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Gender Differences in Risk Factors, Mortality, and Length of Stay of Patients Discharged From a Pakistani Stroke Unit: A Comparative Cross-Sectional Study

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ABSTRACT

BACKGROUND

Differences between women and men in relation to stroke are increasingly being recognized. There is a scarcity of data on gender-based differences in stroke risk factors and outcomes from Pakistan.

METHODS

We enrolled 231 consecutive patients diagnosed with acute stroke. All patients received care along a standardized stroke pathway in a single stroke unit. We analyzed demographic and medical factors, NIHSS scores, and outcomes.

RESULTS

Of 213 consecutive hospitalized patients, 135 patients were men and 76 were women. The male to female ratio was 1.84. The mean age of males was 62.3 ± 13.56 , as compared to females 61.15 ± 11.60 years. Hypertension, smoking, and dyslipidemia were more commonly found in men whereas ischemic heart disease, atrial fibrillation, and history of prior stroke were more frequently encountered in women. However, after adjustment for age and gender smoking in men ($P = .059$) and atrial fibrillation ($P = .054$) and prior stroke ($P = .017$) in women, these were found to be independent predictors of stroke. Diabetes was equally distributed between the two genders. Women were more likely to be dependent prestroke ($P = .524$), have more severe strokes ($P = .142$), and more likely to have a longer hospital stay ($P = .942$). In-hospital mortality was higher in women than in men (6.7% vs 5%; $P = .524$) and they had poorer discharge modified Rankin Scale scores (mRS 5; 8.5% vs 5%; $P = .775$); however, these differences were not statistically significant.

CONCLUSION

There appear to be gender-based differences in the risk factor profile and perhaps outcome in Pakistani patients despite standardized care in a dedicated stroke unit.

Keywords: Gender, stroke, Pakistan, stroke units

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INTRODUCTION

Stroke is the most common cause of sustained disability and the leading cause of mortality worldwide.¹ Although most research and attention to prevention and intervention occurs in high-income countries, more than 85% of strokes occur in low- and middle-income countries.

Stroke can be devastating for all individuals who are affected; however, on a societal level women bear a greater burden of stroke than do men, largely driven by their longer life expectancy and the higher risk of stroke with advancing

age.² There is growing recognition of the clinical and public health importance of stroke in women.³ Existing data suggests that stroke-related outcomes, including disability and quality of life (QOL), are consistently poorer in women than in men, yet the reasons for this are not well understood.² They have a higher rate of poststroke mortality, disability, depression, and dementia compared to men.^{4,5} Cohort studies indicate that women and men have differences in risk factor profiles,^{5,6} acute stroke presentation,^{6,7} and stroke etiology.⁸ However, results from studies on the distribution of risk factors are very inconsistent and differ greatly

between countries. In general, it seems that men suffer more often from atherothrombotic strokes, while cardioembolic strokes are more frequent in women. Women are less likely to smoke cigarettes, drink alcohol, suffer from ischemic heart disease (IHD), carotid artery stenosis, or aortic atherosclerosis, but they seem to present more with diabetes, hypertension, dyslipidemia, and atrial fibrillation.^{5,9,10} Little is known about gender differences in stroke recovery and these have been mostly from Europe^{6,11} and North America.^{4,12} These studies showed that among stroke survivors, women were more disabled on discharge with more physical impairments and limitations in activities of daily living (ADL).^{4,13}

Although international data reflects gender differences in stroke types and subtypes, risk factors, stroke presentation and outcome, there is no published gender-based data from Pakistan on the frequency of modifiable risk factors and stroke outcome to substantiate these findings. The recognition of gender disparities, if any, is the initial step before changes can be made in the health policy aimed at ameliorating the observed asymmetry in stroke outcomes. Hence we performed a gender-based study on differences in stroke presentation, risk factor profile, stroke severity, and outcome in patients hospitalized for acute stroke to a dedicated stroke center of Pakistan.

