

Research Articles

Health screening for new entry medical students at Newcastle University Medicine (NUMed) Malaysia: a 4-year cross-sectional study

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Background

Newcastle University Medicine (NUMed) Malaysia adheres to the UK Medical Schools protocol on screening for blood borne viruses including hepatitis B (HBV), Hepatitis C and HIV as health requirements for new entry medical students' admissions and continuing medical practice. This study specifically aims to assess the outcome of HBV vaccination and the subsequent seroconversion status along with other required vaccinations.

Methods

This 4-year cross-sectional study included 345 new entry Malaysian medical students to NUMed from 2015 to 2018 excluding 80 students with missing data. Demographic data, HBV vaccination status, and HBV surface antibody (anti-HBs) titers were obtained from participants' health screening reports and recorded in a pre-designed data template. Seroconversion status (anti-HBs titer >10 IU/L) measured using an enzyme-linked immunoassay, was determined and seroconversion rates were calculated. None of the participants received a booster anytime prior to testing. Both demographic and vaccination data were matched to investigate seroconversion rate in relation to ethnicity and gender. Chi-square test was used for analysis using Prism with statistical significance defined as $P < 0.05$.

Results

Out of 345, only 223 (64.6%) vaccinated individuals showed seroconversion, while 117 (33.9%) did not seroconvert. Among participants, 121 (35.1%) were male and 224 (64.9%) were female. The majority of the participants were of Chinese ethnicity (62.0%), followed by Malay (19.7%) and Indian ethnicity (18.3%). None of the 345 new entry medical students were tested positive for hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc), indicating an overall HBV prevalence of 0%. A total of 287 participants (83.2%) were vaccinated against varicella-zoster virus, while 58 (16.8%) were not vaccinated. Vaccination coverage of other vaccines, such as measles, rubella, MenQ and yellow fever were 257 (74.5%), 237 (68.7%), 154 (44.6%) and 20 (5.8%) respectively. There is no significant difference in the seroconversion rate of HBV vaccine between male participants (62.0%) and female participants (64.3%, $P = 0.298$). However, there is a statistically significant difference in the HBV seroconversion rate between the 3 ethnicity groups, with students of Malay ethnicity showing the lowest seroconversion rate of 47.1%, followed by those of Indian (68.3%) and Chinese ethnicity (69.6%) ($P = 0.002$).

Conclusions

This is the first study demonstrating a low HBV vaccine seroconversion rate (64.6%) among young new entry medical students at NUMed (median age: 19) following standard recommended 3-dose vaccination. Students of Malay ethnicity showed a significant non-conversion rate of 51.5% ($p=0.002$) as compared to the students of Chinese (29.4%) and Indian (28.6%) origin. Previous studies showed seroconversion rates of over 90% and further studies should be considered to investigate why this young population of Malaysian students did not mount protective antibody titer.

Healthcare workers, including medical students, are at high risk of biological hazards such as hepatitis B virus (HBV) and other vaccine-preventable infection through occupational exposure.¹ Among blood-borne viruses, HBV has the highest risk of viral transmission to non-immune healthcare workers as compared to hepatitis C and HIV.² Studies have reported that 37% of HBV infection among healthcare workers is a result of occupational exposure caused by direct contact with infectious materials such as blood through needle stick injuries or other contaminated body fluids through accidental spillage.^{1,3} There is a high rate (55.9%) of accidental exposure to blood at the start of clinical training among medical students.⁴ Therefore, to mitigate risk of acquisition, health screening for new entry medical students is recommended prior to their clinical training.

HBV infection has a high prevalence worldwide, varying between geographic regions. About 257 million people are living with chronic HBV infection worldwide, which is a leading cause of cirrhosis and hepatocellular carcinoma.⁵ To date, it remains a major global public health concern, resulting in around 1.45 million deaths annually worldwide.⁶ According to the World Health Organization, HBV vaccination coverage amongst health care workers is estimated to be significantly lower in low- and middle-income countries compared to high-income countries (18-39% to 67-79% respectively).⁷

In the United Kingdom (UK), all new entry medical students must be vaccinated against HBV and receive a post-vaccination response test.⁸ Additionally, vaccination status against varicella-zoster, measles, rubella, yellow fever and 4 serogroups of meningococcal disease (A, C, Y, W-135) should be evaluated in the new entry occupational health screening as per the UK and Malaysian occupational health guidelines, as well as admission policy of most medical schools.⁸⁻¹¹

This study aims to evaluate vaccination coverage and subsequent HBV seroconversion in new entry medical students at Newcastle University Medicine (NUMed) Malaysia. In addition, vaccination status against varicella-zoster, measles, rubella, yellow fever and 4 serogroups of meningococcal disease (A, C, Y, W-135) was collected as part of the entry requirements.

