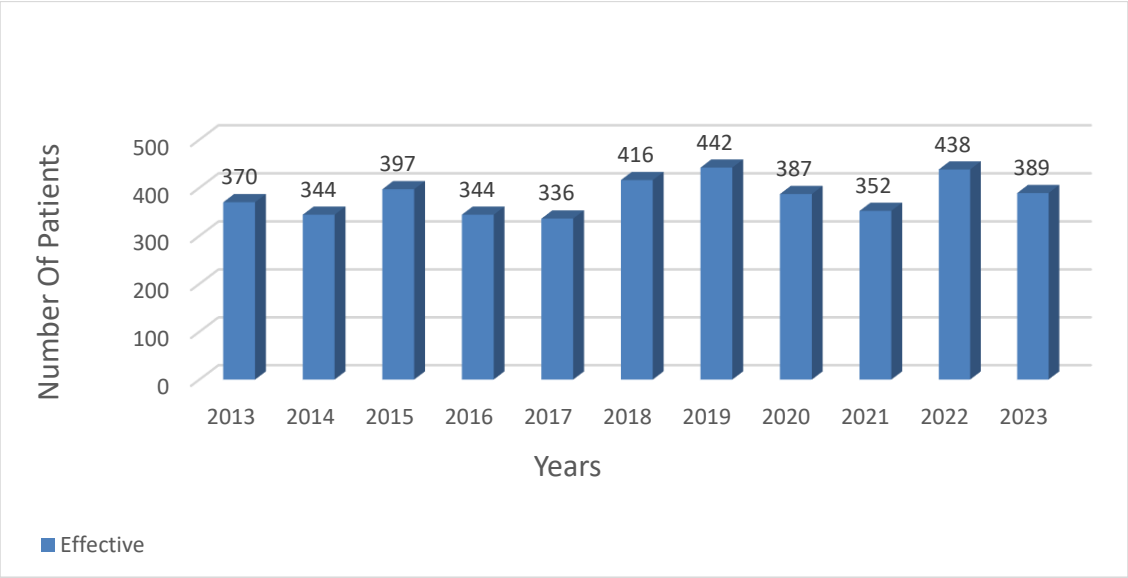

Fig.72: Distribution of EPT infected patients according to the years during the period (2013-2023).

4.2.1.7. Distribution of EPT patients according to the Region during the period (2013-2023)

the **Figure 73** , **Table 18** shows that the highest number of patients was recorded in the Ferdjioua region with a rate of 29.28% . followed by the Chelgoum laid , Mila Region and Tadjenanet respectively , with a rate of 25.53% , 20.57 % and 13.36% respectively during the study period (2013-2023).

Table 18: Number of EPT infected patients according to each region of the porvince Mila.

Regions	Number of Positive Cases	SBI%
Tadjenanet	563	13.36%
Mila	867	20.57%
Chelgoum laid	1076	25.53%
Ferdjioua	1234	29.28%
Ain beida aheriche	475	11.27%

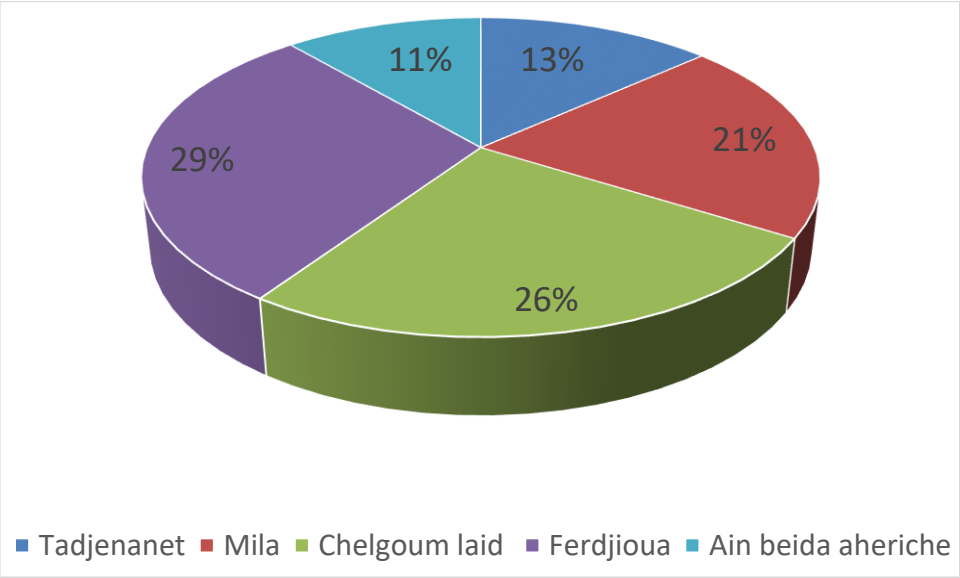

Fig.73: Distribution of EPT patients according to the Region during the period (2013-2023).

4.2.1.8. Distribution of EPT patients according to the Type during the period (2013-2023)

Table 19: Distribution of EPT patients according to the type during the period (2013-2023).

Types	Number of positive cases	SBI%
LYMPH NODE	2444	57.89%
PLEURAL	646	15.33%
PERITONEAL	338	8.02%
OSTEOARTICULAR	203	4.82%
GENITAL	157	3.72%
Intestinal	67	1.59%
Other Types	360	8.54%

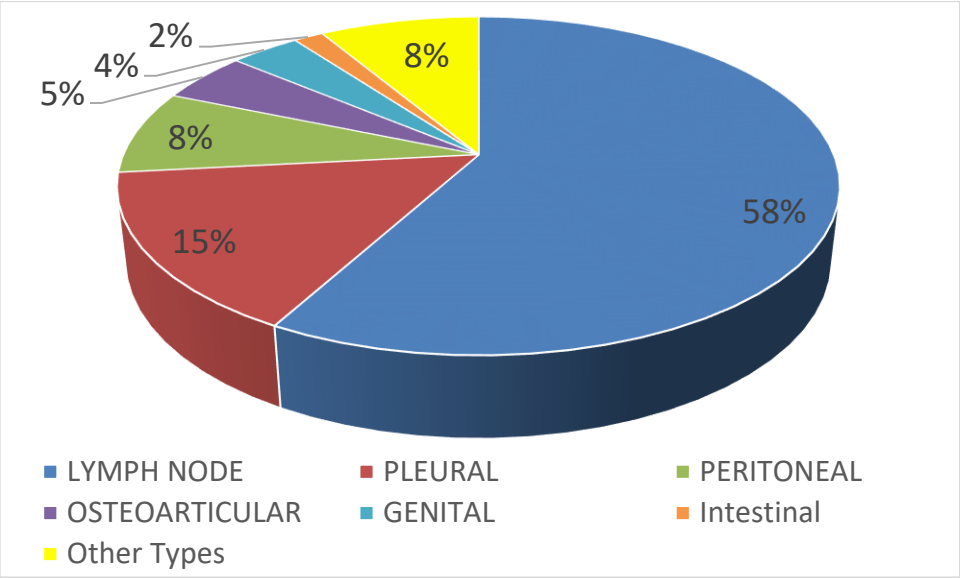

Fig.74: Distribution of EPT patients according to the type during the period (2013-2023).

Figure 74 , **Table 19** shows that the Lymph node tuberculosis is the most widespread type with a percentage of 58% , followed by Pleural tuberculosis with a rate of 15 %, during The study period (2013-2023).

4.3. Prevalence of the population suffering from pulmonary tuberculosis (PT)during the period (2013 - 2023)

4.3.1.Descriptive analysis of the population during the period (2013-2023)

4.3.1.1.The distribution of PT patients according to the infestation rate during the study period (2013-2023)

Fig.75 and **table 20** have show that from 86697 subjects screened for *M. Tuberculosis,* 1816 are infected, the infection rate is (2,094 %) during the study period.

Table 20 : Distribution of PT patients according to infestation rate during the period (2013-2023).

	Effective	**Frequency**
Positive cases	1816	2,094 %
Negative Cases	84881	97,90 %

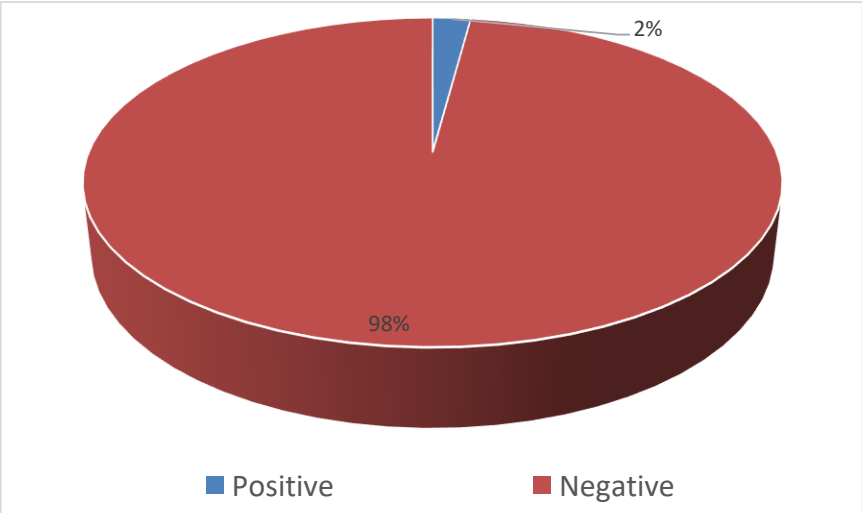

Fig .75: The distribution of PT patients according to the infestation rate during the studyperiod (2013-2023).

4.3.1.2. Distribution of PT infected patients according to sex ratio during the study period (2013-2023)

Our study showed those Men is more exposed to *mycobacterium tuberculosis* by 50.99% in the state of Mila **(Table 21. Figure 76),** the graphs represented in the **Figures 78 , 79, 80** shows thatmen and women me were more infected during the years (2015, 2022). Significantly higherrates of infection were recorded in the summer and spring seasons for both sexes. Also, the months of April and January have seen an increase in the number of cases for both sexes . The results demonstrated statistically significant differencees in the infection rates between genders .

Table 21 : Distribution of PT infected patients according to the sex ratio during the study period (2013-2023).

Sex	Effectives	SBI %
Males	926	50,99 %
Females	890	49,008 %

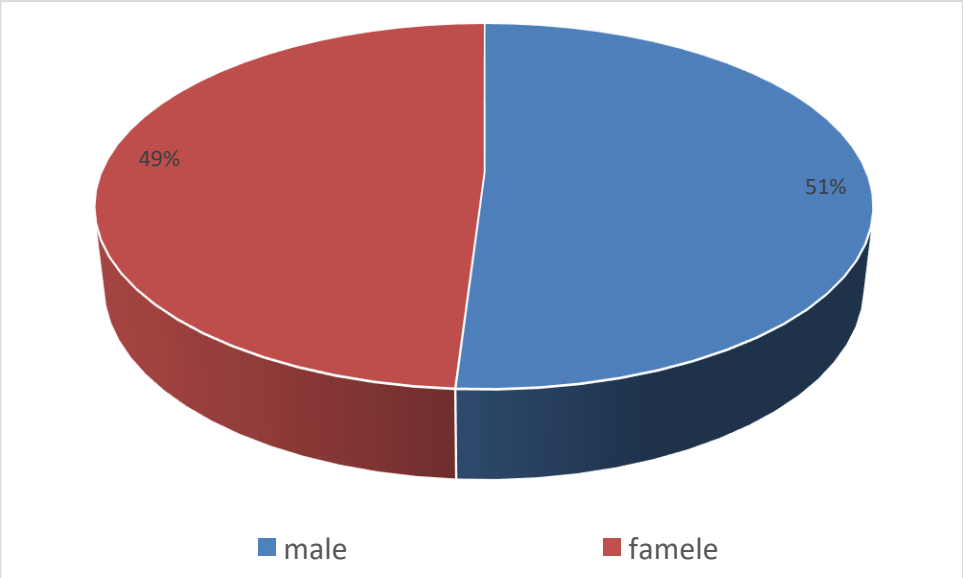

Fig.76: Distribution of EPT infected patients according to the sex ratio during the studyperiod (2013-2023).