METHODS

From February 2010 to August 2010, 213 consecutive patients with CT- or MRI-proven acute ischemic stroke admitted to the stroke unit at the Aga Khan University Hospital—a 550 bed tertiary care center in Karachi, Pakistan—were recruited. A standardized data collection instrument was developed to obtain information on demographics, prestroke ambulatory status, stroke subtype (hemorrhage/infarct), stroke severity, and functional status at discharge. We defined acute stroke as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin” according to the World Health Organization (WHO) criteria.¹⁴

History of hypertension (HTN), diabetes mellitus (DM), stroke or transient ischemic attack (TIA), ischemic heart disease (IHD), valvular heart diseases, atrial fibrillation (AF), and rheumatic heart disease were also noted. Risk factors were defined as follows: Hypertension: a previous record of at least two blood pressure readings of $\geq 160/90$ or the requirement of regular intake of antihypertensive drug(s). Diabetes: as having a random glucose level of > 11.1 mmol/L (200 mg/dl) or the requirement of regular hypoglycemic drugs/insulin. Patients who required regular use of antihypertensive agents and hypoglycemic agents on discharge from the hospital (excluding the acute-phase changes) were also regarded as hypertensive and diabetic. Dyslipidemia was defined as total cholesterol > 200 mg/dl or LDL > 160 mg/dl. Atrial fibrillation was defined by a positive history or the presence of AF on the electrocardiogram (ECG) during the hospital stay or AF on Holter or telemetry. On discharge from the hospital, the length of stay and death or discharge status

was recorded. Either computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain was required for the diagnosis.

The severity of stroke was evaluated by the modified National Institutes of Health (NIH) Stroke Scale¹⁵ on admission and outcome at discharge by the Modified Rankin Scale (mRS).¹⁶ The prestroke functional status of patients was determined by the Oxford Handicap Scale (a measure of disability; 0–2 independent, 3–5 dependent).¹⁷ This study received ethical approval from the Ethical Review Committee of the Aga Khan University. All patients and/or their legal surrogates provided informed consent.

STATISTICAL ANALYSIS

Sample size was calculated by considering the prevalence of stroke and its risk factors in Pakistani population that varies from 12% to 21%. With 5% type I error, 80% power, bound on error of 6% and 20% nonresponse rate, the sample size came out to be 213.¹⁸ All analyses were conducted by using the statistical package for social science SPSS (Release 16.0, standard version, copyright SPSS; 1989–2002). Descriptive analysis was done and is presented as mean \pm standard deviation for quantitative variables and as proportions for categorical variables. Comparisons were made by a Chi-square test and Fisher’s exact test where appropriate to evaluate gender differences in risk factors, stroke severity, length of hospital stay, and outcome at discharge.

RESULTS

Of the 213 patients enrolled in the study with acute stroke, 138 (65%) were men and 75 (35%) were women. Demographic and clinical characteristics of the two groups are described in **Table 1**.

Table 1. Stroke Type, Severity and Prestroke Functional Status According to Sex

	Women, n (%) N = 138	Men, n (%) N = 75	P
Mean age, years	61.15 \pm 11.6	62.25 \pm 13.56	.976
Ischemic stroke, n (%)	63 (84%)	111 (80.4%)	.596
Cerebral hemorrhage, n (%)	12 (16%)	27 (19.6%)	.495
Location of stroke			
Infra-tentorial	21 (28%)	41 (29.7%)	.469
Supra-tentorial	59 (78.7%)	97 (70.3%)	.148
Prestroke functional status			
Independent, n (%)	63 (84%)	124 (89.9%)	.152
Dependant, n (%)	12 (16%)	14 (10%)	.524
Stroke severity			
NIHSS < 8, n (%)	36 (48%)	80 (58%)	.874
NIHSS 8–16, n (%)	29 (38.7%)	40 (29%)	.742
NIHSS > 16, n (%)	10 (13.3%)	15 (10%)	.142

Age Distribution

The mean age was 62.3 ± 13.56 for men and 61.15 ± 11.60 for women with no significant age difference between the two groups ($P = .97$). The prevalence of stroke increased steadily with age for both genders followed by a steep decline after 70 years (Figure 1). Between 61 and 70 years, 32% of the women had strokes. In those greater than 70 years of age, this difference was reversed with more men than women being affected. Stroke in the young (ie, ≤ 40 years) comprised 5.6% of the total sample size and occurred more commonly in men than in women (6.5% vs 4%; $P = .131$).

