



Frequency and Seasonal Distribution of Rotavirus and Adenovirus in Patients with Acute Gastroenteritis

Akut Gastroenteritli Hastalarda Rotavirüs ve Adenovirüs Sıklığı ve Mevsimsel Dağılımı

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Abstract

Aim: The aim of this study was to retrospectively determine the frequency of rotavirus and adenovirus and the distribution of these pathogens by age groups, gender and season in patients admitted to our hospital with gastroenteritis symptoms.

Material and Method: A total of 32755 stool samples collected from patients with gastroenteritis symptoms in the Medical Microbiology Clinic of the Ankara Bilkent City Hospital between January 1 and December 31, 2022 were evaluated retrospectively for rotavirus and adenovirus antigens. Rotavirus and adenovirus antigens were analyzed with the Rapid Cassette Test (Microcult, Biotech) kit. In addition, the distribution of pathogens by age groups, gender and season were examined. Statistical analysis was performed using Jamovi® version 2.3.21.

Results: Antigen test was positive in 9.9% of 32755 stool samples evaluated in our study. Rotavirus was detected in 8.4% and adenovirus in 1.5% of antigen positive samples. Both rotavirus and adenovirus antigen positivity were found to be statistically significantly higher in 0-1 and 2-3 age groups compared to other age groups ($p<0.001$). When the monthly distribution of rotavirus antigen positivity was examined, a statistically significant difference was found in March, April, and May ($p<0.001$).

Conclusion: It was observed that rotavirus has a significant ratio among acute gastroenteritis cases in pediatric age group in our region. Rotavirus should be considered in gastroenteritis in 0-3 age group especially in spring months, and for diagnosis, immunochromatographic-based tests can be easily applied in all health institutions. Detection of the pathogen causing gastroenteritis will contribute to the initiation of appropriate treatment, follow-up of complications, and the prevention of unnecessary antibiotic use.

Keywords: Rotavirus, adenovirus, acute gastroenteritis

Öz

Amaç: Bu çalışmanın amacı, gastroenterit semptomları ile hastanemize başvuran hastalarda rotavirüs ve adenovirüs sıklığını ve bu patojenlerin cinsiyet, yaş ve mevsimlere göre dağılımını retrospektif olarak belirlemektir.

Gereç ve Yöntem: Ankara Bilkent Şehir Hastanesi Tıbbi Mikrobiyoloji Kliniğinde 1 Ocak - 31 Aralık 2022 tarihleri arasında gastroenterit semptomları olan hastalardan alınan toplam 32755 dışkı örneği rotavirüs ve adenovirüs antijenleri açısından retrospektif olarak değerlendirilmiştir. Rotavirüs ve adenovirüs antijenleri Rapid Cassette Test (Microcult, Biotech) kiti ile analiz edilmiştir. Ayrıca patojenlerin cinsiyet, yaş ve mevsimlere göre dağılımı incelenmiştir. İstatistiksel analiz Jamovi® versiyon 2.3.21 kullanılarak gerçekleştirilmiştir.

Bulgular: Çalışmamızda değerlendirilen toplam 32755 dışkı örneğinin %9,9'unda antijen testi pozitif bulunmuştur. Antijen pozitif örneklerin %8,4'ünde rotavirüs ve %1,5'inde adenovirüs tespit edilmiştir. Hem rotavirüs hem de adenovirüs antijen pozitifliği 0-1 ve 2-3 yaş gruplarında diğer yaş gruplarına göre istatistiksel olarak anlamlı derecede yüksek bulunmuştur ($p<0.001$). Rotavirüs antijen pozitifliğinin aylara göre dağılımı incelendiğinde Mart, Nisan ve Mayıs aylarında istatistiksel olarak anlamlı bir fark bulunmuştur ($p<0.001$).

Sonuç: Bölgeimizde pediatrik yaş grubunda akut gastroenterit vakaları arasında rotavirüsün önemli bir orana sahip olduğu görülmüştür. Özellikle bahar aylarında 0-3 yaş grubunda görülen gastroenteritlerde rotavirüs göz önünde tutulmalıdır. Tanı için immüno-kromatografik temelli hızlı kaset testler birinci basamak sağlık kuruluşları da dahil olmak üzere tüm sağlık kuruluşlarında kolaylıkla uygulanabilir. Gastroenterite neden olan patojenin tespit edilmesi, uygun tedavinin başlatılmasına, komplikasyonların takibine ve gereksiz antibiyotik kullanımının önlenmesine katkıda bulunacaktır.

