

## **Psychiatric, behavioral and emotional disorders in Polish children and adolescents with perinatal HIV infection**

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### **Summary**

**Aim.** The aims of the study were to evaluate the prevalence of psychiatric, behavioral and emotional disorders in children and adolescents with perinatal HIV infection and to establish their possible relationships with clinical and sociodemographic variables.

**Material and method.** 56 children with perinatal HIV infection (PHIV+ group), 24 healthy children perinatally HIV-exposed but uninfected (PHEU) and 43 healthy children of uninfected parents (HIV-nA), aged 6–18 years, were assessed. *The Child Behavior Checklist* (CBCL/4–18), completed by parents, and *the Youth Self-Report* (YSR) were used to assess behavioral and emotional disorders, while the semi-structured diagnostic interview K-SADS-PL was used to assess the symptoms of psychiatric disorders.

**Results.** Higher prevalence of psychiatric disorders was found in the PHIV+ group and the PHEU group compared to the HIV-nA group. Anxiety disorders and affective disorders were diagnosed most often. Prevalence of symptoms of emotional and behavioral disorders in the PHIV+ group and in the PHEU group was associated with similar sociodemographic variables (male, not living with the biological caregiver, the experience of stressful life events). Psychiatric disorders were noted more often among PHIV+ subjects whose ARV treatment was started after 12 months of age. Positive correlations were observed between the results of some YSR and CBCL/4–18 problem scales and CD4 counts at the time of the study, higher logarithm of viral load at the start of ARV treatment and at the time of HIV diagnosis.

**Conclusions.** The prevalence of psychiatric disorders in PHIV+ group and the PHEU group is higher in comparison with HIV-nA group. A more serious course of HIV infection and its severity before treatment are associated with the severity of internalizing problems.

**Key words:** HIV infection, psychiatric disorders, behavioral disorders

## Introduction

The results of studies on the prevalence of psychiatric disorders in children and adolescents with HIV (Human Immunodeficiency Virus) have been inconclusive. The reason for this may be: different methodology, large age range of patients, different routes of infections, lack of control groups. However, in all probability, the presence of HIV infection, in conjunction with environmental factors, increases the risk of psychiatric disorders.

In the review of eight studies performed by Scharko [1], ADHD (Attention Deficit/Hyperactivity Disorder) was diagnosed in 28.6%, anxiety disorders in 24.3% and depressive disorders in 25% of children with HIV (not all children had vertical HIV infection). More detailed data have been provided by North American cohort studies [2–8], where psychiatric disorders were diagnosed – at the time of the study or in the preceding 12 months – in 55–61% of PHIV+ children (Perinatally HIV-infected) and 49–62% of PHEU control-group children (Perinatally HIV Exposed but Uninfected) [2, 3, 5, 6, 9], with no significant differences in the prevalence of different psychiatric diagnoses between the two groups. The presence of behavioral and emotional symptoms in children and adolescents with vertical HIV infection has been studied by 3 research groups in the USA [10–14]. The results have revealed higher prevalence rates in PHEU groups (33–38%) compared to PHIV+ groups (25–26%) [10, 11]. Behavioral symptoms were observed in 29% of exposed and 16–19% of infected children, whereas emotional symptoms were diagnosed in 17% and 12%, respectively [10, 12].

In the PACTG219C study (Pediatric AIDS Clinical Trials Group 219C), as many as 52% of children were diagnosed with at least one behavior-related problem [12], and significantly higher, compared to general population, mean scores were observed on all scales, except for anxiety [13]. The caregivers of 22–25% of PHIV+ children reported the presence of school problems, 22–28% – psychosomatic symptoms, 19–20% symptoms of hyperactivity and impulsivity, 8% – anxiety, and 18% – substance abuse (mainly alcohol) [12–14]. The results of the only European study utilizing CBCL (Child Behavioral Checklist) tools on 27 PHIV+ children and control group showed significantly higher scores on all problem scales in the PHIV+ group [15] (children with detectable viral load scoring much higher in *Internalizing problems*, *Social Problems*, *Thought Problems*, *Attention Problems*, and *Delinquent Behavior* scales).

The analysis of the presented studies seems to confirm that PHIV+ children are more susceptible to psychiatric disorders, but perinatal HIV infection may not be the principal or sole contributing factor. Such susceptibility is most likely the consequence of a specific constellation of medical and environmental factors [16]. The role of HIV infection has been confirmed in some studies showing a relationship between the presence of psychiatric disorders and the status of clinical infection. Such results have emphasized the influence of AIDS symptoms (Acquired Immune Deficiency Syndrome) [7, 17], a low level of CD4 lymphocytes [6, 7, 12] and a high viral load

[7, 15] on the presence and severity of symptoms of hyperactivity, conduct disorders and depression.

