Home-based treatment of children with HIV infection or tuberculous meningitis in South Africa

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Introduction

INTRODUCTION

South Africa, with a population of 56.5 million people (2017) and 16.7 million (29.6%) children (0-14 years) [1], is considered a middle-income country in terms of its economy. However, South Africa has health outcomes that are worse than those in many lower income countries. The country's history has had a pronounced effect on the health of its people and the health policy and services of the present day [2].

Historical overview

The roots of a dysfunctional health system in South Africa can be found in policies from periods from the country's history, from colonial subjugation, apartheid dispossession, to the post-apartheid period [2].

Ancestors of the KhoiKhoi and San tribes have lived in Southern Africa between 10,000 and 20,000 years when the first European settlement was established in the Cape of Good Hope in 1652. These settlers, politically controlled by the Dutch East India Company, expanded their occupation into the lands of the amaXhosa. People were dispossessed and forced to work on settler farms together with slaves who were imported from West Africa, Mozambique, Madagascar, India and Indonesia [2].

The British occupation in 1806 forced the native inhabitants into impoverished rural lands (reserves). The British victory in Anglo-Boer War in 1902 brought together two British Colonies (Cape Colony and Natal Colony) and two Afrikaner republics (Orange Free State and Transvaal) after which the Union of South Africa was founded in 1910. Following the discovery of diamonds (1867) and gold (1886), the country transformed from an agricultural to an industrial economy. Coercive legislation, taxes, restricted access and punitive control enforced migration of cheap male labourers required for the mining industry. This became a major determinant of disease patterns in South Africa and neighbouring countries. Racial segregation and failure to provide proper housing for the migrant workers created overcrowded, unsanitary hostels and slums. The high turnover of mineworkers who returned to their families in the reserves contributed to the spread of tuberculosis with infection rates up to 90% in the 1920s [2].

The right-wing National Party came to power in 1948 when the state policy of apartheid consolidated the political exclusion, economic marginalisation social separation, and racial injustices of the preceding 300 years. Racial classification and hierarchy determined where a person could live, work, and go to school, whom they could marry, whether they could vote, and the resources allocated to their education, healthcare, and pensions [2].

Although banned from 1960, anti-apartheid organisations within the country became widespread. State violence and extreme repression increased the mobilisation of civil society in opposition to apartheid. The combined pressure from resistance and reformers

ultimately resulted in the dismantling of apartheid and the country's first democratic elections in 1994 [2].

Since 1994, there have been remarkable achievements: poverty reduction, new housing, sanitation and electricity, and the emergence of an affluent black middle-class. There have also been remarkable failures. The worst have been in the health sector, led by the reluctance of former president of South Africa, Thabo Mbeki, to acknowledge the importance of the human immunodeficiency virus (HIV) epidemic and the corresponding approach of his Health Minister Manto Tshabalala-Msimang [3]. In addition, the widespread emergence of multi-drug resistant (MDR) and extensively drug-resistant (XDR) tuberculosis is a warning sign of serious problems in the health system [4]. Despite increased investments and improved social policies, South Africa has not adequately addressed health disparities. Reasons for this include: an ill-prepared healthcare system to address the changing trend of burden of disease; poor stewardship, leadership, and management; inadequate human-resource capacity, and a poor surveillance system [5].

Current South African health system

South Africa has been a country of contradictions in using evidence to inform health policies and actions [5]. Available scientific information was disregarded and opportunities to implement HIV evidence-based interventions were missed [4, 6]. On the other hand, health data on violence and injury were well implemented [7]. Despite the shortage of health workers, budget shortfalls, and many dysfunctional health facilities [8], community empowerment, non-governmental organisations, and strong civil society have played a significant role in advocating for people's rights, setting an example for other African countries [4, 5].

The current South African health sector is structured based on a national department of health, which is responsible for national health policy. The country has nine provincial departments of health, which are responsible for developing provincial policy within the framework of national policy and public health service delivery. The primary healthcare system (a mainly nurse-driven service in clinics) includes district hospitals and community health centres. Local government is responsible for preventive and promotive services. The private health system consists of general practitioners and private hospitals and is mostly funded through medial schemes [2].

