ORIGINAL ARTICLE

Anti Hbs Antibody Sero-Prevalence among Extended Program of Immunization Vaccinated Children Born between Year 2009-2016 in Urban Community of City Peshawar Pakistan

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ABSTRACT

Objective: To determine the sero-prevalance of antibody against Hepatitis B virus surface antigen among EPI vaccinated children born between year 2009-2016.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Study was carried out among urban area children born in Peshawar city between 2009-2016 from 2 August, 2020 to 30, April 2021.

Materials and Methods: This was descriptive cross-sectional study carried out among children born in city Peshawar "between" 2009-2016, using non-probability convenient sampling technique. After taking the written consent from the parents a predesigned questionnaire was filled. About 3 to 5 ml of blood was collected for anti HBs Ag test through using ELISA technique. Results were collected and analysed using SPSS version 21.

Results: This study included 184 EPI HBV vaccinated children vaccinated "between" 2012 to 2016. Out of 184 children 118 (64.1%) were female belonging to the middle socio-economic class 170 (92.4%). The mean age of the study participants was 7.834 years ±2.045. Anti Hbs antibody titre revealed that out of 184 study participants 75.5% were vaccinated within last 10 years. It was observed that only 33 (17.9%) children out of 184 were immune against HBV (Antibody level > 100 mIU/ml). The study showed that there was no significant difference ($p>0.05$) in the immune status of the children with respect to the demography like age of child $p=0.529$, gender $p= 0.461$, place of vaccination $p=0.918$, economic status $p=0.190$.

Conclusion: The EPI HBV vaccinated children lost protective anti Hbs antibody level after five years of vaccination.

Key Words: *Vaccination, Anti HBs Antibody, Sero-prevalence, HBV Vaccine, Immune Response, Immunization, Children, EPI.*

Introduction

Hepatitis B infection is a grave devastating global public health issue .The causative agent of this infection is hepatitis B virus(HBV).[1] This virus can causes progression of serious liver diseases such as liver cirrhosis, hepatic decompensation and hepatocellular carcinoma[2] , this leads to higher rate of mortality and morbidity.[1] The significant reservoir for HBV is human. The route of transmission of HBV is most common among people who come in contact with blood or body fluids of HBV infected person, unsterilized injections, use of contaminated needles among drug users, and unsafe sexual practices. [1,3] Dr. Baruch was the first to discover hepatitis B virus in 1965. In the beginning, the virus was named as" Australia Antigen". Vaccine therapies are available for Hepatitis B virus infection. HBV vaccine consists of three or four doses, given to the infants over a 6 month period.[4]

Almost 2 billion people are worldwide infected with HBV infection that is one third of the total world population. Among them, are 360 million chronic carriers of HBV which makes 6% of the world population.[5] Chronic HBV infection prevalence differs among regions. The infection rates in USA and Western Europe are low (0.1-2.0%), intermediate (2.0-8.0%) in Japan and Mediterranean countries, and with a high rate of infection (8.0-20.0%) in sub-Saharan and southeast Asia regions.[6] Countries endemic with HBV infections includes Asia, Southern

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Europe, Africa and Latin America.[7] Africa is considered as a whole to have high endemicity levels of HBV infection and the children of Africa aged between 0-14 are at a high risk of HBV infection.[2] A retrospective study conducted in South Korea included the children vaccination data of 2012 to 2015 showed that the titter of Anti Hbs antibodies decreases with increasing age.[8]

Pakistan being a developing country, is also endemic with hepatitis B, and 3% population of the country is infected with the virus.[9] In Pakistan the HBV vaccination coverage varies among different parts of Pakistan and in rural areas the vaccination coverage rate is very low[1] therefore preventive measures should be taken against HBV infection.

The EPI in Pakistan has significant and apparent impact on immunization indicators such as measles, tetanus and poliomyelitis eradication at regional and global level.[10] Despite continuous work, efforts and priorities by the Government of Pakistan, the EPI vaccination in Pakistan did not achieve the framed target of 80% protective level among children. Many factors involved in hindrance of the achievement of benchmarks goal of EPI vaccination in Pakistan are lack of awareness, poor management and limited access to immunization etc.[11] Pakistan started HBV vaccination in EPI from 2009.[12] It has been presumed that EPI vaccination against HBV provide protection for long duration of time. There is no follow up data of HBV vaccine response after 5 year of EPI immunization in Pakistan. Therefore, this study was carried out to determine the HBV vaccine efficacy among children who were EPI vaccinated between 2009 to 2016. The purposes of the study were to determine the Sero-prevalence of anti Hbs antibodies in children born after 2010 and vaccinated against HBV through EPI. Since 2009 when EPI HBV vaccination was started in Pakistan, there found no proper evidence regarding HBV vaccination long term protection. It is important and public health concern to determine the exact duration of protection of any vaccine. This study was conducted to determine anti Hbs Antibody level among EPI vaccinated children born between 2009-2016 in urban community of district Peshawar.