Anahtar Kelimeler: Rotavirüs, adenovirüs, akut gastroenterit



INTRODUCTION

Acute gastroenteritis is among the most common infectious diseases worldwide and can have serious consequences, especially in children and the elderly. The clinical aspect can range from asymptomatic infections to severe illness with dehydration which can be fatal.^[1] Although acute gastroenteritis is usually a self-limiting disease, it can still lead to significant morbidity. It is a major cause of death in underdeveloped countries especially among infants. According to the Centers for Disease Control (CDC), viral gastroenteritis causes the death of more than 200,000 children worldwide annually. Viruses are the most common causative agents of acute infectious gastroenteritis.^[2] More than 20 different viruses have been identified as etiologic agents of viral acute gastroenteritis, rotavirus and adenovirus being among the most common agents.^[3] Rotavirus and adenovirus-associated gastroenteritis is transmitted via fecal-oral route, but it can also be easily transmitted via shared items. In addition, both viruses are non-enveloped and resistant to soap and disinfectants.^[4]

Rotaviruses are double-stranded RNA viruses with a triple-layered capsid surrounding a genome with 11 RNA segments. Ten rotavirus species (A-J) have been classified, based on sequence and antigenic differences of the VP6 protein found in the inner capsid. Type A is the most common cause of infections in children.^[5] The clinical picture of rotavirus-associated acute gastroenteritis includes diarrhea, vomiting, and fever and may lead to a severe condition that may require hospitalization due to fluid loss.^[4]

Adenoviruses, one of the pathogens causing viral gastroenteritis, are double-stranded DNA viruses. Currently, adenovirus is divided into nine subgroups (A-I) and more than 100 genotypes have been identified. Specifically, adenovirus 40 and 41 (species F) serotypes have been classified as causative agents of pediatric gastroenteritis.^[6,7] Clinical features of acute gastroenteritis caused by adenovirus include vomiting, watery diarrhea, mild fever and mild dehydration. Another feature of adenovirus 40-41 serotypes infections is prolonged diarrhea.^[8]

Detection of the causative pathogen in acute gastroenteritis is important for the planning of treatment and the prevention of inappropriate antibiotic use. In the differential diagnosis of viral gastroenteritis, various epidemiological factors such as age, season, geographical region, and socioeconomic conditions in addition to clinical findings may be useful, but laboratory tests are required to confirm the diagnosis.^[9]

The aim of this study was to retrospectively determine the frequency of rotavirus and adenovirus and the distribution of these pathogens by age groups, gender and season in patients admitted to our hospital with gastroenteritis symptoms.

MATERIAL AND METHOD

The study was carried out with the permission of Ankara Bilkent City Hospital Ethics Committee (Date: 10.05.2023, No: E2-23-4081), and in accordance with the principles of the Declaration of Helsinki of the World Medical Association.

A total of 32755 stool samples collected from patients with gastroenteritis symptoms in the Medical Microbiology Clinic of the Ankara Bilkent City Hospital between January 1 and December 31, 2022 were evaluated retrospectively for rotavirus and adenovirus antigens. Patients were divided into age groups as 0-1, 2-3, 4-5, 6-10, 11-15, ≥ 16 . The distribution of rotavirus and adenovirus by age groups, gender and season was determined.

Rotavirus and adenovirus antigens were analyzed with the Rotavirus and Adenovirus Rapid Cassette Tests (Microcult, Biotech, China) that qualitatively identify these antigens by immunochromatographic method, in accordance with the manufacturer's recommendations.

Age and gender data of the patients were obtained from the hospital information management system.

In the presence of more than one positive results on consecutive days, a single positive result was included in the evaluation.

The statistical analysis was performed using Jamovi® version 2.3.21. Normality analysis of the data was assessed by the Shapiro-Wilk test and the difference between groups was calculated by the chi-square test. The p-value of <0.05 was accepted as statistically significant.

