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PREVALENCE OF HEPATITIS B VIRUS AND FACTORS ASSOCIATED AMONG PREGNANT WOMEN IN ADEN CITY-YEMEN

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ABSTRACT

Background: Viral hepatitis during pregnancy is associated with a high risk of maternal complications. Screening for Hepatitis B during pregnancy may help to decide on appropriate antiviral therapy and the institutions to minimize vertical transmission to the newborn infants. **Methods:** A cross-sectional study was conducted during the study period from 12th January to 12th April 2018, a total of 230 pregnant mothers attended the Maternal-Child Health Care at Aden city-Yemen were enrolled in the study. The OnSite HBV 5-Parameter Rapid Test is a chromatographic immunoassay for the qualitative detection of HBsAg, HBsAb, HBeAg, HBeAb, and HBcAb in human serum or plasma. It was intended to be used as a screening test and as an aid in the diagnosis of infection with HBV. Structured questionnaires were used to obtain sociodemographic, obstetrics and medical data (age, education levels, Gestational age, Parity, history of miscarriage, blood transfusion, surgery, Circumcision, dental manipulation and traditional scar) and venous blood was collected and sera was tested for HBV-markers. **Results:** Of the 230 pregnant women enrolled in the study, HBsAg was detected in 25(10.9%) women, HBeAg, HBsAb, HBeAb and HBcAb were detected in (0%, 21.7%, 1.7% and 11.7%), respectively. Univariate analysis and Chi squire test showed that blood transfusion, surgical manipulation and circumcision was significantly associated with HBsAg seropositivity (0.000, 0.000 and 0.004), respectively, the parity and the education level were significantly associated with HBsAg seropositivity (0.03 and 0.000), respectively by Univariate analysis. **Conclusion:** The results of this study suggest that HBsAg have high prevalence among pregnant women in Aden city.

KEYWORDS: Hepatitis B virus surface antigen, Prevalence, Pregnant women, Aden.

INTRODUCTION

Hepatitis B is the most common serious liver infection caused by a double stranded deoxyribonucleic acid (DNA) virus, whose main routes of transmission are: blood transfusion and other blood contact related activities, via open wounds, sexual contact and mother to child (Cheesbrough, 2006).

Mother to infant (vertical) transmission from HBV-infected mother is the commonest mode of transmission worldwide and accounts for 50–60% of chronically infected patients. It is estimated that up to 25% of these patients die prematurely from the complications of chronic HBV infection in later life (cirrhosis, liver failure, liver cancer) *(Beasley, et al., 1981 & McMahon, et al., 1990).*

The risk of perinatal transmission of HBV is related to maternal HBV-DNA levels and the hepatitis B e antigen (HBeAg) status of the mother. Without immunoprophylaxis, vertical transmission occurs in 70–90% if the mother is HBeAg positive (Beasley, et al., 1977). This is reduced to 40% if the mother is HBeAg negative (Alter, 2003). Overall, vertical transmission is reduced to 5–10% with appropriate active and passive immunoprophylaxis (hepatitis B vaccination for all plus hepatitis B immunoglobulin (HBIG) if the mother is HBeAg positive).

However, in infants born to mothers with high HBV-DNA levels, despite immunoprophylaxis 8–32% of infants develop perinatal infection (Van Zonneveld, et al., 2003 & Wiseman, et al., 2009).

Justification of thestudy

No published data are available about prevalence of HBV among pregnant women in Aden city-Yemen. Prenatal screening of HBV provide strategy for both early management of the infects pregnant women as well as vaccination of children in the first 24 hours of life by passive-active immunization, this would prevent the risk of progression into chronic hepatitis & its sequelae. Therefore, this study was aimed at estimating prevalence of hepatitis B virus and factors associated among

pregnant women in Aden city-Yemen.

Methods

Study design, period and area

This was a cross-sectional study conducted for 3 month period at the Maternal-Child Health Care (MCH) in Aden city. Most of these pregnant women would come for a follow up visit. Aden city is located 490 Km southeast of Sana'a. Health institutions in the Zone include: three general hospitals and 7 directorates each has one Maternal-Child Health Care.

