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Original Article

Burgeoning double burden of tuberculosis and diabetes in India: Magnitude of the problem – Strategies and solutions

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ABSTRACT

Background: India reportedly has a fifth of tuberculosis burden worldwide. There is a strong epidemiological evidence for an association between tuberculosis and diabetes mellitus (DM). Patients with diabetes are at increased risk of developing active TB, and have higher rates of treatment failure and death, even when placed on appropriate therapy.

Objective: We sought to perform a comprehensive review of the convergence of these two epidemics in India and strategies for co-management.

Methods: We performed a literature search of current knowledge including observational studies and clinical trials and other position papers, from databases such as, Medline, Embase, worldwide web and other repository of WHO and other international and national reports with the following search terms: tuberculosis, diabetes mellitus, co-epidemics, India, management and strategies.

Results: Combined results from several cohort studies suggest that DM increases the risk of active TB by approximately three fold. This association between TB and DM will become more poignant in the coming years, as the prevalence of diabetes is expected to increase substantially in the developing nations. We describe the epidemiology of each disease in detail, and its convergence. We also discuss the challenges in co-management of TB and DM, including the role of nutrition. The article investigates the barriers, gaps in research data and opportunities to tackle this problem at the policy and grass roots level. The newly evinced approach of public private partnerships with market based partnerships for health (MBPH) need to be explored.

Conclusions: Treatment of diabetes as a co-disease presents an opportunity for collaboration with the current TB control efforts to be expanded. Considering the existing public health infrastructure and the overarching private sectors' role in the co-management, standard

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treatment guidelines which incorporate the core issues in the bi-directional screening and cost-effective management of TB and diabetes need to be developed and enforced.

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1. Introduction

India reportedly has the largest burden of TB cases in the world. According to the World Health Organisation (WHO) estimates of 2009, there were 1.6–2.4 million TB cases in India accounting to one fifth (21%) of the TB cases worldwide.¹ Simultaneously, India also has increasing number of diabetics, more than in any other country of the world.^{1,2} As estimated by WHO, India had 32 million diabetic subjects in the year 2000 and this number would increase to 80 million by the year 2030.² Diabetes has been regarded as one of the key risk factors for TB because of the interaction between the two diseases. More and more research data is reporting the deleterious effects of diabetes on TB associated pathogenesis, infection control and management and leading health experts are expressing their grave concern on the merging epidemic of TB and diabetes in India.³ Combined results from several cohort studies suggest that DM increases the risk of active TB by approximately three fold.³ Our objective is to perform a comprehensive review of the convergence of these two epidemics in India and strategies for co-management.

1.1. Methodology

We performed a systematic literature review of current knowledge including original research such as observational studies and clinical trials, other position papers, from electronic databases such as, Medline, Embase, worldwide web and other repository of WHO and other international and national reports published between 1990 and 2012 with emphasis on the last ten years. We used the following search terms: tuberculosis, diabetes mellitus, co-epidemics, India, management and strategies. We synthesized the literature in the following subheads: as overall description of the epidemiology of each disease and then the information on combined epidemiology; issues in co-management; available services and magnitude of the problem; barriers, challenges and gaps; and co-management, strategies and way forward.

2. Results

The following are the results of the literature review as encompassed in the sub-headings for the review.

2.1. Describing the burden of DM and TB – globally and in India

2.1.1. Epidemiology of TB

Among infectious diseases, mortality from TB continues to be high. In 2010, TB was the second leading cause of death from an infectious disease worldwide (after HIV which caused an estimated 1.8 million deaths in 2008).¹ There were an estimated 8.8 million incident cases of TB globally in 2010. Most of

the estimated number of incident TB cases occurred in Asia (59%) and Africa (26%) with India having the highest number (2.0 million–2.5 million), followed by China (0.9 million–1.2 million). Therefore, India alone accounted for an estimated one quarter (26%) of all TB cases worldwide. Of these 8.8 million TB cases, about 1.1 million (13%) were attributed to HIV. These statistics are alarming in spite of the fact that globally, the absolute number of incident TB cases per year has been falling since 2006 and the incidence rate (per 100 000 population) has been falling by 1.3% per year since 2002.⁴

