

Analysis of clinical symptoms and selected hematological indices in hospitalized children with *Ascaris lumbricoides* infection from the northeastern region of Poland[1]

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ABSTRACT. Ascariasis is the most common soil-transmitted helminth infection in the world. The objective of this study was to analyze the clinical symptoms and selected hematological indices of ascariasis in hospitalized children from the northeastern region of Poland. Patients in the Pediatric Ward hospitalized in the Regional Hospital in Dąbrowa Białostocka in the period of 2005–2007 were included in this retrospective study. The intestinal stage of ascariasis was diagnosed on the basis of positive coprological survey performed using the decantation technique. A total of 938 patients were included in the study, 1801 stool samples were evaluated, and *A. lumbricoides*-positive tests were obtained from 252 children. *Ascaris*-positive young children (≤3 yrs) accounted for 3.0% of all hospitalized children, *Ascaris*-positive preschool-aged children (4–7 yrs) accounted for 8.1% and school-aged children (8–18 yrs) for 15.8%. Seasonal patterns were observed in the prevalence of *A. lumbricoides* (maximum in August–December). There was no relationship between BMI z-score, hemoglobin levels and prevalence of infection with *Ascaris lumbricoides*. Significant predictors of intestinal stage ascariasis in a multivariate logistic regression model were: abdominal pain as a reason for hospital admission (OR–2.19; 95%CI 1.62–2.95; p<0.001) and age from 4 to 7 years (OR–2.0; 95%CI 1.41–2.80; p<0.001). The prevalence rate of ascariasis was not higher in the group of patients with atopic diseases (bronchial asthma, allergic rhinitis, atopic dermatitis) and co-existing ascariasis did not affect the eosinophil counts in the peripheral blood. Ascariasis is still a current pediatric clinical problem characterized by non-specific clinical manifestations, which should be taken into consideration in the differential diagnosis of children's diseases.

Key words: *Ascaris lumbricoides*, ascariasis, abdominal pain, blood, children, Poland

Introduction

Ascariasis is a cosmopolitan intestinal parasitosis estimated to affect approximately 1.4 billion people worldwide, most (73%) in Asia [1,2]. In Poland, the infection rate among children is of the order of several percent [3–5]. The factors playing a key role in the transmission of infection are poor sanitary and epidemiological conditions as well as closed environments and state of health of the exposed subjects [6]. The clinical course in the majority of the infected subjects is asymptomatic; however, those excreting ova constitute a link in the epidemic chain, aiding in the perpetuation of the parasite's life cycle. During development, in growing children, in which the prevalence of

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infection is relatively high, clinical symptoms of ascariasis can mimic other common childhood diseases: respiratory infections, bronchial asthma, skin allergies and gastrointestinal diseases. The consequences of chronic and untreated infections include systemic symptoms, such as disturbances in somatic development or secondary nutritional deficiencies such as anemia, behavioral and sleep disorders [7]. Diagnosis is hampered by lack of sensitive diagnostic tests and is often made only in the event of therapeutic failure of ex juvantibus treatment [3–5,8–11].

The Podlasie region is characterized by high prevalence of ascariasis [5]. The aim of this study was to evaluate the frequency of *A. lumbricoides* infection among hospitalized children, residing in the Podlasie region, and to record the most frequent characteristics of the clinical picture of infection with an assessment of selected hematological parameters.

Materials and methods

The study was carried out among patients of the Pediatric Ward at the Regional Hospital in Dąbrowa Białostocka, in the rural, northeastern region of Poland. Medical documentation of all patients hospitalized from January 2005 to December 2007 was analyzed. Clinical data, blood and stool laboratory results were taken into account in this retrospective analysis. The intestinal stage of ascariasis was diagnosed on the basis of a positive coprological examination. The coprological study was carried out using the decantation technique at intervals of 2–3 days. Fecal samples (approximately 2 g) were homogenized in 3 ml of distilled water. After 2 hours the supernatant liquid was gently removed and the sediment mixed again with water; the procedure was repeated 3 times. After that, slides were prepared for microscopic examination, *A. lumbricoides* eggs were identified by two laboratory specialists. Stool tests for the presence of parasite eggs and *Lamblia intestinalis* cysts were performed on samples from 300 children in 2005, 304 children in 2006 and 334 children in 2007.

