T.R.N.C

NEAR EAST UNIVERSITY

INSTITUTE OF HEALTH SCIENCES

STATISTICAL STUDY OF EPIDEMIOLOGICAL PROFILE OF PULMONARY TUBERCULOSIS AT BANDUNDU PROVINCE FROM 2008 TO 2016, IN THE DEMOCRATIC REPUBLIC OF THE CONGO.

Jury NgunsiaBATEKO

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Assoc.Prof.Dr. lkerEtikan

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DEDICATION

To our father Bateko Anicet and Mother SuzanneSiadi

We dedicate this work.

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To the Associate Professor Dr. lkerEtikan, Head of the Department of Biostatistics, Faculty of Medicine at Near East University in Cyprus; Who had honored us by accepting to lead, to scientifically evaluate and judge this thesis; that he finds here the expression of our deep respect and admiration for his knowledge and the passion that animates him.

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Jury Ngunsia Bateko

ABSTRACT

Statistical study of Epidemiological Profile of Pulmonary Tuberculosis in Bandundu Province

from 2008 to 2016, in the Democratic Republic of the Congo.

Jury NgunsiaBATEKO

Department of Biostatistics

Thesis Supervisor: Assoc.Prof.Dr. IkerEtikan

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Pulmonary Tuberculosis had been described as one of the major infectious diseases ravaging the health of most countries, especially third world nations with weak health care system. The study considered the occurrence and epidemiological profile of Pulmonary Tuberculosis in the provincial region of Bandundu of the Democratic Republic of Congo under the reviewed year of 2008 to 2016.

The epidemiological data werecollected from the Bandundu tuberculosis screening and treatment (TBD) health centersof the province. The data havea total of 40, 619 pulmonary tuberculosis cases, of which the male gender accounted for 21,506 cases and female gender accounted for 19,113 cases. The One-Way ANOVA at a significance level of 0.05 was applied to examine the means difference of the total cases of pulmonary tuberculosis while the Kruska Wallis Test Statistics was applied to to test for significance difference of data that were not found to be normally distributed.

Other test of variables considered in the study were: the cured tuberculosis patients; mortality of patients; the incidence of tuberculosis in the population; the incidence in the male category and the incidence in the female category relative to the years under reviewed(2008-2016).

The incidence cases in the male gender were higher in the year 2015 with [62.50(78.00-210.00)] with cases per 100,000 people. In terms of the female gender, the highest incidence cases were in the year 2016 [56.00(26.00-92.00)]. An increase in the trend of incidence of Pulmonary Tuberculosis was found during our study, though not statistically significant relative to the years under review. In the study, it was found that year 2010 has the highest incidence rate of about 127.70 (27.00 – 207.00) cases per 100,000 people. The year 2013 recorded the highest percentage of dead cases (5.76%) while the year 2016 recorded the highest percentage of tuberculosis cured cases(88.57%)

Keywords: Pulmonary Tuberculosis, Incidence, Mortality, One-Way ANOVA, Epidemiology

TABLE OF CONTENTS

CONVER PAGE	i
TITLE PAGE	ii
APPROVA	iii
DEDICATION	iv
ACKNOWLEDGMENT	v
ABSTRACT	vii
LIST OF TABLES	xi
LIST OF FIGURES	xi
LIST OF ABBREVIATIONS	xiv
CHAPTER ONE	1
1.1 Introduction	1
1.2 Tuberculosis Crisis in the DRC	
1.3 Objectives of the Research	4
1.4 Significance of the Study	4
1.5 Thesis Description	5
1.6 Study Limitations	5
CHAPTER TWO	6
LITERATURE REVIEW	6
2.1: Definition of Concept	6
2.2 Congolese health system	10
2.3 Generality on pulmonary tuberculosis	
2.4 History and epidemiology	
2.5 Evolution of the incidence	
2.5.1 Transmission	14
2.5.2 Bacillary pathogenicity	
2.5.3 Localizations of tuberculosis	17

2.5.4 Evolution
2.5.5 Diagnosis of tuberculosis
2.5.6 Prevention and Treatment
2.5.7 Repressive measures
2.5.8 Anti-Tuberculosis treatment
2.6 Related Searches
CHAPTER THREE
RESEARCH METHODOLOGY
3.1. Type of period and place of study
3.2. Study population:
3.3. Sampling
3.4 Research Method
3.5 Ethics
3.6 Data collection and analysis
CHAPTER FOUR
RESULTS PRESENTATION
4.1 ANOVA of Total Cases of Tuberculosis Relative to the Years (2008 -2019) 46
4.2 ANOVA of Cured Cases of Tuberculosis Relative to the Years (2008 -2019)
4.3: ANOVA of Dead Cases of Tuberculosis Relative to the Years (2008 -2019)53
4.4: ANOVA of Incidence Cases of Tuberculosis Relative to the Years of Study55
4.5: ANOVA of Male Incidence Cases of Tuberculosis Relative to the Years of Study
4.6: ANOVA of Female Incidence Cases of Tuberculosis Relative to the Years of
Study
CHAPTER FIVE
CONCLUSION AND RECOMMENDATIONS
REFERENCE

LIST OF TABLES

		Page N°
Table 1	Estimated incidence of tuberculosis in the six WHO	13
	regions.2008	
Table 2	First-line anti-tuberculosis drugs	32
Table 4.1	Descriptive Statistics of Total Number of Tuberculosis	46
	Cases	
Table 4.2	Test of Homogeneity of Variance Total tuberculosis cases	47
Table 4.3	ANOVA Table for Total Tuberculosis Cases	47
Table 4.4	Descriptive Statistics of Cured Cases of Tuberculosis	49
Table 4.5	Test of Homogeneity of Variance Cured tuberculosis cases	50
Table 4.6	ANOVA Table for Cured Tuberculosis Cases	50
Table 4.7	Post-Hoc Analysis of Tukey's test for Cured Tuberculosis	51
	Cases	
Table 4.8	Descriptive Statistics of Dead Cases of Tuberculosis	53
Table 4.9	: KruskalWallis Test	54
Table 4.10	Descriptive Statistics of Total incidence cases of	55
	Tuberculosis	
Table 4.11	: KruskalWallis Test	56
Table 4.12	Descriptive Statistics of total incidence cases of	57
	Tuberculosis among Males	
Table 4.13	Kruskal Wallis Test	58

Table 4.14	Descriptive	Statistics	of	total	incidence	cases	of	60
	Tuberculosis	among Fer	nales	5				

Table 4.15	Kruskal Wallis Test	61

LIST OF FIGURES

Figure 1:	Decision tree in PATI IV without radiography	25
Figure 2	Tuberculosis incidence rate: All of Quebec, excluding	39
	Montreal and Montreal, By year, 1980-2015	
Figure 4.1	Bar plot of the means of the total tuberculosis recorded	48
	annually	
Figure 4.2	Bar plot of the Means Percentages Cured cases of	52
	Tuberculosis annually	
Figure 4.3	Bar plot of the Percentages Dead Cases of Tuberculosis	55
	Annually	
Figure 4.4	Bar plot of the Median of Incidence Cases of Tuberculosis	57
	Annually	
Figure 4.5	Bar plot of the Median Male Incidence Cases of	59
	Tuberculosis annually	
Figure 4.6	Bar plot of the Median Female Incidence Cases of	62
	Tuberculosis Annually	

LIST OF ABBREVIATIONS

S/No	ABBREVIATIONS	EXPLANATION
1	AEG	Alteration of the general condition
2	AMM	Authorization for the marketing
3	BCG	Bacillus of Calmette and Guérin
4	CMC	Contact morning contact
5	CRP	C-reactive protein
6	CSDT	Health centers for screening and treatment of
		tuberculosis
7	CST	Treatment Health Centers
8	D.R.S.P	the Quebec Regional Directorate of Public Health
9	DRC	Democratic Republic of Congo
10	EM	Microscopic examination
11	HIV	Human immunodeficiency virus
12	IDR	Intra dermo reaction
13	INH	Isonicotinylhydrazine
14	ITL	Slow TB infection
15	IV	Intravenous
16	MAI	Immunosuppressive treatment
17	SCTMR	Tuberculosis and Respiratory Disease Control Service
19	MDR-TB	Multidrug-resistant TB
20	NTP	National Tuberculosis Program
21	PNLS	National AIDS Program

22	PNLS	National AIDS Program
23	ТО	Departure treatment
24	T3	3 months treatment
25	ТВ	Tuberculosis
26	VVA	live virus mitigate
27	WHO	WorldHealthOrganization

CHAPTER ONE

1.1.Introduction

Tuberculosis is one of the critical infectious diseases with high rate of mortality worldwide. It remains an emergency in terms of public health [1]. So far, it is still widespread in sub-Saharan Africa. In this part of the world, measures to combat tuberculosis expansion are negatively impacted by many factors including financial constraints associated with the malfunctioning of the health system put in place and the poverty of the population [13].

According to statistics gatheredby the World Health Organization (WHO), the annual incidence in 1996 increased from 7.3 million to 8.8 million cases in 2002. Moreover, the same source states a projection in which the annual incidence is expected to increase from 9 million cases for the year 2005 to 10 million cases in 2025 [2]. In the same vein, the report of the World Health Organization in 2004 added that out of the 6.2 billion inhabitants of the planet, 2 billion people are already infected with the bacillus of tuberculosis. The incidence of all types of tuberculosis would reach 8.8 million cases, including nearly 4 million cases of highly infectious pulmonary tuberculosis.

In 2013, the WHO reported 9 million new TB cases that would have caused 1.4 million deaths. One-third of the population is infected with TB, which is more than 2 billion people. An estimated 530 000 cases of tuberculosis in children under 15 years, or 6% of all reported cases. [1]. Accordingly, estimates for 2016 inform thatAsian countries have the highest number of new cases, 45% worldwide, followed by Africa,

with 25% of new cases. About 87% of new cases comes from the 30 countries with a high TB burden, including the DRC. Among counties previously mentioned, seven countries accumulate65% of the world's new cases, including South Africa, India, Pakistan, Indonesia, China, Nigeria and the Philippines.