4.3.1.3.Distribution of PT infected patients according to age slices during the period (2013-2023)

According to the data presented in the **Figure 77** we note that the most affected age group is[20-44] years with 851 cases and a rate of 46.86 %, followed by the category [>65] years by 400 cases and a rate of 22.02 The category [0-1] years are the less representative group by 3 cases and a rate of 0,33% over the study period

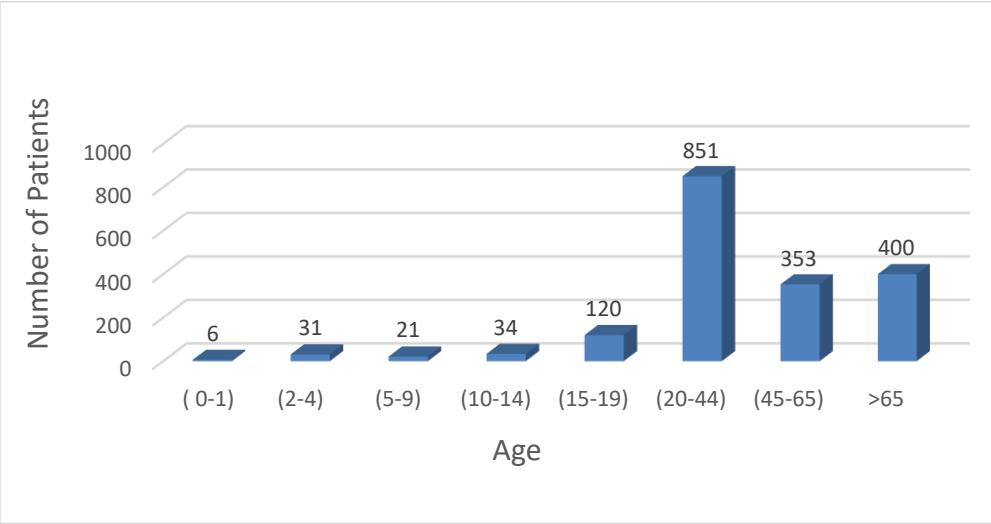

Fig.77 : Distribution of PT infected patients according to age slices during the period (2013-2023).

4.3.1.4.Distribution of PT infected patients according to the months during the study period

The **fig.78,** shows that the highest number of effected cases was recorded during the Month of April,January recorded at 10,35%, 9.30 %, the lowest percentage was detected in the months of February and November at a rate of 6.82%, 7.26% over the study period. The results obtained showed statistically significant differences.

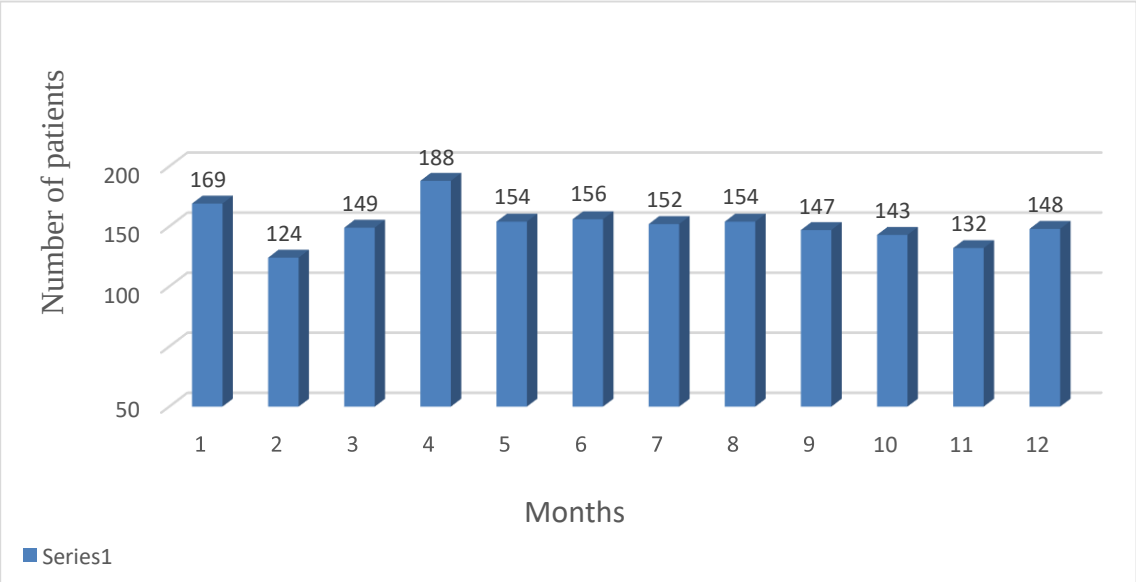

Fig.78: Distribution of PT infected patients according to the months during the study period (2013-2023)

4.3.1.5.Distribution of PT infected patients according to the seasons during the period (2013-2023)

The **Figure 79**, shows that the highest number of infected cases was observed during Spring, followed by the Summer season especially , while the lowest cases were recorded during the Winter season. The results obtained showed statistically significant differences.

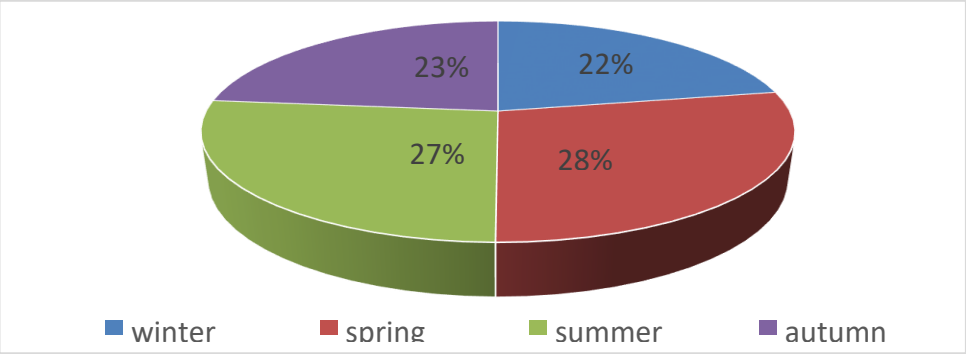

Fig.79: Distribution of PT infected patients according to the seasons during the period (2013-2023).

4.3.1.6.Distribution of PT infected patients according to the years during the period (2013-2023)

The years 2015, 2022,2013 and 2023 recorded the highest rates of Tuberculosis infection, 11.28%, 10.07 % , 9.58 %, and 9.25 %, respectively, compared to other years **(Figure .80),** the rate of Tuberculosis ranged from 7.21 to % 7.81% over the period (2013-2023). The results obtained showedstatistically significant differences.

Fig.80: Distribution of PT infected patients according to the years during the period (2013-2023).

4.3.1.7. Distribution of PT patients according to the Region during the period (2013-2023)

the (**Figure 81)** shows that the highest number of patients was recorded in the Ferdjioua region with a rate of 31.05% . followed by the Chelgoum laid , Mila Region and Ain beida aheriche respectively , with a rate of 31.05% , 24.00 % and 20.75 % respectively during the study period

(2013-2023).

Table 22: Number of PT infected patients according to each region of the porvince Mila

Regions	Number of Positive Cases	SBI%
Tadjenanet	128	7.04%
Mila	377	20.75%
Chelgoum laid	436	24.00%
Ferdjioua	564	31.05%
Ain beida aheriche	311	17.12%

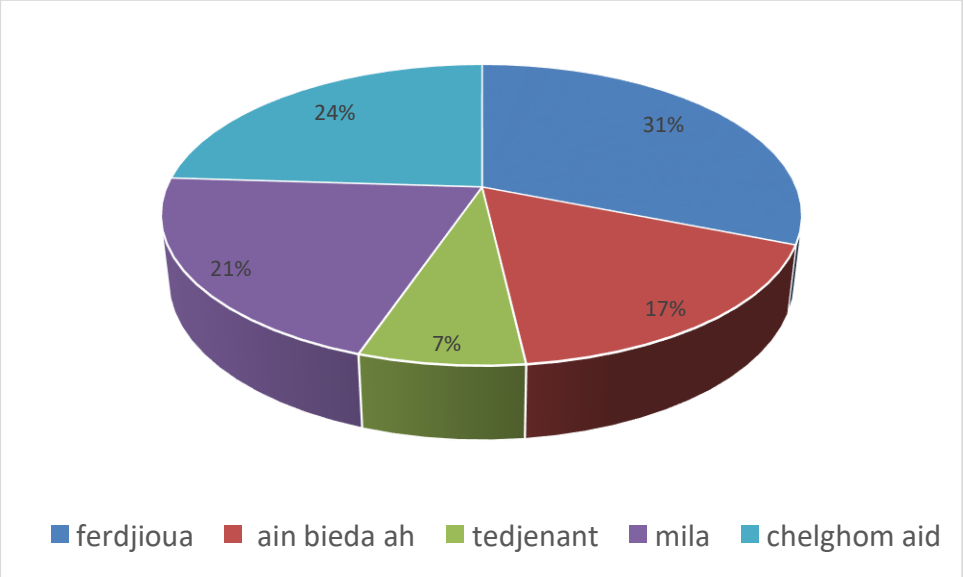

Fig.81: Distribution of PT patients according to the Region during the period (2013-2023).

4.4 Prevalence of the population suffering from pulmonary tuberculosis (PT) during the prospective study period.

4.4.1. Descriptive analysis of the population during the prospective study.

4.4.1.1. Distribution of PT patients according to infection rate during the prospective study

the Figure 82 and Table 23 show that out of 290 people who were examined for tuberculosis, 4were infected, and the infection rate was (1.37%) during the study period.

Table 23 : Distribution of PT patients according to infection rate during the prospective study

	Effective	**Frequency**
Positive cases	04	1.37%
Negative cases	286	98.62%

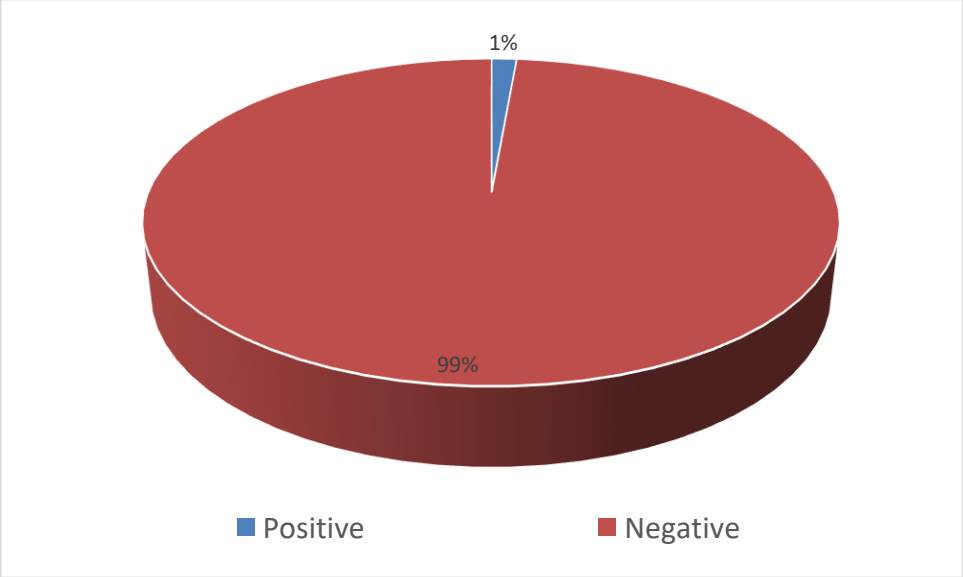

Fig.82: The distribution of PT patients according to the infestation rate during the prospective study.

