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RISK FACTORS;
COMPARISON IN HEPATITIS B AND C CARRIER PREGNANT WOMEN & HEALTHY PREGNANT WOMEN

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ABSTRACT: Objective: To determine the risk factors associated with hepatitis B and C carriers versus healthy pregnant women. **Material and Methods:** It was a single center based, cross sectional comparative study, conducted at Gynae ward II, B-V hospital Bahawalpur. Duration of study was from March to August 2008. 100 patients were enrolled in the two groups, 50 HbsAg/Anti HCV positive women (cases) to compare with 50 healthy women (controls) match for parity. The data were recorded on a proforma. **Results:** 100 pregnant women were enrolled. Sixty eight (68.0%) were aged 25 years or less with a mean age ± S.D of 24.62 ± 3.40. Ten (20%) women had HBV and 40(80%) were HCV positive. The risk factors were compared between the two groups by uni-variate and multivariate analysis which showed that history of dental treatment, blood transfusion, surgery, parenteral treatment and jaundice were significant risk factors for hepatitis B and C carrier status. **Conclusion:** There appears to be a strong co-relation of history of blood transfusion and dental treatment with HbsAg/ Anti HCV carrier state in pregnant women. The anti HCV seropositivity was appreciably high (80%) as compared to HbsAg (20%) in carrier pregnant women.

Keywords: HbsAg, HCV, Pregnancy , Risk factors.

INTRODUCTION

Viral Hepatitis has been a major public health problem for many years worldwide. There are an estimated 300 and 500 million people infected with Hepatitis B and C respectively[1]. Hepatitis B and C virus infections have been the cause of significant morbidity and mortality in western world but more so in developing countries like Pakistan[2]. In Pakistan, 10% of general population and 8% of pregnant females are reported to be carriers of HbsAg. Considering the high prevalence of HbsAg and a crude birth rate of 36 , transmission of HBV will add a large number of carriers in our population, the magnitude of problem is also alarmingly high with Anti HCV carriers of 2 to 20.89% in general population and 29.6% in pregnant women[1,2,4,5].

The incidence of acute viral hepatitis in pregnancy varies globally. It is relatively rare in developed countries, while

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in developing countries acute viral hepatitis is common. The course of acute hepatitis due to HBV and HCV is usually unaffected by pregnancy, except in the case of hepatitis E, where mortality rates is as high as 20% has been reported. The high prevalence of chronic carriers HBV mothers is considered to be the most important factor, serving as reservoirs of HBV and HCV which are transmitted to neonates[3,6,7]. (Vertical transmission).

The rate of infection of infant born to chronic carrier mothers varies among ethnic groups and in different parts of the world. In the USA, high rates of childhood HBV infection were shown by Alaskan Natives, Pacific Islanders and infants of first generation immigrant mothers from countries which are endemic, especially Asia[4]. The rate of HBV vertical transmission from HBsAg-positive carrier mothers to neonate is estimated to be from 0% in Denmark up to 40% in Taiwan. In fact, the most important cause of the spread of HBV in endemic countries is vertical transmission of HBV from chronic carrier mothers to new born. An important factor for the high carrier rate is the high prevalence of HBsAg/HbeAg-positive pregnant women. The maternal presence or absence of HBeAg is the strongest predictor, from 80 to 95% of non-vaccinated infants born to HBsAg/HBeAg positive mothers were reported to become chronic carrier[9]. However, high levels of maternal HBV, DNA is an other strong predictor of persistent infection. Vaccination early in life can, to a certain extent, prevent perinatal transmission and HBV infection later in infancy and childhood[13,29, 30].

HCV accounts for most cases of acute and chronic liver diseases and infects around 3% of the world population including pregnant women[10, 11]. Vertical transmission can occur but is less frequent than HBV[18]. The rate of mother to child transmission of HCV as ranging from 4-50%[17]. Maternal HCV RNA is an important factor for determining infectivity. The higher the viral burden, the higher the risk of transmission[16, 25, 26].