It is also difficult to determine the roles played by other environmental factors, e.g., the disclosure of the diagnosis to the child. Some authors suggest the lack of significance of this factor [2, 9, 18] whereas others have demonstrated that illness awareness along with significant life events increases the risk of mental disorders [19]. The results of some studies have revealed a relationship between the caregiver's own health status and the mental health of a child [2, 20]. Contrary to common belief, children raised by HIV-infected parents do not necessarily experience poorer baseline mental functioning [11, 12]. Furthermore, fewer symptoms of conduct disorders, hyperactivity and school problems were noted in children with vertical HIV infection who lived with their biological parents [12]. Other factors that can have a potentially negative influence include the death of a parent, being raised by an institution, stressful life events, poverty, unsupportive environment, and low parental social skills. A relationship was found between stressful life events, the presence of illnesses in the family and higher severity of symptoms of depression and anxiety in PHIV+ and PHEU children [21].

Considering the aforementioned data, assessment of the prevalence of mental disorders in children and adolescents with perinatal HIV remains a very important field of research that requires further work and conclusions. This study aimed to evaluate the prevalence of psychiatric, behavioral and emotional disorders in children and adolescents with vertical HIV infection and determine possible relationships between the presence of the disorder and clinical and sociodemographic variables.

At the time of the study, 112 children and adolescents under 18 years of age were receiving antiretroviral therapy in Poland [22].

## Material

The study group included 56 patients of the Department of Children's Infectious Diseases of the Medical University of Warsaw with perinatal HIV infection, aged 6–18. The exclusion criteria included the following: other routes of HIV infection, the presence of chronic somatic condition other than HIV infection, the presence of any problem that could limit cooperation, and the lack of child or caregiver consent. Two age- and sex-matched control groups were formed. The first reference group consisted of 24 healthy children and adolescents aged 6–18 with HIV-infected mothers (PHEU group), who were recruited as ex-patients of the Department of Children's Infectious Diseases or as clients of non-governmental organizations dedicated to helping people infected with HIV. The second control group consisted of 43 healthy children and adolescents with uninfected parents or without a history of HIV infection in family members (HIV-non-Affected; HIV-nA), who were recruited through social networking websites and in Warsaw schools.

## Methods

The Polish versions of the *Child Behavior Checklist* (CBCL/4-18) and the *Youth Self-Report* (YSR) [23, 24] were used for the assessment of emotional and behavioral symptoms; the K-SADS-PL (*Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version*; ver.1.0) [25] was used for the assessment of psychiatric disorders. Diagnoses were made based on DSM-IV criteria [26]. The examination was made with the child/adolescent and caregiver participation. Adult participants (older than 18) were invited without their parents/caregivers. The 'or' rule was used, which assumed the equivalence of information collected from the child and the parent [2, 27]. Interviews collected from a child and a parent or a child and a parent alone were included in the statistical analyses.

The term 'in a lifetime' was used in case of a psychiatric disorder diagnosed either at the time of the study or/and in the past. The term 'number of patients' in the context of individual diagnostic groups described the number of individuals diagnosed with a psychiatric disorder at any time (e.g., a child diagnosed with two different anxiety disorders was counted once).

In order to collect sociodemographic data, an original questionnaire, which was filled in by the caregiver, was used. During the initial interview, we collected sociodemographic data on and basic information about the participant and the family, as well as data on environmental and sociodemographic factors. Participation in the study was voluntary. Informed consent forms were signed by both the child and the caregiver prior to the study. The study was approved by the Ethics Committee of the Medical University of Warsaw (approval no: KB 4/2012).

Descriptive statistics are represented as medians with interquartile ranges (IQRs). Between-group comparisons for continuous variables were performed using the Mann-Whitney test. Skewness of some of the dependent variables, the presence of outliers, small sample size, and significant differences in the size of the compared groups determined the choice of used statistics. Nonparametric rank correlation coefficient Spearman's rho was used to estimate relationships between continuous variables. Associations between dichotomous variables were estimated using chi-square or Fisher's exact test. p-values below 0.05 were considered statistically significant.