The incidence of tuberculosis varies worldwide, ranging from a low occurrence between 0 and 9.9 per 100,000 standard populations in Western countries such as North America and Europe. On the other hand, it has an extremely high frequency exceeding 500 per 100,000 Inhabitants per year as seen in South Africa [3]. The distribution of tuberculosis incidence in the world is very unequal. The underdeveloped countries pay the price with 95% of the cases globally. The countriesof theSub-Saharan Africa has overflows of about 85% tuberculosis cases diagnosed with the highest incidence of 250 per 100,000 populations. In Southeast Asia, the highest number of cases is in India and China, which account for 40% of global cases. The Africa region has the most deaths, due to the frequency of coinfection with HIV. [4]

DYE (1999) estimated that in the next few years nearly half of the cases of pulmonary tuberculosis will be positive microscopy cases, which will then be responsible for the transmission of the bacillus in the community and will thus create new infected subjects and new patients. The number of deaths attributable to tuberculosis, meanwhile, will decrease slowly as a result of improved health measures that will help keep patients alive for a short or long period of time. An estimated 37 million lives were saved between 2000 and 2013 through effective treatment and diagnosis [5,7]

1.2.Tuberculosis Crisis in the DRC

Global progress depends on measures that will be applied in countries suffering from the heavy burden of tuberculosis for the prevention and cure of this disease [8].Because currently more than 30% of the African population are infected with Mycobacterium tuberculosis, which constitutes one-third of TB disease cases reported by the WHO, the Democratic Republic of Congo (DRC) is among the 30 countries with a high TB burden in the world and one of the four most affected by drug-resistant tuberculosis in the African region of the World Health Organization (WHO) [10].

It has been found that currently in the DRC 1948 TB care structures refer to Health Centers for Diagnosis and Treatment of TB. These are endowed with quality microscopes, qualified anti-TB drugs and trained staff who are occasionally supervised. All 517 health zones are covered under fee-charging structures, and the Program planned to reach 2065 care facilities during 2017. Although the implementation of all these strategies on the ground, the general picture of the epidemiological situation of tuberculosis results demonstrates a persistently high burden of disease, combined with slow progress in achieving targets and substantially reducing persistent deficiencies. [14] In 2009, the DRC had a high prevalence of tuberculosis with an incidence of 372 per 100,000 inhabitants, nearly 50,000 deaths were attributed to tuberculosis, and in that same year 20% of tuberculosis patients were found to be infected with HIV [15]. The terms of reference for the preventive dialogue on the association of tuberculosis and HIV / AIDS, noted that DR Congo is on the list of countries with the highest number of doubly infected patients. The WHO estimates in 2012 were 210,000 new people affected by the disease, including 16,000

infected with HIV / AIDS. The DRC ranks 8th in countries with the highest burden of infection TB / HIV. Despite the strategies developed to combat these two pandemics by the National AIDS Program (PNLS) and the National Tuberculosis Program (NTP) [10], at the end of 2015, the country recorded 120,508 tuberculosis patients including 515 cases of drug-resistant tuberculosis. Among allcases, 14,061 people were suffering from HIV infection, including 12,681 children aged 0-14 years [16]. A tuberculosis study conducted in the Lubumbashi health zone in Katanga province reveals that the male sex was more affected in 58.75% than the female 41.25%, with a sex ratio of 1.42%. The average age of the patient was 33 ± 15 years. The most affected age group is between 21 and 40 years, i.e. 54.79% of the total population. [14]

1.3.Objectives of the Research

Given the incidence of the disease, the objective of this study is to review the literatures on tuberculosis disease, identify empowered entities in the fight againsttuberculosis and management, to statistically analyze the epidemiological profile of pulmonary tuberculosis in relation to the measures implemented in the Congolese health system. Also, to review the incidence of tuberculosis over the years and investigate if tuberculosis cases recorded differs across gender and year categories in the country.

1.4.Significance of the Study

This study is of paramount importance as a scientific compass, because it allows us to have a global perspective on the epidemiological evolution of pulmonary tuberculosis and to evaluate the scheme aimed at fighting against tuberculosis. Although the treatment and management of this disease is free, it is very unfortunate that TB continues to be one of the causes of mortality, especially in developing countries and most importantly in the Democratic Republic of the Congo. Hence, the study will provide us the insight into the incidences of tuberculosis in the country as well as help health management bodies to review and implement well informed process to favorably support the eradication of this endemic disease.

1.5. Thesis Description

This research is subdivided into five preceding chapters. The first chapter is devoted to the introductory background of the study. The second chapter addresses the review of the literature on pulmonary tuberculosis. The third chapter gives information on the research methodology adopted in the study. The fourth chapter consists of the results analysis and the interpretations while the fifth and last chapter provided the conclusion and summary of the research findings with necessary recommendations for future research.

1.6.Study Limitations

In order to carry out the research, the study only focused on the occurrence of pulmonary TB between years 2008 through the year 2016. It also only focuses on the records of the authorized Bandundu Provincial Health Inspection, DRC.

CHAPTER TWO

LITERATURE REVIEW

2.1. Definition of Concept

Pulmonary tuberculosis is defined as "an infectious disease whose pathogen is Mycobacterium tuberculosis.". The disease is notifiable and contamination is almost exclusively by air in contact with infected subjects. To be infectious, the bacilli must penetrate deep into the alveoli of the lungs, but the contagiousness of the disease is relatively weak and depends on the immune defenses of the subjects. The subjects at higher risk of infection are young children, elderly people with disabilities, people living in precarious socio-economic conditions, under-medicalized or whose immunity is deficient. [17]

The causative agent of TB is a microbe belonging to the family of mycobacteria, more specifically, to the "Mycobacterium tuberculosis complex" identified in 1882 by Robert Koch, and has long been the name "Koch's bacillus". After staining, it is visible under a microscope in the form of a red stick. This particular form earned him the name of "bacillus". Mycobacterium hominies (or tuberculosis): also called Koch's bacillus or BK Mycobacterium bevies: responsible for the tuberculosis of cattle; it is rarely found in humans. [18]. According to Active Study Dictionary (2010, p961) tuberculosis is a "serious infectious disease affecting the lungs". [19]

The definition of Eureka Experts had a slight different version of the previous definitions. They consider pulmonary tuberculosis as "a well-known and easily

contagious lung disease". This disease is on the same list of conditions as pneumonia, pulmonary embolism or cystic fibrosis. The Eureka experts are more interested in the organs that the disease develops moreover. Although the definition of Eureka experts is slightly different from the one found in themedical dictionary and G. Bonaud, there are still some points of similarity on the pathogenicity of pulmonary tuberculosis and other forms of tuberculosis. Pulmonary tuberculosis is an infectious bacterial disease and a contagious disease that primarily attacks the lungs. Indeed, there are also other forms such as extra-pulmonary tuberculosis, which can be renal, ganglionic, and cerebral or bone. [20]

Epidemiology: There are several definitions of epidemiology. According to the Larousse encyclopedia epidemiology is a "Science that studies, among populations (human, animal, even plant), the frequency and distribution of health problems in time and space, as well as the role factors that determine them "[23]. The different branches of epidemiology are characterized by the nature of the questions to be answered, as well as by the methods used for this purpose. Epidemiology was designed to answer the question, "Who is what, when, where and why? [21]".

On the other hand, Future-science defines epidemiology as a "scientific discipline that studies the frequency of diseases (incidence), their distribution in society, risk factors and deaths related to this disease". This information is essential for preventive medicine. [24]. The recognition of epidemiology as a field of study is relatively recent, since the first significant study dates back to 1854 but is one of the pillars of public health and medicine throughout history. [25]

With regard to the conceptual understanding of epidemiology, almost all of the authors listed have a crucial point of convergence on the definition and complement each other.

Prevalence: The Larousse dictionary defines prevalence as "ratio of the number ofallcases of a morbid disorder to the total population size, without distinction between new and old cases, at a given time or during a given period" [23]. Rancheria Health Medicine (2018) defined prevalence as a medical statistical measurement tool. It provides information on the number of people affected by a disease or any other event such as an accident, suicides, within a population at a given time. Prevalence accounts for both new cases and those diagnosed earlier at a specific time. It is mostly expressed in a number of cases per 100,000 inhabitants. [26]

In epidemiology, prevalence refers to the state of health of a population at a given time. The prevalence of a particular disease represents the number of people affected by the disease at a given time. It is usually expressed as a percentage.

There are several types of prevalence that depend on the period for which the measurement is calculated:

-) Instantaneous prevalence: when measured at a specific time;
- Prevalence over a given time: when measured over a period (month, year, etc.).
 It should not be confused with the incidence over the same period that only considers new cases (whereas prevalence also takes into account existing cases);

) Lifetime prevalence: when measuring the proportion of people with a particular pathology during their lifetime. [27]

Incidence: Marion Albouy-Ilaty (2009) considers the incidence as "Number of new cases during a given period relative to the population exposed to the risk of the disease during the same period". [28]. Vulgaris Medical (2018) considered the incidence as "the number of cases of diseases that immerse, the number of people who became sick during a given period in a given population. In other words, it is the number of new annual cases of the disease." [29]

The incidence of a disease is a statistical assessment of the risk for a person or a category of people to develop this disease. Incidence is one of the branches of epidemiology. It is based on statistical studies. [30]

Statistical analysis: Statistical analysis is a component of data analysis. In the context of business intelligence, statistical analysis involves the collection and review of all data samples from a dataset. In the field of statistics, a sample is a representative selection of a population. [31]. Statistical analysis helps to highlight the relationships that may exist between the different data and to draw statistical information that allows to describe more succinctly the main information contained in these data. Other techniques make it possible to group the data in such a way as to make clear what makes them homogeneous. It also helps process a large number of data and to identify the most interesting patterns of the data. [32]

Evaluation: Evaluation is the periodic assessment of a project in terms of efficiency, effectiveness, impact, validity and relevance in the context of the objectives

set. It is generally done as an independent analysis of the context, objectives, results, activities and means to derive that can guide decision-making. [33]

Ngo Bebe (2003) defined evaluation as a systematic process of making judgments about elements or events in reference and using them to improve ongoing activities and promote more effective planning [34].

