

Research Article

Assessment of Stroke Patients and Evaluation of the Status of Hypertension on Them

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Abstract

Background: Stroke is one of the prominent causes of mortality and morbidity in the present context of the current world. Experts have identified several major risk factors for stroke, including high blood pressure, smoking, obesity, diabetes, and preexisting heart disease, among others.

Methods: This is a descriptive type of cross-sectional study. Simple random sampling techniques were used. The researchers themselves collected data using a face-to-face questionnaire. Descriptive statistics was used to analyze the collected data. Stroke patients were assessed through GCS and MRC sum scores. SPSS version 21.0 was used as the statistical tool for this study.

Results: The majority of the stroke patients were diagnosed with a case of hypertension, 100 cases (76.9%). Severity was assessed through the GCS score and MRC sum score. It was found that the score is 2 in the case of the distal portion of the lower limbs and 3 in the case of the proximal and distal portion of the upper limb as well as the proximal portion of the lower limb. So, severity in the case of stroke is more obvious in the distal portion of lower limbs than in the other portions. Ischemic as well as hemorrhagic cases were identified by MRI and CT scans.

Conclusions: This study was done in two hospitals in Dhaka city with 130 respondents. The age group of people was 40-60 years. The objective of the study is to identify the status and effect of hypertension on people suffering from stroke.

Keywords: Stroke, e.g., Ischemic, and Hemorrhagic; Hypertension; GCS score; MRC sum score

Abbreviations

GCS: Glasgow Coma Scale; MRC: Medical Research Council.

Literature Review

Stroke is considered one of the most important factors of morbidity and mortality in the present world. The number of cases and disabilities related to stroke is increasing at an alarming rate. Current statistics on stroke victims and related disabilities reveal that many people are suffering from its effects [1].

As appropriate, experts have given feedback about the liable causes of stroke, e.g., high blood pressure, smoking, obesity, diabetes, pre-existing heart diseases, etc. The impact of stroke is now obvious in the world. An estimated four and a half million deaths occur a year from stroke and about nine million stroke survivors are present [2].

Almost one in four men and nearly one in five women aged 45 years can expect to have a stroke if they live to their eighty-fifth year [3].

There is also an estimation that the present stroke incidence rate is around 2-2.5/thousand population [4].

The rate of recurrence is about 15-40% within 5 years. Estimates suggest that by 2023, the number of patients experiencing a first-time stroke could increase by thirty percent compared to 1983 [5].

The prevalence rate is also estimated to increase to 5/thousand population [6].

Moreover, recently one of the reports published by WHO shows that Bangladesh is now holding the eighty-fourth (84th) position in cases of death as well as cases of mortality due to stroke. The reports also revealed that the age of nearly 82.5 percent of stroke survivors in Bangladesh is between 41-60 years [7].

However, the severity or disabilities occurring due to stroke have not been mentioned in many previous published articles [8].

There is an estimation that of the total 987 patients, the influence of hypertension (67%) was more than other indicators in the occurrence of stroke. It indicates that hypertension is a very important influencing factor in that case [9].

Focusing and targeting some of the Asian countries based on the relevant topics, showed that, stroke, as well as stroke-related disabilities, are now becoming a very important reason for occurring death due to vascular anomalies as well as vascular abnormalities and long-term disabilities. mainly by focusing on and targeting some Asian countries based on the relevant topics [10].

Stroke as well as stroke-related disabilities are now becoming a very important reason of occurring death due to vascular anomalies as well as vascular abnormalities and long-term disabilities [11].

During mid-1989 in Japan, it was seen that there was a relationship between the risk factors of occurring stroke and stroke or stroke-related disabilities or mortality. The studying participants were middle-aged persons (both male & female) Their ages were between 45-60 years. That particular study was performed with a ten-year follow-up. At the beginning of the study, all of the study participants were disease-free. After 10 years of follow-up, it is seen that, of the total participants, about 4.8% of study participants developed incidental stroke and of them, about 60.1% developed infarct in mainly cerebral cortex or ischemic stroke. When there was assessing the risk factors behind the occurrence of this, it was seen that hypertension is responsible for the occurrence of about 32.79% of ischemic strokes while other risk factors were responsible for having of about 17.21% of stroke or stroke-related disorders or disabilities [12].

There was an incident to identify the most important risk factors behind the occurrence of stroke as well as stroke-related disabilities. The study revealed that hypertension is one of the most important risk factors behind this grave situation. Prevalence rate was about 34.5% [13].

