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Original Research Article

Relationship among Sex, Pattern of Weakness and Treatment Outcomes of Post-Stroke Patients: A Register-Based Longitudinal Study

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ABSTRACT:

Introduction: Differences in stroke care and health outcomes between males and females are debated globally. Sex differences in functional outcomes after stroke rehabilitation are poorly investigated in the context of Nepal. This study aimed to explore the relationship among patient's sex, side of weakness, and post-stroke health outcome after rehabilitation in a hilly western region of Nepal. **Methods**: A register-based longitudinal study was conducted in a rehabilitation center including all consecutive patients with stroke who came for rehabilitation (ayurvedic, homeopathic, acupuncture, and physiotherapy) from March 2018 to March 2020. Modified Rankin Scale score at a three-month follow-up after a visit to the center was the main outcome measure. It was reported using relative risk and 95% confidence intervals. **Results**: The study included 384 stroke patients, among them 241 (62.8%) were males. Right-sided weakness was 1.262 times (RR =1.262, 95% CI = 1.016-1.567) more likely in males than in females. Male stroke patients were 1.104 times more likely to achieve a good outcome than females (RR=1.104, 95% CI = 1.007-1.211) and these findings were statistically significant. There was no association between the side of weakness and the outcome. **Conclusion**: More males, compared to females, visited for rehabilitation and achieved a good outcome (mRS0-2) after three-months. Right-sided weakness was more common in males than in females.

Keywords: Health outcome, Right sided-weakness, Sex difference, Stroke, Stroke rehabilitation.

INTRODUCTION:

Stroke is the second leading cause of death worldwide [1] as well as in Nepal after coronary heart disease.[2] Stroke has been reported to affect males and females differently.

Age-specific stroke rates are greater in males as compared to females.[3] Differences in hormonal levels, lifestyle (smoking, alcohol consumption, exercise, diet), the prevalence of hypertension, diabetes, etc. are potential factors that can contribute to sex differences in the incidence of stroke.[4,5]

The relationship of sex with the type of stroke, location of the lesion, side of limb weakness, and quality of life has also been studied.[6,7] A study found that the incidence of right-sided weakness is more common than left-sided weakness due to more frequent involvement of the left middle cerebral artery.[8] It has been observed that females have poorer health outcomes compared

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to males and patients with left hemiplegia tend to recover less well.[6] However, another study reported that there is no significant sex difference in health outcomes.[9]

The literature reveals differences in findings regarding stroke care and health outcomes between males and females.[10,11] Any differences in the outcomes may arise from the role of biologic sex or indirectly through the play of other factors. Several factors such as history prior to the stroke, length of stay in the acute care hospital, types of stroke (hemorrhagic and ischemic), types of motor deficits, aphasia, neglect and dysphasia, types of rehabilitation (physiotherapy, acupuncture, speech therapy, neuropsychological stimulation or rehabilitation) and socioeconomic factors play a role in stroke recovery.[12]

However, the data comparing post-stroke health outcomes between males and females in western Nepal is less available. We, therefore, aimed to study the relationship among sex, pattern of weakness, and treatment outcomes of post-stroke patients in this region.

METHODS:

A register-based longitudinal study was conducted in the Pyuthani Acupuncture, Tansen, Palpa, a rehabilitation center. Pyuthani Acupuncture is a registered polyclinic where patients receive ayurvedic, homeopathic, acupuncture, and physiotherapy treatments. Patients who come directly to the rehabilitation center for clinical signs and symptoms of a stroke are referred to the nearest tertiary health care center. Mostly, stroke patients from the western hilly region directly approach the nearest tertiary care hospital where they receive initial medical care and treatment. After a stay in the hospital, they are referred to the rehabilitation center or by their own will, they reach the rehabilitation center for speedy recovery along with the treatment plan of the hospital. The initial records of consecutive patients with stroke registered in the center from March 2018 to March 2020 were studied. Their three-months-follow-up records were also studied during that period. Clinically diagnosed cases of stroke that met WHO criteria and were confirmed by computerized tomography (CT) scan or magnetic resonance imaging (MRI) in the prior hospital were included in the study.[13]

After approval of the rehabilitation center and Institutional Review Committee of Lumbini Medical College Protocol No: (IRC-LMC 14-G/020) data was collected from September 12 to October 16, 2020. Sample size was calculated to be 384 using the following formula: $n = Z^2p(1-p)/e^2$.[14]Where, n = sample size for infinite population, Z = Z-Score for desired confidence level (95%) = 1.96, p = proportion of patients who achieve good outcome (assumed to be 50% = 0.5, for unknown population), e = desired level of precision = ±5% = 0.05.

