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Leading Article

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Tackling the Problem of Childhood Tuberculosis in Bangladesh

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Understanding global burden of TB in the perspectives of strategies set by WHO for TB eradication

Despite significant progress in TB control, it remains the second leading cause of death in adults with 1.3 million deaths globally[1]. In 2017 an estimated 10 million people developed TB, including 3.2 million women and 1 million children, among which 1.6 million people died from TB, including 300,000 people with HIV[2]. However, 40% of the patients or approximately 3.6 million people with TB were either not detected by the health system or not notified to the local authorities, and therefore missed by the formal health system[3]. According to the 2022 Global Tuberculosis Report from the World Health Organization (WHO), Bangladesh is ranked seventh among the top eight countries with a high TB burden, contributing to 3.6% of global tuberculosis incidences[4,5].

Low- and middle-income countries with higher poverty rates are ranked as higher TB burden. Overcrowded living arrangements, lack of access to healthcare, malnutrition and weakened immune status contribute to increase TB transmission and incidence in poverty-stricken community[6,7]. Social determinant studies showed that higher TB incidence is directly proportionate with poor housing, financial constraint and social and cultural barriers to health care access[8]. Although, since 1993, the National TB Control Program (NTP) of the Government of Bangladesh (GoB), has been offering free treatment to TB patients under DOTS program as recommended by the WHO, research showed that poorest quintile of the household experienced higher Catastrophic Health Expenditure (CHE) for TB than their richest counterpart, 5% vs 1%[9]. The risk of delayed enrolment in the DOTS of the male smear negative patients, might increase the risk of CHE, which improvised the need of social safety-net schemes.

Malnutrition and TB are closely linked with both increasing the risk of TB infection and exacerbating the severity of the disease with the diverse prevalence between 1-92%[10,11]. Malnutrition is currently studied widely in patients with TB, to ascertain this not only as an outcome but also an important risk factor[12]. Individuals with micronutrient deficiency, suffering with weaken immunity and found to be more susceptible to TB infection[10]. Specially in pediatric TB, recent weight loss or not gaining optimum weight or malnutrition at any stage of illness, are well recognized clinical criteria for diagnosing TB[13,14]. A systematic review reporting 7-48% of children <5 years diagnosed with TB had severe malnutrition[10]. A study of 405 malnourished Bangladeshi children hospitalized with severe pneumonia diagnosed as TB in 23%, with 9% of children dying within 3 months of hospital discharge[14].

During pandemic over 50% of the patients with TB were missed or delayed diagnosed, resulting in severe disease progression and increase transmission[15]. The potential biological effects of the interaction of two infections rejuvenating the "Cursed Duet" concept again used for TB and HIV in the past[16]. WHO estimated worsening of TB epidemic globally during COVID-19 pandemic for a strained healthcare systems leading to resource reallocation, staff shortages and increased pressure on healthcare facilities[17,18]. Not only that, lockdowns, quarantine measures, and disruptions in transportation have led to limitations in access to healthcare services increased the difficulties to be tested for TB[15,16].

Current TB Control program in Bangladesh

Among the 1.5 million people who died from tuberculosis (TB) in 2020 globally, around 10% were children[19]. WHO estimates that the range of childhood TB diagnosis is 10-15% for high TB burden countries,

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whereas Bangladesh reported <4.0% in the last ten years[3].

Undoubtedly, there is a low detection rate of TB among children, which indicates an uncontrolled TB infection transmission at the community level, with possibility of a large number of children dying of TB unknowingly. WHO introduced the End TB Strategy to reduce TB mortality by 95% and TB incidence by 90%[1,20]. Under the End TB Strategy, the National Tuberculosis Control Program (NTP) started marching to ensure zero morbidity and mortality related to TB in Bangladesh[21]. With a perpetuating effort, NTP is committed to detecting TB infections early and accurately, followed by appropriate treatment of TB cases to curb the transmission of *Mycobacterium* in the community[14].

