Hepatitis B and measles seroprevalence among Turkish children

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This study was performed to determine hepatitis B and measles seroprevalence among the population under 30 years of age in Turkey. Blood samples of 2,683 subjects from eight provinces of Turkey were studied. Measles IgG was determined by hemagglutinin inhibition method, and hepatitits B surface antigen (HBsAg), anti-hepatitis B surface antibody (anti-HBs) and anti-hepatitis B core antibodies (anti-HBc) were determined by ELISA method. Overall seropositivity for measles was found to be 59.6%. There was a significant difference in seropositivity among provinces. The seropositivity was found to increase with age. The overall seropositivities for HBsAg, anti-HBs and anti-HBc were found to be 5.4%, 17% and 15.1%, respectively. The seroprevalences differed significantly among provinces. Although seroprevalence for anti-HBs and anti-HBc increased with age, HBsAg seropositivity did not change significantly after one year of age. Seroprevalence was not affected by sex. It was concluded that every effort should be given to vaccinate infants as early as possible for hepatitis B and that the coverage of infancy measles vaccination should be increased with a second dose.

Key words: hepatitis B, measles, seroprevalence.

Measles seconded by hepatitis B, are two diseases that we all hope to eradicate in near future. The WHO Regional Office has targeted measles elimination from Europe by 2007[1]. Vaccination is one of the key elements towards elimination as well as disease surveillance. In addition, determining population seropositivity of disease will guide vaccination policy.

In Turkey, universal measles vaccination has been in effect since the implementation of the Expanded Program for Immunization in 1985, thereby increasing the vaccination rate of measles in this country[2]. The vaccination coverage rates are between 62 to 87% in different regions[3]. Infants are vaccinated at nine months of age. A second vaccination at 6-7

years of age at the start of primary school has been in practice for several years. Unfortunately, measles cases and sometimes even epidemics still occur. There has been no nationwide study on the seroprevalence of measles.

Universal infant immunization for hepatitis B started in 1998 in Turkey. Unless the mother is hepatitis B surface antigen (HBsAg) positive, infants receive their first hepatitis B vaccine at three months of age, and vaccination is completed at nine months of age. Although there have been small-scale studies on the seropositivity of hepatitis B, there is no nationwide study.

This study was performed to determine the seroprevalence of hepatitis B and measles in the population under 30 years of age and to identify the relationship of seroprevalence to several characteristics of the study subjects from eight provinces of Turkey.

Material and Methods

This study was carried out between February and December 1998 in eight provinces of Turkey. The blood samples were obtained from the National Varicella and Hepatitis A Seropositivity Study[4,5]. The sampling method of 30 clusters was used for selecting subjects of a predetermined number in rural and urban areas. Details of the sampling method have been reported previously[4-6]. The original sample of the National Varicella and Hepatitis A Seropositivity Study constituted a total of 4,461 subjects, which was considered representative of Turkey[4,5]. In this study, the residual sera from that study were used to determine hepatitis B and measles seropositivity in the population under 30 years of age. Unfortunately, no blood samples were available from one of the provinces in the original series. The number of samples provided by the other provinces were also less than in the original sample. While perhaps not completely representative a total of 2,683 (61% of the original series) blood samples from eight provinces were studied.

The provinces included İstanbul, İzmir, Ankara, Adana, Diyarbakır, Samsun, Trabzon, and Erzurum. No blood sample could be obtained from Edirne province, which was included in the original sampling. Nearly one-third of the Turkish population live in these provinces. They also draw intense migration from neighboring cities and remote areas.

Serum analysis was performed at the Microbiology Laboratory of İstanbul University Faculty of Medicine. Details of serum sampling and transport were reported previously[4,5]. Serum samples were stored and transported to the laboratory in accordance with the principles of cold chain.

Hepatitis B surface antigen, and anti-hepatitis B surface antigen antibody (anti-HBs) and anti-core antibody (anti-HBc) were studied by ELISA method.

Measles IgG was studied by hemagglutinin inhibition method.

The number and percentages of cases were presented and statistical comparison was done using chi-square test.

Results

The original sample of the varicella seroprevalence study, the first part of the seroprevalence project, included 4,461 subjects. A total of 2,683 blood samples were available for this study, with different percentages of samples from each province. The number of cases with full sociodemographic records was 2,157. The number of cases under one year of age was also less than expected in the original data due to the problem of blood sampling in these cases.

The overall anti-HBs, anti-HBc and HBsAg positivities were found to be 17%, 15.1% and 5.4%, respectively (Table I). The distribution of seropositivity according to the provinces is also given in Table I. Although the antibody titers for HBsAg ranged within 13.4% to 24.8% and that for anti-HBc ranged between 11% to 25.6%, there was a dramatic difference in HBsAg positivity among provinces. In Adana, which is one of the southern provinces of Turkey, the HBsAg positivity was 30.1%. In other provinces HBsAg positivity ranged within 2.5 to 7.7% (Table I).

