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PRENATAL SCREENING FOR HBV INFECTION AMONG PREGNANT WOMEN IN BEHERA GOVERNORATE

Thesis

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FIRST AND FOREMOST THANKS TO ALLAH,

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Ebrahim Eid Basyouny Mohammed

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LIST OF ABBREVIATIONS

ALT	**:**	Alanine transaminase
AST	**:**	Aspartate transaminase
CALD	**:**	Culturally and linguistically diverse communities
CCC	**:**	Covalently closed circular
CTLs	**:**	cytotoxic T lymphocytes
DNA	**:**	Deoxyribonucleic acid
EPI	**:**	Expanded Program of Immunization
EQAS	**:**	External quality assurance programs
GRE	**:**	Glucocorticoid responsive element
HBcAb	**:**	Hepatitis B core antibody
HBcAg	**:**	Hepatitis B core antigen
HBeAb	**:**	Hepatitis B envelop antibody
HBeAg	**:**	Hepatitis B envelope antigen
HBIG	**:**	Hepatitis B immunoglobulin
HBsAb	**:**	Hepatitis B surface antibody
HBsAg	**:**	Hepatitis B surface antigen
HBV	**:**	Hepatitis B Virus
HBx	**:**	Hepatitis B X protein
HCC	**:**	Hepatocellular carcinoma
IVD	**:**	Invitro Diagnostic devices
LHBs	**:**	Large Hepatitis B surface protein
MBS	**:**	Medicare Benefits Schedule
MHBs	**:**	Medium Hepatitis B surfaceprotein
mRN	**:**	Amessenger Ribonucleic acid

MTCT	**:**	Mother to child transmission
MTOC	**:**	Microtubule-organizing centre
NHMRC	**:**	National Health and Medical Research Council
NPAAC	**:**	National Pathology Accreditation Advisory Council
NRE	**:**	Negative regulatory element
NSRL	**:**	National Serology Reference Laboratory
ORFs	**:**	Overlapping open reading frames
PCR	**:**	polymerase chain reaction
PER	**:**	protective efficacy rate
RANZCOG	**:**	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RNA	**:**	Ribonucleic acid
SHBs	**:**	Small Hepatitis B surface protein
SIV	**:**	Simian immunodeficiency virus
STIs	**:**	Sexually transmitted infections
TGA	**:**	Therapeutic Goods Administration
USPSTF	**:**	U.S. Preventive Services Task Force
WHO	:	World Health Organization

INTRODUCTION

The hepatitis virus is found in the blood and other body fluids and is transmitted from person to person, the most common routes of infection includes blood transfusions and blood products where there is no screening for blood-borne viruses, medical or dental interventions in countries where equipment is not adequately sterilized, mother to infant during childbirth, sexual transmission (in the case of hepatitis B), sharing equipment for injecting drugs, sharing straws, sharing razors, toothbrushes or other household articles, tattooing and body piercing if done using unsterile equipment ***(Redmond, 2007)***.

Hepatitis B is a major disease of serious global public health proportion. It is preventable with safe and effective vaccines that have been available since 1982. Of the 2 billion people who have been infected with the hepatitis B virus (HBV) globally, more than 350 million have chronic lifelong) infections ***(Mohammed et al, 2003)***.

Viral hepatitis during pregnancy is associated with high risk of maternal complications. There is a high rate of vertical transmission causing fetal and neonatal hepatitis which can have serious effects on the neonate, leading to impaired mental and physical health later in life and is a leading cause in maternal mortality ***(Elinav et al, 2006)***.

Although the CDC (centers for disease control and prevention) and the American Congress of Obstetricians and Gynecologists recommend universal screening of pregnant women for HBsAg, it is important for women's health care providers also to be aware of the groups defined by CDC as being at higher risk for hepatitis B ***(Weinbaum et al, 2009)***.

Groups That Should Be Routinely Screened For Hepatitis B :

- Persons born in regions of the world where hepatitis B prevalence is 2% or higher (including Africa, Asia, Pacific Islands, Middle East, Eastern Europe, Spain, Malta, Mexico, Central America, the Caribbean, areas of South America, and indigenous populations in Alaska, Northern Canada, and Greenland)
- Injection drug users
- Men who have sex with men
- Persons with conditions that may require immunosuppressive or immune-modifying therapy
- Persons with elevated liver enzymes of unknown etiology (ALT; AST)
- Blood or tissue donors
- Pregnant women
- Infants born to HBV-infected mothers
- Hemodialysis patients
- Household members or sexual contacts of HBV-infected persons
- HIV-positive persons ***(Weinbaum et al, 2009)***.

Prevention of vertical transmission entails the diagnosis of acute or chronic HBV infection in pregnant women, This justifies mandatory serum HBsAg testing for all pregnant women ***(ACOG Technical Bulletin, 1992)***.

Peri-natal transmission of this disease occurs if the mother has had acute Hepatitis B infection during late pregnancy, or if the mother is a chronic HBsAg carrier ***(Levy and Koren, 1991)***.

Transmission of HBV infection can be safely and effectively prevented by vaccination. The protective efficacy rate (PER) of vaccination with at least

10 ug recombinant DNA vaccine combined with the administration of immunoglobulin at birth is 95-100% ***(Andre et al, 1994)***.

Women who are acutely infected with hepatitis B virus (HBV), or are chronic carriers of HBV, are likely to transmit the virus to their offspring in the absence of intervention at the time of delivery (the risk being as high as 90%) ***(Chang, 2007)***.