2.2.Congolese health system

The WHO (2000 report) [35] defines the health system as a set of organizations, institutions and resources that aim to achieve health actions. A health action is defined as any effort at the level of personal health care, public health services or through intersectoral initiatives, whose primary purpose is to increase health.

In the DR Congo, the health system comprises 3 levels: Central, Intermediate andOperational (the health zone). It involves several actors, the main being:

-) The inhabitants, better, the beneficiary population,
-) The public or state sector (Ministry of Health structures),
-) The private sector known as lucrative or liberal,
-) The associative and / or denominational or private sector without goal Lucrative
- Multilateral and bilateral organizations [35]

2.3. Generality on pulmonary tuberculosis

Despite the existence of a vaccine and antibiotics, tuberculosis remains one of the leading causes of global morbidity and mortality compared with other infectious diseases such as malaria or all other tropical diseases combined. In fact, WHO estimates that one-third of the world's population is infected, nearly two billion people, most of whom live in developing countries.

Despite the existence of antibiotic treatments against this disease, there has been a resurgence of cases of tuberculosis for fifteen years. In response to this situation, WHO has declared TB a public health priority on a global scale. The resurgence of tuberculosis is closely linked to the emergence of multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains. In addition, the new momentum gained in recent years by this disease could be explained by the movement of people, by the impoverishment of certain populations, by the spread of HIV and by non-rigorous monitoring of treatment. [19, 58]

2.4. History and epidemiology

Shortly after the discovery of the infectious and contagious nature of tuberculosis by J. A. Villemin, R. Koch identified the bacillus responsible for the disease (1882): M. tuberculosis.The initial work of A. Calmette and C. Guérin (1908) culminated in 1921 in the development of the BacilleCalmette-Guérin (BCG) vaccine, the only vaccine used today.

The massive immunization with BCG from 1921, the establishment of a public health policy aimed at improving the care provided to patients, the improvement of living conditions and the discovery of specific antimycobacterial antibiotics after the second war worldwide, have led to a 5 to 6% decline in industrialized countries in the eradication of tuberculosis by the end of the 20th century.

In 1944, S. Waksman discovered the first antibiotic active against tuberculosis: streptomycin. During the next 20 years (1944-1965) many anti-tuberculosis drugs came into being. Five of these antibiotics, isoniazid, ethambutol, rifampicin, pyrazinamide, and streptomycin are said to be major or first-line. [58]

In developing countries, where socio-economic conditions have deteriorated steadily, the annual rate of decline of the disease remains below 1%. To date, despite the existence of a vaccine (BCG) and an effective multidrug therapy set up in the 1970s, tuberculosis remains the leading cause of death due to a single infectious agent. [19]

2.5. Evolution of the incidence

In the late 1970, [43] with the introduction of a treatment based on a Compulsory multidrug therapy for a period of six months, eradication was envisaged for the years 2005-2010 in developed countries. [60] However, tuberculosis is now on the rise. [64] In fact, over the last decade, the number of tuberculosis patients worldwide has increased by 20% and WHO estimates that the number of deaths attributed to tuberculosis will increase to 5 million in 2050. [65] In 2008, the estimated incidence of TB per capita was stable or decreasing in the six WHO regions. However,

the slow rate decline is offset by population growth. As a result, the number of new cases occurring each year continues to increase globally in the WHO regions of Africa, the Eastern Mediterranean and South-East Asia. However, the number of cases reported from the African region is increasing more slowly each year, probably because the HIV epidemic in African countries is also slowing down. In Eastern Europe (mainly the countries of the former Soviet Union), the per capita incidence increased during the 1990s to peak around 2001 and has since declined. [59]

Incidence of any		Prevalence		TB deaths		
	for	m				
WHO region	number	For 100000	number	For 100000	number	For
	(thousands)	inhabitants	(thousands)	inhabitants	(thousands)	100000
	(% global					inhabitants
	total)					
Africa	2828(30)	351	3809	473	385	
America	282(3)	31	221	24	29	03
South Asia	3213(34)	183	3805	216	477	27
Europe.	425(5)	48	322	36	55	06
Eastern	675(7)	115	929	159	115	20
Mediterranean	L					
Western	1946(21)	109	2007	112	261	15
Pacific						
Whole world	9369(100)	139	11093	164	1322	20

Table 1. Estimated incidence of tuberculosis in the six WHO regions 2008.

Source: LAMRIYahiasalaheddine 2014

2.5.1. Transmission

Tuberculosis is an infectious, chronic and contagious disease. Its transmission is through direct human, and is carried out mainly by air, and more rarely by digestive or integumentary trance. The persistence of patients in the population constitutes an infectious reservoir, representing a risk of expansion of the disease. It is the source of screening and prevention strategies and recommendations aimed at stemming the spread of tuberculosis. [36]

It is important to mention that only forms of tuberculosis with open lesions on the outside are contagious; this is essentially the case of pulmonary tuberculosis; especially when bacilli are found in the specimens by direct microscopic examination. [37]. Mycobacterium tuberculosis is transmitted by aerosol emission of micro droplets of mucus in the air, during sputum of a contagious patient, (positive on direct microscopic examination).

A sneeze can release 20 to 40,000 Koch bacilli. The probability of a bacilliform patient contaminating their surroundings is estimated at between 25 and 80%. A person with active pulmonary TB can infect 10 to 15 people a year or more, if no treatment is established. [37]. these vector particles, 0.5 to 5 μ m in diameter, are called "Flügge droplets". They contain within them 1 to 10 tubercle bacilli; enough for an immunocompetent individual, without prior contact with the bacteria, to be contaminated. These droplets will dry out quickly to be reduced to their simplest device, a condensation nucleus, "Wells droplet-nucleus". In this form, they are able to stay for several hours or even more than 6 hours, suspended in the air and will not be eliminated by conventional ventilation.

They will be inhaled by people nearby. The smallest of them $(0, 5 \text{ to } 3\mu\text{m})$ will not be evacuated by the mucociliary carpet of the bronchial tree, which will allow them to cross the respiratory system and reach the pulmonary alveoli, preferentially in the posterior parts of the apical lobes of the lungs. [38]. At this level, the tubercle bacilli will be phagocytosis by innate immunity cells (macrophages, dendritic cells, neutrophils), leading to the formation of a primary infectious focus, called inoculation chance.

This first contact of the organism with Bacillus of Koch represents the primary infection.

The risk of transmission depends on a number of factors:

-) The number of particles emitted (sputum rich in bacilli),
-) The duration of exposure (long and repeated),
-) Ventilation (confined atmosphere),
-) The intrinsic virulence of the bacteria,
-) The immune status of the recipient, subject (extreme age of life <5 years,> 75 years, immunodeficiency, HIV, chronic diseases, diabetes, immunosuppressive treatments).

2.5.2. Bacillary pathogenicity

After penetration of the bacillus in the body, 4 evolutions are possible:

-) The progression from the start to a TB disease,
-) Delayed progression to TB disease,
-) The maintenance of a latent infection, the complete elimination of the bacillus,(70% of the immunocompetent individuals) [39]

After being exposed to TB, a number of people will become infected. The probability of an immunocompetent, unvaccinated individual being infected with the bacillus is estimated at about 30%. [40].Following this primary infection, only 10% of infected individuals will develop TB disease in their lifetime, most often in the first years after this infection. We therefore distinguish the infection from the disease. [37].In 90% of cases, the infection is controlled within 3 to 9 weeks, by the immune response of the infected subject [41]

The tubercle bacilli are contained in the phagocytic cells, within multicellular anatomo-pathognomic structures: the granulomas. The mycobacteria survive there, trapped in the quiescent state, their metabolism and their replicative mode being slowed down; they are said to be "dormant" [39]. This balance between the immune system of the host and the bacilli is characteristic of a latency phase, which can last for months or even years. This is latent tuberculosis infection (LTBI).

The WHO estimates that about 1/3 of the world's population has infected people. In 10% of cases, the infection is not controlled by the immune response put in place; it is outdated or inappropriate. Individuals infected with Mycobacterium

tuberculosis will develop the disease during their lifetime, after a latency phase of varying length; the risk decreases with time. The alteration of the immune system causes a loss of control of the host-bacteria equilibrium, they escape the immune defense mechanisms and resume their multiplication, causing the passage of an ITL to an active tuberculosis infection, known as tuberculosis-disease. We talk about endogenous reactivation, by decreasing immunity. Exogenous reactivation of the infection may be possible, although very rare, induced by another strain of mycobacteria. [42]

2.5.3.Localizations of tuberculosis

a) Pulmonary localization [44] [41]

In the majority of cases, 75%, these lesions preferentially affect the lungs, because of the aerobic nature of Mycobacterium tuberculosis, and its mode of propagation, causing pulmonary tuberculosis. These pulmonary localizations are the most dangerous epidemiologically because they are responsible for the transmission of bacilli; the affected individual will be contagious to those around him. The clinical symptoms of tuberculosis gradually settle and persist for more than 3 weeks. They are not very suggestive and can be classified as systemic or specific organs affected. [45]

General non-specific general symptoms:

-) Alteration of the general state: Asthenia, anorexia, malaise, loss of weight (loss of weight can be = 10kg in severe cases),
-) fever with evening peaks,
-) Night sweats.

Specific respiratory signs:

-) cough more or less productive and frequent,
-) chest pain,
-) dyspnea,
-) in 10% of cases, hemoptysis;

In 1 of 3 cases, the diagnosis of pulmonary tuberculosis is made during hospitalization for other reasons, because of the weakness of the clinical picture.

The chest X-ray remains the essential examination. It allows to highlight typical lesions, sitting preferentially in the posterior segments of the upper lobes or in the apical segments of the posterior lobes (the most oxygenated zones of the lung) and this even in the absence of clinical signs:

-) Nodules, caverns containing a large amount of Koch bacilli.
-) Infiltrates, and effusions;

Bronchogenic or haematogenous dissemination is possible in case of necrosis of these exudative lesions and excavation. Satellite, hilar, or mediastinal lymphadenopathies may be associated.



