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RESEARCH ARTICLE

ANTENATAL SCREENING FOR HEPATITIS B VIRUS INFECTION

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Abstract

Background:- Hepatitis B virus (HBV) infection still has a relatively high incidence and prevalence worldwide. In the post-vaccination era in developing countries, perinatal vertical transmission remains the most common mode of transmission. Prevention of mother-to-child transmission requires screening for HBV surface antigen (HBsAg) in pregnant women to identify which newborns that must be immunized.

Aim:- This study aimed to evaluate the prevalence of HBV infection among pregnant mothers who were attending outpatient clinic of the Obstetric Department, at Benha University Hospital , for routine antenatal care.

Methods:- A cross sectional study included 942 pregnant women. enzyme linked immusorbent assay technique (ELISA) screening test for HBV was done for all women and all Patients with hepatitis B surface antigen positive were subjected to: ALT, AST, Bilirubin (total and direct), HBeAg test and abdominal ultrasound.

Results:- out of 942 pregnant women, 15 were positive for HBsAg (1. 6%) by ELISA test, where ALT, AST and Bilirubin were normal in14 positive cases but high in the 15th positive case, HBeAg was negative in the all 15 positive cases and abdominal ultrasound was normal in 14 positive cases and showed hepatosplenomegally in the 15th positive case. There was no significant association between the seroprevalence of HBV infection (HBsAg) in studied females and their sociodemographic data. There was no statically significance reached by comparing patients with HBsAg +ve and HBsAg –ve regarding Age and Durations of marriage, Blood transfusion, Hospitalization, Major operations, Diabetes Mellitus, Husband with HBsAg +ve and Addiction.

Conclusion:- HBV infection is present among pregnant mothers attending our outpatient services. Therefore we recommend screening for HBV in all Egyptian pregnant mothers to prevent neonatal infection by immunoprophylaxis.

Introduction:-

Of estimated 350 million individuals chronically infected with HBV worldwide, it is generally accepted that at least 50% acquired their infections either perinatally or in early childhood, especially in countries where HBV is endemic [1]. Perinatal vertical transmission is the most common mode of transmission worldwide [2]. Vertically transmitted HBV infection is becoming an important risk factor for acquisition of HBV among children born after the era of mass vaccination in Egypt [3]. High maternal viral load and maternal serum HBV envelope antigen (HBeAg) positivity increase the risk of perinatal transmission [4]. Infants born to mothers known to carry HBV can be treated with HB immunoglobulin. When given with the vaccine within 12-24 hours of birth, the risk of acquiring HBV is reduced by 90% [5].

Prevention of mother-to-child transmission requires screening for HBsAg in pregnant women to identify which newborn should be immunized [6]. This study aimed to evaluate the prevalence of HBV infection among pregnant mothers, and to identify risk factors that may lead to HBV acquisition among these women.

Patients And Methods:-

This study was designed as a cross sectional study to estimate the prevalence of HBsAg among pregnant females. The study was conducted on nine hundred fifty females who were visiting antenatal care clinic in Gynecology and Obstetrics outpatient clinics in Benha University Hospital from January 2013 to January 2015.
The study protocol was approved by Ethical Committee of Benha faculty of medicine,Benha university.
Patients who signed an informed consent were included in the study and were subjected to the following

A- History taking:-

Full medical history taking which includes

- **Personal History:-**

Name
Address
Phone number
Name to contact at emergency
Address of the contact at emergency
Phone number of the contact at emergency

- **General medical history:-**

Date of birth
Expected date of delivery
Place of previous delivery
History of blood transfusion
History of major operation
History of major accidents
Tattooing
I.V drug addiction
Renal dialysis
History of Schistosomiasis
History of antischistosoma therapy
Sexually transmitted diseases
Diabetes mellitus
Number of marriages
Duration of marriage
Family history of hepatitis B
History of husband Hepatitis B
History of husband addiction
Number of deliveries

- **Obstetric History:-**

Number of Pregnancies
History of jaundice needed to be treated in her previous infants
Place of previous deliveries
Duration of previous delivery
Method of previous delivery (Episiotomy, Using suction, Cesarean section, Spontaneous vaginal delivery)

B- Clinical Examination:-

C- Laboratory Investigation:-

Lab investigations included

- **Serum hepatitis B surface antigen (HBsAg):-** using a solid phase enzyme linked immusorbent assay technique (ELISA) , based on the Sandwich principle with use of microtiter plates , was developed for the detection of HBsAg. Results could be read within one day by the naked eye or by colorimeter. The detection level was less than or equal to 5-10 ng of HBsAg/ml .

