

Research article

The burden of pediatric HIV/AIDS in Constanta, Romania: a cross-sectional study

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Abstract

Background: By 1990, 94 percent of the acquired immunodeficiency syndrome (AIDS) cases in Romania were in children less than 13 years of age. The majority of the cases were identified in the city of Constanta. The purpose of this paper was to describe the current burden of pediatric human immunodeficiency virus (HIV) infection in the Constanta county.

Methods: A cross-sectional study was designed to address the primary objective. Between April 1999 and March 2000, all living cases of pediatric HIV infection in the Constanta county were identified from records at the HIV hospital clinic which serves the Constanta county. Standard demographic, social, clinical, treatment and hospitalization data were collected for each study subject. Data were analyzed according to cross-sectional study design methodology.

Results: Of the 762 subjects, the majority were seven to 11 years of age, lived with their parents and attended school. Only 70% of the fathers and 13% of the mothers were employed. Horizontal transmission accounted for 90% of the cases. Most of the children had moderate to severe disease as indicated by their AIDS-defining signs; 40% had AIDS. Less than half of the children were receiving antiretroviral therapy (ART). ART and children of mothers with a high school or greater education were independent predictors of long-term non-progression of HIV disease.

Conclusions: This cross-sectional study demonstrated that ten years after the HIV epidemic was identified in Romania, it remains a health and economic burden. The infected children are very ill, but ART is not available for all. The proportion with vertical transmission has increased from an estimated four % to nine %. Our findings support the need to get HIV therapy to economically challenged countries such as Romania.

Background

Through November 1989, Romania had reported 13 cases of the acquired immunodeficiency syndrome (AIDS) to the World Health Organization (WHO). After the collapse of the Communist regime in Romania in December

1989, there were reports of large numbers of children with human immunodeficiency virus infection (HIV) and AIDS [1]. In early March 1990, the Centers for Disease Control and Prevention was invited to provide epidemiological assistance to establish a national AIDS

surveillance system [2]. In its first report of AIDS cases, the Romanian Ministry of Health reported that 77% of cases were from only five of Romania's 41 districts. Constanta county which includes Constanta, a major port on the Black Sea, had 426 cases; Bucharest, the capital of Romania, had 189 cases; Giurgiu, located on the Danube River where virtually all traffic to Bulgaria from Bucharest passes through, had 119 cases; Bacau, in Moldavia, had 87 cases; and, Galati, also a port on the River Danube, had 74 cases. The majority of the cases (94%) were in children less than 13 years of age. Contaminated blood products and indiscriminate injections with contaminated needles and syringes were the main sources of infection [3]. Only a small percentage (4%) of the pediatric cases resulted from vertical infection.

The most recent global report by the Joint United Nations Programme on HIV/AIDS (UNAIDS) reports 36.1 million people were living with HIV/AIDS, of which 1.4 million were children less than 15 years of age. An estimated 5000 children in Romania were living with HIV/AIDS in 1999 (personal communication, Mark W. Kline, M.D.). The city of Constanta remains the epicenter of pediatric HIV/AIDS in both Romania and Eastern Europe. The purpose of this study was to conduct a population-based cross-sectional study to describe the current burden of pediatric HIV infection in the Constanta county in Romania.

Methods

The study was conducted at the Municipal Hospital in the city of Constanta, Romania. The infectious diseases medical staff cares for all children who seek care for and are diagnosed with HIV infection who live in the Constanta county. The Municipal Hospital has both inpatient and outpatient facilities for children and adolescents with HIV infection. The inpatient area can accommodate up to 65 children and adolescents. The outpatient clinic operates twice per week and sees approximately 20 to 25 patients per session. The majority (97%) of the HIV-infected children seen at Municipal Hospital in Constanta are from the Constanta county. The remaining three % of cases are orphaned or abandoned children from other areas of Romania.

The 1997 population of the Constanta county was 746 700. The child population, zero to 15 years of age, was 161 287. The city of Constanta, in the Constanta county, is located on the eastern border of Romania and is an important shipping port on the Black Sea. The 1999 population was estimated at 339 250 and the child population, zero to 19 years of age, was 88 205.