Materials and Methods

This was a community based, descriptive cross-sectional study carried out during 2 August 2020 to 30 April 2021, among children born in city Peshawar "between" 2009-2016. The sample size of this study was calculated 184 based on the prevalence of anti Hbs level among healthy population 0.5%.[13] The sampling technique used for data collection in this study was non-probability convenient sampling technique. Ethical approval of the study was provided by the ethics committee of Post Graduate Medical Institute Peshawar institutional research and ethics board with Ref No 11007. This study was conducted among the children whose parents were willing to allow their children to participate in this research. Children having the HBV infection in past were excluded from this study. After taking the written informed consent from the parents a predesigned questionnaire was filled. The content of the questionnaire was about the history of the child's HBV vaccination, demography, vaccination time, place of vaccination and family history about HBV infection etc. After collecting data using questionnaire, trained staff of Pakistan Health Research Council (Research centre Khyber Medical College Peshawar) were deputed for blood sampling. About 3 to 5 ml of blood were collected from each child and was processed to determine the induced immunity of the vaccine against the surface antigen of hepatitis B (HBsAg. For anti HBs titre the collected samples were processed and were proceeded for qualitative anti HBs test through ELISA. Results were collected and entered in data form. The data was analysed using SPSS version 21.

Results

This study included 184 EPI HBV vaccinated children vaccinated "between" 2009 to 2016. Out of 184 children greater proportion 118 (64.1%) were female. Most responders (provided data about the child vaccination history) of this study were the mothers of included children 134 (72.8%). It was observed that most respondents belonged to the middle socioeconomic class 170 (92.4%), and these families have only one earning member 167 (90.8%). The mean age of the study participants was 7.834±2.045 **(Table I).**

Study also showed that most of the studied children (47.3%) were vaccinated from primary health centres. The vaccination records of participated children were confirmed verbally from a total 137 (74.5%) respondents. It was found that among 184

participants 75.5% were vaccinated within last 10 years **(Table II).**

It was observed that only 33 (17.9%) children out of 184 were having protective antibody level against HBV **(Figure 1).** The study found no significant difference in the immune status of the children with respect to the demography age of child p=0.529, gender p= 0.461, place of vaccination p=0.918, economic status p=.0.190 **(Table III).**

Table I : Demographic Status of Study Participants

Demographic Status	Description	Frequency	Percentage
Relation with child	Father	29	15.8
	Mother	134	72.8
	Sibling	21	11.4
	Total	184	100.0
Economic status	High	9	4.9
	Middle	170	92.4
	Low	5	2.7
	Total	184	100.0
Age of child	4 years to 5 years	29	15.8
	6 years to 7 years	52	28.3
	8years to 9 years	63	34.2
	10 years to 12 years	40	21.7
	Mean ±Std	7.834±2.045	
	Total	184	100.0
Gender of child	Male	66	35.9
	Female	118	64.1
	Total	184	100.0
Region	Urban	184	100.0
Disability	No	184	100.0

TABLE II: Description of EPI Vaccination History

Demographic Status	Description	Frequency	Percentage
Place of EPI vaccination	EPI Centre	45	24.5
	Health Centre	87	47.3
	Hospital	51	27.7
	Home	1	.5
	Total	184	100.0
Vaccination confirmation	Verbally	137	74.5
	Card	47	25.5
	Total	184	100.0
Last dose of HBV received	Within 5 years	28	15.2
	Within 10 years	139	75.5
	within 11 to 12 years	17	9.2
	Total	184	100.0
Family HBV infection	No	184	100.0
Anti HBs Ab	Yes	184	100.0
Protective level of anti Hbs Ab	Yes	33	17.9
	No	151	82.1
	Total	184	100.0

Table III: Immune Status of Children with Respect to their Demography

Demographic status	description	Immune status		total	P value
		Immune	Nonimmune		
Age of child	4 years to 5 years	6	23	29	0.529
	6 years to 7 years	6	46	52	
	8years to 9 years	12	51	63	
	10 years to 12 years	9	31	40	
	Total	33	151	184	
Gender of Child	Male	10	56	66	0.461
	Female	23	95	118	
	Total	33	151	184	
Place of vaccination	EPI Centre	7	38	45	0.918
	Health Centre	16	71	87	
	Hospital	10	41	51	
	Home	0	1	1	
	Total	33	151	184	
Economic status	High	0	9	9	0.190
	Middle	33	137	170	
	Low	0	5	5	
	Total	33	151	184	