D- Patients with hepatitis B surface antigen positive were subjected to:-

- ALT, AST, Bilirubin (total and direct)
- HBeAg test

Statistical method:-

Sample size calculated based on estimated prevalence of 4%. A sample size of 950 patients gives 95% confidence interval with a width of 4%

Prevalence was calculated as percentage (%) and 95% confidence interval Nonparametric tests were used for comparison of parameters between positive and negative HBsAg females due to small number of HBsAg positive group.

Results:-

The study was conducted on 942 females who were visiting antenatal care clinic in Gynecology and Obstetrics outpatients in Benha University Hospital from January 2013 to January 2015.

The studied females were screened for hepatitis B surface antigen (HBsAg) using ELISA technique. Positive cases were only 15 and they were subjected to

- ALT, AST, Bilirubin (total and direct)
- HBeAg test
- Abdominal Ultrasound.

In the present study the prevalence of HBsAg was around (1. 6%). Sample size calculated based on estimated prevalence of 4%. A sample size of 950 patients gave 95% confidence interval with a width 4%. Prevalence was calculated as percentage (%) and 95% confidence interval.

Where ALT, AST and Bilirubin were normal in 14 positive cases but high in the 15^{th} positive case, HBeAg was negative in the all 15 positive cases and abdominal ultrasound was normal in 14 positive cases and showed hepatosplenomegally in the 15^{th} positive case.

There was no significant association between the seroprevalence of HBV infection (HBsAg) in studied females and their sociodemographic data.

There was no statically significance reached by comparing patients with HBsAg +ve and HBsAg –ve regarding

Age and durations of marriage
Blood transfusion
Hospitalization
Major operations
Diabetes Mellitus
Husband with HBsAg +ve
Addiction

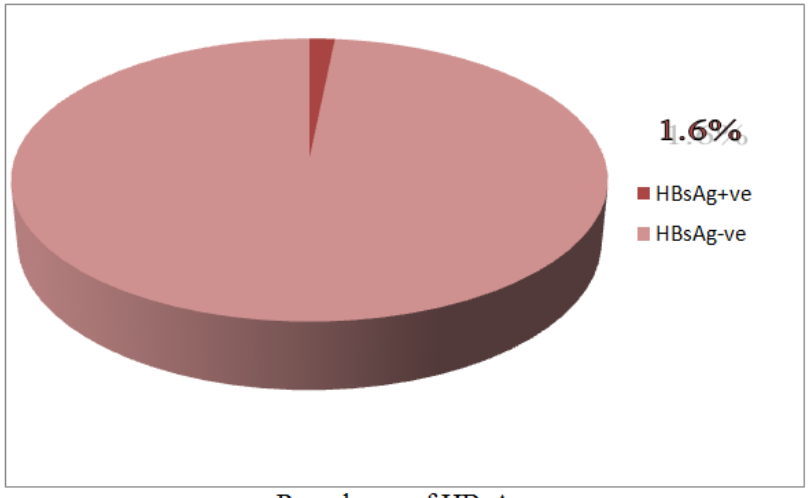
Table (1): Description of the studied patients

Variables	Mean	Standard deviation	Minimum	Maximum	Range
Age, years	26.9	5.56	18	45	27
Duration of marriage, years	4.88	4.47	0.5	25	24.5