When hepatitis B seropositivity was analyzed according to several demographic factors, it was found that sex and place of residence (urban, suburhan, and rural) did not affect the seropositivity (Table II). On the other hand, anti-HBc antibody positivity increased with age after the first year of life. The seropositivity of the first year generally reflects maternal antibodies. However HBsAg positivity did not change with age. The seropositivity remained constant from the first year of life. HBsAg positivity was found to be higher in rural area (Table II).

Table I. Distribution of Hepatitis B and Measles Seropositivity According to Province

Province	No.	Anti-HBs Ab	Anti-HBc Ab	HBsAg	Measles IgG
Adana	163	29 (17.8)	33 (20.2)	49 (30.1)	67 (41.1)
Ankara	688	122 (17.7)	91 (13.2)	17 (2.5)	490 (71.2)
Diyarbakır	153	38 (24.8)	29 (19.0)	9 (5.9)	96 (62.7)
Erzurum	455	61 (13.4)	59 (13.0)	18 (4.0)	269 (59.1)
Samsun	352	53 (15.1)	52 (14.8)	15 (4.3)	217 (61.6)
Trabzon	181	39 (21.5)	46 (25.6)	7 (7.7)	124 (68.5)
İzmir	329	48 (14.6)	54 (16.4)	13 (4.0)	100 (30.4)
Total	2683	457 (17.0)	404 (15.1)	145 (5.4)	1599 (59.6)
P		0.023	<0.000	<0.000	<0.000

Anti-HBs Ab: anti hepatitis B surface antibody; Anti-HBc Ab: anti-hepatitis B core antibody; HBsAg: hepatitis B surface antigen.

The seroprevalence of measles also differed significantly among provinces (Table II). The seroprevalence showed a parallel increase with increasing age (Table II). There was no sex difference in seropositivity (Table II). The highest measles seroprevalence was detected in suburban areas (Table II).

under 30 years of age. This is the first such study in Turkey of this sample size and investigating these characteristics. In this nationwide seroprevalence study anti-HBs positivity was determined as 17%, anti-HBc positivity as 15% and HBsAg positivity as 5.4%. Thus Turkey has a moderate seropositivity for

Table II. Distribution of Hepatitis B and Measles Seropositivity According to Various Sociodemographic Characteristics

Characteristic	No.	Anti-HBs Ab	Anti-HBc Ab	HBsAg	Measles IgG
Age (y)					
0-1	47	13 (27.7)	5 (10.6)	2 (4.6)	14 (29.8)
2-5	329	46 (14.0)	21 (6.4)	17 (5.2)	142 (43.2)
6-10	406	49 (12.1)	39 (9.6)	25 (6.2)	178 (43.8)
11-15	443	54 (12.2)	54 (12.2)	28 (6.3)	244 (55.1)
16-25	663	137 (20.7)	133 (20.1)	37 (5.6)	474 (71.5)
>25	270	58 (21.5)	70 (25.9)	15 (5.6)	207 (76.7)
p		<0.000	<0.000	0.9	<0.000
Sex					
Male	1028	172 (16.7)	155 (15.1)	68 (6.6)	587 (57.1)
Female	1132	186 (16.4)	168 (14.8)	56 (4.9)	675 (59.6)
P		>0.05	>0.05	>0.05	>0.05
Location					
Urban	1621	276 (17.0)	233 (14.4)	84 (5.2)	936 (57.7)
Suburban	134	26 (19.4)	21 (15.7)	5 (3.7)	91 (67.9)
Rural	405	56 (13.8)	68 (17.0)	35 (8.6)	235 (58.0)
P		>0.05	>0.05	0.01	0.03

Discussion

In this study, the serum samples of the National Varicella and Hepatitis A Seropositivity Study were used. That study included 4,387 cases from nine provinces of Turkey and is a representative sample of the country[4,5]. In this study, 61% of the original samples were available for further study. While our study sample may not be totally representative of the country, it nevertheless includes an extensive number of cases from eight provinces of Turkey

HBsAg[7]. The results of this study are comparable to earlier local studies where different seropositivity rates were reported for different provinces[8-11]. Since in most of these studies, risk groups or nonrandom cases were studied our study better reflects the seropositivity of the general population.

The percentages of anti-HBs and anti-HBc were comparable. Indeed, the universal hepatitis B infant immunization program was implemented in 1998 in Turkey. Thus, in accordance with our

results, most of the antiHBs seropositivity in Turkey until today is due to natural infection. Another important aspect of this study, therefore, is that it reports seropositivity results in Turkey just prior to the universal hepatitis B infant immunization program. Although there were significant differences in seroprevalence of anti-HBs and anti-HBc between the eight provinces, the most dramatic difference among provinces was noted for HBsAg positivity. Although HBsAg positivity ranged between 2.5% to 7.7% among seven provinces, the seropositivity was determined as 30.1% in Adana. This suggests that either the daily habits of the population or a genetic defect in that region for controlling the infection leads to high seropositivity for HBsAg. Furthermore, Adana is in the southern part of Turkey, where sickle cell anemia and thalassemia are prevalent; malaria is also common in this province. So these may also play a role in down regulation in producing anti-HBs. We believe that these should be considered in future studies. Another finding in the Adana province that is difficult to explain is the discordance between anti-HBc (20.2%) and HBsAg positivity (30.1%). We could not find similar results in the literature for seroprevalence studies. The only similar results reported were from studies among hepatitis-suspected cases. Perhaps future studies will clarify this finding.

