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The twin epidemics of tuberculosis and diabetes: A case series perspective on co-morbidity and care

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Abstract
Introduction: The dual burden of TB and DM has emerged as a critical public health concern. Diabetes is associated with a twofold increase in the risk of developing TB, leading to poorer treatment outcomes and higher mortality rates. Conversely, TB exacerbates glycemic control in diabetic patients, creating a vicious cycle that complicates management. Globally, the rising prevalence of DM in TB-endemic regions underscores the urgency of addressing this co-morbidity.
Case Series: The presented case series includes six patients (two male and four female) from a tertiary care center, highlighting the interaction of TB and DM across various clinical scenarios:
Male Patients
1. Patient 1: A 34-year-old male with pulmonary TB (PTB) for four years and DM for an equal duration. Despite treatment with metformin and glimepiride, his glycemic control remained poor (HGT 268 mg/dL). GeneXpert testing showed no detectable TB, and HIV was non-reactive.
2. Patient 2: A 72-year-old male with PTB for 1.5 years and newly diagnosed DM. Glycemic control was managed with plain insulin, but fasting blood sugar (FBS) remained critically high (546 mg/dL). GeneXpert revealed rifampicin-sensitive MTB, and HIV testing was non-reactive.
Female Patients:
1. Patient 1: A 50-year-old female with PTB and gross pleural effusion managed with an intercostal drain. Diagnosed with DM three months ago, she was on metformin and glimepiride but exhibited elevated HGT (221 mg/dL). Sputum GeneXpert and fluid cytology results were pending.
2. Patient 2: A 32-year-old female with PTB for one month and DM managed with insulin (6-6-6). GeneXpert detected rifampicin-sensitive MTB.
3. Patient 3: A 51-year-old female with PTB for one month and an eight-year history of DM. Despite treatment with glynase MF, glycemic control was suboptimal. No TB culture growth was noted, and HIV was non-reactive.
4. Patient 4: A 32-year-old female with PTB on Category I therapy. Longstanding DM (HbA1c: 12.2%) was managed with insulin (12-12-10). GeneXpert and LPA confirmed rifampicin and isoniazid-sensitive MTB.
Discussion
Interplay Between TB and Diabetes
The co-morbidity of TB and DM creates a reciprocal influence, where diabetes increases susceptibility to TB and complicates its course, while TB exacerbates glycemic control. Diabetic patients often present with atypical TB symptoms, delayed sputum conversion, and higher rates of drug-resistant TB.
Diagnostic Challenges
1. Latent TB in Diabetics: High-risk populations necessitate enhanced screening, utilizing tools such as IGRA and TST.
2. Hyperglycemia's Impact on TB Diagnosis: Poor glycemic control may mask or modify TB symptoms, complicating the diagnostic process.
Treatment Complexity
1. Drug Interactions: Managing TB-DM co-morbidity often involves adjusting anti-TB regimens to avoid interactions with hypoglycemic agents.
2. Prolonged Therapy: Diabetic patients frequently require extended TB treatment durations to prevent relapse.
3. Adherence Challenges: Dual therapy increases the burden on patients, necessitating robust counseling and support systems.
Integrated Care Strategies
Coordinated Screening: Joint protocols for TB and DM screening in high-risk populations.
Multidisciplinary Teams: Collaboration between pulmonologists, endocrinologists, and primary care providers.
Public Health Interventions: Strengthening healthcare systems to address the dual burden through education, surveillance, and policy reforms.
Conclusion: TB and DM represent a significant global health challenge, particularly in resource-limited settings. The presented case series underscores the complexities of co-managing these conditions and highlights the need for integrated care approaches. Continued research and collaboration between healthcare providers and public health systems are essential to mitigate the burden of these twin epidemics.

Keywords: TB, diabetes, TB, diabetes

Introduction

Tuberculosis and diabetes:

Diabetes is associated with about twice the risk of tuberculosis (TB) disease [1] and a higher risk of multidrug-resistant TB [2]. People with both TB and diabetes are twice as likely to die during TB treatment and have twice the risk of TB relapse after treatment completion [3]. In 2021, about 370 000 new episodes of TB were estimated to be attributable to diabetes [4], and, in 2019, just over 15% of people with TB globally were estimated to have diabetes [5] as compared with 9.3% in the general adult population (aged 20–79 years) [6]. Thus, about 1.6 million people with TB and diabetes require coordinated care and follow-up to optimize the management of both conditions.

The prevalence of diabetes is projected to increase globally by 50% between 2019 and 2045, with a median increase of 99% (interquartile range, 69–151%) in countries with a high burden of TB [6].

