Trends of hepatitis B notification rates in Turkey, 1990 to 2012

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Turkey is a country with intermediate endemicity for hepatitis B, and approximately 4% of the population are HBsAg-positive. A number of measures have been implemented to prevent hepatitis B infection. In 1998, hepatitis B antigen was included in the national immunisation programme, and infants have since been vaccinated with three doses. Catch-up strategies, vaccination for high risk groups and screening measures were also adopted. The aim of this study was to evaluate the impact of the prevention and control strategies on hepatitis B notification rates in Turkey in the period from 1990 to 2012, using data from the national surveillance system. Secular trends revealed that rates showed an initial increasing trend, followed by a steady decline from 2005. The most dramatic decline occurred among children younger than 15 years, highlighting the benefits of vaccination and catch-up strategies. However, vaccination cannot fully explain the decrease in this age group. Socioeconomic development, through interrupting the horizontal transmission may also have contributed. After 2005, a steady decline was achieved also among those 15 years and older. The rates in adults were higher, which indicates that stronger prevention measures are needed to target this group, particularly men.

Introduction

It is estimated that approximately 2 billion people in the world have been infected with hepatitis B virus (HBV) [1,2]. Among those, 360 million are chronic carriers and have a 15% to 25% risk of premature death from consequences such as liver cirrhosis and hepatocellular cancer [1,3]. The burden of hepatitis B differs worldwide. Countries in eastern and southern Europe have a moderate prevalence of chronic hepatitis, and Turkey is classified as a country of intermediate endemicity with approximately 4% of the population HBsAg-positive [2,4]. In a meta-analysis, evaluating seroprevalence studies published between 1999 and 2009, it was determined that the overall HBsAg positivity in Turkey was 4.6% [5].

Rates of HBsAg positivity vary within Turkey. Seroepidemiological studies show a decreasing trend from south-east to west in all age groups [5-12]. In a meta-analysis evaluating studies published between 1999 and 2009, Toy et al. estimated that the prevalence rates of HBsAg positivity in the west, middle and eastern regions were 3.5%, 4.9% and 6.8%, respectively. In the same study, the authors concluded that the lowest prevalence was in children who were younger than 15 years (2.8%) and the highest prevalence was among 25-34 year-olds (6.4%) [5].

In Turkey, hepatitis B vaccine has been on the market since the late 1980s, yet a systematic vaccination policy was not adopted at that time [13]. Since 1998, when hepatitis B antigen was included in the national immunisation programme, infants have been vaccinated with three consecutive doses. Although there have been some changes regarding vaccination schedules, infants have since 2003 received the antigen within the first 72 h after birth, followed by two additional doses at the end of the first and the sixth month of age. Catch-up strategies targeting older age groups are also used as a supplement to routine infant vaccination because studies among children six to 17 years of age, carried out in different parts of the country, indicate a gradual increase in the seroprevalence with rising age [4,10-12,14]. This finding suggests that horizontal transmission, through close contact with infected family members, is the main mode of transmission among children [4,10,14-16]. Vaccination activities were therefore carried out in primary schools during the period 2005 to 2009. In Turkey, eight years of primary schooling is mandatory and children start school at the age of six years. Target age groups which were included in catch-up vaccinations are presented in the Table. In

Table

Target age groups for catch-up vaccinations by school year, Turkey, 2005–2009

School year	Target group
2005–06	Primary school students at the eighth grade (13 years-old)
2006–07	Primary school students at the sixth, seventh and eighth grades (11, 12 and 13 years-old)
2007–08	Primary school students at the third, fourth, fifth, and sixth grades (8, 9, 10 and 11 years-old)
2008–09	High school students at the fourth grade (17 years-old)

Turkey, vaccination policies are adopted at the national level and are the same in all geographic regions.

Also high-risk groups for contracting hepatitis B have been vaccinated free-of-charge since 1998, namely healthcare workers, people who inject drugs, persons with high-risk sexual behaviour, persons who frequently require blood or blood products, haemodialysis patients, close contacts of HBsAg-positive persons, persons residing in orphanages, detention centres and prisons.