One of the most important findings of this study was the relation between HBsAg positivity and age. For anti-HBc and anti-HBs seropositivity as expected increased with age. The study population acquiring the infection increased with age, with a sharp increase during adolescence. However, the HBsAg seropositivity did not show a significant increase with age. It is known that the carrier state develops more commonly when the disease is acquired during the early years of life[12]. According to our findings, most carrier states in Turkey are acquired during the first year of life. Although it has been suggested that infant hepatitis B immunization can be given at 0, 3, 9 months of age, the most commonly practiced schedule is immunization at 3, 4, 9 months. In this study, it was not possible to determine the seropositivity for each month and determine a critical month for immunization. Considering the earlier recommendations[13] and the seropositivity results of our study, it is concluded that every effort should be given to start and complete the universal infant immunization (preferably the 0, 3, 9 month schedule) as soon as possible in the first year of life. In France and Italy it has been shown that HBsAg seropositivity decreased after immunization programs[14,15]. This study is important in that it is probably the last study to present the HBsAg results of the prevaccination era in Turkey.

Our study demonstrates that overall anti-HBs positivity was higher than that of anti-HBc. This can not be explained by natural infection alone and may be the result of hepatitis B vaccination. Although hepatitis B vaccine was added to the infant immunization scheme in Turkey in only the last few years (since 1998), several hepatitis B vaccines have been available in the market for more than 15 years, so this result might also show a higher parental acceptance of the hepatitis B vaccine.

A sex predilection was not detected for hepatitis B infection; the prevalence was similar in both sexes. Although there was no difference between anti-HBs and anti-HBc antibody prevalence according to residence, HBsAg positivity was more prevalent in the rural areas.

The goal of the WHO European Office is to eliminate measles by 2007[1]. In this context, it is important to determine the percentage of susceptible cases so that national and regional vaccination programs can be implemented. In Turkey the overall measles seropositivity was found to be approximately 60% (range 30.4-71.2%). Thus 40% of the 0-30 years of age population is susceptible to measles. Turkey is in the high susceptibility group for all ages. In the Western Europe seroepidemiology study[16] Finland, The Netherlands, The United Kingdom, and France were in the low susceptibility, Denmark and Germany in the intermediate susceptibility and Italy in high susceptibility group. In Italy there were regional differences for vaccination rates across the country (26%-88%), and this different from that observed in the other countries.

In our study, there was a gradual increase of measles seropositivity with age. In Turkey, the Expanded Program of Immunization has been in effect since 1985. We do not have the means to distinguish the seropositivity due to wild infection or vaccination. However, it is possible to speculate that the seropositivity of those

older than 15 years of age is due to wild infection. The seropositivity in that age group was found to be around 75%. In fact, this is lower than expected[17] (90-95% in non-immunized populations) so perhaps even the low level of immunization before 1985 impacted measles disease.

In Turkey, measles vaccine is given at nine months of age. For several years now, a second dose has been given at school entrance at about 6-7 years of age. According to our study, the seropositivity of measles before one year of age determined to be approximately 30%. Measles vaccine coverage for the first dose is reported to be around 62-87% in different provinces. The seropositivity found in our study was far lower than this coverage rate. In the Western European seroepidemilogy study[16], it was reported that the anti-measles antibodies are lower after the first years of vaccination and that levels increase by natural boosters. As the hemagglutinin inhibition method was used for detection of anti-measles antibodies, it is possible that it may have not detected some low seropositive cases in the first years who will later become seropositive by natural boost. On the other hand another study conducted in Turkey reported that 8.1% of nine month-old babies have measles IgG positivity which is due to maternal antibodies[18]. This may also partially explain some of the decreased antibody response at the nine months vaccination. In our study, at 2-5 years of age, the measles seropositivity was found to increase by 50% compared to the first year of life and reach 43.2%. Nevertheless, the seropositive cases are much lower than the reported vaccination coverage. When all these findings are considered together the effectiveness of the first dose of measles vaccine may be questioned. However, as recommended for high susceptibility countries, every effort should be made to increase the infancy vaccination coverage rate as well. A second dose of measles vaccine has been recently implemented for 6-7 year-old children, but the effect of the schedule has not been documented in this study.

Seropositivity for measles was highest in the suburban areas. This may be attributable to the crowded slum life in the suburban residence. There was no sex predilection. A difference was found for the provinces, with İzmir (western) and Adana (southern) provinces having very low seropositivity. Both of these provinces have a hot and moist climate.

In conclusion, this study with a large number of samples from eight provinces of subjects under 30 years old gives a good definition of the hepatitis B and measles seropositivity in Turkey. These findings have implications while developing vaccination programs and other measures of prevention for measles and hepatitis B in Turkey as well as in other countries with similar conditions.

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