## Results

### *Demographic and clinical characteristics*

The PHIV+ group consisted of 56 patients: 30 boys (54.6%) and 26 girls (46.4%); mean age = 164 months. The PHEU group consisted of 24 subjects: 11 boys (45.8%) and 13 girls (54.2%); mean age = 97.5 months, whereas the HIV-nA group consisted of 43 participants: 25 boys (53.2%) and 22 girls (46.8%); mean age = 143 months. Significant differences for between-group comparisons (PHIV+ vs. PHEU and PHIV+ vs. HIV-nA) were found in some demographic parameters (Table 1).

**Table 1. Demographic characteristics in PHIV+, PHEU and HIV-nA groups and results of between-group comparisons (PHIV+ vs. PHEU and PHIV+ vs. HIV-nA)**

	PHIV+ (n = 56)		PHEU (n = 24)		HIV-nA (n = 43)		PHIV+ vs. PHEU	PHIV+ vs. HIV-nA	PHEU vs. HIV-nA
	n (%)		n (%)		n (%)		p	p	p
Male	30 (53.6)		11 (45.8)		22 (51.2)				
Female	26 (46.4)		13 (54.2)		21 (48.8)		0.817	0.897	0.972
Resides with:									
Biological parent	38 (67.8)		18 (75.0)		43 (100.0)				
Adoption/Foster family	10 (17.9)		5 (20.8)		0 (0.0)		0.815	<0.001	0.002**
No data	8 (14.3)		1 (4.2)		0 (0.0)				
Full family	28 (50.0)		20 (83.3)		32 (74.4)		0.046	0.118	0.703
No data	4 (7.1)		0 (0.0)		0 (0.0)				
Delivery:									
In term	25 (44.6)		15 (62.5)		33 (76.7)				
Pre-term or post-term	12 (21.4)		7 (29.2)		8 (18.6)		0.999	0.427	0.550
No data	19 (33.9)		2 (8.3)		2 (4.6)				
Stressful life events of a child	24 (42.9)		15 (62.5)		21 (48.8)		0.959	0.720	0.617
No data	15 (26.8)		1 (4.2)		2 (4.6)				
Education level of mothers:									
Basic or vocational	13 (23.2)		5 (20.8)		0 (0.0)				
Secondary or high education	28 (50.0)		18 (75.0)		40 (93.0)		0.696	<0.001	0.007**
No data	15 (26.8)		1 (4.2)		3 (7.0)				
Mother's contacts with psychiatrist/psychologist	18 (32.1)		13 (54.2)		17 (39.5)		0.730	0.992	0.511
No data	14 (25.0)		1 (4.2)		2 (4.6)				
Education level of fathers:									
Basic or vocational	14 (25.0)		6 (25.0)		0 (0.0)				
Secondary or high education	17 (30.4)		14 (58.3)		34 (79.1)		0.556	<0.001	0.002**
No data	25 (44.6)		4 (16.7)		9 (20.9)				
Father's contacts with psychiatrist/psychologist	11 (19.6)		6 (25.0)		3 (7.0)		0.848	0.025	0.145
No data	26 (46.4)		4 (16.7)		10 (23.0)				
	Med	IQR*	Med	IQR*	Med	IQR*	p	p	p
Age – median (months)	64.0	9.0	7.5	9.6	43.0	1.0	0.010	0.071	0.131

\*interquartile range

\*\*Fisher's exact test

PHIV+ – Perinatally HIV-Infected

PHEU – Perinatally HIV Exposed but Uninfected

HIV-nA – HIV-non-Affected

The clinical characteristics of the PHIV+ group are presented in Table 2 and 3. Data on HIV infection were collected from parents. The presence of missing data stems from the fact that not all parents provided us with information on the matter.

Table 2. Clinical characteristics of the PHIV+ group. Part 1

Awareness of HIV infection	n (%) 33 (58.9)	Ultimate HIV category according to CDC: – A – B – C	n (%) 22 (39.3) 19 (33.9) 15 (26.8)
Smoking during pregnancy	13 (23.2)		
Substance use in pregnancy	7 (12.5)		
Alcohol consumption in pregnancy	3 (5.3)		
HCV infection in children	7 (12.5)		
HIV diagnosis before pregnancy	4 (7.1)		
Current (at the time of the study) HIV category according to CDC: – N – A – B – C No data	n (%) 41 (73.2) 5 (8.9) 0 (0.0) 5 (8.9) 5 (8.9)	Ultimate HIV immunologic status according to CDC: – 1 – 2 – 3	n (%) 14 (25.0) 21 (37.5) 21 (37.5)
Current (at the time of the study) HIV immunologic status according to CDC: – 1 – 2 – 3 No data	n (%) 48 (85.7) 3 (5.3) 0 (0.0) 5 (8.9)	HIV encephalopathy in a child	n (%) 9 (16.1)
ARV treatment initiation: – before the age of 3 months. – before the age of 12 months – no data – never treated	n (%) 7 (12.5) 25 (44.6) 1 (1.8) 2 (3.6)	ARV treatment at the time of the study: – children on medication – children without medication – no data	n (%) 49 (87.5) 2 (3.6) 5 (8.9)

