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Hepatitis B Virus Infection among Egyptian Children Vaccinated during Infancy

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***Abstract*—**This is a national community based project to evaluate effectiveness of HBV vaccination program in prevention of infection. HBV markers were tested in the sera of 3600 vaccinated children. Infected children were followed up for 1 year. Prevalence of HBV infection was 0.39 % (0.28% positive for anti-HBc, 0.03% positive for HBsAg and 0.08% positive for both). One year later, 50% of positive anti-HBc children turned negative with sustained positivity for positive HBsAg cases. HBV infection was significantly higher at age above 9 years (0.6%) compared to 0.2% at age 3-9 years and 0% at younger age ($P<0.05$). Logistic analysis revealed that predictors for HBV infection were history of blood transfusion, regular medical injection, and family history of either HBV infection or drug abuse (adjusted odds ratios 6.2, 5.6, 7.6 & 19.1 respectively). HBV vaccination program produced adequate protection. Adherence to infection control measures and safe blood transfusion are recommended**.**

***Keywords*—**Children, Egypt, HBV Infection, HBV Vaccine.

I. Introduction

HEPATITIS B virus (HBV) infection is a public health problem and a major cause of morbidity and mortality particularly in developing countries [1]. Worldwide, it is estimated that more than 2 billion people have been infected. Of these, approximately 240 million are chronically infected and at risk of cirrhosis and hepatocellular carcinoma [2], [3]. Egypt is considered a country of intermediate prevalence (2%-7%) of HBV infection [4]. In Egypt, there are nearly 2-3 million chronic carriers [5]. The primary routes of HBV transmission are unsafe injections, injection of illicit drugs, blood transfusions, sexual relations and vertical transmission from infected mothers to their newborn. Child to child transmission usually happens in household settings, child day care centers and in schools probably through contact of sores and small breaks in the skin or mucus membranes with blood or skin sore secretions [4], [6]. The risk of becoming a chronic carrier is inversely proportional to age at infection. It ranges from 80%–90% among infants infected during the first year of newborns, 30-50% among children infected before the age of 6 years and <5% among adults [7].

Vaccination is the most effective measure to reduce the global incidence of hepatitis B and hepatocellular carcinoma [8]. The long term protection of HB vaccine is determined by the incidence of break-through infection (positive anti-HBc) as well as chronic carrier state (positive HBsAg) among previously vaccinated individuals [9]. Both are clearly and strongly related to peak antibody concentrations and length of time since vaccination [10]. Breakthrough HBV infection is defined as HBV infection despite receiving the 3 dose series of vaccine [11], [12].

Egypt lacks assessment of maternal infection during pregnancy and early sero-protection 1-3 months after compulsory vaccination on a national basis. This study aimed to evaluate the effectiveness of national HB vaccination program in prevention of HBV infection among Egyptian children.

II. Subjects and Methods

This study is a part of a national community based multi-stage cluster sampling design carried out in the period from July 2010 to June 2013 in 6 governorates representing all geographic regions of Egypt. They are one urban (Cairo), 2 Upper (Beni-Sweif and Assiut), 2 Lower Egypt (Dakahleya and Gharbeya) and one Frontier (Red Sea). The targeted subjects were children aged from 9 months to 16 years who had received the 3 compulsory doses of HBV vaccine during infancy. For sampling process and selecting the clusters, probability proportional to size sampling was used. The sample frame for the current survey was based on the most recent population census 2006. First, implicit stratification by geographic location in each governorate, list of cities and villages were arranged in serpentine order geographically. This stratification was done independently for urban and rural areas. A sampling interval was calculated and accordingly a random number was selected, using a table of random numbers. From this list, number of participating cluster areas in each governorate was identified according to its population size. So, 5 cluster areas from Dakahleya governorate (Mansoura & Meniet-Elnasr cities and 3 villages in Belkas, Talkha & Sinbelawain), 4 from Gharbeya governorate (Tanta city and 3 villages in Samanood, Kotour & Elsanta), 5 urban areas from Cairo governorate (El-Matria, El-Nozha, El-Sayeda Zeinab, El-Sahel & El-Basatien), 2 from Beni-Sweif governorate (El Wasta city and a village in Blevia), 3 from

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Assuit governorate (Assuit city and 2 villages in Abou-Teeg & Abnoob) and one from Red Sea governorate (Hurghada city) were identified. In each selected area, lists of maternal and child health center (MCH), kindergarten and school facilities were identified and 5 facility clusters were randomly selected. They were one MCH or health unit, one kindergarten and 3 schools (primary, preparatory and secondary) according to the age of the targeted children. The participating children aged from 9 months to 16 years who had completed the 3 compulsory doses of HBV vaccine during infancy. Approvals of the ethical committee of Ministry of Health (MOH), National Research Center and from Ministry of Education were obtained. Written signed consent was obtained from each parent.