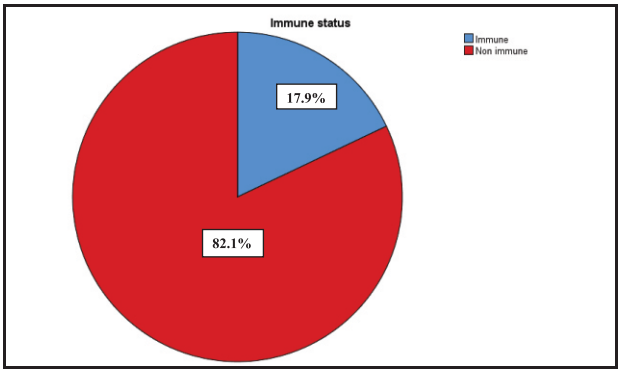

Figure 1: Frequency of Immune Status of Study Participants

Discussion

This study demonstrated the prevalence of HBV vaccination and its effectiveness among children of urban area of district Peshawar vaccinated from 2009 to 2016. The focus of our study was to determine anti Hbs antibodies prevalence among children vaccinated against HBV through EPI. There found no published literatures or findings that justify the long-lasting immunity against HBV after HBV vaccine. In Pakistan, HBV vaccines were included in

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EPI in 2009, therefore the inclusion criteria of this study were set to children born after 2009.

This study was not a novel study focused on children for determination of immune response against vaccine but similar kind of studies among children were observed in other settings where a similar pattern of immune response against vaccination was observed.[14, 15] The sero-prevalence of anti Hbs antibodies in this study (17.9%) was low as compared to another study conducted in south Korea where protective antibody level was 50%.[16] The target population in Korean study was older and recently vaccinated therefore protective antibody level was high. The efficacy of HBV vaccination was tested among the Egyptian children aged 6 to 11 years where the sero-prevalance was 39.3%.[17] All these studies revealed that the sero-prevalance of anti HBs antibodies declined with the age and duration. The low protective anti HBs antibody level in this study was a clue for public health consideration. More in depth studies regarding post immunization prevalence of anti Hbs Level in multi community level with systemic sampling technique is needed to address the issue. Further studies focusing on the active presence of memory cell for this specific antigen among HBV vaccinated children are needed.

Hepatitis B is endemic with higher rate of endemicity and the immunization against the hepatitis B infection needs a broader vaccination coverage, to cope up with this problem.[18] WHO recommended to introduce HBV vaccination in Expanded Program on Immunization (EPI) to eventually eliminate HBV infection and its chronic long lasting impact. EPI is multinational effort whose goal is to immunize children all around the world against the vaccine preventable diseases d of childhood.[19] All of the participants in this study had completed their three doses of HBV vaccination through EPI. This study results showed that the immune status of the participants is 17.9% which is comparatively very low and with passage of time this protective antibody level further decreases. A previously performed studies in Iran, and Egypt reported that the vaccine induced anti HBs Ag level might decreases with age.[20,21] The results of our study in agreement with other studies revealed that anti Hbs antibodies titter start to decrease after primary vaccination, so there is a need of booster dose which induce or trigger anamnestic immune response against HBV infection.[22] Some studies showed that long term immunity is generated against HBV infection by a booster dose.[23]

The findings of this study were consistence with other studies, demonstrated no significant difference when compared the immune status of children with their gender, economic status and anti HBs antibodies level.[17]

The study was limited to a particular time and due to constrain of budget we selected probability convenient sampling technique which was a major limitation of this study. Due to constrains of budget the anti-Hbs Antibody producing memory cell count using HPLC technique could not be determined, which would determine the exact long-lasting immunity against HBV vaccine.

Conclusion

A very high ratio 82.1% EPI HBV vaccinated children lost protective anti Hbs Ag antibodies level after five years of vaccination. The protective anti Hbs antibodies level after 5 year of HBV vaccination was determined very low and need a booster dose of HBV vaccine after five years of vaccination.