As per the national tuberculin survey carried out in India from 2000 to 2003, the annual risk of TB infection (ARTI) was 1.5% and the incidence of new smear-positive TB cases was estimated as 75 new smear-positive cases per 100 000 population. The annual risk of infection was higher in urban areas (2.2%; 1.8%–2.6%; 95% Confidence Interval) than in rural areas (1.3%; 1.0%–1.5%) and higher in the north (1.9%; 1.3%–2.5%) and west (1.6%; 1.0%–2.2%) than in the east (1.3%; 1.0%–1.6%) and south (1.0%; 0.7%–1.4%).⁵ As per reports, an estimated 40% of the Indian population is infected with TB bacillus. The prevalence of TB had been estimated at 3.8 million bacillary cases for the year 2000, by an expert group of Government of India. However the recent estimate by WHO gives a prevalence of 3 million.⁶ As per 2009 data, the prevalence rate of all forms of TB in India was 249 per 100 000 population and the death rate (from all forms of TB excluding HIV) was estimated at 23 per 100 000 population.⁷ On a national scale, the high burden of TB in India is illustrated by the estimate that TB accounts for 17.6% of deaths from communicable disease and for 3.5% of all causes of mortality (WHO, 2004). In 1997, India Revised National Tuberculosis Control Programme (RNTCP) on lines of the internationally recommended DOTS strategy. Since its inception, RNTCP has achieved a treatment success rate of >85% and has consistently managed to maintain the New Sputum Positive (NSP) case detection rate of >70%. As per the latest RNTCP status report (2011) the case fatality rate has remained less than 5% for new cases registered under the programme.

Management of TB/HIV co-infection has been widely understood to be an important factor in TB control. India is the third highest HIV burden country and TB is one of the commonly occurring opportunistic infections of HIV.⁷ Thus, TB mortality could well be influenced by the TB/HIV co-infection, especially in the high HIV burden states of the country. It has been estimated that in 2007, about 4.85% of the incident TB cases in India were HIV-positive. Multi-drug resistance and extensive drug resistant cases add to the growing scourge of the disease. In absolute terms, in 2008, India had 99 000 (range 79 000–120 000) estimated cases of MDR-TB. A large scale population based survey in the state of Gujarat and Maharashtra has indicated multi-drug resistance levels of 3% among new TB cases and 12–17% among previously treated TB patients. High mortality from tuberculosis has serious socio-economic impact affected by high prevalence in the most productive age group of 15–54 years. Almost 70% of TB patients

are among the ages of 15 and 54 years of age. While two thirds of the cases are male, TB takes a disproportionately larger toll among young females, with more than 50% of female cases occurring before 34 years of age. The direct and indirect cost of TB to India amounts to an estimated \$23.7 billion annually.⁷

TB treatment and control efforts are negated by several risk factors which can be broadly classified as biomedical such as HIV infection, diabetes, tobacco, malnutrition, silicosis, and malignancy; environmental (indoor air pollution, poor ventilation) or socio-economic (crowding, urbanization, migration, poverty).⁷ While we discuss the merging epidemics of TB and Diabetes in the Indian context, it is essential to understand the epidemiology of diabetes in India and worldwide.

2.1.2. Epidemiology of diabetes

As per the International Diabetes Federation (IDF) Diabetes atlas,⁸ 366 million people had diabetes in 2011 and this number is expected to rise to 552 million by 2030. In 2011, diabetes caused 4.6 million deaths and accounted for at least USD 465 billion dollars in healthcare expenditures. The greatest numbers of diabetics are in the 40–59 years of age and both sexes are equally affected. Nearly 50% of the cases are undiagnosed. The global prevalence of diabetes among all age groups was estimated to be 2.8% in 2000 and will reach 4.4% in 2030.⁸ Increase in the proportion of people >65 years of age appears to be the most important demographic change to impact diabetes prevalence across the world.

