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Prevalence of antibodies against rubella, CMV and HSV among children in eastern Turkey

Türkiye'nin doğusunda çocuklarda rubella, CMV ve HSV antikorlarının prevalansı

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SUMMARY

Viral infections can lead to a broad range of cutaneous and systemic manifestations in childhood. Infections may occur in-utero, perinatal, postnatal or childhood. The purpose of this study is to determine the IgM and IgG antibodies seroprevalences of rubella virus, cytomegalovirus (CMV) and herpes simplex virus (HSV) in serum samples of pediatric patients, which were sent to our microbiology laboratory and to evaluate the results according to their age groups. A total number of 327 serum samples obtained from the pediatric patients between January 2003 and December 2003 were studied. The antibody levels of rubella IgM - IgG, CMV IgM - IgG and HSV type 1+2 IgM - IgG were detected using TKA 4HD micro-ELISA instrument and kits. IgM seropositivity for rubella, CMV and HSV type 1+2 were found as 3.4% (7/207), 4.3% (8/184), 10.2% (18/177) and the IgG seropositivity rates were 52.6% (131/249), 75.3% (134/178), 10.2% (16/157), respectively. Our results were compatible with the results obtained in other studies and it is an important finding demonstrating the confrontation of children with these viruses in Eastern region of Turkey.

Key Words: *Seroprevalence, Rubella, Cytomegalovirus, CMV, Herpes Simplex Virus, HSV*

INTRODUCTION

Infection with Herpes Simplex Virus (HSV) was first recognized in 1919 (1) and in 1960's antigenically distinct strains; HSV type 1 and HSV type 2 were identified (2). The prevalence of HSV-1 infection increases gradually from childhood, reaching 80% or more in later years (3). In contrast, the seroprevalence of HSV-2 remains low until adolescence and the onset of sexual activity. The incidence of antibodies to HSV-2 in the United States is increasing; currently, about 22% of the general U.S. population is seropositive (4).

Neonatal herpes occurs when genital herpes infection is present and the infant is exposed to HSV in maternal secretions. It is a disease with high mortality and morbidity (5). Infected neonates can present with HSV disease localized to the skin, eyes, and mucosa or with more serious central nervous system or disseminated disease. The mortality rate for untreated neonates with disseminated disease exceeds 70%. Early diagnosis and antiviral therapy while the disease is localized to the skin can substantially reduce the morbidity and mortality associated with neonatal infections (6-8).

Cytomegalovirus (CMV) infections are common and usually asymptomatic in healthy children and adults; however, the incidence and spectrum of the disease in newborns and in immunocompromised hosts establish this virus as an important human pathogen. The seroprevalence of CMV increases with age in all populations and ranges from 40 to 100%. Nearly 10% of women shed CMV in the genital tract at or near the time of delivery, and virus is transmitted to approximately 50% of the newborns but it appears that such perinatally infected infants do not have a

severe disease (9).

CMV infection has been detected in 0.2 to 2.5% of newborn infants and in fewer than 5% of congenitally infected infants develop symptoms during the newborn period; possible manifestations range from severe disease with any combination of intrauterine growth retardation, jaundice, hepatosplenomegaly, petechiae, thrombocytopenic purpura, myocarditis, pneumonitis, central nervous system abnormalities, and chorioretinitis to more limited involvement (9).

Rubella virus characterized by generalized maculopapuler rash both in children and in adults (10). Before the introduction of the rubella vaccine, there were epidemics in springs but after the introduction of the vaccine in 1969 the epidemic cycle was broken (11, 12).

HSV, CMV, and rubella viruses play an important role in childhood viral infections and to investigate the seroprevalence of the antibodies, IgG and IgM antibody levels against these viruses were analyzed in serum samples of pediatric patients, which were sent to our microbiology laboratory in the period of 2003 and 2004.

MATERIALS AND METHODS

A total number of 327 serum samples obtained from the pediatric patients for one-year period, between January 2003 and December 2003 were studied. From these serum samples IgG and IgM antibodies of rubella, CMV, and HSV Type 1+2 were analyzed using TKA 4HD EIA device (Teknolabo A.S.s.I.s.r.l – Italy) and kits. (M.B.S. Srl – Milano - Italy).

RESULTS

As a result of this study, the seropositivity of rubella IgM, rubella IgG, CMV IgM, CMV IgG, HSV Type 1+2 IgM, HSV IgG Type 1+2 were detected as 3.4% (7/207), 52.6% (131/249), 4.3% (8/184), 75.3% (134/178), 10.2% (18/177) and 10.2% (16/157), respectively. The distribution of antibody levels against rubella virus, CMV and HSV Type 1+2 according to age groups are shown in Tables 1, 2 and 3.

