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Original Research

Risk factors associated with hepatitis B virus infection among pregnant women attending the antenatal care unit of the Bamenda Regional Hospital

Nfor Omarine Nlinwe *, Desmond Lungle

The University of Bamenda, Faculty of Health Sciences, Department of Medical Laboratory Science. P.O Box 39 Bambili, Bamenda. North West Region, Cameroon

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ABSTRACT

Objectives: Approximately 257 million people are infected with hepatitis B virus (HBV) especially in the middle and low-income countries, despite the Global Health Sector Strategy on viral hepatitis 2016–2021 which aims to eliminate viral hepatitis as a public health threat by 2030. Hepatitis B virus (HBV) remains a common public health problem in Cameroon with a high prevalence among pregnant women. Therefore, this study was designed to assess risk factors associated with hepatitis B virus infection among pregnant women attending the antenatal care unit of the Bamenda Regional Hospital.

Study design: The study was a health facility-based cross-sectional study carried out from March to May 2020. The inclusion criteria were all pregnant women who came for their first visit.

Methods: A well-structured questionnaire and laboratory test methods were used to collect data from 221 pregnant women who were consecutively enrolled in the study. The OnSite HBsAg Rapid Test (source: CTK Biotech, Inc. REF: R0040), was used to detect HBsAg in serum. Both descriptive statistics and Chi-square (and Fisher's exact) test were used for data analysis.

Results: The prevalence of HBV infection among pregnant women was 4.98% (11/221). Although knowledge, attitude and practice towards HBV by pregnant women were not significantly associated with the risk of infection, there were higher odds of poor practice ($P = 0.0152$) and attitudes ($P = 0.0016$) among those without knowledge on HBV infection.

Conclusions: Free of charge vaccination for those with negative HBsAg test results and extensive health education campaigns against HBV is recommended among pregnant women attending the antenatal care unit of the Bamenda Regional Hospital.

1. Introduction

Although the Global Health Sector Strategy on viral hepatitis 2016–2021 targets to eliminate viral hepatitis as a public health threat by 2030, there is rather an increase in the number of deaths caused by hepatitis [1]. About 257 million people are infected with hepatitis B virus (HBV) especially in the middle and low-income countries [2], with an approximate 2.7 million annual death rate from hepatitis-related deaths [3]. Hepatitis B virus (HBV) causes a common public health problem in Cameroon and across sub-Saharan Africa [4]. In the Limbe and Muyuka health districts of Cameroon, the prevalence of HBV infection among pregnant women was reported to be 5.7% and 7.5% respectively [5]. While all the women in this study assumed poor practices towards HBV, those in the Muyuka health district lacked adequate knowledge of HBV. Being married, increasing age, lack of knowledge, and poor practices toward HBV were potential risk factors [5]. In Uganda, antenatal education was recommended because most pregnant women showed excessively low knowledge and misconceptions about HBV [6]. Studies have reported a significant relationship between knowledge on the transmission/prevention of HBV and the spread of the infection [6,7]. HBV-infected patients were found to lack basic knowledge on the management and control of the disease, a risk factor for the spread of the infection.

Other significant risk factors were found to be involved in sexual activities below 19 years of age, history of multiple sex partners, and sexually transmitted infections [7]. A previous study in the Far North Region of Cameroon which reported a low rate of both HBsAg and HBeAg occurrence projected that perinatal transmission may not be common in that area [8]. Likewise, expected risk factors were found to have no significant outcome in a study with HBsAg prevalence of 12.5%

* Corresponding author.
E-mail addresses: omarinenlinwe@yahoo.ca, omarinenlinwe@yahoo.ca (N.O. Nlinwe), desmondlunglewi8@gmail.com (D. Lungle).

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[9]. Although risk factors were not found to be significantly associated with HBsAg positivity among pregnant women in the Buea Health District in Cameroon [10], HBV infection in pregnant women has been associated with the risk of mother-to-child transmission. With the high (9.7%) prevalence of HBsAg, there was equally a higher chance of mother-to-child transmission [10]. The high (11%) prevalence of HBsAg among pregnant women in Makurdi, Nigeria, also suggested a high risk of vertical transmission [11]. In fact, in areas of high endemicity, the most common means of hepatitis B transmission is from mother to child at birth (perinatal transmission) or by contact with infected blood from a child to an uninfected child below five years of age [2,12].

