Microbiology Research Journal International

Volume 34, Issue 1, Page 36-44, 2024; Article no.MRJI.113386
ISSN: 2456-7043, NLM ID: 101726596
(Past name: British Microbiology Research Journal, Past ISSN: 2231-0886, NLM ID: 101608140)

Evaluation of Non-response to Hepatitis B Vaccines in Individuals Over 15 Years in the Centre Region of Cameroon: A Cross-sectional Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/MRJI/2024/v34i11424

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/113386

Original Research Article

Received: 16/12/2023
Accepted: 21/02/2024
Published: 02/03/2024

ABSTRACT

Background: To investigate the risks factors associated to the non-response of hepatitis B (HB) immunization in participants over the age of 15 years.
Methods: From October 2020 to December 2021, data were collected from individuals aged over 15 years who receive at least one dose of vaccine. An algorithm consisted of three (03) tests researching anti-HBs whose detectability threshold was 10 IU/L and anti-HBc.

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Results: A total of 330 participants were included in this study, among which 158 received three doses of vaccine, of these 83.59% and 6,6% were found positive respectively to anti HBs and anti-HBc. We noted that, age [30 – 40] years [OR= 2.41; CI at 95% (1.24 – 4.80)]; single status [OR=10.80; CI at 95% (1.78 – 114.8)], obesity [OR=2.99; CI at 95% (1.13 – 7.27)], alcohol [OR=10.80; CI at 95% (1.78 – 114.8)]; HEPATITIS vaccine [OR=3.40; CI at 95% (1.24 – 9.10)] were associated with non-response to hepatitis B vaccines.
Conclusion: Non-response to hepatitis B vaccination has been influenced by several risk factors that should be considered during the vaccination process.

Keywords: Anti-HBc; anti-HBs; hepatitis B vaccines.

1. INTRODUCTION

The World Health Organization (WHO) aspires to eradicate HBV infection as a public health issue by 2030, [1] with one of the targets being to reach a hepatitis B surface antigen (HBsAg) prevalence of 0-1% in children aged 5 years [2]. Africa represents for almost 70% of all hepatitis B cases worldwide [3] in this, Cameroon have HBV prevalence rise to 11.2% and ranks among the most impacted countries Africa [4].

Perinatal transmission and horizontal transmission of HBV must be avoided whether World Health Organization put in place strong strategies to make accessible HB vaccine in the whole stratum of society [5]. Following injection of the plasma-derived or recombinant HB vaccines, antibody response to surface antigen (anti-HBs) had been linked to several factors such as intrinsic host factors (such as age, sex, genetics, and comorbidities), perinatal factors (such as gestational age, weight at birth, feeding pattern and maternal factors), extrinsic factors (such as immunity, microbiota, infections and antibiotics) environmental factors (such as geographic location, season, family size and toxins), behavioral factors (such as smoking, alcohol consumption, exercise, and sleep), and nutritional factors (such as body mass index, micronutrients, and enteropathy) to these factors we can add the vaccination schedule, the vaccine route [6–10].

Notwithstanding the identification of risk factors for poor response to HB vaccine, these data could not be generalised whether studies were not done in our context. The aim of this study was to identify the risk factors related with the failure HB vaccination in populations over 15 years.

2. MATERIALS AND METHODS

2.1 Study Design

The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [11].

Settings: Data were collected at four different sites in Centre Region of Cameroon between October 2020 and December 2021. These sites covered the Yaoundé International Vaccination Centre, the Hepato-gastroenterology service of the Yaoundé Military Hospital, the vaccination service of the Mbalmayo District Hospital, and the vaccination service of the Obala District Hospital.

Participants: Our cohort included 15-year-olds who had received least one dose of Hepatic vaccine. Case definition: All participants who had anti-HBs threshold greater than or equivalent to 10 IU/L were classified immunized.

