

Spectrum of Medical Complications During Stroke Rehabilitation and its Associated Risk Factors

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ABSTRACT:

Background: Incidence of stroke is persistently increasing followed by effective medical treatment resulting in high number of stroke survivors. Post stroke recovery is critical necessitating sufficient knowledge, effective prevention and control of chronic diseases, pre-existing complications, and potential risk factors. **Objective:** This study aimed to identify and evaluate potential risks and prognostic factors that can negatively influence post stroke rehabilitation in order to prevent, readily diagnose, and promptly manage the most common manifestations of stroke. **Study Design:** Cross-sectional observational study conducted at Stroke Rehabilitation Center, Lahore, Pakistan with the sample size of 120 patients, selected by using convenient sampling. **Results:** One hundred and twenty stroke survivors admitted in neurorehabilitation center (Age Mean±SD 56.9±12.2) were classified into 4 groups based on Modified Rankin scale: Mild (17.5%), Moderate (26.6%), Moderate to severe (39.1%), and severe impairment (16.6%). The major modifiable post stroke complications included depression (91%) and anxiety (84%). Acute infections (RTI n=69, 58%, UTI n=78, 65%) and poorly managed chronic disorders such as DM (n=59, 49.1%, 95% CI 0.5-2.5), HTN (n=34, 28%, 95% CI 1.7-2.5), and Kidney failure (n=12, 10%, 95% CI 0.4-3.5) were strongly associated with poor prognosis. **Conclusion:** Incidence of stroke was found to be more common in adults (Age: Range=44-69 years, Mean=56.9) with no gender predominance. Most common post stroke complications were depression and anxiety, significantly influencing the recovery process. The severity of the post stroke neurological deficit was positively associated with the frequency of complications and poor neurorehabilitation. Knowledge of post stroke recovery process and effects of various factors on it is essential for the implication of effective clinical and rehabilitation interventions to minimize morbidity and subsequent post stroke disability.

Keywords: brain injury, stroke recovery, neurorehabilitation, disability, stroke management

INTRODUCTION:

In western world, stroke is the fifth most common cause of death and the leading cause of long-term functional disability. [1, 2] Of the estimated 800,000 strokes that are recorded in the United States per annum, majority of the patients end up with mild to moderate permanent disability (Modified Rankin Scale 2-5). [2] Based on population, Pakistan is ranked fifth in the world with 225 million people (median age = 22.5 years). [3] The estimated annual cases of stroke in Pakistan are 250 per 100,000 with the mortality rate of 11-30% of stroke related deaths resulting in 91-70% or 175-227 per 100,000 stroke survivors per year. [4] In Pakistan, stroke is common in adults one decade younger than the same in western countries (mean age \pm SD = 42 \pm 12.6). [4, 5] With the advancement in acute medicine and active stroke management, the mortality rate has remarkably decreased over the last decade. But the overall prevalence of stroke has increased resulting in an increased number of stroke survivors in need of effective neurological rehabilitation to minimize the related morbidity. Functional/neurological deficits after stroke are associated with a considerable financial burden on the patient, family, and society resulting in psychological manifestations such as depression, anxiety, and agitation along with many other complications. Neurological disorders and motor disability are the common manifestations of stroke in survivors. [6] The trajectory of brain recovery after stroke is unpredictable as it depends on several modifiable and non-modifiable risk factors including genetic, sociodemographic, therapeutic, psychoneurotic, and pathophysiologic. Prevention, timely diagnosis, and prompt management of these complications play an important role in the effective neurological rehabilitation of stroke patients. However, the knowledge of these prognostic factors is limited in literature, especially in the developing countries with limited resources [7, 8] It is difficult to assess the frequency of medical complications in stroke patients as it needs examination and monitoring of the patients at different fronts. Also, it greatly depends on the locally acceptable criteria of defining the pathology and its associated risk factors, and methods of investigation. According to multiple studies, the most common post stroke complications are documented as follows: falls, electrolyte imbalance, hypertension, infections, venous thrombosis, and diabetes. Other influential factors include advanced age, post stroke NIHSS score, and GCS score. [5-9] Several regenerative and restorative processes follow the stroke related neurological deficit. Within the first 30 days of stroke, irrespective of the severity, the most dramatic recovery occurs. Then the process of gradual recovery

