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Risk factors and clinical correlates of hepatitis B seroprevalence in Nigerian children

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Abstract: *Introduction:* Establishing risk factors for a disease enables early identification of those with the disease (through screening) as well as targeted prevention and control measures. The significance and relative importance of such risk factors may differ based on geographic location and they may change over time with the institution of control measures. In this study we examined the association between HBsAg seropositivity, some risk factors and clinical features.

Methodology: Consecutive children aged 2 months to 16 years who were admitted to a Children's Emergency Room were recruited. Data on the presence / absence of risk factors such as previous blood transfusion, scarifications, receipt of unsafe injections and previous surgery were obtained. History to ascertain previous or present history of jaundice and pale coloured stool was obtained. Examination to detect hepatomegaly and splenomegaly

was carried out. Blood samples were assayed for HBsAg.

Results: Of the 150 children recruited 84(56%) were male. The mean (SD) age of the children was 33.0(39.1) months. HBsAg seropositivity was 13.9%. Circumcision, scarification, ear piercing, history of blood transfusion, receipt of unsafe injections, present/past history of jaundice and malnutrition were not significantly associated with being seropositive ($p>0.05$).

Conclusion: This study did not identify any pathognomonic clinical feature of hepatitis b seroprevalence. The lack of association between HBsAg seropositivity and the studied risk factors may represent a real improvement in infection control measures. Further research is required to ascertain if there are still some unidentified risk factors for hepatitis B transmission in Nigerian children.

Keywords: Hepatitis B virus, infection, risk factors

Introduction

For many disease conditions there are identifiable risk factors which enable targeted prevention and control measures. Also in the health care setting these risk factors enables heightening the index of suspicion for the diagnosis of a given disease. Hepatitis B virus infection is a global health problem. The hepatitis B virus is transmitted by percutaneous or mucous membrane exposure to infectious blood or body fluids.¹ In developing countries, common modes of transmission are perinatal (mother to child), early child infections (inapparent infections through close interpersonal contact with infected household contacts), unsafe injection practices, unsafe blood transfusion and unprotected sexual contact.² Other frequently listed risk factors include procedures during which sharp objects which may be contaminated are used such as tattoos, ear piercing and circumcision.³⁻⁵

The relative importance of these risk factors varies from

one geographic region to another. For example perinatal transmission is the main route of acquisition of hepatitis B virus infection in South East Asia.⁶ In the United States of America, certain population groups have been identified to be at increased risk such as injection drug users, HIV positive persons, Men who have sex with men, household and sexual contacts of persons with chronic hepatitis B infection.¹

The relative significance of some of these risk factors may also change over time as different interventions are instituted for the control of such risk factors. For example, in the United States of America, since 1972 the blood supply has been screened for hepatitis B making the risk of transfusion transmitted hepatitis B extremely rare.⁷

In Nigeria, the major route of acquisition is thought to be horizontal during childhood and various studies have suggested different risk factors including blood transfusion, children with sickle cell anaemia, circumcision.

Many of these studies were carried out before the widespread adoption of some control measures such as screening of blood before transfusion, creating awareness on transmission routes of blood borne diseases such as Human Immunodeficiency virus. Also some clinical features such as jaundice, tender hepatomegaly are associated with hepatitis b infection. Their presence in a patient may heighten the suspicion of hepatitis B infection. The aim of this study was to evaluate the association of some of these aforementioned risk factors and clinical features with hepatitis b seroprevalence in Nigerian children.

Methodology

The study was carried out at the Children's emergency room (CHER) of the University of Benin Teaching hospital. The University of Benin Teaching Hospital (UBTH) is a 700 bedded hospital. It is a tertiary health facility. It takes care of patients from Edo state and those referred from the neighbouring states of Ondo, Delta, Ekiti, Enugu and Imo. The Children's emergency room is one of four wards that cater for children in the University of Benin Teaching Hospital. Most children beyond the neonatal period who present with an acute illness and who require admission are first admitted in the emergency room.