Clinical symptoms were recorded in the database as binary variables. The presence of a symptom was coded as 1, lack of a symptom as 0. Thereby, we analyzed the history of gastrointestinal signs as a reason for hospital admission (abdominal pain, vomiting/nausea, diarrhea), history of respiratory diseases (recurrent infections, wheezing, bronchial asthma, allergic rhinitis), history of skin symptoms (itching, urticaria, atopic dermatitis). The diagnosis of atopic diseases (bronchial asthma, allergic rhinitis and atopic dermatitis) was considered only if it was made by a specialist allergist in the outpatient clinic of allergic diseases or in the department of allergic diseases.

The nutritional status was determined by body mass index (BMI, weight (kg)/(height (m)^2). The BMI z-score was calculated using gender-specific BMI-for-age growth charts, and values of more than two standard deviations (±2SD) from the mean BMI z-score were assumed to indicate significant departure from normal.

Blood counts were conducted on an 18-parameter hematology analyzer (ABX Micros 60 hematology analyzer, HORIBA Medical) and the hematological parameters of the peripheral blood were also analyzed: hemoglobin (g/dl), hematocrit (%), mean corpuscular volume MCV (fl), platelets (number/mm^3), leukocyte count, WBC (number/mm^3) as well as relative (%) and absolute blood eosinophil counts (number/mm^3). All children with stool positive for *A. lumbricoides* and clinical symptoms were treated with antihelminthic drugs (albendazole, mebendazole or pyrantel).

Statistical analysis

The following tests were applied: the t-Student test to compare variables with a normal distribution (Body Mass Index z score; BMI), the Mann-Whitney U-test to compare variables with non-parametric distribution (age), the Shapiro-Wilk test to verify the distribution of test variables (age, BMI, blood parameters), as well as the chi-square test for independence, and the Yates' chi-square test for comparison of qualitative and categorized variables. In order to evaluate the relationship between the independent variables (predictor factors) and the binary dependent variable (the presence of ascariasis eggs in children's stools) logistic regression was employed. All the potential risk factors of ascariasis were fitted as independent factors in the analysis. In order to identify the best and independent predictors of occurrence of ascariasis among children, all the independent variables that significantly affected the dependent variable in one-factor models, were included subsequently in the multi-factor model. Odds ratios (ORs) and the corresponding 95% confidence intervals (CI) for clinical symptoms and

