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Knowledge and awareness of maternal chronic hepatitis carriers to perinatal antiviral use in prevention of mother-to-child hepatitis B virus transmission

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INTRODUCTION

Hepatitis B virus (HBV) infection is a global health problem. In 2017, an estimated 257 million persons were living with chronic HBV in the world, including 65 million women of childbearing age.[1] Despite immunoprophylaxis with HBV vaccine and hepatitis B immunoglobulin, mother-to child-transmission (MTCT) remains a key mode of viral transmission in high prevalence areas. The rate of HBV MTCT is 10% to 15% in women with high viral load and/ or who are hepatitis B e antigen (HBeAg) positive.[2-5] A high viral load is defined as having a HBV DNA of more than 200,000 IU/ml.

The current guidelines[6,7] advocate starting antiviral therapy for women in the immune-tolerant phase with high viral load during the third trimester of pregnancy to further reduce the risks of MTCT. The short-course of antiviral therapy has been shown to consistently reduce maternal viraemia and vertical transmission. Tenofovir in late pregnancy can result in a 3-fold reduction in MTCT of HBV, when used in combination with immunoglobulin and HBV vaccine at birth.[4]

A global modelling study showed that < 1% of mothers with high viral load received antiviral treatment.[8] In the last 5 years, it was estimated that less than 15% of pregnant women with high viral load in Singapore agreed to treatment.[9] There is an urgent need to understand the reasons for low uptake of this intervention in order to prioritize strategies and accelerate progress to pave the way for the World Health Organization 2030 target of reducing the prevalence of HBV infection to 0.1%.[10]

From a mother's perspective, it was not cost-effective to receive antiviral treatment given the observed medication price and transmission rate in Singapore. The lowest total antiviral treatment cost required to complete antiviral treatment in a restructured hospital in Singapore after

subsidy was for telbivudine at SGD 350.28 (SGD 1 = USD 0.74).[11] In this study, we sought to understand the knowledge and behaviours of mothers with chronic HBV to determine other predictors and barriers to antiviral treatment.

METHODS

This questionnaire-based cross-sectional survey was carried out in National University Hospital of Singapore from January 2018 to December 2019. Eligible participants were chronic HBV carrier pregnant women or women with children less than 5 years old. Ethics approval was obtained from the NHG DSRB Domain F 2017/01209

Participants were recruited using pamphlets and recruitment posters placed in the obstetric, adult and paediatric hepatology and neonatology clinics. The attending healthcare professionals would refer the potential participant(s) to the research assistant(s). The research assistant(s) will then invite the potential subject to take part in the anonymous questionnaire. The research assistant(s) surveyed these participants after implied informed consent was taken. Both research assistants were trained by the primary investigator to ensure standardization of the interview process. These survey questions were translated by the research assistants into a language that the participants could understand.

Participants were surveyed about their socio-economic status, risk aversion, behaviours and knowledge on HBV and their reasons for taking/not taking the antivirals. Participants' risk averseness were assessed through a hypothetical scenario created to assess their risk-taking behaviour and a self-rated Likert scale assessment of their risk averseness.

A knowledge score of HBV awareness was given to the respondents based on the correct answers for 9 questions (each question maximum score of 5, total maximum possible score of 45;

with less than 30 defined as fail) (Appendix, Supplemental Digital Content 1 for knowledge based questions). A knowledge score for the role of antiviral (questions 6 - 8) was given based on correct answers for 3 questions (each question maximum score of 5, total maximum possible score of 15; with less than 10 defined as fail).

Quantitative data non-normally distributed were presented as median and range and compared by Man-Whitney U test. Categorical variables were presented as numbers and percentages and compared by chi-square analysis or Fisher's exact test. $P < 0.05$ was considered statistically significant. All data analysed using SPSS ver 25.0.

RESULTS

57 women were surveyed. The median age was 33 (range 25 - 43) years old. 64.9% were Chinese, with Thais comprising the second largest group surveyed (15.8%). Majority surveyed were degree/post graduate degree holders (50.9%), 64.9% were working full time, 80.7% lived in government housing similar to the national profile. The 17% were pregnant with their first child with the majority surveyed having 1-2 children (47.4%). 3.5% had children with chronic HBV acquired from vertical transmission despite vaccination. (Table I)

54.3% were first diagnosed with chronic HBV more than 5 years ago, with 22.8% being unsure/unable to recall when were they first diagnosed with chronic HBV. 30.3% did not receive any regular clinic follow up for their chronic HBV carrier status. All were reviewed at least once by a hepatologist. One participant (1.75%) had high viral load and none were taking anti-viral.

