

# Racial disparities among Native Hawaiians and Pacific Islanders with intracerebral hemorrhage

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## ABSTRACT

**Objectives:** To evaluate disparities in stroke risk factors and outcome among the Native Hawaiians and other Pacific Islanders (NHPI) in Hawaii who are hospitalized with intracerebral hemorrhage (ICH).

**Methods:** We performed a retrospective study on consecutive patients hospitalized for acute ICH at a single tertiary center on Oahu between 2004 and 2010. Clinical data were obtained from the Get With the Guidelines–Stroke database. Multivariable logistic regression was used to assess the predictors for young ICH (age <45).

**Results:** A total of 562 patients hospitalized for acute ICH (Asian 63%, NHPI 18%, white 16%, other 3%) were studied. The NHPI were younger (mean ages, NHPI  $55 \pm 16$  vs white  $66 \pm 16$  years,  $p < 0.0001$ ), and had higher prevalence of diabetes (NHPI 35% vs white 20%,  $p = 0.01$ ) and history of hypertension (NHPI 77% vs white 64%,  $p = 0.04$ ) compared to white patients. Independent predictors for young ICH were NHPI race (odds ratio [OR] 3.55; 95% confidence interval [CI] 1.33–9.45), being transferred from another hospital (OR 2.03; 95% CI 1.05–3.93), hypertension (OR 0.49; 95% CI 0.27–0.91), previous stroke or TIA (OR 0.21; 95% CI 0.05–0.91), and dyslipidemia (OR 0.15; 95% CI 0.05–0.50).

**Conclusions:** NHPI with ICH are younger and have higher burden of risk factors compared to white patients. Further studies controlling for socioeconomic modifiers are needed to determine factors contributing to the younger age at presentation in this racial group. *Neurology*® 2012;79:675–680

## GLOSSARY

**BMI** = body mass index; **CAD** = coronary artery disease; **CI** = confidence interval; **GWTG** = Get With the Guidelines; **HDL** = high-density lipoprotein; **ICH** = intracerebral hemorrhage; **IVH** = intraventricular hemorrhage; **LDL** = low-density lipoprotein; **LOS** = length of stay; **MI** = myocardial infarction; **NHPI** = Native Hawaiians and other Pacific Islanders; **OR** = odds ratio; **QMC** = Queen's Medical Center.

Intracerebral hemorrhage (ICH) accounts for 10%–15% of the approximately 700,000 annual strokes in the United States<sup>1</sup> and results in disproportionately high morbidity and mortality.<sup>2</sup> In Hawaii, the age-adjusted incidence of ICH is estimated to be 0.6/1,000 person-years<sup>3</sup> in a population that consists of 25% white subjects, 39% Asians, and 10% Native Hawaiians and other Pacific Islanders (NHPI) compared to 0.3/1,000 person-years in a population in Northern Manhattan that consists of 23% white subjects, 12% black subjects, and 65% Hispanic subjects.<sup>4</sup> Recent evidence suggests that the burden of ICH is not borne equally by all, with racial minority groups reported to have a higher incidence and poorer outcomes than white subjects.<sup>5–7</sup> Although NHPI have been reported to have higher prevalence of major cardiovascular risk factors<sup>8–13</sup> and die at a younger age from various cardiovascular disease–related complications compared to other major racial–ethnic groups,<sup>14,15</sup> the specific disease burden related to ICH in this population has not been studied. We hypothesized that NHPI with ICH are younger and have higher burden of risk factors compared to non-Hispanic white subjects.

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**METHODS** We conducted a retrospective observational study using our institution's Get With the Guidelines–Stroke (GWTG–Stroke) registry, a national quality improvement initiative and stroke registry used by many participating hospitals nationwide.<sup>16</sup> Since its inception in 2004, GWTG–Stroke registry has been used in our institution to measure and monitor the quality of hospital-based stroke care delivery.

**Patients.** The Queen's Medical Center (QMC) is a 505-bed medical center located on Oahu, the largest hospital in Hawaii and the tertiary referral center for the Pacific Basin (Hawaii, American Samoa, the Commonwealth of the Northern Mariana Islands, Micronesia, and the US territories of Guam). QMC has the only Joint Commission–certified Primary Stroke Center and the only Neuroscience Intensive Care Unit in Hawaii. Since ICH is a condition that is preferably treated in the Neuroscience Intensive Care Unit,<sup>17</sup> QMC is the primary referral center for acute management of ICH patients from other major islands.