CDC – Centers for Disease Control and Prevention; ARV – antiretroviral

Table 3. Clinical characteristics of the PHIV+ group. Part 2

Specification	At the time of diagnosis	At the time of treatment initiation	At the time of the study
Viremia; Copies of HIV RNA/ml:	n (%)	n (%)	n (%)
>100,000	27 (48.2)	26 (46.4)	0 (0.0)
10,000–100,000	14 (25.0)	16 (28.6)	3 (5.3)
401–10,000	1 (1.8)	3 (5.3)	1 (1.8)
<400	1 (1.8)	1 (1.8)	47 (83.9)
No data	13 (23.2)	10 (17.9)	5 (8.9)
Log <sub>10</sub> ; Copies of HIV RNA/ml:	n (%)	n (%)	
>5 log <sub>10</sub>	22 (39.3)	12 (21.4)	No data
3–5 log <sub>10</sub>	12 (21.4)	19 (33.9)	
<3 log <sub>10</sub>	3 (5.3)	2 (3.6)	
No data	19 (33.9)	13 (23.2)	
% of CD4 lymphocytes	n (%)	n (%)	n (%)
0–14%	13 (23.2)	11 (19.6)	12 (21.4)
15–24%	13 (23.2)	17 (30.4)	16 (28.6)
>=25%	26 (46.4)	23 (41.1)	23 (41.1)
No data	4 (7.1)	5 (8.9)	5 (8.9)
CD4 lymphocytes n/l:	n (%)	n (%)	n (%)
0–199	7 (12.5)	7 (12.5)	0 (0.0)
200–499	10 (17.9)	10 (17.9)	3 (5.3)
500–749	4 (7.1)	5 (8.9)	11 (19.6)
750–999	6 (10.8)	6 (10.8)	17 (30.4)
>1000	26 (46.4)	24 (42.8)	20 (35.8)
No data	3 (5.3)	4 (7.1)	5 (8.9)
Detectable viremia at the time of the study			n (%)
No data	-	-	5 (8.9)
			5 (8.9)

The median age at HIV diagnosis was 13 months. 33 participants (58.9%) were aware of the presence of their HIV infection, they were also aware that the infection was perinatal. 9 patients (16.1%) were diagnosed with HIV encephalopathy, and 5 children (8.9%) had detectable viral loads at the time of the study.

#### *Incidence of mental disorders – results of the K-SADS-PL*

The K-SADS-PL results are shown in Table 4.

Table 4. The results of K-SADS-PL examination.

	PHIV+ (n = 55)		PHEU (n = 24)		HIV-nA (n = 43)	
	At the time of the study n (%)	In a lifetime n (%)	At the time of the study n (%)	In a lifetime n (%)	At the time of the study n (%)	In a lifetime n (%)
Affective disorders						
Melancholic depression						
Dysthymia	1 (1.8)	2 (3.6)	-	-	-	-
Depressive disorder NOS	3 (5.5)	3 (5.5)	1 (4.2)	1 (4.2)	-	-
Adjustment disorder with depressed mood	1 (1.8)	1 (1.8)	-	2 (8.3)	1 (2.3)	2 (4.6)
	-	4 (7.3)	-	1 (4.2)	-	1 (2.3)
TOTAL NUMBER OF PATIENTS*:	5 (9.0)	9 (16.4)	1 (4.2)	3 (12.5)	1 (2.3)	3 (6.9)
Anxiety disorders						
Panic disorder						
Separation anxiety disorder	-	1 (1.8)	-	-	-	-
Social phobia	1 (1.8)	3 (5.5)	-	1 (4.2)	2 (4.6)	2 (4.6)
Agoraphobia	2 (3.6)	3 (5.5)	1 (4.2)	4 (16.7)	-	-
Specific phobias	-	-	1 (4.2)	1 (4.2)	-	-
Generalized anxiety disorder	3 (5.5)	4 (7.3)	1 (4.2)	2 (8.3)	1 (2.3)	1 (2.3)
Obsessive-compulsive disorder	3 (5.5)	4 (7.3)	2 (8.3)	2 (8.3)	1 (2.3)	1 (2.3)
	-	-	-	2 (8.3)	2 (4.6)	2 (4.6)
Post-traumatic stress disorder	-	-	-	1 (4.2)	-	-
TOTAL NUMBER OF PATIENTS*:	8 (14.5)	12(21.8)	4 (16.7)	7 (29.2)	6 (13.9)	6 (13.9)
Attention deficit hyperactivity disorder						
Predominantly inattentive type	-	-	-	-	-	-
Predominantly hyperactive-impulsive type	-	-	1 (4.2)	1 (4.2)	-	-
Combined type	-	-	1 (4.2)	1 (4.2)	-	-
ADHD NOS	4 (7.3)	5 (9.0)	3 (12.5)	3 (12.5)	4 (9.3)	4 (9.3)
TOTAL NUMBER OF PATIENTS*:	4 (7.3)	5 (9.0)	5 (20.8)	5 (20.8)	4 (9.3)	4 (9.3)