A pre-tested closed ended questionnaire was designed to collect data about child age, sex, date of birth and other socio-demographic variables. It also stresses on detailed data concerning child HBV vaccination history. Data of current & past medical history, risky behaviors towards HBV infection (e.g. sharing razors & shaving instruments either at home or at barbers and beauty centers, sharing towels or toothbrushes, unsatisfactory infection control practices including the reuse of contaminated medical or dental instruments,.. etc), history of previous blood transfusion, blood products injection, renal dialysis, and presence of HBsAg positive mother or other family member were also collected. For quality assurance, several training sessions were held for supervisors, interviewers and Ministry of Health staff in each governorate. Peel off barcode sheets were used in order to ensure tracing blood samples and linking laboratory results with other survey data. Face to face interview was carried out with the parents or caretakers of the children. Adolescents above 10 years were also interviewed after their verbal ascent. Anthropometric measurements including height and weight were also taken to assess their nutritional status. Socioeconomic status (SES) was determined according to education of parents, maternal working status, water source, sewage disposable, electricity and family income [13].

III. Blood Sampling and Laboratory Analysis

About 3-5 ml blood sample was withdrawn aseptically from each participant. Serum samples were aliquoted into two labeled sterile cryotubes and were stored at –20°C until laboratory examination. HBV markers detection was carried out in Virology lab –Microbiology Department–Faculty of Medicine, (for Girls) Al-Azhar University, Cairo, Egypt. It was carried out using commercially available enzyme linked immunoassays (ELISA, Dia Sorin-Italy) and according to the manufacturer's instructions. They include qualitative determination of serum hepatitis B surface antigen (HBsAg) and total HBV core antibody (anti-HBc) as well as quantitative detection of serum anti-HBs. According to international standards anti-HBs ≥ 10 IU/L, was considered to be protective against HBV infection [14], [15]. Positive samples for HBsAg and or anti-HBc were retested for confirmation. Chronic infection was defined as the detection of HBsAg on two occasions at least 6 months apart. Breakthrough infection was defined as anti-HBc seropositivity in vaccinated subjects who were not chronically infected. HBV infection was defined as either of the above. Undetectable anti-HBs was defined as <10 (lU/L) [16].

Children with positive HBsAg or anti-HBc and their families (mainly mothers) were followed up one year later to assess their HBV infection status.

IV. Data Analysis and Presentation

Data entry was carried on excel sheet and statistical analysis was done using SPSS software program version 18.0. Chi square was done for qualitative data that presented by numbers and percentages. Logistic regression was done to significantly predict risk factors for HBV infection. P value was considered statistically significant when $P < 0.05$ and considered statistically highly significant if $P < 0.01$.

V. Results

The prevalence of positive total anti-HBc was 0.36% (13/3600 children), positive HBsAg was 0.11% (4/3600 children), where three of them were also positive for total anti-HBc. The overall HBV infection was found among 14 children (0.39%). Follow up for one year was carried out on 12/14 children, as 2 children were dropped out. Persistence of HBsAg was found among all seropositive children (3/3) and that of anti-HBc was found among only 6/12 children (Table I).

Studying different risk factors and risky behavior for HBV infection showed that the highest prevalence of HBV was found in the age group >9 years (0.6%), followed by those aged 3-9 years (0.2%), and none among those <3 years ($P < 0.05$). The prevalence of HBV infection was higher among children with very low SES (0.8%) compared to other SES ($P = 0.05$) (Table II). Delivery history and mode of lactation were not significant risk factors for HBV infection, $P > 0.05$ (Table III). The association between children's current and past medical history and HBV infection is presented in Table IV. It shows that history of blood transfusion and regular medical injection were the only significant risk factors for HBV infection $P < 0.05$. As shown in (Table V) none of the questioned risky behaviors of the studied children was found to be significantly associated with HBV infection ($P > 0.05$). Table VI shows the prevalence of HBV infection among the studied children in relation to the medical history and risky behaviors of their families or friends. The prevalence of HBV infection among children was significantly higher among those with positive family history of either HBV infection or IV drug addict (3.8% & 16.7% respectively) $P < 0.01$. None of the studied friends' medical history and risky behaviors was significantly related to HBV infection. Multivariate logistic analysis revealed that the predictor risk factors for HBV infection among studied children were history of blood transfusion, regular medical injection, positive family history

of IV drug addict and family history HBV infection, with adjusted odds ratio 6.2, 5.6 19.1 &7.6 respectively (Table VII).