A Likert scale of 1 to 5 was used by the respondents to rate their risk averseness, whereby "1" was a person who "does not take any risk" to "5" was a person who "takes risks all the time". The self rated risk profile median score was 2 (range 1 - 5). A hypothetical scenario was also used to assess their risk profile. A choice had to be made between two options: one where the participant would receive an assured sum of $25.00 as pay-out and two, a 50% chance of receiving $60.00 or nothing through a coin toss. 68.5% (37 out of 54 respondents; 3 respondents opted not to answer) chose the first option. 8.8% took part in recreational high-risk activities or had high-risk behaviours. 7.0% acknowledged that they drank and/or smoke. Both the hypothetical scenario and self-reported risk-taking behaviours suggested that the majority of our respondents were risk averse. This correlated with the low Likert score of their self-rated risk profile.

Four questions were asked to assess the mothers' knowledge on HBV (Table II). In questions 1 and 2, which assessed the respondents' knowledge on mode of HBV transmission and symptoms of babies infected with HBV, 64.9% and 40.4% of the respondents, respectively, answered the questions correctly. In questions 3 and 4, which assessed the respondents' understanding of the risk of vertical transmission with/without antiviral use only 21.1% answered correctly. For question 3, 50.9% answered that they did not know the answer and 17.5% replied incorrectly that the risk was <1%. For question 4, 66.7% replied that they did not know the answer.

A knowledge score was given based on 9 questions (Appendix). The median knowledge score was 34 (range 27 - 45). Only 3.5% provided correct answers to all questions. Median knowledge score for the role of antiviral (questions 6 - 8) was 11 (range 7 - 15). Only 10.5% scored full marks for the questions on the role of antiviral while 28.7% answered all questions incorrectly.

In the subgroup of respondents who answered all questions incorrectly, 86.7% (13 out of 15) were non-Singaporeans (10 were native born Chinese; 2 were Vietnamese and 1 identified

herself as “South East Asian”; odds ratio of 2.6 (CI: 0.51 - 13.3; p = 0.25). Most, 93.8% (14 out of 15) lived in government housing; odds ratio of 5.6 (CI 0.66 - 47.4; p = 0.11), 71.4% (10 out of 15) had no tertiary education; odds ratio of 3.25 (CI: 0.94 - 11.2; p = 0.06). No association between age, race, employment status, parity and risk averseness when associated with higher knowledge scores.

87.7% replied that they were willing to take antivirals if it could reduce MTCT HBV from 10% to 1%. We further analysed the respondents who refused to take antivirals. 85.7% (6 out of 7; 4 Chinese and 2 Vietnamese) were non-Singaporeans and did not receive any prior medical review for their chronic HBV status. 85.7% (6 out of 7) lived in public housing. Median knowledge score for these 6 was 39.2 (28 - 45). Median knowledge score for the role of antiviral (questions 6 - 8) for these 6 was 11.1 (range 9 - 15). However, it was interesting to note that when questions 3 and 4, which assessed the respondents’ in depth understanding of the risk of MTCT with/without antiviral use were asked majority said that they did not know of the answer (85.7% i.e. 6 out of 7). One identified incorrectly that the rate of transmission of HBV virus if a baby born to a HBV carrier mother is given the HBV vaccine and immunoglobulin was <1%. No association between differences in employment status, risk averseness, parity or age with antiviral refusal.

The top 3 reasons for taking the antiviral therapy are as follows: A) 21 had read about the antiviral therapy and were convinced that it helped to reduce the rate of HBV transmission to the unborn child, B) 17 stated that they would take the antiviral because the doctors had recommended it and C) 15 would take the antiviral as they were worried that children can become very ill if they are infected by the HBV. One correctly stated that the doctor in view of her high HBV viral load recommended it, and another stated that she had to take the antivirals as she was immunosuppressed.