Ethical clearance for the study was obtained from the UBTH ethical review committee. Verbal consent was obtained from parents of subjects after the objectives and procedure of the study had been explained to them.

Consecutive patients aged 2 months to 16 years admitted to CHER were recruited. Information on bio data such as age, sex, maternal and paternal educational level and occupation was obtained using a proforma. The proforma was pretested at the Institute of Child Health Immunization clinic. The instrument was administered by the researcher. Immunization history was obtained for each child.^f The association between immunization status and HBsAg seroprevalence has been reported elsewhere.⁸ History to ascertain previous or present history of jaundice and pale coloured stool was obtained. Physical examination to detect pallor, jaundice, lymphadenopathy, hepatomegaly, splenomegaly and spider nevi was carried out. The presence or absence of risk factors such as previous blood transfusion, scarification marks, previous injections and surgery was ascertained. Injections that were received outside of health care facilities were considered to be unsafe.

The weight of each child younger than 12 months was measured using an infant weighing scale while a mechanical floor scale was used for children older than 12 months. Infants were weighed nude while older children were weighed lightly clothed. Weight was recorded in kilograms to the nearest 0.05 kilogram

Results

One hundred and fifty (150) children were recruited for the study of whom 84(56%) were males. The mean age (SD) of the children was 33.0(39.1) months with a range of 2-180 months (2months -15 years). Majority of the children 124 (82.7%) were aged below 5 years (Table 1). Infants (younger than 12months) were 53(35.3%) while those older than 10 years (120months) were 8 (5.3%).

Age was available for 146 and 136 mothers and fathers respectively. The mean age (SD) of mothers was 31.9 (5.9) years with a range of 19-50 years while the mean age (SD) of fathers was 38.9(7.2) years with a range of 23-63 years.

Majority of the mothers 59(39.9%) had tertiary education. Only 4(2.7%) mothers did not attempt or complete primary education. Majority of the children 98(72.6%) were from families of high socioeconomic status.

Table 1: Sociodemographic characteristics of 150 children

Characteristic	n	(%)
<i>Gender</i>		
Male	84	56.0
Female	66	44.0
<i>Age group</i>		
<12months	53	35.3
12-59months	71	47.3
60-119months	18	12.0
120months	8	5.3
<i>Maternal Age</i>		
24	11	7.5
25-29	48	32.9
30-34	39	26.7
35-39	31	21.2
40-44	12	8.2
45	5	3.4
<i>Maternal LOE</i>		
I	59	39.9
11	9	6.1
111	35	23.6
IV	41	27.7
V	4	2.7
<i>Socioeconomic Status</i>		
High	98	72.6
Low	37	27.4
<i>Number of persons in HH</i>		
5	84	57.1
>5	63	42.9

I-university degree or equivalent, II- School certificate (Ordinary level GCE) plus teaching or other professional training III- School certificate or grade II teachers' certificate or equivalents IV- modern three, primary six certificate V- Did not complete primary school, illiterate
LOE – Level of education
HH -Household

Risk factors for HBsAg seropositivity

Of the 150 children studied 21(13.9%) were positive for HBsAg. Table 2 shows the relationship between procedures which involves the use of sharps and HBsAg seropositivity. Of the 105 children who had been circumcised, 15(14.3%) were positive for HBsAg while 6 (14.3%) of those who had not been circumcised were

positive. There was no significant association between circumcision and HBsAg status $p=1.000$.

Circumcision was carried out by traditional healers, health care personnel (at home) and health care personnel (at health care facilities) in 12(11.4%), 18(17.1%) and 72(68.6%) children respectively. The person who carried out the circumcision was not known in 3(2.9%) children. Of those circumcised by traditional healers 2 (16.7%) were seropositive compared to 2(11.1%) of those circumcised by health care personnel at home and 10(13.9%) of those circumcised by health personnel at health facilities. The place where circumcision was carried out was not significantly associated with HBsAg seropositivity $p=0.91$.