TABLE I
DEMOGRAPHIC CHARACTERISTICS AND HBV MARKERS OF THE STUDIED CHILDREN AT BASELINE AND FOLLOW UP

Serial no*	Age	Gender	Residence	HBV base line			HBV markers FUP			HBV Markers among Family
				Anti-HBs	HBsAg	Anti-HBc	HBsAg	Anti-HBc	Anti-HBs	
1	10	M	urban	0	+	+	+	+	0	Mother +HBsAg & +Anti-HBc
2	15.8	F	urban	37	-	+	-	-	Not done	Mother + Anti-HBc
3	16.8	F	urban	3	+	+	+	+	4	Mother +Anti-HBc
4	11	F	rural	0	-	+	-	-	0	Mother + Anti-HBc
5	11	F	urban	992	-	+	-	+	1000	All family -ve
6	10	M	urban	404	-	+	-	+	Not done	not available
7	11.8	F	rural	4	-	+	-	-	5	Father/ Brother + Anti-HBc
8	15.8	F	rural	3	-	+	-	-	3	not available
9	16	M	rural	559	-	+	-	+	896	All familly -ve
10	12	M	rural	0	+	+	+	+	0.2	History of blood transfusion Father/ Brother + Anti-HBc
11	9.3	F	urban	439	-	+	-	-	994	All family -ve
12	9	F	urban	210	-	+	-	-	306	All family -ve
13	9.8	F	urban	24	+	-	Lost follow up			NA
14	3.3	M	urban	15	-	+	Lost follow up			NA

M: Males; F: Females; NA: not available
*Patients with serial number 1-4 where from Beni-Sweif governorate, from 5-6 where from Assuit governorate, from 7-10 where from Dakaheya governorate and from 11-14 where from Cairo governorate

TABLE II
SOCIO-DEMOGRAPHIC RISK FACTORS FOR HBV INFECTION AMONG THE STUDIED CHILDREN

Risk Factors	Total n=3600 n (%)	HBV Infected Children n-14 n (%)	Non Infected Children n-3586 n (%)	P value
Gender				
Boys	1743 (48.4)	5(0.3)	1738 (99.7)	0.34
Girls	1857 (51.6)	9(0.5)	1848 (99.5)	
Age group				
≤ 3 years	781(21.7)	0 (0.0)	781 (100.0)	0.036*
3.1-9	921(25.6)	2 (0.2)	919(99.8)	
> 9 years	1898(52.7)	12 (0.6)	1886(98.9)	
Residence				
Urban	1909 (53.0	7 (0.4)	1902 (99.6)	0.88
Rural	1691 (47.0)	7 (0.4)	1684 (99.6)	
SES (total 3506)				
Very Low	1000 (27.8)	8 (0.8)	992 (99.2)	
Low	652 (18.1)	2 (0.3)	650 (99.7)	0.050
Middle	937 (26.0)	3 (0.3)	934 (99.7)	
High	917 (26.2)	1 (0.1)	916 (99.9)	
HAZ (total 3319)				
Stunted (< 2SD)	398 (12.0)	0 (0.0)	398 (100.0)	0.389
Normal (≥ 2SD)	2921 (88.0)	14 (0.5)	2907 (99.5)	
WAZ				
Underweight (< 2SD)	142 (3.9)	0 (0.0)	142 (100.0)	0.33
Normal (≥ 2SD)	3458 (96.1)	14 (0.4)	3444 (99.6)	

HAZ: Height for age Z score; WAZ: Weight for age Z score; *Significant P < 0.05.

TABLE III
HBV INFECTION IN RELATION TO THE DELIVERY HISTORY AND MODE OF LACTATION AMONG THE STUDIED CHILDREN

Risk Factors	Total n=3600 n (%)	HBV Infected children n=14 n (%)	HBV Infected Children n=3586 n (%)	P value
Mother had HBV during pregnancy				
Yes	9 (0.3)	0 (0.0)	9 (100.0)	0.84
NO	3591 (94.7)	14 (0.4)	3591 (99.6)	
Mode of delivery				
Vaginal	2897 (80.5)	11(0.4)	2886 (99.6)	0.86
Cesarean section	703 (19.5)	3(0.4)	700 (99.6)	
Assistance of delivery (total 3338)				
Daya	651(19.5)	2 (0.3)	649 (99.7)	0.62
Nurse	139 (4.2)	0 (0.0)	139 (100.0)	
Doctor	2548 (76.3)	12 (0.5)	2536 (99.5)	
Place of delivery (total 3348)				
Home	906 (27.1)	3 (0.3)	903 (99.7)	
Health unit	93 (2.8)	0 (0.0)	93 (100.0)	0.441
Hospital/private clinic	2171 (64.8)	9 (0.4)	2162 (99.6)	
Not know (answer by child)	178 (5.3)	2 (1.1)	176 (98.9)	
Lactation				
Breast fed	3140 (87.2)	13 (0.4)	3127 (99.6)	0.61
Bottle fed	229 (6.4)	1 (0.4)	228 (99.6)	
Mixed	231 (6.4)	0 (0.0)	231 (100.0)	