Strategies for screening were also adapted. In Turkey, it has been mandatory since 1993 to screen all voluntary blood donations for HBV. All registered sex workers are tested for hepatitis B every three months. Since sex workers are categorised as a high-risk group, vaccinations are offered free of charge. Screening is also carried out when an unregistered sex worker is arrested by the police. Since 2002, couples who appeal for marriage are asked whether they have hepatitis B infection, and counselling is provided, but laboratory analysis is carried out only among the ones who meet the definition of high risk as presented above. Vaccinations are offered to people testing negative. Antenatal screening for HBsAg among pregnant women is not mandatory. Condom use is promoted as a preventive strategy. In Turkey, condoms are freely available at the primary level of care. Advertisements on visual and written media are used for raising awareness about prevention measures.

The aim of this study was to evaluate the impact of the above prevention and control strategies on acute hepatitis B notification rates in Turkey. The main goal was to assess the trend in acute hepatitis B notifications from 1990 to 2012, in order to address future prevention and control activities.

Methods

In this study, data obtained from the National Surveillance System (NSS) were used for evaluating acute hepatitis B notification rates. In Turkey, acute hepatitis B has been notifiable since 1990, and data were collected on a monthly basis by sex, age and province. However, a national guideline encompassing standard case definitions was not in use at that time. In 2004, the Turkish Ministry of Health updated the NSS and introduced standard case definitions for each notifiable disease. According to the newly launched definitions, patients compatible with the clinical picture and positive for anti-HBc IgM and/or HBsAg, were identified as acute hepatitis B cases [17]. Notification was restricted to acute cases. Practically, the newly launched case definition for acute hepatitis B did not differ from the criteria used for acute infections before 2004 in clinical practice. But this was the first time a standard case definition was adopted and circulated to all healthcare institutions throughout the country. Training programmes for physicians were implemented, introducing the case definitions and also emphasising the importance of surveillance.

Notification rates were calculated per 100,000 population. Age groups were defined as 0, 1–4, 5–9, 10–14 and ≥15 years. For calculating regional rates, the Nomenclature of Territorial Units for Statistics (NUTS) was used and provinces were categorised in 12 territorial units [18].

In Turkey, healthcare providers report the number of vaccinated children on a monthly basis to the Ministry of Health through the district and provincial health authorities. Reporting has been carried out electronically since 2011. Hepatitis B vaccination coverage refers to the percentage of fully vaccinated children reaching their first birthday. An infant that has received three doses of hepatitis B vaccine is defined as fully vaccinated. In this study, vaccine coverage data were obtained from the Ministry of Health.