By adopting the international standards formulated by the World Health Organization (WHO) under the Directorate General of Health Services (DGHS), the National Tuberculosis Control Program (NTP) has been working with a mission of eliminating TB from Bangladesh since 1993. The Stop TB Strategy was launched in 2006-2015, and now NTP has published the "National Strategic Plan (NSP) to end tuberculosis in Bangladesh 2024-2030". NSP focuses on increasing case detection by early identification of presumptive TB cases at the Upazila health facility level or private sector, treating with proper drug regimen at proper duration by Directly Observed Therapy Short course (DOTS). NTP has expanded access to digital chest X-rays at the primary health facility level for rapid detection of pulmonary TB. Under the TB REACH program by Interactive Research Development (IRD), Artificial intelligence-based X-ray (Qure.ai) has been used to screen presumptive child TB cases in 50 public and private health facilities since 2019. NTP is operating National TB Reference Laboratories (NTRL) of BSL-2+ level, in Dhaka Rajshahi, Chottogram, Sylhet, and Khulna where pulmonary and extra-pulmonary sample examination using nucleic acid amplification *tests (NAAT)*. Most of these facilities also have GeneXpert for rapid detection of Drug Sensitive (DS-TB) and drug-resistant (DR-TB). Scaling up of WHO recommended shorter, safer, novel all-oral 6-month regimen composed of Bedaquiline fumarate, Pretomanid, linezolid, and Moxifloxacin (BPaLM) for DR-TB, includes pre-XDR and XDR-TB[22].

For successful detection and reporting of TB in the private sector and integration into the national database, a digital notification tool, the "Janao" App, has been introduced by NTP[23].

Barriers of achieving End TB targets in existing capacities

TB diagnosis is tricky because there is a need to differentiate between latent infection and active TB, as well as between pulmonary and extrapulmonary TB[24]. This often presents a challenge because reliable diagnostics to distinguish these forms of TB are often lacking, even in high-income countries[25]. The traditional method of diagnosis by isolating the infectious agents takes several weeks and can only be performed in specialized laboratories. In resource-limited settings, cytology and conventional smear microscopy for acid-fast bacilli (AFB) are the initial diagnostic tools for TB[14]. While fine needle aspiration cytology (FNAC) is a simple and rapid diagnostic technique, the cytomorphological features of Extra pulmonary TB or TB lymphadenopathy[25]. Conventional smear microscopy for AFB lacks sensitivity due to the paucibacillary nature of fine needle aspirates (FNA) and may yield inconclusive or false negatives. Although isolating the TB organism through culture is considered the gold standard in EPTB[26], it has a significant limitation of the 2–4 weeks turnaround time, leading to a delay in the commencement of anti-tuberculosis treatment (ATT), impacting patient management and increasing the risk of complications. Tests like lateral flow and antigen detection assays have limited sensitivity and specificity. In December 2010, the World Health Organization (WHO) approved using GeneXpert MTB/RIF (made by Cepheid, USA) in TB labs[27]. The GeneXpert test is a closed system that relies on real-time polymerase chain reaction (PCR). Even operators with limited technical skills can use it, allowing for the diagnosis of TB and simultaneous detection of rifampicin resistance in just 2 hours[26].

However, the availability of high-tech laboratory tests is only sometimes helpful due to the paucibacillary nature of MTB in children. To meet the End TB target, it is imperative to promote systematic screening for active TB based on careful history taking, clinical examinations, and relevant investigations, even in outpatient settings of rural Bangladesh. This is called Active Case Finding (ACF) of child TB, which is an effective, sustainable approach to increase child TB detection in Bangladesh.

The unavailability of an effective vaccine is another caveat in preventing TB. Although the BCG vaccine primarily protects disseminated forms of TB, such as TB meningitis and military TB, at a young age, its efficacy varies and declines over time. Some promising new and more effective TB vaccines are in the developmental stage, such as M72/AS01E (Phase IIb trials), H4:IC31, and an improved version of BCG vaccine with enhanced efficacy, which could be a game changer in a future world with zero TB[28].

Conclusion:

A comprehensive and multi-faceted approach, including healthcare, education, and community engagement, is required to tackle the problem of achieving the End TB target by 2035. Implementing these strategies requires a collaborative effort from government agencies, healthcare providers, NGOs, and the community. Pediatricians, both public and private, could play an important role in improving the rate of diagnosis, treatment completion and thereby limiting the transmission process in the community. By addressing the various aspects of childhood TB comprehensively, Bangladesh can make significant strides in reducing the burden of this disease among its young population.

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