All patients hospitalized at QMC with a diagnosis of spontaneous ICH between January 1, 2004, and August 31, 2010, were identified using the QMC GWTG–Stroke database. The patients with ICH were identified and registered in the database at the time of admission by imaging and admission diagnosis. A trained nurse reviewer (S.M.A.) at QMC identified consecutive patients admitted to QMC with a principal clinical diagnosis of ischemic stroke, hemorrhagic stroke, or TIA and categorized as such. Case ascertainment of admissions for ICH was conducted by prospective clinical identification and retrospective identification with International Classification of Diseases (9th revision) discharge codes (431 for ICH), followed by chart review of an electronic medical record to confirm case eligibility, or a combination of both approaches. Each subject's medical record was reviewed and recorded into an electronic database using standard criteria and definitions. Patients with recurrent ICH who were previously admitted to QMC with ICH were excluded. We were unable to identify and exclude those who may have had ICH in the past and were hospitalized at another hospital. Patients with ICH related to trauma, ruptured cerebral aneurysm, or ischemic stroke with hemorrhagic conversion were also excluded.

**Baseline characteristics.** Patient demographics, whether the patient was transferred from another hospital, medical history including history of diabetes mellitus, hypertension, atrial fibrillation/atrial flutter, congestive heart failure, prior stroke or TIA, coronary artery disease (CAD), or prior myocardial infarction (MI), peripheral vascular disease, smoking, dyslipidemia, and prosthetic valve replacement were obtained through the GWTG–Stroke database. The race and ethnicity information were collected by the administrative personnel during the registration process or by the nurses during the intake process. Race was initially categorized as NHPI, Asian, white, black, American Indian/Alaska native, or "other" race. Because of the low number of black and American Indian/Alaska native patients in Hawaii, these racial groups were combined with the "other" group in the analysis. Since mixed racial background is relatively common in Hawaii, race was defined as the racial/cultural background that the patient most closely associated with and was based on patient self-identification or family's identification if the patient was incapacitated. The patients were further dichotomized to young ICH (age <45) and older ICH (age ≥45) groups, a generally accepted age dichotomization that has been used to define ischemic strokes in young adults.<sup>18</sup> Additional data on the use of antihypertensive medications, body mass index (BMI), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides were also collected if they were avail-

able. The patients were considered to have hypertension if there was a known history of hypertension prior to admission (self-report, family's report of hypertension, or confirmed history of hypertension in the existing medical record). The patients were considered to have untreated hypertension if they were not taking any antihypertensive medications prior to admission despite the known history of hypertension. The patients were considered to have dyslipidemia if there was a known history of dyslipidemia prior to admission (self-report, family's report, confirmed history of dyslipidemia in the existing medical record, or current use of lipid-lowering agent).

All initial head CT scans were retrospectively reviewed by one of the study investigators (K.N.) using a standardized protocol, blinded to race, ethnicity, and clinical data. Hematoma volume was measured using the previously described ABC/2 method.<sup>19</sup> Presence of intraventricular hemorrhage (IVH) was recorded, and ICH location was coded as lobar, basal ganglia, thalamus, brainstem, cerebellum, or primary IVH.

**Outcome measures.** Hospital length of stay (LOS), in-hospital mortality, discharge ambulatory status, and discharge destination were the selected clinical outcomes.

**Standard protocol approvals, registrations, and patient consents.** We received approval from the QMC Research and Institutional Review Committee to conduct this retrospective review of the prospectively collected QMC GWTG–Stroke database, supplemented by additional clinical data that were obtained from a chart review. Waiver of consent was obtained to conduct this study.