Tablo 1. The seropositivity of Rubella virus among childhood age groups

	Rubella IgM		Rubella IgG	
Age	n*	%	N	%
0-1	2/78	2.5	59/86	68.6
2-6	1/78	1.3	29/108	26.9
7-11	3/36	8.3	30/37	81.1
12-15	1/15	6.7	1 3/38	34.2
Total	7/207	3.4	131/245	52.6

*n: numbers

Tablo 2. The seropositivity of Cytomegalovirus among childhood age groups

	CMV IgM		CMV IgG	
Age	n	%	N	%
0-1	1/36	2.8	39/46	84.8
2-6	6/99	6.1	66/91	72.5
7-11	1/32	3.1	19/27	70.4
12-15	0/17	0	10/14	71.4
Total	8/184	4.3	134/178	75.3

*n: numbers

Tablo 3. The seropositivity of Herpes simplex virus among childhood age groups

	HSV IgM		HSV IgG	
Age	n	%	n	%
0-1	1/56	1.8	3/49	6.1
2-6	8/79	10.1	4/73	5.5
7-11	6/25	24	7/20	35
12-15	3/17	17.6	2/15	13.3
Total	18/177	10.2	16/157	10.2

*n: numbers

DISCUSSION

The antibody levels of rubella IgM were detected as 3.4%, but especially higher in 7-15 age group (8.3% and 6.7%) than 0-6 age group (2.5% and 1.3%). These findings indicate that rubella virus infection is confronted especially above 7 years old. The antibody levels of rubella IgG were higher in 0-1 age group (68.6%) than in 2-6 age group (26.9%) and a second peak was observed in 7-15 age groups (81.1%, 72.2%) The high rate of rubella IgG antibody levels detected in 0-1 age group is caused by the transmitted maternal IgG's. The increase in antibody levels after 7 years of age is because of the acquired rubella infections.

In a study performed on schoolchildren in Korea (13) the rubella IgG rates were found as 65% and 79%, in another study carried out by Guy et al. (14) the rubella infections were detected most frequently in 5-14 age group. Kanbur et al. (15) reported the seronegativity of rubella in girls of 9-10 years old as 15.3%, 11-13 years old as 6.6% and 14-16 years old as 1.3%; and in boys of 9-10 years old as 12%, 11-13 years old as 6.1% and in 14-16 age groups as 6.2%. In a study carried out in Iran (16) a highly significant correlation was detected between the rubella IgG antibody rates of mothers and their babies. Karakoc et al. (17) reported the seropositivity of rubella IgG as 87-94%, in 12-18 years old girls in Adana, Turkiye. In another study conducted in Iran (18) in children of 2-7 years old, the rubella IgG seropositivity was 97% and in Italy (19) in 2-4 and 5-9 age groups, the seropositivity of rubella IgG was 70% and in 15 and older age groups it was detected as 81.8%. In a study performed on 280 people in Erzurum (20), Turkiye, the seropositivity of rubella IgG was reported as 82.5% and IgM seropositivity was 0%.

In a study carried out by Hyde et al. (21) in Atlanta, seropositivity rate of rubella IgG was reported to be 96.2% in children between 6 and 11 years of age. Sallam et al. (22) determined seropositivity rate of rubella IgG as 91.64% in school-age girls in their study performed in Yemen. Serum antibody level against Rubella virus was determined as 95.69% in children in their study performed in Luxemburg by Mossong et al. (23) In their study related to seropositivity rate of rubella IgG, Kanber Kanbur et al. (24) evaluated their scores in children between the ages of 9-16, divided into 3 age groups as 9-11, 11-13 and 14-16. In their study, seropositivity rates of rubella IgG were reported to be 15.3%, 6.6% and 1.3% in girls, and 12.0%, 6.1% and 6.2% in boys respectively. The highest rate was found to be 15.3% in girls in 9-10 age groups. In another study in Edirne, Turkiye by Oner et al. (25) rubella-specific IgG seropositivity rate was reported to be 93.1% in adolescent girls between the ages of 12-17.

The IgM seropositivity for CMV was 4.3% in average and especially higher in 2-6 age group compared to the other age groups. It was assumed that exposure to CMV is most frequent in 2-6 age group. There were no significant differences for IgG levels between all age groups and the seropositivity was detected as 75.3% in average.