continues greatly depending on the additional factors. [10-12] The location and extent of neurological damage is a major determinant of the severity of post stroke disabilities and time required to maximally recover from it. This recovery is a chronic process with unpredictable results, lasting for an undetermined period. Successful and timely introduction of thrombolytic therapy can remarkably improve the prognosis but in developing countries like Pakistan, the supply of thrombolytic agents is scarce. Additionally, inadequate stroke rehabilitation facilities, limited neurologists (1 for 100,000 patients), and shortage of resources result in a poor prognosis of stroke survivors. [13, 14] Post stroke neuronal recovery is a well-studied topic, but still the possible determinants affecting stroke related morbidity are unclear. This study aims to examine and analyze the frequency, types, and nature of different clinical conditions and factors that can influence post-stroke brain recovery. Better knowledge of these influential factors can help in improving stroke rehabilitation and limiting the associated co-morbidities.

Inclusion criteria:

1. Patients of age greater than or equal to 18 years
2. Patients with history of stroke within the past 3 months
3. Patients with mild to severe post stroke disabilities
4. Patients who gave consent to get enrolled in this study

Exclusion criteria:

1. Patients with incomplete previous record
2. Patients younger than 18 years of age
3. Patients who did not give consent to get enrolled in this study

MATERIAL AND METHODS:

In this cross-sectional study, total 120 admitted patients were enrolled according to inclusion and exclusion criteria at stroke rehabilitation center, Lahore, Pakistan. The purpose of those admissions was initial comprehensive acute inpatient stroke rehabilitation. Stroke is defined as an acute, focal or global neurological deficit via cerebrovascular accident, lasting for more than 24 hours. Patients were diagnosed for stroke on the basis of clinical history, examination, and radiographical evidence. On admission, biodata of every patient was recorded including age, gender, ethnicity, marital status etc. (the significant information is explained in the results). The depth of the stroke lesion is defined as cortical and subcortical. The subcortical strokes also included the brain stem strokes. The type of stroke is subdivided into ischemic and hemorrhagic

stroke. The location of the lesion is categorized as right hemisphere, left hemisphere, and bilateral. The duration between the onset of stroke and rehabilitation was more than 3 months for all patients. On clinical examination, the severity of neurological disability of each patient was assessed by using the National Institutes of Health Stroke Scale (NIHSS). It is a well-known, widely accepted tool for the neurological deficit assessment on the basis of 15 brain functions that usually get affected by stroke. This classification consists of 4 categories according to the degree of neurological impairment: Mild (0-5), Moderate (6-10), Moderate to severe (11-15), and Severe (≥ 16). Based on acute emergency admission at the time of stroke and detailed history, chronic or pre-existing medical conditions were recorded for each patient. This included the medical complications that were present before the onset of stroke and during the poststroke hospital stay. The common medical conditions with significant impact are mentioned in the results (which were present in $>5\%$ of the selected patients). The values of body temperature, systolic and diastolic blood pressure, physical examination findings, and the laboratory values of 7 different hematological tests i.e., hemoglobin, creatinine, serum albumin, serum sodium, serum potassium, bicarbonate, and total leukocyte count (TLC) were carefully recorded and analyzed by using statistical analysis tools. During the hospital stay and admission at the rehabilitation facility, the comorbidities were verified and monitored and their effect on the onset of stroke and rehabilitation after stroke was analyzed. Patients were having total of 85 complications before and after the stroke, but only significant figures were included in this study. These complications were mainly related as cardiovascular, pulmonary, hematological, psychological, oncological, endocrine, dermatological, musculoskeletal, gastrointestinal, genitourinary, and trauma related. The disorder itself or the factors related to it and influencing the stroke outcome, were recorded as a single dichotomous variable. For example,

hypertension and frequent change in antihypertensive regimen or noncompliance to the medical treatment, all were included under the heading of comorbidity, hypertension. Each complication was assessed following the clinical criteria specified for it.

Data Analysis:

Medical conditions and hematological abnormalities were analyzed in terms of frequency and percentage. Mean and standard deviation were mentioned where applicable. The p-value of more than 0.05 was considered significant. The data was analyzed with SPSS v.20 for windows.