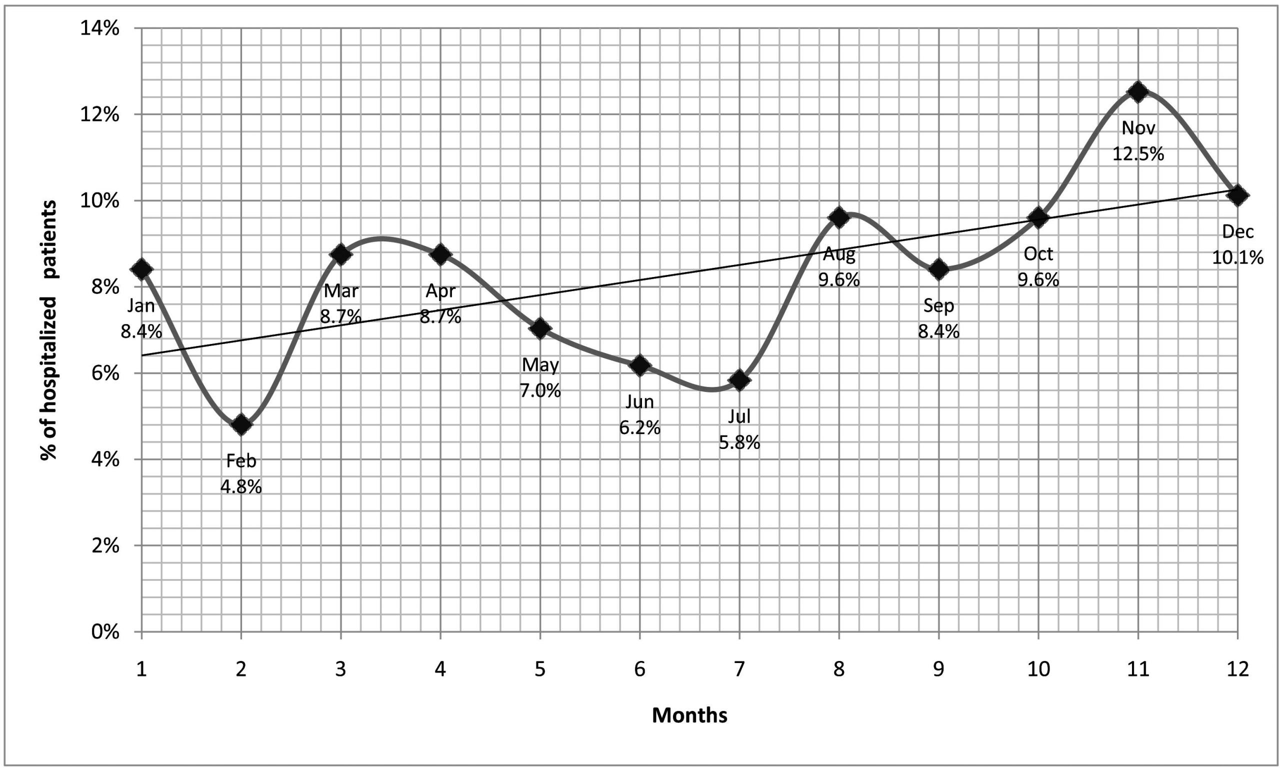

Fig. 1. Seasonal patterns in *A. lumbricoides* isolation rates in hospitalized children. The highest rate was in the late summer and in the autumn.

hematological parameters were estimated. For all the statistical tests used, α=0.05 level of relevance was accepted. The statistical analysis was carried out by means of the STATISTICA 9.0 program.

Results

The study population (n=938) had an age range of 1–18 years. There were 43.2% of boys and 59.8% of children from villages in the region. The analysis was conducted in three age groups: group I: 1–3 yrs (young children), n=145; group II: 4–7 yrs (preschool children), n=207; group III: >7 yrs (school children), n=586 (Table 1). A total of 1801 stool specimen results were analyzed. In 370 children a single coprological examination was carried out, in 267 children it was performed twice, and in 299 children three times. Ascariasis infection was diagnosed in 252 children. In preschool-aged children, the infection was found most often in the first stool sample (63%) (Table 1). Young children with ascariasis accounted for 3.0% of all hospitalized children, preschool children with ascariasis for 8.1% and school children for 15.8%. These groups did not differ in gender distribution. Seasonal patterns in *A. lumbricoides* isolation rates were observed (from August to December) (Fig. 1).

Clinical characteristics of children with *Ascaris*-positive stool

Nutritional status

The average BMI z-score value of the whole group was low: 0.023 (95%CI –0.04–0.09, range –4.37 to 4.36). The BMI z-scores of *Ascaris*-positive and *Ascaris*-negative children did not differ (p=0.2).

Clinical symptoms

Children with stools positive for *A. lumbricoides* eggs presented with a wide spectrum of gastrointestinal symptoms (Fig. 2). Abdominal pain was most frequently observed in school children (72.0%), the least in young children (9.0%). Vomiting and dehydration were the most common causes of hospitalization in the youngest age group (53.6%). Skin symptoms in the form of chronic urticaria or pruritic eruptions occurred equally frequently in the group with and without infection (11.9% vs. 11.5%; p=0.89).

The history of respiratory symptoms occurred in 51.2% (n=129) of the children with a positive stool test and in 42.7% (n=293) of the children with a negative stool test (p<0.02). Among the children with ascariasis, symptoms of bronchial tree obturation (wheezing) were recorded in 9.9%, and in the group with a negative stool test in 10.2%

Table 1. Characteristics of children with ascariasis in three age groups

	≤3 years(n=28)	4–7 years(n=75)	>7 years(n=148)
Median of age (in years)	2.0	5.3	11.9
InterquartiIe range of age (in years)	1.7–2.7	4.0–6.3	9.3–15.0
Percentage of hospitalized (%)	2.99	8.0	15.78
Village (%)*	50.0	65.3	47.6
Male (%)†	46.4	39.5	48.0
Stool samples (n)	42	93	207
Positive first stool sample (%)‡	34.0	63.6	50.0