The case records of all adults aged above 18 years with a diagnosis of stroke (all stroke types presenting with hemiplegia or hemiparesis) and modified Rankin Scale (mRS) finding above 2 at the time of initial presentation to the rehabilitation center[14] were included in the study. To study the health outcome, patients with moderate to severe stroke (mRS>2) were required and we used the consecutive (non-probability) sampling technique. Information about age, sex, history of the patient, side of weakness, the initial level of dependency before rehabilitation (mRS>2 were included), brain imaging data, laboratory reports, diagnosis, and treatment were collected in predesigned case proforma maintaining the confidentiality of the patients' personal information. Patients' health outcome at three-month after registration was evaluated by the mRS from the follow-up records that had been kept based on a telephone interview or follow-up visit to the center. The poor outcome is defined as mRS>2 and good outcome as mRS up to 2.[6] Patients whose records were not complete regarding the information about the study parameters were excluded from the study.

Analysis of the relationship between categorical variables was conducted using the chi-square test. The difference in the mean age of the two groups (male and female) was tested using an independent t-test. Most data were in the form of

categories sex (male and female), male (right- and left-sided weakness), and female (right- and left-sided weakness). The association between sex and clinical outcome at three-month was assessed by the chi-square test. To investigate the relationship between sex and the side of weakness too, a chi-square test was used. The final results were reported using relative risk (RR) and 95% confidence intervals. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS^{TM}) software version 16.0. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS:

A total of 384 stroke patients registered in the rehabilitation center during the two-year period were included in the study. The ratio of males and females visiting the rehabilitation center was 1.68:1. The average age for the occurrence of stroke was 62.4 ± 12.0 years. Most of the stroke patients were in the age group 55-64 years (32.4%) followed by 65-74 years (26.6%). (Table1). There was no significant difference in the mean age of occurrence of stroke between males and females [t(382) = -0.176, p = 0.860].

Table1: Baseline characteristics of the study population.

Variables	Male (N=241) Frequency (%)	Female (N=143) Frequency (%)	Total (N=384) Frequency (%)
Age group (years)			
<44	23 (9.4)	6 (4.1)	29 (7.55)
45-54	31 (12.9)	28 (19.6)	59 (15.4)
55-64	78 (32.4)	48 (33.6)	126 (32.9)
65-74	64 (26.6)	44 (30.8)	108 (28.1)
≥ 75	45 (18.7)	17 (11.9)	62 (16.1)
mRS* (after 3 months)			
Good	214 (88.8)	115 (80.4)	329 (85.7)
Poor	27 (11.2)	28 (19.6)	55 (14.3)

**modified Rankin Score*

Table2: Association between gender and side of weakness.

Gender	Right-sided weakness	Left-sided weakness	Statistics	RR*(95%CI**)
Male	134	107	$\chi2$=4.789,df=1, p=0.029	1.262 (1.016-1.567)
Female	63	80		

**Relative risk, **Confidence interval*

Table 2 shows the findings regarding the side of weakness in relation to the sex of the patients. In male patients, right-sided weakness (55.60%) was slightly more common compared to left-sided weakness whereas left-sided weakness (55.94%) was more common in female patients. Male patients were 1.26 times more likely (RR = 1.262, 95% CI = 1.016-1.567) to have right-sided weakness compared to female patients.

Between-sex contrast of outcome: We observed that the male sex was associated with a 10% greater chance of achieving a good three-month outcome compared to the female sex (RR=1.104,95% CI = 1.007-1.211) as shown in Table 3.

Within-sex contrast of outcome: There was no significant difference in the health outcome between males who had left-sided weakness and males who had right-sided weakness (RR=1.0, 95% CI = 0.913-1.094). There was no significant relationship between the side of weakness and outcomes in the female group either (RR=1.024, 95% CI = 0.869-1.206) (Table 3)

Table3: Association of sex and side of weakness with functional outcome [modified Rankin Score (mRS) good or poor] at three-months.