*table continued on the next page*



Conduct disorders						
Oppositional defiant disorder	-	1 (1.8)	-	1 (4.2)	-	1 (2.3)
Childhood onset type	2 (3.6)	3 (5.5)	-	-	-	-
Adolescent onset type	2 (3.6)	3 (5.5)	-	-	-	1 (2.3)
TOTAL NUMBER OF PATIENTS*:	4 (7.3)	7 (12.7)	-	1 (4.2)	-	1 (2.3)
Substance abuse						
Cannabis	4 (7.3)	4 (7.3)	-	-	-	-
TOTAL NUMBER OF PATIENTS*:	22 (40.0)	29 (52.7)	9 (37.5)	13 (54.1)	10 (23.2)	17 (39.5)
TOTAL NUMBER OF PATIENTS* with nicotine:	23 (41.8)	31 (56.4)	9 (37.5)	13 (54.1)	10 (23.2)	17 (39.5)

\*the diagnosis of more than one disorder was allowable

Of all subjects in the PHIV+ group, 55 patients (98.2%) were investigated, including 45 child-parent dyads. The diagnosis of at least one psychiatric disorder at the time of the study was made in 22 cases (40.0%); such diagnosis in a lifetime was made in 29 cases (52.7%). The most common diagnoses were anxiety disorders (21.8%) and affective disorders (16.4%). All children/adolescents and parents from the PHEU group participated in the K-SADS examination ( $n = 24$ ; 100.0%). At least one psychiatric disorder at the time of the study was diagnosed in 9 subjects (37.5%); at least one diagnosis in a lifetime was made in 13 subjects (54.1%). The K-SADS examination was carried out with 43 children and adolescents in the HIV-nA group (100.0%), along with 42 caregivers. At least one psychiatric disorder at the time of the study was diagnosed in 10 subjects (23.2%); at least one diagnosis in a lifetime was made in 17 subjects (39.5%). The most common diagnoses in both reference groups were anxiety disorders (29.2% in the PHEU group and 13.9% in the HIV-nA group) and ADHD (20.8% in the PHEU group and 9.3% in the HIV-nA group).

No significant differences in the prevalence of any psychiatric disorder were observed in intergroup comparisons. Regardless of that fact, affective disorders in a lifetime were more often diagnosed in the PHIV+ group (PHIV+ 16.4%; PHEU 12.5%; HIV-nA 6.9%), as were conduct disorders (PHIV+ 12.7%; PHEU 4.2%; HIV-nA 2.3%), whereas ADHD (each subtype) was more often diagnosed in the PHEU reference group (20.8%) compared to 9.0% in the PHIV+ group and 9.3% in the HIV-nA group.

## Incidence of emotional and behavioral disorders

### *Results of the CBCL/4-18*

The CBCL/4-18 was completed by 43 PHIV+ group caregivers (77%), 22 caregivers in the PHEU group (91%) and 40 in the HIV-nA group (93%). The median scores for all problem scales, as well as for *Internalizing*, *Externalizing* and *Total Problems*, placed PHIV+, PHEU and HIV-nA groups within the normal range (i.e., below 61T on the T-score scale). The results of intergroup comparisons showed few significantly higher scores among the participants in the PHIV+ group compared to both reference groups (Table 5).

### *Results of the YSR*

At the beginning of the study, 22 children in the PHIV+ group were older than 11. The YSR was also completed if a child reached the age of 11 during the course of the study. Ultimately, the YSR was completed by 38 adolescents (67.8%) in the PHIV+ group, 8 (33.3%) in the PHEU group and 23 (53.5%) in the HIV-nA group. The median scores for the *Internalizing*, *Externalizing* and *Total Problems* scales placed the PHIV+ and HIV-nA groups within the normal range (i.e., below 61T on the T-score scale). Threshold values were observed on the *Somatic Complaints* scale in the PHEU group (62.5T), with median scores for other scales within the normal range. No significant intergroup differences were observed for the YSR scores (Table 5).