Figure 1.0:X-ray of the thorax of a patient with advanced pulmonary tuberculosis

b) Extra-pulmonary localizations

They are generally poor in bacillus and are responsible for disabling or extremely serious forms. Most often, they are found in the elderly immunocompromised subject; and account for about 25% of reported tuberculosis [44]. The most frequent locations are ganglionic, osteoarticular (Pott's disease), pleuropericardic, meningeal, urogenital. The symptoms will be various and varied depending on the site or sites, on a system background poor specific (AEG, fever, sweat).

The anatomical substratum of these lesions is the same: tuberculous granuloma and especially its classification [47].



Figure 1.1: Potts diseases



Figure 1.2: Ganglionic tuberculosis

2.5.4.Evolution

Because of the slow multiplication of bacilli (> 20h), the progression of tuberculosis and the appearance of symptoms are slow. However, the hematogenous and lymphatic spread of the bacilli causes multifocal and disseminated lesions. Vital complications can occur in the absence of treatment.

This is the case of tuberculous meningitis and miliaire tuberculosis, severe forms of tuberculosis, with a high mortality rate, most often affecting young children (<2 years) or adolescents (12 to 15 years), as well as the elderly (> 75 years) and the immunocompromised.

The spontaneous evolution of common pulmonary tuberculosis, in the absence of any treatment, has 3 possibilities in the 2 years following the beginning of the disease:

- o 50% of patients die,
- o 25% recover with functional sequel,
- o 25% develop a chronic form [37].

Systemic pneumonic forms disseminated may evolve, with expansion of exudative lesions, liquefaction of parenchymal tissues, to their necrosis, progressing to a complete destruction of the pulmonary lobe, giving way to cavities.

The destruction is followed by cicatricle fibrosis. This can lead to acute respiratory distress syndrome, or even chronic respiratory failure. Regression of parenchymal foci is slow; from 6 months to 2 years for a complete resolution; even more so for lymphadenopathy.

Under treatment, the course of the disease is favorable, contagiousness decreases rapidly, in 2 to 3 weeks, and resolution of radiological abnormalities slower is shortened to 2 or 3 months. It can, however, persist severe functional sequelae such as scars and calcified nodules, fibrous sequelae, cicatricle atelectasis, bronchial stenosis, localized or diffuse bronchiectasis, para-cicatricle emphysema ..., etc.with chronic respiratory insufficiency. Surgery may be required. [48]

2.5.5.Diagnosis of tuberculosis

Tuberculosis control is based on early detection and diagnosis of cases, especially contagious cases, management of patients (with appropriate and effective treatment) and case-based investigations (looking for secondary cases and source of cases). [49]

The WHO's strategy focuses on the most active, early detection and targeting of populations at risk of developing the disease, as well as the identification of treatment-resistant cases, to control and eradicate the disease, and to limit the transmission and emergence of resistant tuberculosis. [50] In recent decades, great advances have been made in this direction, thanks to the advent of molecular biology techniques (genetic amplification, automated sequencing), allowing the clinician to make a faster diagnosis and more accurate and to propose a tailored treatment to patients.

a.Examination of the patient

Faced with a clinical picture that is not very revealing, the questioning of the patient remains the unavoidable step preceding the diagnosis. He must inquire about the socio-economic conditions of the patient, the underlying ground, current treatments that may interfere.

The interrogation must allow the practitioner to inquire:

• On the profile of the patient, namely his age group, sex, profession, ethnicity, country of origin.
- On the mode and the living conditions of the latter, the context in which it evolves and the communities attended: community, migrants, nomadism, prison environment.
- On the socio-psychological profile: marginality, alcoholism, addiction, drug use IV, smoking, psychological problems followed or not.
- On the existence of pathologies or associated treatments: HIV, MAY, immunosuppressive treatments, corticotherapy, anti-TNFa, diabetes, cancers.
- On the history of the disease, epidemiological context (notion of contagion, travel in endemic area in the two previous years), ant tuberculosis treatment history, existence of previous vaccination, presentation of a clinical picture and frequency of respiratory symptoms or generals.

b. Direct diagnosis: diagnosis of tuberculosis disease

The classical bacteriological diagnosis of TB disease is based on microscopic examination, culture of Mycobacterium tuberculosis, identification of molecular or biochemical methods of the bacilli obtained, and susceptibility tests for antituberculosis drugs. Since the clinical, radiological and histological arguments are not specific for tuberculosis, the detection of the bacillus remains essential for establishing a definitive diagnosis. For diagnostic, clinical and epidemiological purposes, the isolation of the strain is always followed by an identification of the latter and by a systematic study of the susceptibility to the major anti-tuberculous drugs for the mycobacteria of the tuberculosis complex.

c. Sputum collection procedure

Under the conditions of the National Tuberculosis Program in the DRC, 3 sputum samples are requested from the patient and provided in the following way:

- The first sputum during the first interview with the health staff, the spitting is collected on the spot, outside, on the supervision of a member of the trained staff for this (contact);
- Second sputum: the patient receives a small pot, a spittoon to give a spit the next morning as soon as he wakes up (morning);
- Third spitting during the second interview, the day after the first, the patient brings his spittoon and a new spit is collected on site (contact).

In summary: "contact-morning-contact: CMC in two days for anyone presenting in a medical training with respiratory symptoms.

These samples are examined at the nearest laboratory. Thus, the result of the first sample is known on the first day and the other two on the second day. The three samples are given in 24 hours. Among TPM + patients diagnosed by a series of 3 Ziehl exams, 80% are identified thanks to the 1st examination, 15% by the 2nd and 5% by the 3rd examination. The patient has positive microscopy tuberculosis if at least two out of three samples are positive. If the 3 samples are negative, the patient is placed on nonspecific treatment for 10 days and the decision tree continues according to the strategies of the National Program [51].



Figure 1.4: Decision tree in PATI IV without radiography[52].

2.5.6 Prevention and Treatment

The prevention, treatment and management oftuberculosis is based on the detection and early diagnosis of cases, particularly contagious therefore the pulmonary form. The care of infected patients, including appropriate treatment and completed. Investigations, secondary case finding and BCG vaccination are among the most important elements in achieving the disease control objectives [49]

The prevention of transmission can be summarized in two points:

- Reduce the risk of potential contact with Koch's bacillus by means of targeting the contagious patient and his entourage,
-) Reduce the risk of developing TB infection by stimulating the specific immune response through BCG vaccination. [53]

In this case, prevention addresses each stage of the life cycle of the pathogen, namely the reservoir, the transmission and the vector. Thus, the prevention of tuberculosis, a disease with a human-to-human transmission, amounts to reducing the human reservoir of M. tuberculosis and preventing its spread. [53]

a.Classification of the entourage of the patient

The types of contact with the environment are to be evaluated, to identify possible secondary cases. Depending on the proximity and the time spent with the source case, three categories of contacts are defined:

) Close contact: people living under the same roof, or sharing the same room for many hours a day (family, students, colleagues ...),

- Regular contact: people who regularly share the same closed place (social or sports activities carried out with the source case),
-) Occasional contact: people who occasionally share the same closed place (attending the same establishments ...).

The close entourage must have a chest X-ray, an IDR and a medical consultation at T0 and T3 months. Follow-up for 18 months is necessary, consisting of a medical consultation and a chest X-ray. For regular and occasional contact, screening will be done by an IDR at T0 and T3 months. [54]In the case of a positive RDI, prophylactic treatment may be established depending on the immune and vaccine status of the case.

b.Preventive contact measures

Patient

The main measure of prevention of transmission is the early isolation with or without hospitalization of the contagious patient, just after the suspected diagnosis and this until sputum negation, following a suitable treatment. In the past, sanatoriums were intended for the isolation and treatment of tuberculosis patients. Contagiousness depends on several factors: positive EM, location of lesions that can be Pulmonary and / or pharyngeal, intensity and frequency of cough, duration of symptoms, initiation of treatment (rapidly reducing the number of bacilli and the volume of secretions), prescription of invasive examinations (increasing the risk spread by cough: fibroscopy, aspiration ...). The maximum infectious phase persists for 1 to 3 weeks after the start of treatment. The contagious patient must be hospitalized in anisolated and locked individual room, in a unit dedicated to tuberculosis and reported as such. The room

must be well ventilated, ventilated to ensure a regular renewal of air (minimum 6 air changes / hour). Currently flow chambers or negative pressure represent effective means to prevent the spread of the germ. Similarly, any contaminated material must be disinfected.

Another element of preventive strategy is that the patient must be made aware of the risk of contamination that he represents as well as his surroundings. He must limit his contacts with the outside and reduce his movements.Patients should remain isolated until they have been treated for at least 2 to 3 weeks with the usual antituberculosis agents, the time required to achieve clinical improvement, including a reduction in the frequency of coughing, and 3 smear tests. Sputum collected at intervals of 8 to 24 hours were negative. As part of the Standard Precautions, the TB patient must wear a mask in a care environment. [4]

Professionals

Increased vigilance should be given to services designed to accommodate patients at risk of tuberculosis, especially those in whichmulti-resistance may emerge. Limiting staff exposure is a priority. The reinstatement in France since 1996 of simple and effective measures to prevent the risk of transmission of pulmonary tuberculosis has made it possible to control this risk. [54]

Occupational health surveillance has been established, with regular practice of IDR and chest X-ray. [56]. The risk of contact of the nursing staff with the BK is evaluated according to the number of positive EM cases received. Thus 3 risk areas could be defined, in order to determine the frequency and the monitoring methods.

2.5.7 Repressive measures

BCG vaccination is mandatory for children under 6 years of age who are accommodated in a community (including a maternal assistant). It is recommended from the first month of life for children living in a high-risk tuberculosis environment. It is compulsory in the absence of previous immunization for children over 6 years of age, adolescents and young adults attending primary and secondary education institutions as well as some communities and for exposed adults. Vaccination is done intradermally in an age-appropriate dosage. This vaccination only applies to people with tuberculin-negative intradermal reaction.

