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Clinical picture of rotavirus infections in patients hospitalized in the Department of Pediatrics, Medical University of Silesia in Katowice, in the years 2008-2009

Obraz kliniczny zakażenia rotawirusowego u pacjentów hospitalizowanych w Klinice Pediatrii Śląskiego Uniwersytetu Medycznego w Katowicach w latach 2008-2009

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Summary

Introduction. Rotavirus infections are the most common causes of acute diarrhoea in infants and children under 4 years of age. Such infections are mainly transmitted by the gastrointestinal route. They can vary in their course, which may be mild to severe with considerable dehydration and water, electrolyte and acid-base imbalance.

Aim. The aim of the study was a retrospective analysis of the clinical picture of rotavirus infections in children hospitalized in the Department of Pediatrics, Medical University of Silesia, in the years 2008-2009.

Patients and methods. The study involved 226 children: 115 girls (51%) and 111 boys (49%), aged 0-18 years, who were hospitalized in the Department of Pediatrics, Medical University of Silesia in Katowice, in the years 2008-2009 due to acute rotavirus infections. Rotavirus infections were diagnosed on the basis of the clinical picture and positive results of immunoenzymatic stool tests for RV infection. The analysis included: age, sex, clinical symptoms, results of laboratory tests and comorbidities. The obtained results were statistically analysed.

Results. Rotavirus infections mainly occurred in infants and young children (under 3 years of age), i.e. in 185/226 patients (82%). The highest incidence rate was observed from December to March. In infants, the clinical picture was dominated by abundant, watery diarrhoea and vomiting. Abnormalities in laboratory tests were accompanied by hypertransaminasemia (84%) and elevated levels of inflammatory markers (62%). Water, electrolyte and acid-base imbalance was observed more frequently in infants than in older children. In 28/226 (12.4%) children RV infection coexisted with a bacterial infection of the gastrointestinal tract (mostly enteropathogenic *Escherichia coli*, *Campylobacter jejuni* and *Salmonella D-enteritidis*).

Conclusions. RV infections mainly affect children under 3 years of age. The course of disease is varied and, to a large extent, depends on patient's age and comorbidities.

Key words: rotaviruses, children, clinical picture

Streszczenie

Wstęp. Rotawirusy są najczęstszą przyczyną ostrej biegunki u niemowląt i dzieci do lat 4. Do zakażenia dochodzi głównie drogą pokarmową. Infekcje mogą mieć zróżnicowany przebieg – od łagodnego po ciężki, ze znacznym odwodnieniem i zaburzeniami gospodarki wodno-elektrolitowej i kwasowo-zasadowej.

Cel pracy. Celem pracy była analiza retrospektywna obrazu klinicznego zakażeń rotawirusowych u dzieci hospitalizowanych w Klinice Pediatrii SUM w latach 2008-2009.

Materiały i metody. Badaniem objęto 226 dzieci – 115 dziewczynek (51%) i 111 chłopców (49%), w wieku 0-18 lat, hospitalizowanych w Klinice Pediatrii SUM w Katowicach w latach 2008-2009 z powodu ostrych infekcji rotawirusowych. Zakażenie rotawirusowe rozpoznano na podstawie obrazu klinicznego oraz dodatniego wyniku testu immunoenzymatycznego stolca w kierunku zakażenia RV. W analizie uwzględniono: wiek, płeć pacjentów, objawy kliniczne, wyniki badań laboratoryjnych, choroby współistniejące. Otrzymane wyniki poddano analizie statystycznej.

Wyniki. Zakażenie rotawirusowe dotyczyło głównie niemowląt i małych dzieci (poniżej 3 roku życia) – 185/226 pacjentów (82%). Szczyt zachorowalności przypadał na miesiące od grudnia do marca. W obrazie klinicznym u niemowląt dominowała obfita, wodnista biegunka oraz wymioty. Z nieprawidłowości w badaniach laboratoryjnych najczęściej występowała hiper-

transaminazemia (84%) oraz podwyższone wykładniki stanu zapalnego (62%). U niemowląt częściej niż u dzieci starszych obserwowano zaburzenia gospodarki wodno-elektrolitowej i kwasowo-zasadowej. U 28/226 (12,4%) dzieci zakażenie RV współistniało z zakażeniem bakteryjnym przewodu pokarmowego (najczęściej enteropatogenna *Escherichia coli*, *Campylobacter jejuni* oraz *Salmonella D-enteritidis*).