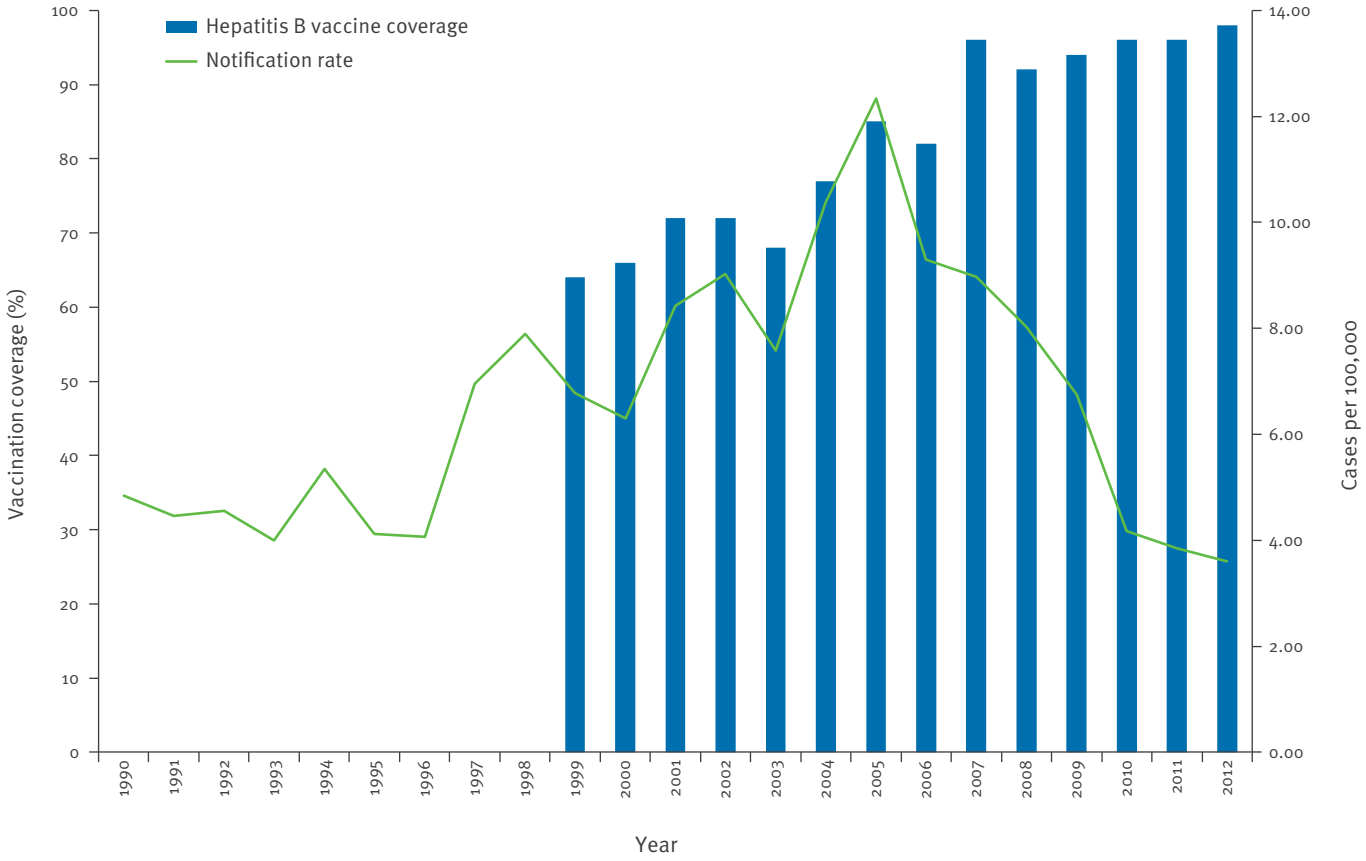
Results

Acute hepatitis B notification rates between 1990 and 2012 are presented in Figure 1. In 1990, the notification rate was 4.8 per 100,000 population. Rates showed an increasing trend and reached 12.3 per 100,000 in 2005. After 2005, there was a steady decline, and the rates in 2011 and 2012 dropped to 3.9 and 3.6 per 100,000, respectively (Figure 1). Vaccine coverage rates between 1999 and 2012 are also presented in Figure 1. In 1999, 64% of infants had been vaccinated with three doses of hepatitis B antigen. Coverage showed an increasing trend and rates above 90% were maintained after 2006 (Figure 1).

Notification rates by age groups are presented in Figure 2. Notification rates in 1997 for children aged <1 year, 1–4 years, 5–9 years and 10–14 years were 8.19, 5.21, 9.54 and 8.74 per 100,000, respectively. Rates for children under the age of 15 years showed a decreasing trend until 2004. In 2001 and 2005 there were small peaks among those younger than 15 years. However, after 2005 a steady decline was observed in all age groups younger than 15 years. The notification rates

Figure 1

Notification rates for acute hepatitis B (1990–2012) and percentage of infants vaccinated with three doses of hepatitis B virus antigen (1999–2012), Turkey*



in 2012 for the 1–4, 5–9 and 10–14 year-olds were 1.8, 0.2, 0.5 and 0.9 per 100,000, respectively.

