Prevalence of anti-hepatitis B and anti-hepatitis A antibodies among school aged children in Western Saudi Arabia

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ABSTRACT

Objectives: To determine the seroprevalence of antibodies to hepatitis B virus (HBV) and hepatitis A virus (HAV) among children in Jeddah, Kingdom of Saudi Arabia (KSA) and to evaluate the need of anti-HAV mass vaccination.

Methods: This study was carried out on random samples of schools located at different regions in Jeddah, KSA during the year 2004. A total of 527 sera, (285 males and 242 females), collected from children aged (4-14 years) were tested for anti-hepatitis B surface (antigen) (HBsAb) and anti-HAV viruses antibodies by enzyme linked immunosorbent assay technique.

Results: Approximately 98% of children received HBV while 49% of received HAV vaccine. For HBV the overall seropositivity was 75% while HAV was 28.7%, whereas seronegativity was 14% for HBV and 70.5% for HAV. Percentage of seropositivity against HBV was elevated in vaccinated versus non-vaccinated children ($p<0.000$). In vaccinated children against HBV, percentage of seropositivity was elevated in children attending public versus those attending private and no schools ($p<0.000$) and in Saudi versus non-Saudi children ($p<0.05$). In vaccinated and non-vaccinated children against HAV, percentage of seropositivity was elevated in children attending public versus those attending private schools ($p<0.000$) and no schools ($p<0.000$) and in males ($p<0.05$) versus females ($p<0.01$). In vaccinated children, percentage of seropositivity for HBV obtained by age range from 4-6 years was 78.7%, for 7-11 years 74.4% and for 12-14 years 72.6%, whereas for HAV virus, seropositivity was 14.8% for 4-6 years, 38.3% for 7-11 years and 28.6% for 12-14 years.

Conclusion: Despite successful coverage of mass vaccination against HBV among school aged children, in Jeddah, KSA, there are high prevalence levels of seronegative with increasing age suggesting outbreak of disease among adolescent. Low prevalence of protective antibodies against HAV in vaccinated and non-vaccinated children may suggest application of mass vaccination program.

Saudi Med J 2006; Vol. 27 (10): 1515-1522

Viral hepatitis has remained a major public health problem worldwide. With the advance in technologies, 8 distinct types of hepatitis viruses have been described so far: Hepatitis A, B, C, D, E, G, TT and SEN viruses.[1] Hepatitis B virus (HBV) infection remains a major contributor to the global disease burden. It is one of the most important infectious agents causing acute and chronic morbidity and mortality worldwide. There are at least 350 million carriers of HBV worldwide.[2] At least one million individuals chronically infected with HBV die each year from chronic liver disease, including cirrhosis and liver cancer.[3] Hepatitis B has a marked tendency to induce a chronic infective status, and

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Received 25th January 2006. Accepted for publication in final form 21st June 2006.

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10% of infected subjects become carriers. Circulating immune complex contributes to the pathogenesis of the extrahepatic manifestation of hepatitis B infection.[4] It is generally agreed that control of hepatitis B is a high-priority public health objects on a worldwide basis. The only practical solution to the problem is recognized as large-scale immunization. It is clear that immune memory remains intact for at least 10 years following immunization.[5] Follow-up studies for up to 10-15 years have shown high safety and continuing immunity.[6] The schedule of HBV vaccination applied in Saudi Arabia consists of 3 doses given at 0, 2, 6 months of life. Hepatitis A is an acute; necroinflammatory disease of the liver, which results from infection by hepatitis A virus (HAV), which is transmitted primarily by fecal oral route.[7] The prevalence of HAV infection is influenced mainly by general hygiene especially in relation to toilet facilities, water supplies and food preparation factors reflecting living standards and socio-economic status.[8] The HAV appears to circulate in most parts of the world, and is responsible for both epidemic and sporadic disease.[9] Most people in hyperendemic areas for HAV have acquired the protective anti-HAV antibody through sub-clinical exposure to the virus in their childhood, which then confirms lifelong immunity against further HAV infection.[10] Lack of such exposure in childhood in low and intermediate endemic areas of HAV might result in a large non-immune population in whom HAV infection has been reported to cause severe adult hepatitis.[11] Several reports from developing nations have suggested a shift in the HAV epidemiology (from high to intermediate or low endemicity), presumably because of improved hygiene and sanitation.[12,13] Such observations have led to a recommendation for mass vaccination of all children in these countries. Vaccination strategies may vary from community to community.[14,15] The present study was undertaken to determine the prevalence of antibodies to HBV and HAV in school aged children in order to evaluate the adequacy of used vaccination policy against HBV, to evaluate the possibility of introducing HAV vaccine and to asses the risk for the diseases outbreak in Jeddah, Kingdom of Saudi Arabia (KSA).