Statistics show that up to 40% of the world's chronic carriers in areas of endemicity were infected through maternal to fetal transmission [13], hence the major mode of HBV transmission in endemic areas [14,15]. Therefore, the effective implementation of preventive measures against perinatal transmission is crucial in the global fight against hepatitis B viral infection, especially in endemic regions. As earlier presented the prevalence of HBV among pregnant women in Cameroon is generally high [4,5,8,16]. Likewise in the northwest region, the incidence of HBV has also been high with a prevalence of 12.6% reported among HIV patients initiating treatment from January 2005 to March 2010 [17]. In 2014 the prevalence of HBV among pregnant women attending antenatal clinics in this region was 7.7% [18]. Meanwhile, in 2015 the prevalence of HBV among pregnant women residing in the Bamenda Health District was 6.0% [4]. Good knowledge and practices toward the HBV were shown to have a significant effect on the infection [4]. Hence in the current study area, there seems to be a reduction in the prevalence of HBV over the years. But to achieve the target of reducing the number of new cases by 90%, by 2030 [19], risk factors associated with perinatal transmission of HBV should be identified and substantially reduced. Therefore, this study was designed to assess risk factors associated with hepatitis B virus infection among pregnant women attending the antenatal care unit of the Bamenda Regional Hospital.

2. Methods

2.1. Study area and study population

This study was carried out at the maternity unit of the Bamenda Regional Hospital (BRH) which is located in the North West Region of Cameroon, Mezam Division, precisely in the Mezam I Sub Division. The approximate population of inhabitants in the Mezam Division is 575,312, with the BRH serving as a referral hospital for the five health districts in this Division. The study population is made up of diverse cultural and religious backgrounds, educational levels, and social statuses [20]. The maternity unit of the BRH has a fully functioning labor room and maternity ward. This unit is taken care of by two obstetricians, three general practitioners, 12 midwives, and nurses. In this unit, the average number of births per month is 320.

2.2. Study design and study participants

This was a health facility-based cross-sectional study carried out from March to May 2020. The inclusion criteria were all pregnant women who came for their first visit at the maternity unit of the BRH, within the study period. The health facility-based study setting was chosen because of the required study population of pregnant women who register for regular antenatal care visits. Moreover, data collected at a specific point in time was deemed adequate to establish a diagnosis of hepatitis B virus, hence justifying the choice of a cross-sectional study design. The inclusion criteria for the study were all pregnant women who came for their first visit at the antenatal care unit of the Bamenda Regional Hospital, within the study period. This is because testing for hepatitis B virus has been made a routine test for all the pregnant women on their first antenatal care visit, at the Bamenda Regional Hospital. Consequently, there were no exclusion criteria. A total of 240 pregnant women registered for their first-time visit during the study period and all were approached with a request to take part in the study. However, 221 (92.1%) gave consent to participate in the study by signing the informed consent form and they were consecutively enrolled in the study.

The minimum sample size for this study was calculated using Fisher's formula:

$$N \text{ (minimum sample size)} = Z^2 \times P\ (1\text{-}P)/d^2$$

Previous prevalence (P) = 7.5% (5)

The error margin (d) used is 0.05, at a 95% interval (Z = 1.96)

Therefore the estimated minimum sample size is approximately 107.

2.3. Ethical consideration

Ethical clearance for this study was gotten from the Ethical Review Committee of the University of Bamenda (the number is 2020/00117H/UBa/IRB). Signed informed consents were gotten from those who accepted to be enrolled in the study.

2.4. Laboratory test methods and data analysis

The OnSite HBsAg Rapid Test (source: CTK Biotech, Inc. REF: R0040), with a lateral flow chromatographic immunoassay, was used to detect HBsAg in serum [21]. Data were obtained using a well-structured questionnaire which was designed for the research and from laboratory analysis. Questions in the questionnaire elicited data to cover the objectives of the study. A four-point Likert-type rating scale [22] was used for the scoring of the knowledge on hepatitis B. The Likert-type rating scale was used because it allows respondents to express their opinion and allows them to be neutral if necessary. The points on the Likert-type rating scale for knowledge on the transmission, signs, and symptoms of hepatitis B were; I don't know, strongly disagree, disagree, agree, and strongly agree. The rating which ranged from 0 to 4 was based on the accuracy of the responses. The midpoint (a cut-off mean) was gotten by adding 4, 3, 2, and 1, and then dividing the sum by 4 to have 2.5 [22]. Means which were more than 2.5 were interpreted as knowledgeable on the transmission, signs, and symptoms of hepatitis B.

