Infectious Diseases of Poverty in Children

A Tale of Two Worlds

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KEYWORDS

• Infectious diseases • Children • Poverty • HIV/AIDS • Malaria • Tuberculosis
• Neglected tropical diseases

KEY POINTS

- Poverty is inextricably linked with infectious diseases, including human immunodeficiency virus (HIV) infection, tuberculosis (TB), malaria and neglected tropical diseases (NTDs).
- Advances have been made in HIV treatment; however, access to and management of antiretroviral therapy (ART) in children still lag behind that of adults.
- TB is the leading infectious cause of mortality worldwide; poverty and young age are significant determinants of progression from TB exposure to disease.
- Malaria remains a leading cause of child mortality; access to effective preventive measures and therapy must reach vulnerable populations.
- Clinicians, both in endemic and nonendemic areas, must be familiar with the epidemiology and clinical manifestations of these infections to ensure prompt diagnosis and treatment.

INTRODUCTION

The phrase "infectious diseases of poverty" (IDoP) is used to describe infectious diseases that are more prevalent among poor and vulnerable populations.[1] IDoP comprises (1) human immunodeficiency virus (HIV) and AIDS, tuberculosis (TB), and malaria—the "big 3" (also referred to as the "Unholy Trinity"); and (2) neglected tropical diseases (NTDs).[2] Poverty has been inextricably linked with infectious diseases since antiquity. Poverty, acting through nongenetic heritable principles, has transformed infectious diseases into "inheritable" conditions. IDoP is seen in pockets of poverty

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in high-income countries as well. IDoP perpetuates poverty by leading to adverse outcomes in pregnancy, child development, and workplace productivity.[3] Gross domestic product, an indicator of the wealth of a country, is the most sensitive surrogate measure of burden of infectious diseases in a country. **Fig. 1** illustrates the positive correlation between poverty and infectious diseases. Substandard housing, lack of access to safe water and sanitation, and inadequate vector control contribute to the efficient transmission of these infections.[4] Other social determinants (eg, gender inequality, unemployment, low educational status, poor nutrition) compound the problem.[5] Strategies to prevent and control infectious diseases require tremendous resources. Therefore, infectious diseases have artificially divided the world into high-income as well as low- and middle-income countries (LMIC), with LMIC bearing the greatest burden of IDoP. However, with globalization and increased interconnectedness of the world, IDoP can transcend this economic divide.

This article provides an overview of IDoP that affect children with a focus on epidemiology, clinical manifestations, diagnosis, management, and prevention. IDoP account for a significant disease burden and high disability-adjusted life-years (**Table 1**).

HUMAN IMMUNODEFICIENCY VIRUS

Epidemiology

Thirty-four years into the HIV epidemic, advances in prevention and treatment have been made. However, challenges remain regarding access to and management of antiretroviral therapy (ART), particularly in LMIC. Established modes of HIV transmission are (1) sexual contact, (2) needle injuries, (3) mucous membrane exposure, (4) mother-to-child transmission (MTCT), and (5) transfusion with contaminated blood products. MTCT continues to fuel the pediatric HIV epidemic in LMIC.[6] The use of perinatal antiretroviral drugs to prevent MTCT (PMTCT) of HIV has resulted in a dramatic decrease (to <2%) in the rate of vertical HIV transmission in the United States.[7]

Despite these successes, progress has not been uniform worldwide. At the end of December 2013, only 23% of the 3.2 million children estimated to be living with HIV were receiving ART and in 2013 alone, 240,000 were newly infected and 190,000 (170,000–220,000) died of HIV-related causes.[8] Poverty is related inextricably to the disparity in global coverage of ART, with LMIC reporting low coverage (**Table 2**). Sub-Saharan Africa, with the highest proportion of people living on less than US$2 per day (see **Fig. 1**), is home to 91% of all children living with HIV.[9]

Clinical Manifestations

The hallmark of HIV infection is progressive depletion of CD4 T cells leading to development of opportunistic infections, AIDS, and death.[7] In acute simian immunodeficiency virus infection, 30% to 60% of all gut-associated CD4 cells become infected, leading to profound depletion within 4 days of infection.[10] Similar CD4 gastroenteropathy occurs with acute HIV infection, albeit at a different pace. During primary infection, HIV infects gut-associated resting and activated memory CD4 cells, leading to breach in the intestinal epithelial barrier with a loss of tight junctions, enterocyte apoptosis, local immune activation, and depletion of CD4 cells.[11] The breach in the mucosal barrier facilitates translocation of pathogenic bacteria and microbial products from the gut lumen to the systemic circulation, leading to chronic immune activation.[12] The time from acute infection to the development of AIDS is defined by a CD4 cell count of less than 200 cells/mm^3 or the appearance of AIDS-defining opportunistic infections or cancers (**Box 1**) and ranges from 6 months to 25 years.