4.4.1.2. Distribution of PT infected patients according to sex ratio during the prospective study

Our study showed those the proportion of men is equal to the proportion of women are exposed to *mycobacterium tuberculosis* by 100 % in the state of Mila **(Table 24, Figure 83),** thegraphs represented in the **Figures 85, 86** shows that men and women they are exposed to the same percentage infected during the within three months. Rates of infection were recorded in the March seasons for both sexes. Also, the months of April and January have seen an increase in the number of cases for both sexes. The results demonstrated statistically significant same in the infection rates between genders

Table 24 : Distribution of PT infected patients according to the sex ratio during the prospective study .

Sex	Effectives	SBI%
Males	2	100 %
Females	2	100 %

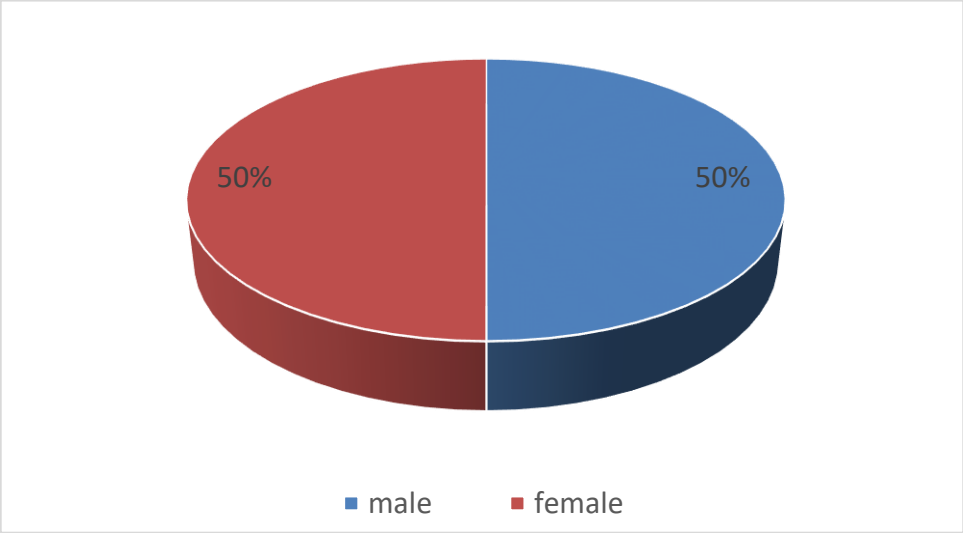

Fig.83: Distribution of PT infected patients according to the sex ratio during the prospective study .

4.4.1.3. Distribution of PT infected patients according to age slices during the prospective study.

According to the data presented in **Figure 84**, we note that the age group most affected is [20-44] years with 2 cases and a rate of 50%, followed by the [45-65] year group and the [>65] year group with 1 case, which is the least represented group according to the cases. By25% during the study period.

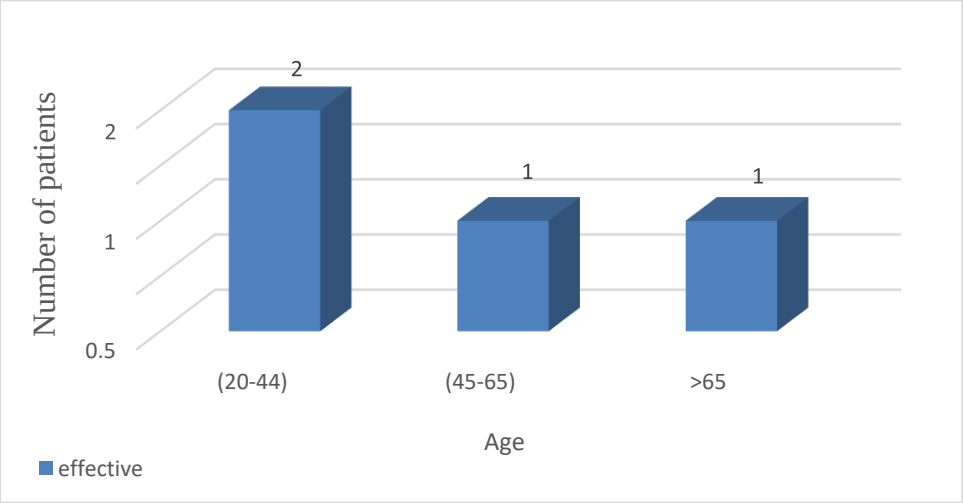

Fig. 84: Distribution of PT infected patients according to age slices during the period the prospective study.

4.4.1.4. Distribution of PT infected patients according to the months during the prospective study period

The **Figure 85** shows that the highest number of effected cases was recorded during the march recorded at 50 %, the lowest percentage was detected in the months of January and February at a rate of 25% over the study period. The results obtained showed statistically significant differences.

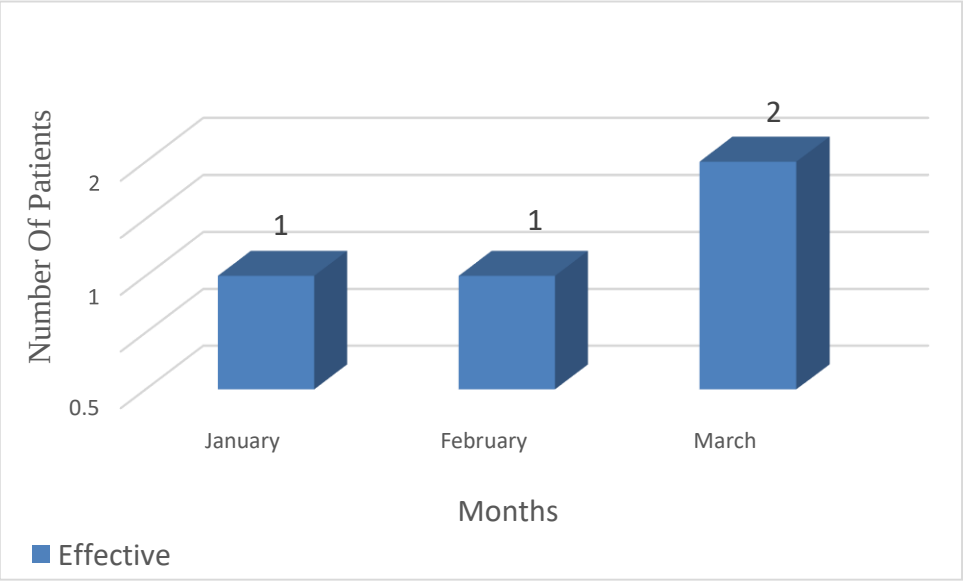

Figure.85: Distribution of patients with PT by months during the during the prospective study period.

4.4.1.5. Distribution of PT infected patients according to the seasons during the period the prospective study

The **Figure 86** shows that the highest number of infected cases was observed during winter and spring in equal proportions. The results obtained showed statistically significant differences .

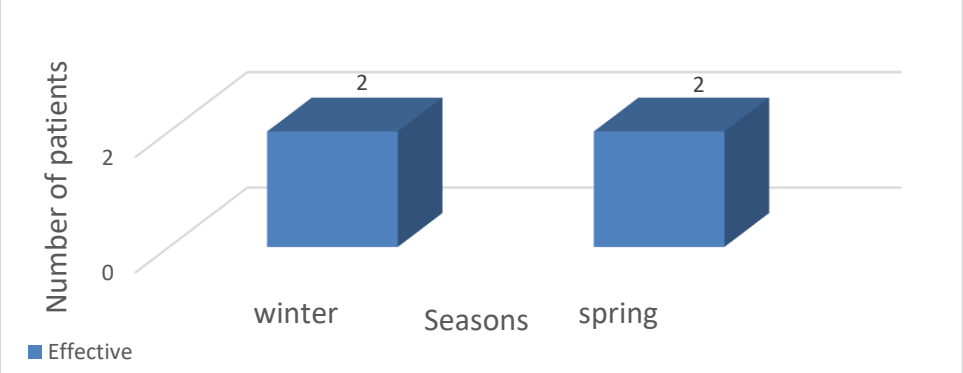

Fig.86: Distribution of PT infected patients according to the seasons during during the prospective study.

4.5. Prevalence of the population suffering from extra pulmonary tuberculosis(PT) during the prospective study

4.5.1. Descriptive analysis of the population during the period the prospective study

4.5.1.1. Distribution of EPT patients according to infection rate during the prospective study

Figure 87 and Table 25 show that out of 25 people who were examined for tuberculosis, 20 were infected, and the infection rate was (80%) during the prospective study.

Table .25 : Distribution of EPT patients according to infection rate during the prospective study.

	Effective	**Frequency**
Positive cases	20	80 %
Negative cases	5	20 %

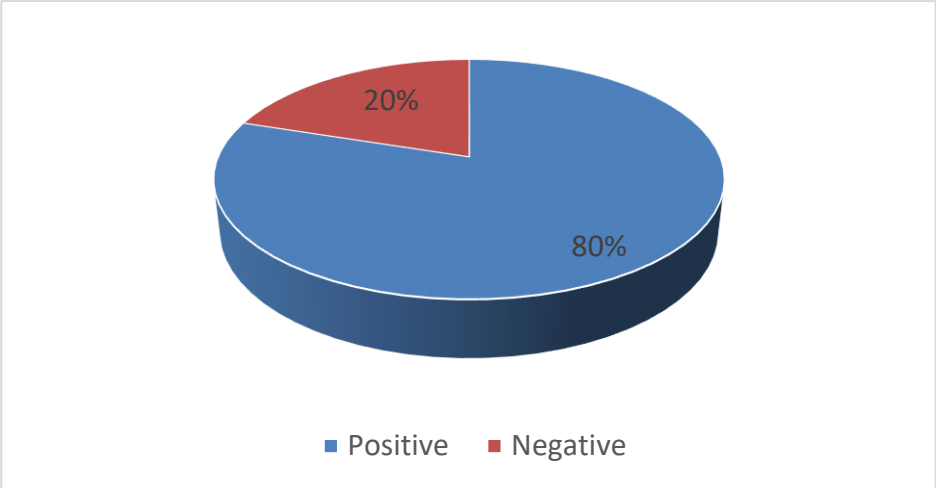

Fig. 87: The distribution of EPT patients according to the infestation rate during the prospective study.

4.5.1.2. Distribution of EPT infected patients according to sex ratio during the prospective study

Our study showed those women are more exposed to *mycobacterium tuberculosis* by 75%in the state of Mila **(Table 26. Figure 88),** the graphs represented in the **Figures 90,91 ,** higher rates of infection were recorded in the winter seasons for both sexes. Also, the months of February and January have seen an increase in the number of cases for both sexes. The results demonstrated statistically significant differences in the infection rates between genders.

Table 26: Distribution of EPT infected patients according to the sex ratio during the prospective study.

Sex	Effectives	SBI %
Males	5	25 %
Females	15	75 %

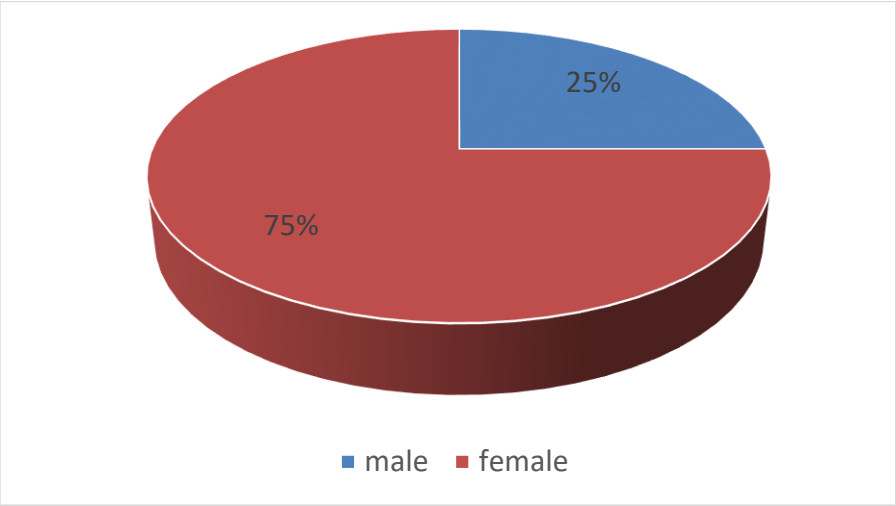

Fig. 88: Distribution of EPT infected patients according to the sex ratio during the prospective study.