This study would help to assess the magnitude of problem among the pregnant women and to determine the possible risk factors associated with increasing number of carriers. There is currently no national system for screening of all pregnant women for HbsAg and HCV and to ensure vaccination for exposed infant.

MATERIAL AND METHODS

The study was conducted at department of Gyneacology and Obstetrics Unit II, Bahawal Victoria hospital Bahawalpur. It was a single center cross sectional comparative study. Duration of study was from March to August 2008. 50 pregnant women found HbsAg/Anti HCV positive were taken as cases and compared with 50 healthy pregnant women controls matched for parity. Sampling technique was non-probability, convenience sampling.

Inclusion Criteria: All pregnant women visiting the antenatal clinic at the Gyneacology and Obstetrics outpatient department, Bahawal Victoria hospital Bahawalpur were tested for Anti-HCV and HbsAg. Fifty women found to be positive were selected as cases. Fifty healthy pregnant women HbsAg/Anti-HCV negative, matched for parity were included as controls.

Exclusion criteria: Patients suffering from active hepatitis, Blood dyscariasis and jaundice were not included in the study.

Data collection: All patients who fulfilled the inclusion criteria were enrolled, the information for groups, cases and controls regarding presence or absence of possible risk factors were recorded on especially designed proforma by taking history. Women fulfilling the criteria were entered in the study as cases after informed consent. The primary outcome measures were the association of previous surgery, dental care, parenteral treatment and blood transfusion with carrier status as compared to the healthy pregnant women (controls). Secondary outcome measures were correlation of history of jaundice and husband's carrier status to cases and controls.

Data Analysis: The data was entered and analyzed by using SPSS version 10.0 software for health statistics.

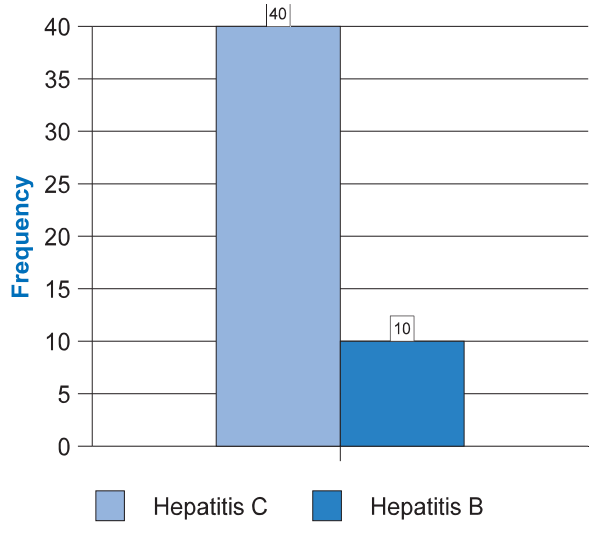
Frequencies of different risk factors and other variables were reported with their percentages. We compared the data between hepatitis B and C carrier women and the non-carrier (normal) women by using uni-variate analysis and result were reported as odds ratio, 95% confidence interval and p-value for categorical variables and student t-test for continuous variables. A multivariate logistic regression model was constructed to identify the risk factors associated with hepatitis B and C carriers. All risk factors found to be significant in uni-variate analysis were included in this forward stepwise model to get the independent risk factors. Odds ratio, 95% confidence interval and p-value were reported for these risk factors.

RESULTS

During the study period, 100 pregnant women were enrolled. Out of these 100 women, 50 were cases i.e carriers and 50 were healthy controls.

Forty (80.0%) of the carrier group were hepatitis C carriers and 10 (20.0%) hepatitis B carriers (details are given in Fig 1).