The cross-sectional study population consisted of all living HIV-infected infants, children and adolescents, 18

months to 18 years of age and known to the medical staff at the Municipal Hospital between April 1999 and March 2000. Even though follow-up was through 18 years of age, all cases were infected during childhood. Before August 2000, there was no systematic surveillance for HIV in the city of Constanta or the Constanta county nor are high-risk pregnant women tested. The majority of newly identified cases are tested for the HIV virus and diagnosed when those individuals seek medical care, usually for an HIV-related illness. Thus, the study population is not complete, i.e. all prevalent cases in the Constanta county have not been identified. Estimates, however, are at least 90-95% of pediatric cases that have been identified and are most likely representative of all the prevalent cases, based on the experience of one of the authors (RM).

A standard data collection form was completed for each case that met the study's inclusion criteria. The form included demographic, social, HIV risk factor, clinical, treatment and hospitalization data. The Center for Disease Control and Prevention's 1994 revised classification system for human immunodeficiency virus infection in children less than 13 years of age was used to determine the clinical category [4]. This system provides mutually exclusive states based on the intersection of four clinical and three immunological categories. Due to the resource-limited environment at the Municipal Hospital in the city of Constanta, CD4-positive cell counts are not available. As a result, the immunological categories were not used to describe the population. Clinical categories classify children with no (category N), mild (category A), moderate (category B) or severe (category C) AIDS-defining signs. Medical record abstraction was the primary method for data collection. For the purposes of this descriptive review of study subjects, long-term non-progressors (LTNP) were defined as those children eight years of age and older, infected with HIV during the first two years of life, and remain classified in the CDC clinical category A.

The data are maintained in a database created with Microsoft Access. Statistical analyses were performed with the SAS software. Descriptive statistics were used to describe the population and Chi-square analysis was used to test for differences between groups. Logistic regres-

sion was used to determine independent factors associated with LTNP while controlling for other factors.

Table 1: Demographic and social factors of HIV infected children and youth Constanta, Romania 1999 2000

Demographic Factors	N	%	Social Factors	N	%
Gender			School		
Male	426	(56%)	Yes	615	(81%)
Female	336	(44%)	No	135	(18%)
			N/A	12	(1%)
Ethnicity			Father Education		
Romanian	614	(81%)	<HS	439	(78%)
ROM*	45	(6%)	HS	91	(16%)
Turkish/Huns	94	(12%)	>HS	33	(6%)
Other	6	(1%)	Mother Education		
Age (yrs)			<HS	472	(81%)
0-6	16	(2%)	HS	85	(15%)
7-11	581	(76%)	>HS	23	(4%)
12-18	165	(22%)	Father Employed		
Residence			Yes	396	(70%)
Parent(s)	599	(78%)	Mother Employed		
Relatives	28	(4%)	Yes	78	(13%)
Orphanage	122	(16%)			
Hospital	13	(2%)			

*ROM = gypsy

This study was approved by the Baylor College of Medicine Institutional Review Board for Human Subject Research and by a Single Project Review Committee for Human Subject Research in Romania and the Romanian Ministry of Health.

Results

Data collection forms were completed for 762 pediatric cases of HIV infection ranging from 18 months to 18 years of age. The demographic and social characteristics of the study population provide great insight to the current pediatric HIV/AIDS population in the Constanta county. The majority of the study subjects are seven to 11 years of age ($\bar{X} = 11.3$; SD = 1.5), of Romanian (Caucasian) ethnicity, and live with their parent(s) or a relative. Most of the children are well enough to attend school. Parental education was commonly stopped before receiving a high school degree. Seventy percent of the fathers reported employment whereas only 13% of the mothers were employed outside of the home.

The mode of transmission of HIV was primarily through transfusions and other medical practices via contaminated needles and syringes. These medical procedures were conducted usually during the first year of life. Perinatal transmission, as defined by the Centers for Disease Control [4], accounted for nine % of the cases. Of the perinatal transmission cases, their dates of birth range from 1987 through 1998.