TABLE IV
HBV INFECTION IN RELATION TO MEDICAL HISTORY OF THE STUDIED CHILDREN

Risk Factors	Total n=3600 n (%)	HBV Infected Children n-14 n (%)	Non Infected Children n-3586 n (%)	P value
History of Jaundice				
Yes	824 (22.7)	2 (0.2)	822 (99.8)	0.53
No	2776 (77.3)	12 (0.4)	2764 (99.6)	
Hospital admission				
Yes	1199 (33.3)	3 (0.3)	1196 (99.7)	0.33
No	2401 (67.3)	11 (0.5)	2390 (99.5)	
Surgical operation				
Yes	684 (19.0)	1 (0.1)	683 (99.9)	0.257
No	2916 (81.0)	13 (0.4)	2903 (99.6)	
Blood transfusion				
Yes	92 (2.6)	2 (2.2)	90 (97.8)	0.048
No	3382 (97.4)	12 (0.3)	3496 (99.7)	
Regular medical injection				
Yes	114 (3.2)	2 (1.8)	112 (98.2)	0.05
No	3486 (96.8)	12 (0.3)	3474 (99.7)	
Attending Dental clinic				
Yes	1359(37.8)	8 (0.6)	1351 (99.4)	0.132
No	2241(62.3)	6 (0.3)	22235 (99.7)	
Rheumatic fever				
Yes	142(3.9)	2 (1.4)	140 (98.6)	0.103
No	3458 (96.1)	12 (0.3)	3446 (99.7)	

*Significant $P < 0.05$.

TABLE V
RISKY BEHAVIORS FOR HBV INFECTION AMONG THE STUDIED CHILDREN

Risk behavior for HBV infection	Total n=3600 n (%)	HBV Infected Children n-14 n (%)	Non Infected Children n-3586 n (%)	P value
Tattooing				
Yes	96 (2.7)	0(0.0)	96 (100)	1.00
No	3504 (97.3)	14 (0.4)	3586 (99.6)	
Sharing scissors, razors & shaving instruments with risky relatives				
Yes	2496 (69.7)	10 (0.4)	2373 (99.6)	1.00
No	1104 (30.3)	4 (0.4)	1100 (99.6)	
Share toothbrush				
Yes	211 (5.9)	2 (0.9)	209 (99.1)	0.196
No	3389 (94.1)	12 (0.4)	3377 (99.6)	
Circumcision (Total 3305)				
Yes	1981 (59.9)	6 (0.3)	1975 (99.7)	0.309
No	1324 (40.1)	7 (0.5)	1317 (99.5)	
Blood donation				
Yes	41 (1.1)	0 (0.0)	41 (100)	1.00
No	3559 (98.9)	14 (0.4)	3545 (99.6)	
Barber change cutter (total 1743 boys)				
Yes	1218 (69.9)	5(0.4)	1213(99.6)	0.331
No	525 (30.1)	0 (0.0)	525 (100.0)	
Pierce the ear (Total 1857 girls)				
Yes	1694 (91.2)	9 (0.5)	1685 (99.5)	1.00
No	163 (8.8)	0(0.0)	163 (100.0)	
Trim nails at Coiffeur (Total 1857 girls)				
Coiffeur	83 (4.5)	0 (0.0)	83 (100)	1.00
Didn't go to Coiffeur	1774 (95.5)	9 (0.5)	1765 (99.5)	

TABLE VI
HBV INFECTION IN RELATION TO FAMILY AND FRIEND RISK FACTORS AND RISKY BEHAVIORS

Risk factors	Total n=3600 n (%)	HBV Infected children n=14 n (%)	Non Infected Children n=3586 n (%)	P value
Family history				
Hepatitis B virus infection				
Yes	56 (1.6)	2 (3.6)	54 (96.4)	0.0001
Don't Know	3544 (98.4)	12 (0.3)	3532 (99.7)	
Hepatitis C virus infection				
Yes	508 (14.1)	1 (0.2)	507 (99.8)	0.48
Don't Know	3092 (85.9)	9 (0.4)	3079 (99.6)	
Blood transfusion				
Yes	120 (3.3)	0 (0.0)	120 (100.0)	0.486
Don't Know	3480 (96.7)	14 (0.4)	3466 (99.6)	
Regular injections				
Yes	474 (13.2)	1 (0.2)	473 (99.8)	0.504
Don't Know	3126 (86.7)	13 (0.4)	3126 (99.6)	
IV drug addict				
Yes	7 (0.2)	1 (14.3)	6(85.7)	0.001
Don't Know	3593 (98.8)	13 (0.4)	3580 (99.6)	
Friends history				
Hepatitis B virus infection				
Yes	20 (0.6)	0 (0.0)	20 (100.0)	0.772
Don't Know	3580 (99.4)	14 (0.4)	3566 (99.6)	
Hepatitis C virus infection				
Yes	80 (2.2)	0 (0.0)	80 (100.0)	0.571
Don't Know	3520 (97.8)	14 (0.4)	3506 (99.6)	
Blood transfusion				
Yes	47 (1.3)	0 (0.0)	44 (100.0)	0.75
Don't Know	3535 (98.7)	12 (0.4)	3086 (99.6)	
Regular injections				
Yes	110 (3.1)	0 (0.0)	110 (100.0)	0.506
Don't Know	3490 (96.9)	14 (0.4)	3476 (99.6)	
IV drug addict				
Yes	9 (0.3)	0 (0.0)	9 (100.0)	0.851
Don't Know	3591 (99.7)	14 (0.4)	3577 (99.6)	