As per recent IDF data, 61.3 million Indians had diabetes in 2011 and this number is projected to rise to 101.2 million in 2030, making it the country with the second highest number of people with diabetes, after China. The total number of deaths attributed to diabetes in India in 2004 were 109 133 and the number of DALYs lost in the same year was 2 263 163 as published by Indian Council of Medical Research (ICMR) 2006 in their assessment of burden of non-communicable diseases.⁹ Literature suggests that Indians have high insulin resistance than other population groups particularly Caucasians, and develop DM at a much younger age.^{10–12} The past two decades have seen an increasing prevalence of type 2 diabetes in both urban and rural areas of the country with prevalence in urban areas being as high as 12%.^{13,14} There has been a sharp increase in prevalence especially in the South Indian cities like Hyderabad (16.6%), Chennai (13.5%) and Bangalore (12.4%), as per the National Urban Diabetes Survey (NUDS) conducted in six large Indian cities in 2001. The prevalence of type 2 diabetes has been on a rise in the peri-urban/urban slum areas across different parts of the country. According to a national NCD risk surveillance, the presence of self reported diabetes was found to be 1.8% in Delhi, 2.3% in Ballabgarh, (North); 6.6% in Chennai and Trivandrum (South); 1.4% in Dibrugarh (East) and 0.6% in Nagpur (Central India).¹⁵ Diabetes prevalence in rural areas has also been catching up with urban estimates as per trends (rural diabetes prevalence increased almost three fold (from 2.4 to 6.4%) in the space of just 14 years).^{16,17} According to Prevalence of Diabetes in India Study (PODIS), estimates based on ADA and WHO criteria, the prevalence of Diabetes in rural areas has been found to be 1.9% and 2.7% respectively.^{18,19} Often lack of awareness and limited availability of quality healthcare facilities in rural areas results in late recognition and rapid progression of the disease, which is often disabling or fatal.^{18–21}

2.1.3. Combined epidemiology of DM and TB and challenges Increasingly, tuberculosis patients are being diagnosed with diabetes and so are diabetes patients with tuberculosis. Of the biomedical risk factors, diabetes poses substantial risk as evidence suggests that the emerging epidemic of diabetes is fanning the spread of TB. A community-based study from South India, as well as multiple studies worldwide has shown diabetes to be an independent risk factor for tuberculosis. Modelling has suggested that diabetes accounts for 15% of all tuberculosis and 21% of smear-positive TB.⁷

Studies globally, have reported the co-epidemic of diabetes and TB in different population settings suggesting that diabetes mellitus increases the risk of active TB.^{3,21} After adjusting for gender and socio-economic factors, in lower income countries, individuals with diabetes are more likely than non-diabetics to have TB. Based on a longitudinal country level analysis the authors.²² also reported that increases in TB prevalence and incidence over time were more likely to occur when diabetes prevalence also increased, suggesting that countries with large population (India, Peru and the Russian Federation) having prevalent tuberculosis and projected increases in diabetes are of particular concern.

Many studies reported that subjects with diabetes were at three fold higher risk of developing TB.^{23,24} In addition, studies that screened for DM among TB patients reported a wide range of DM prevalence among TB patients, ranging from 1.9% to as high as 35%.^{23,24} A recent study conducted in 2011 reported the prevalence rates of diabetes and pre-diabetes to be 10.4% and 8.3%, respectively, among the general population of Tamil Nadu, South India.²⁵

In urban areas, increased prevalence of diabetes in associated with 15.2% greater smear-positive tuberculosis incidence compared to rural areas.²⁴ The study also predicted that in India 18.4% (12.5%–29.9%) of people with pulmonary tuberculosis (both smear-positive and smear-negative) have diabetes, and that in the smear-positive group diabetes prevalence is 23.5% (12.1%–44%).²⁴ Also, in a recent study to determine diabetes prevalence among a cohort of TB cases registered under Revised National Tuberculosis Control Programme (RNTCP) in selected 5 TB units in 3 districts in Tamil Nadu, India, using glycosylated haemoglobin A1C and Oral Glucose Tolerance Test (OGTT), it was found that DM prevalence was 25.3% (95% CI 22.6–28.5) and that of pre-diabetes 24.5% (95% CI 20.4–27.6).²⁶

2.2. Issues in co-management of TB and DM

As discussed in the earlier section, there are a number of barriers that collectively affect co-management of TB and diabetes. While tuberculosis patients are largely managed by the government healthcare system, diabetes patients are mostly handled by private practice. Integrating screening and care requires cooperation between the two sectors and dual action from both sides of providers.