2.2 Variables and Data Sources/ Measurement

Overall, we collected variables such as, gender, age, marital status, study level, vaccination, number of vaccine doses, type of vaccine, BMI (Kg/m^2) by interview of participant. Indeed, we contacted the patients as soon as they arrived at the immunization facilities and explained the aim of our study to gain their consent. We provide them an instructive brochure to familiarise them with our aims, as well as an informed consent letter. When they gave their consent, we provided them a survey sheet to fill out, and a venous blood sample was taken in their arms using a 5 ml EDTA tube.

While, Anti-HBs, Anti-HBc in blood samples were performed after blood was aliquoted before being kept in a freezer at -20° Celsius. An algorithm consisting of three (03) different immunochromatographic assays emphasising anti-HBs and anti-HBc. The positivity result was kept if it was positive on at least two (02) tests, whereas the negativity result was kept if it was negative on at least two (02) tests. All positive

results were confirmed by ELISA and validated by an electrochemiluminescence assay (Cobas e 411).

Bias: To address selection bias, all included participants were submitted to inclusion criterion. to avoid information bias, we well-designed our protocol for data collection and were appropriate define exposure (taking the HB vaccine) and outcome (having Anti-HBs greater than or equivalent to 10 IU/L).

Study size: The minimum study sample size was 153 participants. The calculation of this sample size was made using 11.2% HBV prevalence in Cameroon, [4] this calculation was made using the following formula: $n=P(1-P)(Z_{1-\alpha})^2/i^2$ [12] (with Z1-α= 1.96; i= 0.05; P =prevalence of HBV in Cameroon).

2.3 Data Analysis

The data was entered into Excel 2013 and analysed with Epi Infos 7 software version 7.1.3.3. To represent qualitative data, proportions were used. The logistic regression was utilised with a significance level of 5% to determine the risk factors for non-immunization at a 95% confidence interval.

3. RESULTS

Participants: Our study included 330 participants, the mean ± SD age was 29.7±8.9 years, within the range (21-62) years. Of these participants 158 received three doses of vaccine, 11 received two doses of vaccine, 21 received one dosage of vaccine, and 140 did not receive any dose of the vaccine (Fig. 1).

3.1 Descriptive Data

Distribution of anti-HBs according to vaccination status: Overall, Anti-HBs were shown to be positive in 154/190 (81.01%) of participants who received one, two, or three doses of vaccination and positive in 26/140 (18.99%) who did not receive any dose of the vaccine (Fig. 2).

Distribution of anti HBs according to the number of doses of the vaccine: Overall participants who received tree doses of vaccine had 107/158 (83.59%) rate to positive anti HBs (Fig. 3).

Distribution of Anti-HBc according to vaccination status: Anti-HBc was positive in 7/107 (6.67%) of participants who also tested positive for anti-HBs. The distribution of anti-HBc according to the vaccination status reveals that anti-HBc was found positives in 131/140 (93.33%) of non-vaccinated participants (Fig. 4).

Description of participants according to sociodemographic and clinical characteristics*:* Overall, among the 330 participants included in this study, Yaoundé had the highest proportion of vaccined participants with tree dose of vaccine 46.13% The female gender was the most common, accounting for 42.11% in this group. The most prevalent age group was [20-30] years was representing with 45.18% in those who received tree dose of vaccine. The public sector had the highest representation, accounting for 42.8% and the most represented marital status was that of single people with 44.84% The level of study most represented was the Baccalaureate with 58.33% among those who received tree dose of vaccine (Table 1).

The body mass index was represented by overweight (25 – 29) with 44.52% of vaccined participants with tree dose of vaccine, 67.72% of these received three doses of vaccine. The type of vaccine most recommended was EUVAX with 56% among this group (Table 1).