RESULTS

In our study, a total of 32755 stool samples were examined for the presence of rotavirus and adenovirus antigens. Antigen test was positive in 9.9% (n=3239) of the patients. Rotavirus was detected in 8.4% (n=2761) and adenovirus in 1.5% (n=478) of antigen positive samples. Rotavirus-adenovirus co-infection rate was 2.4%. It was determined that 56% (n=1816) of the antigen positive patients were male and 44% (n=1423) were female, and there was no statistically significant difference between genders (p=0.853). The distribution of rotavirus and adenovirus positivity by gender is given in **Table 1**.

Table 1. Distribution of rotavirus and adenovirus positivity by gender

Gender	Rotavirus positive n (%)	Adenovirus positive n (%)	Total n (%)
Female	1220 (44)	203 (42)	1423 (44)
Male	1541 (56)	275 (58)	1816 (56)
Total	2761 (100)	478 (100)	3239 (100)

In patients with rotavirus antigen, the age range was 0-92, median age 2 [interquartile range (IQR), 4] while the age range was 0-72, median age 3 [interquartile range (IQR), 4] in patients with adenovirus antigen. The age group with the highest antigen positivity was found to be 2-3 (35%) for rotavirus and 0-1 (31%) for adenovirus. Both rotavirus and

adenovirus antigen positivity were found to be statistically significantly higher in 0-1 and 2-3 age groups compared to other age groups ($p < 0.001$). However, there was no statistically significant difference between these two age groups in terms of positivity ($p > 0.05$). A total of 2163 (78%) of the patients with rotavirus antigen positive and 362 (76%) of the patients who were positive for adenovirus antigen were found to be five years old or younger. The distributions of rotavirus and adenovirus positivity by age groups are given in **Figure 1** and **Table 2**.

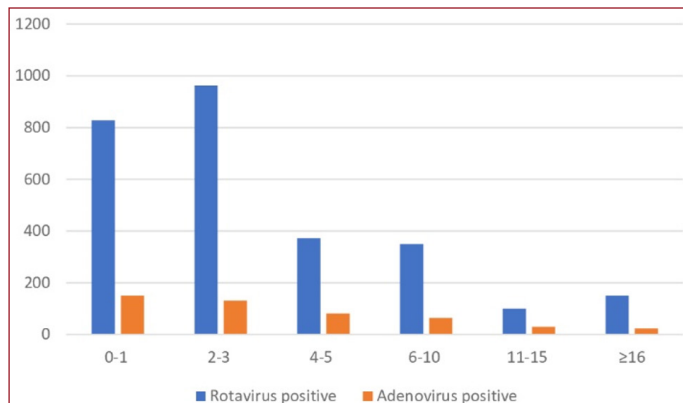


Figure 1. Distribution of rotavirus and adenovirus positivity by age groups

Table 2. Distribution of rotavirus and adenovirus positivity by age groups

Age groups	Rotavirus positive n (%)	Adenovirus positive n (%)
0-1	828 (30)	150 (31)
2-3	963 (35)	131 (28)
4-5	372 (13)	81 (17)
6-10	349 (13)	64 (13)
11-15	99 (4)	29 (6)
≥16	150 (5)	23(5)
Total	2761 (100)	478 (100)

When the monthly distribution of rotavirus antigen positivity was examined, a statistically significant difference was found in March, April and May ($p < 0.001$). When the monthly distribution of adenovirus was assessed, no statistically significant difference was found ($p = 0.154$). The monthly distributions of rotavirus and adenovirus positivity are given in **Figure 2** and **Table 3**.

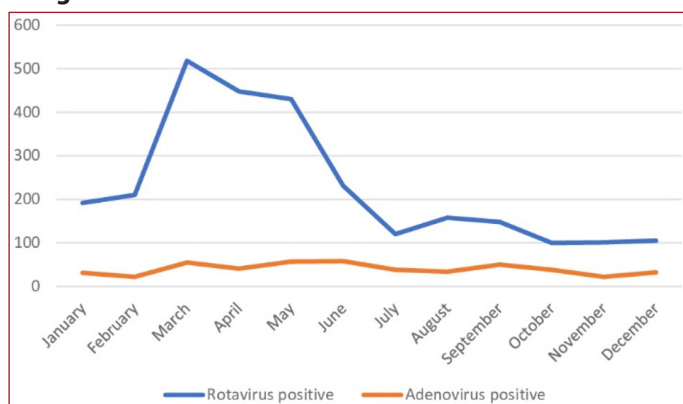


Figure 2. Monthly distribution of rotavirus and adenovirus positivity

Table 3. Distribution of rotavirus and adenovirus positivity by month

Months	Rotavirus positive n (%)	Adenovirus positive n (%)
January	192 (7)	31 (6)
February	210 (8)	22 (5)
March	518 (19)	55 (12)
April	448 (16)	41 (9)
May	430 (16)	57 (12)
June	231(8)	58 (12)
July	120 (4)	38 (8)
August	158 (5)	34 (7)
September	148 (5)	50 (10)
October	100 (4)	38 (8)
November	101 (4)	22 (5)
December	105 (4)	32 (6)
Total	2761 (100)	478 (100)