Since infant vaccination started in 1998, notification rates for the under five years-old in 2002 and 2003 represent the first results for age groups that received vaccination.

The notification rate for those 15 years and older was 6.45 per 100,000 in 1997. Unlike the younger population, rates for this age group showed an increasing trend until 2005 and declined thereafter. The rates in 2005 and 2012 were 15.32 and 4.6 per 100,000, respectively.

Notification rates by age and sex for 2012 are presented in Figure 3. Notification rates for males and females in 2012 were 4.6 and 3.6 per 100,000, respectively. The rates were higher among male than among female infants for 2012, data from previous years showed similar rates (data not shown). Rates were slightly higher among boys during childhood after the first year. Men older than 19 years had higher rates than women. The highest rate difference between men and women was observed in the age group of 30–44 year-olds. Among this age group, the rate difference was 3.3 per 100,000 in 2012.

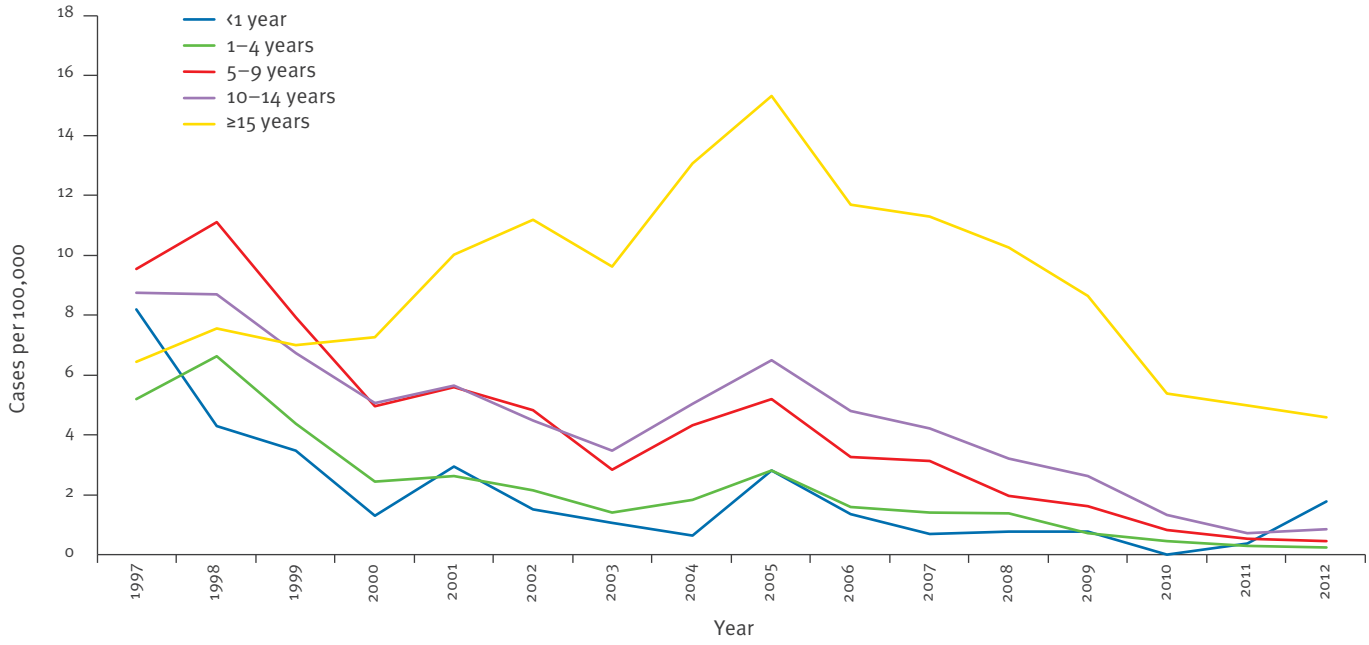
Notification rates are also analysed by geographical region (Figure 4). Highest rates were observed in Istanbul, west Marmara, northern regions and middle Anatolia. Southern regions had lower rates. Eastern Anatolia showed exceptionally low notification rates. Vaccination rates were similar throughout the country, but lowest rates were observed in the eastern regions.

