Gender Influence on Hyperacute Intracerebral Hemorrhage Prognosis: A Demographic, Clinical and Radiologic Analysis

John Christopher V. Ruiz, MD[a], Sherielyn Bayani[a] and Marian Irene Escasura, MD, FPNA[a]

ABSTRACT

Background

There is growing interest in gender differences in acute stroke worldwide. However, no known studies have been published on the differences in prognosis of hyperacute intracerebral hemorrhage between genders among Asians, particularly Filipinos.

Objectives

Compare gender differences in the prognosis of hyperacute intracerebral hemorrhage in terms of baseline demographic and radiologic profile, as well as, clinical outcomes.

Methods

This is a retrospective cohort study involving a chart review of all patients diagnosed with hyperacute Intracerebral Hemorrhage admitted at a tertiary hospital from January 2021 to May 2023. Patients were grouped according to their gender and baseline demographic, radiologic and clinical outcomes were assessed and compared between two groups.

Results

No statistical difference was found between stroke risk factors between the two groups. However, males tend to have higher percentages of intraventricular extension (29.2 %. (n=28) vs 30.6% (n=11) and increased hematoma volume compared to their female counterparts (n=39, 83% vs n=11, 68%). In addition, males had a higher number of ICU admissions (42.7% (n= 41) vs. 33.3% (n= 12) and mortality (46.9%(n=45) vs. 30.6% (n=11), though the results were not statistically significant.

Conclusion

In patients with hyperacute intracerebral hemorrhage, gender does not influence on its radiologic and clinical outcome.

Keywords: *Hyperacute Intracerebral Hemorrhage, Clincal outcomes; Stroke; Gender differences*

INTRODUCTION

Stroke is the second leading cause of death in the Philippines. It has a prevalence of 0·9%; ischemic stroke comprises 70% while hemorrhagic stroke comprises 30%.[1] In the Philippines, a multi-center observational study conducted by the Philippine Neurological Association, reported 10,000 cases of stroke of which 33% comprised Intracerebral Hemorrhage.[2]

Several studies have shown sex differences in incidence, pathophysiology, and outcomes

[a]East Avenue Medical Center

in primary intracerebral hemorrhage patients.[3] Epidemiological studies have shown a higher incidence of Intracerebral Hemorrhage in men. Perihematomal edema after a spontaneous ICH causes both immediate and delayed neurological injury. A study of 387 patients, at the 2-4th day post stroke showed lower PHE values.[4]

There has been conflicting evidence of sex differences in terms of outcome. Women would have worse early or late neurologic outcomes yet other studies find no difference in the 3 to 6 months post ICH.[5] To the best of our knowledge, there have been no studies focusing on gender on clinical outcomes of hyperacute intracerebral hemorrhage

METHODOLOGY

Study Design, setting, and participant selection

This is a retrospective cohort study involving all patients diagnosed with hyperacute Intracerebral Hemorrhage admitted at a tertiary hospital from January 2021 to May 2023. Adult patients, aged 19 and above, with hyperacute spontaneous intracerebral hemorrhage seen in the emergency room within 6 hours post-ictus were included in the study. In addition, those with a diagnosis of stroke mimickers and intracranial bleeding from another source (aneurysm, hemorrhagic conversion, and tumoral bleed) were excluded from the study.

Baseline demographics for patients were acquired and were grouped according to gender (male or female) and were compared in terms of outcome variables (functional outcome, mortality, length of hospitalization and need for ICU admission).

Data Collection and Bias

The sampling method used is non-probability purposive sampling. Study data was acquired from the institution's stroke databank. Unavailable data were accessed through the patient's chart records. Selection bias was addressed by including all available patients in the census fulfilling the criteria.

The study specifically acquired the participant's age, gender, comorbidities, intake of antithrombotics, baseline NIHSS, and baseline ICH score. The etiology of ICH was also patterned to the SMASH- U Criteria, classifying it to be structural, medication, amyloid, systemic, hypertension, or undetermined. The radiographic profile of hyperacute ICH was also described in terms of hematoma Volume, location, presence of edema, and presence of hydrocephalus. Lastly, treatment outcomes described include the need for ICU admission or intubation, mortality, length of hospital stay, and functional outcome.

Sample Size

OpenEpi, Version 3 is used to calculate the minimum sample size requirement. Specifying a 95% level of confidence, a 5% margin of error, and a finite population of 145 patients admitted and diagnosed with hyperacute intracerebral hemorrhage given an Intravenous Nicardipine treatment. A minimum of 106 patients is needed to satisfy the inclusion/ exclusion criteria included in the study for which ours had 132.

Ethical Considerations

The study conforms to the Principles of the Declaration of Helsinki (2013) and was conducted along the Guidelines of the International Conference on Harmonization-Good Clinical Practice, National Ethical Guidelines for Health and Health-Related Research (NEG HHRR) 2017. It complied with the Data Privacy Act of 2012 and the National Ethical Guidelines for Health and Health-Related Research of 2017. The Clinical Protocol and all relevant documents were reviewed and approved by the Institutional Ethics Review Board (IERB 2023- 90).