The children seek medical attention many years after their infection with HIV, thus their mean age at diagnosis is eight and one-half years. The majority (82%) of children have moderate to severe disease as indicated by their AIDS-defining signs; 306 (40%) are diagnosed with AIDS. The most prevalent clinical features since HIV diagnosis for the children categorized in the CDC clinical category A were lymphadenopathy (100%), hepatomegaly (97%) and recurrent or persistent upper respiratory infection, sinusitis or otitis media (97%). For children categorized in the CDC clinical category B, most had been diagnosed with a single episode of bacterial meningitis, pneumonia or sepsis (95%), candidiasis (68%), chronic or recurrent diarrhea (52%), lymphoid interstitial pneumonia (50%) or recurrent herpes simplex virus stomatitis. Those children in the CDC clinical category C suffered from multiple or recurrent serious bacterial infections (97%), wasting syndrome (69%), encephalopathy (51%), esophageal or pulmonary candidiasis (47%) or herpes simplex virus (39%). Cancer, Kaposi's sarcoma or

a lymphoma, had been diagnosed in nine (1%) of the 762 children.

Table 2: Clinical factors of HIV infected children and youth, Constanta, Romania 1999 2000

Clinical Factors	N	%
Transmission		
Perinatal	72	(9%)
Transfusion	231	(30%)
Parenteral	459	(60%)
Year of Diagnosis		
90-92	270	(35%)
93-94	149	(20%)
95-97	231	(30%)
98-99	112	(15%)
Age at Diagnosis		
Mean (SD)	8.5	(2.1)
CDC Clinical Category		
A	135	(18%)
B	320	(42%)
C	306	(40%)
AIDS		
Yes	306	(40%)
Antiretroviral therapy		
Yes	325	(43%)
PCP chemoprophylaxis		
Yes	540	(71%)
Hospitalization for HIV disease		
Yes	96	(13%)

Table 3: Relationship of factors with LTNP* in study subjects 8 years of age or older

Factor	LTNP	Not LTNP	p-value
Birthweight			
≤ 2500	8 (7%)	94 (17%)	0.01
Gender			
Male	57 (49%)	309 (57%)	0.12
Maternal education			
<high school degree	63 (64%)	401 (85%)	0.00
Current ART**			
Yes	65 (51%)	229 (37%)	0.01

*LTNP = long-term non-progressors **ART = antiretroviral therapy

Less than half of the children are receiving antiretroviral treatment, though all were eligible. For those receiving antiretroviral therapy, it was started at a median age of 10.4 years (range: 1.3-18.2). PCP chemoprophylaxis was

initiated at a median age of 7.4 years (range: 0.4-16.0). At some time after their diagnosis of HIV, 96 (13%) of the study subjects had been hospitalized. The primary discharge diagnoses for the majority of hospitalizations were tuberculosis and encephalopathy.

One hundred and twenty-seven (17%) children were defined as LTNP (CDC category A and ≥ eight years of age). Several factors were associated with LTNP including inverse associations with birth weight and maternal education and a positive association with current antiretroviral therapy. The results of a logistic regression model which included these three independent dichotomous variables indicated that the children of mothers with less education were 2.7 times more likely not to be a LTNP (95% CI 1.6-4.5) and children not on antiretroviral therapy to be 1.6 times more likely not to be a LTNP (95% CI 1.01-2.6).

Discussion

Factors associated with the 1989-90 pediatric HIV epidemic in Romania have been reported. Because most of the HIV infected children were born to uninfected mothers, HIV transmission was presumed to be related either to transfusion of unscreened blood or blood products, or to the re-use of unsterilized needles and syringes [3, 5]. This study describes the current HIV-infected child and adolescent population in the Constanta county; the majority of whom were infected during the 1989-1990 epidemic. As a whole, these 762 children and adolescents who are representative of pediatric HIV/AIDS in the Constanta county present a striking burden on the medical resources in the Constanta county; all need treatment but all do not receive it resulting in additional medical outcomes which need medical attention. Because the majority are in the moderate to severe stage of their HIV infection, they require significant medical attention.