Fig-1. Frequency of hepatitis C & C carriers among cases (n=50)



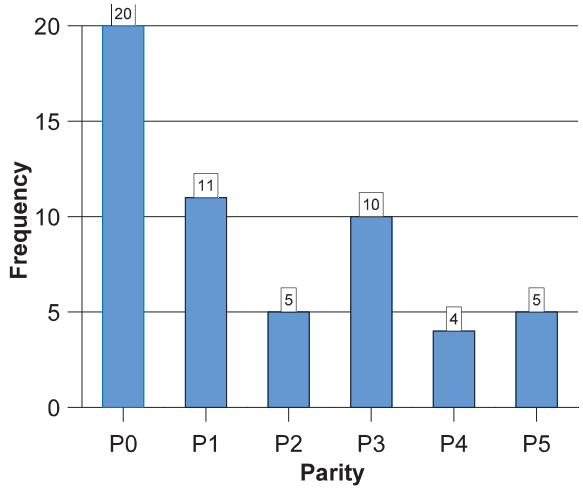
The mean age ± S.D of cases was 24.92 ± 3.83 with range from 20 –30 years, while the mean age ± S.D of control group was 24.3 ± 2.9 with range from 21 –31 years. Comparison of the two groups i.e. the cases (carriers) and control (non-carriers) showed that there was no significant difference in the age distribution. (Table-I).

Table-I. Age distribution in two groups (n =100)

Variable	Cases (n=50)	Control (n=50)	p-value
Age categories Up to 25 years More than 25 years	 0 (60.0%) 20 (40.0%)	 38 (76.0%) 12 (24.0%)	0.13
Mean ± Standard deviation Median Range (Min – Max)	24.92 ± 3.83 25.0 20-30	24.3 ± 2.92 24.0 21-31	0.35

The blood groups of these women were also analyzed. Our results showed that in cases 20 (40%) women and in control group 17 (34%) had B+ blood group. Similarly 10 (20%) cases and 12 (24%) control women had O+ blood group, although the distribution of blood groups not found out to be significant. As the cases and controls were matched for parity, thus the comparison is not relevant. The nullipara and multiparous carrier women is shown. (Fig 2)

Fig-2. Comparison of parity among cases (n=50)



Previous history of surgery was present in 36(72%) of cases and 23(43.4%) of controls with p-value of 0.014. There was also a strong association of past history of dental treatment and carrier status in which 18(36%) of cases and only 3(6%) of controls had undergone dental care with p-value=0.0005. Similarly blood transfusion was reported in 14(28%) of cases and 3(6%) of controls with p-value=0.014. History of jaundice was present in 12(24%) of cases and 3(6%) of controls, p-value=0.02. Similarly 17(34%) of cases and 13(26%) of controls had undergone parenteral treatment which was insignificant statistically. When the carrier status of the husband was ascertained, only 10(20%) of the cases and 1(2%) of controls had husbands positive for hepatitis B or C (Table-II).

Table-II. Various Risk factors associated with carrier status of HBV & HCV (=100)

Risk Factors	Cases (n=50)	Control (n=50)	p-value
Previous H/O Surgery			
Yes	36 (72.0%)	23 (43.4%)	0.014
No	14 (28.0%)	27 (54.0%)	
H/O Dental Treatment			
Yes	18 (36.0%)	3 (6.0%)	0.0005
No	32 (64.0%)	47 (94.0%)	
H/O Blood Transfusion			
Yes	14 (28.0%)	3 (6.%)	0.007
No	36 (72.0%)	47 (94.0%)	
H/O Jaundice			
Yes	12 (24.0%)	3 (6.0%)	0.02
No	38 (76.0%)	47 (94.0%)	
Husband's Carrier Status			
Yes	10 (20.0%)	1 (2.0%)	0.01
No	40 (80.0%)	49 (98.0%)	
H/O Parenteral Treatment			
Yes	17(34%)	13(26%)	0.51
No	33(66%)	37(74%)	

The independent risk factors were also identified by multivariate analysis. The results showed that history of dental treatment, history of blood transfusion and history of jaundice were significant risk factors for cases (Table-III).