4.5.1.3. Distribution of EPT infected patients according to age slices during the prospective study

According to the data presented in the **Figure 89** we note that the most affected age group is [20-44] years with 11 cases and a rate of 55 %, followed by the category [45-65] years by 5 cases and a rate of 25%, And the rest of The categories are the less representative and arête of 5% over the study period

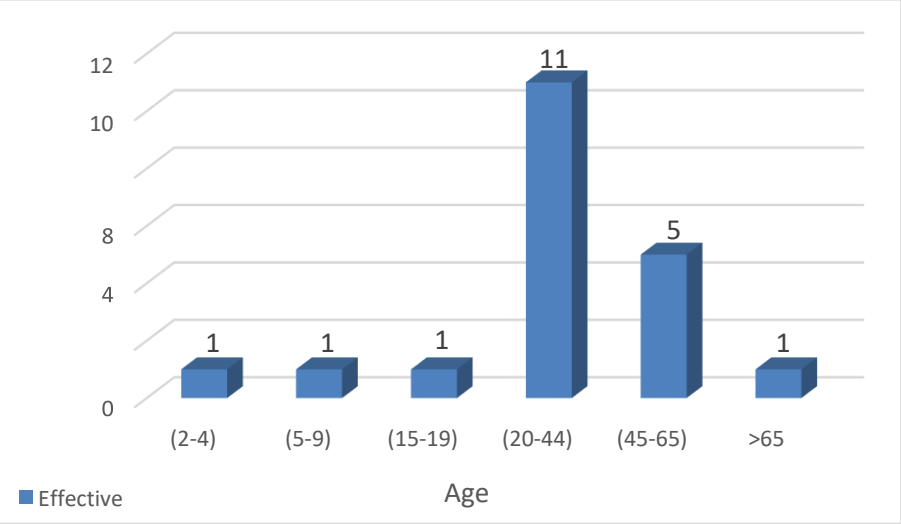

Fig. 89: Distribution of EPT infected patients according to age slices during the prospective study.

4.5.1.4. Distribution of EPT infected patients according to the months during the prospective study

The **Figure 90** shows that the highest number of effected cases was recorded during the

February recorded at 45 %, the lowest percentage was detected in the months of March at arate of 25% over the study period. The results obtained showed statistically significant differences

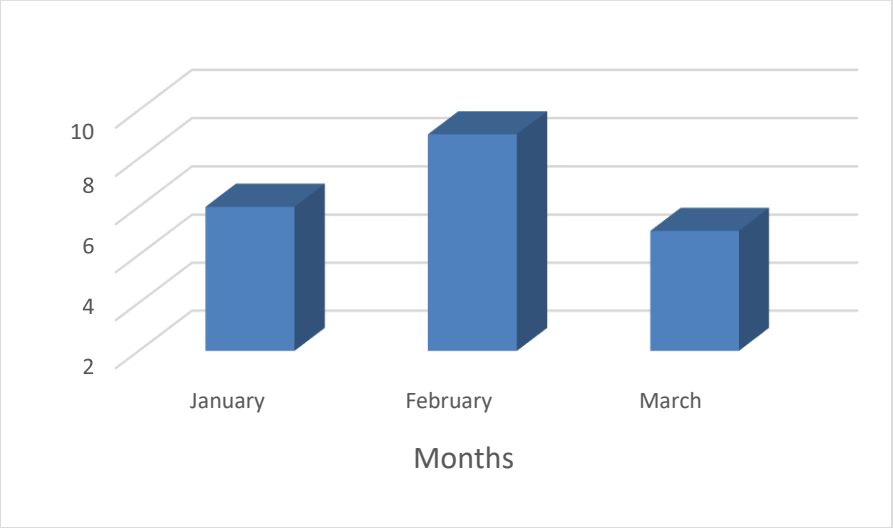

Fig.90: Distribution of patients with EPT by months during the study period, during the prospective study.

4.5.1.5. Distribution of EPT infected patients according to the seasons during the prospective study.

The **Figure. 91** shows that the highest number of infected cases was observed during winter, while the lowest cases were recorded during the spring season. The results obtained showed statistically significant differences

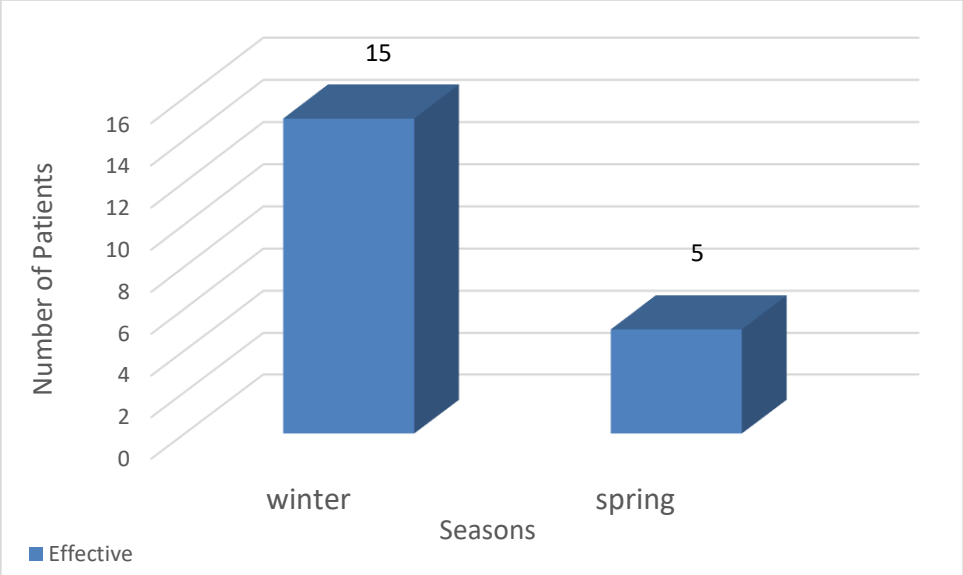

Fig.91: Distribution of EPT infected patients according to the seasons during the prospective study.

4.5.1.6. Distribution of EPT patients according to the Type during the prospective study.

Table 27 : Distribution of EPT patients according to the type during the prospective study.

Types	Number of positive Cases	SBI%
LYMPH NODE	13	65%
PLEURAL	2	10%
PERITONEAL	1	5%
MILIARY	1	5%
Polyserite	1	5%
Ocular	1	5%
PERICARDITIS	1	5%

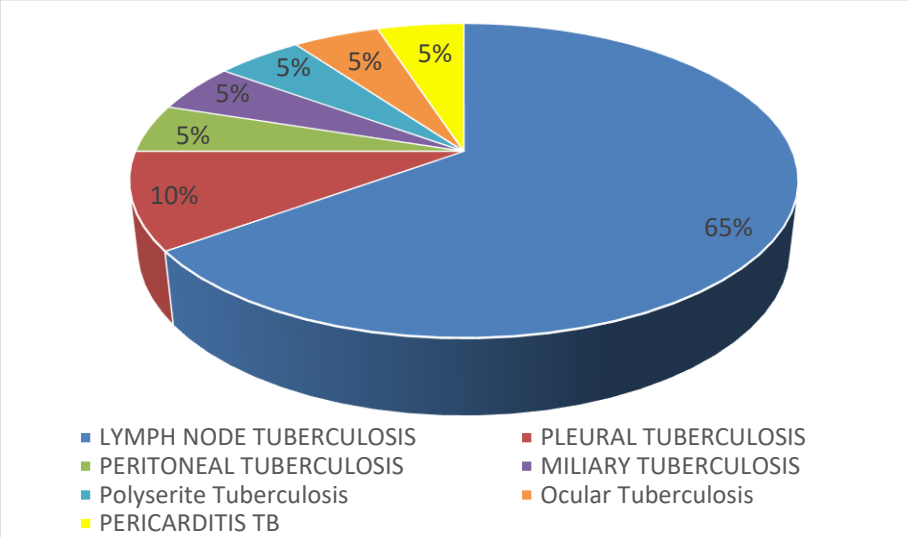

Fig.92: Distribution of EPT patients according to the type during the prospective study**.**

In our work we note that Lymph node tuberculosis is the most widespread type with a percentage of 65%, followed by Pleural tuberculosis with a rate of 10 %, during the studyperiod lasted three month in the state of Mila

4.6. Global performance of human tuberculosis during the prospective study.

4.6.1. Descriptive analysis of the population during the prospective study.

4.6.1.1 The distribution of patients according to the infestation rate during the prospective study.

The **Figure 93** and **(Table.28)** have show that from 311 subjects screened for M. Tuberculosis,

20 are infected, the infection rate is (6.4%) during the study period.

Table.28: Distribution of patients according to infestation rate during the prospective study.

	Effectives	**Frequency**
Positive cases	20	6.4 %
Negative cases	291	93.56 %

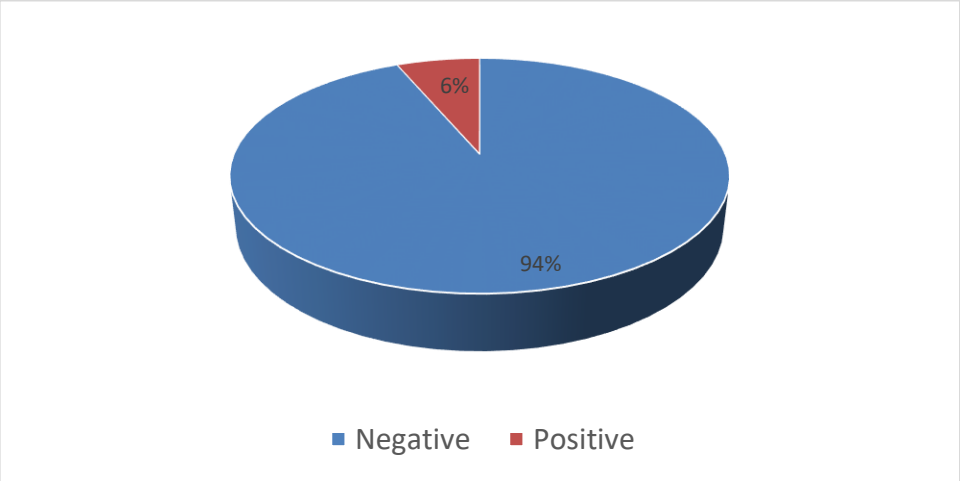

Fig .93: The distribution of patients according to the infestation rate during the prospective study.

4.6.1.2. Distribution of infected patients according to sex ratio during the prospective study.

Our study showed those women are more exposed to *mycobacterium tuberculosis* by 35% in the state of Mila **(Table 29 . Figure 94)**, the graphs represented in the (**figures 96 , 97**) shows that women were more infected during the within three months. Rates of infection were recorded in the February seasons for both sexes. The results demonstrated statistically significant same in the infection rates between genders.

Table 29: Distribution of infected patients according to the sex ratio during the prospective study.