*Significant P < 0.05; **High significant P <0.01

TABLE VII
PREDICTOR RISK FACTORS FOR HBV INFECTION AMONG THE STUDIED CHILDREN

Risk Factors	Univariate analysis		Logistic multivariate analysis	
	OR (95% CI)	P value	AOR (95% CI)	P value
Blood transfusion	6.5 (1.4-29.4)	0.048	6.2(1.3-28.8)	0.021
Regular medical injection	5.2 (1.1-23.4)	0.05	5.6(1.2-26.1)	0.029
Family history of HBV infection	10.9 (2.3-49.9)	0.0001	7.6(1.2-46.9)	0.029
Family history of drug addict injection	45.9 (5.1-408.1)	0.0001	19.1(1.4- 262.4)	0.027

*Significant P < 0.05; **High significant P <0.01
OR odds ratio, AOR adjusted odds ratio; CI confidence interval
Variables entered in the equation were gender, age, blood transfusion, frequent injection, family history of HBV infection, family history of drug injection, and history of rheumatic fever

VI. DISCUSSION

Egypt adopted the implementation of routine infant HBV vaccination in October 1992 and Egyptian DHS surveys reported that Egypt reached 96% vaccination coverage [17], [18]. The long term protection of HB vaccine is determined by the incidence of break-through infection (positive anti-HBc) as well as chronic carrier state (positive HBsAg) among previously vaccinated individuals [9]. "Break through infection" can be defined as an infection in an appropriately vaccinated individual. The majority of breakthrough infections are clinically mild infections with only anti-HBc seroconversion in the absence of HBsAg positivity. However, breakthrough infections can also result in a significant, acute clinical infection; or, in case HBsAg is present, can imply a risk of becoming a chronic carrier. [12], [16].

In the present study, all children confirmed completion of the three doses of hepatitis B vaccine based on the signed birth certificate or the child mothers' recall. The prevalence of HBV breakthrough infection was 0.39 % (0.28% positive for anti-HBc, 0.03% positive for HBsAg and 0.08% positive for both). One year later, only twelve infected children were followed up where and 2 dropped out. Three of the children remained HBsAg positive, indicating chronicity of HBV infection, while 6 children retained positivity to anti-HBc and 6 children seroconverted to negative anti-HBc indicating transient infection. Breakthrough infections can occur in fully vaccinated individuals due to the known/unknown failure of the vaccine (e.g., deteriorated vaccine) or due to inadequate vaccination. Research from Alaska has shown that breakthrough infection was more likely to occur if a child had failed to respond to vaccination or if they developed a lower anti-HBs GMT [12].

The present study revealed that children aged ≤ 3 years had no HBV infection or even any laboratory evidence to suspect vertical or perinatal transmission the mother. The highest prevalence of HBV infection was found in the age group > 9 years (0.6%), followed by age group >3 - 9 years (0.2%), with significant difference between different age groups (P < 0.05).This was in accordance to an Egyptian study conducted by El-Sawy and Mohamed [19] who did not find HBsAg positive sera among 180among children < 5 years, children whereas Shatat et al. [20] in Alexandria, found one child out of 184 children with HBsAg positive. Also, in Alexandria, Reda et al. [21] found that the rate of HBsAg positivity among the same age was 0.8%. On the other hand, a study conducted in Upper Egypt, HBsAg was not detected among the vaccinated primary school children, despite of the presence of risk factors for infection [22].

In China, the carrier rate for HBsAg was 2.0% among vaccinated children aged 0-14 years and was 0.3% among those aged 0-4 years. Children aged 10-14 years had a significantly higher prevalence of HBsAg than children aged 5-9 years and children aged 5-9 years had a higher prevalence than children aged 0-4 years. This was explained by the possibility that children aged 0-4 might have more access to the hepatitis B vaccine and a better hepatitis B vaccine service than children aged 5 onwards [23]. Lai et al. [24] found that seroprevalence of anti-HBc and isolated anti-HBs among children aged 10-14, 14-18, to 18-21 years were 0.4%, 1.9%, and 8.1% (P <0.05).