Antiretroviral therapy has been available in the city of Constanta since 1997; triple therapy became available in 1998. Children with chronic encephalopathy and psychomotor retardation are not placed on therapy nor are children with contraindications. Very few parents refuse antiretroviral therapy. In this study, however, only 43% of the study population in which all were eligible for treatment, were on some type of drug regimen for HIV. As a result of the economic burden of HIV therapy, not all children have the opportunity to receive drug therapy for their HIV.

Under several provisions, the governmental budget from the Minister of Health covers the cost of antiretroviral therapy for HIV for some but not all children. Antiretroviral therapy is usually covered for a total of 500 children in the Constanta county. There are periods of time, how-

ever, when the National Health Security House does not have the funds to cover the costs of therapy for all 500 children. Recently, the lack of funds resulted in stopping treatment for approximately 100 children in Constanta. Antiretroviral therapy for the orphans and abandoned children in Romania is categorized as social assistance. Thirty percent of this social assistance is covered by the budget of the Minister of Health and seventy percent is covered from other sources, such as NGOs, The European Community and UNICEF. It is clear, as with other resource poor nations, that there is inadequate funding for antiretroviral therapy for Romanian children [6].

Because of the lack of laboratory resources in Constanta, it is not possible to monitor antiretroviral therapy with CD4 counts and viral loads. Clinical monitoring of the children on therapy is done monthly and includes body measurements of height and weight, chemical analysis, one-month only prescriptions and medication counseling regarding appropriate methods for taking the medications and adherence.

In contrast to the 1989-1990 epidemic, a large proportion of the currently infected children and adolescents are living with their parents or relatives rather than in orphanages. The majority of the children who were in orphanages in 1989-1990 remain abandoned in the hospital or in family houses. Some children have been placed in foster families through the support of governmental or NGO support.

Social factors relating to the child's place of residence, such as mother's level of education, are independently associated with disease progression in this population. Of interest were the older children who remained categorized in the CDC clinical classification of A and defined as long-term non-progressors. A logistic regression model indicated that children and adolescents whose mothers had attained at least a high school degree and were currently on antiretroviral therapy were more likely to be a LTNP than children of mothers with less education and/or not currently on antiretroviral therapy. It is imperative that health care providers provide instruction and guidance to the mothers with lower levels of education on a level that can be understood and used in the care of their infected children.

Since 1990, donated blood in Constanta county, as well as all Romania, is considered safe. It is screened and tested for HIV and hepatitis B and C. There are disposable medical supplies (needles, syringes, etc.) available throughout health units and hospitals, and the medical staff, regardless of their specialization, has been trained for HIV safe practices. The result of these procedures is, after 1990, no child in Constanta county has been infect-

ed with HIV via horizontal transmission. Infected children continue to be identified monthly in Constanta county, however, they are older horizontal transmission cases (11 years of age or older) or young children with vertical transmission of HIV.

It is unfortunate that perinatal transmission has increased since the early 1990s. The first pediatric HIV epidemic in Romania was documented as nonperinatal [1,2,3]. Nine percent of the study population's direction of transmission was vertical. Prostitution is a major factor associated with this increase of vertical transmission. The majority of the HIV infected women in the city of Constanta were infected by sexual transmission. As noted by Stephenson in her perspective on HIV/AIDS surging in Eastern Europe, increased poverty, unemployment, an ailing public health system, and other manifestations of socioeconomic turmoil have fostered drug use, an increase in prostitution, and epidemics of sexually transmitted disease which, in turn, increase the spread of HIV [7].

Romania has a national HIV prevention program in which each county develops county specific materials. The county of Constanta has developed a program. Evaluations of this program are not available. From the results of this study, it is imperative that proper case management of the infected children be a priority for reducing the burden of this disease in the Constanta district. It is also important that young females be targeted. The reduction in cases of pediatric HIV in Romania will not occur without the reduction in perinatal transmission. In addition, the prevention programs must target those that have not had the opportunity to attain at least a high school education.

Competing Interests

None declared.

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