Introduction to Diabetes (DM)

Diabetes is a chronic condition characterized by high levels of glucose (sugar) in the blood [7] It occurs when the body either doesn't produce enough insulin or can't effectively use the insulin it produces [8]. Insulin is a hormone produced by the pancreas that helps regulate blood sugar levels [8].

Overview and background

Types of diabetes

1. Type 1 Diabetes: This type occurs when the body's immune system attacks and destroys the insulin-producing cells in the pancreas [7]. It usually develops in childhood or adolescence and requires daily insulin administration [7].

2. *Type 2 Diabetes*: This is the most common form of diabetes and occurs when the body becomes resistant to insulin or doesn't produce enough insulin [7]. It is often associated with obesity, physical inactivity, and genetic factors [7].

3. *Gestational Diabetes*: This type develops during pregnancy and usually resolves after childbirth, but it increases the risk of developing Type 2 diabetes later in life [7].

Symptoms: Common symptoms of diabetes include: Increased thirst and frequent urination, Extreme hunger Unexplained weight loss, Fatigue and irritability, Blurred vision, Slow-healing sores or frequent infections [7].

Risk Factors: Risk factors for Type 2 diabetes include: Family history of diabetes**,** Obesity or overweight Physical inactivity**,** Poor diet**,** Age (risk increases with age)**,** Ethnicity (higher prevalence in certain ethnic groups [7].

Complications: Uncontrolled diabetes can lead to serious complications, including: Heart disease and stroke**,** Kidney disease (nephropathy)**,** Nerve damage (neuropathy)**,** Eye damage (retinopathy)**,** Foot problems and infections**,** Skin conditions and Hearing impairment [7].

Prevention and Management

Preventing and managing diabetes involves: Maintaining a healthy diet and weight, engaging in regular physical activity, monitoring blood glucose levels, Taking prescribed medications or insulin, Regular check-ups and screenings for complications [7].

Definition: Tuberculosis (TB)

Tuberculosis (TB) is a potentially serious infectious disease caused by the bacterium Mycobacterium tuberculosis. It primarily affects the lungs but can also impact other parts of the body, such as the kidneys, spine, and brain [9].

Introduction

TB has been a significant public health issue for centuries, historically known as "consumption" due to its wasting effects on the body [10]. Despite advances in medical science, TB remains a leading cause of death from infectious diseases worldwide [11].

Overview

TB is an airborne disease that spreads through droplets released into the air when an infected person coughs, sneezes, or speaks [12]. It can be latent (inactive) or active [9]. Latent TB is not contagious and presents no symptoms, while active TB causes symptoms and can be spread to others [9].

Background

TB has a long history, with evidence of the disease found in ancient mummies [10]. The discovery of the TB bacterium by Robert Koch in 1882 was a breakthrough in understanding and treating the disease [10].

Epidemiology

TB is a global health concern, with millions of new cases each year [12]. It is more prevalent in regions with high population density, poor healthcare infrastructure, and high rates of HIV/AIDS [10]. In 2023, an estimated 10.8 million people fell ill with TB worldwide [12].

TB infection begins when Mycobacterium tuberculosis bacteria enter the body and are inhaled into the lungs [10]. The immune system may initially contain the infection, leading to latent TB [13]. If the immune system fails to control the bacteria, the infection progresses to active TB [13].

Pathogenesis

The pathogenesis of TB involves the bacteria evading the immune system and multiplying within the host [10]. The bacteria can form granulomas, which are clusters of immune cells that attempt to contain the infection [10]. Over time, these granulomas can break down, leading to tissue damage and the spread of the bacteria [10].

Pathology

The pathology of TB includes the formation of tubercles (small nodules) in the lungs, which can become necrotic and form cavities [10]. These cavities can lead to the spread of the bacteria to other parts of the body and cause systemic symptoms [10].

Integrated Care Challenges: Coordinated Screening: Ensuring both diabetes and TB are screened and diagnosed accurately.

Patient Compliance: Managing treatment adherence for both conditions can be challenging.

Healthcare Infrastructure: Strengthening healthcare systems to handle dual diagnosis and treatment. The intersection of Diabetes Mellitus (DM) and Tuberculosis (TB) is a critical area of research, given the significant impact both diseases have on global health [14].

Diagnosis

1. Latent Tuberculosis Infection (LTBI) and DM: Recent studies have shown a positive association between DM and LTBI [15] Individuals with DM are at a higher risk of LTBI progressing to active TB [16]. Improved diagnostic tools like the Interferon-Gamma Release Assay (IGRA) and Tuberculin Skin Test (TST) are being used to detect LTBI in diabetic populations [16].