Methods. ***Subjects.*** This study was carried out on random samples of schools located at different regions in Jeddah, KSA during the year 2004. Blood samples (3 ml) were obtained by venous puncture from (n=527) healthy school aged children (285 males and 242 females); aged 4-14 years (mean ± SD, 8.90 ± 3.34 years). The samples were centrifuged and sera were frozen at –20° until the serological analysis was performed. All subjects were in a good state of health and had a negative history for hematological, renal, hepatic or allergic diseases. The study was approved by the Medical Ethics Committee of King Abdul-Aziz University. Prior permission was obtained from the school authorities and consent was obtained from the parents of the children for venous puncture and medical examination. For each participant, a questionnaire was completed by the students themselves or the helpers in the school who have the student's file to provide some demographic information including name, age, gender, nationality, type of school and vaccination state.

Serological tests. The detection of hepatitis B surface antibodies (HBsAb) is important for follow up patients infected by HBV and in monitoring of recipients upon vaccination with synthetic and natural hepatitis B surface antigen (HBsAg). In this study, HBsAb detection was made using a commercial HBsAb kits (REF#20128) supplied by Dia. Pro. Diagnostic Bioprobes Srl (Milano, Italy). Samples with a concentration <5 WHO mlU/ml are considered negative, with concentration in the range 5-10 WHO mIU/ml are considered into a gray zone and those with concentration >10 WHO mlU/ml are positive for HBsAb. The sensitivity of the test was 100%, specificity 99% and accuracy was 99.5%. Total anti-HAV antibodies were determined using Bioelisa HAV (COD# 3000-1097), supplied by BioKit (Barcelona, Spain). All samples with absorbance value ≤ the cut-off value are considered positive for anti-HAV, while those with absorbance value >cut-off value are considered negative. All values with 10% of the cut-off value are considered equivocal and retested.

Statistical analysis. Data were analyzed using the Statistical Package for Social Sciences software, version 10. The percentages of positive, negative and equivocal sera were calculated according to age, gender, type of school and nationality. The prevalence among different groups was compared using the chi-square test. The $p<0.05$ was considered statistically significant.

Results. This seroepidemiological study shows the overall anti-HBV and anti-HAV antibodies in the sera of 527 school aged children. It was found that of the recruited children, 98% were vaccinated against HBV and 49% against HAV. The overall seropositivity of HBV was 75%, seronegativity was 14% and equivocal rate was 11%, and for HAV the rates were 28.7% for seropositivity, 70.5% for seronegativity and 0.8% for the equivocal rate. In comparing vaccinated versus non-vaccinated children for HBV, percentage of seropositivity was significantly elevated (75% versus

50%, $p<0.000$). Meanwhile, in comparing vaccinated versus non-vaccinated children for HAV, percentage of seropositivity, seronegativity, equivocal rates did not show any significant differences (**Table 1**).