In persons with diabetes there is gross impairment in chemotaxis, phagocytosis, activation and antigen presentation by alveolar macrophages, monocytes and T-lymphocytes and there is decreased phagocytosis by polymorphonuclear leukocytes as well.^{27–30} This impairment is correlated to the degree of hyperglycemia.³⁰ There are other impairments in

the cytokine production and natural killing of the pathogen (in this case *Mycobacterium tuberculosis*). For instance, production of interferon γ , interleukin-12 and intracellular nitric oxide in response to challenge with *M. tuberculosis* bacillus is decreased substantially in diabetic animal models.³¹ Thus, overall cell-mediated immunity, which is of paramount importance in protection against *M. tuberculosis* is grossly impaired in persons with diabetes.²⁷

The issues in co-management of TB and diabetes are reflected in the dichotomous population characteristics which paradoxically affect the co-morbidity. There are a number of barriers to effective treatment and prevention of TB and diabetes. These barriers collectively affect co-management of TB and diabetes. While tuberculosis patients are largely managed by the government healthcare system, diabetes patients are mostly handled by private practice. Integrating screening and care requires cooperation between the two sectors and dual action from both sides of providers.

The radiographic presentation of TB in diabetes may be atypical in persons who are co-affected. There is increased involvement of lower lobe especially in persons > 40 years of age,^{32–34} and multi-lobe involvement with multiple cavities is also noted in diabetics as compared to non-diabetics.^{34,35}

Overall time to sputum culture negativity is prolonged in persons with diabetes as compared to non-diabetics.^{36–40} Latter is postulated be due to higher mycobacterial burden in diabetics as compared to controls.^{41,42}

Almost all oral hypoglycemic agents are metabolized by the cytochrome P450 systems in the liver. Rifampicin, which is the main anchor drug in the management of tuberculosis, is a powerful inducer of the all the P450 systems, including CYP3A4, (where most drugs are metabolized). Due to this inducer effect, there is substantial reduction in the area under the curve of sulfonylureas, thiazolidinediones and the newer hypoglycemic drugs, thus worsening the glycaemic control, which in turn impairs the ability to meet challenge of the pathogen i.e., *M. tuberculosis*.⁴³ In addition, insulin dosages need to be increased in persons on rifampicin.²⁴ Thus closer monitoring of glycaemic control is required during TB treatment among diabetics.

On the other hand, there is reported reduction of 53% in rifampicin concentration with co-administration of oral hypoglycemic drugs, raising concern for treatment failure and development of drug resistance.⁴⁴ Thus there is a need to do therapeutic drug level monitoring in persons co-affected with diabetes and tuberculosis.

Overall experts advocate use of insulin during the first intensive phase of TB management with co-existing DM, followed by oral hypoglycemic drugs, in the maintenance phase of TB treatment. However, metformin has to be used with caution due to concomitant liver injury.

2.3. Available services: magnitude of the problem

2.3.1. Existing services for TB

India has a central tuberculosis prevention and treatment services program - The Revised National Tuberculosis Control Programme (RNTCP) based on the internationally recommended DOTS strategy since 1997. The programme aims to achieve and maintain cure rate of at least 85% among New Sputum Positive (NSP) patients and case detection of at least

70% of the estimated NSP cases in the community. In 2006, the programme was expanded throughout India and had reached over a billion population (1164 million) in 632 districts/reporting units. In 2010, the programme reached out to 1.52 million patients for treatment. The programme's current focus is on ensuring "universal access" to good quality early diagnosis and treatment for all TB patients, regardless of the care provider. Since its inception, RNTCP has initiated more than 12.8 million patients on treatment, thus saving nearly 2.3 million additional lives. In 2010, the NSP case detection rate rose to 86% and the treatment success rate went up by 72%.⁶ The success in case detection can be attributed to the nation-wide network of laboratory services encompassing over 13000 designated sputum Microscopy Centres (DMCs), that are supervised by Intermediate reference laboratories (IRL) at state level, and National Reference laboratories (NRL) & Central TB division at the national level. New testing and treatment modalities have been introduced in the DOTS plus programme to cater to the rising incidence of MDR and XDR tuberculosis.