Sex	Effectives	SBI %
Males	07	35 %
Females	17	85 %

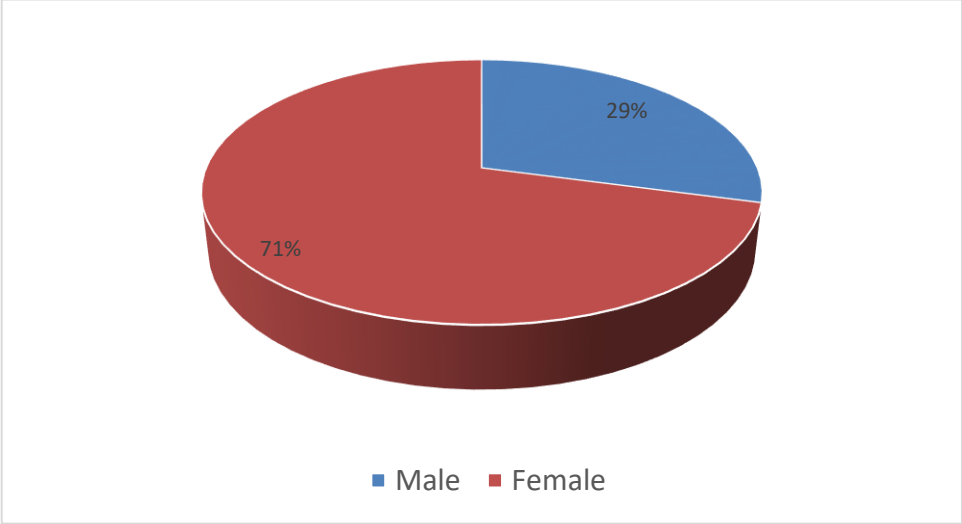

Fig. 94: Distribution of infected patients according to the sex ratio during the prospective study.

4.6.1.3. Distribution of infected patients according to age slices during the prospective study

According to the data presented in the **Figure 95** we note that the most affected age group is [20-44] years with 10 cases and a rate of 50%, followed by the category [45-65] years by 6 cases and a rate of 30%. over during the prospective study.

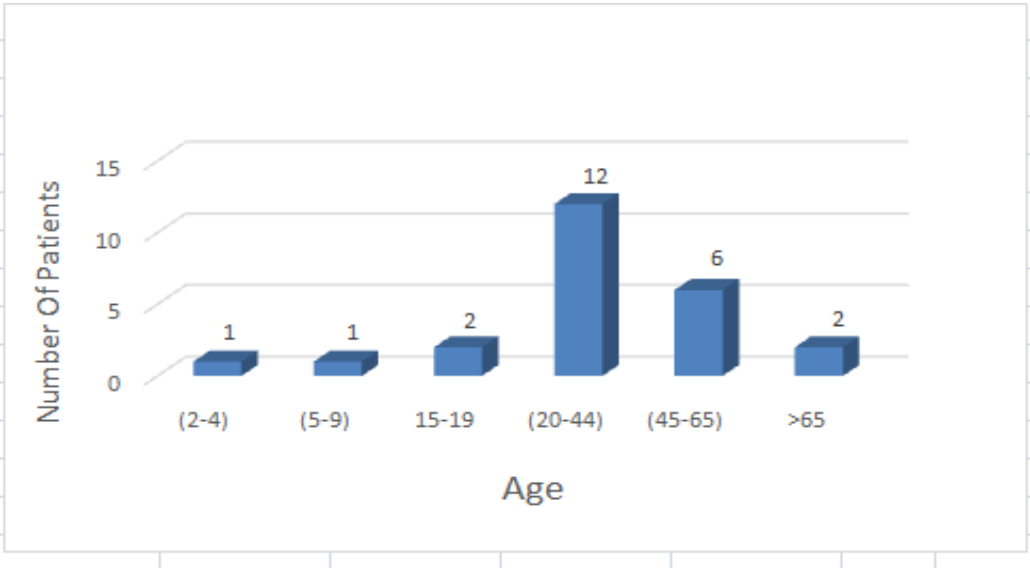

Fig. 95: Distribution of infected patients according to age slices during the prospective study.

4.6.1.4. Distribution of infected patients according to the months slices during the prospective study.

The **figure .96** shows that the highest number of effected cases was recorded during the Month of February. May recorded at 50% during the prospective study. The results obtained showed statistically significant differences.

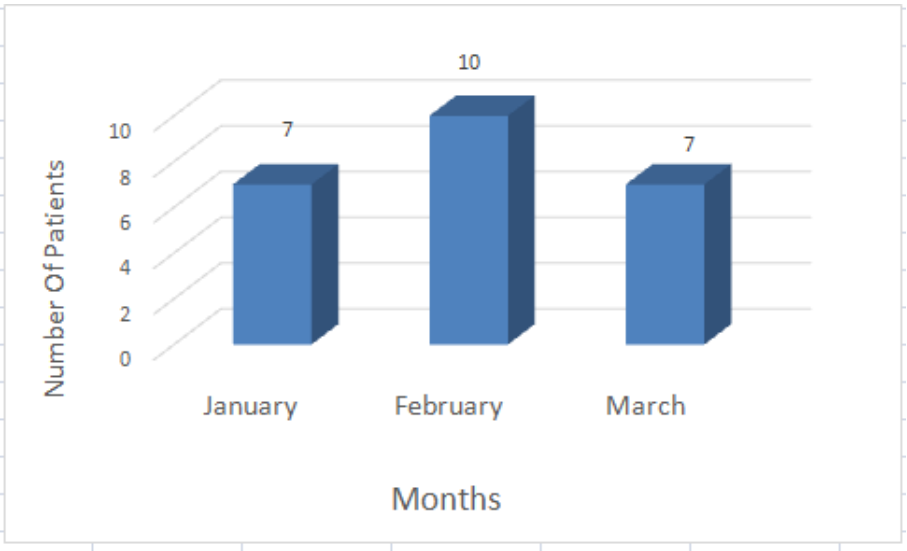

Fig. 96: Distribution of infected patients according to the months during the prospective study.

4.6.1.5. Distribution of infected patients according to the seasons during the prospective study.

The **Figure . 97** shows that the highest number of infected cases was observed during winter of

during the prospective study. The results obtained showed statistically significant differences.

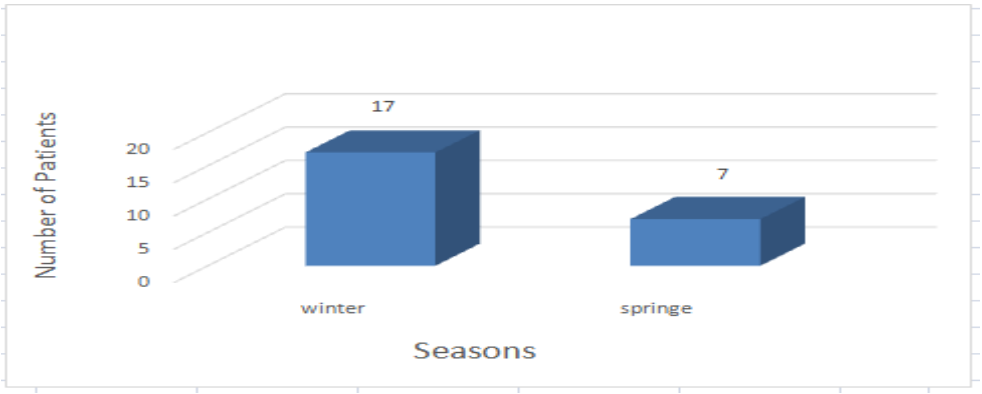

Fig.97: Distribution of infected patients according to the seasons during the prospective study**.**

4.6.1.6. Distribution of infected patients according to type ratio during the prospective study.

In our work we note that Extra Pulmonary Tuberculosis is the most widespread type with a percentage of **83%** , followed by Pulmonary tuberculosis with a rate of **17 %,** during the prospective study.

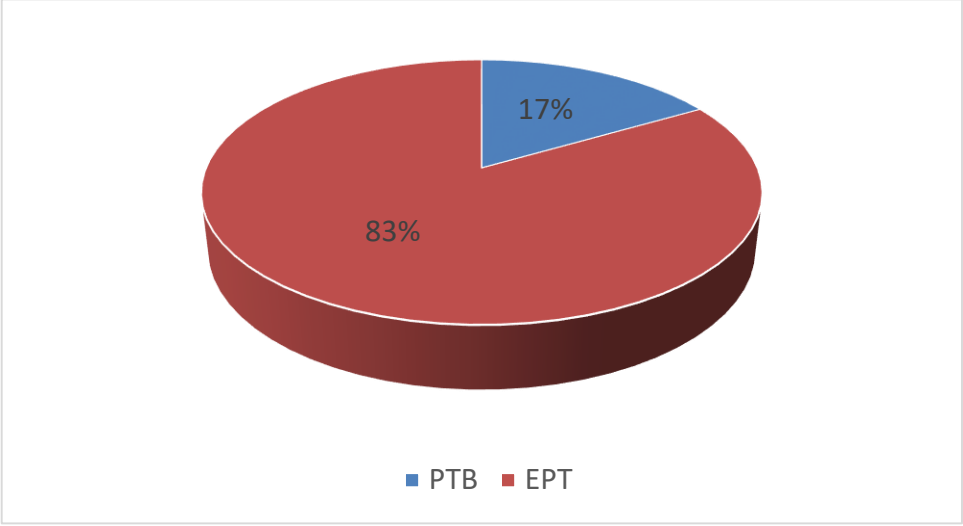

Fig.98: Distribution of infected patients according to the type during the prospective study.

4.7. Correlation between the variation of meteorological parameters and the propagation of *Mycobacteruim tuberculosis* during the period (2023-2023) :

To identify the relationship between meteorological parameters and the propagation of *Mycobacteruim tuberculosis* in the Mila region, we have used the model of diagram using the package {corrplot} in R. Using the package {nlme} in R, we implanted generalized linear

mixed models (GLMMs) to following the relationships: effects of T, Sun, P, WS and H on *Mycobacteruim tuberculosis* dissemination variation.

4.7.1. The relationship between the variation of the average temperature and the number of infected cases during the period (2013-2023):

Linear regression **(Figure 99)** showed that the number of infected cases increases progressively with the increase in the average temperature so there is a very strong positive correlation between the variation of the average temperature (°C) and the number of infected cases during the period (2013-2023).

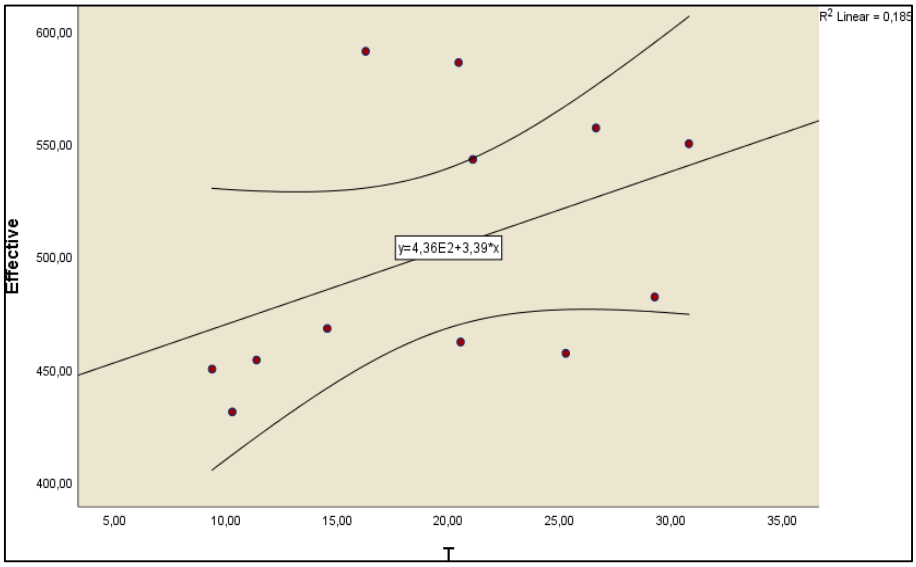

Fig.99: The correlation between the average temperature (°C) and the number of infected cases during the period (2013-2023).

4.7.2. The relationship between the variation of the average precipitation and the number of infected cases during the period (2013-2023):

Linear regression **(Figure 100)** showed that the number of infected cases decreases progressively with the increase in mean precipitation so there is a very strong negative correlation between the variation in mean precipitation (mm) and the number of infected cases during the period (2013-2023).

