**Outcomes of Elimination of Mother-to-Child (EMTCT) Hepatitis B:**

**A Pilot Project in Terengganu 2019-2021**

Abstract

1. **INTRODUCTION**
2. **Background**

Hepatitis B infection is caused by the hepatitis B virus (HBV). It is a global public health problem and causes significant morbidity and mortality. WHO (2022) estimates that 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year and resulted in an estimated 820 000 deaths, mostly from cirrhosis and hepatocellular carcinoma (HCC). Patients with chronic hepatitis B are at increased risk of cirrhosis, hepatic decompensation and responsible for 50–80% of HCC cases worldwide (Aspinall et al., 2011).

The prevalence of chronic HBV infection is high (>8%) in Asia and Southeast Asia, including China, Korea, Indonesia, and the Philippines. In Malaysia, about 1.1 million people are thought to be chronically infected with hepatitis B virus and the estimated prevalence of HBsAg among the population is approximately 4.7%. Following the exposure to HBV, up to about 10% of the patient will progress to chronic hepatitis B, which is defined as persistence of the infection for more than 6 months duration. The chronic hepatitis B then progress to liver cirrhosis and hepatocellular carcinoma in about 15-40% of the patients (Yin & Tong, 2006).

There are 2 major modes of transmission of HBV which are vertical transmission (perinatal transmission), occurring at birth from infected mothers to their newborns and horizontal transmission which can occur through open cuts and scratches; transfusion of blood products; breaks in good practices to prevent blood-borne infections in the health care setting; sexual transmission and risky behavior, including injecting-drug use or tattooing, body piercing, and scarification procedures without the use of sterilized equipment and needles (Nelson et al., 2016).

Strategies for reducing transmission of hepatitis B includes screening pregnant women for HBV infection, providing infant postexposure prophylaxis which are hepatitis B immune globulin (HBIG) and hepatitis B (HepB) vaccine within 24 hours of birth, and maternal treatment with antiviral medications (Nelson et al., 2014). Infant postexposure prophylaxis followed by completion of the vaccine series, is 85%–95% efficacious for prevention of MTCT (Nelson et al., 2014).

Aligned with the WHO commitment of for triple elimination initiatives (HIV, Hepatitis B and Syphilis), Ministry of Health has conducted a pilot project called as EMTCT Hepatitis B to prevent the transmission. There are five strategies have been outlined in this pilot project to achieve this elimination:

1. Universal screening among pregnant mothers for HBsAg at each time of pregnancy when booking.

2. Screening of all pregnant mothers who are HBsAg-positive for HBV DNA as a guide on whether to be given antiviral therapy during pregnancy.

3. Management for HBsAg-positive mothers.

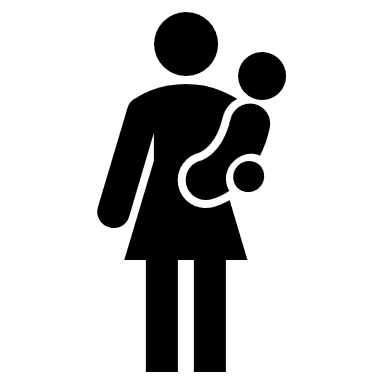
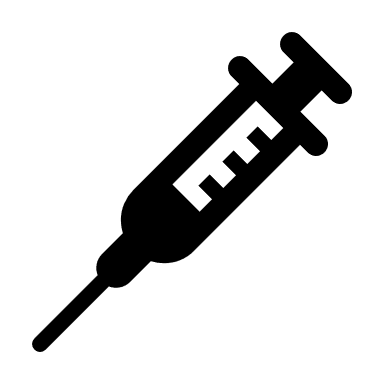
4. Provide Hepatitis B immunoglobulin (HBIG) prophylaxis to infants whose mothers are HBsAg-positive

5. Strengthen complete routine Hepatitis B vaccination for all infants.

1. **Description of project**

In Malaysia, this EMTCT Hepatitis B pilot projects implemented in 3 states which include Terengganu, Pahang, and Kedah. This project was implemented in Terengganu starting on 1st May 2019 involving one (1) health clinic (KK), Klinik Kesihatan (KK) Hiliran, Kuala Terengganu. Following that, on 1st June 2019, this pilot project was expanded to other seven (7) KKs which include KK Kuala Dungun, KK Marang, KK Batu Rakit, KK Kuala Berang, KK Permaisuri and KK Kg. Raja, and involving two (2) hospitals, Sultanah Nur Zahirah Hospital (HSNZ) and Kemaman Hospital. To date, a total of 10 health facilities, eight (8) KKs (1 KK/ district) and two (2) hospitals are involved in this pilot project.