Table -III. Risk factors associated with Hepatitis B and C (forward stepwise Multiple Logistic Regressions)		
Risk Factors	OR (95%CI)	p-Value
H/O Dental Treatment	5.82 (1.44 – 23.57)	0.013
H/O Blood transfusion	4.47 (1.03 – 18.91)	0.045
H/O Jaundice	4.59 (1.06 – 19.87)	0.041

DISCUSSION

Hepatitis B(HBV) and C(HCV) virus infection occurs worldwide. 90% of HBV infection in healthy adults is self limiting followed by recovery and immunity. In the case of acute HCV infection, 75% of the cases are asymptomatic.[1,2] However, 80% of acute HCV infection symptomatic individuals become chronic carriers, in contrast to hepatitis B, in which 5-10% of patients have a chronic disease. These chronic carriers serve as a reservoir of HBV and HCV which are transmitted to neonates.[4,5] the high prevalence of chronic carrier HBV mothers is considered to be the most important factor contributing to the high carrier rate in the Far East. Despite vaccination, HBV infection still occurs in about 10-15% of infants born to chronic carriers[11,20,21].

Vertical transmission of hepatitis B & C virus made this disease of particular significance to the obstetrician[11,12]. In Pakistan, the magnitude of problem is alarmingly high with Anti HCV carriers 2 to 20.89% in general population and 29.6% in pregnant women[1]. Approximately 1% of pregnant women have new born at risk of vertical transmission in developed countries. In Pakistan the figure of HbsAg positive carriers is 3.6-18.6% in general population, 3.16% in pregnant women and 37% in the patients of chronic liver disease[1,2,17,18].

The maternal demographics did not show much difference between two groups. Out of 100 pregnant women, enrolled during the study period, 68(68%) were aged up to 25 years (24.62±3.40), with range from 20-31 years which is almost similar with the age group of the carriers in the studies by other investigators i.e. (29.9±5.2)[5], 20-29 years[22] ,25-34 years[23] and in previous studies from Pakistan (31.88±5.11)[7] .In the United States, hepatitis B mostly affects people between 15 and 39 years old, with the highest incidence between ages 20 to 29 years[9]. This epidemiological cluster represents a major component of the patients seen at centers for women health.

In our study history of previous surgery was considerably high in cases as compared to healthy women (72% Vs 43.4%) with (p-value = 0.014). Similar observations were made by Batayneh N et al[23] and Mehnaz et al[7] in their study. This shows significant likelihood of HBV and HCV transmission through surgical instruments and health care personnel. The overall prevalence figures in health care personnel for HbsAg and Anti-HCV was 5-9% and 4% respectively in different studies done in Pakistan during last five years[12,17,18]. However, studies with large sample size are required to confirm these observations. Health care workers are also at risk for HCV due to occupational exposure. The risk of seroconversion after a percutaneous injury ranges from 3-10%, which is considerably less than following a similar injury from an individual infected with Hepatitis B virus[1,3].

As mentioned earlier intravenous drug abuse (40-50%)[1,2] repeated injections, and infusions are important routes of HBV and HCV transmission especially in developing

countries like Pakistan. In this study there was no significant difference (p value = 0.51) found between cases and controls regarding history of parenteral treatment (34% Vs 26%). However in one study it was found significant (37.5 Vs 10.13%) with p value = 0.01 but the same study shows that history of repeated infusions alone has no significance (p value = 0.28)[8].

Our results signify the strong association between history of dental treatment and HBV or HCV carrier status in pregnant women. The percentage of history of dental treatment among carriers and healthy controls is 36% and 6.0% respectively (p value = 0.005). Similar strong association as also observed by Batayneh N et al[23] with percentage of as high as 76.6% in HbsAg positive women and 77.6% collectively for HBV carriers including other serum markers as well. In developing countries like Pakistan facilities for dental care are almost negligible, especially in rural areas. This strong association may truly depict one mode of transmission of HBV and HCV infection through contaminated needles and syringes used by quacks during dental treatment, leading to the carrier status of considerable portion of population.