Table 2 showed the overall seropositivity, seronegativity and equivocal rates in vaccinated and non-vaccinated children against HBV and HAV grouped by gender, type of school and nationality. In vaccinated children against HBV, percentage of seropositivity was significantly elevated in children attending public school compared to those in private or no-school (39% versus 24% and 12%, $p<0.000$) and in Saudi versus non-Saudi children (42% versus 34%, $p<0.05$). In non-vaccinated children against HBV, no significant difference was noticed regarding gender, type of school or nationality. In vaccinated children against HAV, percentage of seropositivity was significantly elevated in children attending public

Table 1 - Prevalence of antibodies against hepatitis B and hepatitis A in school aged children (n=527) in Jeddah, Saudi Arabia grouped by vaccination state.

Variable	Seropositive N (%)	Equivocal N (%)	Seronegative N (%)
Hepatitis B virus			
Vaccinated (n=517)	389 (75)	55 (11)	73 (14)
Non Vaccinated (n=10)	5 (50)	2 (20)	3 (30)
P-value	$p<0.000$	$p<0.000$	$p<0.000$
Total (n=527)	**394 (75)**	**57 (11)**	**76 (14)**
Hepatitis A virus			
Vaccinated (n=259)	74 (29)	3 (1)	182 (70)
Non Vaccinated (n=268)	77 (29)	1 (0.4)	190 (71)
P-value	$p>0.05$	$p>0.05$	$p>0.05$
Total (n=527)	**151 (28.7)**	**4 (0.8)**	**372 (70.5)**

Table 2 - Prevalence of antibodies against hepatitis B and hepatitis A in vaccinated and non-vaccinated children (n=527) in Jeddah, Saudi Arabia grouped by gender, type of school and nationality.

Variable	Gender (% to vaccination)			School (% to vaccination)				Nationality (% to vaccination)			Total (% to vaccination)
	Male (n=285)	Female (n=242)	*P*-value	Private (n=161)	Public (n=287)	No school (n =79)	*P*-value	Saudi (n=298)	Non- Saudi (n=229)	*P* value	(n=527)
Hepatitis B virus											
Vaccinated (n=517)											
Seropositive	204 (39)	185 (36)	>0.05	124 (24)	202 (39)	63 (12)	<0.000	216 (42)	173 (34)	<0.05	**389 (75)**
Equivocal	28 (6)	27 (5)	>0.05	18 (4)	30 (6)	7 (1)	<0.001	36 (7)	19 (4)	<0.05	**55 (11)**
Seronegative	49 (10)	24 (4)	<0.01	15 (3)	49 (10)	9 (2)	<0.000	38 (7)	35 (7)	>0.05	**73 (14)**
Non- Vaccinated (n=10)											
Seropositive	2 (20)	3 (30)	>0.05	0 (0)	5 (50)	0 (0)	-	3 (30)	2 (20)	>0.05	**5 (50)**
Equivocal	0 (0)	2 (20)	-	2 (20)	0 (0)	0 (0)	-	2 (20)	0 (0)	-	**2 (20)**
Seronegative	2 (20)	1 (10)	>0.05	2 (20)	1 (10)	0 (0)	>0.05	3 (30)	0 (0)	-	**3 (30)**
Hepatitis A virus											
Vaccinated (n=259)											
Seropositive	26 (10)	48 (19)	<0.05	30 (12)	38 (15)	6 (2)	<0.000	35 (14)	39 (15)	>0.05	**74 (29)**
Equivocal	0 (0)	3 (1)	-	0 (0)	1 (0.4)	2 (08)	>0.05	1 (0.4)	2 (1)	>0.05	**3 (1)**
Seronegative	84 (32)	98 (38)	>0.05	51 (20)	101 (39)	30 (12)	<0.000	95 (37)	87 (34)	>0.05	**182 (70)**
Non- vaccinated (n=268)											
Seropositive	50 (19)	27 (10)	<0.01	26 (10)	44 (16)	7 (3)	<0.000	51 (19)	26 (10)	<0.01	**77 (29)**
Equivocal	1 (0.4)	0 (0)		1 (0.4)	0 (0)	0 (0)	-	1 (0.4)	0 (0)	-	**1 (0.4)**
Seronegative	124 (46)	66 (25)	<0.000	53 (20)	103 (38)	34 (13)	<0.000	115 (43)	75 (28)	<0.01	**190 (71)**