Variables	mRS0-2 (good)	mRS >2 (poor)	Statistics	mRS (good) RR*(95%CI**)
Male	214	27	$\chi2$=5.132,df=1, p=0.023	1.104 (1.007-1.211)
Female	115	28		
Male (Left-sided weakness)	95	12	$\chi2$=0.00,df=1, p=0.996	1.000 (0.913-1.094)
Male (Right-sided weakness)	119	15		
Female (Left-sided weakness)	65	15	$\chi2$=0.08,df=1, p=0.778	1.024 (0.869-1.206)
Female (Right-sided weakness)	50	13		
Left-sided weakness (Total)	160	27	$\chi2$=0.004,df=1, p=0.950	0.997 (0.919-1.082)
Right-sided weakness (Total)	169	28		

**Relative risk, **Confidence interval*

Moreover, right-sided weakness and left-sided weakness in the entire cohort had no significant difference in the health outcome (RR = 0.997,95% CI = 0.919-1.082) as shown in Table 3.

DISCUSSION:

This study aimed to determine the relationship between the stroke patient's sex and side of weakness, explore the relationship between the patient's sex and post-stroke health outcome, and assess the relationship between the side of weakness and post-stroke health outcome.

The ratio of the number of males and females visiting the rehabilitation center was 1.68:1. A higher incidence of stroke in males may be responsible for this sex difference. The difference in access to the facility cannot be ruled out though. Previous studies have suggested that several factors such as hypertension, hyperlipidemia, type 2 Diabetes Mellitus, overweight, and obesity as well as genetic, hormonal, and anatomic factors add sex

differences in stroke. Besides this, sex differences in lifestyle, level and pattern of dietary intake, smoking, and drinking behavior also contribute to risk for stroke.[4] A previous study has shown that the risk factors namely hypertension, chronic heart failure, and atrial fibrillation were more common in female patients. On the other hand, smoking and alcohol consumption were more common in male patients.[5]

We observed that male patients were 1.26 times more likely to have right-sided weakness compared to female patients. The difference in the right and the left-sided weakness may be due to more frequent involvement of the left middle cerebral artery in ischemic stroke in general.[8] However, we were not able to assess this possibility directly in our sample. Also, the cause of this sex difference is not clear. However, when observed, the difference in the side of involvement is important because the weakness of the dominant side (usually the right side) leads to more severe disability.

Our data showed that men and women both benefited from stroke rehabilitation as 85.67% of all patients (88.8% males and 80.4% females) achieved a good functional recovery (mRS<2). This finding is consistent with the previously published studies (85.7%, 88.5% overall good outcomes).[10,15]

The present study showed that the patients suffering from a stroke who were males were 1.10 times more likely to achieve a good health outcome after stroke rehabilitation in three months compared to female patients. Different factors, like genetic, sex hormones, lifestyle, clotting status, social relationship might separately or collectively help to describe gender differences in stroke.[16] A previous study explained that post-stroke depression [17] or post-stroke memory decline in the brain hemispheres was responsible for the poor outcome from a stroke.[18] It has been found that more women suffered depression after stroke which affected recovery and quality of life.[19]

A previous study also showed that women experienced worse outcomes after stroke than men. [20] However, in another study, males and females recovered equally well after rehabilitation. Many hypotheses have been formulated to explain the findings but all of them were insufficient.[21,22] Condonnier et al. have reported sex differences in access to rehabilitation services and variation in stroke care across different countries.[21]

Our findings may not be generalized to all patients with stroke but are representative of moderate- to severe stroke patients who undergo physiotherapy and acupuncture rehabilitation. Some limitations need to be mentioned. First, our study was limited to a single center in the western hilly region of Nepal. Data of patients who had not come for follow-up and had not responded in the telephone interview at three months could not be obtained. Second, the register-based study did not allow the collection of many important clinical determinants of functional outcomes. Demographics, such as education, living conditions (alone or with others), and marital status, could not be determined from the available clinical records. We were also not able to consider important clinical outcomes such as quality of life and depression. These factors are known to influence the worse prognosis in women which is often reported in the available literature.[23] Future studies are needed to assess the responsiveness of women and men to physical, cognitive, and social interventions during the post-stroke period. Both subjective (i.e. quality of life) and objective (i.e. cognitive functioning, depression, disability) outcome measures will be useful for the purpose.

CONCLUSION:

We observed that right-sided weakness was slightly more common than left-sided weakness in male patients whereas the reverse was true for females. We did not find any significant association between the side of weakness and outcome. However, male patients were slightly more likely to achieve good outcome compared to female patients. We hope that this knowledge is helpful to optimize the care of female patients and minimize the unequal burden of stroke in males and females. Further studies are required

to determine the factors responsible for the observed sex differences.

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