Transmission, which appears to occur intrapartum can be prevented in 95% of cases by administering hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine at birth. As the efficacy of HBIG decreases sharply in newborns after their first 48 hours of life, the injection should be administered immediately after birth ***(Tharmaphornpilas et al, 2009)***.

The first dose of hepatitis B vaccine should be administered within 12 hours of birth, followed by 2 additional doses at 1 and 6 months ***(Tharmaphornpilas et al, 2009)***.

High rates of vertical HBV transmission are due to the presence of hepatitis B envelope antigen (HBe-Ag) and the absence of HBe-Ab (or anti-HBe, the antibody to HBe-Ag), in maternal serum. Up to 90% of the newborns of women with serum HBe-Ag and no serum HBe-Ab are chronic carriers, compared with 15% of the newborns of women with serum HBe-Ab ***(Kabir et al, 2006)***.

Using this background information, the epidemiology of viral hepatitis during pregnancy is essential for health planners and program managers ***(Ejele and Ojulu, 2004)***.

AIM OF THE WORK

This work is designed as pilot cross sectional screening study.

The primary aim of this work is to detect the prevalence of HBV infection among pregnant women who attend the antenatal clinic of the Medical National Institute of Damanhur.

The secondary aim is the early detection of disease and prevention of transmission of infection to others especially the household contacts and to an altogether new generation (fetus) and thereby decrease the pool size.

Chapter (1)

HEPATITIS B VIRUS

The hepatitis B virus (HBV) is the prototype member of a family of hepatotropic DNA viruses, the *Hepadnaviridae,* that replicate by reverse transcription of an RNA pregenome. HBV infects humans, whereas other hepadnaviruses infect mammals (orthohepadnaviruses) or birds (avihepadnaviruses) ***(Schaefer, 2007).***

HBV comprises eight genotypes (A to H) with distinct virological characteristics and geographic distributions ***(Kramvis et al, 2005; Schaefer, 2007)***.

Host range:

HBV primarily infects humans, although chimpanzees, Chacma baboons, and tree shrewsare also susceptible to infection ***(Hu et al, 2000; Cao et al, 2003).***

Target cells:

HBV is primarily an hepatotropic virus, and hepatocytes are the only confirmed site of replication for all members of this virus family. Although the virus has been detected in other cells such as bile duct epithelial cells, peripheral blood mononuclear cells and cells in the pancreas and kidneys, the evidence for viral replication in these cells is controversial ***(Seeger and Mason, 2000).***

Epidemiology of infection:

HBV is one of the most common infectious viruses worldwide. It is estimated that more than two billion people are infected. Approximately 360

million of these are chronically infected ***(Lee, 1997; Chen et al, 2007; Dienstag, 2008).***

Approximately one million people die each year from HBV-related chronic liver disease, including liver cirrhosis and hepatocellular carcinoma (HCC) ***(Mahoney, 1999).***

HCC is one of the most common cancers in the world, and chronic HBV infection is responsible for 50–90% of HCC in high-risk areas ***(Chen et al, 1997).***

Prevalence and geographic distribution:

There is a wide variation of HBV infection in the world ***(Custer et al, 2004; CDC, 2012).***

Approximately 45% of the world population lives in areas where chronic HBV infection is highly endemic (> 8% of the population are HBsAg-positive); 43% live in areas where endemicity is intermediate (2–7% HBsAg-positive); and 12% live in areas where endemicity is low (< 2% HBsAg-positive) ***(CDC, 2012).***

The prevalence of chronic HBV infection is lowest in North America, Northern and Western Europe, Australia and New Zealand; intermediate in Japan, the Middle East, Eastern and Southern Europe and parts of South America; and highest in sub-Saharan Africa, the Amazon Basin, the People's Republic of China, the Republic of Korea, Taiwan (China), and several other countries in South-east Asia ***(Chen et al, 2000; Custer et al, 2004).***

The worldwide variation in the endemicity of HBV infection is influenced primarily by the predominant age at which infection occurs and the modes of transmission by which it occurs. In areas of high endemicity, the

lifetime risk of HBV infection is more than 60%, and most infections are acquired from perinatal and child-to-child transmission, when the risk of developing chronic infection is greatest. In these areas, acute hepatitis B is uncommon because most perinatal and early childhood infections are asymptomatic. However, rates of liver cancer and cirrhosis in adults are very high. Chronic carriage is thought to result from vertical transmission in China, Taiwan (China), and the Republic of Korea ***(Chen et al, 2000).***

In low endemicity areas, most HBV infections occur in adolescents and young adults with relatively well defined high-risk groups, including injection drug users, homosexual males, health care workers, and patients who require regular blood transfusion or haemodialysis. In countries where adult horizontal transmission patterns are the principal transmission routes, the incidence of HBV infection is highest in adults ***(Custer et al, 2004).***

Genotype A is prevalent in Europe, Africa, and North America. Genotype B is prevalent in Taiwan (China), China, Thailand, South-east Asia, and genotype C is prevalent in China, Japan, the Republic of Korea, and South-east Asia ***(Devesa et al, 2004).***

Genotype D is predominant in India, Mediterranean areas, and the Middle East region. Genotype E is limited to West Africa. Genotypes F and G are mostly found in Central and South America. Genotype H has been observed in Mexico and Central America ***(Devesa et al, 2004).***

Compared with patients infected with the HBV genotype B, those infected with genotype C have a significantly lower rate of spontaneous HBeAg seroconversion ***(Furusyo et al, 2002; Kao et al, 2004),*** a higher histological activity index of necroinflammation or fibrosis score ***(Lindh et al, 1999; Chan et al, 2002; Kobayashi et al, 2002; Lee et al, 2003),*** and a higher