Table 3 - Prevalence of antibodies against hepatitis B and A in vaccinated and non-vaccinated (4-6 years aged) children (n=156) in Jeddah, Saudi Arabia grouped by gender, type of school and nationality.

Variable	Gender			School				Nationality			
	Male (n=98)	Female (n=58)	*P*-value	Private (n=41)	Public (n=39)	No school (n=76)	*P*-value	Saudi (n=73)	Non- Saudi (n=83)	*P*-value	Total (n=156)
Hepatitis B virus											
Vaccinated (n=155)											
Seropositive	75 (48.4)	47 (30.3)	<0.05	32 (20.6)	30 (19.4)	60 (38.7)	<0.000	56 (36.1)	66 (42.6)	>0.05	**122 (78.7)**
Equivocal	7 (4.5)	5 (3.2)	>0.05	2 (1.3)	3 (1.9)	7 (4.5)	>0.05	6 (3.9)	6 (3.9)	>0.05	**12 (7.7)**
Seronegative	15 (9.7)	6 (3.9)	<0.05	7 (4.5)	5 (3.2)	9 (5.8)	>0.05	11 (7.1)	10 (6.5)	>0.05	**21 (13.5)**
Non-vaccinated (n= 1)											
Seropositive	1 (100)	- -	-	- -	1 (100)	- -	-	- -	1 (100)	-	**1 (100)**
Equivocal	- -	- -	-	- -	- -	- -	-	- -	- -	-	**- -**
Seronegative	- -	- -	-	- -	- -	- -	-	- -	- -	-	**- -**
Hepatitis A virus											
Vaccinated (n= 81)											
Seropositive	3 (3.7)	9 (11.1)	>0.05	5 (6.2)	2 (2.5)	5 (6.2)	>0.05	8 (9.9)	4 (4.9)	>0.05	**12 (14.8)**
Equivocal	- -	2 (2.5)	-	- -	- -	2 (2.5)	-	- -	2 (2.5)	-	**2 (2.5)**
Seronegative	42 (51.9)	25 (30.9)	<0.05	18 (22.2)	19 (23.5)	30 (37)	>0.05	31 (38.3)	36 (44.4)	>0.05	**67 (82.7)**
Non-vaccinated (n=75)											
Seropositive	10 (13.3)	1 (1.3)	<0.01	2 (2.7)	3 (4)	6 (8)	>0.05	5 (6.7)	6 (8)	>0.05	**11 (14.7)**
Equivocal	- -	- -	-	- -	- -	- -	-	- -	- -	-	**- -**
Seronegative	43 (57.3)	21 (28)	<0.01	16 (21.3)	15 (20)	33 (44)	<0.01	29 (38.7)	35 (46.7)	>0.05	**64 (85.3)**

(Data are represented by number (percent (٪) to total number

Table 4 - Prevalence of antibodies against hepatitis B and A in vaccinated and non-vaccinated (7-11 years aged) children (n=235) in Jeddah, Saudi Arabia grouped by gender, type of school and nationality.