REFERENCES

1. Khan A, Ullah O, Attaullah S, Sohail S, Nisar N and Ijaz H. SERO-PREVALANCE OF ANTI HBSAG AMONG FEMALE UNIVERSITY STUDENTS OF DISTRICT PESHAWAR. *Pakistan Journal of Public Health*. 2018; 8: 181-4.
2. Zampino R, Boemio A, Sagnelli C, et al. Hepatitis B virus burden in developing countries. *World J Gastroenterol*. 2015; 21: 11941-53.
3. Meireles LC, Marinho RT and Van Damme P. Three decades of hepatitis B control with vaccination. *World J Hepatol*. 2015; 7: 2127-32.
4. Yuen M-F, Chen D-S, Dusheiko GM, et al. Hepatitis B virus infection. *Nature reviews Disease primers*. 2018; 4: 1-20.
5. Ijaz H, Nisar N, Sohail S, Attaullah S, Ullah O and Khan A. Sero-Prevalance of Anti Hbsag among Female University Students of District Peshawar. *Pakistan Journal of Public Health*. 2018; 8: 181-4.
6. Liaw Y-F and Chu C-M. Hepatitis B virus infection. *The lancet*. 2009; 373: 582-92.
7. Ali M, Idrees M, Ali L, et al. Hepatitis B virus in Pakistan: a systematic review of prevalence, risk factors, awareness status and genotypes. *Virol J*. 2011; 8: 102.
8. Lee KH, Shim KS, Lim IS, et al. Changes in hepatitis B virus antibody titers over time among children: a single center study from 2012 to 2015 in an urban of South Korea. *BMC Pediatr*. 2017; 17: 164.
9. Khan F, Shams S, Qureshi ID, et al. Hepatitis B virus infection among different sex and age groups in Pakistani Punjab.

Virol J. 2011; 8: 1-5.
10. Zaidi SS, Hameed A, Rana MS, et al. Identification of measles virus genotype B3 associated with outbreaks in Islamabad, Pakistan, 2013–2015. *Journal of Infection and Public Health*. 2018; 11: 540-5.
11. Haq Z, Shaikh BT, Tran N, Hafeez A and Ghaffar A. System within systems: challenges and opportunities for the Expanded Programme on Immunisation in Pakistan. *Health research policy and systems*. 2019; 17: 1-10.
12. Donadel M, Scobie HM, Pastore R, et al. Comprehensive Vaccine-Preventable Disease Surveillance in the Western Pacific Region: A Literature Review on Integration of Surveillance Functions, 2000–2021. *Global Health: Science and Practice*. 2022; 10.
13. Cárdenas-Perea ME, Gómez-Conde E, Santos-López G, et al. Hepatitis B surface antibodies in medical students from a public university in Puebla, Mexico. *Hum Vaccin Immunother*. 2016; 12: 1857-62.
14. Zhu W, Higgs BW, Morehouse C, et al. A whole genome transcriptional analysis of the early immune response induced by live attenuated and inactivated influenza vaccines in young children. *Vaccine*. 2010; 28: 2865-76.
15. Hendrikx LH, Felderhof MK, Öztürk K, et al. Enhanced memory B-cell immune responses after a second acellular pertussis booster vaccination in children 9 years of age. *Vaccine*. 2011; 30: 51-8.
16. Lee KH, Shim KS, Lim IS, et al. Changes in hepatitis B virus antibody titers over time among children: a single center study from 2012 to 2015 in an urban of South Korea. *BMC Pediatrics*. 2017; 17: 164.
17. Norouzirad R, Shakurnia AH, Assarehzadegan M, Serajian A and Khabazkhoob M. Serum Levels of Anti-Hepatitis B Surface Antibody Among Vaccinated Population Aged 1 to 18 Years in Ahvaz City Southwest of Iran. *Hepat Mon*. 2014; 14: e13625.
18. Lavanchy D and Kane M. Global epidemiology of hepatitis B virus infection. *Hepatitis B virus in human diseases*. Springer, 2016, p. 187-203.
19. Gupta N, Nelson BD, Kasper J and Hibberd PL. *The MassGeneral Hospital for Children handbook of pediatric global health*. Springer Science & Business Media, 2013.
20. Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recommendations and Reports*. 2018; 67: 1.
21. Norouzirad R, Shakurnia AH, Assarehzadegan M-A, Serajian A and Khabazkhoob M. Serum levels of anti-hepatitis B surface antibody among vaccinated population aged 1 to 18 years in ahvaz city southwest of iran. *Hepatitis monthly*. 2014; 14.
22. Poorolajal J and Hooshmand E. Booster dose vaccination for preventing hepatitis B. *The Cochrane database of systematic reviews*. 2016; 2016: Cd008256.
23. Ma J-C, Wu Z-W, Zhou H-S, et al. Long-term protection at 20–31 years after primary vaccination with plasma-derived hepatitis B vaccine in a Chinese rural community. *Human Vaccines & Immunotherapeutics*. 2020; 16: 16-20.

CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

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