Wnioski. Infekcje RV dotyczą głównie dzieci do lat 3. Przebieg choroby jest zróżnicowany, w dużym stopniu zależy od wieku pacjenta i chorób współistniejących.

Słowa kluczowe: rotawirusy, dzieci, obraz kliniczny

INTRODUCTION

Acute infectious diarrhoea is the most common cause of morbidity and mortality among children all over the world. Improved living conditions, easier access to health care, early fluid therapy and prophylactic vaccination led to a considerable improvement of the epidemiologic situation.

At present, the most common causes of acute infectious diarrhoea in Polish children are viral infections, especially those caused by rotaviruses. More than 140 million rotavirus infections are reported yearly worldwide. Generally, 25 million children are outpatients, whereas 2 million require hospitalization, and approximately 600 000 children die, mostly those in developing countries. Infections usually affect children under 4 years of age, mainly infants. Characteristic symptoms of rotavirus infection include: watery diarrhoea, often accompanied by vomiting, fever and abdominal pain. Symptoms usually persist for up to 5-7 days (1-5).

AIM OF STUDY

Aim of study was a retrospective analysis of the clinical picture of rotavirus infections in children hospitalized in the Department of Pediatrics, Medical University of Silesia, in the years 2008-2009.

PATIENTS AND METHODS

The study involved 226 children: 115 girls (51%) and 111 boys (49%), aged 0-18 years (mean 2.3 years), who were hospitalized in the Department of Pediatrics, Medical University of Silesia in Katowice, in the years 2008-2009 due to acute rotavirus infections. Rotavirus infections were diagnosed on the basis of positive results of immunoenzymatic stool tests (ELISA method) for RV infection. The analysis included: age, sex, seasonal nature of infections (month of hospitalization), clinical symptoms on admission, results of laboratory tests (inflammatory markers – blood count and C-reactive protein, aminotransferase levels, parameters of water-electrolyte and acid-base balance).

In all our patients bacteriological stool tests were performed. Moreover, comorbidities were analysed in the group of subjects. The obtained results were statistically analysed.

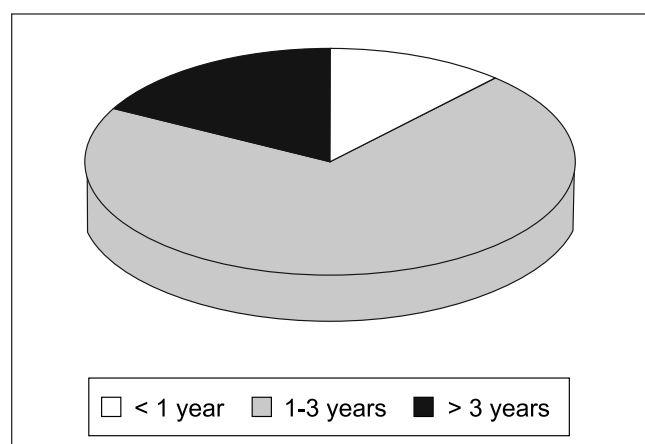
Statistical analysis was performed according to procedures available for the MedCalc software. Quantitative variables were presented in the form of arithmetic

mean and standard deviation. Qualitative variables were presented as absolute values and percentages. Intergroup differences were verified by means of the Chi-Square Test for qualitative variables. The assumed statistical significance level was $p < 0.05$.

RESULTS

The analysed group of patients was divided into 3 age subgroups: group 1 included infants – 27/226 (12%), group 2 (the largest) included children aged 1-3 years – 158/226 (70%), and group 3 including children over 3 years of age, which only constituted 18% (41/226) of the whole study population. The differences were statistically significant.

Over 3/4 of the analysed patients were children under 3 years of age (82% – 185/226) (fig. 1).



AGE	Number of patients	Percentage of analysed group
< 1 yr	27	12.0%
1-3 yrs	158	70.0%
> 3 yrs	41	18.0%
Total number of patients	226	100.0%

Chi ² test	24.885
Significance level	$p < 0.0001$

Fig. 1. Age analysis of the subjects with rotavirus infections.

Among the analysed patients, rotavirus infections were slightly more frequent among girls than boys; girls constituted 51% (115/226 patients), whereas boys

49% (111/226 patients). In the group of infants, boys fell ill more frequently (18/27 – 67%) than girls (9/27 – 33%). In the other age subgroups, no significant statistical differences were observed in the distribution.