Table (2): Descriptive characteristics of the Studied Patients

	Number 942	Percentage %
Blood transfusion	12	1.27%
History of hospitalization	43	4.56%
History of major operations	38	4.03%
Diabetes Mellitus	2	0.2%
Family history of hepatitis B	5	0.53%
History of husband with hepatitis B	14	1.48%
History of husband addiction	218	23.1%
Number of pregnancies		
1	432	45.8%
2	235	26.8%
3	171	18.1%
4	74	7.8%
5	20	2.1%
6	7	0.7%
7	1	0.1%
8	2	0.2%
History of jaundice in previous infants needed to be treated	17	1.8%
HBsAg +ve	15	1.6%

Fig. (1): Prevalence of HBsAg +ve among studied population



Prevalence of HBsAg
1.6% , 95 CI, 0.79 – 2.39%

Patients with HBsAg +ve were only15 patients that make statistical analysis for categorical or dichotomous variables difficult because of small number per cells.

- All patients with HBsAg +ve had HBeAg –ve (15/15), 100%).
- Out of 15 patients with HBsAg +ve, 14 patients (93.33%) had normal ALT&AST.

Discussion:-

The prevalence of HBV varies between 2% in developed countries where the prevalence is low to about 8% in developing countries where infection is endemic with sex, age and socioeconomic status as important risk factors for infection [7,8]. Countries are classified as having low endemic rates (<2%), intermediate endemic rates (2-8%), or high endemic rates (>8%) positive for HBsAg [9]. The prevalence of HBV in Egypt is of intermediate endemicity (2-8%) [10,11]. **Badawy and El-Salahy** [12] reported a rate of materno-fetal transmission in 51.8% of HBsAg-positive women in Egypt.

Our study showed that out of 942 pregnant women, 15 were positive for HBsAg (1.6%) with 95% confidence interval. this result is in agreement with **El-Shabrawi et al., (2013)** [13] from Egypt, **Khalil et al., (2005)** [14] from Saudi Arabia and **El-Magrahe et al., (2010)** [15] from Libya who reported that 1.75%, 2.4% and 1.5% of their studied women were positive for HBsAg, respectively. **Eke et al., (2011)** [16] from Nigeria and **Sharifi-Mood et al**., **(2004)** [17] from Iran, reported higher prevalence rates of HBV of 8.3%, and 6.5% respectively. Other studies from the North Africa and Middle East reported rates of 4% from Tunisia **Hannachi et al., (2009**) [18], 4.3% from Jordan **Batayneh and Bdour, (2002**) [19], From Pakistan, **Taseer et al., (2010)** [20] and **Azhar et al., (2011)** [21] also reported prevalence rates of seropositive HBsAg among pregnant women of 4.6% and 5.7%, respectively. High prevalence rates of HBsAg were also reported from Ghana (10.5%) **Damale et al., (2005)** [22] and Yemen (13.2%) **Al-Shamahy, (2000)** [23].

Prevalence of HBV infection varies in different parts of the world. In addition, this prevalence varies from country to country, from one region to another region and from one group to another group in a country [24] **.** This difference can explain the difference of prevalence among pregnant females.

Factors influencing incidence and prevalence of HBV infection in a particular community in addition to ethnicity and immigration patterns include intravenous drug use and high-risk sexual activity were documented by **Wright,(2006)** [25].

Pregnant women are considered at a higher risk due to increased exposure to risk factors (as blood transfusion, intravenous drugs or surgical procedures) [26]. However, our results showed that 54.2% of cases were multigravidae with no significant difference between both multigravidae and primigravidae. This is in agreement with **El-Shabrawi et al., (2013)** [13]**, Eke et al., (2013)** [16]and **Buseri et al., (2010)** [27]. However, **Azhar et al**., **(2011)** [21]reported a higher frequency of HBV infection among multigravidae**.** It might be at increased risk of HBV infection among multigravidae because of their past pregnancies, hospital admission, blood transfusion and/or any surgical procedure in the past [28].Therefore, with each pregnancy and childbirth chances of exposure to HBV become greater.

Blood transfusion continues to cause hepatitis B infection in countries, where blood donor is not screened. Transmission of HBV from transfusion of unscreened blood continues to be a problem and may account for a majority of infections among children and adults [29]. In our study, history of previous blood transfusion was not observed in a significant number of cases. Our study comes in agreement with **El-Shabrawi et al., (2013)** [13]**, Khalil et al., (2005)** [14]and **Vázquez-Martínez et al., (2003)** [30] However; other studies reported that blood transfusion was an important risk factor for acquiring HBV infection [20, 31].