Extensive dermatoses in evolution are a temporary medical contraindication to BCG vaccination and congenital or acquired immunodeficiency due to HIV a definitive contraindication.

The ID sensitivity test must be performed:

-) to verify the absence of tuberculosis before a primary vaccination, except infants under three months of age who are vaccinated without prior testing;
-) during investigations around a case of tuberculosis;
-) As an aid to the diagnosis of tuberculosis;
- As a reference test in the context of occupational surveillance. [57]

a.Vaccine policies

Vaccine policies differs from country to country because of differences of opinion as to its place as a tool for fighting tuberculosis.

Some have never opted for routine vaccination of their population (USA, Netherlands), others have adopted repeated vaccination (Poland). In England, vaccination is carried out during adolescence. Germany has stopped vaccination for all children, while Sweden is reconsidering this decision and advocating vaccination of children at risk. In the European Union, it was only Greece and France to keep this widespread vaccination of children under 6 years old.

In 1995, WHO no longer recommends re-vaccination, as no scientific evidence demonstrates the usefulness of this practice and the epidemiological context no longer justifies it. [48]

b.Contraindications and Precautions [61]

The BCG SSI® vaccine should not be given in case of hypersensitivity to any of its components.

Before any primary vaccination, (except for newborns until they are 3 months), an IDR is performed in order to exclude any prior contact with the tubercle bacillus. The BCG vaccine is a VVA, it is necessary to ensure the immunocompetence of the subject. Immunosuppression is a contraindication to vaccination. Thus BCG is contraindicated for all people receiving systemic corticosteroid therapy or immunosuppressive therapy, people with malignancies, primary or secondary immunodeficiency's, and HIV-infected patients.

c.Undesirable effects

Some complications may occur as a result of this vaccine. Their frequency varies according to the strain and dose administered, the immune status, and the age of

the patient. Adverse effects should be reported to the regional pharmacovigilance center.Intradermal injection is difficult and must be well controlled. Indeed, a technical error (too deep injection, overdose) increases the risk of local adverse effects. A local reaction and / or satellite adenopathy of less than 1 cm are expected vaccine reactions after intradermal injection of BCG.

Most of the complications are local regional in the form of adenitis or ulceration with discharge greater than 1 cm in size, sometimes accompanied by fever and evolving in rare cases to caseation and fistulation. These local complications are well known (1 to 2%), they can last for several months, but tend to heal spontaneously.

An update on the management of local abscesses and adenopathy's following BCG vaccination was developed at the end of 2007 and validated by the AMM commission. In case of abscess at the site of injection or lymphadenopathy, parents should be reminded of the principles of their care which are based above all on educational and hygienic measures. Indeed, abscesses and lymphadenopathies heal without anti-infectious treatment or surgery in the vast majority of cases.

2.5.8 Anti-Tuberculosis treatment

a.Preventive treatment

According to **G.Gonnaud** (2007), Preventative treatment avoids in 70 to 90% of cases the transition from the stage of latent tuberculosis infection to that of the disease. The initiation of a preventive treatment is not systematic in the infected subjects, whose intradermal reaction is positive It is preferentially prescribed in those

who have a higher risk of developing the disease; for example, subjects who have recently been infected, and subjects with "risk factors" who strongly reduce immunity.

Taking a single drug is justified because the small number of microbes involved in latent infections, resistance is not likely to develop. Most often, Rimifon is prescribed daily for 6 months. In special cases, 2 drugs are indicated: Rifadine and Rimifon for 3 months. [18]. An anti-tuberculosis treatment aims to cure patients with disease and to avoid relapses favoring the emergence of resistant strains, but also must allow to destroy the source of bacillary contamination represented by microscopically positive patients, with the ultimate aim of stemming the progression of tuberculosis and to eradicate it.

It is important to note that for at least 35 years, or even 45 years, the treatment of tuberculosis has changed little or nothing, apart from that of multi-resistance. This treatment uses a combination of four first-line anti-TB drugs, isoniazid, rifampicin, pyrazinamide and ethambutol [4]

	Daily Administration		Intermittent Administration			
Drug			3x/week			
	Children	Adult	Maximum	Children	Adult	Maximum
			Dose mg /			Dose mg /
			day			day
Isoniazid	5-10(15)	5	300	10	10(15)	900
Rifampicin	10-20	10	600	10	10	600
Pyrazinamide	25-40	25	2000	35-50	35	2000
Ethambutol	15(25)	15(25)	1600	30	30	2000

 Table 2. First-line anti-tuberculosis drugs

Source [46]

In general, quadritherapy is prescribed for 2 months, followed by dual therapy with rifampicin and isoniazid. It is important to realize that in this combination, antibiotics play a different role, which allows us to understand the underlying reason for this combination of antibiotics. Isoniazid (iNH) is a potent bactericide that reduces bacterial burden by more than 92% in two days. It is followed by rifampicin. Pyrazinamide has very low bactericidal activity at the start of treatment. The other phenomenon to be understood is the activity of these different anti-tuberculous drugs on the bacilli, either in rapid multiplication or in slow multiplication, in acid or neutral medium.

Isoniazid acts on the bacilli extremely fast multiplication while it acts very weakly on the slow-growing bacilli, it has some activity on the bacilli in an acidic pH whereas it has practically no activity in neutral pH, especially caseous foci. Rifampicin, on the other hand, has activity at the three stages of propagation described above. Pyrazinamide mainly has activity on slow-growing bacilli, at acidic pH, and therefore macrophages, and practically no activity on slow-multiplying bacilli in a neutral pH, especially caseous foci.

Ethambutol, meanwhile, acts weakly on the different growth phases, its role is mainly to prevent the selection of isoniazid-resistant bacilli. In summary the iNH and the major early bactericidal, 95% of the inoculum is swept in two days, (bactericidal effect of 18 mg / day with an increasing effect up to 300 mg / day). Pyrazinamide has active bactericidal activity in acidic medium, it has reduced the risk of relapse after six months of treatment, from 22 to 8%. Rifampicin is bactericidal, active on rapidly metabolizing bacteria and slowed down. It has reduced the risk of relapse after six

months from 6 to 3%. Ethambutol is bacteriostatic, the interest is especially if there are resistant iNH strains [63].

Depriving of iNH in a TB treatment will result in a less rapid conversion of sputum; depriving oneself of rifampicin will prolong the duration of treatment until 18 months; depriving yourself of pyrazinamide may prolong the duration of treatment at 9 months [63]. The standard regimen consists of a two-month, initial phase quadritherapy combining iNH, rifampicin, pyrazinamide and ethambutol. Then a dual therapy in the continuation phase lasting 4 months, associating iNH and rifampicin. There are intermittent regimens with an initial two-month phase and daily quadripharmacy (iNH, rifampicin, pyrazinamide and ethambutol) and a continuation phase with weekly intakes of iNH and rifampicin [47].

It is important to note that the intermittent regimen is only in the maintenance phase and should not be applied to immunocompromised patients, particularly HIV patients. The treatment of extra-pulmonary tuberculosis is identical to the treatment of pulmonary tuberculosis, in any case, in terms of the associated scheme. In additive drugs, we have pyridoxine which is vitamin B6 at the dose of 20 mg/day, 250 mg /week, it prevents peripheral neuropathy caused by iNH. In practice, it is systematically administered, but it may not be done. Its use is especially recommended for at-risk patients such as pregnant or breastfeeding women, alcoholics, the elderly, undernourished people, diabetics, patients with renal failure, HIV-infected persons and breast-fed children.

This vitamin B6 should be given during pregnancy at a slightly higher dose of 25 mg/day. In pregnant women, do not forget to administer vitamin K during the last

two weeks of pregnancy, 10 mg/day, and also to the newborn 1 mg/day, because there is a risk of bleeding. The breastfeeding woman with tuberculosis should receive full treatment with conventional quadric-chemotherapy. Treatment must be rapid to prevent transmission of TB to the child. The mother and her baby are often together and the baby must continue, especially in developing countries, to be breastfed.

Active tuberculosis in children should be excluded and isoniazid preventive therapy should be given for 6 months and later BCG vaccination [47]. Corticosteroids are indicated in meningitis and pericarditis. In children, they can be used in miliary tuberculosis or mediastinal ganglionic forms resulting in compression with a reduction in bronchial diameter of more than 50%. Corticosteroids have also been used in immune reconstitution syndromes in patients receiving antiretroviral therapy. When cortisone is used, it should be remembered that it has an interaction with rifampicin and it is advisable to increase the dose to 1.5 mg/kg/day [47].

a) Duration of treatment

The duration of treatment is 6 months for pulmonary tuberculosis as well as for extra-pulmonary tuberculosis, except in neuro-meningeal tuberculosis where it takes 9 to 12 months. For osteoarticular tuberculosis, there is a discussion between a conventional treatments of 6 months versus a treatment of 9 to 12 months.

b) Surveillance of TB treatment

The patient is required to be seen again twice during the first month and once a month until one-year post-diagnosis.

Hepatic tests Renal function, serum uric acid, complete blood test, CRP and HIV test and visual function should be performed at the start of treatment. Hepatic tests can be repeated at 15 days, in the first month and in the second month to monitor the possible toxicity of anti-TB drugs. A blood count check can be done in the second month. Chest X-ray is performed at admission in the second month and at the end of treatment. It can be checked in the 12th month if there are sequelae. The direct sputum examination will be done upon admission, at 15 days. This examination, at 15 days, allows especially three times to be able to leave the patient of quarantine when it is negative. It must also be done in the second month. In the case whereit is positive in the second month, it must be done again in the third month. If it always remains positive, it is necessary to discuss the failure of the treatment and to evoke the possibility of a resistance. If the patient has a positive direct examination at the 5th month, the patient must be considered to have a treatment failure, reevaluate and rediscuss an adaptation of treatment according to the resistance found [47]. The treatment of tuberculosis must be extremely regular. Health professional must be vigilant. Management of irregular catches or interruption of treatment will take into account the patient's situation.