Sample size calculation and sampling procedures

A total of 230 pregnant women will be studied. Sample size for this study was calculated using the following formula:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where n= expected minimum sample

Z = standard, corresponding to 95% confidence i.e. 1.96

P= prevalence of Hepatitis B virus (10.8%) according to previous study for the prevalence of HBV in Sana'a, Yemen *(Murad, et al., 2013).*

d= maximum likely error taken as 4%. Hence, minimum sample size calculated was 231, then we approximated into 230.

A fixed questionnaire was applied to gather relevant sociodemographic characteristics (age and education level) and obstetric characteristics (gestational age and parity). Then the possible risk factors (e.g. history of blood transfusion, surgery, Circumcision, dental manipulation, miscarriage & the presence of traditional scar). After this a venipuncture was performed and 5mL blood collected in a tube for Hepatitis B serology. A mark was put in the clinic card of all enrolled mothers to avoid repeat inclusions during their subsequent visits. The OnSite HBV 5-Parameter Rapid Test (CTK Biotech, Inc. 6748 Nancy Ridge Drive, San Diego, USA) for the qualitative detection of HBsAg, HBsAb, HBeAg, HBeAb, and HBcAb in human serum or plasma was used. It is intended to be used as a screening test and as an aid in the diagnosis of infection with HBV.

Statistical Analysis: Data was entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0. Descriptive analyses, using means, percentage and frequency, were calculated. Univariate analysis and Chi-Square were employed to assess the association of factors with hepatitis B virus infection. A P-value of ≤ 0.05 was regarded as significant.

Ethical Considerations: Ethical approval for the study was given by the Ethics Review Committee at University of Science & Technology-Aden branch and from Ministry of Health at Aden-Republic of Yemen. Informed oral consent was obtained from the pregnant women who agreed to participate in the study.

RESULTS

During the study period of three months between 12th January to 12th April 2018, a total of 230 pregnant mothers attended the Maternal-Child Health Cares in Aden city were enrolled in the study. The age of the women studied ranged from 18 to 43 years with a mean of 30.6±6.9. There was a steady increase in the age groups of the women (when we grouped the age of such women) with a peak in the 38−43year 50(21.7%), a decline towards the 18−22 year age groups 38(16.5%). Table(1).

Level of education: Majority of the women tested 59(25.7%) were educated up to the secondary school & postsecondary level, while the lower frequency was seen in housewife followed by primary education level 48(20.9%) and 64(27.8%), respectively. Table (1).

The gestational age: The frequency of the gestational age of the pregnant women since it divided into first trimester, second trimester & full term was 90(39.1%), 64(27.8%) and 76(33%), respectively. Most cases were seen in the first trimester followed by full term and least extend the second trimester, Table (1).

Number of Conception (Parity): There was a steady increase in the percentage of the number of parity from primigravida, second gravida and multigravida (31.3%, 33% & 35.7%), respectively, Table (1). Those having vaccine was 56 out of the 230 pregnant women, i.e. (24.3%).

Table 1: Sociodemographic and Obstetric characteristics of pregnant women in Aden-Yemen.

Age Groups (Year)	Frequency	Percent
18-22	38	16.5
23-27	46	20.0
28-32	47	20.4
33-37	49	21.3
38-43	50	21.8
Education level:		
Housewife	48	20.8%
Primary level	64	27.8%
Secondary level	59	25.7%
Postsecondary level	59	25.7%
Trimester level:		
First trimester	90	39.2
Second trimester	64	27.8
Full term	76	33.0
Parity:		
Primigravida	72	31.3
Second gravida	76	33
Multigravida	82	35.7

History of blood transfusion, surgery, circumcision, dental manipulation, traditional scar and miscarriage:

Majority of the women tested was 151(65.7%) never had blood transfusion and 79(34.3%) had blood transfusion, also the majority of pregnant women had no surgery was 193(83.9%) and 37(16.1%) had surgery. Those having circumcision, dental manipulation, traditional scar and miscarriage was 11(4.8%), 13(5.7%), 7(3%) and 20(8.7%), respectively, Table (2).

