Ph. D. Thesis

HIV infection in children: epidemiological and clinical aspects in Constanta County

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Key words: HIV/AIDS infections, children, epidemiology, common illnesses
Introduction

The global AIDS epidemic is one of the greatest challenges facing our generation. AIDS is a new type of global emergency—an unprecedented threat to human development requiring sustained action and commitment over the long time.

In many parts of the world, HIV/AIDS is still seen as a death sentence, a disease from which there is no recovery. But with the ever-improving availability of antiretroviral therapy, HIV is increasingly recognized as a chronic rather than terminal illness. This transition requires special adjustments especially in the pediatric and adolescent populations.

The paper “HIV infection in children—epidemiological and clinical aspects in Constanța County” consists in 193 pages: 71 pages about the state of knowledge in HIV/AIDS infection and 122 pages of personal contribution.

The author wants to show that the children with a chronic illness such as HIV/AIDS face unique challenges that make their lives more difficult. It is important to understand the long-term effects these challenges can have on the children and their caregivers, whether that's their parents, extended family, or others in the community.

With proper support from their health care providers and their community, the burden of childhood with HIV/AIDS will seem less great.

The first part of the thesis is structured in 9 chapters focuses on the state of the art data regarding HIV/AIDS infection: Historical data, Epidemiology, Etiology, Pathophysiology, Classification and Clinical manifestations in HIV infection. The information is presented using 29 tables and 18 figures.

The main historical data about HIV infection are systematically displayed, in terms of international and Romanian chronology. The historical aspects are followed by the theoretical part of the thesis describing the main data regarding HIV infection: etiology, epidemiology, classification system and clinical categories of HIV infection.

The second part of the paper: the personal contribution represents two thirds of the thesis, containing 94 tables and 60 figures. There are seven chapters: Objectives, Material and Methods, Results, Discussions, Clinical cases, Conclusions, References and finally an appendix.

The aim of the study was to describe the demographic and clinical aspects of HIV-infected children in the Pediatric Department on the County Hospital of Constanța.

Material and Methods An observational study on 153 patients diagnosed with HIV infection in the Pediatric Department of the County Hospital of Constanța from 1990-2002. We conducted a complex analysis extending the observation until 2008.
Discussion and conclusions

On the 153 subjects, the majority (144 cases; 94.11%) were born between 1987-1989; most of them were born in 1988 (62.75%).

The mode of transmission was primarily through transfusion of unscreened blood and other medical practices via injections with improperly sterilized equipment: 32.67%; 48.36% with nosocomial transmission and 13.07% of patients had received parenteral treatment at home and in the hospital. Perinatal transmission accounted for 5.22% of cases.

At the onset: 62.09% of cases were grouped into B category with moderately severe symptoms and 37.90% developed severe symptoms and were classified as category C.

In the early stage of the HIV infection the patients presented in 68.62% of cases lymphadenopathy; moderate unexplained weight loss (60.13%), hepatosplenomegaly: enlarged liver and spleen in 49.01% of cases and one third of children had respiratory infections.

At the end of the study, 96 children (62.74%) died with AIDS and there are 57 survivors (37.2%). The age of the survivors ranges between 14 and 22 years with the highest number at the age group of 21-22 years: 37 cases. The majority of the survivors are in the clinical category C: 55 patients (96.49%) and two patients in the clinical category B. According to the degree of the immunosuppression: 25 patients (43.85%) were allocated to severe immune suppression (C3), 24 cases with moderate immunosuppression (C2) and 25 cases with mild immunosuppression (C1).

The cutaneo-mucous manifestations were due either the opportunistic infections either the therapeutical side effects. Oral candidiasis was the most frequent disorder of the mouth: 60 cases (39.2%) followed by stomatitis due by herpes virus (20 cases) and in a few cases lingual papillomatosis and hair leukoplakia of the tongue. Esophageal candidiasis appeared in 5.2 % cases. Viral infections were observed in patients with severe immunosuppression. Among bacterial infections, one of the most incriminated bacteria was Staphylococcus aureus followed by Streptococcus. Among fungal infections the most common disorder was candidiasis dermatosis (3.2%).

The most common neurologic manifestations of pediatric HIV infection was progressive encephalopathy (60%) from the total cases with nervous system abnormalities. Opportunistic infections accounted in 16 patients and included: toxoplasmosis, cryptococcus and cytomegalovirus infection, TB meningitis and multifocal demyelinating leukoencephalopathy (PML).

Mycobacterium tuberculosis infection were diagnosed in 60 patients, and extrapulmonary TB (incuding pleuritis, pericarditis, meningitis and disseminated disease) were observed in 23 cases.

The cardiac manifestations of HIV infection included cardiomyopathy, wich was the most common manifestation found in ten cases, followed by miocarditis (3 cases), endocarditis (2 cases) and pericardial effusion (2 cases).

Renal disorders are encountered at all stages of HIV infection in 39.21% of cases, the most frequent cause was represented by urinary tract infections (47 cases). Nephrotic syndrome was found in 6 cases. Seven children in treatment with indinavir developed renal complications such as renal pains and hematuria.
Opportunistic intestinal parasitosis occurred in 76.08% of cases, especially in patients with severe immunosuppression. Polyparasitosis predominated (with protozoa).

A common co-infection was HIV and hepatitis. There were 84 patients (54.9%) with chronic hepatitis B infection.

Lipodistrophy was diagnosed in 20 patients. The drugs implicated in lipodistrophy etiology included PIs (in 15 cases) and associated treatment with PIs and NRTIs (in 5 cases). Lypodistrophy was more frequent in patients at age of 14-21 years old with severe immunosuppression. There were a slight female predominance. Lypodistrophy comparing to male lipoatrophy predominated.

Kaposi's sarcoma was diagnosed in 3 patients. In 2 cases the lesions affected the skin and the oral mucosa, and in one case the lesions were found only on the skin. All the patients died in a few months after the diagnosis.

From the total number of patients who have died (96), 32 presented wasting syndrome associated with encephalopathy in 26 cases.

The highest death-rate (69.79%) was found on children born in 1988.

The death rate over studied cases revealed a high mortality in institutionalized children.

The number of deceases was increased in children who had poor living conditions.

Considering the age on HIV finding, the death analyse showed that 90.91% of the patients have died at the age group of 0-2 years-old (p=0.0034, with is significantly hight)

Considering the age, the death occurred in patients with age between 8 and 16 (66.66%), the medium age was 8.2.

The deceases' analysis according on clinical stage of initially HIV infection revealed a significant statistical relation (p<0.05) between the two clinical categories: death occurred in 60% of patients diagnosed in stage B and in 67.24% of patients diagnosed in stage C.

The average period of time (years) from the moment considered infectious (1988) was 6 years for stage B, 8 years for stage C: in patients alive and 4 years for stage B, 8 years for stage C: in dead patients (p<0.0001).

There is a tardy AIDS detection on patients in C-stage, equally survivor and dead children.

The cases' analyse concerning the period of death from the diagnosis showed that 82.29% of patients died in the first 6 years from the diagnosis.

The survival from the moment of the diagnosis was increased in children in stage B (4 years) comparing to the children in stage C (3 years), the statistical relation being extremely significant (p<0.0001, p<0.0002).
References

2. Ministerul Sanătății, Compartimentul de Evaluare și Monitorizare a Infecției HIV/SIDA –Institutul de Boli Infecțioase “Prof. Dr. Matei Balș”. Date statistice HIV/SIDA în România, iunie 2009
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I supervised practical lessons in pediatrics and license thesis.

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