



Seroprevalance of Hepatitis B, Hepatitis C and Hepatitis D in Children Between 0-18 Years of Age Attending to Our Hospital

Hastanemize Başvuran 0-18 Yaş Arası Çocuklarda Hepatit B, Hepatit C ve Hepatit D Seroprevalansı

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Abstract

Objective: Detection of seroprevalence and possible transmission routes of hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis D virus (HDV) in children between the ages of 0 and 18 accepted our hospital due to any complaints.

Material and Methods: From blood taken from 208 patients that accepted to our hospital children's policlinics due to any complaint, serology of Hepatitis B, Hepatitis C (HBsAg, anti-HBs, anti-HBc IgG, anti-HBc IgM, anti-HCV) via chemiluminescent microparticle immunoassay (CMIA) method and serology of hepatitis D (anti-HDV) via enzyme-linked immunosorbent assay (ELISA) method were examined.

Results: The anti-HBs positivity was 68.3%, HBsAg positivity was 0.0%, anti-HBc IgG positivity was 0.5% and anti-HBc IgM positivity was 0.0% in a total of 208 patient group. The status of hepatitis B immunization was found as 100% according to the our questionnaire.

Conclusion: When the results of our study were evaluated, seroprevalance of anti-HBs was higher than the average of Turkey, seroprevalance of HBsAg, anti-HDV total and anti-HCV were lower than the average of Turkey. Campaigns about vaccination and transmission routes and public awareness activities should continue.

Keywords: Hepatitis B, hepatitis C, hepatitis D, seroprevalance

Özet

Giriş: Bu çalışmanın amacı hastanemize herhangi bir şikayetle başvuran 0-18 yaş arası çocuk hastalarda hepatit B virüs (HBV), hepatit C virüs (HCV) ve hepatit D virüs (HDV) seroprevalansının ve muhtemel bulaş yollarının saptanmasıdır.

Gereç ve Yöntemler: Hastanemiz çocuk polikliniklerine herhangi bir şikayetle başvuran 208 hastadan alınan kanlardan kemilüminesan mikropartikül enzim immünassay (CMIA) tekniği ile hepatit B, hepatit C serolojileri (HBsAg, anti-HBs, anti-HBc IgG, anti-HBc IgM, anti-HCV) ve sandwich enzim-linked immunosorbent assay (ELISA) yöntemi ile de hepatit D serolojisi (anti-HDV total) çalışıldı. Elde edilen veriler SPSS 15.0 programı kullanılarak bilgisayar ortamında değerlendirildi.

Bulgular: Çalışmaya alınan 208 hastada anti-HBs pozitifliği %68.3, HBsAg pozitifliği %0.0, antiHBc IgG pozitifliği %0.5 ve anti-HBc IgM pozitifliği %0.0 saptandı. Hepatit B aşılama durumu yapılan anket sonucunda %100 olduğu saptandı. Bu hastaların tümünde anti-HDV total ve anti-HCV negatif saptandı.

Sonuç: Çalışmamızda saptanan bulgular değerlendirildiğinde anti-HBs seroprevalansı Türkiye ortalamasının üstünde, HBsAg, anti-HDV total ve anti-HCV seroprevalansı Türkiye ortalamasının altındadır. Aşılama ve bulaş yolları hakkında kampanyalar ile halkın bilinçlendirilmesi çalışmalarına devam etmelidir.

Anahtar Kelimeler: Hepatit B, hepatit C, hepatit D, seroprevalans

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Introduction

Viral hepatitis maintains its importance in developing and developed countries (1). HBV infection, in the acute phase, threatens life and cause serious complications such as chronic hepatitis, hepatocellular carcinoma (HCC) and cirrhosis in advanced cases (2). HBV has been found responsible for 30% of all cirrhosis cases and 53% of all HCC cases in studies carried out in different regions. In terms of HCV, these rates have been reported respectively as 27% and 25% (3,4). While HBV seroprevalence changes from region to region in our country, HBsAg positivity has been determined between 3.9-12.5% and anti-HBs positivity between 20.6-52.3% (5,6). HCV seroprevalence in the world has been confirmed as 0.5-2% and in our country as 0.3-1.8%. Cirrhosis develops within 20-30 years in 10-20% of cases infected with HCV and HCC is seen in 15% of these cases (7). HDV infection occurs as a co-infection with HBV or as a superinfection by being subsequently concomitant to chronic HBV infection (8). Acute stage in HDV superinfection rises up to 90% and prognosis is more severe when compared to co-infection. The risk of fulminant hepatitis is between 2-20% in co-infection and progresses fatally in 70% of the cases (9). In seroprevalence studies conducted in our country, it has been reported between 1.05-5.2% in hepatitis B carriers, between 6.35-22% in cases with acute B-type viral hepatitis and between 31.1-58% in cases with chronic liver disease (10).