Table 2: Most Risk factors tested in questionnaires.

Variable tested	Yes n(%)	No n(%)	Total
Blood transfusion	79(34.3%)	151(65.7%)	230(100%)
H/O surgery	37(16.1%)	193(83.9%)	230(100%)
Circumcision	11(4.8%)	219(95.2%)	230(100%)
H/O Dentalmanipulation	13(5.7%)	217(94.3%)	230(100%)
Traditional scar	7(3%)	223(97%)	230(100%)
H/O Miscarriage	20(8.7%)	210(91.3%)	230(100%)

H/O= History of.

The results of the 230 pregnant women screened for HBV using OnSite HBV 5- Parameter Rapid Test were as following: The total Seroprevalence of HBsAg was seen in 25 cases (10.9%); those having HBsAg & HBcAb positive together 10(4.3%), those only having HBsAg positive 11(4.8%) while those having HBsAg, HBeAb & HBcAb positive were 4(1.7%). The level of HBeAg and the level of HBsAb were not detected in all the twenty five women who tested positive for HBsAg, while the level of HBeAb was detected in 4 pregnant women (1.7%). The vaccinated women (i.e. HBsAg-Negative; HBsAb-Positive; HBeAg-Negative; HBeAb-Negative and HBcAb-Negative) were seen in 37(16.1%), Table (3).

Table 3: Interpretation of 5 Parameter of HBV-Serology test.

Serological Markers of HBV	Frequency	Percent
HBsAg-N; HBsAb-N; HBeAg-N; HBeAb-N; HBcAb-N (Not Infected)	155	67.4
HBsAg-P; HBsAb-N; HBeAg-N; HBeAb-N; **HBcAb-P** (Infected)	10	4.3
HBsAg-P; HBsAb-N; HBeAg-N; HBeAb-N; HBcAb-N (Infected)	11	4.8
HBsAg-N; **HBsAb-P**; HBeAg-N; HBeAb-N; HBcAb-N (Vaccinated)	37	16.1
HBsAg-N; **HBsAb-P**; HBeAg-N; HBeAb-N; **HBcAb-P** (Interpretation Unclear[1])	13	5.7
HBsAg-P; HBsAb-N; HBeAg-N; **HBeAb-P**; **HBcAb-P** (Infected & Less Likelihood of transmissibility)[1]	4	1.7
Total	230	100.0

N=for Negative; P=for Positive. 1=Interpretationunclear;fourpossibilities:

1. *Resolved infection (most common).*
2. *False-positive anti-HBcAb.*
3. *"Low level" chronicinfection.*
4. *Resolving acute infection.*

Thefrequencyofeachmarkerinseparateeventswasseenbelowin(Table4).
HBeAg was not detected in all pregnant women screened for HBV.

Table 4: Frequency of the Serological markers.

Serological markers	Frequency	Percentage
HBsAg (n=230)	25	10.9
HBeAg (n=230)	0	0
HBsAb (n=230)	50	21.7
HBeAb (n=230)	4	1.7
HBcAb (n=230)	27	11.7

The association of HBsAg with HBsAb it show a statistical significant association (χ^2=7.791, df=1, P=0.005). HBsAb was not seen in the 25 positive cases. However HBeAb was found in 4 cases of positive HBsAg with highly a statistical significance (χ^2*=33.381, df=1, P=0.000*). (Table 5).

Table 5: The Association between HBsAg with both HBsAb & HBeAb.