RESULTS:

Among 120 stroke patients, most of the patients were of age less than 70 years with the mean age of 56.9 years and standard deviation of 12.2 years. The results showed slight male predominance (M=63, 52.5%, F=57, 47.5%) with male to female ratio M:F = 1.10:1. This minimal gender bias was found coincidental rather than significant with a p-value of 0.92. The type of the stroke in selected patients was mainly ischemia (n=86, SD=71.6, p-value <0.03) where the rest of the cases were categorized as hemorrhagic (n=34, SD=29.4, p-value 0.09). The mean duration of onset of stroke and admission to the rehabilitation facility was 48.2 ± 11.3 days (less than 3 months duration). Based on the depth of stroke, most of the patients had subcortical stroke (n=61, 50.9%, p-value 0.03). The subcortical stroke also included brainstem stroke with marked fluctuations in blood pressure and GCS level. The incidence of cortical stroke was almost similar to the subcortical with the difference of 2 cases, so it can be assumed that the risk of developing either of those strokes would be the same. Depending on the location of the stroke, the lesions were found to be more prevalent in the left hemisphere (n=47, 39.1%). All the demographic data and stroke features are tabulated in Table 1.

Age	Mean		SD (\pm)
	56.9		12.2
Gender	Frequency (n)	Percentage %	p-value
	Male	63	52.5
Female	57	47.5	0.43
Type of Stroke			
Ischemic	86	71.6	<0.03
Hemorrhagic	34	29.4	0.09
Depth of Stroke			
Cortical stroke	59	49.1	0.92
Subclinical stroke	61	50.9	0.03
Side of stroke			

Right hemisphere	42	35	0.01
Left hemisphere	47	39.1	0.43
Bilateral hemisphere	11	9.1	1.92

Table 1. Demographic data and characteristics of stroke in selected patients

A number of pre-existing comorbidities were noted on the basis of clinical history and examination of each patient. The previous medical record was also analyzed to verify the information and to assess the severity of the disease. Top on the list, the comorbidities that significantly influenced the stroke (onset and prognosis) were Hypertension n=34, 28% (p-value <0.025), History

of previous stroke n=38, 32% (p-value <0.012), Diabetes Mellitus n=28, 23% (p-value <0.037), Kidney failure n=12, 10% (p-value < 0.001), malignancy n=10, 8% (p-value 0.042), and clinical depression n=30, 25% (p-value <0.023). P-value less than 0.05 was considered significant. Table 2.

Pre-existing risk factors	Frequency (n)	Percentage %	p-value
Hypertension	34	28%	<0.025
Pneumonia	69	58%	
Previous stroke	38	32%	<0.012
Cardiac arrhythmia	15	13%	
Feeding tube	41	34%	
Foley catheter	32	27%	
Diabetes mellitus	28	23%	<0.037
Coronary artery disease	43	36%	
Osteoarthritis	38	32%	
Substance abuse	16	13%	
Kidney failure	12	10%	<0.001
Pressure ulcer	58	48%	
Hydrocephalus/ventriculoperitoneal shunt	36	30%	
Malignancy	10	8%	<0.042
Peptic ulcer disease	41	34%	
Clinical depression	30	25%	<0.023
Seizure disorder	52	43%	
Tracheostomy	28	23%	
Benign prostatic hypertrophy	34	28%	
Peripheral vascular disease	35	29%	
Hypothyroidism	43	36%	
Valvular heart disease	29	24%	

Table 2. Frequency of pre-existing clinical condition and comorbidities before the onset of stroke and at the time of admission to the rehabilitation center

About 85% (102/120 patients) were having single or multiple abnormalities in hematological reports. The blood analysis of the patients was performed to check for hypoalbuminemia 48%, leukocytosis 36%,

Hemoglobinemia 34%, bicarbonate levels 43% (either high or low), hyponatremia 36%, hypokalemia 32%, and elevated urea/creatinine levels 28%. Table 3.