Explanations: Chi^2 Pearson Test * p=0.48; † p=0.12; ‡ p<0.002

(p=0.9). The prevalence of *A. lumbricoides* infection was not higher in the group with allergies as compared to allergy-free children. The percentage of patients infected in the bronchial asthma group was 26.3% (n=25/70) (p=0.9), in the allergic rhinitis group 15.0% (n=3/17) (p=0.2), in the atopic dermatitis group 20.0% (n=5/20) (p=0.4) and in the urticaria group 19.1% (n=4/17) (p=0.4).

In children with ascariasis, various disease symptoms were diagnosed concurrently: gastroesophageal reflux disease (3.3%), constipation (2.5%), arrhythmia and syncope (1.7%), cow's milk protein allergy (1.6%), dysuric symptoms (0.5%), hypomagnesemia/hypocalcemia (0.4%), sinusitis (0.2%), hypostatura (0.2%), vertigo (0.2%), metatarsal arthritis (0.1%), stomatitis aphthosa (0.1%).

Analysis of hematological parameters

There were no differences in the hemoglobin concentrations, white blood cell count and the average red blood cell volume (MCV) between the two groups in the respective age categories (Fig. 3). Absolute eosinophilia in both groups was within normal limits, in the group of infected children amounting to 242.2±164.9/mm^3 and in the group of non-infected children to 246.3±300.6/mm^3(p=0.34). In children with gastrointestinal symptoms, the eosinophil cell count was higher in the infected children than in the control group (level of significance p=0.06). Ascariasis in children with allergic diseases did not affect the severity of eosinophilia in the peripheral blood (Fig. 4). There

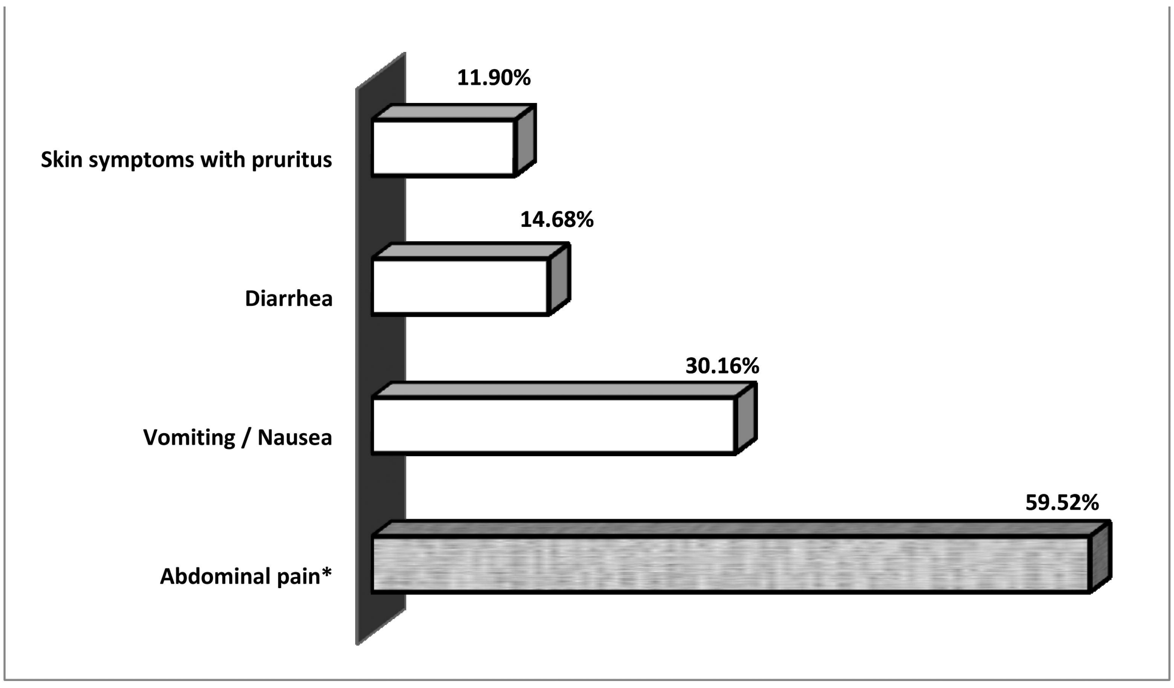

Fig. 2. Clinical symptoms in *Ascaris*-positive children demonstrated on hospital admission. Abdominal pain was the only symptom more common in *Ascaris*-positive vs. *Ascaris*-negative group (* p<0.001; test *U*).