DISCUSSION

Acute gastroenteritis is a cause of morbidity and mortality in low- and middle-income countries, especially in children under 5 years of age. Viruses are the most common etiologic agents of acute infectious gastroenteritis, followed by bacteria and parasites. Among viral gastroenteritis agents, rotavirus and adenovirus are the leading causes of diarrhea worldwide.^[7] The frequency of these pathogens is influenced by geographical, environmental or socio-economic factors.^[3] In studies conducted in different countries, the prevalence of rotavirus was reported to vary from 9.7% to 35.9% and the prevalence of adenovirus from 2.5% to 17.1%.^[3,10-15] In studies conducted in different regions in Türkiye, rotavirus and adenovirus frequency rates were reported to vary from 6.7% to 20.2% and from 1.3% to 17.6% respectively.^[4,16-20] The difference in results of these studies may be due to both regional, climatic and socio-economic factors, and diagnostic methodology. In this study, rotavirus frequency was 8.4%, adenovirus frequency was 1.5%, rotavirus-adenovirus coinfection rate was 2.4% and these results are compatible with the national data. In line with previous studies conducted in our country, no statistically significant difference ($p = 0.853$) was found in this study between genders in patients with antigen positivity.^[4,9,17-21]

The age groups with the highest antigen positivity were 2-3 years (35%) and 0-1 year (30%) for rotavirus, and 0-1 (31%) and 2-3 years (27%) for adenovirus. Both rotavirus and adenovirus antigen positivity were statistically significantly higher in the 0-1 and 2-3 age groups compared to other age groups ($p < 0.001$). Consequently, as the distribution of antigen positivity was examined according to age groups in this study, it was found that infection with both viruses was mostly observed in the age group of 3 years old and younger, which was compatible with the previous studies in our country.^[16,17,19,21,22]

The epidemiology of the disease has changed drastically in countries which included rotavirus vaccine in their national vaccination programs. While rotavirus caused gastroenteritis

mostly in children under 5 years of age before it was included in the vaccination program in such countries, it was found to cause gastroenteritis in older age groups who were not vaccinated after it was included in the vaccination program.^[23] In Türkiye, rotavirus vaccine has not yet been included in the national vaccination program but the vaccine is available on demand. According to the results of our study, the dramatic decrease in rotavirus infection over 5 years of age may be explained by partial immunity caused by previous rotavirus infections.

Although rotavirus is recognized as an important cause of gastroenteritis in children, it is also responsible for adult gastroenteritis. Immunity to rotavirus is not complete, and most people will have more than one infection throughout their lives. Reinfections are asymptomatic or mildly severe.^[24] It has been reported that approximately 50% of parents of children with rotavirus disease develop rotavirus infection and half of them develop mild disease. This has been attributed to the fact that rotavirus-specific CD4+ T cells and neutralizing antibodies decrease over time and are insufficient to prevent reinfection.^[5] In this study, the frequency of rotavirus was found to be 3.4% in adults over the age of 20, and therefore, rotavirus should be considered in adult gastroenteritis even though its incidence is low.

Despite the fact that rotavirus infections are seen all year round in tropical climates, they are seen especially in winter and early spring in countries with temperate climates including Türkiye.^[19] In a national meta-analysis of 38 studies, Güzel et al.^[25] found the highest incidence of rotavirus in spring and winter. In our study, consistent with the literature, we found that rotavirus infections start to increase in winter and peak in spring. A statistically significant difference was found in March, April and May ($p < 0.001$). Levy et al.^[26] concluded in their metanalysis of 34 epidemiologic studies from different countries that rotavirus is definitely more prevalent during the cooler months in globally temperate regions, but that seasonal peaks of infections can vary from autumn to spring. In our study, when the monthly distribution of adenovirus was examined, no statistically significant difference was found ($p = 0.154$) and adenovirus did not show any seasonal characteristics.