Frequencies (sums and percentages) were calculated for the socio-demographic factors and the different attitudes and practices toward hepatitis B. A fourfold (2 × 2) contingency table displaying the frequency distribution for knowledge, attitude, and practice toward HBV was entered into Graph Pad Prism version 8.2.1. In each of the four cells, the contingency table had frequencies for knowledge, attitude, and practice by both HBV positive and negative cases. Chi-square (and Fisher's exact) test was used to determine the relative risk, attributable risk, odds ratio, and likelihood ratio of HBV occurrence in exposed groups. The sensitivity and specificity for the prediction of risk of HBV in exposed pregnant women were also determined by Chi-square (and Fisher's exact) test. Regression analysis was used to determine the effect of socio-demographic factors on knowledge of HBV infection.

3. Results

The prevalence of HBV infection among pregnant women was 4.98% (11/221). Up to 59.28% of the pregnant women were among the 27–38years age group, while most were urban dwellers (68.33%), married (82.81%), and Christians (93.21%). Although 60.18% of the women were college graduates, 54.75% (121/221) were housewives and 61.09% (135/221) were in the low (<30,000 F RS) monthly income class (Table 1).

Out of the 221 pregnant women, 48.87% (108/221) knew about the hepatitis B virus. While 59.28% (131/221) have not heard of a disease caused by hepatitis B virus, 33.94% (75/221) do not know that hepatitis B can cause liver cancer and 62.9% (139/221) agreed/strongly agreed

Table 1
Socio-demographic information among pregnant women attending ANC.

		Pos (%)	Neg (%)	Column total (%)
	Row total	11 (4.98)	210 (95.02)	221
Age (in years)	15–26	3 (3.66)	79 (96.34)	82 (37.1)
	27–38	8 (6.11)	123 (93.89)	131 (59.28)
	39–49	0	8 (100)	8 (3.62)
Residence	Urban	7 (4.64)	144 (95.36)	151 (68.33)
	Rural	4 (5.71)	66 (94.29)	70 (31.67)
Marital status	Single	1 (2.94)	33 (97.06)	34 (15.38)
	Married	9 (4.92)	174 (95.08)	183 (82.81)
	Widowed	1 (33.33)	2 (66.67)	3 (1.36)
	Divorced	0	1 (100)	1 (0.45)
Religion	Orthodox	0	5 (100)	5 (2.26)
	Muslim	0	9 (100)	9 (4.07)
	Christian	11 (5.31)	196 (94.69)	207 (93.21)
Educational status	No formal education	0	2 (100)	2 (1.36)
	Able to read and write	0	18 (100)	18 (8.14)
	Elementary education	2 (7.69)	24 (92.31)	26 (11.76)
	Secondary education	4 (9.52)	38 (90.48)	42 (19)
	College	5 (3.76)	128 (96.24)	133 (60.18)
Occupational status	Self-employed	2 (8.7)	21 (91.3)	23 (10.41)
	Government employed	2 (5.41)	35 (94.59)	37 (16.74)
	Housewife	5 (4.13)	116 (95.87)	121 (54.75)
	Not employed	2 (5)	38 (95)	40 (18.1)
Monthly income (FRS)	<30,000	6 (4.44)	129 (95.56)	135 (61.09)
	30,000–250,000	5 (6.49)	72 (93.51)	77 (34.84)
	>250,000	0	9 (100)	9 (4.07)

that hepatitis B can affect all age groups. 56.56% (125/221) agreed/strongly agreed that hepatitis B can be transmitted from mother to child, 68.78% (152/221) agreed/strongly agreed that hepatitis B is curable and 77.38% (171/221) agreed/strongly agreed that vaccine is available for hepatitis B (Table 2).

The pregnant women with urban residence had more knowledge (P = 0.0254) than those who lived in rural areas, likewise those with higher educational status (P = 0.0004) and monthly income (P = 0.0252) (Table 3).