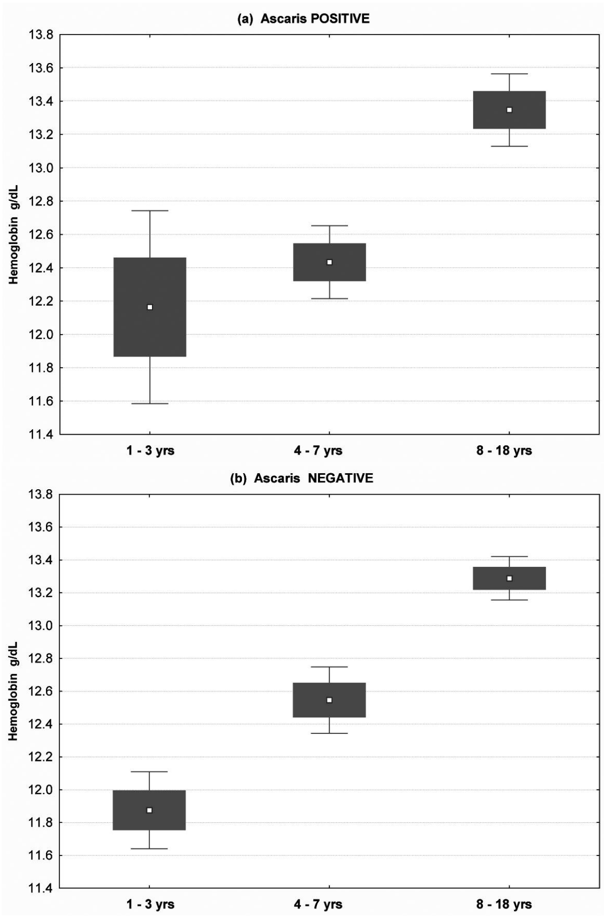

Fig. 3. Mean hemoglobin concentration in *Ascaris*-positive and *Ascaris*-negative children in the respective age categories (ANOVA p=NS)

were no differences in the assessed clinical and morphological parameters between the years 2005, 2006, 2007.

The probability of occurrence of ascariasis in relation to each of the fitted factors was calculated using logistic regression (Table 2). Significant variables were included in the multivariate regression model. In this model, two predictor factors were connected with a two-fold increased risk for ascariasis: abdominal pain and age between 4 and 7 years (Table 3).

Discussion

The aim of this study was to evaluate the clinical symptoms of ascariasis in hospitalized children. Children included in the study came from the region where the percentage of infection among 7-year-old school children was estimated 11 years ago at 40% among rural children and 18.4% among urban children (mean 24.1%), and 8 years ago at 15.8% on average (95% CI 14.2–17.4%) [5,8].

In the study population of the hospitalized children, the risk of ascariasis calculated using the odds ratio identified to children between 4 and 7 years of age as particularly at risk, and this can be associated with lack of good hygiene habits that are typical of this age group and attendance at nurseries and preschools.

A seasonal occurrence of outbreaks of infection was observed, prevalence being the highest in the second half of the year in late summer and in the autumn. This observation is consistent with the idea of greater exposure to infection in this period in the warm months of the summer (playing in the sand, greater consumption of vegetables and fruit from home gardens, often naturally contaminated by soil).