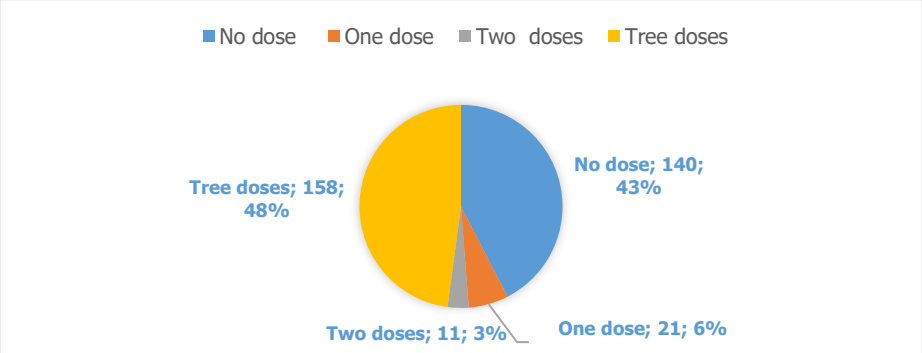

Fig. 1. Distribution of participants by vaccine dose

Table 1. Sociodemographic and clinical data of participants

Sociodemographic and clinical variables	Vaccination (Tree doses) N=158 (%)	Vaccination (None, one and two doses) N= 172 (%)
Study sites		
Yaounde	143 (46.13)	167 (53.87)
Obala	8 (72.73)	3 (27.27)
Mbalmayo	7 (77.78)	2 (22.22)
Gender		
Male	78 (55.71)	62 (44.29)
Feminine	80 (42.11)	110 (57.89)
Age (years)		
[20 – 30[	89 (45.18)	108 (54.82)
[30 – 40[	49 (43.75)	63 (56.25)
[40 – 50[	2 (100.00)	0 (0.00)
≥50	18 (94.74)	1 (5.26)
Occupation		
Public sector	107 (42.80)	143 (57.20)
Informal sector	22 (44.00)	28 (56.00)
Pupil/student	29 (96.67)	1 (3.33)
Marital status		
single	139 (44.84)	171 (55.16)
Divorced	19 (95.00)	1 (5.00)
Study level		
GCE Ordinary Level	21 (42.00)	29 (58.00)
GCE Advance Level	70 (58.33)	50 (41.67)
Bachelor	28 (40.00)	42 (60.00)
Master	19 (63.33)	11 (36.67)
PhD	20 (33.33)	40 (66.67)
BMI (Kg/m²)		
Normal (18.5 – 24)	70 (48.28)	75 (51.72)
Overweight (25 – 29)	69 (44.52)	86 (55.48)
Obesity (≥30)	19 (63.33)	11 (36.67)
Vaccination		
Yes	128 (67.37)	62 (32.63)
No	30 (21.43)	110 (78.57)
Number of vaccine doses		
1	11 (52.38)	10 (47.62)
2	10 (90.91)	1 (9.09)
3	107 (67.72)	51 (32.28)
None	30 (21.43)	110 (78.57)
Type of vaccine		
EUVAX	28 (56.00)	22 (44.00)
HEPATITIS	8 (40.00)	12 (60.00)
GENEVAC	19 (95.00)	1 (5.00)
I don't know	73 (73.00)	27 (27.00)

GCE: General Certificate of Education

Table 2. Assessment of non-immunization in patients who received 3 vaccine doses according to sociodemographic data

Sociodemographic variables	Immunization		OR (95% CI)	P- value
	No N=51 (%)	Yes N= 107 (%)		
Study sites				
Yaounde	48 (33.57)	95 (66.43)	2.02 (0.59 – 6.94)	0.38
Obala	1 (12.50)	7 (87.50)	0.28 (0.02 – 1.68)	0.43
Mbalmayo	2 (28.57)	5 (71.43)	0.83 (0.16 – 4.10)	0.99
parenting				
Yes	40 (33.61)	79 (66.39)	1.28 (0.60 – 2.76)	0.56
No	11 (28.21)	28 (71.79)	0.77 (0.36 – 1.66)	0.56
Gender				
Male	22 (31.88)	47 (68.23)	0.96 (0.49 – 1.85)	0.99
Feminine	29 (32.58)	60 (67.42)	1.03 (0.52 – 2.01)	0.99
Age (years)				
[20 – 30[	23 (30.26)	53 (69.74)	0.83 (0.43 – 1.61)	0.61
[30 – 40[	27 (44.26)	34 (55.74)	2.41 (1.24 – 4.80)	0.01
[40 – 50[	1 (33.33)	2 (66.67)	1.05 (0.07 – 9.19)	0.55

