

Epidemiological and Clinical Insights into Pulmonary Tuberculosis among Diabetic Patients: A Descriptive Retrospective Study in N'Djamena, Chad

ABSTRACT

Introduction: association with HIV tuberculosis is a real public health problem according the International Union Against Tuberculosis and Lung Disease. The objective of this work is to study the epidemiological, progressive and therapeutic aspects of pulmonary tuberculosis in diabetic

Methods: This is a descriptive retrospective study evaluating the association between pulmonary tuberculosis and diabetes in the pneumo-physiology department of the Reference National University Hospital Center over a period of 3 years about 51 cases.

Results: During our study period, we collected 51 cases of pulmonary tuberculosis and diabetes out of a total of all hospitalised patients. with a prevalence of Tuberculosis/Diabetes co-infection of 5.6%. The sex ratio was 2.18 in favour of men. The average age was 52.3 ± 13.8 years with extremes ranging from 20 to 80 years old. The notion of tuberculosis infection was found in 21.6% of cases. Other comorbidities were present, such as hypertension (41.2%, n=21) and HIV (15.7%, n=8). The GenXpert results revealed MTB Detected in 62.7% of cases with 9 cases of Rifampicin Resistance Detected. The type of diabetes found was mainly Type 2 diabetes (88.2%) and the most common complication was diabetic foot. The treatment consisted of a quadruple therapy, Oral Antidiabetic (OAD) and insulin, or a combination of both.

Conclusion: This study shows that the association of tuberculosis and diabetes is a reality in our countries. The prevalence remains relatively high and the treatment regimen remains the same. Prevention of TB and correct management of diabetes could reduce the prevalence of this pandemic.

Keywords: tuberculosis, diabetes, prevalence, N'Djamena, Chad

INTRODUCTION

Tuberculosis remains a major public health problem in developing countries particularly in Africa and notably in Chad. According to the World Health Organization (WHO), in 2020, the total number of tuberculosis cases was estimated to be 10 million (9 to 11.1 million), a number which has remained relatively stable over the last decades. [1] Approximately, 10% of subjects infected with Koch's Bacillus develop tuberculosis disease while the vast majority, 90% present with primary tuberculosis infection which can progress to tuberculosis disease during immune deficiencies such as HIV infection, immunosuppressive therapy, long-term corticosteroid therapy and diabetes which will favor the outbreak of the disease within 5 to 10 years[1]. Diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin or when the body is not able to effectively use the insulin it produces. In 2017, the number of people with diabetes worldwide was estimated to be 425 million and is expected to reach 629 million by 2045. According to the International Union Against Tuberculosis and Lung Disease (UICTMR), 16% to 46% of with tuberculosis suffer from diabetes. Every year, 10 million new cases are recorded and up to 5 million people die from complications. Africa has the lowest prevalence, which is 3.2% compared to the rest of the world which is above 8%, but has the highest rate of undiagnosed cases (above 50%) [2]. Diabetes is known to weaken the immune system, leaving individuals vulnerable to infections including tuberculosis. In Africa, little is known in the literature for the frequency of TB in diabetic patients; hence the interest of this work.

MATERIALS AND METHODS

❖ **Study Design:** The pneumo-physiology department of the Reference Nationale University Hospital Center served as our study setting. This is a descriptive retrospective study from January 1, 2019 to December 31, 2021, i.e. in a duration of 3 years.

❖ **Setting and study population**

✓ **Inclusion criteria :** all patients with the combination of diabetes (whatever the type) and tuberculosis (whatever the location) have been hospitalized during this study period with complete medical records and with an age ≥ 15 years old and all patients with the combination of diabetes and tuberculosis who also have other comorbidities as well.

✓ **Non-inclusion criteria** : were not included in our study:

-all patients aged <15 years old;

-patients whose medical records were incomplete;

-patients infected with tuberculosis but not diabetic.

-outpatient department

❖ **Data Collection and Analysis:** Data was entered into Microsoft Word and Microsoft Excel 2019 software and analyzed using SPSS Version 25. For the analysis, the differences observed between the results will be assessed by using the Student's T-Test and the Fisher Exact Test. The level of statistical significance of the p-value is 0.05.