Table 5. The comparison of CBCL/4-18 and YSR scales median scores: PHIV+ vs. PHEU and PHIV+ vs. HIV-nA (Mann Whitney U Test)

CBCL/4-18 6-18 years	PHIV+ n = 43		PHEU n = 22		HIV-nA n = 40		PHIV+ vs. PHEU	PHIV+ vs. HIV-nA
	Med	IQR	Med.	IQR	Med	IQR	p	p
Withdrawn	3.0	4.00	1.0	2.50	1.00	2.50	0.010	0.047
Aggressive Behavior	8.0	8.50	7.5	9.75	3.00	7.50	0.956	0.047
Externalizing Problems	11.0	11.00	9.0	13.00	4.50	10.25	0.813	0.042
6-11 years	n = 23		n = 18		n = 21			
Withdrawn	3.00	4.00	1.00	1.00	1.00	2.00	0.025	0.020
Social Problems	3.00	5.00	1.00	2.00	1.00	2.00	0.049	0.075
Delinquent Behavior	2.00	1.00	2.00	4.00	0.00	2.00	0.523	0.011
Aggressive Behavior	9.00	8.00	8.00	11.00	5.00	7.00	0.763	0.023
Externalizing Problems	11.00	8.00	10.00	14.00	6.00	9.00	0.602	0.015
Total Problems	31.00	19.00	27.00	24.00	18.00	20.00	0.661	0.039
12-18 years	n = 20		n = 5		n = 19			
Attention Problems	6.00	5.25	1.00	2.00	3.00	5.50	0.040	0.515

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YSR	n = 38		n = 8		n = 23		lp	p
	Med	IQR	Med	IQR	Med	Med		
Somatic Complaints	1.50	4.00	5.50*	5.25	3.00	3.00	0.070	0.174

\* 62.5T.

PHIV+ – Perinatally HIV-Infected

PHEU – Perinatally HIV Exposed but Uninfected

HIV-nA – HIV-non-Affected

YSR – Youth Self-Report

CBCL/4-18 – Child Behavioral Checklist

### Relationships with clinical and sociodemographic factors

Due to the small sizes of the various age groups, analyses of relationships between K-SADS-PL, CBCL/4-18 and YSR scores and clinical and sociodemographic factors were conducted for a single group of children (6–18 years).

#### *PHIV+ group*

The analysis of the presence of psychiatric disorders, as diagnosed by the K-SADS-PL, and clinical factors showed significant differences in the prevalence of any psychiatric disorder in a lifetime in children who started ARV treatment after the age of 12 months ( $p = 0.045$ ). Externalizing problems (including ADHD or CD) were diagnosed more often in children treated before the age of 3 months ( $p = 0.011$ ).

Significant differences in CBCL/4-18 or YSR scores were observed across subgroups relative to sex, living with a biological parent, being raised in an intact family, the experience of a stressful event, and such clinical factors as illness awareness, HIV infection clinical class and encephalopathy (Table 6).

Table 6. Significant differences in YSR and CBCL/4-18 scores in subgroups depending on sociodemographic and clinical factors: PHIV+ group

	Med	IQR	Med	IQR	p
YSR	Girls (n = 14)		Boys (n = 24)		
Delinquent Behavior	2.00	2.00	4.00	3.25	0.015
Aggressive Behavior	2.00	2.00	4.00	3.25	0.015
Externalizing Problems	4.00	4.00	8.00	6.50	0.015
YSR	No-awareness of HIV infection (n = 8)		Awareness of HIV infection (n = 30)		
Delinquent Behavior	2.00	2.25	3.50	4.00	0.043
Aggressive Behavior	2.00	2.25	3.50	4.00	0.043
Externalizing Problems	4.00	4.50	7.00	8.00	0.043