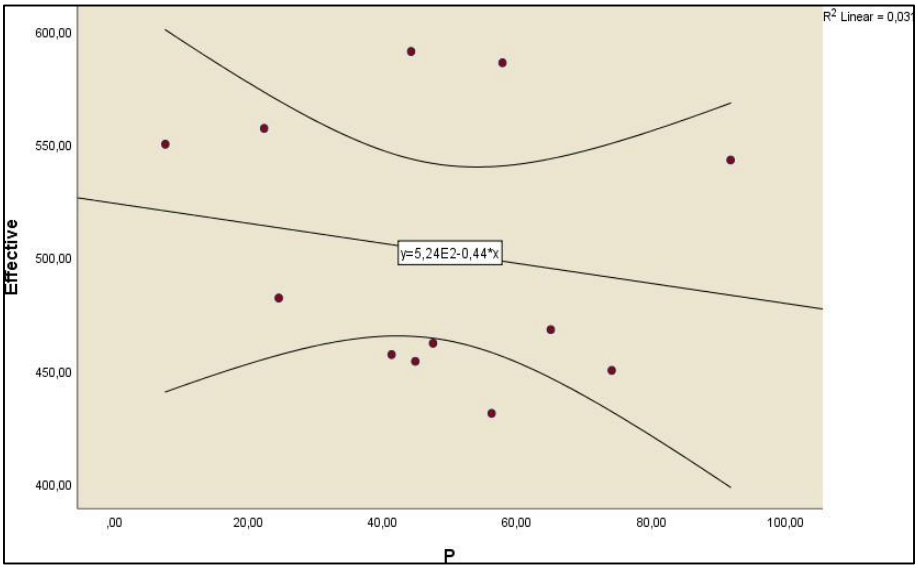

Fig. 100: The correlation between the average precipitation (mm) and the number of infected cases during the period (2013-2023).

4.7.3. The relationship between the variation of the average wind speed and the number of infected cases during the period (2013-2023):

Linear regression **(Figure 101)** showed that the number of infected cases increases progressively with the increase in the average wind speed so there is a very strong positive correlation between the variation in mean wind speed (knots) and the number of infected cases during the period (2013-2023).

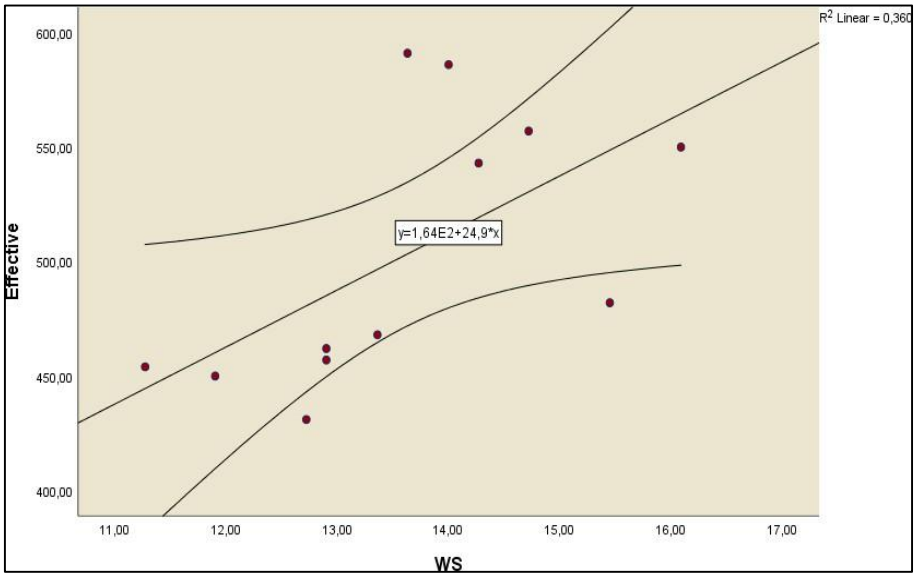

Fig. 101: The correlation between the average wind speed (knots) and the number of infected cases during the period (2013-2023).

4.7.4. The relationship between the variation of the average humidity and the number of infected cases during the period (2013-2023):

Linear regression **(Figure 102)** revealed that the number of infected cases decreases progressively with increasing humidity, so there is a very strong negative correlation between the average humidity (g/m3) and the number of cases infected during the period (2013-2023).

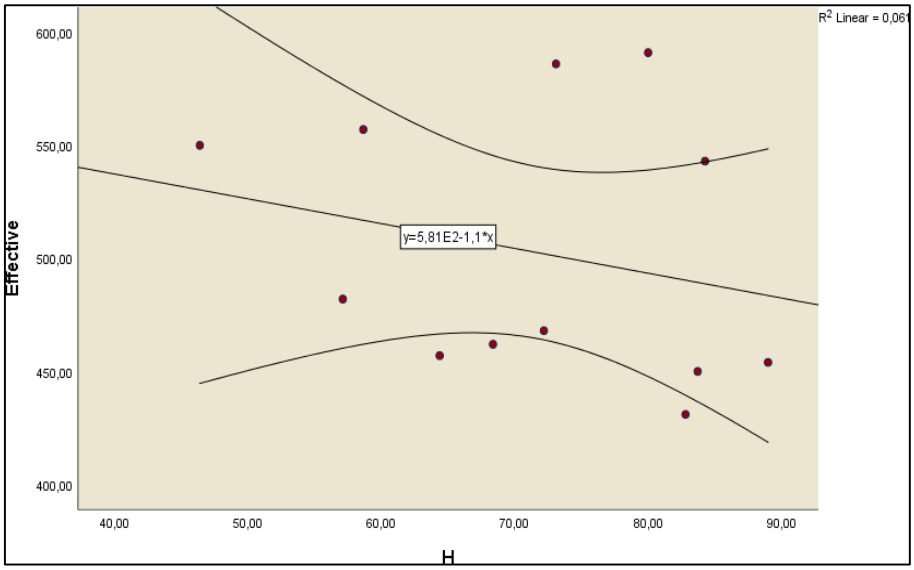

Fig. 102 : The correlation between the average humidity (g/m3) and the number of infected cases during the period (2013-2023).

4.7.5. The relationship between the variation of the average sunshine duration and the number of infected cases during the period (2012-2022) :

Linear regression **(Figure 103)** showed that the number of infected cases increases progressively with the increase in the average sunshine (hours) so there is a very strong positive correlation between the variation of sunshine (hours) and the number of infected cases during the period (2013-2023).

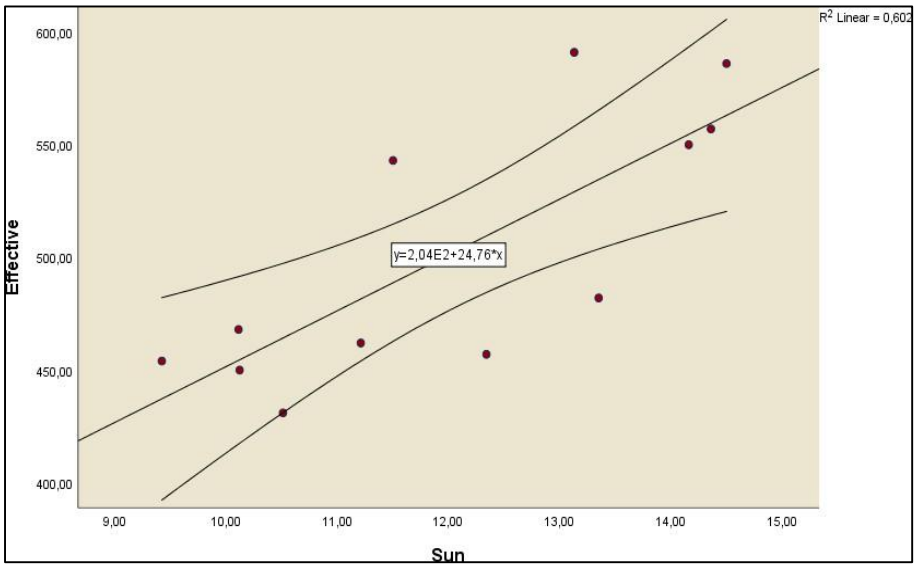

Fig.103 : The correlation between the average sunshine duration (hours) and the number of infected cases during the period (2012-2022).

Chapter V:

Discussion

5. Discussion

Tuberculosis is an infectious disease caused by the *Mycobacterium tuberculosis* of which humans are the main Host .Tuberculosis is spread from person to person through the air. When a person with pulmonary TB coughs, sneezes, or spits, they release TB bacilli into the air. You only need to inhale a little to become contaminated. Pulmonary tuberculosis can infect all organs of the body through the blood vessels, and this is called extrapulmonary tuberculosis. This work aimed to determine the prevalence of Tuberculosis diagnosed in the 5 regions (Tadjenanet , Mila , Chelgoum laid , Ferdjioua , ein bida ahrich) over a period (January 2013 to December 2023). In this study, the comparison of our results with the results of the scientific literature allowed us to identify The tuberculosus and to highlight the relationships of tuberculosis with different criteria such as age and sex of patients, years, months, types and weather parameters.

We treated 91700 cases of which 6031 were positive, which corresponds to a total infection rate of 6.58 % during the period (January 2013 to December 2023) , 4.6% positive cases from the global are extrapulmonary tuberculosis And the reason for their spread is due to agricultural activities and livestock raising

our results was consistent with a study in South Africa where Tuberculosis (TB) continues to be a public health issue of concern in South Africa.Workers in the agricultural sector are generally at increased risk of Tuberculosis due to multiple interacting factors such as , co-worker infection, and occupations falling within the lower socio-economic sectors. **(Mlangeni *et al.*, 2023).**

which is comparable to the results found in other studies where Our results were lower than studies conducted In 2006 in pakistan , approximately 44% tuberculosis cases are to be found (Ahmad, et al., (2013)). And in 2015 , Cameroon is a country with high TB incidence with a high prevalence in the city of Yaoundé (17%) . **(Tchatchouang *et al.*, 2015).**

The reason for the high rates of tuberculosis infection in these two countries compared to Algeria is due to poverty, lack of hospitality, low standard of living, and poor health conditions.

Poverty is a powerful determinant of tuberculosis. Crowded and poorly ventilated living and working environments often associated with poverty constitute direct risk factors for tuberculosis transmission. Undernutrition is an important risk factor for developing active disease.

We found positive cases of pulmonary TB at a rate of 1.98 %, which is lower than positive

cases of extra pulmonary TB.

We explain this by smoking, drug addiction, immune diseases that weaken the immune system, poor nutrition, and travel. our results was consistent with a study in in Beijing , from(2004 to 2011) ,The pathogenesis and spread of infectious diseases are determined by many factors, including social and economic factors, ecological conditions, the human immune system, and health care methods.(**Long Yan *et al.*,2018).**

In Taiwan Entry and exit ratio for TB susceptible and infected and , the transmission population. (Chung-Min *et al.*, 2008) .

in Iran. from 2006 to 2011 Another reason involves a hampered immune function caused by vitamin-D deficiency in cold seasons . **(Fallahi *et al.*, 2019).**

the lymph node tuberculosis is predominantly (57.89%) then to the pleural tuberculosis (15.33%) and the PERITONAL tuberculosis (8.02%). we observe that the other types are rare . the lymph nodes is a secondary lymphatic organ which contains mature lymphatic cells whose main role is lymphatic drainage and the elimination of germs such as BK in the human body.

Lymph nodes are located in many parts of the body, including the neck, armpit, chest, abdomen (belly), and groin. They contain immune cells that can help fight infection by attacking and destroying germs that are carried in through the lymph fluid. There are hundreds of lymph nodes throughout the body.

our results consistent with a study in india where Lymphadenopathy is the common form of extrapulmonary tuberculosis (TB) in the developing country like India. **(Singh and Tiwari, 2016).**

Our study reveals that tuberculosis is more common in females (64%) than in males (36%) , the same thing on the extra Pulmonary TB affects (84.25%) from women in Mila City .

We explain this increase for women because Women are at increased risk of progression to disease during their reproductive years.