2.6. Related Searches

Mr. MassingaLoembé and Mr. P. Grobusch(2014) in one report of the WHO explored a study on the Epidemiology of Tuberculosis in Gabon during the period 2003-2013. According to the authors, all age groups are affected with a prevalence of incidence at the age of 15 to 44. Sex ratio and 1.3 to 1.7 in men compared to women. Importantly, the same source reports that mortality rate is 10.3% with therapeutic

success approaching 53.2%. The incidence at the end of 2013 was 423 cases per 100,000 inhabitants. [55]

For S. Hamidi (2015), formerly a country with a high prevalence of tuberculosis, since the beginning of the 1980s Algeria has joined the group of countries with moderate prevalence thanks to the application of technical measures for tuberculosis control, its incidence in 2013 is 81 cases per 100,000 populations, a Retrospective Study was conducted during the 2010-2014 period at the Boughar MCTS. 612 new cases of tuberculosis were respectively assessed during the last 5 years from 2010 to 2014 with 114, 161, 143, 93, 101 cases per year. An incidence of Pulmonary Tuberculosis was 21.66 per 100,000 populations in 2010 and 16.56 per 100,000 in 2014, as were PET cases with a decrease in incidence of 80.9 per 100,000. In 2011, the population was 47.77 cases per 100 000 inhabitants in 2014. Pulmonary tuberculosis reaches the women. A cure rate of new cases estimated at 97% at the end of treatment [60]

F.H.Okemba-Okombi and al (2016) conducted a study on the epidemiological profile in Congo Brazzaville from 2010 to 2015, the aims of the study were to identify the evolution of the incidence of tuberculosis and describe its epidemiological profile in the Republic of Congo from 2010 to 2015. After a comprehensive descriptive study, during 6 years the results show a reasonable growth between 2010 and 2012, then a decrease in incidence between 2013 and 2015 that reached a stable around 381 to 382 cases per 100,000 inhabitants. The median age of cases reported in Congo is 35 years

with a peak in 25 to 34 years. The therapeutic success oscillates between 68 and 78%. [52]

D.R.S.P Quebec (2017) The Regional Direction of Public Health of Quebec has produced a descriptive analysis of the epidemiological surveillance data of tuberculosis, the data were collected in Quebec from 2012 to 2015. The objective of the study is to help the professionals who work in the public health field to better target their surveillance program and help treating physicians make the right medical decisions. 953 people were compiled for an average of 240 cases per year and an average annual incidence rate of 2.9 per 100,000. According to the authors the highest annual rate, 3.4 cases per 100,000 populations, was recorded in 2012. The incidence rate for Quebec has fallen almost constantly over the past 25 years, from 12.8 cases per 100,000 people in 1980 to 2.5 in 2009. Changes in incidence it then reversed: it increased in 2010, peaked in 2012, and then began to fall again in 2013 before reaching a new low of 2.5 cases per 100,000 people in 2014.

For the period 2012-2015, the average annual incidence rate is 5.6 per 100,000 people in Montreal and 2.1 per 100,000 in the rest of Quebec. Increased morbidity is observed in males in their twenties and increases from age 65. The average annual incidence rate for men is 3.4 per 100,000, while it is 2.5 for women.



Figure 2: Tuberculosis incidence rate: All of Quebec, excluding Montreal and Montreal, by year, 1980-2015

In general, the most affected age group is between 20 and 59 years old with 57.1% and 60 years with 26.8%. Are less important The average age of tuberculosis cases in Quebec differs according to the origin of the population; Average age among non-Aboriginal people and 55.3 years, among persons born outside Canada 44.5 years and among Inuit 20.7 years.

Age-specific incidence rates are very different for non-native-born Canadians and those born outside Canada. The average annual incidence increases gradually with age among the first, reaching 2.3 per 100,000 in the over 65 years. On the other hand, for persons born outside Canada, the incidence is highest in the 15-24 age group 22.2 per 100,000, decreases between 35 and 64, and then increases in the group of 65 years or older with 17.0 cases per 100,000 [67]

CHAPTER THREE

RESEARCH METHODOLOGY

3.1. Type of period and place of study

This survey is descriptive transversal with a longitudinal view of the phenomena, carried out with tuberculosis patients who have been screened and have followed anti-tuberculosis treatment, during the period from 2008 to 2016.

The investigation took place in the province of Bandundu which is one of 26 provinces of the Democratic Republic of Congo. The Bandundu Province is located entirely in the South-West part of the country. It thus extends between the 1st and the 8th degree of South latitude and the 16th to the 21st degree of East longitude. This area covers 295,658 km² of surface or 12.6% of the national territory and thus constituting the 4th Province of the Republic in relative order of magnitude.

It is bordered:

-) In the North by the Province of Ecuador.
-) In the South by the People's Republic of Angola with which it shares 1,200 km of the border.
-) In the East by the province of Kasaï-Occidental.
-) In the West by the Province of Bas-Congo and the Republic of Congo-Brazzaville with which it shares 345 km of the border.

Bandundu province has 24 health zones with a total of 88 tuberculosis screening and treatment (TBD) health centers and 432 treatment health centers (CSTs).

3.2. Study population:

Our study included all pulmonary TB patients throughout Bandundu province who were notified to the national TB program during the study period. The general population of the various health zones was taken into account for the impact assessment with a total of 40,619 tuberculosis patients.

3.3. Sampling

The sampling was exhaustive and random including tuberculosis patients of Congolese nationality, consulted and treated in health facilities in the province of Bandundu during the period mentioned.

Criteria for inclusion:

) Any pulmonary tuberculosis with positive and negative microscopy notified.

Criteria for non-inclusion:

- Extra-pulmonary tuberculosis notified during the study period
-) Tuberculosis patients from the surrounding provinces

The variables of the study included different names of the health zones, variable population of the year; here we will have the population per year of each structure, variable patient age of 0-4 years, 5-14 years and 15 years and over. We will have the number of patients presented by respective age group and by year according to tuberculosis with positive and negative microscopy. The total tuberculosis variable

per year, variable prevalence per year. It should be noted that the variables we mentioned above will be repetitive in the years that cover the period of the survey.

3.4.Research Method

Usually, when making a contrast and comparison between two populations, this is done by the independent t-test (Parametric test) or Wilcoxon signed rank test (Non-parametric test). However, when we have more than two groups of independent populations, the method used for this comparison is the Analysis of Variance (ANOVA). Suppose, there are three groups of patients subjected to three treatment methods, namely treatment A, treatment B, and treatment C. To test for the mean difference of these methods, the One –Way Anova method is adopted. Therefore, it can be stated that ANOVA is an extension of an Independent t-test statistic.

The ANOVA basically examines the null hypothesis that there is no mean difference among the groups while the alternative hypothesis assumes that at least one of the group's mean differs from the others [68]. The F-distribution statistics is used to test this hypothesis.

Ho: $\mu_1 = \mu_2 = \mu_3 = \dots = \mu_n$

Hi: $\mu_1 = \mu_2 = \mu_3 = \dots = \mu_n$

A basic ANOVA table is given below.

Source of Variation	SS	df	MS	F
Between Samples	SSB	k-1	MSB = SSB/K-1	F=MSB/MSW
Within Samples	SSW	n-k	MSW=SSW/n-k	
Total	SST=SSB+SSW	n-1		

There are basically two sources of variation in the One- Way ANOVA, namely **Between Group Variation (SSB)** which explains the variation attributable to the differences between the samples mean of each group and the grand (total) mean of all the observational units. And this variation is weighted by the respective sample size of each peculiar group. The**Within Sample Variation (SSW)** is the variation attributed to the weighted total of all sample individual variations and this variation is computed with the respect of the degrees of freedom.

The Mean of the squares of the variances are derived by dividing the Sum of squares variances by an appropriate degree of freedom (MS = SS/df). The resulting Mean Squares of the variation for the between samples (MSB) and the Mean Squares of the within samples(MSW) also known as the pooled estimate of the variance are used to compute the test statistics from the F-distribution table which is a right tailed distribution test with a degree of freedom of k-1 numerator and n-k denominator.

Test Statistic(F) = $\frac{M}{MSW}$

Where K= number of groups, and

n = total number of observational units

Assumptions of ANOVA

-) The data are expected to be randomly independent
-) The observational units are expected to be normally distributed
-) There should be homogeneity of variances of the group samples

However, in ANOVA, the assumptions of the normal distribution condition are not stringent [70, 71] especially if there is a balance in the number of samples in each group, the within group variances are homogenous and skewness in the group distribution are not large. In terms of sizes, if the sample sizes are moderately large (15 n < 40) or large (40), any skewness are considerably okay in this instance [71].

3.5.Ethics

The data that we present in this study does not present an ethical problem, since it does not directly implicate indirectly the privacy of the patients, nor the professional secrecy of the health institutions of the place, which in fact, it must contribute to the emergence of the health situation of the population with respect to different diseases.

Approval from authorities was solicited and acquired to allow the researchers to contribute to the improvement of the health situation related to the tuberculosis to have a general idea of the disease.

3.6.Data collection and analysis

The information expected was collected on a survey form based onfrom the quarterly notifications of detection, treatment, and annual activity reports of the national tuberculosis program. To carry out this study some calculation software notably Excel and statistical software package called statistical package for social sciences (SPSS) version 20 were used. The descriptive statistics were utilized to give the patterns of the data and the One – Way ANOVA was employed for hypothesis testing. A 95% significance level was utilized throughout the study.