**Statistical analysis.** Data were analyzed using commercially available statistical software (SPSS 19.0, Chicago, IL). Patient characteristics were summarized using descriptive statistics appropriate to variable type. The NHPI and Asian racial groups were compared to white subjects (reference group) using  $\chi^2$  test or Fisher exact test for categorical data and 2-tailed *t* test for normally distributed, continuous variables. Multivariable regression analyses using a logistic regression model with a forward stepwise procedure, with  $p < 0.1$  for addition of variables, were performed to identify factors predictive of young ICH. Odds ratio (OR) and 95% confidence interval (CI) were calculated from the  $\beta$  coefficients and their standard errors. Data are presented as means  $\pm$  SD, and levels of  $p < 0.05$  were considered statistically significant.

**RESULTS** Between January 2004 and August 2010, 573 consecutive patients with a possible diagnosis of ICH were identified. After case confirmation with retrospective CT analyses, the following patients were excluded: 3 patients with traumatic ICH, 3 patients with ICH related to subarachnoid hemorrhage from ruptured cerebral aneurysm, 2 patients with ischemic stroke with hemorrhagic transformation, 2 patients with recurrent ICH at QMC, and 1 patient without radiographic evidence of ICH. In the final analyses 562 consecutive patients admitted to QMC with a diagnosis of acute nontraumatic, nonaneurysmal, spontaneous ICH were included (Asian 63%, NHPI 18%, white 16%, other 3%). Demographics, cardiovascular risk factors, hospital LOS, and in-hospital mortality data for the NHPI, Asians, and

**Table 1** Characteristics of ICH patients at The Queen's Medical Center: 2004-2010<sup>a</sup>

	NHPI	Asian	White
No. of patients	100	352	92
Transferred from another hospital	27 (27)	64 (18)	22 (24)
<b>Risk factors</b>			
Age, y	55 ± 16 <sup>b</sup>	67 ± 17	66 ± 16
Female	40 (40)	172 (49)	39 (42)
Diabetes mellitus	35 (35) <sup>c</sup>	78 (22)	18 (20)
Hypertension	77 (77) <sup>c</sup>	267 (76) <sup>c</sup>	59 (64)
Atrial fibrillation/atrial flutter	10 (10)	41 (12)	16 (17)
Congestive heart failure	0 (0)	4 (1)	2 (2)
Previous stroke or TIA	16 (16)	69 (20)	19 (21)
Coronary artery disease or prior MI	10 (10)	42 (12)	15 (16)
Peripheral vascular disease	0 (0)	5 (1)	1 (1)
Smoking	17 (17)	44 (13)	11 (12)
Dyslipidemia	22 (22)	112 (32)	29 (32)
Prosthetic heart valve	1 (1)	5 (1)	0 (0)
<b>CT characteristics</b>			
Location			0.65
Basal ganglia	43 (43)	112 (35)	37 (40)
Lobar	24 (24)	84 (24)	29 (32)
Thalamus	12 (12)	70 (20)	12 (13)
Brainstem	9 (9)	25 (7)	4 (4)
Cerebellum	5 (5)	32 (9)	6 (7)
Primary IVH	6 (6)	15 (4)	4 (4)
IVH	41 (41)	167 (47)	47 (51)
Hematoma volume, cm <sup>3</sup>	33 ± 49	39 ± 56	40 ± 52
Hospital LOS, d	13 ± 19 <sup>c</sup>	11 ± 17	7 ± 10
In-hospital mortality	22 (22) <sup>c</sup>	91 (26)	33 (36)
Ambulatory at discharge	22 (22)	70 (20) <sup>c</sup>	28 (30)
Discharged home	27 (27)	57 (16) <sup>c</sup>	25 (27)

Abbreviations: IVH = intraventricular hemorrhage; LOS = length of stay; MI = myocardial infarction; NHPI = Native Hawaiians and other Pacific Islanders.

<sup>a</sup> Baseline patient characteristics. NHPI and Asians were compared to white patients (reference group). Data are n (%) or mean ± SD.

<sup>c</sup>  $p < 0.05$  Compared to white patients.

<sup>b</sup>  $p < 0.0001$  Compared to white patients.

white subjects are summarized in table 1. Univariate analyses showed that NHPI were younger ( $p < 0.0001$ ) and had higher prevalence of diabetes and hypertension ( $p < 0.05$ ), higher hospital LOS ( $p = 0.01$ ), and lower in-hospital mortality ( $p = 0.03$ ) compared to white subjects. Head CT data were available in 556 (99%) ICH patients. The hematoma size, location, and prevalence of secondary IVH were not different across racial groups.