Hematological features	Frequency (n)	Percentage (%)
Hypoalbuminemia	49	48%
Leukocytosis	37	36%
Hemoglobinemia	35	34%
Abnormal bicarbonate levels	44	43%
Hyponatremia	37	36%
Hypokalemia	33	32%
Elevated urea & creatinine levels	29	28%

Table 3. Hematological features of the patients with abnormal lab reports (N=102)

Analysis of multiple factors that play a significant role in the prognosis of stroke is summarized in Table 4. Five of the total 13 factors were found strongly related to the outcome of stroke rehabilitation, including 4 categories of NIHSS score (mean±SD = 30±4.8, 95% confidence

interval: lower value= 1.6, upper value= 2.3, and p-value <0.01), other factors include history of uncontrolled hypertension 28%, renal failure 10%, Hospital stay >7 days 74%, and cardiac arrhythmias 38% as described in table 4.

Prognostic Factors	Frequency (n)	Percentage (%)	95% Confidence Interval (CI)	p-value
Mild NIHSS (0-5)	21	18%	1.6-2.3	<0.01
Moderate NIHSS (6-10)	32	27%		
Moderate to severe NIHSS (11-15)	47	39%		
Severe NIHSS (16-27)	20	17%		
Feeding tubes	41	34%	2.1-2.8	
Foley's catheter	32	27%	0.5-3.1	
Tracheotomy	28	23%	0.4-3.6	
Pressure ulcer	58	48%	1.7-2.5	
Hypoalbuminemia	32	27%	0.3-2.9	
Abnormal electrolytes	74	62%	2.1-3.5	
History of uncontrolled hypertension	34	28%	1.7-2.5	<0.001
Renal failure	12	10%	0.4-3.5	<0.01
Normal hemoglobin	52	43%	0.3-2.6	
Duration of hospital stay (>7days)	89	74%	1.4-3.2	0.002
Cardiac arrhythmia	46	38%	1.7-2.4	<0.005
Chest infections	51	43%	1.6-3.8	

Table 4. Complications/factors significantly influencing the stroke rehabilitation requiring acute medical care or transfer to the tertiary care facility for better management.

Thirteen most common medical complications (occurred in >5 patients) were analyzed and are described in table 5 in detail. The frequency of these complications was stratified in 4 subgroups based on NIHSS score of total 120 patients at the time of recovery. A positive correlation was noted between the occurrence of these complications and severity of the neurological impairment. Incidence of the complications in all

subgroups are as follows (in descending order): Depression n=91, Anemia n=85, Anxiety/agitation n=84, falls n=79, urinary tract infection n=78, nutritional deficiency n=76, electrolyte imbalance n=74, joint/soft tissue pain n=68, hyperglycemia n=59, acute urinary retention n=56, acute respiratory tract infection n=30, clostridium difficile enteritis n=17, and cellulitis n=14. Table 5.

Medical Complications	Mild impairment NIHSS=0.5 (n=21)	Moderate impairmet NIHSS=6-10 (n=32)	Moderate to severe impairment NIHSS=11-15 (n=47)	Severe Impairment NIHSS=10-27 (n=20)	Mean	Standard Deviation	Confidence Interval (CI)
	Frq (%)	Frq (%)	Frq (%)	Frq (%)			
Nutritional deficiency	4 (3.3%)	18 (15%)	36 (30%)	18 (15%)	62.5	0.2	1.8-2.1
Anemia	11 (9.2%)	23 (19.2%)	32 (26.7%)	19 (15.8%)	70.75	1.4	0.4-1.5
Acute urinary retention	9 (7.5%)	17 (14.2%)	18 (15%)	12 (10%)	47	2.7	2.6-3.2
Clostridium defficile enteritis	2 (1.7%)	4 (3.3%)	7 (5.8%)	4 (3.3%)	14	0.8	1.1-2.5
Anxiety/agitation	14 (11.7%)	21 (17.5%)	31 (25.8)	18 (15%)	70.5	3.5	0.4-1.6
Electrolyte imbalance	12 (10%)	19 (15.8%)	27 (22.5%)	16 (13.3%)	62	2.7	0.9-1.4
Hyperglycemia	6 (5%)	8 (6.7%)	32 (26.7%)	13 (10.8%)	49.25	3.8	0.5-2.5
Cellulitis	1 (0.8%)	3 (2.5%)	6 (5%)	4 (3.3%)	11	2.1	1.3-3.5
Acute respiratory failure	8 (6.7%)	6 (5.0%)	8 (6.7%)	8 (6.7%)	24	2.6	1.8-2.3
Joint/soft tissue pain	13 (10.8%)	26 (21.7%)	17 (14.2%)	12 (10%)	59	3.2	2.3-4.7
Falls	18 (15%)	24 (20%)	27 (22.5%)	10 (8.3%)	71.5	4.3	1.7-2.4
Urinary tract infections	10 (8.3%)	18 (15%)	34 (28.3%)	16 (13.3%)	66	2.8	0.09-1.7
Depression	17 (14.2%)	24 (20%)	33 (27.5%)	17 (14.2%)	78.25	4.4	0.07-1.4

Table 5. Most common medical complications that develop or exacerbate during stroke rehabilitation, based on NIHSS score.