Discussion

Notification rates of acute hepatitis B showed a decreasing trend among those younger than 15 years between 1997 and 2004. The most dramatic decline was observed among children under the age of five years, highlighting the benefits of vaccination which had been introduced in 1998. However, in 2001 and 2005, the downward trend changed and notification rates peaked among children under 15 years of age. The trend change in 2005 could be related to the introduction of the new notification system. In 2004 with the change of the Communicable Disease Notification System, a standard case definition was adopted for acute hepatitis B infection [19,20]. Although the newly launched criteria were not different from those used in daily practice before, revisions may have created awareness among health personnel and led to an increase in notification rates. After 2005 and until

Figure 2

Notification rates for acute hepatitis B by age group, Turkey, 1997–2012



2012, the rates have been declining steadily among all age groups under 15 years.

The first infant cohort was vaccinated in 1998 as part of the national immunisation programme. This group reached the age of five in 2003 explaining the decrease in the rates for 5–9 year-olds after 2003. Children younger than 15 years had been vaccinated by 2007 through catch-up activities, therefore the decrease after 2007 for children aged 10–15 years was also expected. However, not all the decline can be explained by vaccination activities. Epidemiological studies in Turkey show that HBsAg positivity is more prevalent among socioeconomically disadvantaged groups, and that horizontal transmission is the main route of transmission [4,9,10,12,14-16,21]. In a study carried out in one of the hospitals in Turkey during 2001–05, it was determined that HBsAg carrier rate was higher among fathers than among mothers. However, in the present study, it was determined that the children of mother index cases had higher rates of HBsAg compared with the children of father index cases. So in intra-familiar transmission, mother-to-child has been suggested as the main route. Since mothers mostly are not working and spend longer time with their children, their risk of transmitting the virus is higher compared to fathers. [16]. Socioeconomic development, leading to improved living conditions, less crowded families, improved sanitation and hygiene practices could have interrupted intra-familiar transmission and contributed to the decreasing trends [22-25]. A study in Italy showed that the decrease in acute hepatitis B was more apparent before the introduction of the mass immunisation. The authors concluded that the improved socioeconomic