2. HbA1c Testing: Research indicates that using HbA1c for diagnosing diabetes in TB patients provides more accurate results compared to self-reported diabetes [16].

3. Diagnostic Challenges: Diabetic patients may have atypical presentations of TB, making diagnosis difficult [17]. Additionally, the immune response in diabetic patients can affect the accuracy of TB tests like the Tuberculin Skin Test (TST) and Interferon-Gamma Release Assays (IGRAs) [14]

4. Screening: Regular screening for TB in diabetic patients is crucial but often underutilized due to resource constraints and lack of integrated care systems [14].

Treatment

1. Integrated Care: The World Health Organization (WHO) emphasizes the importance of integrated and patient-centered care for individuals with both TB and DM [14]. This includes coordinated treatment plans to manage both conditions effectively [14].

2. Drug-Resistant TB and DM: Studies have found that DM is a risk factor for adverse outcomes in drug-resistant TB (DR-TB) and multidrug-resistant TB (MDR-TB) patients [15]. Controlling hyperglycemia during TB treatment can improve outcomes [15].

3. Drug Interactions: Managing TB treatment in diabetic patients can be complicated by potential drug interactions between anti-TB medications and diabetes medications [17].

4. Adherence: Ensuring adherence to both TB and diabetes treatment regimens can be challenging, especially in resource-limited settings [18].

5. Extended Treatment Duration: Diabetic patients often require longer treatment durations and are at higher risk of treatment failure and relapse [17].

Prevention

1. Collaborative Framework: WHO's Collaborative Framework for Care and Control of TB and Diabetes aims to establish mechanisms for collaboration, detect and manage TB in patients with diabetes, and vice versa [14].

2. Public Health Interventions: Enhanced surveillance and monitoring of the joint burden of TB and diabetes are crucial for effective public health interventions [14].

3. Research Needs: More research is needed to develop effective strategies for the co-management of TB and diabetes, especially in developing countries [18].

Treating tuberculosis (TB) in patients with diabetes presents several challenges at different levels of investigation, treatment, and prevention.

Common Co-morbidities: Co-morbidities can significantly complicate the treatment of both diabetes and tuberculosis (TB).

1. HIV Infection: HIV weakens the immune system, making individuals more susceptible to TB [19] TB is a leading cause of death among people with HIV [19].

2. Undernutrition: Malnutrition impairs immune function and increases the risk of TB [19]. It also complicates the management of diabetes by affecting glucose metabolism.

3. Mental Health Disorders: TB and its treatment can exacerbate mental health issues, such as depression and anxiety, which can interfere with treatment adherence.

4. Chronic Obstructive Pulmonary Disease (COPD): COPD can worsen TB symptoms and complicate treatment due to overlapping respiratory issues.

5. Chronic Kidney Disease (CKD): CKD can affect drug metabolism and clearance, complicating the treatment of both TB and diabetes.

Impact on Treatment

- **Drug Interactions:** Co-morbidities often require multiple medications, increasing the risk of drug interactions and side effects.
- **Treatment Adherence:** Managing multiple conditions can be overwhelming for patients, leading to poor adherence to treatment regimens.
- **Healthcare Coordination:** Coordinated care is essential but often lacking, leading to fragmented treatment and poorer outcomes.

Complications Exacerbated by Diabetes: Diabetes can exacerbate several complications of tuberculosis (TB), making them more difficult to treat.

1. Pulmonary TB: Diabetes increases the risk of developing pulmonary TB and can lead to more severe disease progression [20].

2. Extrapulmonary TB: Diabetes can also increase the risk of TB spreading to other parts of the body, such as the lymph nodes, bones, and central nervous system [20].

3. Drug-Resistant TB: Patients with diabetes are at a higher risk of developing multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) [14].

4. Poor Treatment Outcomes: Diabetes is associated with higher rates of treatment failure, relapse, and death during TB treatment [16].

5. Increased Risk of Infection: Diabetic patients have a weakened immune system, making them more susceptible to TB infection and complications [20].

Case series

Male ward Total Patient 39, Diabetes patients 2

1. 34 years male K/c/o PTB Since 4 YEARS. K/c/o DM Since 4 YEARS. Pt.is on Tab. metformin 500mg bd and Tab. Glimepiride 2MG BD 19.9.24 HGT 268, Sputum GeneXpert 24.9.24 MTB Not Detected, 20.9.24 HIV NR. No HTN/Kidney Disease.
2. 72-year male, K/C/O PTB SINCE 1.5 YEAYS. Cat 1. 2 months back. 8 months back sputum GeneXpert mtb low rifa (s). No HTN/Kidney Disease, K/C/O DM 2 months back on Plain Insulin 10-10-8, HIV NR, 2 months back FBS 546.