Sociodemographic variables	Immunization		OR (95% CI)	P- value
	No N=51 (%)	Yes N= 107 (%)		
≥50	0 (0.00)	18 (100.00)	-	0.004
Occupation				
Woker	51 (36.96)	87 (63.04)	-	0.0005
Pupil/student	0 (0.00)	20 (100.00)	-	0.0005
Marital status				
Single	50 (36.23)	88 (63.77)	10.80 (1.78 – 114.8)	0.004
Divorced	1 (5.00)	19 (95.00)	0.09 (0.008 – 0.56)	0.004
Study level				
GCE Advance Level	28 (35.44)	51 (64.56)	1.33 (0.66 – 2.57)	0.49
Bachelor	2 (6.90)	27 (93.10)	0.12 (0.02 – 0.48)	0.0008
Master	11 (36.67)	19 (63.33)	1.27 (0.57 – 2.84)	0.66
PhD	10 (50.00)	10 (50.00)	2.36 (0.87 – 6.40)	0.07

GCE: General Certificate of Education

Table 3. Assessment of non-immunization in patients who received 3 vaccine doses according to clinical data

Clinical variables	Immunization		OR (95% CI)	P- value
	No N=51 (%)	Yes N= 107 (%)		
BMI (Kg/m²)				
Normal (18.5 – 24)	25 (30.12)	58 (69.88)	0.81 (0.42 – 1.54)	0.61
Overweight (25 – 29)	15 (27.27)	40 (72.73)	0.69 (0.33 – 1.40)	0.37
Obesity (≥30)	11 (55.00)	9 (45.00)	2.99 (1.13 – 7.27)	0.03
Personal history				
Alcoholism	50 (36.23)	88 (63.77)	10.80 (1.78 – 114.8)	0.004
Smoking	19 (41.30)	27 (58.70)	1.75 (0.88 – 3.65)	0.13
Type of vaccine				
EUVAX	12 (30.77)	27 (69.23)	0.91 (0.40 – 1.92)	0.99
HEPATITIS	11 (57.89)	8 (42.11)	3.40 (1.24 – 9.10)	0.01
GENEVAC	1 (5.00)	19 (95.00)	0.09 (0.008 – 0.56)	0.004
I don't know	27 (33.75)	53 (62.25)	1.14 (0.60 – 2.19)	0.73

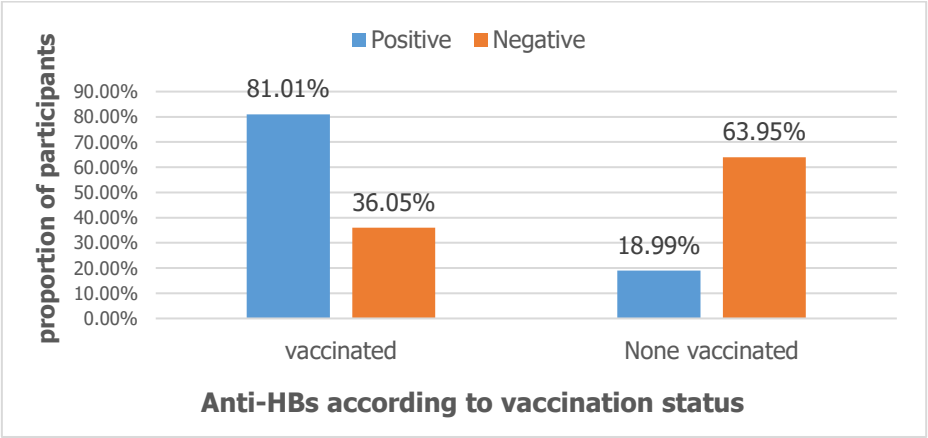

Fig. 2. Distribution of anti- HBs according to vaccination status

3.2 Outcome Data

Risk factors of non-immunization in patients having received 3 doses of vaccine according to sociodemographic data: Overall assessment of non-immunization in patients who received 3 doses of vaccine according to sociodemographic data were registered a total of 158 participants who received 3 doses of vaccines. We note that, age [30 – 40 [years [OR= 2.41; CI at 95% (1.24 – 4.80)], single [OR=10.80; CI at 95% (1.78 – 114.8)], were associated with non-immunization (Table 2).