The aim of this study was to detect the seroprevalence of HBV, HCV AND HDV and their possible mode of transmission in pediatric patients between 0-18 years of age applying to our hospital with any kinds of complaints.

Materials and Methods

This study was carried out analyzing Hepatitis B, Hepatitis C, and Hepatitis D serology (HBsAg, anti-HBs, anti-HBc IgG, anti-HBc IgM, anti-HCV, anti-HDV total) in 208 patients applying to the Pediatric Outpatient Clinic of Cumhuriyet University Medical School for any complaints between 22.12.2014 and 01.01.2016. Patients with chronic diseases, immunodeficiency and previously diagnosed hepatitis diseases were excluded from the study.

3 cc of venous blood was taken from patients included into the study and were centrifuged for 4 min at 3500 rpm. Hemolyzed samples were excluded from the study due to the fact that they could give inconsistent results. Anti-HDV total tests were studied in the Microbiology Laboratory of Cumhuriyet University Medical with the sandwich ELISA method by a device called Triturus (Spain) and by microelisa kits of Dia.pro Diagnostic (Italy) from samples on which

positivity was detected via HBsAg, anti-HBs, anti-HBc IgG, anti-HBc IgM, anti-HCV and HBsAg, anti-HBc IgG, anti-HBc IgM tests with CMIA technique and fully-automated ELISA method of Architect Plus i2000 SR Abbott (USA) among the samples kept under -80 centigrade degree until the date of the study.

A 12-question questionnaire was conducted by a healthcare professional after having received the approval of all patients and their families. The age and gender of the persons, the state of Hepatitis B vaccination, the conditions that could create a risk in terms of transmission of hepatitis infection (tooth extraction and/or dental treatment, blood transfusion, surgery, having a tattoo done, getting a piercing, perforating injury, history of circumcision), and whether or not there were individuals in the family, relatives or around the person that had had Hepatitis B, C or D infection or still had active infection were questioned.

The study was approved by Cumhuriyet University Clinical Research Ethics Committee with decision numbered 2014-12-02 and dated 16.12.2014 and was financial supported by Cumhuriyet University Scientific Research Projects with project number T-638. Informed consent was received from the patients.

Statistical Analysis

The data acquired in the study were analyzed on SPSS (Statistical Package for Social Sciences) for Windows 15.0 program. Chi-square test was used for comparing intergroup rates. Significance was evaluated at $p < 0.05$. Kolmogorov-Smirnov test was used to analyze if numeric data conformed to normal distribution. The mean of the ones that conformed to normal distribution and the median value of the ones that did not conform to normal distribution were given.

Results

208 patients between the ages of 0 and 18 were included into the study. Whether or not the age values of the patients conformed to normal distribution was evaluated with Kolmogorov Smirnov test and the age values of the patients were detected to not conform to normal distribution. While minimum age of the patients was 15 days, maximum age was 204 months and median age was found as 87 months. 97 (46.6%) of the patients were females and 111 (53.4%) were males. Age range of the patients included into the study was as follows: 65 patients (31.3%) in 0-2; 30 patients (14.4%) in 3-5; 24 patients (11.5%) in 6-8; 23 patients (11%) in 9-11; 35 patients (16.8%) in 12-14; and 31 patients (15%) in 15-18 (Figure 1).