The components include universal screening of hepatitis B, anti-viral treatment for those who indicated, active (4 doses + 1 booster of hepatitis B vaccine) and passive (Hepatitis B immunoglobulin) immunization. Finally, the outcome was to screen the child for Hepatitis B surface antigen (HBsAg) and Hepatitis B antibody tests at 9 months old.

1. **Objectives of the study**
   1. General Objectives
2. To determine the outcomes of EMTCT program in preventing Hepatitis B transmission to children.

**Infant Care & Screening at 9/12**

* Other 3 doses of Hepatitis B vaccine
* HBsAg ELISA test
* Hepatitis B Antibody test

**Immunization of Newborn**

* Hepatitis B Immunoglobulin at birth
* Hepatitis B vaccination at birth
  + - 1. Specific Objectives

1. To describe the socio-demographic characteristics of cases.
2. To describe the clinical status of mother with Hepatitis B.
3. **METHODOLOGY**

An observational study design was used in this study. Pregnant women in the selected health clinics and hospitals were screened for HBsAg using the Rapid Test Kit - RTK HBsAg, including mothers who have been screened or who have been vaccinated against hepatitis B before. This screening was done to pregnant mothers at each time of pregnancy when booking. RTK will be performed at the selected hospitals (Hospital Sultanah Nur Zahirah and Hospital Kemaman - PAC, antenatal ward, or delivery room) if the mother has never been screened or has never made an antenatal visit at the Health Clinic (unscreened/unbooked).

For pregnant women with reactive RTK results, the mother will be referred to a medical officer or family physician for clinical evaluation including risk factor assessment. For confirmation test, venous blood will be collected for HBs Ag EIA. The lab will continue to run HBeAg and anti-HBe tests on the same sample if the HBsAg verification test is positive. The mother will be notified to the District Health Office using the notification form and the mother will be referred to the Gastroenterology and Hepatology Specialist Clinic preferably before 24 weeks of gestation.

Prior to the date of the appointment with the specialist, all HBsAg-positive pregnant women who have been referred to a gastrologist will be given an appointment to have FBC, LFT, INR, and HBV DNA blood tests. The mother will be evaluated clinically based on history, physical examination and clinical tests. For HBsAg positive mothers with active disease/hepatitis or advanced fibrosis or cirrhosis, it is recommended to start treatment including antivirals.

When a mother with HBsAg positive is referred to the O&G clinic, an assessment will be carried out to rule out potential causes/obstetric disorders that cause abnormal liver function in mothers who have been diagnosed with hepatitis flare, active disease/hepatitis, fibrosis, or cirrhosis.

All these HBsAg positive mothers will undergo antenatal/obstetric evaluation and planning related to the time and method of delivery will be determined based on obstetric and non-obstetric factors including Hepatitis B disease status. They must give birth in a hospital with specialised care.

Infants whose mothers have hepatitis B will receive hepatitis B immunoglobulin prophylaxis (HBIG) (HBsAg-positive) within 12 hours after birth and no later than 48 hours and hepatitis B Vaccine dose 1 should be given as soon as possible (or within 12 hours).

Post Hepatitis B Vaccination Testing (PVST) should be performed at the age of 9 to 12 months. The outcome classified into 3 categories:

1) responder (HBsAg negative and presence of antibody >10 ui/l)

2) non-responder (HBsAg negative and antibody <10 ui/l)

3) infected

Infants with a positive HBsAg result should continue follow-up treatment with a Pediatrician. Summary flow of management of Hepatitis B mothers is shown in **Fig. 1**.