In Taiwan, the prevalence of isolated anti-HBc was 1.2% (21/1734) among children after 18 years post vaccination. One of the possible reasons for isolated anti-HBc includes resolved HBV infection in subjects with very low anti-HBs titers or loss of anti-HBs positivity [25]. Core antibodies typically persist for life, regardless of whether the infection resolves or remains chronic. While among vaccinated children, anti-HBc can be disappeared indicating transient infection [26]. In Thailand, 17 years post-vaccination there have been no HBV cases with evolving chronicity, although transient presence of HBsAg or transient and/or long-term presence of anti-HBc antibody indicated that there has been exposure to HBV, but none of these subjects had clinical symptoms [27]. In Gambia, 3.6% of children at baseline had positive ant-HBc became anti-HBc negative during follow up [16].

In present study, at baseline, the anti-HBs level <10 IU/L was found among the 3 children with positive both anti-HBc and HBsAg and among 3/10 children with positive anti-HBc, while, anti-HBs was above 100 IU/L among 5/10 children with only positive anti-HBc. After 1 year, transient infection (losing anti-HBc positivity) was found among 5/8 followed up children with positive anti-HBc (the 3 children with anti-HBs <10 IU/L and 2/5 children with anti-HBs > 100 IU/L). Isolated anti-HBc can also be due to false-negative HBsAg test results. Concentrations of HBsAg that are below detection limits or mutations in the major antigenic determinant, namely the "a" determinant, of HBsAg that are associated with occult HBV infection can lead to false-negative HBsAg results [28]. In addition, isolated anti-HBc seropositivity may result from

the presence of anti-HBc during the "window period" following acute HBV infection, when antigenemia with HBsAg has resolved and anti-HBs has not yet developed [25]. Zanetti [29] stated that although breakthrough infections do occur in vaccinated populations, there is no disease or carriage, suggesting that protection lasts longer than detectable antibodies (humoral immunity). However in current study, 3 children with positive HBsAg remain positive after 1 year follow up indicating chronic infection.

In Alaska, there were 23 breakthrough infections (defined by the presence of anti-HBc), were detected among 1530 vaccinated children and adolescents who were followed up yearly for 11 years and at year 15 post-vaccination. These breakthrough infections occurred more frequently among post vaccination non-responders than among responders [30].

In the current study, the prevalence of HBV infection was higher among girls (0.5%) than boys (0.3%), $P > 0.05$, while it was similar among children in urban and rural areas (0.4%). A systematic review on HBV infection in Iran revealed that prevalence of this infection is approximately 2.14% and it was higher among males than females [31]. While, in Gambia, older age and male gender among children and adolescents were independently associated with increased risk of HBV infection [16]. In Cambodia, the proportion of children who had positive HBsAg was 0.33% in urban, 1.41% in rural and 3.45% in remote area [32].

Logistic multivariate analysis in the present study, revealed that, the significant predictor risk factors for HBV infection were history of blood transfusion, regular medical injection, family history of HBV infection, and family history of intravenous drug addict with AORs (95%CI) were 2(1.3-28.8), 5.6(1.2-26.1), 7.6(1.2-46.9), 19.1(1.4- 262.4) respectively. This was in accordance to a Brazilian study, where out of 95 children aged <19 years with positive HBsAg, about 33% of them had family history of chronic carrier and 44% had positive anti-HBc suggesting the possibility of intra-familial transmission [33].

In the present study, HBV markers were evaluated in the families of 10 out of 14 infected children, where 40% of them had positive for HBsAg, anti-HBc or both among their mothers. A Turkish study, found high HBsAg positivity rate in children whose mothers were HBsAg positive (25.2%) than those whose fathers were HBsAg positive (2.5%), $P < 0.01$). Positive HBsAg mother or father did not affect HBV infection rate at 0-10 year age group. However, having HBsAg positive mother significantly increased the infection rate more than HBsAg positive father in 11-20 years, $P < 0.001$ [34]. In the current study, evidence of mother HBV infection was found in two out of the three children chronic infection (persistence positivity of HBsAg after 1 year follow up) while the third had history of blood transfusion. Horizontal transmission and mother-to-infant transmission of HBV are demonstrated by strong family clustering occurring through frequent exposure to blood (e.g., through contact with skin lesions), saliva (e.g., through sharing of toothbrushes and candy), or breast milk [35], [36]. A study conducted in Egypt showed that HBV transmission is community rather than iatrogenic-acquired [6], however, Chen et al. [37] stated that under the recommended prophylaxis, breastfeeding is not a risk factor for mother-to-child transmission of HBV. Therefore, clinicians should encourage HBV-infected mothers to breastfeed their infants.

VII. Conclusion

The present study shows that primary infant vaccination with a recombinant HBV vaccine confers long-term protection against HBV infection that evolves towards chronicity. Health education should focus more on dealing with HBV-positive family members and nosocomial infections. Safety measures for transfusion of blood and its products should be strictly controlled and ensured by all hospitals and the local governments.

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References

[1] C. J. Chen, and H. I. Yang, "Natural history of chronic hepatitis B", J Gastroenterol Hepatol., 26(4):628-38, Apr. 2011.