Of the 58 children whose ears were pierced, 32(55.2%) were done at home using sterile pin ear rings while 21 (36.2%) were done in health facilities using sterile pin ear rings. One child had the ears pierced at home using a sewing needle. HBsAg was positive in 4(12.5%) of those whose ears was pierced at home and this was not significantly different from the 5(23.8%) among those whose ears were pierced in a health facility $p=0.46$.

Previous blood transfusion, receipt of unsafe injections, previous surgery, and having had scarifications were not significantly associated with being positive for HBsAg ($p>0.05$).

Table 2: Association between HBsAg serostatus and some risk factors

Risk factor	HBsAg serostatus				p-value
	Positive		Negative		
	n	%	n	%	
<i>Scarifications</i>					
Yes	3	15.0	17	85.0	1.00
No	18	14.3	108	85.7	
Total	21		125		
<i>Unsafe injections</i>					
Yes	4	21.1	15	78.9	0.48
No	17	13.5	109	86.5	
Total	21		124		
<i>Blood transfusion</i>					
Yes	2	18.2	9	81.8	0.66
No	19	14.2	115	85.8	
Total	21		124		
<i>Surgery</i>					
Yes	1	50.0	1	50.0	0.27
No	20	14.0	123	86.0	
Total	21		124		
<i>Circumcision</i>					
Yes	15	14.3	90	85.7	1.00
No	6	14.3	36	85.7	
Total	21		126		
<i>Ear Piercing</i>					
Yes	9	15.5	49	84.5	0.81
No	12	13.0	80	87.0	
Total	21		129		

Comparison was by Fishers Exact test

Clinical features and HBsAg seropositivity

Of the 22 children who had a past history of jaundice 4 (18.2%) were HBsAg positive and this was not significantly different from 17(13.5%) of those who did not have a past history of jaundice.(Table 3) Similarly the presence of jaundice in the patients was not significantly

associated with being HBsAg seropositive $p=0.59$. Past history of pale stools, presence of pallor, hepatomegaly, splenomegaly and lymphadenopathy were not significantly associated with being seropositive.

There were 32 moderately/severely malnourished children. Of these 8(25%) were HBsAg seropositive compared to 12(11.3%) of those who were not malnourished. Nutritional status was not significantly associated with being seropositive $P=0.08$.

Table 3: Association between hepatitis B serostatus and some clinical features

Clinical features	HBsAg Serostatus				**pvalue
	Positive		Negative		
	n	%	n	%	
<i>History of pale stools</i>					
Yes	2	28.3	4	66.7	0.20
No	18	13.4	116	86.6	
Total	20		120		
<i>Past History of jaundice</i>					
Yes	4	18.2	18	81.8	0.52
No	17	13.5	109	86.5	
Total	21		127		
<i>Jaundice</i>					
Yes	0	0	7	100	0.59
No	20	14.6	117	85.4	
Total	20		124		
<i>Pallor</i>					
Yes	3	11.1	24	88.9	0.73
No	17	13.8	106	86.2	
Total	20		130		
<i>Hepatomegaly</i>					
Yes	9	20.0	36	80.0	0.20
No	11	11.3	86	88.7	
Total	20		124		
<i>Splenomegaly</i>					
Yes	1	6.3	15	93.7	0.47
No	19	15.1	107	84.9	
Total	20		122		
<i>Lymphadenopathy</i>					
Yes	0	0	4	100.0	1.00
No	20	14.5	118	85.5	
Total	20		122		
<i>Nutritional status</i>					
Moderately/severe*	8	25.0	24	75.0	0.08
Normal	12	11.3	94	88.7	
Total	20		118		

*moderately/severe underweight **All comparisons were by Fishers Exact Test

The commonest provisional diagnosis was Pneumonia 33(22.3%), closely followed by malaria 31(21.0%).and then gastroenteritis 18(12.2%). Other diagnoses are as shown in table 4. These diagnoses were similar to those of children who were HBsAg positive. Table 5.