There were 123 patients (22%) who were transferred from other hospitals. Among these patients (Asian 52%, NHPI 22%, white 18%, other 8%), the racial distribution was different compared to those

who were directly admitted (Asian 65%, NHPI 17%, white 16%, other 2%,  $p = 0.001$ ). Furthermore, these patients were younger (mean age:  $58 \pm 18$  vs  $66 \pm 17$ ,  $p < 0.0001$ ), had higher prevalence of CHF (4% vs 0.2%,  $p = 0.0003$ ) and IVH (60% vs 44%,  $p = 0.003$ ), and lower prevalence of prior stroke or TIA (10% vs 22%,  $p = 0.003$ ) and lower mortality (20% vs 29%,  $p = 0.049$ ) compared to those who were directly admitted. The distribution of hematoma location was different between the 2 groups (transferred patients: basal ganglia 33%, lobar 29%, thalamus 16%, brainstem 3%, cerebellum 12%, primary IVH 8%; vs directly admitted patients: basal ganglia 39%, lobar 24%, thalamus 18%, brainstem 8%, cerebellum 7%, primary IVH 4%,  $p = 0.014$ ). There was no difference in the prevalence of other risk factors, hematoma size, or other discharge outcomes between the 2 groups.

Univariate analyses showed that the young ICH group (age <45 years) had different racial distribution ( $p = 0.001$ ), higher prevalence of patient being transferred from another hospital ( $p < 0.0001$ ), higher hospital LOS ( $p < 0.05$ ), and lower prevalence of hypertension ( $p < 0.0001$ ), atrial fibrillation/atrial flutter ( $p = 0.001$ ), previous stroke or TIA ( $p = 0.001$ ), CAD or prior MI ( $p = 0.004$ ), and dyslipidemia ( $p < 0.0001$ ) compared to the older ICH group (table 2). In multivariable analyses, independent predictors for young ICH were NHPI race (OR 3.55; 95% CI 1.33–9.45;  $p = 0.01$ ) compared to white subjects, being transferred from other hospital (OR 2.03; 95% CI 1.05–3.93,  $p = 0.04$ ), hypertension (OR 0.49; 95% CI 0.27–0.91;  $p = 0.02$ ), previous stroke or TIA (OR 0.21; 95% CI 0.05–0.91;  $p = 0.04$ ), and dyslipidemia (OR 0.15; 95% CI 0.05–0.50;  $p = 0.002$ ).

Further comparative analyses of cholesterol and BMI were performed in a subset of patients with available data. Cholesterol data were available in 238 (42%) patients. NHPI had lower HDL level than white subjects ( $p < 0.05$ ) but similar LDL, total cholesterol, and triglyceride levels (table 3). The BMI data were available in 376 (67%) patients. The NHPI group had higher BMI compared to white subjects ( $p < 0.0001$ ; table 3), suggesting higher prevalence of obesity.

Since hypertension is one of the major causes of ICH, we also analyzed the ICH patients with a pre-existing diagnosis of hypertension (NHPI = 77, Asian = 267, white = 59) and assessed the proportion of those with untreated hypertension prior to admission. The results demonstrate that NHPI had higher prevalence of untreated hypertension compared to Asians (NHPI 45% vs Asians 31%,  $p = 0.02$ ), and a trend toward higher prevalence of un-