Healthcare seeking in India leads patients to their nearest available healthcare provider predominantly from private sector, and a large proportion of health spending is from out-of-pocket.⁴⁵ On similar lines, almost half of the TB patients are highly likely to visit private healthcare for diagnosis and treatment of TB. A recent population survey based on 64th round of NSS data reported that the proportion of patients attending private outpatient facilities for TB care was marginally higher than for government facilities.⁴⁵ However, a higher percentage of patients attended public health facilities for in-patient care. Women and individuals from higher educational background were more likely to seek care at a private facility. Also, more urbanites attended private health facilities vis-a-vis their rural counterparts.⁴⁶ However, the private sector suffers from its own infirmities and lacunae. Care provided by the private sector lacks adherence to national or international standards of care and resulting in case mismanagement.^{47–50} The private facilities have exhibited poor handling of cases leading to delayed diagnosis, inadequate treatment, acquired drug resistance and high rate of relapse - highlighting the need for regulation of the private sector with respect to case management and the widespread irrational use of first-line and second-line anti-TB drugs.⁵¹ In 2006, the total market of first-line anti-TB drugs in India was USD 94 million. The public sector purchased drugs worth \$24 million while the private sector accounted for the remaining, highlighting the important role of the private sector in TB treatment.⁵⁰ The scourge of this poor practice is reflected in India accounting for over a fifth of the global MDR-TB burden, with indicators showing a rising trend.⁵² Upon seeking care from the private sector, most patients approach a government facility while some discontinue treatment. The prevailing stigma for TB diagnosis persists as reflected in the lack of uptake of the public health services for TB treatment. To streamline tuberculosis prevention and treatment services, the RNTCP has now involved private practitioners throughout the country through the public private mix model. Collaboration of the private and public sector through the PPM model can go a long way in resolving some of the issues and challenges of TB control in India.⁵² Many non-

governmental organisations have also been roped in for advocacy, communication and social mobilisation (ACSM) as well as for bridging prevention and treatment services at the grass roots.

2.3.2. Existing services for diabetes

Following the rising burden of diabetes and other lifestyle diseases in the country,⁵³ the Non-Communicable Diseases program aims at promoting healthy lifestyle through massive health education and mass media efforts at country level and provisions opportunistic screening of persons above the age of 30 years; establishment of Non-Communicable Disease (NCD) clinics at CHC and district level; and development of trained manpower and strengthening of tertiary level health facilities. It is expected to screen over 70 million adult population (30 years & above) for diabetes and hypertension, early diagnosis of NCDs and treatment at early stages. To fill the gap in the health delivery system, about 32 000 health personnel would be trained at various levels to provide opportunistic and targeted screening, diagnosis and management of NCDs. Integration of NCD interventions with the existing National Rural Health Mission (NRHM) framework and facilities at the state level is one of the primary aims of the programme. The launch of the programme is a very important and positive step towards NCD interventions in the country. However, its outcome and impact needs to be carefully monitored and evaluated in the times to come.

Management of diabetes requires establishing a continuum of care involving preventive, diagnostic and therapeutic services.¹⁷ Care-seeking for diabetes in India is hugely variable with differential costs and outcomes. The diabetics either visit the government doctors serving a public health facility of municipal, district, state or national level (such as health centre, district or a teaching hospital) or visit private clinics, nursing homes, hospitals, general practitioners and specialists.^{54,55} Treatment at a public facility is either low cost or free of charge but is often marred by limited infrastructure and resources and high patient volumes; whereas, the private clinics offer services at a huge out-of-pocket cost which leads to financial drains in case of prolonged treatment and care. Yet, evidence suggests that low and middle income group of patients prefer private hospital care.³⁹ Some other important factors that determine the choice of provider as well as intention to seek treatment are awareness, knowledge and resources available with care seeker. Some studies have looked at the perceptions and attitude of patients and providers towards treatment and care and the overall impact on delivery of care.⁵⁶

Reported clinical outcomes of diabetes management in India have been largely poor and sub-optimal.^{57–59} The lack of adequate health infrastructure, facilities, equipment, drugs, and trained healthcare personnel adds to the woes along with poor awareness and knowledge of type 2 diabetes among the masses.^{60–62}

Indian healthcare system also suffers from physical and financial (particularly private care) inaccessibility issues with seventy percent of the population in rural areas where access to primary healthcare system is limited and often inadequate. Lack of proper transportation and ambulance services to the regional health centres for further management of diabetes is a considerable barrier in diabetes care provision.⁶⁰ Inadequacy

of trained workforce is another problem that limits efficient healthcare provision, especially in the rural areas. Given the deficiencies of the current healthcare infrastructure and resources in rural areas, recruiting trained personnel for guidance on nutrition, lifestyle changes, family support and counselling, treatment, and appropriate referrals will be a herculean task.