South Africa spent 8.2% of its gross domestic product on health in 2015. The public healthcare sector accounts for half of these expenditures (53.6%), where 44.0% is spent by the private sector and 2.4% external expenditures [9]. Only 18.1% of the population had a medical-aid scheme providing access to private healthcare and 81.9% mainly relied on the public sector. Households more likely consult public compared to private doctors, clinics or hospitals when they fall ill or have an accident (69.3% versus 28.9% respectively) [10]. The

maldistribution of resources between the public and private health sectors, relative to the population that each serves, reflects inefficiencies and inequities [11].

The South African constitution binds the state to work towards the progressive realization of the right to health. In 2004, the National Health Act was passed which legislates for a national health system incorporating public and private sectors to provide equitable healthcare services. It defines both the district health system and primary healthcare as provincial responsibilities [2]. In 2011, the Green Paper was launched which describes the principles for developing National Health Insurance (NHI) to improve access to quality healthcare services and provide financial risk protection against health-related catastrophic expenditures [12]. The White Paper on the NHI published in 2017 describes a healthcare financing system that is designed to pool funds to actively purchase and provide access to quality, affordable personal healthcare services for all South Africans based on their health needs, irrespective of their socioeconomic status. The NHI is intended to move South Africa towards Universal Health Coverage [13]. The individual, societal, financial, and political costs of South Africa's huge burden of disease are overwhelming the country's resources. Stewardship in health is required to enable South Africa's commitment and ambitions to ensure economic prosperity and social cohesion [4, 5].

HIV infection in South Africa

In 2016, South Africa was home to 0.9% of all children (age 0-14) globally [14] and accounted for 15.2% of the global HIV infected children [15]. South Africa has more people on treatment for HIV than any other country in the world [16]; anti-retroviral treatment (ART) coverage for children was 55% in 2016 [17].

The two key barriers to obtaining ART in South Africa until 2004 were the state's support of acquired immunodeficiency syndrome (AIDS) denialism and high prices [8]. In November 2003, the government decided to provide free AIDS treatment. Large expenditures on the AIDS epidemic have strained the health system [8, 18], at the same time, AIDS advocacy has resulted in a large increase in financial investment in healthcare [8]. The level of community involvement in health facilities that has come about because of the combined efforts of health workers and AIDS activists is unprecedented. In addition, the effect of successfully implementing ART and mother-to-child transmission prevention on life expectancy is massive [8].

South Africa has national guidelines for the management of HIV in children, adolescents and adults [19, 20]. In 2012, South Africa presented the first integrated National Strategic Plan for HIV, STIs and TB in response to the dual epidemics of HIV and tuberculosis [21]. The latest document for 2017-2022 builds on significant progress and addresses gaps identified in the previous five years [22].

The paediatric ART regimen is characterised by life-long, twice daily treatment with a combination of three medicines on average [23]. An outpatient ART clinic is visited monthly; every two months when appropriate for selected cases. HIV counsellors are available to support adherence and facilitate the HIV disclosure process.

TB infection in South Africa

In 2016, South Africa accounted for 5.6% of the global tuberculosis (TB) incidence in children [24, 25]. The National Tuberculosis Programme, established in 1994 faced the challenge of integrating tuberculosis services into a weak primary healthcare system and the emergence of the HIV epidemic, which led to TB case rates quadrupling between 1994 and 2012. The growing burden of MDR and XDR tuberculosis in 2006 added a further burden to the overstretched health services [6, 21]. With the implementation of the national strategic plan on HIV, sexually transmitted infections and TB [22], South Africa has made notable progress to improve TB control although the burden remains enormous [21].