Amongst those who gave reasons for making the choice of not taking the antivirals, the top 4 most common reasons for not taking the antiviral therapy were: A) 6 were not convinced that the antiviral was required to reduce the risk of vertical transmission to their unborn child B) 5 felt that the HBV vaccination alone was good enough to reduce the transmission risk to their child, C) 4 replied that they did not understand their doctors' explanation, D) 3 were uncertain of the side effects of the antivirals and hence were not keen to take the antivirals, E) 2 stated that their HBV viral load was low and hence did not see the need to take the antivirals.

45.6% (26 out of 57) stated that S$14.00 to S$20.00 per week (i.e. S$2 to S$2.90 daily) over 12 weeks was a reasonable price to pay for an antiviral therapy which could reduce the vertical transmission rate of HBV virus from 10% to 1%.

DISCUSSION

We showed that mothers with chronic HBV carriers in Singapore lacked sufficient knowledge regarding HBV virus transmission and prevention. Alarmingly, 78.9% of the mothers were not aware of the role of antivirals to reduce MTCT. This was regardless of age, education, compliance to regular medical appointments and degree of risk aversion.

Our surveyed population was generally risk averse. 50.9% surveyed were degree holders and above, with 64.9% working full time and 47.4% had at least 1 child or more at the time of the survey. In other words, more than half of our surveyed population was a group of highly educated and fully employed working mothers.

Compared with other studies,[12-14] respondents seemed to be more knowledgeable about HBV transmission routes. 64.9% of respondents were aware of the various modes of HBV transmission as compared to 46.7% in China,[15] and 10.3% in Nigeria.[16] It is noteworthy that

information related to HBV was relatively accessible to women and their families at our study sites. Free pamphlets on HBV transmission obtained from the Singapore Health Promotion Board were placed in the waiting areas.

While more than half of our study respondents were aware of the transmission modes of HBV, and the need for HBV vaccine and immunoglobulin, 21.1% were aware of the role of antivirals in reduction of MTCT from 1%–5% to less than 1%. Amongst the 28.7% respondents who answered all knowledge based questions on antivirals incorrectly, the majority were citizens from developing countries, lived in government housing and had no formal tertiary education.

When we looked at the respondents who declined the use of antivirals, the majority of the individuals were non-Singaporeans, lived in public housing and received no prior medical review for their chronic HBV status. There is a knowledge gap in the role of antiviral for this population that needs to be addressed urgently. Education campaigns should be targeted at this group of high risk mothers from lower socioeconomic and education levels as they are the most likely to forgo treatment, especially if it is costly.

While 80.7% in this study agreed that they would take the antivirals when offered, in the last 5 years, it was estimated that less than 15% of pregnant women with high viral load in Singapore agreed to treatment.[9] We examined the reasons behind this discrepancy and found that it was due to lack of medical knowledge for these mothers. Firstly, more than half of the mothers who did not use antivirals believed that HBV vaccination alone was good enough to reduce the transmission risk to their child. Some reported that they did not understand their doctors' explanation. Lastly they were sceptical of the side effects. 3.5% of our respondents correctly identified their reasons for not taking antivirals (i.e. low HBV viral load). In line with the meta-

analysis from WHO,[17] more education is required for mothers with high viral load 200,000 IU/ml to accept treatment to reduce MTCT.

In our previous study,[11] one of the primary reasons we identified for pregnant women with high viral load for not choosing antiviral treatment to prevent HBV vertical transmission is that the consequent reduction in MTCT rates appears to be small. In this study, cost was also explored as a possible reason for poor uptake of antivirals to reduce MTCT. While none of our respondents reported that cost was a prohibitive factor for taking the antivirals during their pregnancy, those surveyed were only willing to pay between S$2.00 to S$2.90 daily for 12 weeks to reduce their MTCT risk from 10% to 1%. None of the current antiviral drugs used except for Lamivudine is priced at this level.[11] This information could serve to inform policy makers of the amount of financial subsidies required to improve uptake of antiviral treatment.

We recognise that the results from this survey might not be applicable to all maternal HBV carriers as the sample size is small. Also, the self-reported HBV compliance to regular medical appointments, use of antivirals and immunisation practices of the respondents cannot be validated.