Various methods such as Latex agglutination (LA), Enzyme-linked immunosorbent assays (ELISA), immunochromatographic method and Reverse transcriptase-polymerase chain reaction (RT-PCR) are used to detect rotavirus in stool samples. Latex agglutination is widely used for rapid testing, but its sensitivity is lower than ELISA. Immunochromatographic method has been found to have higher sensitivity and specificity compared to ELISA.^[27] In a study comparing the gold standard RT-PCR with the immunochromatographic method and ELISA, the sensitivity and specificity of both methods were found to be relatively low.^[28] The limitation of this study is that the virus was detected by the immunochromatographic method but RT-

PCR, which is more sensitive for diagnosis, was not used. On the other hand, the immunochromatographic method has its own advantages on the grounds that it is simple to perform, faster and easy to read the results, it is useful for testing a single sample and readily available, and it is also cost-effective and does not require additional equipment. Therefore, immunochromatographic method is widely used for the diagnosis of rotavirus and adenovirus gastroenteritis in health institutions, including primary care.

CONCLUSION

It has been observed in this study that rotavirus has a significant ratio among acute gastroenteritis cases in the pediatric age group in our region. Rotavirus should be considered especially in gastroenteritis of the 0-3 age group in spring months. Immunochromatographic-based sensitivity high-speed antigen tests can be easily applied in all health institutions for diagnosis. Detection of the pathogen causing gastroenteritis will contribute to the initiation of appropriate treatment, follow-up of complications, and the prevention of unnecessary antibiotic use. Therefore, we consider that our study to determine the regional frequency and the distribution of rotavirus and adenovirus as the causative agents of gastroenteritis by age groups, gender and season is useful in terms of contributing to the epidemiological data of the country and presenting data for the national vaccination program plans.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Bilkent City Hospital Ethics Committee (Date: 10.05.2023, No: E2-23-4081).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

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REFERENCES

1. Kang G. Viral Diarrhea. In: Stella R.Q, editors. International Encyclopedia of Public Health. Academic Press (Second Edition), 2017;360-367.
2. Stuempfig ND, Seroy J. Viral Gastroenteritis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
3. Amodio E, De Grazia S, Genovese D, et al. Clinical and Epidemiologic Features of Viral Gastroenteritis in Hospitalized Children: An 11-Year Surveillance in Palermo (Sicily). *Viruses* 2022;15(1):41.