2.4. Need for bi-directional screening: barriers, challenges and gaps

To improve the overall outcomes of TB and DM it is important that diabetic patients attending both government and private providers should be screened for symptomatic TB and this will be done at every visit. Similarly, in the patients diagnosed with any form of TB a history of diabetes and screening for diabetes to be done. The screening for diabetes can be done using measurement of a simple postprandial or random or fasting glucose followed by gold standards such as glycosylated haemoglobin (HbA1C), and 75 g 2 h, Oral Glucose Tolerance Test (OGTT). However, considering the enormous pressures put on the already over-stretched public health systems in resource limited settings, it may be impractical to perform these sophisticated tests and/or follow the glycaemic control rigorously.

China has taken the lead in registering success with the TB-DM bi-directional screening. China had piloted a 9-month project that tested the implementation of bi-directional screening of TB/DM in September, 2011.^{63,64} The project was evaluated in May 2012. This can be replicated in India considering the lesson learnt from the China model.

2.4.1. Barriers/challenges/gaps in treatment provision of diabetes

Diabetes care in India often suffers due to lack of adequate infrastructure inclusive of clinical and support services capable of offering a continuum of care. Wherever available, support services are expensive, often leading to the patient's unwillingness to pay for them. There is hardly any insurance available for diabetes, which results in high out-of-pocket costs spent in private care. The country has absolute paucity of personnel trained to tackle the surge of increasing non-communicable diseases (NCDs). Availability of diabetologists are limited and the general practitioners are overburdened, treating acute illnesses—fever, infections, injury and other trauma left with a smaller amount time and interest towards a chronic illness like diabetes. Inadequate numbers of nurse educators and dieticians and no podiatrist makes diabetes care-seeking and care-giving, a difficult task.⁵⁶ Management of chronic diseases needs heightened commitment and responsibility both on the part of patient and the provider. It is hard to expect the already overburdened doctors to single-handedly manage diabetes and its complications.

The provider's perception and attitudes along with their competency to treat plays a crucial role.⁵⁶ In India, diabetes management is largely the domain of general care practitioners and consultant physicians; however specialist care is on the rise with availability of diabetologists, endocrinologist especially in the urban areas. As opposed to the therapeutic care, where a clinician reserves most of the responsibility for intervention and care, chronic disease management requires

the ownership, understanding and participation from the patient and each case must be tackled using a friendly and counselling orientated approach. The doctors need to understand the pharmacological regimen and advice the patient on preventive solutions through maintenance of exercise and diet. Careful follow-up and reinforcement is equally important. Thus, what is required is a comprehensive care package where each diabetic patient is registered in an ongoing treatment and prevention programme.

2.4.2. Barriers/challenges/gaps in treatment provision of TB
Treatment of tuberculosis in India is governed by a number of socio-economic and healthcare factors which interfere with proper management of the disease and adherence to treatment regimen. Study has shown that people, especially those from low-income backgrounds face significant barriers towards treating and curing their illness.⁶⁵ There are economic barriers (those arising out of complex healthcare seeking pathways, high opportunity costs from utilizing government healthcare facilities as well as high out-of-pocket costs when care is sought from a private provider); geographic barriers (pertain to distance from TB treatment services); socio-cultural (stigma and lack of knowledge about TB and available services for TB) and health system barriers (lack of health system responsiveness). Apart from this, there are behavioural barriers which often contribute to diagnosis delay and treatment compliance. Motivation, perceived severity of disease, and self efficacy were found to be the key differences among compliers and non-compliers of TB treatment.⁶⁶

A significant proportion of the population still shuns the existence of TB from their neighbours and relatives. As per National Family Health Survey (NFHS) III, 15.6% urban and 17.2% rural households would want to keep a family member's TB secret from their neighbours. Twenty percent respondents with nil education and 18.6% respondents belonging to the lowest wealth index responded in a similar manner. Studies worldwide have reported that women bear the highest burden of stigmatizing behaviours.⁶⁷ Also it is well-established that health seeking behaviour to access care with AYUSH (Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy) and/or spiritual providers adds a considerable delay in diagnosis and missed opportunities for timely care. As described in an earlier section, the healthcare system and the DOTS treatment regimen is in itself not very effective in delivering patient friendly services. The DOTS program lacks patient-centred approaches resulting in limited access and acceptability among the end users.⁵²