In our study, previous hospital admission was reported in 4.56% of cases, which was not significant. Our study does not come in agreement with **El-Shabrawi et al., (2013)** [13] **and Ahmadi et al., (2011)** [32]. Who reported that previous surgery and hospitalization were observed in a higher percent of HBsAg positive cases than HBsAg negative controls but the difference between both groups was not of statistical significance.

History of previous surgeries was reported in 4.03% of our cases, which was also not significant. History of previous surgeries is a major risk factor for transmission of HBV [20]. Our study comes in agreement with **Khalil et al., (2005)** [14] and **Vázquez-Martínez et al., (2003)** [30] who reported a nonsignificant distribution of previous

surgeries in the transmission of HBV infection among their studied women. However; **El-Shabrawi et al., (2013)** [13] reported that history of previous surgeries was reported in 80% of their cases, which was also significant.

Rural residence could be a risk factor for HBV infection. Socioeconomic conditions among the poor and less educated, and crowded living condition especially in the rural areas, may contribute to HBV exposure [33]. In our study, most of HBsAg-positive women were belonging to rural areas with poor socioeconomic and low educational status.

In our study, husband infected with hepatitis B was reported in 53.3% of cases, with statistical analysis was difficult, but it appears that pregnant females with HBsAg +ve had higher prevalence 53.3% of husband with HBsAg +ve than patients with HBsAg –ve (0.7%). Our study comes in agreement with **El-Shabrawi et al., (2013)** [13]who reported that husbands with HBsAg +ve were observed in a higher percent of HBsAg positive cases than HBsAg negative controls.

History of husband addiction was reported in 26.7% of our cases, However, although statistical analysis was difficult, but it appears that pregnant females with HBsAg +ve had higher prevalence 26.7% of husband addiction than patients with HBsAg –ve 1.8%. Our study comes in agreement with **Khalil et al., (2005)** [14] and **Vázquez-Martínez et al., (2003)** [30] who reported a significant distribution of husband addiction in the transmission of HBV infection among their studied women.

Our study showed that out of 942 pregnant women, 15 were positive HBsAg and all of the positive cases were HBeAg negative. Our study comes in agreement with **Ahmadi et al., (2011)** [32] who reported that HBeAg negative was observed in high percent of their HBsAg positive cases.

HBeAg-negative variant accounts for more than 80% of CHB in Egypt [34]. And represents a late phase of HBV infection characterized by persistent viral replication, progression of liver disease, and early development of cirrhosis [35].

Reductions in HBeAg prevalence among HBsAg positive women between 1990 and 2005 could be related to improved hepatitis B vaccination coverage. This may explain decreases particularly observed in Egyptian women (reduction up to 14 %) [36].

One of the most common mutations in HBV occurs in the precore or core promoter regions. This precore mutation stops the virus from producing or secreting the e antigen, despite its inability to secrete this protein, these mutated viruses are able to live and replicate without it [33]**.**

Patients with the precore mutation have +ve HBsAg and –ve HBeAg and they often have normal liver enzymes levels, unfortunately Patients with this e antigen negative often have active liver disease **Eke et al., (2011)** [16]**.**

The prevalence of these mutations ranges from 20 to 90%among patients from Europe and the Middle East including Egypt, Libya, Tunisia, Algeria and Morocco **(WHO, 2013)** [37].

In our study, normal ALT level was reported in 14 cases of the 15 positive cases 93.33%, which was highly significant. Our study comes in agreement with **Ahmadi et al., (2011)** [32] from Iran who reported that normal ALT level was observed in high percent of their HBsAg positive cases.

Recent preliminary reports showed that 12 – 43 % of Egyptian patients with chronic HBV infection and HBsAg positive had persistently normal ALT levels [34]**.**

Conclusion:-

In the post-vaccination era in Egypt, HBV infection prevalence among pregnant females is low.
Most of HBV-infected pregnant women are asymptomatic and unaware of their infection until being unraveled by screening; therefore, antenatal screening of pregnant women for HBsAg is important to identify which newborn should be immunized.
The study is considered as a pilot study, to help in implementing a national program for prevention of vertical transmission of HBV as the schedule of HBV vaccine in our country is at the age of 2, 4, 6 months.

