

PREVALENCE AND RISK FACTORS OF HYPOGLYCAEMIA AMONG NON-DIABETIC RESPONDENTS: FINDINGS FROM NATIONAL HEALTH MORBIDITY SURVEY (NHMS) 2015.

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ABSTRACT

Background: Hypoglycaemia among non-diabetes patients are not common but the aetiologies point out to factors such as sepsis, liver disease, malnutrition, alcohol related disorders and malignancies. The objective of this study is to investigate the prevalence and potential risk factors associated with non-diabetic hypoglycaemia

Materials and Methods: This study used data of the National Health and Morbidity Survey (NHMS) 2015, a cross sectional design, applied two stage stratified cluster sampling. Descriptive statistics for the complex sampling and multiple logistic regression were applied to estimate the prevalence of hypoglycaemia in non-diabetes population and factors associated in Malaysia

Result: A total of 18373 respondents aged 18 years and above were analysed. The overall prevalence of non-diabetic hypoglycaemia among Malaysia adults were 10.2% (95% CI 9.27-11.23). Non-diabetic hypoglycaemia was significantly associated with males (AOR=1.24, 95% CI=1.03-1.49), age group 18-24 years (AOR=2.61, 95% CI= 1.91-3.57), age group 25-44 years (AOR=1.93, 95% CI=1.41-2.63), other Bumiputra (AOR=1.79, 95% CI= 1.30-2.45) and others ethnicity (AOR=1.64, 95% CI=1.18-2.29), normal weight (AOR=1.48, 95% CI= 1.20-1.82) and underweight (AOR=1.60, 95% CI= 1.17-2.18).

Conclusion: Lower Body Mass Index (BMI) and underweight respondents, younger age group, males, Bumiputras and other ethnicity, were significantly associated with non-diabetic hypoglycaemia. The outcome of this study warrants insights into treating this group of patients. Therefore, clinicians should dwell into the aetiology of hypoglycaemia in non-diabetic patients and treat the underlying cause.

Keywords: Hypoglycaemia, Non-diabetes, low sugar, NHMS

1.0 Introduction

Hypoglycaemia is defined by either one of the following two conditions: a) low plasma glucose level (<4.0 mmol/L) OR b) development of autonomic or neuroglycopenic symptoms in patients treated with insulin or OADs which are reversed by caloric intake [1].

Symptoms of hypoglycaemia are as below:

Autonomic	Neuroglycopenic
<ul style="list-style-type: none"> • Trembling • Palpitation • Sweating • Anxiety • Hunger • Nausea • Tingling 	<ul style="list-style-type: none"> • Difficulty in concentrating • Confusion • Weakness • Drowsiness • Vision changes • Difficulty in speaking • Headache • Dizziness

(Clinical Practice Guidelines Diabetes Malaysia 2015)

Hypoglycaemia among non-diabetes patients are not common but the aetiologies might point out to certain factors such as sepsis, liver disease, malnutrition, alcohol related disorders and malignancies (2). It is common in non-diabetic patients in critical care (2,3). Tsajinamoto (2015) study (4) showed that non diabetes patients had higher mortality with hypoglycaemia than non-diabetic patients (22.1% vs 1.6%). His study also revealed that age, pre-existing advanced liver disease cancer and sepsis were predictors of deaths in non-diabetic patients. Non diabetes hypoglycaemia patients had higher mortality (4) than large scale cohort studies (14.9% vs 3.8%). Hypoglycaemia in these non-diabetes patients can be diagnostically challenging and may indicate a poor prognosis especially in the ICU setting given severe nature of illnesses and insufficient nutritional intake (5).

Hypoglycaemia among non-diabetes admission accounts for 13 episodes per 10000 admission per year. (6). Estimates tends to be higher in patients above 63 years old (6). Most of cases of admission that occurred was caused by conditions such as alcohol dependency, renal failure, and sepsis (6). The in-hospital death was reported as 14.9% (7).

Currently there are a few researches available that investigates non diabetes hypoglycaemia but mostly are done in clinical settings. Non diabetes hypoglycaemia has never been studied and used in Malaysia population studies or survey. The objective of this study is to investigate the prevalence and potential factors of respondents associated with non-diabetic hypoglycaemia using data from the Malaysia National Health and Morbidity Survey (NHMS) 2015. Outcome of this study can then be used by tertiary clinics or hospitals to further manage patients with non-diabetic hypoglycaemia.