**Table 2** Characteristics of young ICH patients<sup>a</sup>

	Age <45 y	Age ≥45 y	p
No. of patients	68	494	
Transferred from another hospital	28 (41)	95 (19)	<0.0001
Age, y	35 ± 8	69 ± 14	<0.0001
Female	25 (37)	232 (47)	0.11
Race			0.001
NHPI	23 (34)	77 (16)	
Asian	33 (49)	319 (65)	
White	8 (12)	84 (17)	
Other	4 (6)	14 (3)	
<b>Risk factors</b>			
Diabetes mellitus	12 (18)	121 (25)	0.21
Hypertension	36 (53)	375 (76)	<0.0001
Atrial fibrillation/atrial flutter	0 (0)	68 (14)	0.001
Congestive heart failure	0 (0)	6 (1)	0.36
Previous stroke or TIA	3 (4)	103 (21)	0.001
Coronary artery disease or prior MI	1 (2)	67 (14)	0.004
Peripheral vascular disease	0 (0)	6 (1)	0.36
Smoking	11 (16)	65 (13)	0.50
Dyslipidemia	4 (6)	161 (33)	<0.0001
Prosthetic heart valve	0 (0)	6 (1)	0.36
<b>CT characteristics</b>			
Location			0.65
Basal ganglia	31 (46)	180 (37)	
Lobar	16 (24)	123 (25)	
Thalamus	11 (16)	86 (18)	
Brainstem	3 (5)	35 (7)	
Cerebellum	3 (5)	42 (9)	
Primary IVH	3 (5)	23 (5)	
IVH	33 (49)	230 (47)	0.76
Hematoma volume, cm <sup>3</sup>	36 ± 37	38 ± 56	0.79
Hospital LOS, d	14 ± 23	10 ± 15	0.046
In-hospital mortality	16 (24)	137 (28)	0.47
Ambulatory at discharge	16 (24)	106 (22)	0.75
Discharged home	17 (25)	94 (19)	0.25

Abbreviations: IVH = intraventricular hemorrhage; LOS = length of stay; MI = myocardial infarction; NHPI = Native Hawaiians and other Pacific Islanders.

<sup>a</sup> Characteristics of the young (age <45) and older (age ≥45) ICH group. Data are n (%) or mean ± SD.

treated hypertension compared to white subjects (NHPI 45% vs white subjects 31%,  $p = 0.11$ ), suggesting a possible racial disparity in primary prevention.

**DISCUSSION** Our results based on a single-center study demonstrate that NHPI admitted with spontaneous ICH are significantly younger, by more than 10 years, and have higher prevalence of diabetes and hypertension compared to white patients. In multi-

variable analyses adjusting for ICH risk factors, NHPI race was an independent predictor of young ICH. The age disparity seen in our study is similar to the age disparities reported in other ICH observational studies comparing non-Hispanic white subjects to Maoris from New Zealand,<sup>20</sup> Mexican Americans,<sup>21</sup> and black patients<sup>22,23</sup> with ICH, and supports the idea that minority racial groups have a significantly younger age at presentation with ICH. Since NHPI have been historically grouped with Asians into a single racial category in many studies, prior ICH studies may have masked substantial differences in disease characteristics and outcomes among the NHPI group. Indeed, to our knowledge, this is the first study to characterize the clinical characteristics of NHPI who were hospitalized with acute ICH.

Although we acknowledge the limitation of a single-center study and its lack of generalizability, we believe this is an important first glance at the possible racial disparities in stroke risk factors seen in the state of Hawaii. Interestingly, NHPI had longer hospital LOS compared to white patients even though they shared similar ICH size and location, which suggests that the disease severity was likely similar between the 2 groups. We speculate that the insurance status, the disposition environment, and the geographical location of patients' homes may have played a major role in this observation.

Our study also demonstrates that NHPI with ICH are more likely to have characteristics of the metabolic syndrome (diabetes, obesity, and lower HDL) compared to white subjects, which is consistent with the prior studies that showed higher prevalence of cardiometabolic risk factors among the community-dwelling NHPI compared to other racial-ethnic groups.<sup>8-13</sup> However, it is uncertain how these cardiometabolic health disparities impact the incidence and long-term outcome of ICH among the NHPI population. Although low levels of LDL cholesterol have been linked with increased risk of death after ICH,<sup>24</sup> no studies have investigated the effect of HDL cholesterol on ICH. Furthermore, the proportion of hypertensive ICH patients who were untreated for hypertension prior to admission was significantly higher among NHPI compared to Asians even though there was no difference in the prevalence of reported hypertension. This finding suggests a possible disparity in community-based primary prevention between these 2 races. Further study addressing the socioeconomic status, access to health care, insurance status, and cultural beliefs toward health care is needed to determine the important factors driving this disparity.