Statistical Analysis

Data were downloaded by the researcher into Excel Format. Microsoft Excel Data Analysis version 2017 and SPSS version 27 will be used for data processing and analysis. Descriptive analyses will be presented as frequencies and percentages for categorical variables. For continuous variables, Mean and standard deviation with a parametric distribution will be utilized. Independent T-test will be used to compare the means of the clinical outcomes between hyperacute ICH patients between male and female, while Mann Whitney U for non-parametric distribution. Whereas, the chi-square test for independence or the Fisher exact test was used if the variables were categorical. Logistic regression analysis is used to examine the association of gender (independent variable) with clinical outcome (dichotomous dependent variable). The Crude ratio will be utilized to determine the effect measure from the binary logistic regression model. Whereas Adjusted odds ratio is the effect measure from multivariate logistic regression. The test will be performed using SPSS27 software at a 5% level of significance.

RESULTS

A total of 132 patients fulfilled the inclusion criteria (n=96) for the males and (n= 36) for the females. The demographics of this study consist of age, baseline NIHSS, ICH, and hematoma size. Baseline ICH values show higher scores for the male group compared to the female. History of co-morbidities was seen more in the male group in terms of previous stroke history 4.54% (n=6) vs. 2.27% (n=3); type 2 DM 2.27% (n=3) vs. 2.27% (n=3); intake of antithrombotics 1.51%(n=2) vs. 0.7%(n=1) although there were relatively few patients for both groups. For the social history of patients, the frequency of patients having a history of alcohol intake was 44.69% (n=59) vs 8.3%

Table 1. Baseline Demographic Characteristics of the Study Participants

	Male	Female	P- Value
AGE mean (SD)	52.2 (9.29)	54.8 (10.5)	0.631
Baseline NIHSS mean (SD)	17.9 (9.23)	16.4 (9.62)	0.991
Baseline ICH			
0	34 (35.4)	13 (36.1)	0.879
1	24 (25.0)	11 (30.6)	
2	14 (14.6)	4 (11.1)	
3	10 (10.4)	5 (13.9)	
4	13 (13.5)	3 (8.3)	
5	1 (1.0)	0 (0)	
Baseline Hematoma Size mean (SD)	19.4 (17.9)	20.3 (20.8)	0.404
RISK FACTORS			
Heart Disease	0 (0)	0 (0)	-
Hypertension	61 (64.2)	22 (61.1)	0.072
Type 2 DM	3 (3.2)	3 (8.3)	0.217
Stroke	6 (6.3)	3 (8.3)	0.672
Intake of Anti Thrombotics	2 (2.2)	1 (2.8)	0.846
History of Smoking	47 (51.6)	4 (11.4)	<0.001
History of Alcohol Intake	59 (64.8)	11 (31.4)	<0.001
History of Drug Use	1 (1.1)	0 (0)	0.677

Table 2. Mechanism and Radiologic Profile Intracerebral Hemorrhage

	Male	Female	P-value
MECHANISM OF ICH			
Structural	1 (1.0)	1 (2.8)	0.467
Medications	0 (0)	0 (0)	-
Amyloid	0 (0)	0 (0)	-
Systemic	0 (0)	0 (0)	-
Hypertension	95 (99.0)	35 (100.0)	0.544
Undetermined	0	0	
NEUROSURGICAL INTERVENTION			
Minimally Invasive	0	0	
Decompressive Hemicraniectomy	1 (0.75	0	
Evacuation of Hematoma	1 (0.75)	0	
RADIOLOGIC PROFILE OF BLEED			
Intraventricular Extension	90 (93.8)	30(83.3)	<0.001
Location of Hematoma			
Putamen	0	0	
Thalamus	18(18.8)	8(22.2)	0.876
Basal Ganglia	40(41.7)	13(36.1)	0.655
External Capsule	13(13.5)	6(16.7)	0.562
Pons	15(15.6)	4(11.1)	0.511
Cerebellum	2(2.1)	1(2.8)	0.812
Lobar	8(8.3)	4(11.1)	0.621
Hematoma Expansion	12(30.8)	2 (20.0)	0.501

Table 3. Treatment Outcomes of Hyperacute Intracerebral Hemorrhage Patients

	Male	Odds Ratio (CI)	Female	Odds Ratio (CI)	P- Value
Mortality (Expired)	45 (46.9)	2.005 (0.888-4.529)	11 (30.6)	0.499(0.221-1.13)	0.094
MRS (3-6)	24 (25.0)	1.696(0.745-3.858)	13 (36.1)	0.590 (0.259-1.340)	0.208
Hematoma Expansion	12(30.8)	1.778 (0.327-9.66)	2 (20.0)	0.562(0.104-3.055)	0.505
Rebleed	12(30.8)	1.778 (0.327-9.66)	2 (20.0)	0.562(0.104-3.055)	0.505
Adverse Events	45 (46.9)	1.561 (0.709-3.44)	13 (36.1)	0.641(0.291-1.41)	0.269
Need for ICU Admission	41 (42.7)	1.491(0.668-3.326)	12 (33.3)	0.671(0.301-1.50)	0.329
Length of Hospitalization-average SD	8.21(7.66)	-0.267(-0.653-0.120)	10.6 (12.0)	0.267(-1.20-0.653	0.175

(n= 11), followed by smoking at 28% (n=37.8) vs. 22% (n= 43.1) and a few with an unknown history.