	HBsAb		Total	HBeAb		Total
	Positive	Negative		Positive	Negative	
HBsAg Positive	0(.0%)	25(100%)	**25(100%)**	4(16%)	21(84%)	**25(100%)**
HBsAg Negative	50(24.4%)	155(75.6%)	**205(100%)**	0(.0%)	205(100%)	**205(100%)**
Total	**50(21.7%)**	**180(78.3%)**	**230(100%)**	**4(1.7%)**	**226(98.3%)**	**230(100%)**

χ2=7.791, df=1, **P=0.005** χ2=33.381, df=1, **P=0.000**

Table (6) show the association between HBsAg with HBcAb, it show that the 25 positive HBsAg only found in 14 cases of positive HBcAb, while the 13 cases of positive HBcAb was found in negative HBsAg; this

positivity had 4 interpretations in which the most common is resolved infection as mentioned before in table (3).

Table 6: The Association between HBsAg with HBcAb.

	HBcAb		Total	P-Value
	Positive	Negative		
HBsAg Positive	14(56%)	11(44%)	**25(100%)**	**χ2=53.033, df=1, P=0.000**
HBsAg Negative	13(6.3%)	192(93.7%)	**205(100%)**	
Total	**27(11.7%)**	**203(83.3%)**	**230(100%)**	

The association between the socio-demographic and the Obstetric characteristics of the study participants and HBsAg serostatus

1) **The Association with the Age groups:** The association between HBsAg and the various age groups was evaluated and show no statistical significant (P=0.4). However, the prevalence of HBsAg was highest among 28-32year age groups i.e. (17%) and the lowest prevalence of HBsAg was seen at 33-37year age groups i.e. (4.1%). **Table (7).**
2) **The Association with Educational levels**: The association of HBsAg and the various levels of education was evaluated and it show no a statistical significant (P=0.3), while high prevalence of HBsAg was seen among primary education level (17.2%). **Table (7).**
3) **The Association with the Stage of Conception:** The association of HBsAg with the 1st trimester, 2nd trimester and the full term was evaluated and it show no a statistical significance (P=0.3), but high prevalence was seen in the 2nd trimester 10(15.6%). **Table (7).**
4) **The Association with the Number of Parity:** The association of HBsAg with the number of parity was also evaluated and it show a statistical significant (P=0.03), and the prevalence of HBsAg with number of parity either Primigravida, second gravida and multigravida was (3.9%, 10.9% and 16.7%), respectively. **Table (7).**

Table 7: The association between the socio-demographic and Obstetric characteristics of the study participants and HBsAg serostatus.

Socio-demographic characteristics		HBsAg		Total
		Positive	Negative	
Age groups (Years)	18-22	4(10.5%)	34(89.5%)	**38(100%)**
	23-27	6(13%)	40(87%)	**46(100%)**
	28-32	8(17%)	39(83%)	**47(100%)**
	33-37	2(4.1%)	47(95.9%)	**49(100%)**
	38-43	5(10%)	45(90%)	**50(100%)**
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	*χ^2=4.434, df=4, P=0.4*			
Education level	Housewife	5(10.4%)	43(89.6%)	48(100%)
	Primary	11(17.2%)	53(82.8%)	64(100%)
	Secondary	4(6.8%)	55(93.2%)	59(100%)
	Postsecondary	5(8.5%)	54(91.5%)	59(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	*χ^2=4.015, df=3, P=0.3*			
Stage of Conception	1st Trimester	9(10%)	81(90%)	90(100%)
	2nd Trimester	10(15.6%)	54(84.4%)	64(100%)
	Full Term	6(7.9%)	70(92.3%)	76(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	*χ^2=2.258, df=2, P=0.3*			
Number of Parity	Primary-gravida	3(3.9%)	73(96.1%)	76(100%)
	Second-gravida	7(10.9%)	57(89.1%)	64(100%)
	Multigravidae	15(16.7%)	75(83.3%)	90(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	***χ^2=6.881, df=2, P=0.03***			

The Seroprevalence of HBsAg in Relation to the various risk factors among pregnant women in Aden-City, 2018

The association between HBsAg with the various risk factors under study in questionnaire was evaluated, it show only a statistical significant of association between HBsAg and the history of blood transfusion & history of surgical manipulation (P=0.000 & 0.02), respectively. While the other risk factors such as history of

circumcision, dental manipulation, history of miscarriage and presence of traditional scar show no a statistical significant (P-value=0.07, 0.7, 0.4 and 0.3), respectively. (Table 8).