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YSR	C class (n = 8)		Non-C class (n = 30)		
Delinquent Behavior	2.50	2.75	5.00	2.50	0.025
Aggressive Behavior	2.50	2.75	5.00	2.50	0.025
Externalizing Problems	5.00	5.50	10.00	5.00	0.025
CBCL/4-18	No HIV encephalopathy (n = 32)		HIV encephalopathy (n = 8)		
Anxious/Depressed	2.50	3.00	5.00	4.25	0.042
CBCL/4-18	Biological parent (n = 30)		No biological parent (n = 13)		
Social Problems	1.00	3.00	3.00	4.00	0.013
YSR	Full family (n = 16)		One-parent family (n = 19)		
Somatic Complaints	0.50	2.25	2.00	3.50	0.048
CBCL/4-18	No stressful life events (n = 15)		Stressful life events (n = 24)		
Somatic Complaints	0.00	1.50	2.00	2.25	0.029

YSR – Youth Self-Report

CBCL/4-18 – Child Behavioral Checklist

PHIV+ – Perinatally HIV-Infected

No statistically significant relationships were found between the incidence of psychiatric disorders, as measured by K-SADS-PL, and clinical or sociodemographic factors. Statistically significant correlations between clinical factors and CBCL/4-18 or YSR results are shown in Table 7.

**Table 7. Relationships between CBCL/4-18 and YSR scores and clinical factors: PHIV+ group**

	Viral load – Diagnosis (Logarithm)		Viral load – ARV treatment initiation (Logarithm)		CD4 % at the time of the study	
	rho	p	rho	p	rho	p
CBCL/4-18						
Anxious/Depressed	-	-	0.37	0.024	-	-
Social Problems	0.57	<0.001	0.59	<0.001	-	-
Attention Problems	-	-	-	-	0.10	0.039
Internalizing Problems	-	-	0.33	0.044	-	-
Total Problems	-	-	0.34	0.037	-	-
YSR						
Delinquent Behavior					0.08	0.004
Aggressive Behavior					0.08	0.004
Externalizing Problems					0.08	0.004

PHIV+ – Perinatally HIV-Infected

CD4 – limfocyty CD4

ARV – antiretroviral

YSR – Youth Self-Report

CBCL – Child Behavioral Checklist

### *PHEU group*

Significantly higher CBCL/4-18 scores were observed on the following scales: *Delinquent Behavior* ( $p = 0.035$ ) and *Externalizing Problems* ( $p = 0.041$ ) in boys; *Somatic Complaints* ( $p = 0.042$ ) and *Internalizing Problems* ( $p = 0.045$ ) in children living with their biological parent; and *Internalizing Problems* ( $p = 0.043$ ) in children who experienced a stressful event in their lifetimes. No significant correlations were found between CBCL/4-18 scores and sociodemographic factors.

## **Discussion**

Our study is the first to have evaluated the majority of HIV infected individuals aged 6–18 in Poland. The prevalence rates of mental disorders in subjects were lower compared to the results of American studies, which have described the prevalence of psychiatric disorders in 55–61% of PHIV+ children and 49–62% of PHEU children [2, 3, 5, 6, 9]. The most common diagnoses in children with perinatal infection included anxiety disorders and affective disorders. Our result is in line with other reports about the profiles of psychiatric disorders in the general population of children and adolescents [28, 29], which have shown the highest prevalence for anxiety disorder. Anxiety disorder is a predominant diagnosis also in PHIV+ children, with the prevalence of 24–49% [2, 3, 6, 9]. The high prevalence of externalizing problems in PHEU children found in our study (including ADHD or CD) is similar to the results of other studies (24–27%) [2, 3, 9].

Contrary to the K-SADS-PL assessments, the results of the CBCL/4-18 and YSR did not place PHIV+ group within clinical thresholds in any problem scales. The same results were reported by Mellins et al. [9], who found that the high prevalence of psychiatric disorders (55%) observed in direct interviews was not confirmed by the results of questionnaires (CBCL/4-18 and *the Child Depression Inventory* [30] filled in by the caregiver and the child).

Taking into consideration intergroup comparisons, it can be concluded that the severity of internalizing problems is greater in children with perinatal HIV infection compared to HIV-exposed healthy children. They are also characterized by a greater severity of externalizing problems in comparison with healthy children of healthy parents. The results are compatible with the study of Gortmaker et al. [31], which showed an increased prevalence of conduct disorders in children diagnosed with a chronic condition. One of the hypotheses explaining this phenomenon emphasizes the negative influence of a chronic condition on social interactions and family systems, which is one of the risk factors for conduct disorders. Different results can be found in the study of

Gadow et al. [4], where the prevalence of parent-reported conduct disorder in PHIV+ children was significantly lower than in PHEU children (4.8% vs. 9.3%). According to the authors, the result could be explained by the influence of a high level of control over the functioning of an infected child and his/her caregivers (via regular medical appointments, treatment regimen), leading to the stabilization of such behavior and enabling a quick reaction in the event of dysfunctional behaviors. The results of our study showed that external control was insufficient as regards the prevention of conduct disorders in the PHIV+ group (including frequent use of tobacco and cannabis abuse not observed in the reference groups).