**Screening & Counselling**

* Rapid Test Kit (RTK) HBsAg
* Confirmation test HBsAg ELISA
* HBeAg & Hepatitis B Viral Load

**Co-morbidities Screening**

* HIV test, Syphilis, Hepatitis C
* FBC, Liver Function Test, INR
* Ultrasound Hepatobiliary System

**Maternal Care**

* Referral to Medical and O&G care
* Assessment for anti-viral therapy
* Timing and delivery mode

**Immunization of Newborn**

* Hepatitis B Immunoglobulin at birth
* Hepatitis B vaccination at birth

**Infant Care & Screening at 9 months old**

* Other 3 doses of Hepatitis B vaccine
* HBsAg ELISA test
* Hepatitis B Antibody test

**Fig. 1: Summary flow of management of Hepatitis B Mothers**

1. **RESULTS**

A total of 18,725 pregnancy women were screened for RTK HBsAg in selected health facilities and hospitals, and 62 (0.33%) tested positive. The total number of screenings by health facilities and year of screenings are shown in **Table 1**. Out of those tested positives, 6 had miscarriages, 4 babies died, 30 babies were not due for testing and 2 missing data (**Fig. 2**). A total of 20 babies (32.3%) completed the 9-month follow up.

**No. of Antenatal Mother Screened**

n = 18,725

Negative, n = 18,863

Negative, n = 0

**Positive HBsAg RTK**

n = 62 (0.33%)

**Eligible for analysis**

* Mother, n = 62
* Child: Due, n = 32

Not Due, n = 30

**Discard**

* Abortion, n = 6
* Infant Death, n = 4
* Missing data, n = 2

**Completed Data & Follow up**

n = 20

**Fig. 2: Flow of Data Collection**

**Table 1: Total number of screenings and Hepatitis B cases among pregnant women in Terengganu in 2019 (May-Dis) - 2021.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Health Facilities/**  **Year** | **May – Dis 2019** | | **2020** | | | **2021** | | **Total No.of Screening** | **Total No. of Hep B Cases** |
| **No.of Screening** | **No. of Hep B Cases** | **No.of Screening** | **No. of Hep B Cases** | **No.of Screening** | | **No. of Hep B Cases** |
| KK Chukai | 465 | 0 | 840 | 5 | 774 | | 1 | 2079 | 6 |
| KK Kuala Dungun | 706 | 3 | 1349 | 5 | 1246 | | 9 | 3301 | 17 |
| KK Marang | 400 | 1 | 784 | 3 | 735 | | 2 | 1919 | 6 |
| KK Kuala Berang | 278 | 0 | 565 | 0 | 591 | | 1 | 1434 | 1 |
| KK Hiliran | 1231 | 7 | 1633 | 3 | 1486 | | 3 | 4350 | 13 |
| KK Batu Rakit | 531 | 3 | 1007 | 2 | 914 | | 2 | 2452 | 7 |
| KK Permaisuri | 351 | 1 | 551 | 2 | 564 | | 5 | 1466 | 8 |
| KK Kg Raja | 408 | 2 | 654 | 1 | 607 | | 1 | 1669 | 4 |
| Hospital Sultanah Nur Zahirah | 11 | 0 | 26 | 0 | 0 | | 0 | 37 | 0 |
| Hospital Kemaman | 5 | 0 | 13 | 0 | 0 | | 0 | 18 | 0 |
| **Total** | **4,386** | **17** | **7,422** | **21** | **6,917** | | **24** | **18,725** | **62** |

**Table 2: Sociodemographic Data for Hepatitis B cases among pregnant women in Terengganu in 2019 (May-Dis) - 2021**

|  |  |  |
| --- | --- | --- |
| **Sociodemographic Data (n=62)** | **Frequency** | **Percentage (%)** |
| **Age (Year)** | | |
| 20-24 | 3 | 4.8 |
| 25-29 | 12 | 19.4 |
| 30-34 | 25 | 40.3 |
| 35-39 | 16 | 25.8 |
| 40-44 | 6 | 9.7 |
| **Race** | | |
| Malay | 60 | 96.8 |
| Myanmar | 1 | 1.6 |
| Thailand | 1 | 1.6 |
| **Occupation** | | |
| Government | 22 | 35.5 |
| Self-employed | 9 | 14.5 |
| Housewives | 31 | 50.0 |
| **Risk Factors** | | |
| Vertical Transmission | 8 | 12.9 |
| No risk factors | 54 | 87.1 |

The sociodemographic data for these positive cases is shown in **Table 2**. Most cases (96.8%) were Malay and housewives (50%). Majority of the cases aged within 30-34 years old (40.3%), followed by 35-39 years old (25.8%). About 87.1% mothers with positive Hepatitis B had no risk factors identified and only 12.9% of them had mothers/ siblings with Hepatitis B (vertical transmission).