METHODS

STUDY DESIGN AND SETTING

Across-sectional study was undertaken at Newcastle University Medicine (NUMed) Malaysia, a branch campus of University of Newcastle upon Tyne, UK which is located in the Iskandar Puteri district of Johor, Malaysia. The study population consisted of 345 new entry Malaysian medical students from a total of 425 new students enrolled in 4 cohorts of intake (2015-2018). Due to missing data on their occupational health screening report, 80 students were excluded from the study.

DATA COLLECTION

Data were collected from participants' occupational health screening reports and recorded in a pre-designed data tem-

plate on Microsoft Excel. Demographic characteristics such as age, gender and ethnicity were identified in this way. Vaccination status against HBV, varicella-zoster, measles, rubella, yellow fever and 4 main serogroups of meningococcal disease (A, C, Y, W-135) were identified from their self-reporting questionnaire with evidence of vaccination attached prior to their occupational health assessment.

Aside from the immunisation requirement recommended by Newcastle University MBBS Admission Policy and NUMed Occupational and Immunisation Policy, this study also investigated the vaccination coverage of Quadri-valent Meningococcal (MenQ) vaccine and yellow fever vaccine as recommended by UK Department of Health and Ministry of Education, Malaysia respectively.^{8,10}

HBV seroconversion status was identified using an enzyme-linked immunoassay (ELISA). A student was considered to have seroconverted if their HBV surface antibody (anti-HBs) titer was >10 IU/L. Both demographic and vaccination data were matched to investigate the association between seroconversion rate and demographic characteristics such as ethnicity and gender.

All participants including those from overseas had HBV vaccination all Malaysian citizens were given full course HBV vaccination as early as 0, 1 month and 6 months old as part of the respective national vaccination programme using Engerix hepatitis B vaccine.

STATISTICAL ANALYSIS

Data obtained from the participants' health screening reports were entered in a pre-designed data template on Microsoft Excel. Comparative statistical analysis with Chi-square test was performed using Prism, where specific statistical investigations will be shown where relevant. The statistical significance threshold was $P < 0.05$.

RESULTS

DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

This study included 345 new entry medical students from 4 cohorts of intake between 2015-2018. The median age of participants was 19 years with an interquartile range (IQR) of 1 year (19-20 years). Among participants, 121 (35.1%) were male and 224 (64.9%) were female. The majority of the participants were of Chinese ethnicity (62.0%), followed by Malay (19.7%) and Indian ethnicity (18.3%). None of the 345 new entry medical students were tested positive for hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc), indicating an overall HBV prevalence of 0%.

Further details are shown in [Table 1](#).

VACCINATION AND SEROCONVERSION STATUS

A total of 340 participants (98.6%) were vaccinated against HBV with the recommended standard 3-dose vaccination, while 5 (1.5%) were not vaccinated. However, out of all participants, only 223 (64.6%) participants seroconverted with anti-HBs titer levels >10 IU/ml, meanwhile 117 (33.9%) did not mount protective anti-HBs level.

A total of 287 participants (83.2%) were vaccinated

Table 1: Demographic characteristics of new entry medical students at NUMed Malaysia from 2015-2018.