In Pakistan the estimated prevalence rates for HbsAg for healthy blood donors ranged between 2-14%[8]. The HCV prevalence was recorded between 00-20.89% for the same group[8,24]. That is why blood transfusion is considered to be the major risk factor for HBV and HCV carrier status in general population as well as in pregnant women. Our study also supports this speculation because there is significant difference in the percentages of history of blood transfusion between carriers and healthy controls (28.0% Vs 6.0%). This shows strong association of this risk factor with HBV and HCV carrier status (p value = 0.007), which was also observed in other parts of world[19]. In a study by Tajiri et al[24] blood transfusion was found as a significant risk factor in 12% of pregnant women. But in previous studies the figure was found insignificant i.e. 37.5% Vs 21.58% in carriers and non carriers respectively (p value=0.28)[7] Similar observation were also recorded by other investigators[23]. Infection from blood transfusion mostly before 1989 accounts for 5% of HCV infected patients. But the institutional HCV testing of blood banks has reduced the risk of HCV to 0.3% per unit of transfused blood[25, 29].

Recently it has been reported that pregnancy does not induce a deterioration of HCV associated liver disease, and conversely that HCV infection does not seem to increase the risk of obstetric complications. Gestational cholestasis is the most common liver disorder of pregnancy. The incidence of cholestasis of pregnancy is significantly higher among women positive for HCV antibodies than in women negative for HCV antibodies. another study suggest that pregnancy worsen histopathological characteristics of the liver in women with chronic HCV infection[19,22,26,27].

There appears to be a strong co-relation between history of jaundice and women's carrier status in our study. The history of jaundice was found in 24.0% of carriers, while in healthy controls it was only 6.0%. Although the significant number of women have no history of jaundice (76% of cases and 94% of controls). Still it is found to be a significant risk factor for the carrier state (p value = 0.02). In a similar study Lin HH [6], among pregnant women with jaundice considerable number of women were found HbsAg and HCV positive with figure of 3.16% and 6.42% respectively. The relationship of liver disease with HbsAg and HCV carrier status is also found in other studies, e.g. 10.20% in patients with provisional diagnosis of hepatitis by Tayyab GN et al[18], the prevalence of anti HCV in patients with acute or chronic liver disease ranges from 29.63% by. Wang J et al[16], to 43.06% by Mehmood A et al[17]. Studies for identification of risk factors by other investigators Pakistan & abroad also found it significant. In a study by Mehnaz et al[7], history of jaundice was found in 50% of carriers as compared to non carrier (11.89%) with p value =0.001.While screening of pregnant Jordanian women revealed that 4.3% were HbsAg positive with acute or chronic hepatitis[23,28].

Thus HbsAg and anti HCV carrier status was found to be strongly associated with history of blood transfusion, dental treatment, and jaundice in population studied. The anti HCV seropositivity was appreciably high (40%) as

compared to HbsAg (10%) in carrier pregnant women. There is an urgent need to expand, extend and standardize work done on HBV and HCV prevalence in order to get more reliable estimates [22,30].

Standard care in obstetrics and Gyneacology often includes routine screening of HbsAg and anti HCV in all pregnant women in developed countries. We recommend that in Pakistan, all females of child bearing age should be screened for hepatitis B and C antigenemia and their offspring should be provided with active or passive prophylaxis according to their serological status[20, 27, 30].

CONCLUSION

We found higher prevalence of HbsAg and anti HCV in pregnant women than studied before by other investigators, along with strong association of history of blood transfusion, dental treatment and jaundice. Increasing number of carriers among pregnant women indirectly depicts increasing prevalence rate among children and young adults because of potential risk of vertical transmission.

There is a need of effective health education program to provide standardized educational aids to facilitate counseling of population at risk about prevention of hepatitis B and C virus infection. Health education, vaccination against HBV at birth, screening of blood donors for HbsAg, anti HCV, and strict use of disposable syringes must be observed. Vaccination against HBV already introduced for newborn should be available to population at large.

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