4. Gür Vural D, Torun E.G, Biyık İ, Tanrıverdi Çaycı Y, Bilgin K, Birinci A. Akut gastroenteritli olgularda rotavirüs ve adenovirüs sıklığının araştırılması. *Kırıkkale Üni Tıp Derg* 2022;24(2):289-94.
5. Crawford SE, Ramani S, Tate JE, et al. Rotavirus infection. *Nat Rev Dis Primers* 2017;3:17083.
6. Kumthip K, Khamrin P, Ushijima H, Maneekarn N. Enteric and non-enteric adenoviruses associated with acute gastroenteritis in pediatric patients in Thailand, 2011 to 2017. *PLoS One* 2019;14(8):e0220263.
7. do Nascimento LG, Fialho AM, de Andrade JDSR, de Assis RMS, Fumian TM. Human enteric adenovirus F40/41 as a major cause of acute gastroenteritis in children in Brazil, 2018 to 2020. *Sci Rep* 2022;12(1):11220.
8. Dey RS, Ghosh S, Chawla-Sarkar M, et al. Circulation of a novel pattern of infections by enteric adenovirus serotype 41 among children below 5 years of age in Kolkata, India. *J Clin Microbiol* 2011;49(2):500-5.
9. Güreşer AS, Karasartova D, Taşçı L, Boyacıoğlu Zİ, Taylan Özkan HA. Çorum'da Akut Gastroenteritli Çocuklarda Rotavirüs ve Adenovirüs Saptanma Sıklığı. *Flora Dergisi* 2017;22(2):58-66.
10. Cho SR, Chae SJ, Jung S, et al. Trends in acute viral gastroenteritis among children aged ≤ 5 years through the national surveillance system in South Korea, 2013-2019. *J Med Virol* 2021;93(8):4875-82.
11. Najafi A, Najafi S, Vahdat K, Kargar M, Javdani N. Importance of viral pathogens in children with acute gastroenteritis in the south of Iran. *Ann Saudi Med* 2013;33(2):124-9.
12. Thwiny HT, Alsalih NJ, Saeed ZF, Al-Yasari AMR, Al-Saadawe MAA, Alsaadawi MAE. Prevalence and seasonal pattern of enteric viruses among hospitalized children with acute gastroenteritis in Samawah, Iraq. *J Med Life* 2022;15(1):52-7.
13. Levidiotou S, Gartzonika C, Papaventsis D, et al. Viral agents of acute gastroenteritis in hospitalized children in Greece. *Clin Microbiol Infect* 2009;15(6):596-8.
14. Wang LP, Zhou SX, Wang X, et al. Etiological, epidemiological, and clinical features of acute diarrhea in China. *Nat Commun* 2021;12(1):2464.
15. Cornejo-Tapia A, Orellana-Peralta F, Weilg P, et al. Etiology, epidemiology and clinical characteristics of acute diarrhea in hospitalized children in rural Peru. *J Infect Dev Ctries* 2017;11(11):826-32.
16. Varışlı AN, Tekin S, Bıçak İ. How much trouble rotavirus and adenovirus cause in patients with acute gastroenteritis?: Four-year results. *Klimik Derg* 2019;32(1):67-70.
17. Aytaç Ö, Şenol FF, Öner P, et al. Akut gastroenteritli hastalarda Rotavirüs ve Adenovirüs sıklığı. *Türk Hij Den Biyol Derg* 2020;77(2):179-84.
18. Bozok T, Şimşek T. Üçüncü basamak bir hastanede rotavirüs, enterik adenovirüs ve enterik parazit enfeksiyonlarının prevalansı ve demografik özellikleri: Altı yıllık retrospektif kesitsel çalışma. *Mersin Univ Sağlık Bilim Derg.* 2021;14(2):199-207.
19. Kirişçi Ö, Muratdağı G. Bir Devlet Hastanesine Akut Gastroenterit ile Başvuran Hastalarda Rotavirüs ve Enterik Adenovirüs Enfeksiyonu Sıklığı. *Sakarya Tıp Dergisi* 2019;9(4):585-91.
20. Öner SZ, Kaleli İ, Demi RM, Mete E, Çalışkan A. Rotavirus and adenovirus prevalence in patients with acute viral gastroenteritis in Denizli, Turkey, 2017-2021. *J Med Virol* 2022;94(8):3857-62.
21. Terzi HA, Aydemir Ö. Akut Gastroenteritli Hastalarda Rotavirüs ve Adenovirüs Sıklığının Araştırılması; Sakarya. *Sakarya Tıp Dergisi* 2018;8(4):746-52.
22. Rad AY, Gözalan A. Detection of Rotavirus and Enteric Adenovirus Antigens in Outpatients with Gastroenteritis. *Türkiye Klinikleri Dergisi* 2010;30(1):174-9.
23. LeClair CE, McConnell KA. Rotavirus. [Updated 2023 Jan 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
24. Anderson EJ, Weber SG. Rotavirus infection in adults. *Lancet Infect Dis* 2004;4(2):91-9.
25. Güzel M, Akpınar O, Kılıç MB. Prevalence of Rotavirus-Associated Acute Gastroenteritis Cases in Early Childhood in Turkey: Meta-Analysis. *Children (Basel)* 2020;7(10):159.
26. Levy K, Hubbard AE, Eisenberg JN. Seasonality of rotavirus disease in the tropics: a systematic review and meta-analysis. *Int J Epidemiol* 2009;38(6):1487-96.
27. Dhiman S, Devi B, Singh K, Devi P. Comparison of Enzyme-Linked Immunosorbent Assay and Immunochromatography for Rotavirus Detection in Children Below Five Years with Acute Gastroenteritis. *J Clin Diagn Res* 2015;9(9):6-9.
28. Artiran S, Atalay A, Gökahmetoğlu S, et al. Investigation of Rotavirus with Various Methods in Children with Acute Gastroenteritis and Determination of Its Molecular Epidemiology in Kayseri Province, Turkey. *J Clin Lab Anal* 2017;31(2):e22030.