The IgM seropositivity in 0-1 age group was found out to be 2.8%. This result was compatible with detection of CMV as a cause of congenital infection in newborns in rates of 0.2% to 2.5% (9). It was reported that specific IgM antibodies were detectable for 3-4 months in average. In 5% of the patients, this period could be as long as 2 years and again CMV-IgM seropositivity could be detected in reinfection and reactivation besides primer infection (19, 26). The high rate of CMV IgG seropositivity seen in 0-1 age group (84.8%) is considered to be mostly because of the maternal antibodies transmitted to the baby.

In a study performed by Hizel et al. (27), the CMV IgG seropositivity of 318 children (1 day

to 15 years of age) and 745 women were analyzed and the rates were detected as 99% for women and 90.6% for children. The seropositivity rates were 94.5% in 0-5 months age group, 77.6% in 6-12 months age group, and 94% for 11-15 years age group in addition it was reported that only in 7 out of 55 CMV IgG positive infants, CMV IgM positivity was detected. The high rate of seropositivity in 0-5 month old infants was explained to be caused by primer infection or by the transmission of maternal antibodies to the newborn.

In similar studies performed in Turkiye (28, 29) the CMV antibody prevalence was reported to be 86-99% in adults and in another study (30) the serum samples of 143 pregnant women and their babies cord blood were analyzed for CMV IgG and the seropositivity was detected as 96%. Tuncer et al. (31) reported that they have detected the pregnant women to be 29.3% CMV IgG seropositive, 11.9% CMV IgM seropositive and from their babies cord blood the IgG antibodies were detected in 22.9% and could not have detected any IgM seropositivity. In a similar study of Orak et al. (32), the seropositivity of CMV IgG antibodies was detected as 99.5%.

In a study associated with the seroprevalence of CMV infections, which was carried out in the USA by Staras at al. (33), the seroprevalence rate was reported to be 58.9% in children at the age of 6 and over and to increase gradually in consistent with age level. In 819 Swedish children between 9 and 12 years old, Svahn et al. (34) Performed CMV IgG measurements between 1967-1968, 1977-1978 and 1997, and found the scores as 31%, 53% and 58%, respectively. In a study carried out in children from Finland during the first eight years of their age by Aarnisalo et al. (35), antibody level against CMV was determined to be 27% in 7 month-old children. This level was found to be increasing slowly to the level of 41% in 8-year-old children.

As we examine the antibody levels for HSV Type 1+2, it is seen that IgM seropositivity is lowest in 0-1 age group (1.8%), gradually increased in 2-6 age group (10.1%), highest in 7-11 age group (24%) and decreasing again in 12-15 age group (17.6%). According to these findings, it is assumed that most frequent encounter with HSV is in 7-11 age group, followed by 12-15 age group. The HSV IgG Type 1+2 levels were observed to be 6.1%-5.5% in 0-6 age group, however increased up to 35% in 7-11 age groups and again decreased to 13.3% in 12-15 age groups. The rates of HSV IgG and IgM Type 1+2 similarly make a peak in 7-11 age groups which indicates that encounter with HSV is most frequent in this group.

In a study performed by Aarnisalo et al. (35), HSV antibody level was determined to be 2% with in the first 8 years of life. It was also determined the same study that the rate increases 17% in 8-year-old children. Fusun et al. (36) found HSV-1 IgG seroprevalence to be 62.6% in atopic children in Samsun, Turkiye. In another study performed in individuals during their childhood by Tang et al. (37), HSV-1 IgG seroprevalence was determined as 38.9% and HSV-2 IgG seroprevalence as 15.9%. Kasubi et al. [38] determined HSV-1 antibody level as 73% in a study performed in Tanzania while determining HSV-2 antibody level as 15%. In 819 Swedish children between the ages of 9 and 12, Svahn et al. (34) performed HSV IgG measurements during the periods of 1967-1968, 1977-1978 and 1997, and determined the rates as 35%, 32% and 38%, respectively. In a study performed in children between 0 and 19 years old, Tunback et al. (39) accumulated 2106 samples of serum, and found HSV-1 seroprevalence as 35% and HSV-2 seroprevalence as 0.5%.

In a study performed by Kıyan et al. (40) from the serums of mothers with pregnancy problems and their babies cord bloods, HSV-1 IgM was investigated and in mother's serums HSV IgM

seropositivity was detected as 9.6%, however there was no positivity in cord bloods.

In our study, the kits used were for HSV Type 1 and 2 antibodies, and because the onset of HSV 2 antibodies are seen usually after adolescence, the antibodies detected in 2-25 age groups are considered to be HSV Type 1 antibodies.

As a conclusion, the results of our seroprevalence research for IgM and IgG antibodies of HSV, CMV, and rubella viruses were compatible with the results obtained in other studies and it is an important finding demonstrating the confrontation of children with these viruses in Eastern region of Turkiye.