It has long been observed by obstetricians that pregnancy is associated with a more prevalent onset of active tuberculosis (TB) and also more rapid progression of TB disease compared with the non-pregnant state. **(Bates *et al.*, (2015).**

our results are consistent with a study at 2013 , women were more likely than men to have concurrent extra-pulmonary TB **(Lin *et al.*, 2013).**

but the pulmonary TB is more common in males (50.99%) than in females (49.008 %) in

Mila City . where males were found to be more numerous, It has been shown that the percentage of females infected with pulmonary tuberculosis is (49%) , which is less than the percentage of females infected with extra pulmonary tuberculosis (64%) and we explain this increase for males because Due to smoking and taking drugs that damage the lungs and immune system and accordung to the study conducted in pakistan (September 2013) and in Spain Between 2012 and 2020, it was found that ,poorer nutritional status, no early medical care, lack of proper treatment protocol because the patient of TB left their treatment before the completion. **(Tauseef *et al.*, 2013)**

Behavioural risk factors,usually more frequent in men than in women (i.e. imprisonment, alcohol abuse, drug use, or smoking), seem to also play an import-ant role. (María *et al.*,2020).

Our results regarding the effect of age for the age groups included in this study ranged from newborns to ≥65 years, and the age group [20-44] was the most affected by Tuberculosis with an infection rate of 51.93% , the same thing on the EPTB , where mainly affects subjects aged between 20 to 44 years (55.87%) , then between 45 to 65 years (19.54%). the same thing on the PTB , and the age group [20-44] was the most affected by pulmonary Tuberculosis with an infection rate of 46.8% , followed by age ≥65 years with an infection rate of 22.02%.

there is a progressive increase in the notification of tuberculosis rate with age. Most cases of TB in the elderly are linked to the reactivation of lesions that have remained dormant.The awakening of these lesions is attributable to changes in the immune system related to senescence. **(Caraux-Paz *et al.*, 2021).**

Specific for TB, numerous age-related comorbidities, such as diabetes, obesity, malnutrition, chronic respiratory diseases, cancer, and other underlying medical conditions, can result in an increased risk for developing active TB disease .(Fontánez and Turner (2022)).

Increased risk of TB disease and mortality are associated with populations that have compromised immunity, such as HIV-infected individuals, **.(Fontánez and Turner 2022).**

The risk of TB susceptibility and mortality is significantly increased in individuals aged 65 and older, confirming that the elderly represent one of the largest reservoirs for M.tb infection. The elderly population faces many challenges that increase their risk of developing respiratory diseases, including TB. The challenges the elderly face in this regard include the following: decreased lung function, immuno-senescence, inflammaging, adverse drug effects, low tolerance to anti-TB drugs, lack of suitable diagnoses/interventions, and age- associated comorbidities. **.(Fontánez and Turner 2022).**

This agrees with the results of the study done in The city of Shenzhen (china) The incidence was lowest amongst the age group 0–14 . In contrast, the TB incidence increased in the age groups 45–54, 55–54, and especially in those aged ≥65 . (Zhu *et al.*, 2018) , the same in Morocco(the province of Kenitra) . The 30 - 44 age group is the most affected by 42%, followed by that of 15 - 29 years (29%), the oldest 75 - 90 are the least affected . This study has shown that the determinants of tuberculosis are manifold and relate mainly to unfavorable socioeconomic conditions, linked to poverty, population growth, human migration, which explains the incidence of the disease from the point of socio-economic view. **(Bouchra *et al.*,(2020).**

Our results are consistent with a study in iraq (2011) , the most common affected age group was between 21-40 years (31.9%) patients. **(Ali *et al.*, 2011).**

The results obtained show that the infestation rate during the period (2013-2023) was very high in 2022, 10.28% compared to other years where we notice that the prevalence of infection by Tuberculosis have been fluctuating from one year to another. insufficient testing and treatment for latent TB may have fueled a rise in active cases.

Poor TB case detection leads to increased transmission and high TB prevalence rates **(Amenuvegbe *et al.*, 2016).**

On the other hand we observed a slight increase in positive cases during the years 2019 - 2015 with SBI vary between 10.11% and 9.99% this can be explained by a better control of clinical and biological diagnosis by health personnel which would lead to the detection of more cases.

our results are consistent with a study In 2022, the largest number of new TB cases occurredin WHO's South-East Asian Region (46%), followed by the African Region (23%) and the Western Pacific (18%). **(WHO , 2022).**

but for the extra pulmonary tb ,The results obtained show that the infestation rate during the period (2013-2023) was very high in 2019, 10.49% compared to other years where we notice that the prevalence of infection by Extra Pulmonary Tuberculosis have been fluctuating from one year to another. insufficient testing and treatment for latent TB may have fueled a rise in active cases Or perhaps because of the Corona pandemic, which contributed to the activation of latent tuberculosis .

COVID-19 may also lead to unmasking of latent infections such as TB. **(Daneshvar *et al.*, 2023).**

On the other hand we observed a slight increase in positive cases during the years 2022-2018 with SBI vary between 10.39% and 9.86% this can be explained by a better control of clinical and biological diagnosis by health personnel which would lead to the detection of more cases , Or perhaps due to the lack of coronavirus cases in 2022 .

The results obtained show that the infestation rate pulmonary TB during the period (2013- 2023) was very high in 2015 ,2014 and 2022 , 11.28%, 10.57 % and 10.07 % and compared to other years where we notice that the prevalence of infection by Tuberculosis have been fluctuating from one year to another.

insufficient testing and treatment for latent TB may have fueled a rise in active cases. We explain the increase in the percentage during the period 2014 and 2015 due to the increase in population, which is comparable to the results found in other studies in World Health.

Organization 2014 I have that Tuberculosis (TB) remains one of the world's deadliest communicable diseases. In 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease, 360 000 of whom were HIV-positive. TB is slowly declining each year and it is estimated that 37 million the death toll from the disease is still unacceptably high and efforts to combat it must be accelerated if 2015 global targets, set within the context of the Millennium Development Goals (MDGs), are to be met. Of the estimated 9 million people who developed TB in 2013 , more than half (56%) were in the South-East Asia and Western Pacific Regions.

A further one quarter were in the African Region, which also had the highest rates of cases and deaths relative to population. India and China alone accounted for 24% and 11% of total cases, respectively.22 October 2014, Geneva - Recent intensive efforts to improve collection and reporting of data on tuberculosis (TB) are shedding new light on the epidemic, revealing that there are almost half a million more cases of the disease than previously estimated.

while in the period 2022 we explain this due to the decline in people's immune systems after the period of the Corona -virus 19. hich is comparable to the results found in other studies in World Health Organization 2022 Until the coronavirus (COVID-19) pandemic, TB was the leading cause of death from a single infectious agent, ranking above HIV/AIDS. During the COVID-19 pandemic, WHO has also collected provisional monthly or quarterly national TB case notification data on an ongoing basis from more than 100 countries with about 90% of the world's TB cases And it turns outThe most obvious and immediate impact on TB of disruptions caused by the COVID-19 pandemic was a large. **(Tedros , and Tereza 2022).**

On the other hand weobserved a slightincrease in positive cases during the years 2016 - 2019 this can beexplained by And a change in lifestyle a better control of clinical and biological

diagnosis by health personnel .

The analysis of the distribution according to regions revealed that *Mycobacterium tuberculosis* notes a predominance in the region of Ferdjioua (29.86%) and chelgoum (25.07%) Due to the large amount of agricultural activity and livestock raising, the high pollution in these areas, and the lack of health facilities but in mila region the cases of tuberculosis are less (20.56 %)because there is a lot of health facilities and less rate of pollution , Ain beida aheriche the rate of tuberculosis cases is less compared to the other regions (12.96%) because the population is smaller compared to other regions. in Tadjenanet region the cases of tuberculosis are less (11.44%) Due to the less amount of agricultural activity and livestock raising .

the same thing for the pulmonary tuberculosis according to analysis of the distribution according to regions On the spread of tuberculosis pulmonary varies from on region to another . we recorded the the highest percentage in the city of ferdjioua , chelghoum laid and mila 31.05% , 24.00%, and 20.75% this is explained by commercial exchanges ,administrative work , and an increase in the number of local residents.

as for the ain eida ahriche and tadjenanet 17.12% and 7.04% , regions , the lowest percentage was recorded . the is explained by the small population andof agricultural activity.

For the Extra pulmonary tb , The analysis of the distribution according to regions revealed that *Mycobacterium tuberculosis* notes a predominance in the region of Ferdjioua (29.28%) and chelgoum (25.53%) Due to the large amount of agricultural activity and livestock raising, the high pollution in these areas, and the lack of health facilities but in mila region the cases of tuberculosis are less (20.57%)because there is a lot of health facilities and less rate of pollution , in Tadjenanet region the cases of tuberculosis are less (13.36%) Due to the less amount of agricultural activity and livestock raising , Ain beida aheriche the rate of tuberculosis cases is less compared to the other regions (11.27%) because the population is smaller compared to other regions.

our results was consistent with a study in Ethiopia where the majority of inhabitants in this area engaged in agriculture. As the climate condition is suitable for cattle production, these farmers practice mixed cattle farming in addition to crop cultivation. Previous studies conducted on bovine TB in herds in the study area have indicated high prevalence of the disease. Thus, MTC prevalence in both human and cattle in the area suggest the possibility of existence of transmission between farmers and their cattle. .**(Ameni *et al.*, 2013).**

our results was consistent with a study in South Africa where Tuberculosis (TB) continues to be a public health issue of concern in South Africa. Workers in the agricultural sector are generally at increased risk of EPTB due to multiple interacting factors such as , co-worker

infection, and occupations falling within the lower socio-economic sectors. **(Mlangeni *et al.*, 2023).**

The analysis of the distribution according to seasons showed that the majority cases of Tuberculosis indicate a prevalence in Spring of 28.42%, followed by a slight increase in summer and autumn of 26.45% and winter 23%, while the presence of Tuberculosis decreased during the cold winter , the same thing for the extra pulmonary tuberculosis where The analysis of the distribution according to seasons showed that the majority cases of Tuberculosis indicate a prevalence in Spring of 28.59%, followed by a slight increase in summer and autumn of 26.26% and 22.61%, while the presence of Tuberculosis decreased during the cold winter . and the same thing for the pulmonary tuberculosis where The analysis of the distribution according to seasons showed that the majority cases of Tuberculosis pulmonary indicate a prevalence in Spring of 28%, followed by a slight increase in summer and autumn of 27% and 23%,

the risk of TB increased in line with the temperature in all groups **(Fares ,2011).**

our results are consistent with a studies in Mongolia, South Western Cameroon , Hong Kong , India , Japan too . The spring and summer peaks of tuberculosis cases are clearly demonstrated in most of this studies . **(Fares ,2011).**

our results are consistent with a study in Korea , While the trough season was winter from 2006 to 2016, the peak season was spring between 2013 and 2016. **(Eunhee ,and Jongmyeon ,. 2006).**

our results are consistent with a study in pakistan (2021) , where EPTB has been shown to demonstrate seasonal variation, with higher incidence in the spring/summer months and lower incidence in the autumn/winter; **(Butt *et al.*, 2021).**

We note that the rate of Tuberculosis by month is high during the months of April 9.79% , May 9.71%, June 9.24% . The other increase is recorded during the month of July 9,12% . the same thing for the extra pulmonary tubercuosis where we note that the rate of Extra pulmonary Tuberculosis by month is high during the months of may 9.87% , april 9.56%, July 9.37% . The other increase is recorded during the month of march 9,23% , the same thing for the pulmonary tuberculosis We note that the rate of Tuberculosis by month is high during the months of April 10.35% , May 8.48%, June 8.59% . The other increase is recorded during the month of July 9,12% , that confirms the Spring and Summer predominance.

Because the highest prevalence of the tuberculosis occurs at the moderate temperature of the spring season.

TB notification rates increase with temperature . **(Gelaw *et al.,* 2019)**

Our results are consistent with a study in india (2011) ,The total EPTB cases were highest during the quarter Q2 (April to June) **(Behera and Sharma 2011).**

Based on our results, we noticed that as the temperature , the sunshine and the wind speed increased, the number of tuberculosis cases increased, and as the precipitation and the humidity rate increased, the number of cases decreased.