Table 5: Provisional diagnosis of children who were HBsAg seropositive

Provisional diagnosis	n	%
Bronchopneumonia	8	38.1
Malaria	4	9.5
Gastroenteritis	3	14.3
Accidental poisoning	2	9.5
Tuberculosis	1	4.8
Septicaemia	1	4.8
Shigellosis	1	4.8
Nephrotic syndrome	1	4.8

Table 4: Provisional diagnosis of the studied children

Provisional diagnosis	n	%
Bronchopneumonia	33	22.3
Malaria	31	21.0
Gastroenteritis	18	12.2
Meningitis	14	9.5
Tonsillitis	8	5.4
Septicaemia	7	4.7
Soft tissue infections	6	4.1
Asthma	3	2.0
Seizures	3	2.0
Malignancy	3	2.0
Accidental poisoning	3	2.0
Bronchiolitis	2	1.4
Head injury	2	1.4
Acquired Immunodeficiency syndrome	2	1.4
Tuberculosis	2	1.4
Viral encephalitis	1	0.7
Intracranial space occupying lesion	1	0.7
Chronic liver disease	1	0.7
Pertussis	1	0.7
Tetanus	1	0.7
Chronic renal failure	1	0.7
Nephrotic syndrome	1	0.7
Haemophiliac	1	0.7
Congenital heart disease	1	0.7
Shigellosis	1	0.7

Discussion

None of the risk factors examined in this study was significantly associated with being seropositive for HBsAg. Historically the first recorded cases of Hepatitis B (formerly called serum hepatitis) are thought to be those that followed the administration of smallpox vaccines containing human lymph administered to shipyard workers in Germany in 1883.⁹ In the early and middle parts of the 20th century serum hepatitis was repeatedly observed following the use of contaminated needles and syringes while the role of blood as a vehicle for transmission was further emphasized in 1943 by Beeson when he described jaundice that had occurred in seven recipients of blood transfusion.⁹ However the screening of blood before transfusion has all but eliminated transfusion of blood/blood products as a source of hepatitis B infection in some developed countries.⁷

Although some previous studies have reported blood transfusion to be a risk factor for hepatitis b infection in children,^{3,4} in this study blood transfusion was not significantly associated with hepatitis B infection. This is in keeping with some other studies in Nigerian children.¹⁰ The lack of association between seropositivity and blood transfusion may be due to improved screening of blood before transfusion that has been adopted in the national guidelines on blood transfusion.¹¹ However, the differing results obtained between studies may be due to differential implementation of the national guidelines on blood transfusion, but may also reflect earlier horizontal transmission which is thought to be the major route of transmission in Nigerian children.

Scarification marks were not significantly associated with hepatitis B status. This is similar to findings from studies in Eastern Nigeria.¹² In one study it was noted that traditional healers request new blades from their clients to carry out scarifications.¹² The current drive to raise awareness on the transmission routes of Human immunodeficiency virus (HIV) which has similar routes of transmission as the hepatitis B virus may also have contributed to such improved practices.

Unsafe injections were not associated with an increased risk of being positive for the hepatitis B surface antigen in this study. This is in keeping with a study from Ilorin in which none of the children seropositive for HBsAg had a history of use of unsterile needles.³ The finding in this study was however in contrast with findings in Abakaliki in which unsafe injections was reportedly the commonest route of hepatitis B infection.¹³ Also in Pakistan HBsAg seropositivity was higher in children who had received therapeutic injections and this was attributed to recycling of needles.¹⁴ It is also possible that the same awareness drive on transmission routes for HIV may have resulted in improved practices among those who administer injections outside of health care settings resulting in the lack of association between HBsAg seropositivity and unsafe injections in this study. Improved practices with sharps were also observed with ear piercing in this study as most of the ear piercing was done with sterile pin ear rings. Thus ear piercing was not significantly associated with a higher prevalence of hepatitis B surface antigen. This was similar to findings in Pakistan.¹⁴