This study has several limitations. First, the data on sympathomimetic drug abuse (i.e., methamphet-

**Table 3** Comparison of cholesterol and BMI between different racial groups<sup>a</sup>

	NHPI	Asian	White
Total cholesterol, mg/dL	177 ± 41	184 ± 45	171 ± 48
LDL, mg/dL	113 ± 36	111 ± 48	102 ± 39
HDL, mg/dL	40 ± 10 <sup>b</sup>	50 ± 15	49 ± 16
Triglycerides, mg/dL	116 ± 69	121 ± 93	101 ± 59
BMI, kg/m <sup>2</sup>	32 ± 10 <sup>c</sup>	25 ± 6	26 ± 4

Abbreviation: BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; NHPI = Native Hawaiians and other Pacific Islanders.

<sup>a</sup> Comparison of total cholesterol, LDL, HDL, triglycerides, and BMI among races. NHPI and Asians were compared to white patients (reference group). Data are mean ± SD.

<sup>b</sup>  $p < 0.05$  Compared to white patients.

<sup>c</sup>  $p < 0.0001$  Compared to white patients.

amine and cocaine) were not available and were not accounted for in the analyses. Since sympathomimetic drug abuse is considered one of the major etiologies of spontaneous ICH in the young, and NHPI have a higher prevalence of methamphetamine abuse compared to other major racial-ethnic groups in Hawaii,<sup>25–27</sup> it is unclear whether younger age at ICH observed in NHPI is related to high prevalence of methamphetamine abuse. Second, Asian race was not further specified (i.e., Japanese, Filipinos, Chinese, Korean), and thus it is unclear if similar age disparities exist between NHPI and each of the specific Asian races. Third, our prediction model for young ICH, based on a stepwise logistic regression, is limited due to the few subjects with young ICH. Fourth, due to the lack of long-term outcome data in our study, we were unable to assess any potential disparities that may exist in long-term outcome among the NHPI population as previously shown in black stroke patients in the United States,<sup>28,29</sup> and the Pacific people in New Zealand.<sup>30</sup> Fifth, we do not have complete data on anticoagulation use and were not able to incorporate it in the final model, which could have affected our results. However, we have attempted to adjust for this to the best of our ability by incorporating the pertinent risk factors in the model such as atrial fibrillation/atrial flutter, prosthetic heart valve, peripheral vascular disease, and history of prior stroke that are often associated with anticoagulation use. Finally, since this is a single-center observational study, our results may not be generalizable to other populations since there may have been a referral bias at our institution; for example, because our institution is a tertiary referral center, there may have been a referral bias toward more severe ICH patients as ICH patients with small hematomas and minor neurologic symptoms may not have been transferred to our facility. Also, it is possible that some of the older ICH patients with preexisting do-not-resuscitate orders or those with terminal illness

may not have transferred to our facility, creating a possible selection bias toward younger ICH patients. However, only 22% of our patients were transferred from another hospital, and the rest of the patients were brought directly to our Emergency Department from the scene; thus, we believe that our study population is reasonably representative of the Honolulu County. We have adjusted for this referral bias factor in our final multivariable model.

Our study offers a first look at the possible racial disparities in stroke risk factors among NHPI with ICH, which has not been described previously. Prospective statewide, multicenter studies controlling for socioeconomic modifiers and the impact of substance abuse are needed to determine factors contributing to the younger age at ICH presentation in this unique racial group.

### AUTHOR CONTRIBUTIONS

K.N. participated in the conception and design of the study, the analysis and interpretation of data, and was responsible for drafting and finalizing the manuscript. M.A.K. participated in the analysis and interpretation of data and helped to draft and finalize the manuscript. T.B.S. participated in the analysis and interpretation of data, and helped to draft and finalize the manuscript. S.M.A. participated in the acquisition of data, analysis and interpretation of data, and finalization of the manuscript. C.W.C. participated in the conception and design of the study, study supervision, analysis and interpretation of the data, and helped to draft and finalize the manuscript. All authors read and approved the final manuscript.

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### DISCLOSURE

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Mark these dates on your calendar for exciting continuing education opportunities, where you can catch up on the latest neurology information.

### Regional Conference

- October 26–28, 2012, Las Vegas, Nevada, Encore at Wynn Hotel

### AAN Annual Meeting

- March 16–23, 2013, San Diego, California, San Diego Convention Center