Female total patient 13, diabetes 4

1. 50-year female K/c/o PTB on cat 1, since 4 months. With right gross pleural effusion ICD in situ.

KCO DM: 3 months on T. METFORMIN 500MG AND T. GLIMIPERIDE 2MG 1od 15 days back HGT 221
No HTN, Kidney Disease Sputum GeneXpert, fluid cytology awaited

2. 32 years female, PTB 1 month, KCO DM on PI 6-6-6. 15 days, No Htn Kidney disease, Truenaat 1.10.24 MTB detected rifa – Sensitive, HIV NR 5.10 24.
3. 51 years female KCO PTB 1 month, KCO DM:8 years on glynase MF BD, HIV NR No HTN/ Kidney Disease, Culture NO growth
4. 32 years female KCO PTB on cat 1, 2months HB1AC 12.2 KCO DM since 3 years on PI 12-12-10.

HIV NR, Sputum GeneXpert MTB medium RIFA-Sensitive LPA- MTB MEDIUM Rifa, INH -S.

Discussion:

TB and diabetes: The data provided offers a cross-sectional snapshot of patients with concurrent diabetes mellitus (DM) and pulmonary tuberculosis (PTB) admitted to a TB hospital. This case series presents an opportunity to discuss the complex interplay between diabetes and TB, focusing on the increased susceptibility of diabetic individuals to TB, the impact of diabetes on TB management, and the implications for public health.

Background and Clinical Context

Diabetes is a known risk factor for TB due to its immunosuppressive effects, which impair host defense mechanisms and increase the risk of both TB reactivation and relapse. The cases included here exemplify how diabetes affects TB progression and complicates clinical management, especially concerning glycemic control and TB treatment outcomes. Studies suggest that diabetic patients are three times more likely to develop active TB compared to non-diabetic individuals, often resulting in more extensive lung disease, increased bacterial load, and prolonged time to culture conversion.

Case-by-Case Analysis

Male Patients

1. 34-Year-Old Male

PTB for 4 years, DM for 4 years, HGT of 268 mg/dL: Despite being on dual oral anti-diabetic therapy (metformin and glimepiride), this patient's blood glucose remains poorly controlled, which could hinder immune function and response to TB therapy. Although his sputum GeneXpert shows no detectable MTB (Mycobacterium tuberculosis), persistent hyperglycemia may predispose him to TB reactivation.

2. 72-Year-Old Male:

PTB for 1.5 years, DM diagnosed 2 months ago, FBS of 546 mg/dL: This elderly patient has very high fasting blood sugar, managed with plain insulin. A previous GeneXpert test showed MTB low with rifampicin-sensitive status. Poor glycemic control in this case could be due to delayed diagnosis of diabetes or ineffective initial management, highlighting the importance of frequent glycemic monitoring and prompt initiation of insulin therapy in diabetic TB patients.

Female Patients

1. 50-Year-Old Female:

PTB with gross pleural effusion, DM diagnosed 3 months ago, HGT of 221 mg/dL: This patient presents with an additional complication of pleural effusion, requiring an intercostal drain. TB and diabetes together can lead to increased inflammation, making complications like pleural effusion more likely.

2. 32-Year-Old Female:

PTB for 1 month, newly diagnosed DM on plain insulin (6-6-6): Though recently diagnosed with DM, this patient's case exemplifies early intervention with insulin therapy, which is critical in maintaining glycemic control, especially in TB cases where oral agents may be less effective due to fluctuating insulin requirements.

3. 51-Year-Old Female:

PTB for 1 month, DM for 8 years on Glynase MF: Despite prolonged DM, there's no evidence of HTN or kidney disease. However, the chronicity of diabetes may compromise her immune response, slowing down her recovery from TB. Culture results showing no growth suggest a response to TB treatment, but diabetes control remains crucial.

4. 32-Year-Old Female:

PTB for 2 months, HBA1C of 12.2%, DM for 3 years on plain insulin (12-12-10): This patient's high HbA1c suggests poor long-term glycemic control, which could exacerbate her TB infection. The GeneXpert and LPA results show rifampicin and INH sensitivity, yet this drug-sensitive profile requires effective diabetes management to ensure a favorable TB outcome.