Hospitalizations due to rotavirus infections were the most common in winter and in early spring, i.e. from December to March, whereas the least common – from May to August. The difference was statistically significant ($p < 0.05$) (fig. 2).

The clinical picture of rotavirus infections was varied. All examined children suffered from acute diarrhoea. Additionally, vomiting (120/226 – 53%), fever (44/226 – 19.4%), and abdominal pain (38/226 – 16.8%) were observed.

Neurological symptoms, usually in the form of apathy or agitation, anxiety and headache were observed in 99/226 children (43.8%) (tab. 1).

In the youngest patients, the clinical picture was dominated (apart from diarrhoea) by the symptoms of dehydration (22/27 – 81.5%). The incidence of severe dehydration decreased with age, reaching 25% in the group of older children (10/41).

Vomiting was most common in children from group 2 (1-3 yrs) – 98/158 (62%), and less frequent in older children – 15/41 (37%). In infants vomiting was observed in only 26% (7/27). The difference was statistically significant ($p = 0.0014$).

Fever was not a characteristic symptom, and occurred at a similar frequency in all age groups.

Abdominal pain occurred in 38/226 patients (16.8%) with rotavirus infections, mostly in older children. The difference was statistically significant ($p < 0.001$).

Neurological symptoms occurred in 99/226 patients (44%), least frequently in children under 1 year of age, however, the difference was not statistically significant.

The most common laboratory abnormalities included increased inflammatory markers and elevated aminotransferase levels (fig. 3).

Elevated aminotransferase levels were observed in 190/226 patients (84%).

The levels of alanine aminotransferase (ALT) were elevated in 51/226 patients (22.6%), whereas elevated levels of aspartate aminotransferase (AST) were observed in 176/226 subjects (77.9%). ALT levels exceeding two-fold the upper limit of normal were only observed in 3 patients (3/226), whereas AST levels – in 5 children (5/226). In all patients without any other liver diseases, the elevated aminotransferase levels normalized during observation. The proportion of patients with hypertransaminasemia increased with age, reaching 52% (14/27) in infants, 87% (138/158) in children aged 1-3 years, and 93% (38/41) in older children. However, the difference was not statistically significant.

Increased values of inflammatory markers (CRP protein, leukocytosis) were significantly more frequent in the youngest children (< 1 yr: 21/27 – 78%). The difference was statistically significant ($p = 0.0013$).

Table 1. Evaluation of the frequency of clinical symptoms in children with rotavirus infections.

Clinical symptoms	Frequency	AGE			Statistical significance
		< 1 yr	1-3 yrs	> 3 yrs	
Vomiting	120/226 (53%)	7/27 (26%)	98/158 (62%)	15/41 (37%)	$p = 0.0014$
Abdominal pain	38/226 (16.8%)	2/27 (7.4%)	12/158 (7.6%)	24/41 (58.5%)	$p < 0.001$
Fever	44/226 (19.4%)	4/27 (15%)	33/158 (21%)	7/41 (17%)	NS
Neurological symptoms	99/226 (43.8%)	5/27 (19%)	77/158 (49%)	17/41 (41%)	NS
Dehydration symptoms	102/226 (45.1%)	22/27 (81.5%)	70/158 (44%)	10/41 (25%)	$p = 0.003$

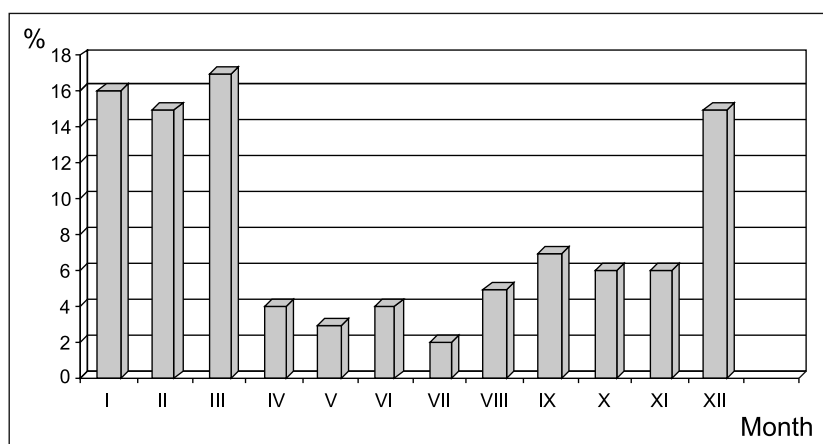


Fig. 2. Seasonal nature of rotavirus infections in the analysed population.