[2] J. J. Ott, G. A. Stevens, J. Groeger, and S. T. Wiersma, "Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity", Vaccine: 30: 2212-2219, 2012.

[3] WHO, "Prevention & Control of Viral Hepatitis Infection: Framework for Global Action", 2012. http://www.who.int/.

[4] WHO, "Vaccines and Biologicals. Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents". DEPARTMENTWHO/V&B/01.31 http://www.who.int/vaccinesdocuments/, 2001.

[5] A. El-Zayadi, "Hepatitis B Virus Infection: "The Egyptian Situation", Arab J Gastroentol., 8(3): 94-98, 2007.

[6] A. P. Jimenez, N. S. El-Din, M. El-Hoseiny, M. El-Daly, M. Abdel-Hamid, S. ElAidi, Y. Sultan, N. El-Sayed, M. K. Mohamed, and A. Fontanet, "Community transmission of hepatitis B virus in Egypt: results from a case-control study in Greater Cairo", Int J Epidemiol., 38(3):757-65, 2009.

[7] World Health Organization (WHO), "Hepatitis B fact sheet No. 204.", July 2013. Available at: http://www.who.int/mediacentre/factsheets/fs204/en.

[8] A. R. Zanetti, P. Van Damme, and Daniel Shouval, "The global impact of vaccination against hepatitis B: A historical overview", Vaccine, 26: 6266-6273, 2008.

[9] J. Poorolajal, M. Mahmoodi, R. Majdzadeh, S. Nasseri-Moghaddam, A. Haghdoost, and A. Fotouhi, "Long-term protection provided by hepatitis B vaccine and need for booster dose: a meta-analysis", Vaccine, 8; 28(3):623-31, Jan. 2010.

[10] M. A. van der Sande, P. Waight, M. Mendy, P. Rayco-Solon, P. Hutt, T. Fulford, C Doherty, S. J. McConkey, D. Jeffries, A. J. Hall, and H. C. Whittle, "Long-term protection against carriage of hepatitis B virus after infant vaccination", J Infect Dis., 1;193(11):1528-35, Jun. 2006.

[11] M-H. Chang M-H, "Breakthrough infection in vaccinated children in Taiwan: surveillance for HBV mutant," Antiviral Therapy, 15:463-469, 2010.