❖ **Sample size determination** : We systematically selected all patients hospitalised in the department during the study period. This gave us 910 patients, 51 of whom were co-infected with tuberculosis and diabetes.

RESULTS

The prevalence of tuberculosis in diabetic patients was 5.6% (n=51/910). The average age of the patients was 52.3 ± 13.8 years old, with extremes ranging from 20 to 80 years old. The most represented age group is 60 years and above with 35.3%. We noted a male predominance of 68.6% (n=35) with a sex ratio of 2.18. Married couples constituted 62.7% (n=32), followed by single people with 13.7% (n=7). High blood pressure is the most represented comorbidity with 41.2% (n=21), followed by HIV infection with 15.7% (n=8). There were 33.3% (n=17) of patients who had a history of previous TB and who completed treatment. The most common general signs were anorexia followed by physical asthenia and weight loss, which was 88.2% (n=45), 74.5% (n=38) and 62.7% (n=32) respectively. Cough, fever and chest pain were the most common functional signs, which were 100% (n=51), 84.3% (n=43) and 80.4% (n=41) respectively. The GenXpert results revealed MTB Detected in 62.7% (n=32) of cases with 9 cases (28.10%) of Rifampicin Resistance.

Radiological abnormalities consisted of alveolar and alveolar-interstitial syndrome in 31.4% each (n=16). The most common location was in the left lung, which was 45.1% (n=23). The duration of diabetes was on average 6.13 ± 4.5 years with extremes ranging from 0.1 to 20

years. Patients who had diabetes for 10 years represented with 33.3% (n=17). Type 2 diabetes represented 88.2% (n=45) compared to Type 1 diabetes which represented 11.8% (n=6). There were 16 patients that had diabetes-related complications, which were diabetic foot in 13.7% (n=7), followed by 3.9% in neuropathy and retinopathy each. The discovery of diabetes was incidental in 41.2% (n=21). Biologically, the average blood glucose level was 2.4 ± 1.04 g/dl with extremes ranging from 0.5 to 5.34 g/dl. The treatment was with insulin in 49% of cases. Insulin therapy associated with oral antidiabetics was in 5.9% of cases. All of the patients had received multiple antituberculosis drug therapy according to the National Tuberculosis Control and Protocol Guidelines. 52.9% (n=27) of patients were cured. Those who didn't come for follow-up sessions represented 27.5% (n=14). Those deceased were 19.6% (n=10).

DISCUSSION

Our study included 910 patients hospitalized in the pneumo-phthisiology department and 51 patients of whom had tuberculosis due to diabetes (5.6%). This prevalence is similar to that of different african authors including Diarra et al in Mali [3], Djenebou et al in Mali [4] and Morad et al in Morocco [5] who reported 5.7%, 5.2 % and 5.2% respectively. In this study, we noted a male predominance (68.6%) with a sex ratio of 2.18. This result agrees with those of several other authors who had shown a male predominance such as, Toure et al., [6] and Kouismi et al., [7] in Senegal, who reported 68% and 60%, respectively. This male predominance is explained by the fact that tuberculosis and diabetes are more present among men in Africa. The average age of the patients in our study was 52.3 ± 13.8 years as reported in most of the data in the literature, notably, Touret al [6], Djenebou et al [4], and Diarra et al [3] reported the average age of 53.4 years, 51.5 years and 52.4 years, respectively. The age group most affected in our study population is that of the 60 years and above (35.30%). In our study, hypertension was present in 21 patients (41.2%). This data is consistent with the data of Aynaou H. et al in Oujda [8] who found a frequency of association between hypertension and diabetes in 55% of cases. In this series, 8 patients (15.7%) were co-infected with HIV. This prevalence of co-infection is similar to that of the World Health Organization [9], which stated that 13% of people who developed tuberculosis worldwide were immunosuppressed by HIV. The history of previous tuberculosis is found in 33.3% of cases. Adrianinianna et al., in Madagascar [10] and Rhanim et al., in Morocco [11] had found 26.42% and 16.3% respectively. A