Variable	Gender			School				Nationality			Total (n=233)
	Male (n=118)	Female (n=115)	*P* value	Private (n=62)	Public (n=169)	No school (n=2)	*P* value	Saudi (n=134)	Non-Saudi (n=99)	*P* value	
Hepatitis B virus											
Vaccinated (n=227)											
Seropositive	84 (37)	85 (37.4)	>0.05	47 (20.7)	120 (52.9)	2 (0.9)	<0.000	97 (42.7)	72 (31.7)	>0.05	**169 (74.4)**
Equivocal	12 (5.3)	16 (7)	>0.05	9 (4)	19 (8.4)	- -	>0.05	20 (8.8)	8 (3.5)	<0.05	**28 (12.3)**
Seronegative	19 (8.4)	11 (4.8)	>0.05	3 (1.3)	27 (11.9)	- -	<0.000	12 (5.3)	18 (7.9)	>0.05	**30 (13.2)**
Non-Vaccinated (n=6)											
Seropositive	1 (16.7)	2 (33.3)	>0.05	- -	3 (50)	- -	-	2 (33.3)	1 (16.7)	>0.05	**3 (50)**
Equivocal	- -	1 (16.7)	-	1 (16.7)	- -	- -	-	1 (16.7)	- -	-	**1 (16.7)**
Seronegative	2 (33.3)	- -	-	2 (33.3)	- -	- -	-	2 (33.3)	- -	-	**2 (33.3)**
Hepatitis A virus											
Vaccinated (n=115)											
Seropositive	17 (14.8)	27 (23.5)	>0.05	16 (13.9)	28 (24.3)	- -	>0.05	18 (15.7)	26 (22.6)	>0.05	**44 (38.3)**
Equivocal	- -	1 (0.9)	-	- -	1 (0.9)	- -	-	1 (0.9)	- -	-	**1 (0.9)**
Seronegative	29 (25.2)	41 (35.7)	>0.05	15 (13)	55 (47.8)	- -	<0.000	39 (33.9)	31 (27)	>0.05	**70 (60.9)**
Non-Vaccinated (n=118)											
Seropositive	24 (20.3)	21 (17.8)	>0.05	14 (11.9)	30 (25.4)	1 (0.8)	<0.000	29 (24.6)	16 (13.6)	>0.05	**45 (38.1)**
Equivocal	1 (0.8)	- -	-	1 (0.8)	- -	- -	-	1 (0.8)	- -	-	**1 (0.8)**
Seronegative	47 (39.8)	25 (21.2)	<0.01	16 (13.6)	55 (46.6)	1 (0.8)	<0.000	46 (39)	26 (22)	<0.05	**72 (61)**

Data are represented by number (percent (%) to total number)

school compared to those in private or no-school (15% versus 12% and 2%, $p<0.000$) and in females versus males children (19% versus 10%, $p<0.05$). In non-vaccinated children against HAV, percentage of seropositivity were significantly elevated in children attending public school compared to those in private and no-school (16% versus 10% and 3%, $p<0.000$), in males versus females children (19% versus 10%, $p<0.01$) in Saudi versus non-Saudi children (19% versus 10%, $p<0.01$) (**Table 2**).

Table 3 showed prevalence to HBV and HAV in children aged (4-6 years). For HBV, vaccinated children aged 4-6 years, the overall percentage of seropositivity was 78.7%, equivocal was 7.7% and seronegativity was 13.5%. The percentage of seropositivity was significantly elevated in children who did not attending school compared to those in private and public schools (38.7% versus 20.6% and 19.4%, $p<0.000$). Meanwhile, percentage of seropositivity was significantly elevated in males versus female children (48.4% versus 30.3%, $p<0.05$). In this age group, only one child was not vaccinated against HBV and his serum showed seropositivity. For HAV, vaccinated children aged 4-6 years, overall percentage of seropositivity was 14.8%, equivocal was 2.5% and seronegativity was 82.7%. For HAV, in non-vaccinated children aged 4-6 years, overall percentage of seropositivity was 14.7%, equivocal was 0% and seronegativity was 85.3%. In this unvaccinated group, percentage of seropositivity was significantly elevated in males versus females (13.3% versus 1.3%, $p<0.01$).