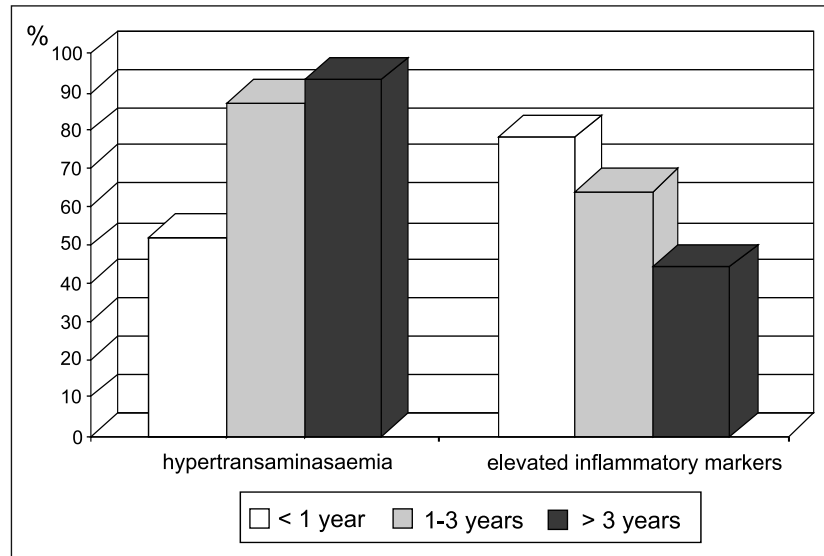


Fig. 3. Results of laboratory tests in patients with rotavirus infections.

The incidence of increased inflammatory markers decreased with age; among the patients in group 2 (1-3 yrs) increased values were observed in 101/158 children (64%), whereas among older children (> 3 yrs) such values were demonstrated in 18/41 patients (44%).

Acid-base imbalance, usually manifested as metabolic acidosis, occurred in 74/226 patients (33%). Metabolic acidosis was most common in infants – 18/27 (68%) and younger children (1-3 yrs) – 41/158 (26%). In the group of youngest children, decreased potassium concentrations were more common (statistical significance) than in the older age groups ($p = 0.0054$).

The abdominal ultrasound revealed enlarged lymph nodes (mostly mesenteric) in 9/40 cases: in 3 children aged 1-3 and in 6 children over 3 years of age. In all cases, enlarged lymph nodes were observed in patients with *Campylobacter jejuni* infection.

In all patients bacteriological stool tests were performed. **Concomitant bacterial infections of the**

gastrointestinal tract, diagnosed in 28/226 children, were usually caused by enteropathogenic *E. coli*, *Campylobacter jejuni* and *Salmonella* (fig. 4). Co-existing bacterial infections mainly affected patients over 3 years of age. The difference was statistically significant ($p < 0.0001$).

Infections caused by enteropathogenic *E. coli* were observed in 11/226 patients (5%). *Campylobacter jejuni* infections were diagnosed in 12/226 patients (5%), mostly in children over 3 years of age – 8/41 (20%), but in only 4/185 younger patients (2%). Infections caused by *Salmonella* were observed in 6/226 patients (2.7%). The proportion of infections among younger children (1-3 yrs) was 0.13% (2/158 patients), whereas in older children – 10% (4/41 patients). No *Salmonella* infections were diagnosed in infants.

Among comorbidities, upper respiratory tract infections occurred most frequently, usually in older children (16/41 – 39%), whereas body mass and/or height deficiency was mainly observed in children under 3 years of age (36/185 – 19.5%) (tab. 2).

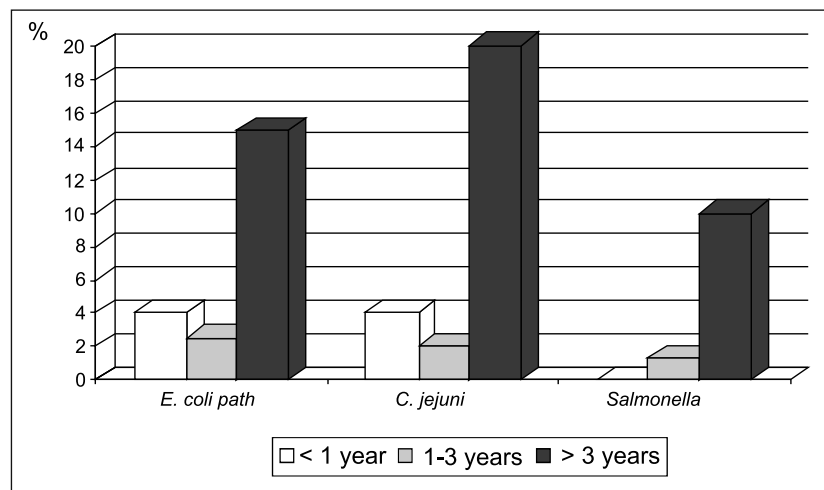


Fig. 4. Coexistence of bacterial and rotavirus infections in children.