Figure 3

Notification rates for acute hepatitis B by sex and age group, Turkey, 2012

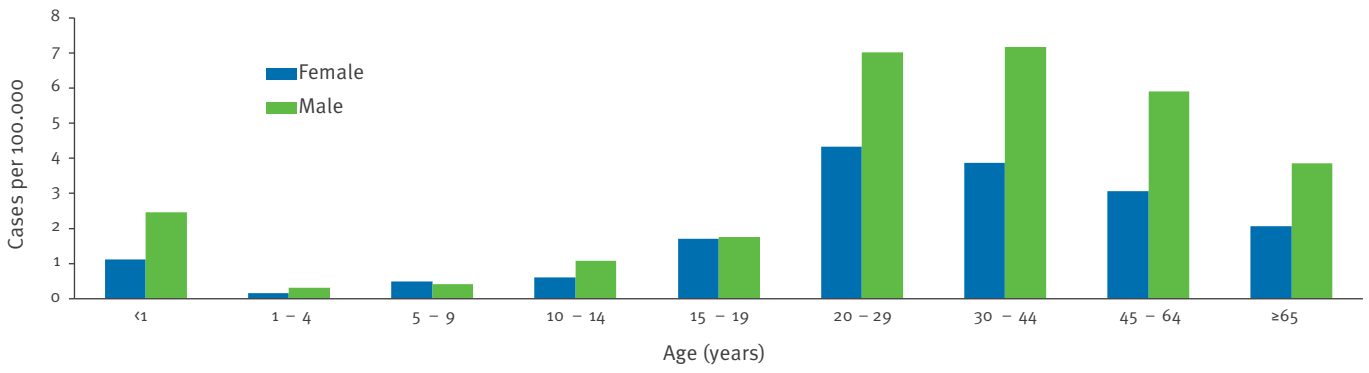
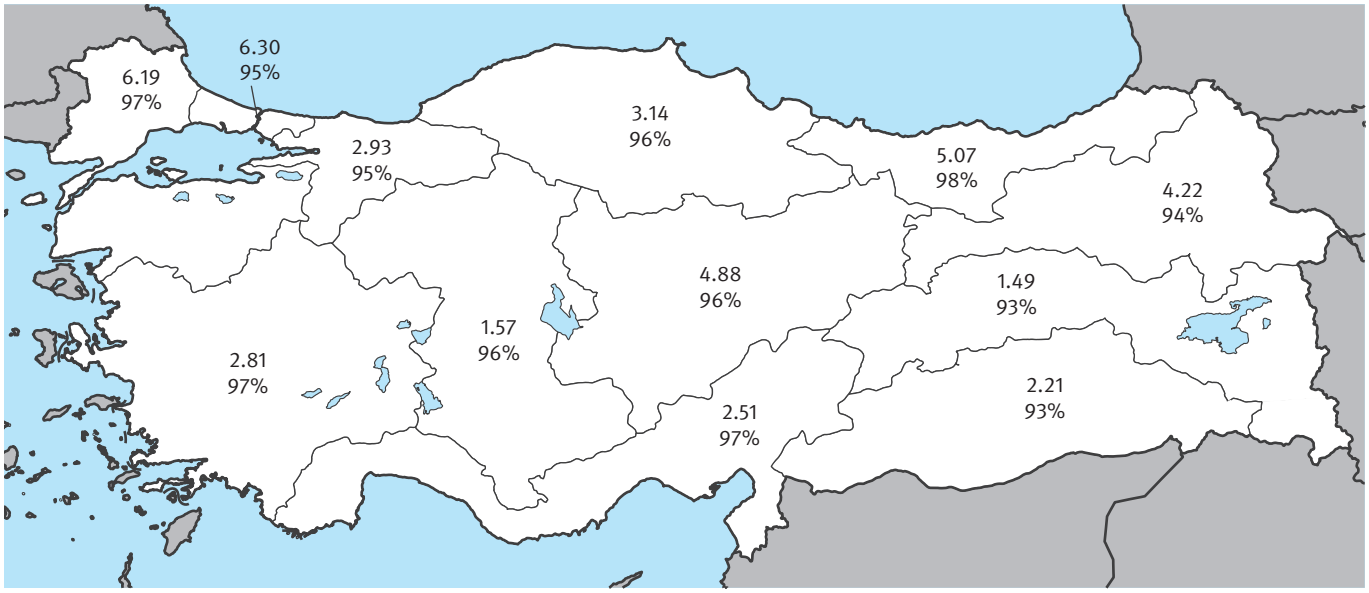


Figure 4

Notification rates for acute hepatitis B cases per 100,000 and percentage of infants vaccinated with three doses of hepatitis B virus antigen, by region, Turkey, 2012



Source: Kartenwerkstatt; http://commons.wikimedia.org

and sanitary conditions in the country had resulted in declining rates [22].

The notification rates for those 15 years and older followed an upward trend until 2005 and a decrease thereafter. Introduction of standard case definitions in 2004 and prevention activities among adults may have had an impact, but are not sufficient to explain the trend change after 2005. There is not any information on the uptake of vaccination outside the national immunisation programme. Still, the continuing downward trend after 2005 suggests that there is a true reduction in hepatitis B infections also among this age group.

Adults still had relatively higher rates of hepatitis B seroprevalence compared with children, highlighting the need to strengthen vaccination services targeting adults. In Turkey, hepatitis B vaccines are provided free of charge to individuals at high-risk for contracting the virus. It is therefore important to assess individuals at every opportunity at consultations in primary care and to offer vaccination for high-risk groups. It is important to remember that both patients and healthcare providers can be reluctant to report high-risk sexual practices, particularly in traditional societies. Information should therefore be provided about the risk factors for contracting hepatitis B infection and benefits of vaccination [26].