Circumcision was not significantly associated with being positive for hepatitis B surface antigen. Most of the circumcisions (85.7%) were carried out by health care personnel at home or in health facilities. That these health workers are unlikely to use contaminated instruments for the procedure may explain the lack of association of circumcision with being seropositive for HBsAg. This assertion is corroborated by findings in a study from northern Nigeria where those who had traditional circumcision were more likely to be seropositive for hepatitis B virus infection compared to those who had circumcision done in health facilities.⁴

The finding that blood transfusion, ear piercing, scarification marks, and use of contaminated sharps were unassociated with being seropositive is contrary to findings in many studies in Nigerian adults.¹⁵⁻¹⁷ These differences may be due to the fact that these adults most likely acquired their infection years ago in their childhood before the advent of control measures for blood borne infections became widely adopted in Nigeria both at health facility and at community levels.

A history of jaundice in the past or the presence of jaundice in the current illness was not significantly associated with being positive for hepatitis B surface antigen. This is similar to findings in Ilorin where none of the children who were seropositive had a history of jaundice.³ Similarly, the clinical features of hepatomegaly, splenomegaly and lymphadenopathy which may be present either in acute or chronic hepatitis B infection were

not significantly associated with hepatitis B surface antigen status in this study. This suggests that these clinical features are not specific and sensitive enough to discern hepatitis B infection. Moreover these are features that are present in more common conditions of children such as malaria and septicaemia. Also children with acute hepatitis are more likely to be asymptomatic. The finding in this study is however in contrast to that in Port Harcourt where hepatomegaly and jaundice were the commonest features in children who were seropositive.¹⁸

That study may have been biased in that the children evaluated were those in whom hepatitis B was highly suspected.

The provisional diagnoses of the children showed that these were similar in both those who were hepatitis B seronegative and those who were seropositive. Most of the diagnoses were not referable to the liver. The one child who had a diagnosis of chronic liver disease was not even seropositive for hepatitis B. Thus it is advisable that health care workers should observe standard precautions when handling any patient or clinical specimen.

A significant proportion of the children studied (23.2%) were either moderately or severely underweight. This is comparable to the findings of 28.3% for moderately or severely underweight in the Nigerian Multiple Indicator Cluster Survey in 2011.¹⁹ Malnutrition is known to be a risk factor for many infectious diseases.^{20,21} Few studies have evaluated this factor as a possible risk factor for hepatitis B. In this study malnutrition was not significantly associated with being seropositive. This is in keeping with findings from a study on Turkish children with chronic hepatitis B infection in whom no significant difference was found in levels of alanine amino transferase, histological activity and HBV DNA levels between those who were malnourished and those who were not.²²

The lack of association of HBsAg seroprevalence with the studied risk factors may represent a real improvement in infection control measures such as improved blood screening, observance of standard precautions and an informed population on prevention of blood borne diseases at community level. Research is required to ascertain if there are still as yet some unidentified risk factors for hepatitis B transmission in children in Nigeria.

Health care workers have been identified as being occupationally at risk for hepatitis B infection.²³ This risk is determined by the prevalence of hepatitis B in the patient population and by their rate of exposure to procedures during which exposure to blood or blood products is likely. The prevalence of HBsAg among the children studied is high therefore there is a need to adopt measures to protect health care workers in this setting. Continued observance of standard precaution is mandatory as hitherto identified risk factors were not predictive of seropositivity in this study. A higher index of suspicion will be required for diagnosis of hepatitis B in children more especially as hepatitis B infection in children is mostly asymptomatic. Immunization of health care workers will be a worthy strategy to protect health care workers while universal infant immunization will reduce HBsAg seroprevalence at community level.

Author's contribution

AES conceptualized the study, was involved in data collection, analysis and interpretation, wrote the initial draft and approved the final draft

ANO contributed to the concept, was involved in data analysis and interpretation and approved the final draft.

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