Recommendations:-

1. Screening of pregnant females for HBsAg and evaluation of females for treatment and neonatal immunoprophylaxis.
2. Screening of contacts with high risk of partners as addict.
3. Screening and vaccination of contacts with HB infected partners.
4. Study for long follow up of infected pregnant females and their children.

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Ethical Approval:-

The study protocol was approved by Ethical Committee of Benha Faculty of Medicine, Benha University.

References:-

1. **Alter MJ (2003)**: Epidemiology of hepatitis B in Europe and worldwide. J Hepatol.; 39(Suppl. 1):64-69.
2. **Mast EE, Weinbaum CM, Fiore AE, et al., 2005):** A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. MMWR Recomm Rep; 55:1-3.
3. **El-Raziky MS, El-Hawary MA, et al., (2012):** Patterns of hepatitis B infection in Egyptian children in the era of obligatory hepatitis B vaccination. Arab J Gastroenterol; 13(1):1-3.
4. **Chowdhury SD (2009):** Perinatal transmission of Hepatitis B. Hep. B Annual.; 6:80-88.
5. **Libbus MK and Phillips LM (2009):** Public health management of perinatal hepatitis B virus.Public Health Nursing (Boston, Mass).; 26:353–361.
6. **Jara P and Bruguera M (2008):** Hepatitis B in pregnant women and children. Enferm Infecc Microbiol Clin.; 26:675.
7. **Odusanya OO,. Alufohai FE, Meurice FP, Wellens R, Weil J and Ahonkhai VI (2005):** Prevalence of hepatitis B surface antigen in vaccinated children and controls in rural Nigeria.International J Infect Dis.; 9:139-143.
8. **Alikor EA and Erhabor ON (2007):** Seroprevalence of hepatitis B surface antigenaemia in children in a tertiary health institution in the Niger delta of Nigeria. Niger J Med.; 16:250-251.
9. **Sharma P and Steele RW (2011):** Pediatric Hepatitis B. 2011. Available online at: http://emedicine.medscape.com. (accessed on July16, 2011).
10. **Attia MA (1998):** Prevalence of hepatitis B and C in Egypt and Africa. Antivir The ; 3:1-9.
11. **El-Zayadi A (2007):** Hepatitis B Virus Infection the Egyptian Situation. Arab J Gastroentero.; 8:94-98.
12. **Badawy HA and El-Salahy E (2000):** Materno-fetal transmission of hepatitis B infection. J Egypt Public Health Assoc.; 75:357-67.
13. **El-Shabrawi M, Mohamed MF, , Hamdi MS, Ehab M, Khamiss SS and El-Karaksy H, (2013):** Prevalence of Hepatitis B Virus Infection among Egyptian Pregnant Women - A Single Center Study, International Journal of Tropical Disease & Health 3(2): 157-168.
14. **Khalil MK, Al-Mazrou YY, Al-Jeffri M, et al., (2005):** Serosurvey of hepatitis B surface antigen in pregnant Saudi women. East Mediterr Health J; 11:640-647.
15. **El-Magrahe H, Furarah AR, El-Figih K, et al., (2010):** Maternal and neonatal seroprevalence of Hepatitis B surface antigen (HBsAg) in Tripoli, Libya. J Infect Dev Ctries; 4:168-170.
16. **Eke AC, Eke UA, Okafor CI, Ezebialu IU, et al., (2011):** Prevalence correlates and pattern of hepatitis B surface antigen in a low resource setting. Virol J; 8:12.
17. **Sharifi-Mood B, Keykhah F, Moghadam ES, et al., (2004):** Prevalence of Hepatitis B Surface Antigen inPregnant Women in Zahedan, Iran. Hepat Mon; 4:161–163.
18. **Hannachi N, Bahri O, Mhalla S, et al., (2009):** Hepatitis B virus infection in Tunisian pregnant women: Risk factors and viral DNA levels in HBe antigen negative women Pathol Biol (Paris); 57:e43-47.
19. **Batayneh N and Bdour S (2002):** Risk of perinatal transmission of hepatitis B virus in Jordan.Infect Dis Obstet Gynecol; 10:127-132.
20. **Taseer IU, Ishaq F, Hussain L, Safdar S, et al., (2010):** Frequency of anti-HCV, HBsAg and related risk factors in pregnant women at Nishtar Hospital, Multan. J Ayub Med Coll Abbottabad; 22:13-16.
21. **Azhar T, Khan IA, Mohsein S, Usman J, et al., (2011):** Antenatal screening for hepatitis B and C virus infection in pregnant women in a tertiary care hospital of Rawalpindi;3,18,145.