Up to 78.28% (173/221) of the pregnant women will go to a health facility if they found out they have hepatitis B and 74.21% (164/221) would communicate to a physician about their illness. Also, 92.76% (205/221) will go to a health facility as soon as they realize they have symptoms of hepatitis B. Generally 44.8% (99/221) of the women did not know the cost of diagnosing and treating hepatitis B, meanwhile, 18.55% (41/221) thought it is expensive. The worry of most (36.36%) of those who tested positive for HBsAg was the fear of death while most (42.38%) of those who tested negative were afraid of transmitting the disease to family members if diagnosed with hepatitis B. All (100%) of those who tested positive thought they could get hepatitis B and only 18.18% (2/11) thought they are infected with hepatitis B. However 72.38% (152/210) of those who tested negative thought they could get it while only 0.48% (1/210) thought she is infected with hepatitis B (Table 4).

Table 2
Knowledge on hepatitis B virus among pregnant women attending ANC.

	Num (%) Knowledgeable = 108 (48.87%)				
	I don't know (%)	Strongly Disagree (%)	Disagree (%)	Agree (%)	Strongly Agree (%)
Have you heard of a disease caused by the hepatitis B virus?	0	98 (44.34)	33 (14.93)	43 (19.46)	55 (24.89)
Can hepatitis B affect the liver?	61 (27.6)	22 (9.95)	14 (6.33)	54 (24.43)	69 (31.22)
Can hepatitis B cause liver cancer?	75 (33.94)	33 (14.93)	22 (9.95)	45 (20.36)	46 (20.81)
Are nausea, vomiting, and loss of appetite common symptoms of hepatitis B?	89 (40.27)	38 (17.19)	34 (15.38)	40 (19.05)	20 (9.52)
Can hepatitis B affect all age groups?	50 (22.62)	27 (12.22)	5 (2.26)	47 (21.27)	92 (41.63)
There is no symptom of hepatitis B in some patients?	72 (32.58)	48 (21.72)	21 (9.5)	43 (19.46)	37 (16.74)
Can hepatitis B transmit through contaminated blood?	57 (25.79)	33 (14.93)	15 (6.79)	37 (16.74)	79 (35.75)
Can hepatitis B be transmitted by blades of ear or nose pierces?	59 (26.7)	33 (14.93)	26 (11.76)	38 (17.19)	65 (29.41)
Can hepatitis B be transmitted by unsafe sex?	58 (26.24)	40 (18.1)	19 (8.6)	39 (17.65)	65 (29.41)
Can hepatitis B be transmitted from mother to child?	54 (24.43)	26 (11.76)	16 (7.24)	54 (24.43)	71 (32.13)
Is hepatitis B curable/ treatable?	48 (21.72)	11 (4.98)	10 (4.52)	86 (38.91)	66 (29.86)
Is vaccination available for hepatitis B?	36 (16.29)	6 (2.71)	8 (3.62)	56 (25.34)	115 (52.04)

Table 3
Regression analysis on the effect of sociodemographic factors on knowledge of HBV infection.

Variable	|t|	P value	*P*-value summary
Intercept	1.105	0.2705	Ns
B: Age (in years)	0.5625	0.5744	ns
C: Residence	2.253	0.0254	*
D: Marital status	0.4238	0.6722	ns
E: Religion	0.8833	0.3781	ns
F: Educational status	3.626	0.0004	***
G: Occupational status	0.4211	0.6741	ns
H: Monthly income	2.254	0.0252	*

|t| = t value, ns = not significant P value, * = significant P value.

Up to 63.64% (7/11) of the women who tested HBV positive and 57.14% (120/210) of those who tested negative had earlier screened for hepatitis B. Generally 53.39% (118/221) asked their barber to change the blade while 91.86% (203/221) would go for further investigation and treatment when diagnosed with hepatitis B. 36.66% (4/11) of those who tested hepatitis B positive indicated to have been vaccinated while only 26.19% (55/210) of those who tested negative were vaccinated (Table 5).

Table 4
Attitude towards hepatitis B virus among pregnant women attending ANC.