Table 4 showed prevalence to HBV and HAV in children aged (7-11 years). For HBV, in vaccinated children, overall percentage of seropositivity was 74.4%, equivocal was 12.3% and seronegativity was 13.2%. In vaccinated children against HBV, percentage of seropositivity were significantly elevated in children attending public school compared to those in private and no schools (52.9% versus 20.7% and 0.9%, $p<0.000$). In this age group, 6 children were non-vaccinated against HBV and their serum showed seropositivity of 50%, equivocal rate of 16.7% and seronegativity rate was 33.3%. For HAV, vaccinated children aged 7-11 years, overall percentage of seropositivity was 38.3%, equivocal of 0.9% and seronegativity was 60.9%. For HAV, in non-vaccinated children aged 7-11 years), overall percentage of seropositivity was 38.1%, equivocal was 0.8% and seronegativity was 61%. In this non-vaccinated group, percentage of seropositivity was significantly elevated in children attending public compared to those in private or no- schools (25.4% versus 11.9% and 0.8%, $p<0.000$).

Table 5 showed prevalence to HBV and HAV in children aged 12-14 years. For HBV, vaccinated

Table 5 - Prevalence of antibodies against hepatitis B and A in vaccinated and non vaccinated (12-14 years aged) children (n=138) in Jeddah, Saudi Arabia grouped by gender, type of school and nationality.

Variable	Gender			School				Nationality			Total (n=233)	
	Male (n=118)	Female (n=115)	*P* value	Private (n=62)	Public (n=169)	No school (n=2)	*P* value	Saudi (n=134)	Non-Saudi (n=99)	*P* value		
Hepatitis B virus												
Vaccinated (n=135)												
Seropositive	45 (33.3)	53 (39.3)	>0.05	45 (33.3)	52 (38.5)	1 (0.7)	<0.0001	63 (46.7)	35 (25.9)	<0.01	**98**	**(72.6)**
Equivocal	9 (6.7)	6 (4.4)	>0.05	7 (5.2)	8 (5.9)	- -	>0.05	10 (7.4)	5 (3.7)	>0.05	**15**	**(11.1)**
Seronegative	15 (11.1)	7 (5.2)	>0.05	5 (3.7)	17 (12.6)	- -	<0.05	15 (11.1)	7 (5.2)	>0.05	**22**	**(16.3)**
Non-Vaccinated (n=3)												
Seropositive	- -	1 (33.3)	-	- -	1 (33.3)	- -	-	1 (33.3)	- -	-	**1**	**(33.3)**
Equivocal	- -	1 (33.3)	-	1 (33.3)	- -	- -	-	1 (33.3)	- -	-	**1**	**(33.3)**
Seronegative	- -	1 (33.3)	-	- -	1 (33.3)	- -	-	1 (33.3)	- -	-	**1**	**(33.3)**
Hepatitis A virus												
Vaccinated (n=63)												
Seropositive	6 (9.5)	12 (19)	>0.05	9 (14.3)	8 (12.7)	1 (1.6)	<0.05	9 (14.3)	9 (14.3)	>0.05	**18**	**(28.6)**
Equivocal	- -	- -	-	- -	- -	- -	-	- -	- -	-	**-**	**-**
Seronegative	13 (20.6)	32 (50.8)	<0.01	18 (28.6)	27 (42.9)	- -	>0.05	25 (39.7)	20 (31.7)	>0.05	**45**	**(71.4)**
Non-Vaccinated (n=75)												
Seropositive	16 (21.3)	5 (7)	<0.05	10 (13.3)	11 (14.7)	- -	>0.05	17 (22.7)	4 (5.3)	<0.01	**21**	**(28)**
Equivocal	- -	- -	-	- -	- -	- -	-	- -	- -	-	**-**	**-**
Seronegative	34 (45.3)	20 (26.7)	>0.05	21 (28)	33 (44)	- -	>0.05	40 (53.3)	14 (18.7)	<0.000	**54**	**(72)**