It was found out from the questionnaire conducted on the patients included into the study that 100% had age-appropriate hepatitis B vaccination. 142 (68.3%) of the patients had anti-HBs positivity and while hepatitis B vaccination had already

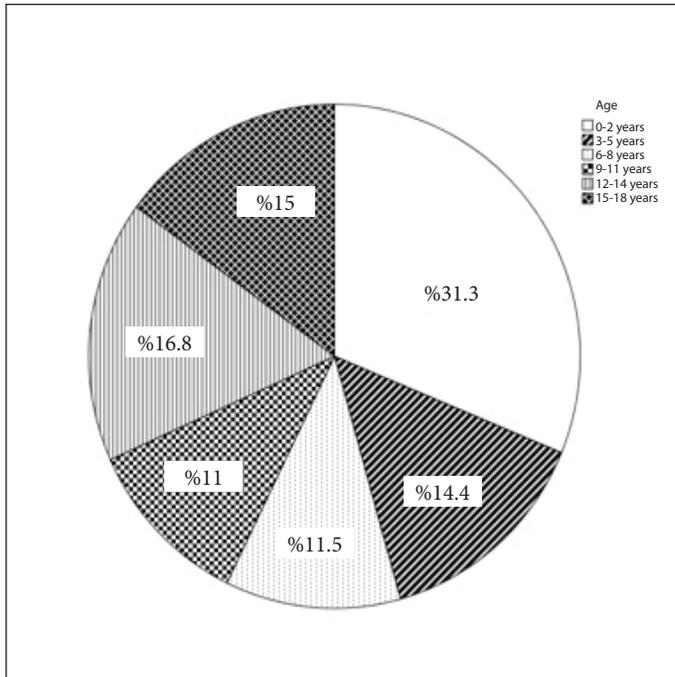


Figure 1. Age-Range Distribution Graphic of the Patients

been given, 66 (31.7%) of the patients had anti-HBs negativity. When the state of anti-HBs was compared as regards gender, 73 (51.4%) of the ones with anti-HBs positivity were male and 69 (48.6%) were female patients. Among the patients with anti-HBs negativity, 38 (57.6%) were males and 28 (42.4%) were females. Table 1 shows anti-HBs distribution as for age range. When anti-HBs was as for age range was evaluated, it was found statistically significant ($p=0.004$). The period when protectiveness based on vaccination is the highest was detected as the first three years with 84.6% anti-HBs positivity and the period when protectiveness based on vaccination is the lowest was detected as 3-6 years with 53.3% anti-HBs positivity. HBsAg and anti-HBc IgM negativity were detected in all patients included into the study.

Anti-HBc IgG was detected positive in one patient (0.5%) in the study. History like icterus, malaise, loss of appetite, vomiting, and rash suggesting acute hepatitis infection, individual history of HBV infection or carrier in the family was not detected in this nine-month-old patient. Besides, liver function tests of the patient was found normal (AST: 43 IU/L, ALT: 23 IU/L). In the patient with anti-HBc IgG positivity, anti-HDV total was determined negative.

Anti-HCV was detected negative in all patients included into the study.

Discussion

Transmission of hepatitis infection in central endemic regions including our country occurs mostly through non-parenteral modes (11). After having established the relation between acquiring the infection in early period and becoming chronic, hepatitis B vaccination gained importance in order to prevent infection in children. It has been reported that infection can be seen in vaccinated cases. However, there is no finding that the infection becomes chronic in vaccinated cases. In a study by Karaoğlu et al. (12) carried out on vaccinated children, previous HBV infection was found as 0.5% and in a study by Mc Mahon et al. (12) conducted on Alaskan natives, HBV infection was determined as 1%; however, symptoms for chronic infection were not confirmed on any patient. In our study, one patient (0.5%) was detected as having had HBV infection but not become chronic despite being vaccinated, which was concordant to other studies.

HBsAg seroprevalence that differ among regions in our country has been found between 3.9 and 12.5% and anti-HBs seroprevalence has been determined as 20.6-52.3% (5,6). Aypak et al. (14) found HBsAg positivity as 0.0% and anti-HBs positivity as 66.4% in Ankara between the years 2010 and 2011 in a study with 530 pediatric patients between the ages of 2 and 12. While Kaya et al. (15) determined hepatitis B vaccination

Table 1. Anti-HBs distribution according to age range ($p=0.004$)

