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Global health approach needed to save children with TB meningitis

A pragmatic approach is needed owing to the complexity of the diagnosis

COMMENT

PROFESSOR REGAN SOLOMONS

A FILE picture of Dr Regan Solomons checking on the progress of a baby who was treated for TB meningitis and discharged from Tygerberg Hospital. | Independent Newspapers archive

SOUTH Africa has one of the highest burdens of tuberculosis (TB) worldwide, including tuberculous meningitis (TBM) – the most devastating form of TB and associated with high mortality and morbidity.

Young children are especially at risk of developing TBM. Children aged two to four years are the most at risk as this is also within the time period that children's brains are still developing and particularly vulnerable.

Managing childhood TBM in our country is challenging due to the complex nature of the disease and our specific health-care context. As we join people around the globe in celebrating World Children's Day on November 20, we should also realise that addressing these challenges will require an understanding of the current status, the obstacles, and potential solutions for managing TBM in South Africa's children.

Early diagnosis of the disease is notoriously difficult and often delayed. The onset is mostly insidious (days to weeks) and early symptoms such as low-grade fever, cough, vomiting, irritability and lethargy are non-specific and can be confused with flu.

Neck stiffness is often absent during early disease in children. Vomiting without preceding nausea should alert clinicians to the possibility of increased pressure inside the skull (intracranial pressure). An important factor that differentiates the symptoms of TBM from common illnesses such as the flu is their persistence, although this feature is often missed if a patient does not see the same health professional consistently. Household contact with an adult with pulmonary TB (TB of the lungs) within the previous year should heighten suspicion of TBM.

To diagnose TBM definitively requires evidence of Mycobacterium tuberculosis – the bacterium that causes TB – in the fluid that surrounds the brain and spinal cord (cerebrospinal fluid). However, tests are more often than not suboptimal in children and supporting evidence in the form of cerebrospinal fluid cell count, chemistry, chest X-rays and brain imaging is required.

Tuberculous meningitis is mostly based on a doctor's suspicion that a child may have the disease and empirical anti-tuberculous therapy is started. It is almost usually too late to reverse neurological impairment once clinical features of advanced TBM including meningeal irritation, coma, seizures, signs of raised intracranial pressure, cranial nerve palsies (weakness of the nerves responsible for eye movements, visions, hearing, facial movements and swallowing), hemiparesis (weakness on one side of the body) and movement disorders become manifest.

Left untreated, children will die, which highlights the importance of early diagnosis and treatment. However, even if diagnosed and treated, up to 20% of children die and of those surviving over half are left with a neurological disability. A further complicating factor is that TB, and therefore TBM, is prevalent in impoverished socio-economic settings where poverty and food insecurity are rife. For many children in South Africa, especially in rural and informal urban areas, access to health-care facilities is limited, compounding already delayed diagnosis and treatment.

The World Health Organization (WHO) recommends treatment for childhood TBM similar to that used for pulmonary TB, with either a six or 12-month option. The six-month regimen – also called the Cape Town regimen as it was developed and is the standard of care at the Department of Paediatrics and Child Health at the Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital – was proposed as an alternate regimen by the WHO in 2022, based on reduced mortality as shown in a systematic review and meta-analysis of observational studies. To be effective, drugs must be able to prevent death and neuro-disabilities in children whose brains are still developing. Several of the first-line drugs are not effective in penetrating the brain. Increasing doses of first-line drugs and second-line drugs without toxicity are being evaluated in ongoing clinical trials globally.

Steroids are part of the standard of care in childhood TBM. For example, low doses of thalidomide have been shown to be effective in some children with TBM; however, broader use as well as the usefulness of other drugs like aspirin require careful study. In South Africa, the double burden of TB and HIV can result in co-infection, which makes it more difficult to treat TBM and HIV in children, who may rapidly develop severe HIV, the correct timing for the introduction of antiretroviral therapy is unknown.

Younger children with TBM and stroke, independently of each other, can suffer worse neurological disabilities, despite recent progress in the management of TBM. Prediction of outcomes, especially after a stroke, is important for setting realistic and attainable treatment goals, informing caregivers properly, facilitating discharge planning, and anticipating possible consequences for home and school adjustments. Long-term outcomes in children with TBM include cerebral palsy, vision impairment, hearing loss, cognitive impairment, epilepsy and behavioural disturbance.

Given the complexity of the diagnosis, management as well as social determinants underpinning childhood TBM, a pragmatic global approach is needed. More accurate and accessible diagnostic tests for TBM in children, such as improved methods for the analysis of cerebrospinal fluid and point-of-care tests, must be developed and implemented. Anti-tuberculous drugs whose mechanisms have been studied in children, with paediatric-specific dosage and duration of treatment need to be developed and guidelines formulated and implemented. Similarly, the optimal timing of antiretroviral therapy, as well as dosage and duration of treatment of other drugs needs to be developed specifically for children, and not down-sized from adult use.

Emphasising a global child health approach to TBM to maintain the big picture, education and training is essential for health-care professionals to recognise and manage childhood TBM, including guidance on anti-tuberculosis drug dosing and monitoring. Improving awareness among communities and caregivers about the signs and symptoms of TBM in children is a compulsory preventative approach to encourage early diagnosis and care-seeking. Equitable access to care and consistent and adequate paediatric antituberculous drugs from primary health-care level upwards is also essential. Telemedicine and outreach as a complementary approach to TBM health care, especially to the lesser-served rural areas is useful but underutilised. Ongoing research on childhood TBM, including surveillance to monitor prevalence and outcomes, is imperative to reduce deaths and neurodisabilities associated with it.

Managing childhood TBM in South Africa is complex and challenging which requires a multi- and inter-disciplinary approach involving improved public health, education, research, and policy. Collaboration between government, health-care practitioners and world-class local researchers is crucial to address these challenges and save children's lives.

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