When analyzing the relationships with clinical factors, we found that psychiatric disorders in a lifetime were more common in PHIV+ subjects whose ARV treatments were started after 12 months of age. On the other hand, externalizing disorders (ADHD or CD) were more often observed in children treated before 3 months of age. It seems that this may be related both to environmental factors that prevented the child from being diagnosed with HIV early enough, and to untreated HIV neuroinfection. Considering that the examined children were mostly the first family members diagnosed with HIV infection, it can be assumed that in some cases the initiation of ARV treatment before 3 months of age could have been caused by severe HIV infection symptoms.

When analyzing the results of the CBCL/4-18 and YRS, one may hypothesize that the severity of infection before treatment (assessed on the basis of viral load (log<sub>10</sub>) at the moment of diagnosis and at the moment of ARV treatment initiation) is associated with the occurrence of internalizing problems, especially parent-reported ones, whereas better clinical status (assessed on the basis of CD4 lymphocytes levels and lower than Class C infection status) is related to a higher severity of externalizing problems per children's reports. Nichols et al. [32], who noted greater severity of behavioral problems in children with 'better' courses of the infection (i.e., later onset of the highest viral load and smaller decreases of CD4 lymphocytes across the lifespan), indicate lower probability of the presence of challenging behaviors in children with more severe courses of infection (due to greater control exerted by both parents/caregivers and the medical environment). The contradictory results of the study of Bomba et al. [15] showed a correlation between viral load at the time of the study and greater scores on the CBCL/4-18 *Delinquent Behavior* scale. In the current study, viremia was undetectable in the PHIV+ group, although the prevalence of conduct disorders was higher than in the reference groups.

More frequent occurrence of emotional and behavioral symptoms in the group of children and adolescents with perinatal HIV infection and in the group of healthy infection-exposed individuals is associated with similar sociodemographic variables (male gender, not living with a biological parent, stressful life events; for the group with perinatal HIV infection, additionally having one-parent family). The influence of not living with a biological parent can be interpreted in the context of the fact itself and how the caregiver perceives the child's behavior and mood [10, 11]. The multid-

dimensionality of the problem was shown in the results of the study of Gadow et al. [4], who reported worse functioning of PHIV+ children who lived with their biological parents. On the other hand, Mellins et al. [2] and Elkington et al. [20] found that better clinical status of an HIV+ parent was related to better mental health of a child as well as lower severity of conduct and somatization problems.

In our study, boys scored significantly higher on *Delinquent Behavior*, *Aggressive Behavior* and *Externalizing Problems* scales, but only in their own assessment (YSR), and not in the assessment of parents/caregivers (CBCL / 4-18). On the other hand, in the PHEU control group, it was the caregivers who significantly more often reported the occurrence of symptoms in the area of *Delinquent Behavior* and *Externalizing Problems* in boys. This may indicate the limited capacity of the caregivers of HIV-infected children to provide information about additional problems.

Awareness of one's own perinatal HIV infection seems to be another important factor affecting mental health, yet the consequences remain ambiguous. Infection-aware subjects reported more externalizing symptoms on *Delinquent Behavior*, *Aggressive Behavior* and *Externalizing Problems* scales. Furthermore, the YSR scales scores correlated positively with age. However, the group of illness-aware children was significantly older, which means that the higher score may not be directly related to infection awareness as such.

There are several important limitations of the study. The first is the limited size of the experimental group and control groups, which resulted in statistical limitations and made it impossible to perform analyzes taking into account more than one factor. Consequently, the study is mainly descriptive and does not permit conclusions to be drawn about any relationships between variables. We failed to recruit a control group of infection-exposed children who could be age-matched. It seems that the difficulty in recruiting older children was due to the fact that mothers of children with perinatal HIV infection in subsequent pregnancies were already under specialist care and gave birth to healthy children. Another limitation is the lack of a socio-economic status criterion in the matching process.

## Conclusions

The prevalence of psychiatric disorders in children and adolescents with perinatal HIV infection and perinatally HIV-exposed but uninfected children and adolescents is higher in comparison with healthy children of healthy parents, but the profile of the diagnosis is characteristic of the general population of children and adolescents. A more serious course of HIV infection and its severity before treatment are associated with the severity of internalizing problems. Better current clinical status and severity of HIV infection are correlated with greater severity of externalizing problems.

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