A higher proportion of males had hematoma volume greater than 30ml compared to females (n=39, 83% vs n=11, 68%). The presence of Intraventricular extension was also noted to have a significantly higher frequency in males 29.2 %. (n=28) compared to females 30.6% (n=11). The most common location of hematoma was at the basal ganglia 41.7 % (n=40) vs. 36.1% (n=13), followed by the thalamus 18.8% (n=18), vs. 22.2% (n=8). external capsule 13.5%, (n=13) vs. 16.7% (n= 6), pons 15.6%, (n=15) vs. 11.1% (n=4). lobar 8.3% (n=8) vs. 11.1% (n=4)., cerebellum 2.1% (n=2) vs. 2.8% (n=1), and putamen 0% (n=0).

For the clinical outcomes, results show a point towards significantly good functional outcomes (MRS 0-2) for the female 36.1% (n=13) vs. 25%(n=24). Mortality rate was higher among male patients 46.9%(n=45) vs. 30.6% (n=11). The average length of hospitalization was 8.21 (SD= 7.66) vs. 10.6 (SD= 12) days. ICU admission rate was also higher for the male group 42.7% (n= 41) vs. 33.3% (n= 12) as well as adverse event 46.9% (n=45) vs. 36.1% (n=13).

Due to the significantly heterogeneous finding of intraventricular extension in our comparison groups, this has been added as a confounding variable further subdividing the group into HICH male patients with IVE vs. HICH Female patients with IVE. Mortality rates showed significant statistical difference (P- value 0.001) in male patients with IVE at 25% (n= 24) compared to female counterpart at 19.4% (n= 7) but was not significant for the other outcomes.

DISCUSSION

In Sakamoto et al 2017's study of 211 patients with hyperacute intracerebral hemorrhage, the median NIHSS Score was 13. In our study, the baseline NIHSS was shown to be severe with a median of 16 stating that regardless of gender HICH patients have poorer prognosis. For the mechanism of Intracerebral Hemorrhage, hypertension remains to be the leading cause.[6]

Based on our study, the male gender had poorer functional outcomes compared to their female counterpart but was not significant 25% (n=24) vs. 36.1% (n=13), (P-value .208).

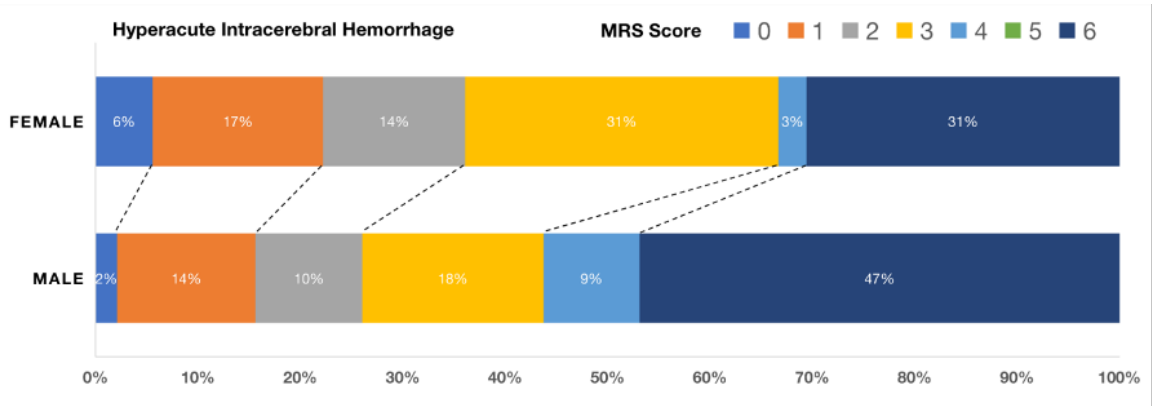
CONCLUSION

In patients with hyperacute intracerebral hemorrhage, gender does not influence on its radiologic and clinical outcome.. Prospective, multicenter study is suggested to provide generalizability of the study results.

FUNDING

This research was independently conducted and was not funded by any

Figure 1. MRS Distribution Based on Gender in Patients with Hyperacute ICH



pharmaceutical company. The findings and conclusions presented in this study are solely the result of our research efforts and do not represent the interests or influence of any pharmaceutical company.

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