[12] M. E. Tosti, B. McMahon, M. van der Sande, H. Whittle, C-F. Jan,and Y. Poovorawan, "Viral hepatitis," This issue of Viral Hepatitis reviews topics covered at the VHPB's autumn meeting held on November 17-18, 2011 in Milan, Italy. Viral hepatitis, Vol. 20-2, July 2012.
[13] S. I. Fahmy and A. F. El-Sherbiny, "Determining simple parameters for social classifications for health research". The Bulletin of the High institute of Public Health; vol. XIII, 5: 95-103, 1983.
[14] WHO, Hepatitis B, WHO/CDS/CSR/mLYO/2002. 2:1–76. 2002.
[15] A. Zanetti, A. Parlato, L. Roman, M. G. Desole, G. Ferrera, F. Giurdanella, M. Zuliani, P. Richard, S. Thomas and A. Fiquet, "Challenge with a hepatitis B vaccine in two cohorts of 4–7-year-old children primed with hexavalent vaccines: An open-label, randomised trial in Italy," Vaccine, 30: 5770– 5775, 2012.
[16] M. Mendy, I. Peterson, S. Hossin, T. Peto, M. L. Jobarteh, A. Jeng-Barry, M. Sidibeh, A. Jatta, S. E. Moore, A. J. Hall, and H. Whittle, "Observational Study of Vaccine Efficacy 24 Years after the Start of Hepatitis B vaccination in two Gambian villages: no need for a booster dose," PLoS One, 8(3):e58029, 2013.
[17] F. El-Zanaty, and W. Ann, "Egypt Demographic and Health Survey 2003," Cairo, Egypt Ministry of Health, El-Zanaty and Associates, and Macro International, 2003.
[18] F. El-Zanaty, and W. Ann, "Egypt Demographic and Health Survey 2008," Cairo, Egypt Ministry of Health, El-Zanaty and Associates, and Macro International, 2009.
[19] I. H. el-Sawy, and O. N. Mohamed, "Long-term immunogenicity and efficacy of a recombinant hepatitis B vaccine in Egyptian children," East Mediterr Health J., 5: 922-932, 1999.
[20] H. Z. Shatat, A. M. Kotkat, and Z. I. Imam, "Follow-up study of the immunogenecity and efficiency of hepatitis B vaccine in Egyptian children," J Med Res Inst., 21: 126-136, 2000.
[21] A. A. Reda, M. A. Arafa, A. A. Youssry, E. H. Wandan, M. Ab de Ati, and H. Daebees, "Epidemiologic evaluation of the immunity against hepatitis B in Alexandria, Egypt," European Journal of Epidemiology, 18: 1007-1011, 2013.
[22] A. G. Soliman, M. S. Hassan, N. A. Makhlouf, Z. Mohamed, Z. Abd Elrhman, and K. A. Khalaf, "Screening for HBsAg among Vaccinated School Children in Upper Egypt," J Am Sci., 9(7):404-406, 2013. (ISSN: 1545-1003). http://www.jofamericanscience.org.
[23] X. Li, Y. Zheng, A. Liau, B. Cai, D. Ye, F. Huang, X. Sheng, F. Ge, L. Xuan, S. Li, and J. Li et al., "Hepatitis B virus infections and risk factors among the general population in Anhui Province, China: an epidemiological study," BMC Public Health, 12:272, 2012. http://www.biomedcentral.com/1471-2458/12/272.
[24] M. W. Lai, T. Y. Lin, K. C. Tsao , C. G. Huang, M. J. Hsiao, K. H. Liang, and C. T. Yeh, "Increased seroprevalence of HBV DNA with mutations in the s gene among individuals greater than 18 years old after complete vaccination," Gastroenterology, 143(2):400-7, Aug. 2012.
[25] F. H. Su, C. H. Bai, F. Y. Chu, Y. S. Lin, C. T. Su, and C. C. Yeh, "Significance and anamnestic response in isolated hepatitis B core antibody-positive individuals 18 years after neonatal hepatitis B virus vaccination in Taiwan," Vaccine, 8; 30(27):4034-9, Jun. 2012.
[26] CDC, "A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States," Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part 1 Immunization of Infants, Children, and Adolescents. MMWR Morb Mortal Wkly Rep. 54(RR-16):1-23, 2005.
[27] Y. Poovorawan, V. Chongsrisawat, A. Theamboonlers, K. Srinivasa, Y. Hutagalung, H. L. Bock, and B. Hoet, "Long-term benefit of Hep B vaccination among children in Thailand with transient hepatitis B virus infection who were born to Hepatitis B surface antigen-positive mothers," J Infect Dis., 200:33-8, 2009.
[28] K. M. Weinberger, T. Bauer, S. Bohm, and W. Jilg, "High genetic variability of the group-specific a-determinant of hepatitis B virus surface antigen (HBsAg) and the corresponding fragment of the viral polymerase in chronic virus carriers lacking detectable HBsAg in serum," Journal of General Virology, 81:1165–74, 2000.
[29] A. R. Zanetti, L. Romanò, C. Giambi, A. Pavan, V. Carnelli, G. Baitelli, G. Malchiodi, E. Valerio, A. Barale, M. A. Marchisio, D. Montù, A. E. Tozzi, and F. D'Ancona, "Hepatitis B immune memory in children primed with hexavalent vaccines and given monovalent booster vaccines: an open-label, randomised, controlled, multicentre study," Lancet Infect Dis., 10:755-61, 2010.
[30] B. J. McMahon, "The natural history of chronic hepatitis B virus infection". Hepatology, 49: S45–S55, 2009.
[31] S. M. Alavian, B. Hajariazdeh, M. AhmadzadAsl, A. Kabir, and K. Bagheri Lankarani, "Hepatitis B virus infection in Iran: a systematic review," Hepat Mon., 8:281–294, 2008.
[32] B Mao, MK Patel, K Hennessey, RJ Duncan, K Wannemuehler and SC Soeung, " Prevalence of chronic hepatitis B virus infection after implementation of a hepatitis B vaccination program among children in three provinces in Cambodia," Vaccine, 13;31(40):4459-64, 2013 Sep.
[33] A. P. Compri, I. Miura, G. Porta, M. F. Lemos, C. P. Saraceni, and R. C. Moreira, "Hepatitis B virus infection in children, adolescents, and their relatives: genotype distribution and precore and core gene mutations," Revista da Sociedade Brasileira de Medicina Tropical, 45(3):301-304, may-jun., 2012.
[34] H. S. Barut , Ö. Günal , A. Göral , and I. Etikan, [Prevalence of hepatitis B virus infection in children of HBsAg positive parents]. Mikrobiyol Bul., 45(2):359-65, Apr. 2011.
[35] L. G. Davis, D. J. Weber, and S. M. Lemon, "Horizontal transmission of hepatitis B Virus," Lancet, 1:889-893, 1989.
[36] Y. Zheng, Y. Lu, Q. Ye, Y. Xia, Y. Zhou, Q. Yao, and S. Wei, "Should chronic hepatitis B mothers breastfeed? A meta-analysis," BMC Public Health, 11:502, 2011.
[37] X. Chen, J. Chen, J. Wen, C. Xu, S. Zhang, Y. H. Zhou, and Y. Hu, "Breastfeeding is not a risk factor for mother-to-child transmission of hepatitis B virus," PLoS One, 8(1):e55303, 2013.