REFERENCES

1. Lowenstein A. Aetiologische Untersuchungen über den fieberhaften, Herpes. Muench. Med Wochenschr. 1919; 66, 769-70.

2. Roizman B, Pellett P.E. The family Herpesviridae: a brief introduction. In: Knipe DM and Howley PM, eds. Fields Virology. Lippincott Williams and Wilkins, Philadelphia: 2001: 2381-2397.

3. Nahmias AJ, Lee FK, Beckman-Nahmias S. Seroepidemiological and sociological patterns of herpes simplex virus infection in the world. Scand J Infect Dis 1990; 69: 19-36.

4. Fleming DT, McQuillan GM, Johnson RE, Nahmias, AJ, Aral SO, Lee FK, St. Louis ME. Herpes simplex virus type 2 in the United States, 1976 to 1994. N Engl J Med 1997; 337: 1105-1111.

5. Prober CG, Sullender WM, Yasukawa LL, Au DS, Yeager AS, Arvin AM. Low risk of Herpes simplex virus infections in neonates exposed to the virus at the time of vaginal delivery to mothers with recurrent Herpes simplex virus infections. N Engl J Med 1987; 316: 240-244.

6. Kimberlin DW, Coen DM, Biron KK, Cohen JI, Lamb RA, McKinlay M, Emini EA, Whitley RJ. Molecular mechanisms of antiviral resistance. Antiviral Res 1995; 26: 369-401.

7. Whitley RJ, Arvin AM. Herpes simplex virus infection. In: Remington J. Klei J, eds. Infectious Diseases of the Fetus and Newborn Infant, W. B. Saunders Co, Philadelphia: 1995: 354-376.

8. Whitley RJ, Kimberlin DW. Treatment of viral infections during pregnancy and the neonatal period. Clin Perinatol 1997; 24: 267-283.

9. Murray PR, Baron EJ, Pfaller MA, Jorgensen JH, Yolken RH. Manuel of Clinical Microbiology. In: Hodinka RL, eds. Human Cytomegalovirus. ASM Press, Washington DC: 2003: 1304-1318.

10. Mandell GL, Bennett JE, Dolin R. Principles and Practice of Infectious Diseases. Churchill Livingstone Inc, New York: 1995: 1459-1465.

11. Horstmann DM. Rubella, The challenge of its control. J Infect Dis 1971; 123: 640-644.

12. Krugman S. Present status of measles and rubella immunization in the United States: A medical progress report. J Pediatr 1977; 90: 1-5.

13.Ki MR, Choi BY, Kim MH, Shin YJ, Park TS. Rubella seroprevalence in Korean children. J Korean Med Sci 2003; 18: 331-336.

14. Guy RJ, Andrews RM, Robinson PM, Lambert SB. Mumps and rubella surveillance in Victoria, 1993 to 2000. Commun Dis Intel 2003; 27: 94-99.

15. Kanbur NO, Derman O, Kutluk T, Kinik E. Age specific Rubella seroprevalence of an unvaccinated population of adolescents in Ankara, Turkiye. Jpn J Infect Dis 2003; 56: 23-25.

16. Doroudchi M, Samsami Dehaghani A, Emad K, Ghaderi A. Placental transfer of rubella specific IgG in fullterm and preterm newborns. Int J Gynaecol Obstet 2003; 157-162.

17. Karakoc GB, Altintas DU, Kilinc B, Karabay A, Mungan NO, Yılmaz M, Evliyaoglu N. Seroprevalence of Rubella in school girls and women. Eur J Epidemiol 2003; 18: 81-84.

18. Doroudchi M, Dehaghani AS, Emad K, Ghaderi AA. Seroepidemiological survey of Rubella immunity among three populations in Shiraz, Islamic Republic of Iran. East Mediterr Health J, 2001; 7: 128-138.

19. Rawlinson WD. Diagnosis of human Cytomegalovirus infection and disease. Pathology 1999; 31: 109-115.

20. Yazgı H, Arseven G, Dilli N, Ayyıldız A. Erzurum yöresinde anti-rubella antikor sıklığının değerlendirilmesi. Türk Mikrobiyol Derg 1996; 26: 117-119.

21. Hyde TB, Kruszon-Moran D, McQuillan GM, Cossen C, Forghani B, Reef SE. Rubella immunity levels in the United States population: has the threshold of viral elimination been reached? Clin Infect Dis 2007; 44: 465-466.

22. Sallam TA, Raja'a YA, Benbrake MS, Al-Shaibani KS, Al-Hababi AA. Prevalence of rubella antibodies among schoolgirls in Sana'a, Republic of Yemen. East Mediterr Health J 2003; 9: 148-151.