Age range	Patient number n (%)	Anti-HBs positive n (%)	Anti-HBs negative n (%)
0-2 years	65 (%31.3)	55 (%84.6)	10 (%15.4)
3-5 years	30 (%14.4)	16 (%53.3)	14 (%46.7)
6-8 years	24 (%11.5)	14 (%58.3)	10 (%41.7)
9-11 years	23 (%11)	14 (%60.8)	9 (%39.2)
12-14 years	35 (%16.8)	19 (%54.2)	16 (%45.8)
15-18 years	31 (%15)	24 (%77.4)	7 (%22.6)

as 69%, HBsAg positivity as 66.4%, and anti-HBs positivity as 71.3% in pediatric patients between the ages of 0-18 in Van in 2010, Ayvaz et al. (16) found anti-HBs positivity as 73.9%, HBsAg and anti HBC IgG positivity as 0.16% in their study conducted on 607 pediatric patients, aged 7, in Sivas in 2008. There are various studies conducted on other regions, as well (17-20). Age-appropriate Hepatitis B vaccinations were proved to have been given to 100% of our patients as a result of the questionnaire conducted on our cases. HBsAg and anti-HBC IgM were detected negative in all patients. Even though anti-HBs was detected positive in 68.3% of the patients and negative in 31.7% in the ones with hepatitis B vaccination, anti-HBC IgG was confirmed positive in 0.5%. Difference in socio-economic levels of the groups and the easiness to reach healthcare services in cities were considered among the reasons why there was a difference between the positivity rates of anti-HBs.

Anti-HBs result was found statistically significant to the detriment of advanced age. The period when protectiveness based on vaccination is the highest was detected as the first three years with 84.6% anti-HBs positivity and the period when protectiveness based on vaccination is the lowest was detected as 3-6 years with 53.3% anti-HBs positivity. That there was no regular decrease with age in anti-HBs positivity rate was thought to be related to the fact that patient number in age groups included into the study was not equal, there was a limited number of patients, intensifier Hepatitis B vaccination may have been given in advanced ages, and that immunity may have responded differently in different patients.

There was no statistically significant difference when anti-HBs was evaluated according to gender, which was interpreted as the fact that protection rate formed through vaccination is independent of age.

In various studies conducted with present vaccines, it has been reported that immune response at a rate of 15% may not develop in HBV vaccinated individuals. While antibody levels formed after primary HBV vaccination reduce fast in the first year, these levels decrease more slowly afterwards in vaccination non-responsiveness. Gender (being male), smoking and obesity-like factors are thought to be responsible factors in these individuals. Additionally, non-compliance to vaccination schema, the fact that vaccines have been kept without complying to cold chain rules and the fact that the vaccines were administered without the proper technique also play part in vaccination non-responsiveness. Vaccination non-responsiveness has also been reported to be hereditary. In a genetic analysis study conducted on a total of 200 pediatric patients, of whom 100 were responsive to HBV vaccination and the other 100 were not, allele 2 frequency in the IL-1RN VNTR gene was found significantly higher in the non-responsive group. According to this result, it has been taken into consideration

that there may be a relation between allele 2 in IL-1RN and hepatitis B vaccination non-responsiveness(21). Pre-vaccination HBV indicators in non-responsive individuals should be checked. If the individual was vaccinated when carrying, anti-HBs will not develop. Anti-HBs response begins early on in some individuals after vaccination but the level is low and not detected by routine serologic tests. These individuals are considered low-responsive. In some cases, the individual is a hepatitis B carrier but HBsAg level is too low to be detected in routine tests. Therefore, HBsAg and, if necessary, ALT and HBV DNA are recommended to be tested in these non-responsive individuals (22-26).

HbsAg positivity rates in the pediatric age group were detected as 1.05% in Taiwan (2006), 2.4% IN Pakistan (2009), 7.5% in Mongolia (2007), 1.7% in Arabia (2008) and 0.66% in Belgium (2003)(27-31). Not having detected HBsAg positivity in our study was thought to be based on the fact that HBV infection is prevented and carriers are reduced as a result of hepatitis B vaccination program, socio-economic levels are improved, and the efficiency of policies followed towards informing the public an healthcare workers about the mode of transmission along with protection methods.

Intravenous drug users rank first due to the fact that the epidemiology of HCV infection whose vaccination has not been developed yet has seen a noteworthy change since 1990s in blood donors and in countries that perform HCV antibody scanning tests and use disposable medical products (32). HCV infection has become an important health issue due to elevation in in the rate of acute stage and the fact that its prevalence increases with advanced age (33).