Risk factors of non-immunization in patients having received 3 doses of vaccine according to clinical data: Risk factors of non-immunization in patients who received 3 doses of

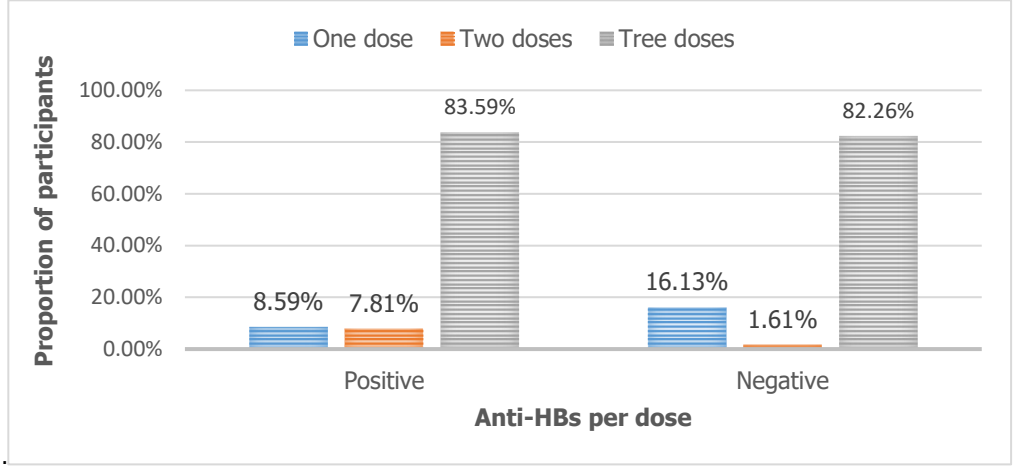

Fig. 3. Distribution of anti HBs according to vaccine doses

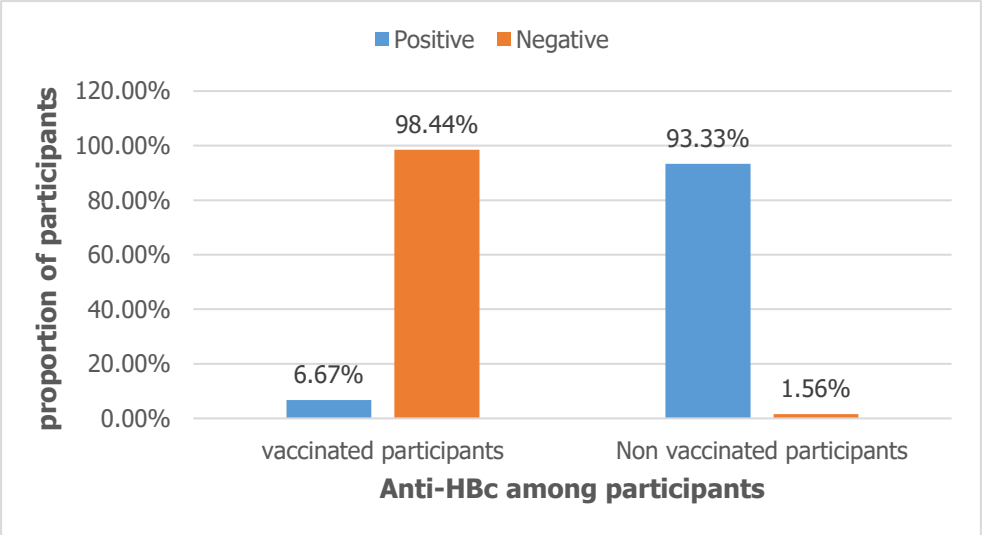

Fig. 4. Distribution of Anti-HBc according to vaccination status

vaccine based on clinical data revealed that, obesity [OR=2.99; CI at 95% (1.13 – 7.27)], alcohol [OR=10.80; CI at 95% (1.78 – 114.8)], HEPATITIS Vaccine [OR=3.40; CI at 95% (1.24 – 9.10)] were associated with non-immunization (Table 3).