Variable	Frequency (n)/Median	Percentage (%) / Interquartile range
Cohort		
2015	52	15.1%
2016	80	23.2%
2017	116	33.6%
2018	97	28.1%
Age, years (n=345)		
Median	19	19.0-20.0
Gender		
Male	121	35.1%
Female	224	64.9%
Ethnicity		
Chinese	214	62.0%
Malay	68	19.7%
Indian	63	18.3%

Table 2: Vaccination rate in the study cohort from 2015-2018

Vaccines	Vaccinated	Non-vaccinated	No data
Hepatitis B	340 (98.6%)	5 (1.4%)	0 (0%)
Varicella Zoster	287 (83.2%)	58 (16.8%)	0 (0%)
Measles	257 (74.5%)	15 (4.3%)	73 (21.2%)
Rubella	237 (68.7%)	33 (9.6%)	75 (21.7%)
MenQ	154 (44.6%)	112 (32.5%)	79 (22.9%)
Yellow fever	20 (5.8%)	284 (82.3%)	41 (11.9%)

against varicella-zoster virus, while 58 (16.8%) were not vaccinated. Vaccination coverage of other vaccines, such as measles, rubella, MenQ and yellow fever were 257 (74.5%), 237 (68.7%), 154 (44.6%) and 20 (5.8%) respectively. However, there were participants with missing or incomplete data on vaccination status of measles (21.4%, n=74), rubella (21.7%, n=75), MenQ (22.9%, n=79) and yellow fever (11.9%, n=41).

Further details are shown in [Table 2](#).

FACTORS ASSOCIATED WITH HBV SEROCONVERSION

Among the vaccinated participants, there is no significant difference in the seroconversion rate of HBV vaccine between male participants (62.0%) and female participants (64.3%, $P = 0.298$). However, there is a statistically significant difference in the HBV seroconversion rate between the 3 ethnicity groups, with students of Malay ethnicity showing the lowest seroconversion rate of 47.1%, followed by those of Indian (68.3%) and Chinese ethnicity (69.6%) ($P = 0.002$). This is shown in [Table 3](#).

DISCUSSION

The overall seroprevalence of HBV in Malaysia ranges from 1.1-5% and is slightly higher than the estimated overall prevalence rate in the South East Asia region (2%).¹²⁻¹⁴ The present study identified a HBsAg seroprevalence of 0% among medical students at Newcastle University Medicine Malaysia. The HBsAg seroprevalence in the study population is lower than those identified in previous studies on medical students in Brazil (0.5%), Mexico (0.5%) and Taiwan (1.7%).¹⁵⁻¹⁷

With the implementation of early clinical exposure component in the Newcastle MBBS curriculum, it is important to ensure up-to-date vaccination status and seroprotection as recommended by occupational health assessment guidelines. To evaluate seroconversion in this study, an anti-HBs titer level of >10 IU/ml, which is a universal indicator of protective immunity, was used.^{18,19}

While over 98% of the study population received the recommended standard 3-dose vaccination, only 64.6% of participants demonstrated evidence of post-vaccination seroconversion. This is the first study demonstrating a low HBV seroconversion rate in young adults with a median age of 19

Table 3: HBV seroconversion status according to demographic characteristics among new entry medical students at NUMed Malaysia from 2015-2018

Variable	Total	Vaccinated		Non-vaccinated	P-value
		Seroconverted (>10 IU/L)	Non-responder (<10 IU/L)		
Cohort					
Total cohort	345	223 (64.6%)	117 (33.9%)	5 (1.5%)	
2015	52	52 (100.0%)	0	No record	
2016	80	52 (65.0%)	26 (32.5%)	2 (2.5%)	
2017	116	59 (50.9%)	54 (46.5%)	3 (2.6%)	
2018	97	60 (61.9%)	37 (38.1%)	0	
Gender					
Male	121	75 (62.0%)	45 (37.2%)	1 (0.8%)	
Female	224	144 (64.3%)	76 (33.9%)	4 (1.8%)	0.298
Ethnicity					
Chinese	214	149 (69.6%)	63 (29.4%)	2 (0.9%)	
Malay	68	32 (47.1%)	35 (51.5%)	1 (1.5%)	
Indian	63	43 (68.2%)	18 (28.6%)	2 (3.2%)	0.002

years. The findings on the HBV seroconversion rate in this study is lower than those of previous studies by Guho et al, Obiri-Yeboah et al, Cardenas-Perea et al, Dassah et al and Perera et al, ranging from 88.7-100%.^{15,20-23}

Among 340 vaccinated participants, 117 (33.9%) participants were anti-HBs negative or had a titer level of <10 IU/ml following HBV vaccination. This corresponds to about 3 out of 10 medical students being non-responders to HBV vaccination, resulting in high risk of HBV acquisition if accidental exposure occurs during clinical training. This poses an occupational health concern to non-responders, considering that the incidence rate of hepatitis B has since increased more than five-fold from 2.26 per 100,000 in 2008 to 12.65 per 100,000 population in 2015 in Malaysia.²⁴ Appropriate measures such as a further course or booster dose of vaccination is recommended for non-responder or non-vaccinated students, as per the UK Department of Health and NUMed Occupational Health and Immunisation policy. Post-booster testing of antibody titer should be conducted to ensure seroconversion.