precarious immunity most often exposes diabetic patients to a new episode of tuberculosis, whether by reinfection or by endogenous reactivation of latent tuberculosis. Concerning the signs, in our study, 88.2% were anorexic, 74.5% had physical asthenia and 62.7% had weight loss. These data corroborate with those of other authors, notably in Tekpa et al., in Bangui [12] who reported that the main signs were long-term fever in 96.82% of cases and deterioration of general condition in 75.91% of cases. This noted difference would be due to variations in the epidemiological or clinical profile of the patients. Cough is present in all patients followed by chest pain in 80% of the cases. The same is done by Tekpa et al., in the Central African Republic [12] which reports 71.81% cases of chronic cough. The GenXpert results revealed MTB Detected in 62.7% (n=32) of cases with 9 cases (28.10%) of Rifampicin Resistance. , these results are identical to those of Diop et al., in Senegal [13] who obtained a positive result in 62% of the cases in accordance with the African literature [14]. On the other hand, the study by MoustahfirElidriss et al., in Morocco [15] shows a positivity rate of 43.7%. This result, slightly lower than ours, could be explained by the difference in the population studied and the size of the sample used. GeneXpert remains the most appropriate test for the diagnosis of tuberculosis [16]. In our study, the sensitivity to rifampicin is 71.8% compared to 28.1% in resistance. This result is similar to that of Creswell et al., in Nepal [17] with 21.1% of resistance to rifampicin. On the other hand, in Mali and the DRC [18,19], resistance to rifampicin is slightly lower than that of ours with 15.9% and 18.02%, respectively. This difference can be justified by the fact that in our study we have cases of recurrence of tuberculosis among the patients investigated and this reduces the rate of sensitivity to rifampicin and increases the rate of resistance. Radiologically, in our series, tuberculous lesions are bilateral in 45.1%. This bilateralization of lesions is found in several studies and seems to be accentuated by diabetes. In the case of Mezghani et al., in Tunisia [20] and Morad et al., in Morocco [5] they had found 63% and 46% of bilateral lesions, respectively. Unilateral lesions on our radiographs were predominated by 39.1%, on the left. Which is similar to the result of Toure et al., in Senegal [6] who found 27% of lesions on the left lung as well. Most studies report that radiological lesions are atypical in cases of pulmonary tuberculosis and diabetes. Therapeutically, almost all of our patients are treated according to the National Tuberculosis Control and Protocol Guidelines using the 2RHZE/4RH regimen. This is consistent with the data of Djenebou et al., [4] and Diarra et al., [3] in Mali who found that 87.5%

and 84.2%, respectively, received the same treatment regimen. In our study, Type 2 diabetes is predominant with 88.2%. This result is consistent with most studies, notably those of Maalej et al., in Tunisia [21] and Sibomana et al., in Rwanda [22] which found 92% and 91.3%, respectively, of Type 2 diabetes. The high frequency of Type 2 diabetics in our series could be explained by the fact that our study population is mainly made up of people aged over 60 years old and that patients aged less than 15 years were excluded from the study. Additionally, Type 2 diabetes is the most common type of diabetes in sub-Saharan Africa. Biologically, HbA1c was high on admission and the average blood sugar level was 2.4g/dl \pm 1.04 in our series. Our data are superior to those of Rhanim et al., in Morocco [11] who reported a mean blood sugar level of 1.92 \pm 0.98g/dl and a 67% glycemic imbalance. In our study, the most frequent complications are diabetic foot with 13.7% followed by neuropathy and nephropathy with 3.9% each with a non-significant difference (p=021). Our results corroborate with those of other authors [10]. The study by Yan et al., in Denmark [23] 10.5% of the patients had diabetic foot. In our series, the evolution was favorable, which was marked by 52.9% of the patients that had gotten cured. This lethality is higher than that of the literature, in particular those of Toure et al., in Senegal [6] and Maalej et al., in Tunisia [21] which found 7.4% and 8%, respectively. While Viswanathan et al., in India [24] reported a very low rate of 2% deaths. This high rate of death could be explained by the older age of most of our patients and the delay in coming to see a health practitioner. Dooley et al., in the USA [25] shows that the risk of death is twice as high in diabetic tuberculosis patients then those in non-diabetic patients.