The clinical symptoms of ascariasis depend on the life cycle of the parasite. In the first phase of infection with the invasive egg, during migration of larvae into the lungs, there are general symptoms (body temperature increasing to 38.3°C), a dry nonproductive cough, symptoms of airway obstruction (dyspnea, wheezing, and even hemoptysis) and skin symptoms (pruritus, urticaria) [1]. The non-specific nature of the symptoms, their similarity to common infections or allergies, and additionally the fact that this is a nondiagnostic phase (for approximately 40 days from the infection onset, there is an absence of parasite eggs in stools) significantly hinder diagnosis. In hospitalized children with *A. lumbricoides* eggs in the stool, 51.2% had a documented history of symptoms of respiratory infection. However, it is not clear whether these were connected with the infection or had other causes. Pulmonary manifestations of ascariasis are rarely a complication of the intestinal phase; however, in children in this phase there is a possibility of reinfection. Indeed, a past *Ascaris* infection leaves no resistance and does not protect against reinfection, and the risk of reinfection depends on constant exposure to *A. lumbricoides* eggs [12,13].

While discussing other symptoms in children with a positive stool test, we must also consider a random occurrence of disease in children with asymptomatic infection. In the second (intestinal) phase of ascariasis, symptoms from the gastrointestinal tract occur, which are characterized by great diversity. In the intestinal phase, ascariasis symptoms may mimic an acute abdomen (peritonitis and appendicitis), which is associated with the intestinal migration of mature individuals that have

Table 2. Predictor factors of infection with *A. lumbricoides* in hospitalized children

	OR	95% CI	p
Town	**1.48**	1.04–2.12	**0.031**
Village	**0.67**	0.47–0.96	**0.031**
Female	0.90	0.67–1.20	0.463
Male	1.11	0.83–1.49	0.465
1–3 years	**0.61**	0.39–0.94	**0.027**
4–7 years			
>7 years	0.79	0.59–1.07	0.123
BMI z-score <1SD	0.98	0.28–3.46	0.974
Abdominal pain	**2.07**	1.54–2.78	**<0.001**
Vomiting	1.05	0.75–1.44	0.766
Diarrhea	0.83	0.56–1.25	0.377
Urticaria	1.04	0.65–1.65	0.874
Bronchial asthma	0.97	0.59–1.60	0.915
Allergic rhinitis	0.47	0.14–1.64	0.238
Atopic dermatitis	0.63	0.21–1.91	0.419
Hemoglobin level <11 g/dl	1.06	0.69–1.65	0.780
Eosinophilia in blood >3%	0.89	0.67–1.18	0.414

the ability to crawl into the pancreatic duct, the biliary ducts and the appendix [14]. They are reported in a significant percentage of patients, particularly the abdominal pain (87%) and, less frequently diarrhea (15%) [15]. Among children with abdominal pain, the risk of ascariasis was twice as high (OR=2.2) as in children without abdominal pain. Skin lesions described in the course of ascariasis have different symptoms: utricaria, cutaneous pruritus, Schonlein-Henoch syndrome [16].

Recently, the relationship between parasitic infections and allergies has been discussed [17–22]. Clinical symptoms of ascariasis may mimic the symptoms of allergic disease and some authors suggest the participation of intestinal parasites in immunomodulation [22]. IgE antibody are an important component of the immune resistance to helminth infections [23]. There are two different IgE responses to helminthic infections. The first is synthesis of IgE specific to parasite antigens (sensitisation), the second is non-specific polyclonal synthesis of IgE, which results in highly elevated total serum IgE level [23,24]. It is assumed that parasitic infections with a high total IgE may protect against allergens, i.e. by blocking mast cell response to an allergen, which is explained by a lower percentage of positive skin prick tests in children with infection [21]. Parasitic worms may survive in their mammalian hosts by switching off inflammatory immune responses and inducing a tolerant response to parasite antigens [25]. Thus, the parasites can protect against allergies, especially among chronically infected children by increasing the secretion of regulatory immunoreactive cytokines (IL-10 and TGF-beta and reduced secretion of IL-4) [22,26–28].