For the outcome of the infants of Hepatitis B mothers is shown in **Table 4**. The results showed that all infants were responders (20/20) and none of them were infected.

**Table 3: The clinical status of mother with Hepatitis B in Terengganu in 2019 – 2021**

|  |  |  |
| --- | --- | --- |
| Variables | N=62 | % |
| Hepatitis B ‘e’ Antigen (HBeAg) |  |  |
| 1. Reactive | 50 | 80.0 |
| 1. Non-Reactive | 12 | 20.0 |
| Co-infection (Reactive) |  |  |
| 1. HIV | 0 | 0 |
| 1. Hepatitis C | 0 | 0 |
| 1. Syphilis | 0 | 0 |
| Complications (Yes) |  |  |
| 1. Cirrhosis | 0 | 0 |
| 1. Chronic Liver Disease | 0 | 0 |
| 1. Hepatocellular Carcinoma | 0 | 0 |
| Hepatitis B Viral Load (iu/ml) |  |  |
| 1. < 20,000 | 56 | 90.3 |
| 1. 20,000 – 200,000 | 2 | 3.2 |
| 1. > 200,000 | 4 | 6.5 |

**Table 4: Outcome of infants of Hepatitis B mothers in Terengganu in 2019 – 2021**

|  |  |  |
| --- | --- | --- |
| **Outcome of the babies (n=20)** | **Frequency** | **Percentage (%)** |
| **1st dose Hepatitis B vaccine** |  |  |
| Given Hepatitis B vaccine | 20 | 100 |
| **HBIG** |  |  |
| Given HBIG | 20 | 100 |
| **HBsAg @ 9 month of age** |  |  |
| Negative | 20 | 100 |
| **Hep B Antibody** |  |  |
| ˃10 iu/l | 20 | 100 |

1. **DISCUSSION**

A total of 18,725 pregnant women in Terengganu from 2019 to June 2021 were screened for Hepatitis B. Out of that, 62 positive cases of Hepatitis B were reported. The positive rate in this study was 0.33%. It is similar to study in Netherlands and UK (Visser et al., 2019). The initial impact showed a promising result as it successfully prevents the transmission of Hepatitis B infection to children as result of continuous care and multidisciplinary efforts for the elimination. By giving hepatitis B vaccinations, only can prevent 72% of transmission but with EMTCT program it will prevent by 99.2% of transmission (Lee et al., 2006).

Our study had several limitations. Limitation for this study was small sample size, this is because 48.3% babies not due for HBsAg testing yet. In addition, this study was conducted in selected antenatal clinics and therefore results of the study may not be representative of the entire pregnant women in Malaysia. Further study should be conducted to determine continuous care and outcomes of this project.

We did not perform a cost analysis of the project. Nevertheless, the additional cost of integrating the HBV intervention into the existing flow would be limited. In term of cost-effectiveness, the EMTCT program showed to be a cost-effective in long term.

1. **CONCLUSION**

The World Health Organization (WHO) has set a global target of eliminating mother-to-child transmission of hepatitis B by 2030. This goal is achievable through the implementation of effective prevention strategies, such as providing universal access to antenatal care, immunisation, and treatment.

The EMTCT of hepatitis B has had a significant impact on the health of mothers and their children. By preventing the transmission of the virus from mother to child, the risk of chronic hepatitis B infection and its associated complications is greatly reduced. This has resulted in improved health outcomes for mothers and their children. Hence, all pregnant women should be tested for HBV, infants born to mothers who test positive for HBsAg should receive HBV immunisation and HBIG prophylaxis within 12 hours of delivery and completed the hepatitis B vaccinations to prevent the transmission to the children. Serologic testing for infection and immunity at age 9 months should be done to make sure the child is non-infective.

Our results demonstrate that Hepatitis B screening among pregnant mothers is important, and this screening programme should be extended to all health clinics in Terengganu and even nationwide. However, to implement this screening expansion requires a large financial allocation.

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