2.0 Materials and Methods

This study used data from Malaysia National Health and Morbidity Survey (NHMS) 2015. NHMS 2015 is a nationwide survey on non-communicable diseases (NCD), risk factors and other health problems for adults aged 18 years and above. It is funded by Ministry of Health; Malaysia and the results are used by the government to develop policies and monitor trends in NCDs all over Malaysia.

2.1 Sampling

The sampling frame was updated in 2014 prior to sampling process. Based on the frame, areas in Malaysia were divided into Enumeration Blocks (EB). The sampling design used two staged stratified random sampling. Primary stratum made up of states of Malaysia and federal territories while the second stratum made up of urban and rural strata. Sampling involve 2 stages; the Primary Sampling Unit (PSU), which were Enumeration Block (EBs) and the second sampling Unit (SSU) which was Living Quarters (LQs) within the selected EBs. A total of 10,428 LQs were selected from the total EBs in Malaysia. Twelve LQs were randomly selected from each selected EBs. Data collection was done from Mac 2015 till June 2015.

2.2 Questionnaires

Structured validated questionnaires were used to collect data. There were two types of questionnaires; face to face interview. The face to face interview questionnaires were programmed into an application and the data collection was done using tablet. The self-administrated questionnaires were prepared in hardcopies. Prior to data collection, a training course was conducted for all data collectors.

2.3 Clinical Assessment

Clinical assessment (weight, height, waist circumference, blood pressure measurement, fasting blood sugar and fasting blood cholesterol) was done by trained nurses. For measurement of weight, Tanita personal Scale HD 319 was used. For measurement of height, SECA Stadiometer 213 was used. Both tools were validated and calibrated. Omron Japan Model HEM-907 which had been validated and calibrated was used for blood pressure measurement, while PA CardioChek which had been validated was used to assess fasting blood glucose and cholesterol.

2.4 Data Analysis

In this study, we analysed data comprised of 16361 respondents aged 18 and above which is the final sample after removing all the missing and exclusion group, pregnant women, post-natal (less than 60 days at time of visit), bed ridden due to chronic / prolonged illness,, injury/ accident, having physical disability that can affect the normal standing including on wheel chair, body deformities such as no hand and leg, spondylolysis except deaf, blind and mute.

We described the prevalence of non-diabetic hypoglycaemia and characteristics associated with 95% confidence interval (CI). Univariate analysis using binary logistic regression was then applied for all socio-demographic, dietary and lifestyle factors to get the crude OR and p-value. Variables having a p-value less than 0.25 from the univariate analysis were included in the initial multivariate logistic regression model. The strength of association for each risk factor

was assessed using crude and adjusted odds ratios (AOR). All the analyses were performed using SPSS software version 25.

2.5 Ethnical Approval

This study had obtained ethical approval from the Medical Research and Ethics Committee (MREC), Ministry of Health, Malaysia, bearing registration number NMMR -14-1064-21877. Prior to each interview, the purpose of the survey and methods used during the survey was explained to the respondent and information handed out via the participant's information sheet, before informed written consent was taken.

3.0 Result

Table 1: Prevalence of hypoglycaemia among non-diabetic patients in Malaysia

Variable	Estimated population	n	%	95%CI	
				Lower	Upper
Overall	1718072	1543	10.2	9.27	11.23
Socio-demographic					
Sex					
Male	1010338	854	11.4	10.20	12.66
Female	707734	689	8.9	7.85	10.10
Age group (years)					
18 - 24	517412	362	15.1	13.22	17.25
25 - 44	905704	753	11.2	9.89	12.61
45 - 64	226467	309	5.4	4.65	6.36
65+	68489	119	6.0	4.69	7.61
Ethnicity					
Malay	723338	901	8.8	7.82	9.88
Chinese	313422	194	8.3	6.54	10.59
Indian	75669	76	7.1	5.08	9.85
Other Bumiputras	314852	216	16.1	13.02	19.77
Others	290791	156	15.9	12.28	20.44
Locality					
Urban	1207184	805	9.6	8.53	10.75
Rural	510888	738	12.1	10.16	14.26
Household income group (RM)					
Less than RM1000	234836	219	10.8	8.63	13.39
RM1000 - 1999	333936	317	12.0	10.21	13.97
RM2000 - 2999	291034	286	10.4	8.66	12.44
RM3000 - 3999	233589	212	10.9	8.89	13.23
RM4000 - 4999	160584	138	9.7	7.45	12.57
RM5000 - 5999	129645	105	9.7	7.17	13.07
RM6000 - 6999	69529	65	7.9	5.41	11.52
RM7000 - 7999	52716	50	7.8	4.93	12.23
RM8000 - 8999	42470	27	7.6	4.51	12.46