Data are represented by number (percent (%) to total number)

children, overall percentage of seropositivity was 72.6%, equivocal was 11.1% and seronegativity was 16.3%. In vaccinated children against HBV, percentage of seropositivity rates was significantly elevated in Saudi versus non-Saudi children (46.7% versus 25.9%, $p<0.01$), meanwhile percentage of seropositivity was significantly elevated in children attending public school compared to those in private and no schools (38.5% versus 33.3% and 0.7%, $p<0.000$). In this age group, only 3 children were not vaccinated against HBV and their serum showed seropositivity, equivocal and seronegativity rates of 33.3% for all. For HAV, vaccinated children aged 12-14 years, overall percentage of seropositivity was 28.6%, equivocal was 0% and seronegativity was 71.4%. Percentage of seropositivity was significantly elevated in children attending private school compared to those in public or no- schools (14.3% versus 12.7% and 1.6%, $p<0.05$). For HAV, non-vaccinated children aged (12-14 years), overall percentage of seropositivity was 28%, equivocal was 0% and seronegativity was 72%. In this non-vaccinated group, percentage of seropositivity was significantly elevated in males versus females (21.3% versus 7%, $p<0.05$) and in Saudi versus non-Saudi (22.75 versus 5.3%, $p<0.01$).

Discussion. Hepatitis B and hepatitis A are parental and enteric transmitted viral diseases occurring in epidemic and sporadic forms especially in developing countries.[16,8] In the present study, 98% of the children were vaccinated against HBV. On the other hand, overall incidence of seropositivity for HBV surface antibodies (HBsAb) among participated children was (75%), which was significantly higher among vaccinated compared to non-vaccinated children and decreased by increasing age of vaccinated students. In vaccinated children, significant elevation of seropositivity against HBV antibodies was found in public school students comparing to those in private and no school children. These results can be explained by crowdedness of classes in public schools, so students are liable to catch natural infection that strengthens their immunity state. These results indicate success of HBV vaccination program in KSA between young age children. Meanwhile, decrease seropositivity incidence with older children needs further evaluation of vaccination program by giving booster dose in adolescent.

Saudi Arabia is considered to be endemic area for hepatitis B virus infection. In 1992, it was reported that by adult age 7% of population have HBsAg and approximately 70% had one or more HBV markers. During same year, overall prevalence of HBsAg was 6.7%, with at least one HBV markers being positive in 19.7% persons tested.[17] Introduction of HBV vaccination in KSA Expanded Program of Immunization shifted the high endemicity to intermediate endemicity,[18] decreased prevalence of HBsAg in children from 6.7% to 0.3%[19] and of anti-HBcAg from approximately 4.2% to under 0.5%.[18] Jizan region in South-Western area of KSA was noted for high prevalence of HBsAg carrier rate.[20] The vaccination schedule for hepatitis B employed in this study was at 0, 2, 6 months. Clinical studies showed no significant difference in immunogenicity whether 0, 1, 2 or 0, 1, 6 months schedule[21] is used for immunization purpose. Marsano et al,[22] have established that 0, 1, 2 months vaccination schedule gives a rate that is quicker than and identical to rate of sero-protection of standard vaccination schedule at 0, 1, 6 months. In most developed countries, the age-specific prevalence curve of anti-HAV has a sigmoid shape, with a low prevalence among children and adolescents and a high prevalence among elderly due to improvements in standard of living and sanitation.[9] Vaccination policy against HAV is elective in KSA. In the present study, 49% of healthy children included in this study, were vaccinated against HAV. The overall incidence of seropositivity for HBV antibodies among vaccinated and non-vaccinated children was (29% for both). The equal results of seropositivity between vaccinated and non vaccinated children could be explained by that most of our children who participated are old and exposed to outside environment that liable them to catch natural immunity against HBA or inappropriate used vaccination strategy. The prevalence of anti-HAV antibodies was higher in public school comparing to those in private or no schools children. These results can be explained by the crowdedness of the classes in public school students so they can catch natural infection that strengthens their immunity state. Parallel to other studies,[23,24] the present study revealed that, in vaccinated children the seronegativity was higher in males compared to females. Dentico et al[25] reported that gender factor is one of the parameters influencing response following vaccination. The seroprevalence of anti-HAV antibody in younger children, particularly preschool age group (4-6 years), would be important to assess magnitude of actual target population at risk for HAV infection. The present study showed that seropositivity against HAV was low in age group (4-6 years) then rise in (7-11 years) and decline again in (12-14 years) in both vaccinated and non-vaccinated children which indicates decline of seropositivity against HAV in KSA among young and adolescent. Similar previous studies were carried out in different regions of KSA. A community-based study in 14