Row Total		Pos (%), N = 11	Neg (%), N = 210
What would be your reaction if you found that you have hepatitis B?	Fear	0	6 (2.86)
	Sadness	1 (9.09)	8 (3.81)
	Go to the health facility	7 (63.64)	166 (79.05)
	Multiple actions	3 (27.27)	30 (14.29)
Whom would you communicate to about your illness?	Physician	9 (81.82)	155 (73.81)
	Parents	0	4 (1.9)
	Husband	1 (9.09)	43 (20.48)
	No one	1 (9.09)	8 (3.81)
What will you do if you think that you have symptoms of hepatitis B?	Go to the health facility	10 (90.91)	206 (98.1)
	Go to traditional healers	1 (9.09)	2 (0.95)
	Go to health facility and traditional healers	0	2 (0.95)
If you had symptoms of hepatitis B, at what stage would you go to the health facility?	As soon as I realized the symptoms	10 (90.91)	195 (92.86)
	After 2–4 weeks of the appearance of the symptoms	1 (9.09)	7 (3.33)
	After my treatment fails	0	5 (2.38)
	Will not go to the health facility	0	3 (1.43)
How expensive do you think is the diagnosis and treatment of hepatitis B	Cheap	1 (9.09)	6 (2.86)
	Free	0	9 (4.29)
	Moderately expensive	1 (9.09)	42 (20)
	Expensive	4 (36.36)	37 (17.62)
	I do not know	5 (45.45)	94 (44.76)
What worries you if you are diagnosed with hepatitis B?	Cost of treatment	2 (18.18)	25 (11.9)
	Fear of transmitting the disease to family members	1 (9.09)	89 (42.38)
	Fear of death	4 (36.36)	37 (17.62)
	Fear of discrimination by the society	0	3 (1.43)
	Multiple fears	1 (9.09)	31 (14.76)
	Nothing to worry about	3 (27.27)	25 (11.9)
Do you think you can get hepatitis B?	Yes	11 (100)	152 (72.38)
	No	0	58 (27.62)
Do you think you have hepatitis B?	Yes	2 (18.18)	1 (0.48)
	No	9 (81.82)	209 (99.52)

Lack of knowledge on HBV and poor practice towards HBV was not significantly associated with the odds of being infected with HBV. The attributable risk indicates that 10% of HBV infections were significantly (P = 0.0003) caused by poor attitude towards HBV. From the specificity, 46.19% of those with good attitudes were significantly (P = 0.0003) not at risk of HBV infection. Those with no knowledge of HBV infection had significantly higher odds of having poor attitudes and practice toward HBV (Table 6).

Table 5
Practice towards hepatitis B virus among pregnant women attending ANC.

	Pos (%), N = 11		Neg (%), N = 210	
	Yes (%)	**No (%)**	**Yes (%)**	**No (%)**
Have you done the screening for hepatitis B before now?	7 (63.64)	4 (36.36)	120 (57.14)	90 (42.86)
Do you ask your barber to change the blade?	8 (72.73)	3 (27.27)	110 (52.38)	100 (47.62)
When diagnosed with hepatitis B, would you go for further investigation and treatment?	10 (90.91)	1 (9.09)	193 (91.9)	17 (8.1)
Have you got yourself vaccinated against hepatitis B?	4 (36.36)	7 (63.64)	55 (26.19)	155 (73.81)
Do you avoid meeting hepatitis B patients?	4 (36.36)	7 (63.64)	86 (40.95)	124 (59.05)

4. Discussion

The 4.98% prevalence of HBV among pregnant women in the current study could be considered high especially with the possibility of perinatal transmission. Findings from an earlier study carried out five years ago reported a higher prevalence of 6% among pregnant women in the Bamenda health district [4]. However compared to findings from a study in the South-West and Far-North regions of Cameroon, the prevalence of HBV in the recent study is relatively low. The prevalence of HBV among pregnant women was 5.7%, 7.5%, and 9.7% in Limbe, Muyuka, and Buea respectively, all located in the South-West region [5,10]. A higher prevalence of 10.2% and 20.4% among pregnant women was reported in a rural settlement, in the Far North region [8,23]. The lower prevalence in the current study confirmed findings from a previous study that categorized the North-West region under low HBV seroprevalence [24]. The Far-North and South-West regions were categorized under high and medium HBV seroprevalence respectively [24]. The prevalence of HBsAg among pregnant women in Eastern parts of Germany was low (0.48%) [25], compared to the current study. This may be expected since Cameroon falls under the middle and low-income countries with a higher prevalence of HBV [2].