Discussion Points

1. Immunological Impact of DM on TB Progression: Diabetic patients, due to impaired cellular immunity, exhibit a greater susceptibility to TB and delayed response to TB medications. Hyperglycemia can impair macrophage and T-cell function, leading to increased bacterial survival and TB persistence, as observed in the glycemic readings of the patients here.
2. TB Reactivation and Relapse Risk: Long-standing diabetes (especially poorly controlled) is associated with a higher risk of reactivation or relapse of TB, particularly in elderly and immunocompromised patients. The 34-year-old male and 72-year-old male

cases represent these risk profiles, with persistent or recurrent TB likely linked to their diabetic status.

3. TB Management in the Presence of Diabetes: For optimal outcomes, a multidisciplinary approach is essential, involving glycemic control alongside TB therapy. Insulin is often preferred for glycemic control in TB-DM patients due to fluctuating glucose levels during the infectious phase, as seen in patients receiving insulin regimens here. The effectiveness of TB treatment can be significantly hindered by poor glycemic control, underscoring the need for adequate insulin therapy and frequent monitoring.
4. Public Health Implications: The co-prevalence of TB and diabetes, particularly in regions with a high TB burden, signals the need for integrated TB-DM management programs. Routine screening for diabetes in TB patients could help in early diagnosis and management, thus reducing the TB burden.
5. Considerations for Future Management: The data emphasizes the need for customized treatment regimens, considering both TB and DM as chronic conditions. Case-specific therapeutic adjustments (e.g., insulin titration, possible drug-drug interaction monitoring) could potentially improve outcomes. Further research might explore if standard TB treatment durations suffice or if extensions are needed in poorly controlled diabetics to prevent relapses.

Conclusion

This case series highlights the interrelated challenges of managing TB in diabetic patients. The complex interaction between TB and DM requires careful management, especially of hyperglycemia, to avoid delays in TB treatment response, reactivation, and potential complications. Optimizing both glycemic control and TB therapy through integrated care models could significantly improve patient outcomes.

Summary

This case series presents a cross-sectional analysis of patients with concurrent tuberculosis (TB) and diabetes mellitus (DM) admitted to a TB hospital. Among the 39 male and 13 female patients in the ward, 2 male and 4 female patients had both TB and DM. Each case shows the heightened clinical complexities when these two conditions coexist. Poor glycemic control was prevalent, with most diabetic patients requiring either insulin or oral antidiabetic medications, and many displaying persistently high glucose levels. Key observations include the impact of diabetes on TB reactivation risk, delayed immune response, and a tendency for complications, such as pleural effusion.

Conclusion

The coexistence of TB and diabetes poses significant challenges to patient management and treatment outcomes. Diabetes increases the risk of TB reactivation, slows response to TB treatment, and predisposes patients to additional complications. The cases analyzed highlight the necessity for integrated care that includes intensive glycemic monitoring and tailored TB therapy to enhance recovery and prevent relapse. Improved TB-DM care models, involving both endocrinology and pulmonology expertise, could help mitigate the public health impact of this comorbidity and improve patient outcomes.

Message for the Community: Social and Economic Impact

Tuberculosis (TB) and diabetes mellitus (DM) together have significant social and economic repercussions, particularly for those in vulnerable communities. TB is a disease that impacts productivity, leading to job loss and financial strain, especially for families with primary earners affected. Diabetes, when coupled with TB, further complicates health and increases healthcare costs, draining household resources. Community awareness is crucial, encouraging regular screening for diabetes among TB patients and raising understanding of the TB-DM connection. Empowering communities through education and accessible healthcare services can prevent disease spread, ensure early intervention, and reduce the social and financial burden on families.

Message for Future Perspectives or Way Forward

Moving forward, it's vital to integrate TB and diabetes management within healthcare systems to improve patient outcomes and reduce the TB burden. Screening for diabetes in TB patients, ensuring glycemic control, and adopting a multidisciplinary approach can greatly impact the success of TB treatment. Community-based support, greater health literacy, and policy initiatives focused on TB-DM co-management can create a sustainable, comprehensive model. Investment in research on TB-DM interaction, alongside expanding resources for low-income patients, will help mitigate the combined impact of these diseases and improve long-term health outcomes.

Message to the medical fraternity and healthcare workers

For healthcare professionals and particularly those who develop TB in their later years, often with diabetes, this message is one of caution and encouragement. Older age and chronic conditions like diabetes increase vulnerability to TB reactivation. Healthcare workers should take preventive measures, like regular screenings, vaccinations, and adherence to infection control practices. They should also prioritize their own health and seek early intervention when necessary. As a dedicated medical community, understanding the double burden of TB and diabetes not only strengthens our response to these diseases but also emphasizes the need for self-care, ultimately enhancing our ability to serve our patients and society effectively.

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