Tuberculous meningitis (TBM) is the most severe form of TB and frequently occurs in early childhood [26]. In the Western Cape of South Africa, 14.9% of all culture confirmed TB cases in children (<13 years) at two major referral hospitals had TBM [27]. Different to WHO standard guidelines for TBM treatment of 12 months [28], the Western Cape of South Africa standard is a short-intensified 6-months, once-daily treatment regimen with a combination of four medicines (isoniazid, rifampicin, pyrazinamide and ethionamide) [29]. In-hospital treatment is the gold standard for children with neuro-tuberculosis due to complexity of care and serious consequences of non-adherence to anti-TB treatment [30]. Long-term hospitalization can negatively affect the child and family [31]. Short intensified treatment at home, under certain conditions, is a viable alternative to in-hospital treatment of children with drug-susceptible TBM [29, 30]. In the home-based treatment setting, the out-patient clinic is visited monthly and provided a dedicated programme nurse to coordinate follow-up appointments and support adherence and a social worker is available to the families in the program.

Adherence to treatment

The sheer magnitude of the HIV and tuberculosis epidemics in South Africa have stimulated the development of innovative means of delivering healthcare [6]. With increasing access to care, it is important to focus on treatment outcome and adherence.

Adherence to long-term therapy for chronic illnesses in developed countries averages at 50%. In developing countries, the rates are even lower. Many patients experience difficulties with following treatment recommendations. Poor adherence to long-term therapies severely compromises the effectiveness of treatment, making it a critical issue

in population health both from the perspective of quality of life and health economics. Interventions aimed at improving adherence would provide a significant positive return on investment through primary prevention of risk factors and secondary prevention of adverse health outcomes. Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments [32].

Although South Africa has guidelines and strategic plans in place that address adherence [20, 22], this information is not specifically tailored to children. Adherence is a dynamic process [32] not only affected by health system challenges [33] but also child, caregiver, clinical and socio-economic characteristics [34, 35]. Often, simple adherence support strategies that healthcare providers can use in busy clinics which greatly improve the quality of patient support that children and their caregivers receive before the child's health deteriorates [36]. Understanding factors contributing to well-functioning healthcare programs for children can improve care provided.

Outline of the thesis

The difference in healthcare structure, treatment regimen, duration of treatment and effect of the condition on daily functioning between HIV infection and tuberculous meningitis provided for a diverse population to study paediatric home-based treatment. The general aim of this thesis was to study home-based treatment of paediatric HIV (group 1) or tuberculous meningitis (group 2) in South Africa. This resulted in the following research questions:

- What is the level of adherence in children on ART and which factors affect adherence?
- What is the prevalence of disclosure of the child's HIV status to the child, and which factors are associated with this disclosure process?
- What are the barriers to adherence and perceptions of caregivers of children on home-based treatment for tuberculous meningitis?
- What are the costs and what is the cost-effectiveness of home-based treatment compared to in-hospital treatment of paediatric TBM?
- What is the effect of a treatment-support intervention on adherence, quality of life and family functioning in both groups (HIV and TBM)?

Part 1 focusses on paediatric HIV. In **chapter 2** we address the first research question: using multiple measures and definitions, we describe adherence in 195 children and factors affecting their adherence (child, caregiver, clinical and socio-economic characteristics). **Chapter 3** focuses on disclosure of HIV status to the child in the same population and explore the effect of child, caregiver, clinical and socio-economic characteristics on the

disclosure process.

Part 2 focuses on paediatric TBM. **Chapter 4** introduces the health-belief model to support the understanding of barriers and facilitators of adherence in children treated at home for tuberculous meningitis. In **chapter 5** we evaluate the costs and cost-effectiveness of home-base treatment versus in-hospital treatment for tuberculous meningitis in children.

Part 3 brings together both paediatric populations in a home-based treatment setting: **Chapter 6** evaluates a treatment-support intervention which was developed in collaboration with stakeholders at multiple levels. This intervention was implemented and evaluated in two paediatric populations receiving treatment at home for HIV or tuberculous meningitis.

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PART I

Home-based treatment of paediatric HIV infection