In the current study, the prevalence of HBV was higher among those who resided in the rural area (5.71%: 4/70) than in the urban area (4.64%: 7/151). Also, HBV was significantly high in a rural setting in the Far-North region of Cameroon [8,23]. In the Southeastern region of Turkey, the prevalence of HBsAg was higher in the rural setting, with the low educational level being a risk factor in the urban areas [26]. Another study in Iran also reported a higher prevalence of HBV in rural settings and among those with low educational levels [27]. Contrary to the current study, HBsAg was significantly higher in urban than rural populations in Gabon [28]. Urban residence, high educational level, and increased monthly income had significant effects on increase knowledge on HBV among the pregnant women in this current study. However, only 48.87% of the pregnant women in the current study knew hepatitis B. The lack of knowledge, poor practice, and attitude towards HBV was not significantly associated with the risk of infection. But the higher odds of poor practice (P = 0.0152) and attitudes (P = 0.0016) among those without knowledge on HBV (Table 6) suggest higher chances for future risk. In Northern and Central Uganda, pregnant women without knowledge on prevention/transmission of HBV were more at risk [6]. Also, the lack of knowledge on HBV was a risk factor for infection among pregnant women in Lagos, Nigeria [7], and in the Eastern parts of Germany [25].

In the current study, although the attitudes of the pregnant women towards hepatitis B were generally good, it remains disturbing that some of the women still had poor attitudes. For example, 25.79% (57/221) of the women opted that they will not communicate to a physician about their illness, while 44.8% (99/221) do not know the cost of diagnosing and treating HBV. The practice towards HBV by some of the women was

Table 6
Risk of HBV infection among pregnant women.

Risk of poor attitude, practice, and no knowledge on HBV infection.							
Variable	Relative Risk (95%)	Attributable Risk (95%)	Odds Ratio (95%)	Sensitivity (95%)	Specificity (95%)	LR	*P*-value
Not Knowledgeable	1.67 (0.54–5.24)	0.023 (−0.04-0.1)	1.72 (0.53–5.36)	63.64 (35.38–84.83)	49.52 (42.83–56.23)	1.26	0.5395
Poor Attitude	0 (0–0.33)	0.1 (0.02–0.16)	0 (0–0.33)	0 (0–25.88)	46.19 (39.58–52.94)	0	0.0003***
Poor Practice	0.92 (0.31–2.76)	0 (−0.06-0.08)	0.92 (0.31–3.24)	45.45 (21.27–71.99)	52.38) (45.64–59.03)	0.95	>0.9999
Risk of no knowledge of HBV on poor attitude and practice toward HBV							
Variable	**Relative Risk (95%)**	**Attributable Risk (95%)**	**Odds Ratio (95%)**	**Sensitivity (95%)**	**Specificity (95%)**	**LR**	***P*-value**
Poor Attitude	2.05 (1.46–18.74)	0.52 (0.16–0.58)	Infinity (3.02-infinity)	8.85 (4.88–15.53)	100 (96.57–100)	–	0.0016**
Poor Practice	1.43 (1.08–1.92)	0.17 (0.03–0.3)	1.98 (1.14–3.38)	60 (50.44–68.86)	56.9 (47.81–65.54)	1.39	0.0152*

*Significant P values.

also poor. Up to 42.53% (94/221) of the pregnant women had not done the screening for HBV even though they have been sexually active. Although 54.3% (120/221) had earlier screened and tested negative for HBV, only 45.83% (55/120) got themselves vaccinated against HBV while up to 54.17% (65/120) did not. This demonstrates poor practice towards HBV and also indicates a lack of post-screening follow-up. Instead, 36.36% (4/11) of those who tested positive and did not need the vaccine, had been vaccinated. The cost of the vaccine and lack of knowledge are the possible reasons for the lack of vaccination by some of those who had earlier been tested negative. As earlier indicated, the cost of the vaccine has contributed to the high infection rates in poor countries [29].

5. Conclusion

The seroprevalence of HBsAg among the pregnant women attending the antenatal care unit of the Bamenda Regional Hospital was 4.98% (11/221). Knowledge, attitude, and practice towards HBV by pregnant women are not significantly associated with the risk of infection. However, there are higher odds of poor practice and attitudes among those without knowledge of HBV infection. The current practice of routine screening of pregnant women and free-of-charge vaccination of all babies against HBV in the study area is highly commendable. Nevertheless, to ensure rational control and management of the disease among pregnant women, free-of-charge vaccination should immediately be given to those with negative test results. Extensive health education campaigns against HBV are also recommended during antenatal care visits.

Limitation of study

Because this study had a relatively small sample size and was a cross-sectional study carried out in a single center, it is difficult to make causal inferences.

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Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Conflict of interest and authorship conformation form

✓ All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

✓ This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue.

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