On the other hand, there are reports that chronic or moderately severe ascariasis may increase the risk of symptoms of asthma and allergy to airborne allergens [18]. Increased bronchial hyperreactivity provoked by exertion was noted in children with serologically confirmed ascariasis [17]. Alcantara-Neves et al. reported that *Ascaris lumbricoides*

Table 3. Predictor factors of intestinal stage of ascariasis in hospitalized children in multiple logistic regression analysis

	OR	95% CI	P
Abdominal pain	2.19	1.62–2.95	<0.0001
Age between 4 and 7 years	2.00	1.41–2.80	<0.0001

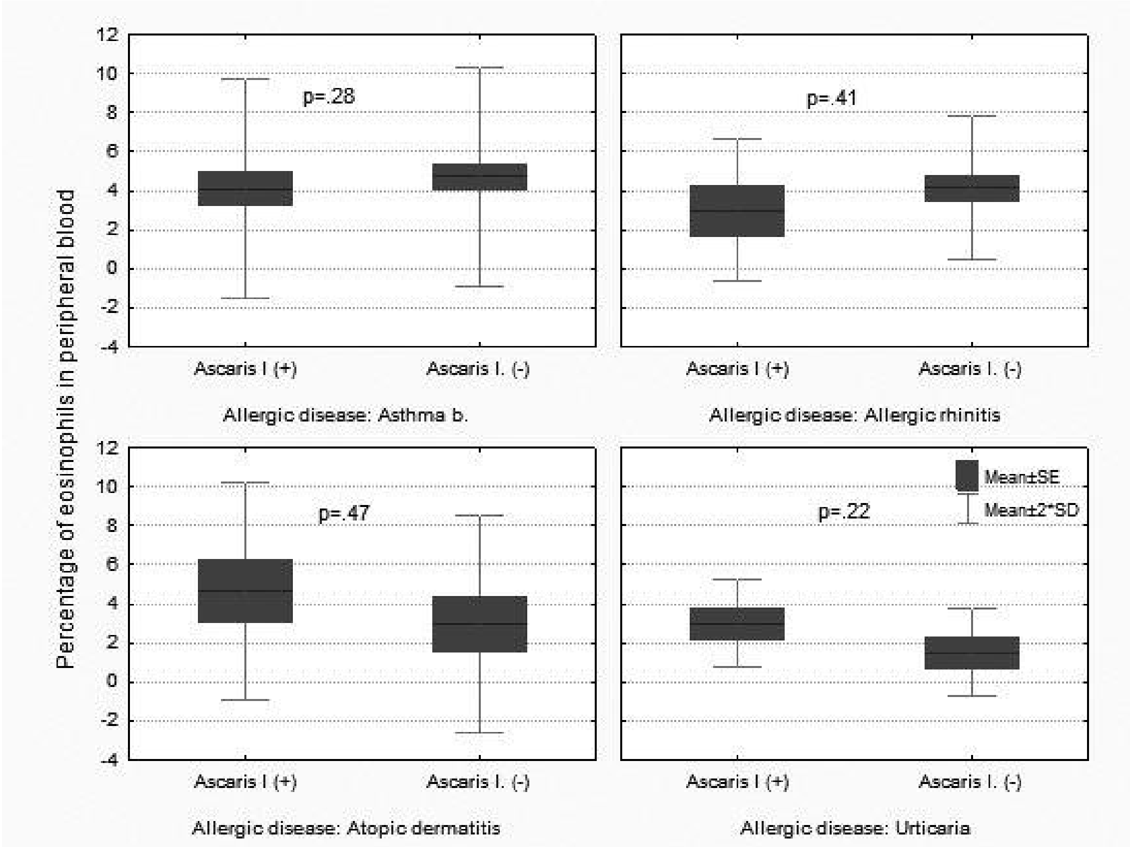

Fig. 4. Comparison of peripheral blood eosinophilia in children with allergic diseases with and without *A. lumbricoides* infection

sensitization, but not *A. lumbricoides* infection, was associated with wheezing and atopy in early childhood [29]. We found no increased prevalence of chronic *A. lumbricoides* infection (confirmed by presence of *A. lumbricoides* eggs in the stool) in children with atopic diseases (asthma, allergic rhinitis and atopic dermatitis) compared to children without atopy. Since anti-*Ascaris* IgE antibodies were not detected in the study children, the association between *A. lumbricoides* sensitization atopic diseases was not assessed in the current study.