2.4.3. How nutrition affects diabetes and tuberculosis?

Body mass has a distinct relationship with both diabetes and TB. Low body mass and diabetes have been treated as distinct risk factors for TB; alternatively, diabetes is more frequent among people who are overweight. As such, concurrent over and under nutrition is a widespread problem in developing countries.⁶⁷ Other than the nutritional profile of an individual, tuberculosis is also impacted by socio-demographic and environmental factors such as poverty, urbanization, migration and overcrowding.⁶⁸ Review of six studies by Lönnroth et al. concluded that there is a log-linear inverse relationship between TB incidence and BMI, within the BMI range

18.5–30 kg/m².⁶⁹ While diabetes enhances the risk of pulmonary tuberculosis, a greater body mass index is protective.

Tuberculosis incidence in India varies by age and sex and differs between rural and urban areas. It changes with age directly and indirectly through its effects on BMI and DM as risk factors. A recent study examined the consequences for TB epidemiology and control of changes in BMI, diabetes, population age structure and urbanization by studying a combination of nutritional and demographic data for over a decade (1998–2008) in relation to TB incidence in two contrasting countries - India (high TB burden) and Korea (low TB burden).⁷⁰ This study estimated that the strongest adverse effect on TB incidence per capita in India was the fall in BMI (from 21.3 to 20.9 kg/m²) among men living in rural areas (85% in 2005). Due to the coinciding over and under nutrition among different subsets of the population, TB incidence in India would have increased (2.9% increase in annual TB incidence) both because of falling BMI in one part of population and because of the overall rise in diabetes prevalence. The study concluded that the dynamics between BMI, TB and DM resulted in an extra 0.90 million cases among people with diabetes between 1998 and 2008. Thus overall there is increase in cases of TB and DM.

2.5. Co-management of the TB-DM epidemic – strategies and way forward

Having described the catastrophe of this emerging co-epidemic in the above sections, this section highlights the strategies and collaborative framework that must be adopted for prevention, control and management of the dual epidemic of diabetes and tuberculosis.

In recent times, there has been a significant thrust placed on the burgeoning dual epidemic of TB and diabetes both globally and in India. Given the absence of international guidelines for joint management of tuberculosis and diabetes, in 2011 WHO and the International Union Against Tuberculosis and Lung Disease (the Union) came up with the provisional collaborative framework for co-management of TB and diabetes. The framework is based on the evidence compiled from systematic reviews and existing guidelines on the diagnosis and management of TB and diabetes. The framework is expected to serve as a guide to national programmes, clinicians and others engaged in care of patients and prevention and control of diabetes and TB on how to establish a coordinated response to both diseases, at organizational and clinical levels.⁷¹ India too has been waking up to the emergent epidemic. It is only in 2011 that the RNTCP annual report has for the first time regarded diabetes as an important risk factor for TB. As described earlier, the Indian government has come up with a national NCD management program. The private sector too has started advocating and taking keen interest in tackling the dual epidemic.

As understood from the combined epidemiology of TB and Diabetes, diabetes can worsen clinical course of TB and TB can worsen glycaemic control in people with Diabetes. Early diagnosis (of patients having either or both conditions by two-way testing), careful clinical management as well as provision of optimal care within a healthcare service continuum could be an important step in curtailing this dual

epidemic. Focussing on the private sector (health and non-health providers) while establishing horizontal and vertical linkages with the public sector could yield a best possible start given the fact that 75–80% of the Indian population seeks care at the private provider level. This holds true for both diabetes and tuberculosis. Public–private partnerships in health have the potential to provide an immense thrust to the public health outcomes.⁷² Some successful examples exist within the Indian context. A literature review of 14 public–private mix projects under the RNTCP concluded that the case notification rates for TB were higher after implementation of a public–private mix project. It was found that these projects maintained acceptable treatment outcomes. Corporate based and non-governmental organisations served as the main source of service provision.⁴⁷ Another review published by the WHO revealed that the potential for public private partnerships in early case detection of TB, especially favouring the pro-poor needs to be exploited more rigorously while involvement of a wide variety of private players needs to be brought in.⁵² The experience and lessons of the DOTS PPM mix collaboration can serve as a stepping stone to forge public private partnerships for co-management of the dual epidemic. Moreover, the optimal follow-up and treatment of TB and DM co-affected patients needs to be better studied and

defined. Thus there is an emergent need for education of the providers and formulating standard guidelines for the co-management of TB and DM. The current RNTCP guidelines make a mention for random blood sugar testing as a means to screen for diabetes among other screening tests. However, the challenges of the co-management of diabetes with TB are not addressed in the current guidelines and form a severe short-coming not only for addressing diabetes but other co-morbidities as well.⁶⁵