Data stratified by sex indicated that notification rates were comparable until adulthood. From the age of 20 years, however, rate differences between men and women increased. In the age group 30–44 years, the rate difference was 3.3 per 100,000. Seroepidemiological studies carried out in different parts of Turkey among adults also show higher rates of HBsAg positivity among men [5,9,21,27,28]. Sex differences suggest a higher rate of exposure to risk factors among men. Unfortunately in Turkey, routes of transmission are not reported for notified cases, but we can consider several reasons for men to predominantly contract the infection. High-risk behaviours such as having multiple sexual partners, male homosexual contact, using intravenous drugs, or sharing contaminated blades in barber shops may be more prevalent among men [6,29]. High-risk groups, particularly males, should be asked about potential exposure and offered vaccination at every opportunity.

Notification rates differed by geographical region, with the highest rates identified in Istanbul, western Marmara, the Black Sea and middle Anatolia. We need to be cautious in comparing these rates because access to healthcare, diagnostic capacity and notification rates may vary widely. Seroepidemiological studies show that residents of eastern, particularly south-eastern, Anatolia have higher rates of HBsAg positivity compared to the other regions [6,10,11]. Also the meta-analysis carried out by Toy et al. which evaluated studies published between 1999 and 2009, identified the highest rates in the eastern parts of Turkey [5]. Our results for south-eastern Anatolia could therefore be an underestimation and may be related to low access to healthcare, underdiagnosis and/or notification practices. Eastern parts are the least developed regions in Turkey. So we expect there a higher rate of underestimation than in the other regions. Efforts

should be made to understand the regional differences and eliminate their causes.

In 2008 and 2012, notification rates for acute hepatitis B in Turkey were 8.0 and 3.6 per 100,000, respectively. In Europe (among 27 European Union Member States and three European Economic Area countries), the notification rate of acute hepatitis B was 0.8 per 100,000 in 2010 [30]. Among the countries reporting acute cases, the Czech Republic (2.3 per 100,000), Romania (2.3 per 100,000) and Lithuania (2.1 per 100,000) had the highest notification rates [30]. The rates notified from Turkey were higher than in other European countries, although direct comparison between countries is not possible, due to differences in surveillance systems. It is hard to predict the level of underestimation and project the actual rates. However, a study conducted in one Turkish city in 2003 provides a clue on the rate of underestimation: Durusoy and Karababa compared data obtained from serology laboratories with the notifications received by the Provincial Health Directorate in order to understand the completeness of acute hepatitis B notifications in 2003 in Izmir, the third largest city in Turkey located in the west near the Aegean coast. At that time, the notification rate of acute hepatitis B in Izmir was 6.4 per 100,000. Yet by capture–recapture analyses, the authors calculated the notification rate as 52.2 per 100,000 (95% confidence interval: 39.9–64.5 per 100,000) [31].

The reported rates therefore suggest an underestimation. However, secular trends indicate that the rates are declining. With the available data, it is not possible to determine the quantitative impact of each preventive measure on notification rates. Although it is possible to assume that all measures had interacted synergistically, the trend among the younger age groups highlighted in particular the importance of universal vaccination and catch-up strategies. The impact of infant and school vaccination on acute hepatitis B notification rates had been demonstrated in a number of studies [23,32-34]. Still, vaccination can only partly explain the decline in hepatitis B infections among children. Since horizontal transmission is an important route particularly among groups with low socioeconomic status, improved living conditions, interrupting the horizontal transmission, may have contributed to the downward trend.

Conclusion

Secular trends reveal that the notification of acute hepatitis B is decreasing in all age groups in Turkey. High vaccination coverage and catch-up strategies had a positive impact among young age groups. Although a decreasing trend was achieved for adults after 2005, these rates remain high and demand strengthened prevention measures targeting adults, particularly men.

*Erratum:

The correct illustration for Figure 1 was uploaded on 25 November 2013.

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