RM9000 - 9999	29027	28	9.3	5.48	15.35
RM10000 and above	140706	96	9.3	6.80	12.71
Anthropometric					
Body mass index					
Underweight	156108	138	13.7	11.06	16.83
Normal	945261	787	12.2	10.93	13.61
Overweight	387960	385	8.0	6.85	9.32
Obese	211752	208	7.6	6.35	9.11
Life style					
Physical activity (2 category)					
Active	1194246	1081	10.4	9.39	11.60
Inactive	491264	425	9.9	8.65	11.22
Alcohol intake					
Non drinker	1379504	1342	9.8	8.89	10.76
Ex-drinker	28396	20	11.0	6.42	18.11
Current drinker	207753	108	14.2	11.09	17.99
Unclassified	89997	55	11.7	8.39	15.96
Smoking					
Current tobacco smoker	519497	444	12.3	10.72	14.15
Current non-smoker	1187620	1084	9.6	8.62	10.65
Fruit and vegetable intake					
Not adequate	1604502	1443	10.3	9.30	11.32
Adequate	99680	83	10.4	7.81	13.82

Table 2: Univariate and multivariate analyses of risk characteristics toward hypoglycaemia among non-diabetic patient in Malaysia

Variable	Crude OR	95%CI		P-value	AOR	95%CI		P-value
		Lower	Upper			Lower	Upper	
Socio-demographic								
Sex								
Female	1.00				1.00			
Male	1.31	1.13	1.52	<0.001	1.24	1.03	1.49	0.023
Age group (years)								
65+	1.00				1.00			
45 - 64	0.90	0.68	1.21	0.493	0.96	0.70	1.32	0.813
25 - 44	1.98	1.50	2.62	<0.001	1.93	1.41	2.63	<0.001
18 - 24	2.80	2.11	3.73	<0.001	2.61	1.91	3.57	<0.001
Ethnicity								
Malay	1.00				1.00			
Chinese	0.94	0.71	1.26	0.693	0.99	0.73	1.33	0.922
Indian	0.79	0.55	1.15	0.225	0.81	0.55	1.19	0.282
Other Bumiputras	1.99	1.51	2.63	<0.001	1.79	1.30	2.45	<0.001
Others	1.97	1.42	2.73	<0.001	1.64	1.18	2.29	0.004
Locality								
Rural	1.00				1.00			

Urban	0.77	0.61	0.97	0.029	0.89	0.69	1.15	0.370
Anthropometric								
Body mass index								
Obese	1.00				1.00			
Overweight	1.06	0.85	1.32	0.635	1.02	0.82	1.28	0.841
Normal	1.69	1.38	2.07	<0.001	1.48	1.20	1.82	<0.001
underweight	1.93	1.44	2.58	<0.001	1.60	1.17	2.18	0.003
Life Style								
Physical activity								
Active	1.00				1.00			
Inactive	0.94	0.81	1.08	0.384	1.00	0.86	1.16	0.962
Alcohol intake								
Non drinker	1.00				1.00			
Ex-drinker	1.14	0.64	2.02	0.663	1.00	0.56	1.78	0.998
Current drinker	1.53	1.15	2.02	0.003	1.21	0.89	1.65	0.229
Unclassified	1.22	0.86	1.73	0.277	1.06	0.72	1.55	0.782
Smoking								
Current non-smoker	1.00				1.00			
Current tobacco smoker	1.33	1.12	1.57	0.001	0.97	0.79	1.19	0.767
Fruit and vegetable intake								
Adequate	1.00							
Not adequate	0.98	0.71	1.36	0.909	0.95	0.69	1.31	0.743

*Classification table-89.0%, Nagelkerke Pseudo R²=0.068

The overall non-diabetes hypoglycaemia among Malaysia adults were a total of 1543 respondents (10.2%). Male respondents were 854 (11.4%) while females were 689 (8.9%). The highest incidence of hypoglycaemia was among the age group of 25-44 years which were 753 respondents (11.2%). In terms of ethnicity, Malays had the highest prevalence of hypoglycaemia 901 (8.8%) followed by Chinese 194 (8.3%) and other Bumiputras 216 (16.1%). Locality showed urban population had higher incidents of hypoglycaemia 805 (9.6%) compared to rural 738 (12.1%). Those with income group of RM1000-RM1999 had the highest incidence of hypoglycaemia 317 (12.0%).