In conclusion, our findings suggest a need to update and improve the quality of education programmes targeting women of childbearing age about the benefits of antiviral use, in addition to the practice of giving HBV vaccination and immunoglobulin at birth for babies born to maternal HBV carriers. In particular, educational efforts should be focused on vulnerable individuals who are less educated, with lower socio-economic status. This is because pregnant women's awareness and perception to their illness largely impact treatment decisions. It is perhaps timely to review existing educational pamphlets and antenatal educational programs to ensure that key messages are effectively conveyed to the target audience. Additionally, from a health system perspective,

providing subsidies for antiviral treatment to ease the financial concerns of parents is likely to reduce long-term expenses generated by chronic HBV co mplications.

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Table I: Socio-demographic and clinical characteristics of mothers (n=57)

Characteristics	n (%)
Median Age in years (IQR)	33 (25 - 43)
Nationality	
• Chinese	37 (64.9)
• Thailand	9 (15.5)
• Indians	5 (8.8)
• Malays	1 (1.8)
• Others	15 (22.4)
Highest education level (n=55)	
• Primary	2 (3.5)
• Secondary	13 (22.8)
• Diploma or equivalent	11 (19.3)
• Degree	20 (35.1)
• Postgraduate degree	9 (15.8)
Employment	
• Full time	37 (64.9)
• Part time	20 (35.1)
Housing type	
• Government	46 (80.7)
• Private property	11 (19.3)
First diagnosed with HBV	
• <5 years ago	13 (22.8)
• >5 years ago	31 (54.3)
• Unable to recall	13 (22.8)
Follow up for HBV n=56	
• 3-6 monthly	24 (42.9)
• 12 monthly	15 (26.8)
• Never	17 (30.3)
Number of children	
• 0	17 (29.8)
• 1-2	27 (47.4)
• 3-4	10 (17.5)
• 5 or more	3 (5.3)
Children with HBV MTCT	
• Yes	2 (3.5)
• No	55 (96.5)

Table II: Questions assessing knowledge.

Questions assessing knowledge	Correct (n=57) (%)
1. How does a person get infected with hepatitis B? (*There can be more than 1 correct answer)* **a. Direct contact with blood of hepatitis B carrier** **b. From mother to baby during the birth process** c. Sharing a meal with hepatitis B carrier	64.9
2. Babies infected with hepatitis B virus have the following symptoms, if any: a. Fever b. Yellow eyes c. Tea colored urine **d. No symptoms at all**	40.4
3. What is the rate of transmission of hepatitis B virus if a baby born to a hepatitis B carrier mother is given the hepatitis B vaccine and immunoglobulin? a. < 1 % **b. 1-5%** c. 5-10% d. I do not know the answer	21.1
4. What is the rate of transmission of hepatitis B virus if a hepatitis B carrier mother receives antiviral therapy during her pregnancy? **a. < 1 %** b. 1-5% c. 5-10% d. I do not know the answer	21.1

Option in bold type is the correct answer.

APPENDIX

Supplemental Digital Content 1 for knowledge based questions.
Knowledge based component of survey, which comprised of 9 questions. Maximum score of 45 marks. We have bracketed the mark allocated for each answer below.

	Strongly Agree	Agree	I am not sure	Disagree	Strongly disagree
Q1. Most people with chronic hepatitis B were infected at birth or during early childhood.	(5)	(4)	(3)	(2)	(1)
Q2. Infected infants at birth will develop chronic infection for life.	(5)	(4)	(3)	(2)	(1)
Q3. Many people with chronic hepatitis B virus infection do not know that they are infected since they do not feel or look unwell.	(5)	(4)	(3)	(2)	(1)
Q4. Chronic infections with hepatitis B virus may eventually lead to serious health problems, including liver damage, liver cancer, and even death	(5)	(4)	(3)	(2)	(1)
Q5. Some people who were infected during early childhood may remain infected for most of their life because they cannot eradicate the virus from their bodies	(5)	(4)	(3)	(2)	(1)
Q6. Antiviral therapy is recommended for pregnant mothers with high viral load of hepatitis B virus.	(5)	(4)	(3)	(2)	(1)
Q7. Antiviral therapy during pregnancy could reduce mother to child transmission rate significantly so that the child may not be affected.	(5)	(4)	(3)	(2)	(1)
Q8. The potential risks of taking antiviral treatment during pregnancy outweigh the risk of transmission.	(1)	(2)	(3)	(4)	(5)
Q9. Shaking hands with hepatitis B carriers or talking to them can lead to you being infected with hepatitis B.	(1)	(2)	(3)	(4)	(5)