CHAPTER FOUR

RESULTS PRESENTATION

4.1. ANOVA of Total Cases of Tuberculosis Relative to the Years (2008 -2019)

Table 4.1: Descriptive Statistics of Total Number of Tuberculosis Cases (N = 40,619 Cases)

Year	Mean ± SD	Median (Min – Max)
2008	159.92 ± 61.32	154.50 (61.00 – 276.00)
2009	170.38 ± 69.60	163.50 (59.00 – 303.00)
2010	190.17 ± 71.42	175.50 (83.00 – 345.00
2011	182.67 ± 66.99	176.50(82.00 - 345.00)
2012	175.46 ± 55.47	171.50(98.00 - 299.00)
2013	175.67 ± 54.99	178.00(84.00 - 261.00)
2014	200.42 ± 75.19	204.00 (64.00 - 331.00)
2015	214.04 ± 65.27	218.50(82.00 - 346.00)
2016	223.75 ± 78.07	220.00(59.00 - 394.00)
Total	112.05 ± 34.147	

 \mathbf{H}_0 :There is no significance mean difference in the total cases of tuberculosis recorded annually.

 $\mathbf{H}_{\mathbf{i}}$: There is a significant mean difference in the total cases of tuberculosis recorded annually.

Decision Rule: H_0 is not assumption if p-value < 0.05.

Table 4.2: Test of Homogeneity of Variance

Total tuberculosis cases

Levene Statistic	df 1	df 2	p-value
0.683	8	207	0.706

The Levene test was conducted to test the homogeneity of the variance. Since the p-value > 0.05, it can be concluded that the variances across the groups are similar.

Table 4.3: ANOVA Table for Total Tuberculosis Cases

ANOVA

TOTAL TUBERCULOSIS

	Sum of Squares	df	Mean Square	F	р
Between Groups	85253.731	8	10656.716	2.380	0.018
Within Groups	926994.708	207	4478.235		
Total	1012248.440	215			

The ANOVA was significant F (8, 207) = 2.380, p-value = 0.018. Since the p < 0.05, the H₀was not assumption. Thus, it can therefore be concluded that the annual total tuberculosis cases recorded differs in annual basis.

The Post-Hoc Analysis comparisons to evaluate pairwise differences among group means were conducted with the use of Turkey's test. The tests revealed that there is a significant pairwise differences between the tuberculosis cases recorded in the year 2008 and the year 2016, p = 0.030. This implied that the total cases of tuberculosis reported in the year 2016 (Mean = 223.75, SD = 78.07) is higher than all other years recorded cases in the study while the lowest reported cases of tuberculosis

were in the year 2008 (Mean = 159.92, SD = 61.32) compared to all other years. The total cases of tuberculosis reported in the year 2016 are statistically significant as well as the number of total cases recorded in the year 2008.



Figure 4.1: Bar plot of the means of the total tuberculosis recorded annually

Because the SPSS output for the line mean plots figure is not to scale, the transformation of the graph to a scaled bar-plot is considered appropriate. From the bar-plot above, it can be seen that there was a downward reduction in annual cases of tuberculosis between the year 2010 and 2014. However, the year 2008 has the lowest number of cases recorded while the year 2016 has the highest annual cases of tuberculosis.

Year	Ν	% of Cured Case	Mean ± SD	Median (Min – Max)
2008	2965	80.40%	128.96 ± 51.31	120.50 (48.00 – 237.00)
2009	3218	84.10%)	143.29 ± 57.84	140.50 (48.00 – 276.00)
2010	3846	84.26%	160.25 ± 58.93	157.00 (66.00 – 256.00)
2011	3735	85.19%	155.63 ± 52.43	147.50 (54.00 – 236.00)
2012	3534	83.92%	147.25 ± 45.08	148.50 (63.00 – 230.00)
2013	3504	83.11%	146.00 ± 49.42	151.50 (48.00 – 230.00)
2014	3777	84.19%	181.83 ± 61.79	181.50 (44.00 –296.00)
2015	4368	85.03%	182.00 ± 55.18	182.00 (53.00 – 298.00)
2016	4756	88.57%	198.17 ± 75.99	188.00 (48.00 – 370.00)
Total	33,703	85.3%	160.38 ± 59.89	

4.2 ANOVA of Cured Cases of Tuberculosis Relative to the Years (2008 - 2019) Table 4.4: Descriptive Statistics of Cured Cases of Tuberculosis (N= 33,703)

Hypothesis Test

 H_0 : There is no significance difference in the cured cases of tuberculosis recorded relative to years.

 H_1 : There is at least a significant difference in the cured cases of tuberculosis recorded relative to the years.

Decision Rule: H_0 is not assumption if p-value < 0.05.

The normality test was conducted using the Schapiro-Wilk Test of Normality. The p-values for each of the years from year the 2008 through year 2016 were given as follows: 0.687, 0.823, 0.246, 0.259, 0.793, 0.584, 0.981, 0.827 and 0.504 respectively. Since the p - values > 0.05, we considered that the categorical data classifications were normally distributed.

Table 4.5: Test of Homogeneity of Variance

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Levene Statistic	df 1	df 2	p-value
0.711	8	207	0.682

The Levene test was conducted to test the homogeneity of the variance. Since the p-value > 0.05, it can be concluded that the variances across the group are similar.

Table 4.6: ANOVA Table for Cured Tuberculosis Cases

ANOVA

Cured Tuberculosis Cases					
	Sum of Squares	df	Mean Square	F	р
Between Groups	96879.416	8	12109.927	3.718	<0.001
Within Groups	674197.208	207	3256.991		
Total	771076.625	215			

The ANOVA was significant F (8, 207) = 3.718, p-value = 0.0001. Since the p < 0.05, the H₀ was being rejected. Thus, it can therefore be concluded that the cured tuberculosis cases reported differ in annual basis.

The Post-Hoc Analysis comparisons to evaluate pairwise differences among group means were conducted with the use of Tukey's test. The tests revealed that there are significant pairwise differences between cured tuberculosis cases reported in the following table.

pairwise comj	parison years	P-value
2008	2014	0.040
2008	2015	0.039
2008	2016	0.001
2009	2016	0.028
2013	2016	0.046

Table 4.7:Post-Hoc Analysis of Tukey's testfor Cured Tuberculosis Cases

However, the cured tuberculosis cases do not significantly differ from the other years considered in the study since there *pvalues* > 0.05.

In terms of percentage cured patients, it can be inferred that more patients were cured in the year 2009 (84.10%); 2014 (84.19%); 2015 (85.03%) while the highest cured cases was recorded in the year 2016 (88.57%) but the lowest cured percentage of cases was recorded in the year 2008(80.64%).



Figure 4.2: Bar plot of the Means Percentages Cured cases of Tuberculosis Annually

The graph above shows that less cases of Percentage cured tuberculosis was reported in the year 2008. The cured cases also increase up to the year 2010. However, the Percentage cured cases began to deteriorate as from year 2011 through between years 2013. The Percentage cured cases peak again from year 2014 through the year 2016. The year 2016 has the highest number of Percentage cured cases.

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Year	Ν	% of Dead Cases	Mean ± SD	Median (Min – Max)
2008	184	4.79%	7.64 ± 4.57	7.00(1.00 - 18.00)
2009	214	5.23%	8.92 ± 5.77	7.00 (1.00 – 23.00)
2010	243	5.32%	10.13 ± 5.55	9.50 (1.00 – 23.00)
2011	175	3.99%	7.29 ± 6.13	6.50 (0.00 - 26.00)
2012	223	5.29%	9.29 ± 5.36	8.00 (3.00 – 21.00)
2013	243	5.76%	10.13 ± 5.55	9.50 (1.00 – 23.00)
2014	222	4.60%	9.25 ± 5.91	8.00 (1.00 -27.00)
2015	209	4.00%	8.71 ± 5.34	8.50 (0.00 – 18.00)
2016	219	4.07%	9.13 ± 5.29	9.00 (2.00 – 19.00)
Total	1,932	4.78%	8.94 ± 5.49	

Table 4.8: Descriptive Statistics of Dead Cases of Tuberculosis (N= 1,932 cases)

Hypothesis Test

H₀: There is no significance difference in dead cases of tuberculosis recorded relative to the years under study.

 H_1 : There is at least a significance difference in dead cases of tuberculosis recorded relative to the years under study.

Decision Rule: H_0 is not assumption if p-value < 0.05.

The normality test was conducted using the Schapiro-Wilk Test of Normality. The p-values for each of the years from year the 2008 through year 2016 were given as follows: 0.219, 0.145, 0.664, 0.001, 0.026, 0.664, 0.055, 0.378 and 0.077 respectively. The year 2011 and year 2012 p-values < 0.05, hence the normality assumption is violated. Hence, the Kruskal Wallis non-parametric test will be used.

	Death Per Years
Chi-Square	7.828
df	8
p-value	0.450

 Table 4.9: KruskalWallis Test

TheKruskaWallis test shows that 2 (8) = 7.828, p = 0.450. Since the p > 0.05, the H_o will be accepted. Thus, it can therefore be concluded that death cases of the tuberculosis ailment are not statistically significantly different in the year categories. In terms of the percentage of cases from the figure 4.3 below, it can be observed that the year 2009 through 2013 have the highest percentage of dead cases. The year 2013 had the highest percentage of dead cases of the years under review, while the year 2015 had the lowest percentage of dead cases. However, all these are not statistically significant as indicated by the Kruska Wallis Test.



4.4: ANOVA of Incidence Cases of Tuberculosis Relative to the Years of Study

Year	Mean ± SD	Median (Min – Max)
2008	112.66 ± 33.41	110.35 (44.00 - 179.00)
2009	119.28 ± 38.37	127.70 (27.00 – 207.00)
2010	121.86 ± 57.47	116.35 (37.00 – 344.00)
2011	108.88 ± 30.91	108.25 (45.00 - 151.00)
2012	101.67 ± 23.61	106.35 (45.00 – 151.00)
2013	99.08 ± 19.87	102.30 (46.00 – 133.00)
2014	119.28 ± 22.44	111.10 (44.00 – 141.00)
2015	121.03 ± 30.32	117.55(78.00 - 210.00)
2016	118.07 ± 32.59	117.20 (61.00 – 179.00)
Total	112.05 ± 34.15	

Table 4.10: Descriptive Statistics of Total incidence cases of Tuberculosis

Hypothesis Statement

H_o: There is no significance difference in the incidence cases of tuberculosis reported relative to the years under study.