Our results are consistent with a study in Brazil, 2003–2012 where More cases of TB were reported in the FD when the temperature was between 20◦C and 23◦C (72.4%of cases), in line with several studies carried out in different places, includ ing: New York (20–25◦C); Spain (16–24◦C) ; Cape Town, South Africa (13–23◦C) ; UK (11.7◦C and 21.1◦C)4; and Peru. How ever, TB was also diagnosed at higher temperatures: 39◦C in Cameroon16; 21–39◦C in Northern India11; and 20–38◦C in Kuwait.43 Lower temperatures have been identified in Japan (5◦C) and Mongolia (−5◦C to 9◦C).22 In general, TB incidences were higher in milder temperatures. **(Fernandes *et al.,* 2017).**

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Our prospective study during the first three months of 2024 at the Bacteriology Laboratory and the Service for the Control of Tuberculosis and Respiratory Diseases (S.C.T.M.R.) at the Public Clinical Institution of Bouarrouj-Mila confirms our analytical study by obtaining the same results with regard to the influence in terms of gender that prevails in the spring and summer seasons, and age, As well as regions. On the distribution of tuberculosis in humans The category is between [20-44] and The elderly are most affected > 65 years. Older adults have an increased susceptibility to viral infections and subsequent superimposed bacterial infections. Altered immune responses in older people are responsible for many diseases.

Conclusion

Conclusion

Tuberculosis remains one of the deadliest infectious diseases and has claimed millions of lives for many years. Although significant progress has been made towards controlling the global burden of TB over the past decade, more efforts are still needed to eliminate it.

Tuberculosis (TB), an infectious disease caused by the tuberculosis bacillus, *Mycobacterium tuberculosis.* In most forms of the disease, the bacillus spreads slowly and widely in the lungs, and is a notifiable disease, favoured by HIV and distressing socioeconomic factors. Despite the existence of a monitoring program for anti-TB drugs, TB remains a serious public health problem in the country. Algeria. Our bibliographic research and internal training have allowed us to expand the scope of the research deepening our knowledge of tuberculosis. We conducted this descriptive, analytical, retrospective study at the level of: Directorate of Health and Population (DSP) - Mila.

During an extended period From January 2013 to December 2023 and a three-month prospective study (January to March 2024).

The results obtained showed that (6.63%) of the subjects were carriers of tuberculosis. among the positive cases, and the percentage of women reached 64.09%, followed by man 35.91%. There may be biological or behavioural factors that make women more susceptible to including differences in sex hormones or social and environmental factors related to lifestyle.

Age also plays an important role in the spread of these bacteria. The age group [20-44] is the most exposed to the tuberculosis linked to high activity which involves exposure to risk factors.

- This may be due to lifestyle and behavioural factors in this age group. This may include diet, habits or exposure to potential pathogens in the work or living environment.

- People over 65 years of age are also affected and this is linked to allow immunity.

Lack of effect on children under 14 years of age which may be due to better management burden through prevention methods such as the BCG vaccine. Extra pulmonary TB is more common than pulmonary TB. Predominance of bothlymphnode and pleural forms.

Meteorological parameters have an important influence on the increase or decrease in the number of cases infected with *Mycobacterium tuberculosis*, including the Temperature,

sunshine duration and wind speed According to our results, spring , summer and autumn suare the seasons most associated with increased tuberculosis . Due to high temperatures, and changes in humidity and wind speed Where temperature, average monthly sunshine duration, and wind speed come into play, An important role in its spread. Through the results of our prospective study lasting three months (from January to March, 2024), we conclude that there is a great similarity with those of retrospective study (2013-2023).

In conclusion, it should be noted that this study represents an important contribution to our understanding of the relationship between *M tuberculosis* and weather parameters and provides a basis for future research in this area. We hope that the results of this study will contribute to the development of prevention and control strategies for tuberculosis and thus improve the health of individuals and society in general. Effective treatment is a necessary condition, but it is far from sufficient, it is not enough to diagnose and treat patients, but to attack the source. It is imperative to strengthen the fight against tuberculosis by creating other treatment centers .More efforts and research should be directed in this area to Epidemiological study of tuberculosis distribution in the Mila region correlation with meteorological parameters

In Conclusion in, the end we hope that our data will move in the direction of better consideration of local epidemiology, better understand the transmission and spread pathways of this disease and develop effective preventive measures. It is important to understand that weather and environmental factors are not the only factors contributing to the spread of tuberculosis and the relevant health authorities must work together to implement comprehensive preventive measures targeting all factors affecting the prevalence of this condition.

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Annex

Annex

One-Sample Test

Test Value = 0

	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Sex	265,861	6030	,000	1,642	1,63	1,65
Age	345,839	6030	,000	6,158	6,12	6,19
Month	149,121	6030	,000	6,402	6,32	6,49
Seasons	180,970	6030	,000	2,502	2,47	2,53
Years	147,392	6030	,000	6,042	5,96	6,12
Type	58,909	6030	,000	2,875	2,78	2,97
Region	200,228	6030	,000	3,123	3,09	3,15

ANOVA ONE WAY

		Sum of Squares	df	Mean Square	F	Sig.
Sex	Between Groups	2,898	10	,290	1,261	,247
	Within Groups	1383,783	6020	,230		
	Total	1386,680	6030			
Age	Between Groups	52,721	10	5,272	2,766	,002
	Within Groups	11476,320	6020	1,906		
	Total	11529,041	6030			

Month	Between Groups	227,307	10	22,731	2,048	,025
	Within Groups	66806,822	6020	11,097		
	Total	67034,129	6030			
Seasons	Between Groups	24,171	10	2,417	2,100	,021
	Within Groups	6927,553	6020	1,151		
	Total	6951,724	6030			
Type	Between Groups	194,915	10	19,492	1,358	,193
	Within Groups	86422,819	6020	14,356		
	Total	86617,734	6030			
Region	Between Groups	66,649	10	6,665	4,571	,000
	Within Groups	8777,798	6020	1,458		
	Total	8844,448	6030			

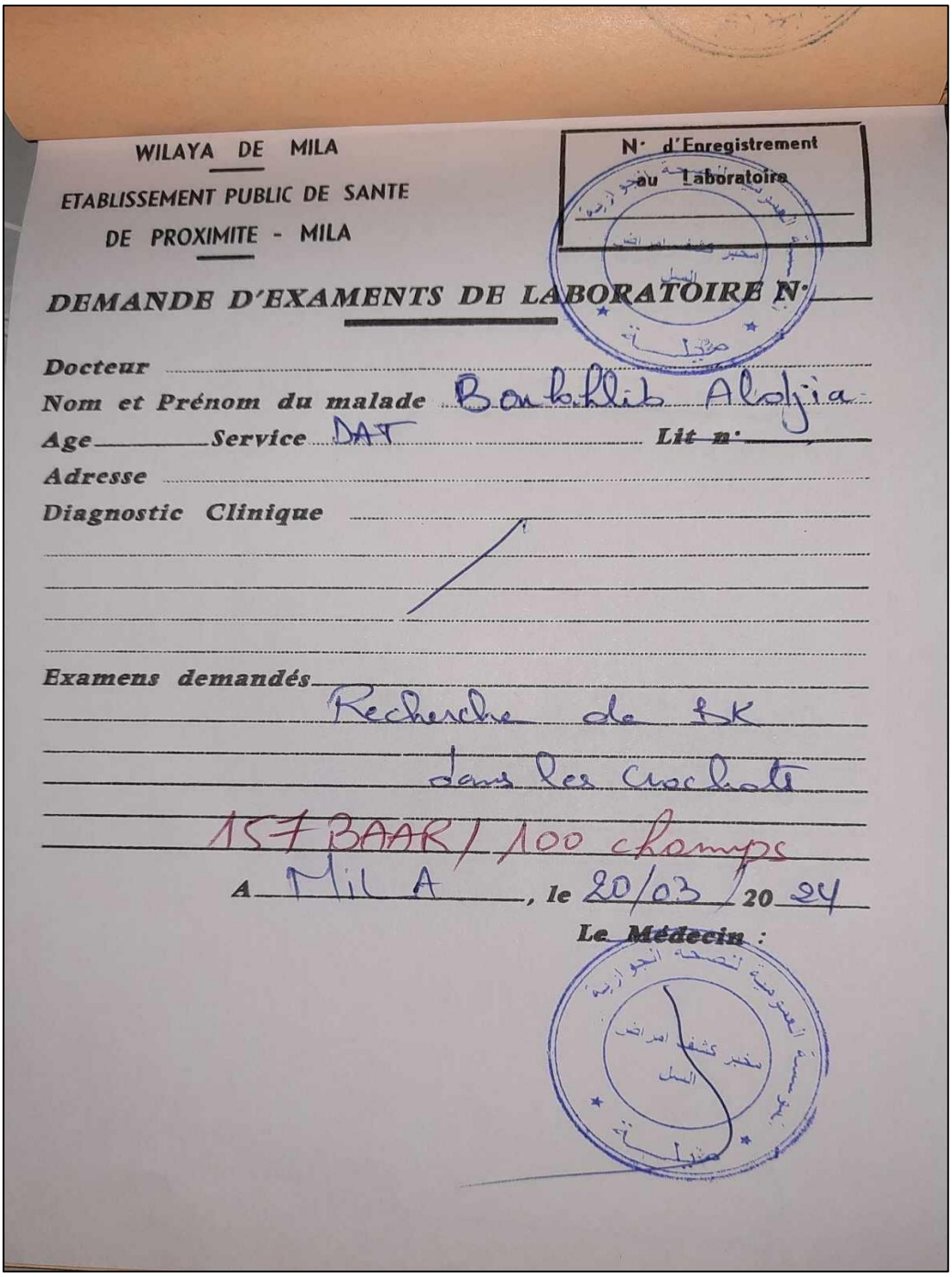
MANOVA

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	Sex	3,350[a]	12	,279	1,215	,266
	Age	57,235[b]	12	4,770	2,502	,003
	Region	68,852[c]	12	5,738	3,935	,000
	Type	320,651[d]	12	26,721	1,863	,034
Intercept	Sex	2316,609	1	2316,609	10078,109	,000

	Age	32431,510	1	32431,510	17013,261	,000
	Region	8260,982	1	8260,982	5665,095	,000
	Type	5703,377	1	5703,377	397,730	,000
Month	Sex	,383	1	,383	1,664	,197
	Age	,084	1	,084	,044	,834
	Region	,003	1	,003	,002	,962
	Type	47,264	1	47,264	3,296	,069
Seasons	Sex	,023	1	,023	,099	,753
	Age	3,501	1	3,501	1,837	,175
	Region	1,518	1	1,518	1,041	,308
	Type	9,649	1	9,649	,673	,412
Years	Sex	2,926	10	,293	1,273	,240
	Age	52,906	10	5,291	2,775	,002
	Region	66,708	10	6,671	4,575	,000
	Type	201,458	10	20,146	1,405	,171
Error	Sex	1383,330	6018	,230		
	Age	11471,806	6018	1,906		
	Region	8775,596	6018	1,458		
	Type	86297,083	6018	14,340		
Total	Sex	17641,000	6031			
	Age	240207,000	6031			
	Region	67648,000	6031			
	Type	136467,000	6031			
Corrected Total	Sex	1386,680	6030			
	Age	11529,041	6030			

Region	8844,448	6030			
Type	86617,734	6030			

Operating Sheet



WILAYA DE MILA

ETABLISSEMENT PUBLIC DE SANTE

DE PROXIMITE - MILA

N° d'Enregistrement au Laboratoire

DEMANDE D'EXAMENTS DE LABORATOIRE N°

Docteur

Nom et Prénom du malade Barkallah Alaoua

Age Service DAT Lit n°

Adresse

Diagnostic Clinique

Examens demandés Recherche de BK dans les crachats

157 BAAR / 100 champs

A Mila, le 20/03/2024

Le Médecin :