23. Mossong J, Putz L, Schneider F. Seroprevalence of measles, mumps and rubella antibodies in Luxembourg: results from a national cross-sectional study. Epidemiol Infect 2004; 132: 11-18.

24. Kanbur NO, Derman O, Kutluk T, Kinik E. Age specific rubella seroprevalence of an unvaccinated population of adolescents in Ankara, Turkey. Jpn J Infect Dis 2003; 56: 23-25.

25. Oner N, Vatansever U, Karasalihoglu S, Tatman Otkun M, Ekuklu G, Kucukgurluoglu Y. Rubella seroprevalence among Turkish adolescent girls living in Edirne, Turkey. Turk J Pediatr 206; 48: 288-293.

26. Daniel Y, Gull I, Peyser MR, Lessing JB. Congenital cytomegalovirus infection. Eur J Obstet Gynecol Reprod Biol 1995; 63: 7-16.

27. Hizel S, Parker S, Önde U. Seroprevalence of Cytomegalovirus infection among children and females in Ankara, Turkiye. Pediatr Int 1999; 41: 506-509.

28. Ustaçelebi Ş, Köksal I, Cantürk H. Hamilelikte TORCH etkenlerine karşı antikorların saptanması. Mikrobiyol Bült 1986; 41: 1-8.

29. Cengiz,AT, Cengiz L, Ataoglu H, Kayan M, Aksoy E. Sağlıklı doğum yapan annenin serumunda ve bebeğin kordon serumunda CMV IgG antikorlarının araştırılması. Türk Mikrobiyol Cem Derg 1990; 41: 176-181.

30. El-Nawawy A, Soliman AT, El Azzouni O, Amer ES, Karim MA, Demian S, El Sayet M. Maternal and neonatal prevalence of toxoplasma and cytomegalovirus (CMV) antibodies and hepatitis-B antigens in an Egyptian rural area. Early Human Development 1997; 47: 97-109.

31. Tuncer I, Bitirgen M, Şendil AZ ve ark. Anne ve yenidoğanda sitomegalovirus antikorlarının araştırılması. S Ü Tıp Fak Derg 1990; 5: 16-20.

32. Orak S, Kocabay K, Yılmaz M, Kılıç S, Özekici Ü. Cytomegalovirus antibodies in cord blood samples. Turk J Med Sci 1994; 41: 123-125.

33. Staras SA, Dollard SC, Radford KW, Flanders WD, Pass RF, Cannon MJ. Seroprevalence of cytomegalovirus infection in the United States, 1988-1994. Clin Infect Dis 2006; 43: 1152-1153.

34. Svahn A, Berggren J, Parke A, Storsaeter J, Thorstensson R, Linde A. Changes in seroprevalence to four herpesviruses over 30 years in Swedish children aged 9-12 years. J Clin Virol 2006; 37: 118-123.

35. Aarnisalo J, Ilonen J, Vainionpää R, Volanen I, Kaitosaari T, Simell O. Development of antibodies against cytomegalovirus, varicella-zoster virus and herpes simplex virus in Finland during the first eight years of life: a prospective study. Scand J Infect Dis 2003; 35: 750-753.

36. Fusun AI, Mahir I, Zafer Y, Semra OG, Asuman B, Recep S, Fadil O. Distribution of HSV-1 IgG antibodies by two methods comparing in Turkish atopic children. New Microbiol 2007; 30: 109-112.

37. Tang JP, Yang YJ, Zhang D, Li LP. Serologic examination for childhood herpes simplex virus infection. Zhongguo. Dang Dai Er Ke Za Zhi 2006; 8: 476-478.

38. Kasubi MJ, Nilsen A, Marsden HS, Bergström T, Langeland N, Haarr L. Prevalence of antibodies against herpes simplex virus types 1 and 2 in children and young people in an urban region in Tanzania. J Clin Microbiol 2006; 44: 2801-2807.

39. Tunbäck P, Bergström T, Andersson AS, Nordin P, Krantz I, Löwhagen GB. Prevalence of herpes simplex virus antibodies in childhood and adolescence: a cross-sectional study. Scand J Infect Dis 2003; 35: 498-502.

40. Kıyan M, Cengiz L, Cengiz AT, Kara F, Uğurel MŞ. Gebelikle ilgili sorunları bulunan anne serumlarında ve kordon serumlarında ELISA ile Herpes simplex virus-1 (HSV-1) IgM'in araştırılması. İnfeksiyon Derg 1991; 5: 121-123.