Table 8: The Seroprevalence of HBsAg in Relation to the various risk factors among pregnant women in Aden-City, 2018.

Risk Factors		HBsAg		Total
		Positive	Negative	
H/O Blood Transfusion	Yes	24(30.4%)	55(69.6%)	79(100%)
	No	1 (0.7%)	150(99.3%)	151(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	***χ^2=47.278, df=1, P=0.000***			
H/O Surgery	Yes	8(21.6%)	29(78.4%)	37(100%)
	No	17(8.8%)	176(91.2%)	193(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	***χ^2=5.263, df=1, P=0.02***			
H/O Circumcision	Yes	3(27.3%)	8(72.7%)	11(100%)
	No	22(10%)	197(90%)	219(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	*χ^2=3.208, df=1, P=0.07*			
Dental Manipulation	Yes	1(7.7%)	12(92.3%)	13(100%)
	No	24(11.1%)	193(88.9%)	217(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	*χ^2=0.144, df=1, P=0.7*			
H/O Miscarriage	Yes	1(5%)	19(95%)	20(100%)
	No	24(11.4%)	186(88.6%)	210(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	*χ^2=0.779, df=1, P=0.4*			
Traditional Scar	Yes	0(0.0%)	7(100%)	7(100%)
	No	25(11.5%)	198(88.8%)	223(100%)
Total		**25(10.9%)**	**205(89.1%)**	**230(100%)**
P-Value	*χ^2=0.880, df=1, P=0.3*			

H/O= History of.

Using Univariate analysis in which HBsAg as dependent variable and sociodemographic, obstetric characteristics and the possible risk factors as mentioned in questionnaires as independent variables. We found that there a statistical significant association between HBsAg with the age, level of education, gestational age and parity, (OP=0.6, 95% CI=0.013-0.187, P=0.02); (OP=0.5, 95% CI=0.005-0.165, P=0.04); (OP=0.6, 95% CI=0.008-0.149, P=0.03) and (OP=0.9, 95%.

CI=0.103-0.231, P=0.000), respectively. However, the parity show highly statistical significant with high observed power (OP). Regarding the risk factors history of blood transfusion, surgery and circumcision was highly statistical significant association with high power with the HBsAg in Univariate analysis. (Table 9).

Table 9: Univariate analyses for the socio-demographic Obstetric characteristics and possible risk factors for HBsAg among pregnant women in Aden city-Yemen.

Variable	OP	95% CI	P-Value
Age groups (Years)	0.6	0.013-0.187	0.02
Education level	0.5	0.005-0.165	0.04
Stage of Conception	0.6	0.008-0.149	0.03
Parity	0.9	0.103-0.231	0.000
H/O Blood Transfusion	1	0.242-0.366	0.000
H/O Surgery	0.9	0.116-0.316	0.000
Circumcision	0.8	0.088-0.457	0.004
Dental Manipulation	0.1	-0.094-0.248	0.4
H/O Miscarriage	0.1	-0.088-0.188	0.5
Traditional Scar	0.05	-0.232-0.232	1.000

OP=Observed Power.

DISCUSSION

The overall Seroprevalence HBsAg in our study was seen in 25 cases (10.9%); those having HBsAg & HBcAb positive together 10(4.3%), those only having HBsAg positive 11(4.8%) while those having HBsAg, HBeAb & HBcAb positive were 4(1.7%). This result is in conformity with a previous study done among pregnant women at the Al-Thawra hospital in Sana'a-Yemen by Murad, et al., (2013) who investigate the seroprevalence and associated risk factors for HBsAg and anti-HCV antibody; of the 400 pregnant women enrolled in his study, HBsAg and anti-HCV were detected in 43 (10.8%; 95% CI: 8.0–14.0%) and 34 (8.5%, 95% CI: 6.0–11.5%), respectively (Murad, et al., 2013). The overall prevalence of Hepatitis B surface antigen (HBsAg) in the Yemen Republic was found in 18.5% healthy individuals and 24.1% patients with chronic liver disease (P = 0.03) (El Guneid, et al., 1993), this shows that a higher proportion of population of Yemen Republic has ever been exposed to hepatitis B virus.