Stroke Types and Risk Factor Distribution

The MRI brain was available in 181 (85%) and CT in 32 patients (15%). Strokes were categorized into ischemic and hemorrhagic. Ischemic stroke was the predominant subtype in both the groups. There were 81.7% of all patients that had ischemic stroke and 18.3% had ICH. Of these, 70.8% patients had supratentorial and 29% had infratentorial strokes. The distribution of these stroke types did not differ between men and women. Also, 84% of women and 80% of men had ischemic strokes. Females had a higher rate of cerebral infarct, which is comparable ($P = .592$). The distribution of conventional risk factors was remarkably similar between men and women (Table 2).

Prestroke Functional Status

We observed that prestroke, women were significantly more disabled at baseline than their counterparts as assessed by the Oxford Handicap Scale. Twelve out of 75 women (16%) were already dependent in their functional status prestroke ($P = .524$) and most of these were in the 60–70 year age group.

Stroke Severity

Eighty out of 138 (58%) men and 36 out of 75 women (48%) had milder strokes (NIHSS < 8), whereas, 15 men (10.8%) and 10 women (13.3%; $P = .142$) had severe strokes (NIHSS > 16).

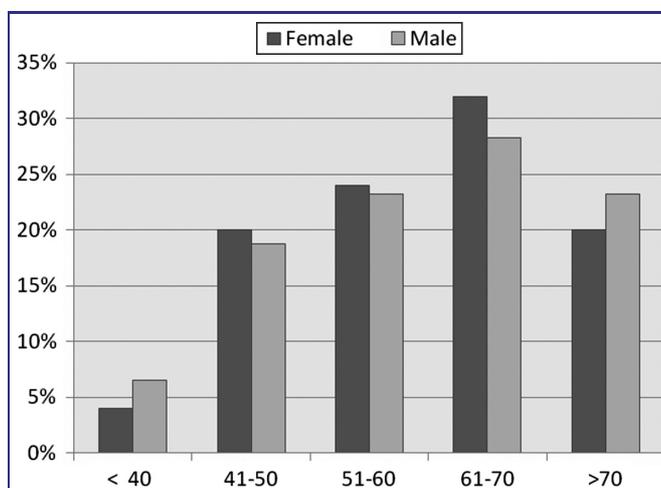


Figure 1. Prevalence of stroke by age and gender showing more women with stroke up to 70 years with the trend then reversing after 70 years.

Table 2. Risk Factor Distribution According to Gender

	Women n (%)	Men n (%)	P
Hypertension, n (%)	62 (82.6%)	110 (79.7%)	.165
Diabetes, n (%)	33 (44%)	62 (44.9%)	.572
Dyslipidemia, n (%)	23 (30.7%)	58 (42%)	.105
Atrial Fibrillation, n (%)	10 (13.3%)	4 (2.9%)	.054
Ischemic heart disease, n (%)	24 (32%)	35 (25.3%)	.242
Smoking, n (%)	1 (1.33%)	51 (37%)	.059
Prior stroke, n (%)	16 (21.3%)	18 (13.04%)	.01

Women Men P

There were 38.7% of women and 29% of men that had moderate strokes (NIHSS 8–16; $P = .142$). The mean NIHSS score was 9 for women and 4.8 for men.

PATIENT OUTCOMES

Mortality and Functional Outcomes

Five out of 75 women (6.7%) and 7 out of 138 men (5%) died in the first 7 days after a stroke ($P = .524$). All of these deaths were in-hospital mortalities. Fatality rate was 5.6%. Three men and three women who died from acute ischemic stroke had NIHSS of 16 and above. Women were more likely to die from ischemic strokes of severe intensity (60% vs 40%; $P = .237$) while men had a higher mortality from cerebral hemorrhage (57% vs 43%; $P = .374$). The outcome of stroke based on stroke severity is shown in Table 4.