22. **Damale NKR, Lassey AT, Bekoe V (2005):** Hepatitis B virus seroprevalence among parturients in Accra, Ghana. Intern J Gynecol and Obstet; 90:240-241.
23. **Al-Shamahy HA (2000):** Prevalence of hepatitis B surface antigen and risk factors of HBV infection in a sample of healthy mothers and their infants in Sana'a, Yemen. Ann Saudi Med; 20:464-467.
24. **Merat S and Malekzadeh R (2003):** Hepatitis B in Iran. Arc Irn Med J; 4:192-201.
25. **Wright TL (2006):** Introduction to chronic hepatitis B infection. Am J Gastroenterol; 101(Suppl 1):S1–S6.
26. **Beasley RP, Hwang LY, Lee GC, et al., (1983):** Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. Lancet; 2:1099-1102.
27. **Buseri F, Seiyaboh E, Jeremiah Z, et al., (2010):** Surveying Infections among Pregnant Women in the Niger Delta, Nigeria. J Glob Infect Dis; 2:203–211.
28. **Khattak ST, Ali Marwat M, Khattak ID, et al., (2009):** Comparison of frequency of hepatitis b and hepatitis c in pregnant women in urban and rural area of district Swat. J Ayub Med Coll Abbottabad; 21:12-15.
29. **Prescott LM, Harley JP, Klein DA, et al., (2002):** Hepatitis B in: Microbiology 5th ed. London: MacGraw/Hill; 889.
30. **Vázquez-Martínez JL, Coreño-Juárez MO, Attlan M, et al., (2003):** Seroprevalence of hepatitis B in pregnant women in Mexico. Salud Publica Me; 45:165-170.
31. **Shamsuddin K and Marmuji L Z (2010):** Weighted analysis of prevalence and risk factors of hepatitis B infection among antenatal mother in Ipoh. Singa pore Med J; 51:800.
32. **Ahmadi M, Toghyani R, Shahidi S, Izadi M, Reza, et al., (2011):** Prevalence of HBsAg and high-risk behaviors in pregnant women referring to Urban Health Centers in Isfahan province. IJNMR; 16:47-54.
33. **Bwogi J, Braka F, Makumbi I, et al., (2009):** Hepatitis B infection is highly endemic in Uganda: findings from a national serosurvey. Afr Health Sci; 9:98-108.
34. **El-Zayadi A, Badran HM, Ahmed S, Khaled Z, et al., (2009):** Evaluation of Liver Biopsy in Egyptian HBeAg-Negative Chronic Hepatitis B Patients at Initial Presentation: Implications for Therapy; 3:178 – 83.
35. **Chu CJ, Keeffe EB, Han SH, et al., (2003):** Prevalence of HBV precore/core promoter variants in the United States. Hepatology; 38: 619 – 28.
36. **EL-Zayadi AR ,Ibrahim EH , Badran HM (2008):** Anti-HBc screening in Egyptian blood donors reduces the risk of hepatitis B virus transmission. In Transfusion medicine; 2: 55-61
37. **World Health Organization, (2013):** health information support, Eastern Mediterranean Region. 3.2 Hepatitis B Virus. http://www.who.sci.eg/Publications/Regionpublications/Transfusion_Microbiology/Transfusion_3.2htm≠3.2.1.