The consequences of chronic and untreated infections may include systemic symptoms, such as disturbances of somatic development, secondary nutritional deficiencies, i.e. anemia, and behavioral and sleep disorders. In the study groups, behavioral disorders and parasomnias were observed in just a few patients, and lower hemoglobin concentrations in children with ascariasis were not observed. Children with ascariasis also did not differ from uninfected children in the intensity of peripheral blood eosinophils, with the exception of children with gastrointestinal symptoms. Noteworthy is the fact that there was a low percentage of children with nutritional disorders (BMI z-score >2 standard deviations) among all hospitalized children; only 4 children were diagnosed with malnutrition and 9 with obesity, which accounts for 1.4% of all the hospitalized patients. This observation can be considered a consequence of the economic status of the families and nutrition, and in some children may also be an indirect sign of parasitic disease [7,30]. Therefore, when analyzing the clinical symptoms in children with a positive stool test, it should be taken into account that the majority of the infected subjects are asymptomatic and it is possible to accidentally discover ova in stool without any links to the symptoms.

Conclusions

This study was based on a selected population of hospitalized children and may not be representative of the general population of children [31]. A limitation of this study is the risk of a false-positive stool test for the presence of *Ascaris lumbricoides* eggs, which despite considerable experience of the laboratory was not verified by other methods (i.e. anti-*Ascaris lumbricoides* IgE and IgG4 antibodies). However, serological testing of antibodies against *Ascaris* also has its limitations, such as cross-reactivity with other parasites [32]. The possibility of false-negative results, which characterize the initial phase of infection, should also be considered. It would be interesting also to investigate the coexistence of other intestinal parasites, especially *Enterobius vermicularis*, the most common parasitosis in Polish children with an incidence estimated at 12.5% to 40–50% [3,4,8,9]. The retrospective nature of the analysis prevented full insight into the symptomatology of the disease, i.e. tracing the sequence of the emergence of specific symptoms or monitoring the effectiveness of therapy. Despite these limitations, the study draws attention to the problem of ascariasis, as a disease that is still relevant, and which despite non-specific multiorgan manifestations should be considered in the differential diagnosis, especially of abdominal pain.

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Analiza objawów klinicznych i wybranych wskaźników hematologicznych u hospitalizowanych dzieci z zarażeniem *Ascaris lumbricoides* z rejonu północno-wschodniej Polski

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Analizą retrospektywną objęto dzieci hospitalizowane w latach 2005–2007 w Oddziale Dziecięcym Szpitala w Dąbrowie Białostockiej. Jelitowe stadium zarażenia *A. lumbricoides* rozpoznawano na podstawie dodatniego wyniku badania koprologicznego wykonywanego metodą dekantacji w odstępach 2–3 dni. Do oceny czynników predykcyjnych zarażenia zastosowano metodę regresji wielorakiej. Przeanalizowano wyniki 1801 próbek kału pobranych od 938 pacjentów; u 252 dzieci wykryto jaja *A. lumbricoides*. Dzieci z zarażeniem *A. lumbricoides* w wieku do 3 lat stanowiły 3,0%, w wieku przedszkolnym (4–7 lat) – 8,1%, a w wieku szkolnym (8–18 lat) – 15,8% hospitalizowanych dzieci.

Odnotowano sezonowość częstości wykrywania *A. lumbricoides* z najwyższym odsetkiem w miesiącach sierpień–grudzień. Znamiennymi czynnikami predykcyjnymi zarażenia *A. lumbricoides* w modelu regresji wielorakiej były dwie zmienne: ból brzucha jako przyczyna przyjęcia do szpitala (OR-2,19; 95%CI 1,62–2,95; p<0,0001) i wiek przedszkolny (OR-2,0; 95%CI 1,41–2,80; p<0,0001). Nie stwierdzono zależności między obecnością zarażenia a stanem odżywienia dzieci wyrażonym wskaźnikiem BMI *z*-score oraz niedokrwistością. W podgrupie dzieci z chorobami atopowymi nie stwierdzono częstszego występowania zarażenia ani nie odnotowano wpływu zarażenia na liczbę eozynofili we krwi obwodowej.

Zarażenie *A. lumbricoides* jest aktualnym problemem klinicznym wśród dzieci hospitalizowanych, co należy uwzględnić w diagnostyce różnicowej chorób, zwłaszcza u pacjentów z bólami brzucha w wieku przedszkolnym.

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