In the immediate poststroke period (7 days after stroke), mild disability (mRS ≤ 2) was observed in 41% of the men and 35% of the women. Six women (8.5%) and seven men (5.3%; $P = .775$) were severely disabled and bedridden requiring constant nursing care (Rankin score 5), whereas, 40 women (56.3%) and 70 men (53.4%; $P = .742$) were moderately disabled (Rankin score 3 or 4), requiring assistance to attend to own bodily needs (Table 3). There was no significant difference in the functional outcome between men and women after accounting for age and prestroke functional status.

Seventy-four percent of the men and 82.7% of the women had less than a 7-day hospital stay, whereas, 26.1% of the men and 29.3% of the women stayed for more than 7 days. Thus, female patients had a longer in-hospital stay ($P = .942$). Those with a longer hospital stay also had more severe strokes and either died or were more disabled at discharge (Figure 2).

Table 3. Outcomes According to Gender

	Women	Men	P
Rankin score, 0–2, n (%)	25 (35.2%)	54 (41.2%)	.874
Rankin score, 3–4, n (%)	40 (56.3%)	70 (53.4%)	.742
Rankin score, 5, n (%)	6 (8.5%)	7 (5.3%)	.775
Death, n (%)	5 (6.7%)	7 (5.1%)	.524
Length of hospitalization, >7 days, n (%)	22 (29.3%)	36 (26%)	.942

Table 4. Correlation Between Severity (Admission NIH Score) and Outcome Status (mRS at Discharge)

NIH Score (on admission)	mRS at Discharge							
	Dead		≤2		3-4		5	
	M n (%)	F n (%)	M n (%)	F n (%)	M n (%)	F n (%)	M n (%)	F n (%)
<8	0	0	45 (83.3%)	23 (92%)	34 (48.6%)	13 (62.5%)	1 (0.75%)	0
8-16	2 (28.5%)	1 (20%)	9 (16.7%)	2 (8%)	27 (38.3%)	23 (57.5%)	2 (28.6%)	2 (40%)
>16	5 (71.4%)	4 (80%)	0	0	9 (12.9%)	4 (10%)	4 (57%)	3 (60%)

DISCUSSION

The present study is one of the first prospective observational studies to examine gender differences in stroke subtype, risk factors, and outcome of stroke patients in Pakistan from a center where standardized care is provided. Women and men were comparable for age at stroke onset but with increasing age there was a trend toward increased prevalence of stroke with the highest between 61 and 70 years of age in females. This trend reversed after 70 years because Pakistan is one of the few countries in the world with an inverse sex ratio: the number of older men is more than women. We also report a higher rate of young stroke (<40 years). This is in conformity with the previous epidemiologic data on stroke from this region, which shows that the average age of patients with stroke in developing countries is 15 years younger than that in the developed countries.¹⁹ Overall, women have greater stroke severity at presentation with mean NIHSS of 4.8 in men and 9 in women. They have worse baseline functional status than men, are less likely to have an excellent outcome (mRS < 2), and more likely to have a longer hospital stay. These are preliminary trends that require detailed exploration. There are also differences with respect to the prevalence of stroke risk factors. Women are more likely to have AF and prior stroke (which may have contributed to their premorbid condition), whereas, men with stroke are more likely to have a history of smoking. We also report among women a greater tendency of diabetes, hypertension, and IHD; however, none of these were found to be independent predictors of stroke outcome with regard to gender.