districts of KSA, showed a significant decrease in seroprevalence of anti-HAV between 1989 and 1997 across all age groups up to 12 years for all districts except one bordering Yemen.[17] In all of the districts except for this one, endemicity for HAV shifted from high or intermediate to intermediate or low over the time period.[26] Study in Riyadh involved children aged up to 15 years reported that by 11 years of age, only 45% of them were anti-HAV-positive, indicating intermediate endemicity in this city.[27] Another study also in Riyadh (urban area) revealed 24.7% of children were seropositive to HAV by age of 12 years.[28] The above studies and the present one indicate that pattern of endemicity of HAV infection is shifting in KSA.[26] Patterns of endemicity found in other developing countries, differ from that reported in KSA, where despite improvement in gross national product, seroprevalence of anti-HAV antibodies remain high.[29] On contrary, seroprevalence study in Eastern region of KSA (Dammam) showed that hepatitis A virus infection starts dramatically high in school-age children, and then rise gradually with an increase in age reflecting high endemic of HAV in this region.[30] The results obtained by above studies indicated that there are very great differences between regions in KSA in terms of epidemiology of HAV infection. There is low natural protection against hepatitis A and changing epidemiological pattern of HAV infections may have several consequences. Availability of hepatitis A vaccine will necessitate determination of strategies for its use. Such strategies should be based upon disease epidemiology. The result obtained by this study showed decrease prevalence of seropositivity against HAV in both vaccinated and non-vaccinated children. However, different studies approximately immunogenicity of HAV vaccines support their use in pre- and possibly post exposure prophylaxis against hepatitis A virus infection. Appropriate prophylactic measures, as strategies for active immunization should be considered. In the future, the strategy for the use of hepatitis A vaccine may be similar to that recently recommended for hepatitis B vaccine, that of universal infant immunization. In this way, all persons would eventually have immunity to infection and transmission of HAV could potentially be eliminated.[31] The lower anti-HAV prevalence in children under age of 14, found in this survey, suggest that if improvements in sanitary conditions keep occurring in this areas, fewer people will acquire the virus, meanwhile it will increase the number of susceptible persons. Thus, possibility of future hepatitis A outbreaks in this area should not be ignored.

Limitation of study. The study population was confined to children who lived in urban area limited to city of Jeddah. It is important to consider many other regions of country could also be suffering similar changes in HAV epidemiology due to improvements in sanitary standards. Therefore, it is relevant to stimulate new large population-based studies with adequate sample size, and should be undertaken in different regions of country prior to recommending mass vaccination for HAV in KSA.

In conclusions, HBV immunogenicity had been improved but still there is high prevalence of seronegativity among school age children especially with increasing age and booster doses at adolescent may be recommended. The ultimate goal of preventing HBV-related chronic liver disease and hepatocellular carcinoma in KSA is foreseeable in the near future. Seroprevalence of hepatitis A is likely to decrease due to improvements in environmental and socio-economic conditions and mass vaccination against HAV is recommended in this area to prevent outbreak of disease among children. In the future, the strategy for use of hepatitis A vaccine may be similar to that recently recommended for hepatitis B vaccine, that of universal immunization.

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