Table 2. Comorbidities in children with rotavirus infections.

Comorbidities in children with rotavirus infections	< 1 yr	1-3 yrs	> 3 yrs
Body mass and/or height deficiency	6/27 (22.2%)	30/158 (19%)	7/41 (17%)
Urinary tract infections	6/27 (22.2%)	19/158 (12%)	3/41 (7%)
Upper respiratory tract diseases	1/27 (4%)	40/158 (26%)	16/41 (39%)

DISCUSSION

Rotavirus infections are the most common causes of acute diarrhoea in children. Epidemiological data has shown that in 2009 there were 207 500 cases of rotavirus infections in Poland, and 6.500 children required hospitalization. At present, the number of rotavirus infections is decreasing due to popularization of prophylactic vaccination.

In the period of two years, 226 children with rotavirus infections were hospitalized in the Department of Pediatrics at the Medical University of Silesia, which constituted 5% of all hospitalizations. Recently, the number of hospitalizations has slightly decreased due to recommendation of rotavirus vaccination in our country (6-8).

Rotavirus infections are seasonal. In the temperate climate zone, increased incidence is observed late in autumn, in winter and in early spring. In our group of patients this infection was also significantly more frequent from December to March (over 60%) (1, 9).

The highest morbidity rates are observed in the age range from 9 to 24 months. In our analysis, children in this age group were also most often hospitalized due to rotavirus infections; children under 3 years of age constituted 82%. The greatest morbidity in this age range is associated with increased exposure to a contact with ill children and lack of immunity to rotavirus antigens. However, tests on the murine model have revealed that the number of receptors for enterotoxin produced by NSP4 rotaviruses decreases with age. This is probably why the greatest susceptibility to such infections is observed among the youngest children (11).

Generally, rotavirus infections are acute and last up to 4-8 days. The incubation period is 12-96 hours (average 48-72 hours), and contagiousness persists for 2-5 days after cessation of diarrhoea. Group A rotaviruses (division depends on VP7 protein) includes two subgroups: subgroup 1 – the clinical picture is dominated by vomiting, and subgroup 2 – fever and severe diarrhoea are more common, whereas vomiting is less frequent (4, 11). Among our patients, vomiting was observed in 53% (120/226), fever in 19.4% (44/226), whereas abdominal pain in 16.8% (38/226) subjects. According to some authors, vomiting may occur in up to 96%; in our study population, vomiting affected a smaller percentage of subjects, which may be connected with a different RV genotype in Poland. Dehydration occurred at a similar rate (83 vs 81.5%), but fever was less frequent.

In neonates and premature babies, a connection was established between rotavirus infection and necrotising enterocolitis (statistically significant difference, 66 vs 30%) (12). Asymptomatic course of disease is rarely observed in this age group. Rotavirus infections may result in both febrile and fever-independent convulsions. Contributing factors may include water-electrolyte and acid-base imbalance. There are some literature reports on encephalitis, cerebellitis and encephalopathy in the course of rotavirus infections (10). In our study group, neurological symptoms, usually manifested as apathy or agitation, anxiety and headache, were observed in 43.8% (99/226). These symptoms were transient and resolved after proper hydration, restoring acid-base and water-electrolyte balance.

Elevated aminotransferase levels, especially aspartate aminotransferase, have been observed in literature in almost half of the examined children with acute rotavirus diarrhoea; in most cases, these values did not exceed two-fold the upper limit of normal. In the majority of patients, the elevated levels of aminotransferases were transient and normalised spontaneously during observation.