Respondents who had normal BMI had highest incidence of hypoglycaemia 787 (12.2%), followed by underweight 385 (8.0 %). Respondents who were physical active had higher incidents of hypoglycaemia 1081 (10.4%) compared to those who were inactive 425 (9.9%). In terms of alcohol intake, non-drinker had higher episodes of hypoglycaemia 1342 (9.8%) compared to current drinker 108 (14.2%). Non-smokers had higher incidence of hypoglycaemia 1084 (7.2%) compared to smoker 444 (12.3%). Those who were consuming inadequate vegetables and fruits had higher incidents of hypoglycaemia 1443 (10.3%) compared those consuming adequate vegetables and fruits 83 (10.4%).

A univariate regression analysis found the non-diabetic hypoglycaemia was significantly associated with male gender, age groups 18-44 years, ethnicity, locality, lower BMI, and smoking. The multivariate regression analysis revealed that male (AOR=1.24, 95% CI=1.03-1.49), age group 18-24 years (AOR=1.96, 95%CI= 1.3-2.97),), age group 25-44 years

(AOR=1.93,95%CI=1.41-2.63), Bumiputra (AOR=1.79, 95%CI= 1.30-2.45) and others ethnicity (AOR=1.64, 95%,CI= 1.18-2.29),normal weight (AOR=1.48,95%CI= 1.20-1.82) and underweight (AOR=1.60,95%CI= 1.17-2.18), were significantly associated with non-diabetic hypoglycaemia.

4.0 Discussion

Hypoglycaemic disorders are rare in persons without diabetes, recommendations for their evaluation and management must rely largely on clinical experience. Clinical Practice Guidelines Diabetes Malaysia 2015 does not highlight non diabetes management. Currently, there is no data available on hospitalization of non-diabetic hypoglycaemia in Malaysia. Most of the clinical guidelines for hypoglycaemia are for diabetic patients except for Endocrine Society for the United States 2011 (8).

Non diabetes hypoglycaemia is mainly caused by malignancies, cerebrovascular diseases, infection, major organ failure, alcohol related disorders (9). Malnutrition was the leading cause of non-diabetes hypoglycaemia in a Japanese study, followed by alcohol related disorders, infection, and post gastrectomy (7). In a study in UK, most common comorbidities of non-diabetes hypoglycaemia were sepsis, kidney disease, alcohol related disorder, followed by pneumonia, cancer, and liver diseases (6).

This present study revealed that respondents with lower than normal BMI (<18.5kgm²) and normal BMI were more common in non-diabetic hypoglycaemia. Studies have showed that lower BMI patients with non-diabetic hypoglycaemia are significantly associated in higher in hospital mortality (12). This could be due to people with lower BMI might be also be suffering from malnutrition. A study from Japan has revealed the association between malnutrition and higher incidence of hypoglycaemia among non-diabetic patients (12).

Study revealed that non diabetes hypoglycaemia is more prevalent in respondents aged >60 years and above (9,10,11,12), where else our present study showed the age group of 18-24 are more significantly associated. According to other study, younger patients and those who have lower BMI tends to be more susceptible to non-diabetes hypoglycaemia (9,12). These studies also revealed that males were more susceptible of getting non diabetes hypoglycaemia which is aligned with our present study (9,10,11).

Limitations of this study was it did not consider dietary factors which is crucial for causing and managing hypoglycaemia. Our study did not identify the true causes of non-diabetes hypoglycaemia. There has been no similar study that has been carried out to the author's knowledge. This study also has an advantage of having a large sample size and was a population-based study.

5.0 Conclusion and recommendation

In conclusion, non-diabetes hypoglycaemia is prevalent in Malaysia. Investigating the probable risk factors of this population might be useful for clinicians to treat them when hospitalized. This study showed that it warrants insights into treating this group of patients. Therefore, clinicians should dwell into the aetiology of hypoglycaemia in non-diabetes patients and treat the underlying cause.

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Declaration

These authors declare that there is no conflict of interest in any form

Authors contribution

Author 1: Proposal planning and introduction.

Author 2: Analysis and Methodology

Author 3: Analysis and results

Author 4: Discussion writing

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