This study showed no significant difference in the HBV seroconversion rate between genders ($P = 0.298$). The finding from the current study is consistent with those of previous studies that reported no gender difference in seroconversion rate after HBV vaccination.^{25,26}

Using comparative statistical analysis, this is the first study demonstrating a significant difference in the HBV seroconversion rate between the ethnicity groups, with the lowest seroconversion rate of 47.1% found among participants of Malay ethnicity ($P = 0.002$).

All participants are from the same age group of 18-20 years. According to the Malaysian National Immunisation Programme (NIP), all Malaysian citizens are given full course HBV vaccination as early as 0, 1 month and 6 months old.²⁷ Hence, the non-responders identified in this study may have responded initially after their HBV vaccination

with subsequent declining anti-HBs titer to below protective or undetected level over time as reported in previous studies by Norouzirad et al and El-Sayed et al.^{28,29}

This raises the possibility of antibody titres declining over time for those who were immunized previously.

The main limitations of this study include small and selected sample size, missing or incomplete data and potential self-reporting errors in the occupational health screening report. Nevertheless, this study could serve as a pilot for further studies with larger sample sizes to test the findings discussed here.

This is the first study demonstrating a low HBV seroconversion rate (64.6%) among young new entry NUMed medical students (median age: 19) following standard recommended 3-dose vaccination. Students of Malay ethnicity showed a statistically significant non-conversion rate of 51.5% ($P = 0.002$) as compared to the Chinese (29.4%) and Indian (28.6%) ethnicity groups. These students are at higher risk of HBV acquisition if accidental exposure occurs, especially when the HBV incidence rate in Malaysia has increased steadily over years.²⁴ Further research is needed to investigate whether there is a genetic basis to explain this difference.

Further course or booster dose of vaccination is strongly recommended for non-responder and non-vaccinated students as advised by the UK Department of Health, Newcastle University MBBS Admission Policy and NUMed Occupational Health and Immunisation policy.^{8,9,11} Post-booster testing of antibody titer should be conducted to ensure protective adequate seroconversion.

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ETHICS APPROVAL

The study protocol was approved by the Newcastle University Ethics Committee (UEC) and Faculty of Medical Sciences (FMS) Research Ethics Committee, Newcastle University. The data collected was kept confidential in a pseudonymised form using reference code numbers and stored in a password-protected institutional drive which will only be accessible to the researchers. Non-responders or non-vaccinated participants will be channeled to an occupational health provider for a further course or booster dose of vaccination and followed by post-booster testing of antibody titer to ensure seroconversion, as advised by UK Department of Health, Newcastle University Admission Policy and NUMed Occupational Health and Immunisation Policy.

INFORMED CONSENT

As part of health screening for entry to medical school, informed consent from each student was given.

AUTHORSHIP CONTRIBUTIONS

WP Goh: Methodology, Software, Investigation, Resources, Data Curation, Writing- Original draft preparation, Writing

- Review & Editing, Formal analysis, Visualization and Project administration. **G Evans:** Conceptualization and Writing - Review & Editing. **E Hurn:** Software, Formal analysis and Writing - Review & Editing. **A Leong:** Investigation, Data Curation and Writing - Review & Editing. **Lim YK:** Investigation, Data Curation and Writing - Review & Editing. **YT Saw:** Investigation, Data Curation and Writing - Review & Editing. **B Subramaniam:** Investigation, Data Curation. **ZJ Tan:** Software, Investigation, Data Curation and Writing - Review & Editing. **ELC Ong:** Conceptualization, Methodology, Formal analysis, Resources, Data Curation, Writing - Review & Editing, Visualization and Supervision.

CONFLICT OF INTEREST

The authors are academic staffs at Newcastle University Medicine (NUMed) Malaysia.

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