 H_1 : There is at least a significant difference in the incidence cases of tuberculosis reported relative to the years under study.

Decision Rule: H_ois not assumptionif p-value < 0.05.

The normality test was conducted using the Schapiro-Wilk Test of Normality. The p-values for each of the years from year the 2008 through year 2016 were given as follows: 0.979, 0.669, 0.001, 0.904, 0.684, 0.012, 0.002, 0.051 and 0.390 respectively. The p-values < 0.05 for the year 2010, 2013, 2014 and 2015 respectively, hence the normality assumption is violated. Hence, we will proceed to use the Kruska Wallis Test Statistic.

Table 4.11: KruskalWallis Te

	Death Per Years
Chi-Square	14.436
df	8
p-value	0.071

The Kruska Wallis test shows that 2 (8) = 14.436, p = 0.07. Since the p > 0.05, the H_o will be accepted. Thus, it can therefore be concluded that incidence cases of tuberculosis are not statistically significantly different in the year categories.



Figure 4.4: Bar plot of the Median of Incidence Cases of Tuberculosis Annually

4.5: ANOVA of Male Incidence Cases of Tuberculosis Relative to the Years of Study

 Table 4.12: Descriptive Statistics of total incidence cases of Tuberculosis among

 Males

Year	Mean ± SD	Median (Min – Max)
2008	58.54 ± 18.13	59.50 (44.00 - 179.00)
2009	64.42 ± 18.32	64.50 (27.00 - 207.00)
2010	63.71 ± 29.38	59.50 (37.00 - 344.00)
2011	57.75 ± 15.72	57.50 (38.00 - 180.00)
2012	54.63 ± 12.65	56.00 (45.00 - 151.00)
2013	52.13 ± 11.88	53.50 (46.00 - 133.00)
2014	55.58 ± 13.79	57.00 (44.00 - 141.00)
2015	65.13 ± 18.13	62.50 (78.00 - 210.00)
2016	61.83 ± 18.78	62.50 (61.00 - 179.00)
Total	59.30 ± 18.30	

Hypothesis Statement

 H_0 : There is no significance difference in the incidence male cases of tuberculosis reported relative to the years under study.

 H_1 : There is at least a significant difference in the incidence male cases of tuberculosis reported relative to the years under study.

Decision Rule: H_0 is not assumption if p-value < 0.05.

The normality test was conducted using the Schapiro-Wilk Test of Normality. The p-values for each of the years from year 2008 through year 2016 were given as follows: 0.815, 0.544, 0.001, 0.353, 0.977, 0.828, 0.082, 0.033 and 0.364 respectively. The p-values < 0.05 for the year 2010 and the year 2015 respectively, hence the normality assumption is violated. Hence, the Kruska Wallis Test Statistic will be used.

Table 4.13:Kruska Wallis Test

	Male Incidence Cases
Chi-Square	12.161
df	8
p-value	0.144

The Kruska Wallis test shows that 2 (8) = 12.161, p = 0.144. Since the p > 0.05, the H_o will be accepted. Thus, it can therefore be concluded that male incidence cases of tuberculosis are not statistically significantly different in the year categories.




The figure above shows that incidence of tuberculosis were high in the year 2009 [64.50(27.00-207.00) cases], year 2015[62.50(78.00-210.00) cases] and year 2016[62.50(61.00-179.00) cases] but lower in the year 2013[53.50(46.00-210.00) cases]. However, these differences were not found to be statistically significant.

4.6: ANOVA of Female Incidence Cases of Tuberculosis Relative to the Years of Study

 Table 4.14: Descriptive Statistics of total incidence cases of Tuberculosis among

 Females

Year	Mean ± SD	Median (Min – Max)
2008	54.33 ± 17.31	55.50 (22.00 - 91.00)
2009	54.79 ± 22.42	54.00 (10.00 - 110.00)
2010	58.21 ± 29.49	54.00 (16.00 - 167.00)
2011	51.29 ± 16.41	53.50 (13.00 - 78.00)
2012	47.17 ± 12.54	51.50 (19.00 - 72.00)
2013	46.92 ± 11.91	47.00 (19.00 - 63.00)
2014	50.13 ± 12.87	51.50 (19.00 - 71.00)
2015	56.08 ± 14.57	56.00 (30.00 - 102.00)
2016	56.20 ± 15.61	56.00 (26.00 - 92.00)
Total	52.79 ± 17.92	

Hypothesis Statement

 H_0 : There is no significance difference in the female incidence cases of tuberculosis reported relative to the years under study

 H_1 : There is at least a significant difference in the female incidence cases of tuberculosis reported relative to the years under study.

Decision Rule: H_0 is not assumption if p-value < 0.05.

The normality test was conducted using the Schapiro-Wilk Test of Normality. The p-values for each of the years from year the 2008 through year 2016 were given as follows: 0.708, 0.668, 0.001, 0.630, 0.061, 0.121, 0.514, 0.068 and 0.732 respectively. The p-values < 0.05 for the year 2010, hence the normality assumption is violated. Hence the normality assumption is violated.

Hence, the Kruska Wallis Test Statistic will be used.

	Female Incidence Cases
Chi-Square	9.966
df	8
p-value	0.267

Table 4.15:Kruska Wallis Test

The Kruska Wallis test shows that 2 (8) = 9.966, p = 0.267. Since the p > 0.05, the H_o will be accepted. Thus, it can therefore be concluded that female incidence cases of tuberculosis are not statistically significantly different in the year categories.



Figure 4.6: Bar plot of the Median Female Incidence Cases of Tuberculosis Annually

The plot above shows that the female incidence cases for the year 2015 [56.00(30.00-102.00) cases] and the year 2016[56.00(26.00-92.00) cases] all have highest incidence cases of tuberculosis in the female gender while the year 2013 [47.00(19.00-63.00)] had the lowest female incidence tuberculosis cases. However, these differences are not found to be statistically significance.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

In summary, the study shows that the annual cases of tuberculosis vary across all years (2008-2016) that have been meticulously reviewed. The highest annual total cases of tuberculosis recorded under the review occurred in the year 2016, while the lowest recorded cases of tuberculosis were recorded in the year 2008. An increase in the trend of incidence of Pulmonary Tuberculosis was found during our study, though not statistically significant in relative to the years under review. In the study, it has been found that year 2009 has the highest incidence rate of about [127.70 (27.00 -207.00)] cases per 100,000 people closely followed by the year 2015 with about [117.55(78.00 – 210.00)] incidence cases per 100,000 people and the year 2016 with [117.20 (61.00 - 179.00)] incidence cases per 100,000 people and the year. The least incidence cases occurred in the year 2013 with about [102.30 (46.00 - 133.00)]incidence cases per 100,000 people. There was an increasing trend of tuberculosis incidence between the years 2008 through the year 2009. This was followed by a downward plunge from the year 2010 to the year 2013. However, it increased in the year 2014 and the year 2015 before a slight reduction occurred again in the year 2016 which had an incidence occurrence of about [117.20 (61.00 - 179.00) incidence cases per 100,000 people.

Mutatis mutandis, similar trend increase in tuberculosis cases has been reported in several countries in Africa and other developing regions of the world. A study conducted in Congo Brazzaville on TB from the year 2010 to 2012 showed results of a reasonable growth between 2010 and 2012. Then a decrease in the incidence between 2013 and 2015 which reached a stability around 381 to 382 cases per 100,000 populations [52]. The armed conflict and the displacement of the population, could explain this outbreak of the incidence of TB in general in Congo Brazzaville and Congo Kinshasa. Comparatively, an upward trend in the number of new cases was also evident in Gabon from 2003 to 2007, with a drop in 2009 to resume its path from 2010 to 2012, when it stabilized with 423 cases per 100,000 inhabitants [55].

From the gender perspective, the incidence cases in the male gender were higher in the year 2009 with [64.50 (27.00 – 207.00)] cases per 100,000 people. There was a brief decline of incidence cases between the years 2011 through the year 2013. However, it has been discovered an upward trend from the year 2014 through the year 2016, even though the differences observed are not statistically significant. In terms of the female gender, the highest incidence cases is in the year 2015 [56.00 (30.00 - 102.00)]cases per 100,000 people] and closely followed by the year 2016[56.00 (26.00 - 92.00)]cases per 100,000] and year 2008[55.50 (22.00 - 91.00)] cases per 100,000 while the lowest rates were in the year 2013[47.00 (19.00 - 63.00)]cases per 100,000 and the year 2014[51.50 (19.00 - 71.00)] cases per 100,000.

Taking into account the mortality aspect, deaths resulting from tuberculosis were much higher in the year 2013 with 5.76% and the year 2010 with 5.32%. This situation is linked to the breakage of drugs in the health structures and the massive displacement of the population; which leads to poor patient care. In addition to the above situation, factors like poverty of the population and malnutrition were also found as important elements in the increased death rate. The death rate lowered in the

year 2011 with 3.99% cases. Even though this assertion was not found to be statistically significant.

The percentage cured TB cases was higher in the year 2016 with 88.57% cases, but lower in the year 2008 with 80.40% cured cases. This was not found to be statistically significant.

Considering all aforementioned statistical data, it was concluded an increase in the trend of incidence of Pulmonary Tuberculosis was found during our study, though not statistically with a difference significant relative to the years under review.

It logically can be inferred that the health system for the management of TB patients is still to be improved all around the Bandundu province in the Democratic Republic of the Congo for efficient and tangible reduction in the incidence and mortality of TB patient's pulmonary tuberculosis.

Taking into accountresults of data and findingsdisplayed in this study, the following recommendations are made:

At the PNLT Level

-) Introducing the method of active screening of patients in high prevalence settings.
-) Implementing measure of screening and therapeutic management of patient after essential screening
-) Applying the Active Screening Measures to the immediate entourage of the patient and preventive treatment.
-) Organizing a platform for educational lessons, information and public awareness campaigns;

) Creating structures able to archive data for their best and further exploration.

To TB patients

• Reinforcinggood compliance with the treatment, including the rules of hygiene of life.

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