CONCLUSION

This study shows that the association of tuberculosis and diabetes is a reality in our countries. The prevalence remains relatively high and the treatment regimen remains the same. Prevention of TB and correct management of diabetes could reduce the prevalence of this pandemic.

Ethical Approval: For our study, we received research authorization from the Faculty of Human Health Sciences of N'Djamena and the management of the Reference National University Hospital Center.

REFERENCES

1. Toujani S, Ben Salah N, Cherif J, Mjid M, Ouahchy Y, Zakhama H, et al. Primary infection and pulmonary tuberculosis. *Rev pneumol clin*. 1 Apr 2015;71(2):7382.
2. Wirth T, Hildebrand F, Allix-Bguec C, Wlbeling F, Kubica T, Kremer K, et al. Origin, Spread and

- Demography of the Mycobacterium tuberculosis Complex. *PLOS Pathogens*. Sep 26, 2008;4(9):e1000160.
3. Diarra B, Diallo A, Maiga M, Sanogo M, Diallo MH, Baya B, et al. Tuberculosis and diabetes in Bamako, Mali: prevalence and epidemiological characteristics of the association. *Rev Mal Infect Microbiol* 20Apr 2014;24-6.
 4. Djenebou T, Sylla SD, Djibril S, Massama K, Khadidia O, Noumou SD, et al. Tuberculosis among diabetics in Bamako. *Health Sci Dis [Internet]*. 25 Oct 2020 [cited 31 Oct 2022]; 21(11). Available at: <http://hsd-fmsb.org/index.php/hsd/article/view/2365>
 5. Morad S, Benjelloun H, Moubachir H, Zagbha N, Bakhatar A, Yassine N, et al. Clinical, radiological and progressive profile of pulmonary tuberculosis in diabetics. *Rev Mal Respir* 1 Jan 2015; 32:A225.
 6. Toure N O, Dia Kane Y, Diatta A, Ba Diop S, Niang A, Ndiaye EM, et al. Tuberculosis and diabetes. *Rev Mal Respir*. Sep 1, 2007;24(7):869-75.
 7. Kouismi H, Hammi S, Bouti K, Rhanim A, Ataouna K, Razine R, et al. Pulmonary tuberculosis and diabetes mellitus profile. *Integrative Journal of Medical Sciences*. 2015;2(1).
 8. Aynaou H, Latrech H. Cardiovascular comorbidity in hypertensive type 2 diabetic patients. *Ann Endocrinol* 1 Oct 2014;75(5):376.
 9. World Health Organization. *Global Tuberculosis Report 2013*. World Health Organization; 2013. 303 p.
 10. Andrianiana MMA, Raheison RE, Razanamparany T, Raharinalona SA, Rakotomalala ADP, Andrianasolo RL. [Epidemiologic-clinical, biological and radiological characteristics of pulmonary tuberculosis in patients with diabetes in Antananarivo, Madagascar]. *Pan Afr Med J*. 2022; 42:49.
 11. Rhanim A, Zemed N, Marc K, Soualhi M, Zahraoui R, Benamor J, et al. Diabetes and pulmonary tuberculosis: clinical, radiological and biological aspects. *Rev Mal Respir*, Jan 2015; 32:A224.
 12. Tekpa G, Fikouma V, Tengothi RMM, Longo J de D, Woyengba APA, Koffi B. Epidemiological and clinical aspects of tuberculosis in hospitals in Bangui. *Pan Afr Med J*. May 15, 2019; 33:31.
 13. Diop SA, Massaly A, Ka D, Manga NM, Fortes-Dgunonvo L, Ndour CT, et al. Use of the GeneXpert test for the diagnosis of tuberculosis in the infectious diseases department of the Fann University Hospital. *Pan Afr Med J [Internet]*. July 16, 2016 [cited Dec 14, 2022]; 23(1). Available at: <https://www.ajol.info/index.php/pamj/article/view/139630>
 15. Moustarhfir Elidrissi A, Benjelloun H, Zagbha N, Yassine N. Contribution of GeneXpert in the diagnosis of pulmonary tuberculosis. *Rev Mal Respir*. 1 Jan 2017; 34:A215.
 16. Kohli M, Schiller I, Dendukuri N, Dheda K, Denkinger CM, Schumacher SG, et al. *Cochrane Database of Systematic Reviews [Internet]*. 2018 [cited Dec 21, 2022];(8). Available at:

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012768.pub2/full>

17. Creswell J, Rai B, Wali R, Sudrungrot S, Adhikari LM, Pant R, et al. Introducing new tuberculosis diagnostics: the impact of Xpert® MTB/RIF testing on case notifications in Nepal. *Int J Tuberc Lung Dis*. May 2015;19(5):545-51.
18. Okemba-Okombi FH, Itoua A, Biniakounou JB, Illoye-Ayet M, Bemba ELP, OssalAbacka KB, et al. Contribution of GeneXpert in the diagnosis of pulmonary tuberculosis: preliminary study and perspectives in the Republic of Congo. *Rev Mal Respir*. 1 Jan 2015;32:A211.
19. Toloba Y, Cisse AB, Soumare D, Ouattara K, Kanoute T, Kone D, et al. Contribution of GeneXpert in the diagnosis of tuberculosis and resistance to rifampicin in Mali after 22 months of acquisition. *Rev Mal Respir*. 31 Jan 2017; 34:A216-7.
20. S. Mezghani, H. Laadhar, A. Hayouni, M. Benzarti, M. Jerray. The association of pulmonary tuberculosis and diabetes mellitus. *EM-Consult*. 17 Apr 2008; 20(HS1):153-66.
21. Maelej S, Belhaoui N, Bourguiba M, Mahouachi R, Chtourou A, Taktak S, et al. Pulmonary tuberculosis causes diabetes imbalance: Retrospective study of 60 patients in Tunisia. *The Medical Press*. 1 Jan 2009;38(1):20-4.
22. Sibomana T, Manirakiza M, Ndirahisha E, Mbonicura JC, Nkurunziza E, Ndikumwenayo F, et al. Epidemiological, clinical and radiological analyzes of the association of diabetes and pulmonary tuberculosis in a hospital environment in Bujumbura. Prospective study of 23 cases. *JacclInfectiol*. 2020;2(4):1-4.
23. Yan Lin, Anthony D Harries, Julia A Critchley, Philip Owiti, Anders Dejgaard, Ajay M V Kumar, et al. Diabetes-tuberculosis management: guide to essential elements for good practice. Paris Bagsvaerd (Denmark): International Union against Tuberculosis and Lung Diseases World Diabetes Foundation; 2019. 116 p.
24. Viswanathan V, Vigneswari A, Selvan K, Satyavani K, Rajeswari R, Kapur A. Effect of diabetes on treatment outcome of smear-positive pulmonary tuberculosis report from South India. *Journal of Diabetes and its Complications*. 2014; 28(2):162-5.
25. Dooley KE, Tang T, Golub JE, Dorman SE, Cronin W. Impact of Diabetes Mellitus on Treatment Outcomes of Patients with Active Tuberculosis. *Am J Trop Med Hyg* Apr 2009; 80(4):634-9.

Annexes

Table 1: Distribution of patients according to other comorbidities

Comorbidities	Number (N = 51)	Percentage
Hypertension	21	41.2
HIV	8	15.7
Cardiopathy	3	5.9
Asthma	3	5.9
Hepatitis C	3	7.7
without comorbidities	13	25,5

Table 2: Distribution of patients according to symptoms of tuberculosis

Symptoms	Number (N = 51)	Percentage
Cough	51	100
Fever	43	84.3
Chest pain	41	80.4
Mucus secretion	29	56.9
Dyspnea	9	17.6
Hemoptysis	8	15.7
Night sweats	4	7.8

Table 3: Distribution of patients according to type of chest injury

Lesions	Number	Percentage
Alveolar syndrome	16	31.4
Alveolar-interstitial syndrome	16	31.4
Mixed syndrome	13	25.5
Pleural effusion	6	11.8
Total	51	100

Table 4: Distribution of patients according to diabetic complications

Complications	Number	Percentage
No complications	35	68.6
Diabetic foot	7	13.7
Nephropathy	2	3.9
Retinopathy	2	3.9
Ketoacidosis	2	3.9
Cerebrovascular accident	1	1.9
Hypoglycemia	1	1.9
Neuropathy	1	1.9
Total	51	100