In our study this percentage was higher, reaching 84%. In all patients without any other liver diseases, the elevated aminotransferase levels normalized during observation. Teitelbaum demonstrated elevated levels of alanine aminotransferase in 20% of patients with rotavirus infections, and in more than 70% – elevated levels of aspartate aminotransferase (13). These values also normalized spontaneously; they were probably associated with a damaged intestinal barrier and secondary viremia. Kacerka et al. observed more frequent bacterial infections of the gastrointestinal and respiratory tracts in the course of rotavirus infections (31% patients). The authors also demonstrated frequent coexistence of hypertransaminasemia in these groups of patients (14). It has been established that rotavirus infections in *Salmonella* carriers increase several times a risk of bacteraemia (15). In our analysis, concurrent bacterial infections of the gastrointestinal tract were observed in 28/226 children; they were usually caused by enteropathogenic *E. coli*, *Campylobacter jejuni* and *Salmonella*. Co-existing bacterial infections mainly affected patients over 3 years of age. In this patient population, increased inflammatory markers and hypertransaminasemia were more frequently observed (15, 16). Among comorbidities, upper respiratory tract infections were most frequently observed, usually in older children.

CONCLUSION

1. Rotavirus infections primarily affected children aged 1-3 years.
2. The highest incidence was observed from December to March.

3. The clinical picture of rotavirus infections in infants was dominated (apart from diarrhoea) by dehydration, whereas in children over 1 year of age – by vomiting, neurological symptoms and features of upper respiratory tract infections.

BIBLIOGRAPHY

1. Benerjee I, Ramani S, Primrose B et al.: Comparative study of the epidemiology of rotavirus in children from a community-based birth cohort and hospital in South India. *J Clin Microbiol* 2006; 44: 2468-2474.
2. Desai R, Esposito D, Lees C et al.: Rotavirus – coded deaths in children United States 1999-2007. *Pediatr Infect Dis J* 2011; 30: 986-988.
3. Bruijning-Verhagen P, Sankatsing V, Kunst A et al.: Rotavirus – related hospitalizations are responsible for high seasonal peaks in all – cause pediatric hospitalizations. *Pediatr Infect Dis J* 2012; 31: 244-249.
4. Kuchar E, Nitsch-Osuch A, Szenborn L, Ołdak E: Rotawirusy jako czynnik etiologiczny zakażeń szpitalnych w Polsce – przegląd systematyczny z metaanalizą 11 badań. *Przegl Epidemiol* 2012; 66: 409-415.
5. Lopez-de-Andres A, Jimenez-Garcia R, Carrasco-Garrido P et al.: Hospitalizations associated with rotavirus gastroenterocolitis in Spain 2001-2005. *BMC Public Health* 2008; 8: 109-116.
6. Begue R, Perrin K: Reduction in gastroenterocolitis with the use of pentavalent rotavirus vaccine in a primary practice. *Pediatrics* 2010; 126: 40-46.
7. Albrecht P, Albrecht-Stanisławska A: Nadeszła era szczepień przeciwrotawirusowych. *Ped Współ Gastroenterol Hep Żyw Dziecka* 2006; 8: 215-219.
8. Munos M, Walker C, Black R: The effect of rotavirus vaccine on diarrhea mortality. *Int J Epidemiol* 2010; 39 (suppl. 1): i56-i62.
9. Perl S, Goldman M, Berkovitch M et al.: Characteristics of rotavirus gastroenteritis in hospitalized children in Israel. *IMAJ* 2011; 13: 274-277.
10. Szajewska H, Chmielewska A: Powikłania zakażenia rotawirusowego – przegląd piśmiennictwa. *Ped Współ Gastroenterol Hep Żyw Dziecka* 2008; 1: 7-11.
11. Hagbom M, Sharma S, Lundgren O, Svensson L: Towards a human rotavirus disease model. *Curr Opin Virol* 2012; 2: 408-418.
12. De Villiers FP, Driessen M: Clinical neonatal rotavirus infection: association with necrotizing enterocolitis. *S Afr Med* 2012; 6: 620-624.
13. Teitelbaum J, Daghistani R: Rotavirus causes hepatic transaminase elevation. *Dig Dis Sci* 2007; 52: 3396-3398.
14. Kacerka A, Wójcik K, Kuydowicz J et al.: An evaluation of the relationship between rotavirus diarrhoea and bacterial infection and acute hepatitis in children. *Gastroenterol Pol* 2009; 16: 446-448.
15. Hung T, Liu M, Hsu C, Lin Y: Rotavirus infection increases the risk of bacteremia in children with nontyphoid *Salmonella gastroenteritis*. *Eur J Clin Microbiol Infect Dis* 2009; 28(4): 425-428.
16. Kawashima H, Ishii H, Ioi H et al.: Transaminase in rotavirus gastroenteritis. *Pediatrics International* 2012; 54: 86-88.

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