4. DISCUSSION

Our study included 330 people, with women constituting the majority (57.58%). This result is similar with the study of Braka et al., who observed a 57% female ratio in Uganda in 2006. This can be explained by the fact that our research sample was largely made up of nursing workers, the majority of whom were female [13] The ages of the respondents varied from 21 to 61. This age range is identical to that described by Noah et al., Yaoundé Central Hospital, who reported a range of 21 to 57 years [14].

Our results showed a strong association between age (30-40 years) and non-response to the vaccine [OR= 2.41; CI at 95% (1.24 – 4.80)]. However, the work of Fonzo et al indicates that individuals vaccinated during adolescence, showed a protective anti-HBs titre 12.2% while 50.3% of those vaccinated in the first year of life showed a titre below the established threshold [15]. Studies have shown that teenagers who receive immunisations had higher levels of vaccine-induced immunity in terms of both antibody titer and the proportion of participants with a titer above 10 IU/L, regardless of the time interval between the last dose and the serological test [16–18]. Our results suggest that

the older age, is at risk of not responding to the vaccine, beside this factor others factors is correlated with a lower risk of titre <10 IU/L as well as an extension of time between 2nd and 3rd dose [16–20]. These results are confirmed by Stefanati et al., Verso et al; Mastrodomenico et al. [18–20]**.**

Our results showed that 8.59% of participants who received 1 dose of hepatitis B vaccine gained antibody levels anti-HBs ≥ 10 IU/L, while the study by Szmuness et al [21] in 1980 demonstrated that 31.4% of participants with 1 dose of hepatitis B vaccine gained levels of anti-HBs ≥ 10 mIU/Ml [21,22]**.** In our study, 7.81% of those who received two doses of immunisation show a seroconversion. This result is different to that Schiff et al observed. Indeed, Schiff et al observed more than 90% of seroconversion after two vaccination doses [23].The seroconversion percentage for the third vaccine dose was 67.7%, which contradicts the findings of Burgess et al in 2001, who observed a seroconversion rate of 98.1% following the last immunisation dose [24]. This difference might be explained by the fact that their research cohort was 12 to 15 years old, but ours included people beyond the age of 15.

Our results show that some participants were exposed to HBV (anti-HBc positive) respectively 6.67% of participants with a titer anti-HBs ≥ 10 IU/L and 93.33% of participants having a titer <10 IU/L. This is largely at the rate (65%) of exposure to HBV (positive anti-HBc) found in the work of Shaha et al. [25] and observed in the general population of Bangladesh (> 40%) [26]. A plausible explanation is that the study was conducted in an area with high HBV prevalence [4]. Our findings is far above (6.6%) with those of Lok et al, who reported 11.9% of anti-HBc in individuals who were positives to anti-HBs after vaccination [27]. This result suggests that, health care worker may test anti-HBc in patient before providing the HB vaccine.

5. CONCLUSION

As shown by the results of this study, non-response to HB vaccination in subjects who received 3 doses of vaccine was associated with several risk factors like intrinsic host factors, environmental factors, behavioural factors, and nutritional factors. These suggest that health care workers must consider this risk factors when providing vaccines.

This study highlights the prevalence of anti-HBc in individuals how were anti-HBs ≥ 10 IU/L and Risk factors associated with non-response to Hepatitis B vaccine in our context.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

This study was a cross-sectional study and received the approval of the regional ethics committee at N°: 1282/CRERSHC.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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