HCV seroprevalance varies between 0.2%-2.6% in a limited number of studies conducted in our country (7,34). In these anti-HCV seroprevalance studies, Ayvaz et al. (16) found HCV seroprevalance as 0.6% in 607 pediatric patients, aged 7, in Sivas in 2008, Banak et al. (35) as 0.7% in patients above the age of ten in Adana in 2002, Zeyrek at el. (36) as 0.0% in children between the ages of 0 and 6 in Şanlıurfa in 2001, and Kaplan et al. (37) as 5.1% in hemodialysis patients in Sivas in 2011. The rates determined in studies conducted on children in terms of anti-HCV positivity in some countries were found as follows: 2.1% in Taiwan (2006); 2.1% in Pakistan (2009); 5.4% in Mongolia (2007), 0.0% in Arabia (2008), 0.12% in Belgium (27-31). As in some other studies indicated, anti-HCV seroprevalance was determined as 0.0% in our study. The reasons for this may be attributed to the fact that HCV seroprevalance is low in our country, HCV is transmitted through blood (the rate of the patients receiving blood-blood products in our study was 2.9%), hemophilia, organ transplant patients and hemodialysis patients who are in the HCV risk group were not included into our study, and to success of the studies conducted towards

protection or to the low number of patients included into the study.

HDV is a defective RNA virus necessitating HBV for replication and spread. In recent years, there has been a decrease in HBV and HDV seroprevalence in more specifically western regions thanks to education and vaccination studies conducted against HBV (38). In various HDV seroprevalence studies conducted on HBsAg-positive pediatric patients, Yaşar et al. (39) found 0.0% in children under the age of 15 in Istanbul in 2010, Koruk et al. (40) found 1.5% in children between the ages of 1-18 in Şanlıurfa in 2009, Akbulut et al. (41) found 0.0% in children between the ages of 7 and 14 in Elazığ in 2000, and Sönmez et al. (42) found 0.0% in children between the ages of 0 and 6 in Malatya in 2000. In our study, only one patient was tested positive for anti-HBc IgG in HBsAg, anti-HBc IgM, and anti-HBc IgG tests and HDV total in this patient was negative. This result is concomitant to previously conducted studies, and the most important mode to prevent HDV infection is to prevent transmission, vaccinating those who did not suffer hepatitis B infection or those who did not develop immunity to HBV through vaccination, and educating all towards modes of transmission.

HDV seroprevalence rates in the pediatric age group in some countries are as follows: 18% in Greenland (2007); 6.1% in Mongolia (2006) and 0.9% in Moldova (1994) (43-45). Hepatitis B vaccination program conducted in our country just as in other countries with low seroprevalence rates, studies carried out towards preventing the transmission of viral hepatitis and increase in the socio-economic level are believed to make hepatitis B and hepatitis D no longer a problem in the future.

In conclusion, as in many viral diseases, there is no definitive treatment of infections arising from HBV and HDV. Nonetheless, HCV infection has become a treatable disease with regimes with and without interferon as a result of various studies (46). Therefore, the most important issue is the prevention of the transmission of these viruses. The main goal in protection from HDV is to provide individuals that have not suffered hepatitis B disease or gained immunity to HBV with HBV vaccination and with education against modes of transmission. It is foreseen with the studies carried out that the decrease in the frequency of HBV, HCV and HDV infections will continue in the upcoming years. We are of the opinion that this study conducted on determining HBV, HCV and HDV seroprevalence in pediatric patients applying to our hospital will shed light on broader and more comprehensive studies that will be carried out in Sivas and Turkey in subsequent years.

Ethics Committee Approval: The study was approved by Cumhuriyet University Clinical Research Ethics Committee with decision numbered 2014-12- 02 and dated 16.12.2014.

Informed Consent: Informed Consent was received from the patients.

Peer-review: The article is arranged according to the reviewers and we accepted this last form of manuscript.

Author Contributions: Concept - FD; Design - AK; Supervision - AK; Data Collection and/or Processing - FD, AZ, BAA, PKB, CC; Analysis and/or Interpretation - FD, AZ, BAA, PKB, CC; Writing - FD, İOŞ; Confirmation - FD, AK, AZ, İOŞ, BAA, PKB, CC

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: This study was financial supported by Cumhuriyet University Scientific Research Projects with project number T-638.

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