Market based partnerships for health which has been developed successfully for family planning and other such services could be a winning strategy wherein the private provider network within and outside DOTS is strengthened to diagnose, treat and manage diabetes and tuberculosis simultaneously and with equal priority. Private providers which can be possibly roped in the network include general practitioners (MBBS doctors); AYUSH practitioners; druggists and chemists; pathology laboratories; diagnostic centres and non-governmental organisations (NGOs). Each of these providers can become important stakeholders in the private provider network and can be encouraged and capacitated to provide different services under the network. The box below and the Fig. 1, demonstrates roles that each of these private providers and different stakeholders could uptake.⁷³

Fig. 1 – Co-management of tuberculosis and diabetes through public private provider network – A conceptual framework.

Provider Roles in PP Network

- **MBBS Doctors** – diagnosis, treatment and referral for complications to the RNTCP centres/diabetes clinics and referral hospitals.
- **AYUSH Doctors** – identification of symptomatics, glucose testing, collection of sputum and referral to the RNTCP centres/Allopathic Doctors in the network for diagnosis and treatment
- **Druggist, chemists and others** – referral and DOTS provision, provision of testing equipments and reservoir of patient education materials
- **Laboratories** – Intervention cell microscopy centres (ICMC) for sputum examination and diagnosis and glucose testing
- **NGOs** – DOTS providers and referral units to coordinate with the existing RNTCP centers, screening camps, preventive check ups

It may be based on the strategies where Private Providers who agree to participate in the RNTCP and the National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS), diabetes management may be given incentives such as tax-waivers, and/or provision of discounted essential services such as electricity and water, besides increased visibility and popularity in the community in terms of supporting talks, and other such forums for knowledge dissemination, etc. The supply of better services can be backed by enhanced demand for TB/DM package services through strategies like patient education and preventive screening for TB and diabetes, better treatment opportunities, management of complications and consistent follow-up to be coupled with supportive services of a dietician, lifestyle counsellors and other allied services. We have tried to put together a comprehensive conceptual framework for co-management of the dual epidemic (Fig. 1). It would be the mandate of the governance to provide access to relevant and timely information, and have complete accountability, transparency and reporting and meaningful involvement of the PP for the co-management of the two epidemics. Screening for TB in patients with diabetes as well as screening for diabetes in TB patients is crucial. Diabetes may increase the risk of adverse treatment outcomes in TB patients, thus special attention may be needed to ensure high-quality TB treatment in people with diabetes. DOTS providers must be trained for diagnosis and treatment of diabetes and the issues in co-management as outlined above.

3. Conclusion

Progress towards TB control in India is as important to global public health as it is to India, due to substantial immigration to foreign countries of persons from the Indian sub-continent and vice versa. There is a strong epidemiological evidence for a link between tuberculosis and diabetes. There is need to formulate standard guidelines for both diseases together. But before that, there is a need for future research to answer many questions about the co-management of diabetes and

tuberculosis and better understand the epidemiology of the co-epidemics. Further research on who should be screened for diabetes or vice versa and its cost-effectiveness needs to be done. Access to diabetes services varies greatly between the regions, and also the healthcare systems are structured to address acute, not chronic diseases despite the recent interest among the international and bilateral agencies to address the NCDs. Therefore till such time that the systems are geared to handle chronic illnesses, the most practical way to deal with these co-epidemics is the rapid case finding of persons with tuberculosis and to expand services to screen and manage for diabetes. The estimated additional costs of treating diabetes for the duration of the DOTS up to \$ 91million.⁷³ The impact of type 2 diabetes on TB is underappreciated at the grass roots level of healthcare, and in the light of its epidemic status in many countries such as India, it should be actively considered by TB control programmes with better financial support to expand these services. It is well-known that the current operational infrastructure and funds for the RNTCP program, are robust, and can be rapidly expanded to include diabetes, and this can be aided by public private partnerships models such as market based partnerships for health to control costs.

Conflicts of interest

All authors have none to declare.

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