However, a study done in Nigeria showed that the prevalence to be 4.3% (Akani, et al., 2005), in Sudan the prevalence found was 5.6% (Elsheikh et al, 2007) which less than our study. The prevalence of HBV estimated by our study also compares well with what was reported in Republic of South Sudan (11%) of pregnant women were positive for HB-surface antigen (Anthony, et al., 2017).

The association between HBsAg and the various age groups was evaluated in our study. The level of significance established by the current study indicated that age of an individual does not determine the HBV status (P=0.4). Mbaawuaga, et al., (2008) also found there no a statistical significant association. The differences in prevalence rate among the age groups may be due to many of pregnant women tested in this survey may have not been exposed to hepatitis B vaccine; since only 37(16.1%) has been vaccinated.

The association of HBsAg and the various levels of education was evaluated and it show no a statistical significant (P=0.3), while high prevalence of HBsAg was seen among primary education level 11(17.2%). (Table 7). Dahie, and Heyle, (2017) also found that high prevalence of HBsAg among women with low economic status. Okeke, et al., (2015) also found that socioeconomic status showed Junior Staff having the highest prevalence rate of (4.8%). However, these study didn't show any significant statistical difference in terms of age, socioeconomic status or educational level similar to our finding. Murad, et al., (2013) also found that there are no a statistical significant association between HBsAg & the educational level.

Regarding the association of HBsAg with the number of parity in our study, it show a statistical significant (P=0.03), in which the prevalence of HBsAg with number of parity either Primigravida, second gravida and multigravida was (3.9%, 10.9% and 16.7%), respectively, (Table 7). Several studies showed that a statistical significant association of HBsAg with the number of parity, similar to our study. Murad, et al., (2013) reported that in multivariate analysis there was a statistical significant association, i.e. (P=0.03). Dahie, and Heyle, (2017) also reported that mothers with gravidity of 7 and more (multigravidae) were 2.1 times (OR 2.1, 95%CI 1.31-3.04) more likely to get hepatitis B compared to mothers with gravidity between 1-6 (Primigravida & second gravidae). This may due to that multigravidae were frequently exposed to risk of blood transfusion & the surgical manipulation.

The association between HBsAg with the various risk factors under study in questionnaire was evaluated in our study, it show only a statistical significant of association between HBsAg and the history of blood transfusion & history of surgical manipulation (P=0.000 & 0.02), respectively, (Table 8). It has been observed that previous history of surgery, multiple injection therapy, and blood transfusion was a risk factor among anti-HCV and HBsAg-positive pregnant women (Altinbas, et al., 2010). On the contrary, Hasan, et al., (2015) did not find a statistically significant association between job, history of transfusion, history of tattooing, jaundice, dentistry procedure, gestational age and the risk of HBV infection. Altinbas, et al., 2010, has been observed that previous history of surgery, multiple injection therapy, and blood transfusion was a risk factor among anti-HCV and HBsAg-positive pregnant women.

The high parity, older age and blood transfusion were independently associated with HCV among pregnant women (Khan, et al., 2008 and AbdulQawi, et al., 2010). Other risk factors such as early age of sexual debut, history of multiple sexual partners, and past history of sexually transmitted infection were found to be significantly associated with HBV among pregnant women (Rabiu, et al., 2010). As a result of social and religious reasons, these factors are difficult to be investigated in our country. Perhaps if these risk factors were investigated, different results might have been obtained.

CONCLUSIONS

The results of this study suggest that HBsAg have high prevalence among pregnant women. History of blood transfusion, surgical manipulation and circumcision was a risk factor for HBsAg. The obstetric and socio-economic factors (i.e. the multiparty parity as well as the low education level) was associated with HBV-infection.

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