We think it is important to relate these differences because the demographic- and gender-based data from Pakistani populations is disconcerting with regard to absolute numbers

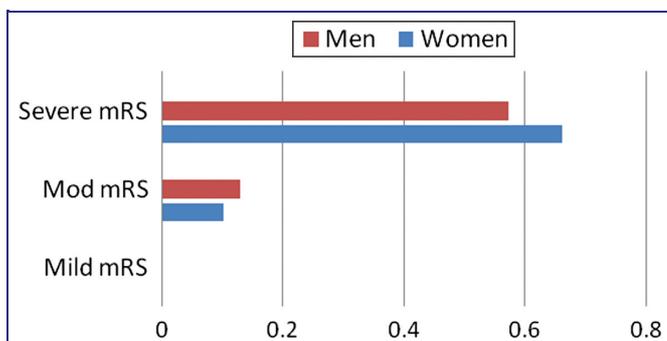


Figure 2. Correlation of NIHSS > 16 with discharge mRS in both men and women, women being more significantly disabled at the same measurable neurologic deficit.

and distribution of risk factors. Pakistan is the sixth most populous country in the world with an estimated population of 188.8 million (based on 2008 WHO population estimates) of which 48.5% are women.²⁰ It has one of the highest noncommunicable disease (NCD) burdens accounting for 59% of the total disease load.²¹ Existing population-based morbidity data on NCDs in Pakistan shows that one in three adults over the age of 45 years suffers from high blood pressure and metabolic syndrome.²² The prevalence of cardiovascular and cerebrovascular disease is 21%, diabetes 11%, dyslipidemia 35%; whereas, 40% of the men and 12.5% of the women use tobacco in one form or the other.²³

According to the National Health Survey of Pakistan (NHSP) 1998, men have a higher prevalence of hypertension than women but this pattern reverses after 45 years. For women, prevalence rates of hypertension rises sharply after 35–44 years compared to men. Thirty-four percent of the men and 12.5% of the women in Pakistan use tobacco regularly.²⁴ The risk of coronary artery disease is higher in females than in males (30% vs 23.7%).²⁵ Women also have a higher prevalence rate of dyslipidemia (40%) with a steeper increase in prevalence rate with age.²⁴ According to a WHO report on Pakistan's demographics, the proportion of population 65 years and older will move from 3.9% in 2000 to 5.4% in 2025, with women bearing the greater burden of old age.²¹ Pakistan has an annual estimated stroke incidence of 350 000 new cases each year²⁶ with a life-time prevalence of stroke/TIA of around 20% equally shared between men and women.²⁷ Despite these high prevalence rates there are no large scale epidemiological studies regarding stroke risk factors, outcomes, and their relation with gender.

The 7-day stroke outcome showed that women had more physical impairments and limitations in mobility, as measured by the Modified Rankin Scale. In a study of 2725 stroke survivors from a 10-year cohort, it was observed that 38% women were disabled at discharge (Barthel index < 60) with 22% women being discharged to a long-term care facility.²⁸ The causes of sex differences in functional outcomes and QOL have yet to be fully elucidated. Differences in outcome can be explained by the fact that compared with men, women have poorer prestroke functional status and greater comorbidities. Other factors like depression and lack of social support for women may also have contributed to this difference; however, this may not be sufficient to adequately explain the observed differences.⁵ Stroke severity is often cited as a potential explanation for sex differences in stroke outcomes, although the available data suggests that differences in stroke severity between men and women are small to nonexistent.^{2,9} Clearly,

more studies that assess stroke survivors in both subjective (eg, health related QOL) and objective (eg, cognitive functioning, depression) measures are needed to determine the causes of these differences in outcomes.

Our study is the first of its kind in Pakistan reporting gender differences in stroke risk factors and outcomes. The strengths of our study are enrollment in a single hospital providing organized stroke care and prospective data collection. Any observed differences in outcome are likely real as stroke care was standardized. However, the study has limited generalizability given that it describes the result of a single tertiary care center. This is only a cross-sectional survey and no conclusions on longitudinal trends in risk factor control or treatment could therefore be drawn. Follow-up was also limited to hospital discharges and mortality. Most importantly the major weakness of this study is that the small numbers make it difficult to draw conclusive, statistically significant observations and we can only report on trends that need further exploration.

CONCLUSION

In summary, preliminary observations in a developing country like Pakistan suggest that gender-based differences exist in risk factor profiles and perhaps outcomes. This limited study highlights the need to explore these differences further as men and women are at equal high risk for NCD including stroke in Pakistan.

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