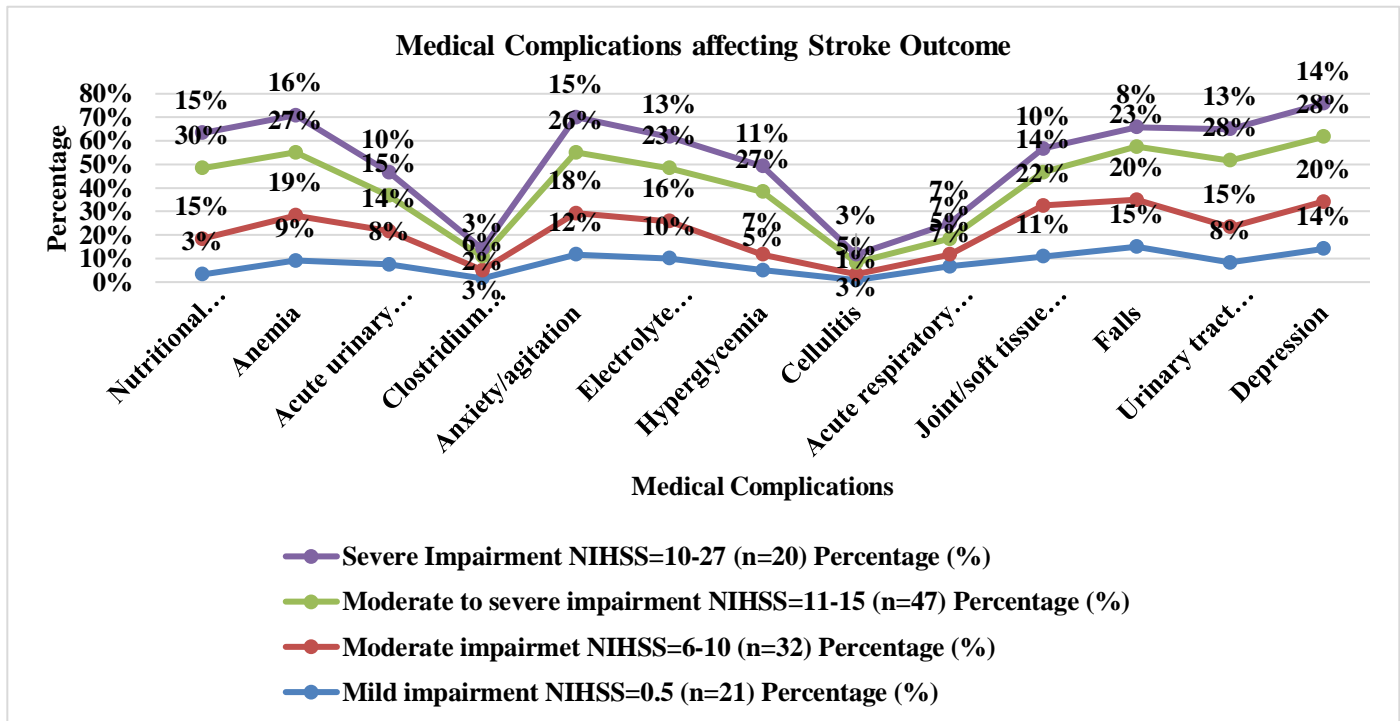


Fig 1. Medical complications strongly associated with poor prognosis in stroke patients

DISCUSSION:

Multiple studies have identified old age as a significant prognostic factor in developing countries. However, in our study, most of the stroke patients were adults with the mean age of 56.9 years. None of the selected patients was older than 70 years. The results show that in our setup, stroke is more common among young people. There is a need for a detailed study on a larger scale to verify this finding. [15, 16] Post stroke depression (PSD) is the most prevalent neuropsychiatric manifestation of stroke affecting more than one third of the stroke survivors. Extensive literature review reveals that the incidence of PSD is considerably higher in females than males. In multiple studies, it is hypothesized that females are more prone to develop post stroke complications and slow or incomplete recovery. However, in this study, no significant gender predominance was noted. Nonetheless, the females are found to suffer from psychological manifestations more than the males, including depression, anxiety, agitation, and suicidal thoughts. These factors can directly affect the stroke rehabilitation by affecting the will power to get better and indirectly by decreased appetite (malnutrition, electrolyte imbalance, anemia etc.), lack of interest in physical activities, and poor hypertension/ diabetes control. [16-19] There are a few explanations to it including amine hypothesis which states that the stroke results in decreased bioavailability of bioamines such as dopamine, serotonin, and norepinephrine. Chronic disease, tragic events before stroke, lack of social support/family support, female gender, moderate to severe post stroke disability, and history of chronic depression can make the patient more susceptible to develop PSD. The severity of symptoms of PSD is higher in first 3 months of stroke and gradually decreases with recovery. [20] However, reportedly, PSD can greatly influence post stroke recovery and jeopardize mental health and quality of life. So the relationship between PSD and post stroke recovery can be explained as a vicious cycle. PSD slows down the recovery, adding more to the depression and the cycle goes on. Post stroke antidepressant prescription remarkably improves cognitive as well as motor recovery. It can also extend the window of neuroplasticity hence the neurorehabilitation. In our study, most common post stroke complications include depression and anxiety/agitation affecting 91 and 84 of the total 120 patients, respectively. [19-22] Patients with comorbidities such as hypertension, diabetes, renal failure, especially if it is uncontrolled or severe, are associated with poor post stroke recovery and prognosis. Likewise, severity of post stroke disability (measured by Modified Rankin scale MRs) is also found negatively correlated

with the post stroke neurorehabilitation. Other medical complications that are explained in the results are associated with the slow recovery by causing hematological abnormalities, prolonged hospital stay, added financial burden, sepsis, and possible drug-drug interactions. [23, 24] Acute infections are also negatively associated with stroke recovery. In our study, the most common infections were pneumonia (n=30) and urinary tract infections (n=78). As they are usually hospital acquired so they can be considered as modifiable risk factors. Due to neurological deficit resulting in poor gag and cough reflex, recurrent respiratory tract infections (RTIs) can occur. Effective chest physiotherapy, good posturing, nebulization, and feeding tube can prevent RTIs. Prolonged hospital stays, indwelling catheters (intravenous, foley), mechanical ventilation, or mask ventilation can subject a patient to develop RTI or UTI. If left untreated or poorly managed, can lead to immobilization, generalized fatigue, low mood, septicemia, affecting the blood chemistry, increased levels of inflammatory markers in the bloodstream and hence, delayed neuronal recovery. Pulmonary infections are also found to be associated with other complications such as DVT. [25] The strength of this study is that we comprehensively analyzed the prognostic or influential factors in post stroke hospitalized patients. These results can enable physicians and neurologists to effectively manage and prevent comorbidities to improve patient's outcomes and functional rehabilitation by paying special attention to the mentioned influential factors. The limitation of this study is that it only described the prognostic factors in patients admitted at the rehabilitation center. Cross sectional study design was not able to analyze the final outcomes in detail. Rural and non-hospitalized patients were not analyzed in this study.

CONCLUSION:

The high incidence of stroke and increased number of stroke survivors demand availability of effective and accessible neurorehabilitation centers for everyone. A better understanding of the pattern, pathophysiology, and factors influencing the post stroke recovery can remarkably improve the preexisting therapeutic and rehabilitation therapies for better outcome. Knowledge and effective management of non-pathological, modifiable prognostic factors can significantly boost the recovery process. The combination of determinants of stroke recovery should be individualized and every patient should receive a personalized recovery plan to ameliorate their co-morbidities for better prognosis. In Pakistan, limited study on the modifiable post stroke prognostic factors is done. A comprehensive,

multicentric study including large number of urban as well as rural population should be conducted for improved post stroke clinical/rehabilitation interventions and prevention strategies.

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