It is revealed that hypertension is one of the major leading risk factors liable for the occurrence of ischemic stroke in the case of both males and females [14].

There is a strong correlation between hypertension and stroke. From this study, it could be observed that, of the total study participants about two-thirds of the participants were suffering from hypertension, and among the participants suffering from hypertension, almost 46% had a familial history of hypertension. This study revealed a strong association between hypertension and stroke [15].

It can be observed that about 85% of stroke survivor participants developed hypertension before stroke. This study also identified urbanization as an important potential risk factor responsible for this condition as more than 68% of the stroke survivors were urban dwellers [16].

It also can be observed that among the stroke participants, patients suffering from ischemic stroke were the highest (about 72%). While assessing the risk factors, it showed that hypertension is one of the most important potential risk factors responsible for this condition. About 57.3% of the stroke patients gave a history of having hypertension before stroke [17].

It was revealed that there is a strong association between hypertension and stroke [18].

It was also revealed that there is a strong association between hypertension and stroke. Hypertension is more important than all other potential risk factors in this field [19].

It was also revealed that the modifiable risk factor or the most important risk factor was systemic hypertension for the occurrence of stroke [20].

It was revealed about the status of hypertension related to stroke, shows that hypertension is one of the major predominant factors in the occurrence of stroke in most countries of Asia [21].

It was also regarded considering hypertension as a risk factor and as an important modifiable risk factor of stroke [22].

It was also regarded that rising blood pressure may be a great danger in case of occurring of acute stage ischemic stroke [23].

It was also revealed that the major risk factors liable for the occurrence of hemorrhagic stroke states that extreme rising of blood pressure in any acute position may cause rising of the risk of hemorrhagic stroke [24].

It is also revealed that strokes as well as cerebrovascular accidents possess the third-ranking position in case of mortality and morbidity in Bangladesh. This study reveals that hypertension played a major role in cases of ischemic or hemorrhagic stroke [25].

It can be estimated that stroke can cause a long-term disability in the public health concern. Therefore, focusing on prevention is important. One of the most prominent aims of reducing or controlling or preventing the prevalence of stroke and stroke-related disabilities is to treat modifiable risk factors, such as arterial hypertension, which is a leading modifiable contributor to stroke. So, adequately reducing Blood Pressure (BP) among hypertensive patients is very necessary to prevent the occurrence of stroke or stroke-related disabilities [26].

It can also be estimated that hypertension or high blood pressure can lead to 75% or more in case of occurrence of acute stroke. There is also evidence of BP modulation of acute stroke [27].

It is also evident that high blood pressure/hypertension is present in 80% case of patients experiencing acute stroke and epidemiologically associated with poor outcomes It can be also said that the patients experiencing cerebral hemorrhage due to acute stroke have a long history of suffering from high blood pressure [28].

On the other hand, controlling high blood pressure is essential for controlling stroke [29].

There is a variation in blood pressure during the acute phase after the onset of any stroke. It is observed that rapidly lowering blood pressure causes escape from the dangerous harm of stroke [30].

It is also observed that hypertension is one of the most prevalent factors in the stroke population and is one of the most important modifiable risk factors for the occurrence of stroke. On the other hand, hypertensive disorders promote stroke [31].

It is evident that hypertension and its consequences are associated with over 50% of ischemic and 70% of hemorrhagic strokes but despite good control of blood pressure (BP), there remains a 10% risk of recurrent cerebrovascular events [32].

The cerebrovascular pulsatility differs between young and middle-aged adults despite similar changes in cerebral pulsatile damping during blood pressure-dependent, but not blood pressure-independent increases in large artery stiffness [33].

Management of high blood pressure is closely associated with reducing of acute phase of stroke [34].

It is revealed that hypertension is regarded as a threat for long-term stroke but procedures for management of hypertension in acute stroke are less certain [35].

It is also regarded as arterial hypertension as one of the major risk factors for the occurrence of acute stroke or stroke-related disabilities [36].

It can be said that most strokes occur among persons with resistant hypertension; approximately half of strokes could be prevented by blood pressure control [37].

From close observation it can be said that raised blood pressure is closely associated with the acute phase of stroke. High blood pressure may occur due to many reasons such as consumption of high salt or excessive sodium intake, alcoholism, smoking, obesity, diabetes mellitus, or renal hypertension (due to high renin/aldosterone) [38].

It can be said that the prevalence of stroke due to cerebral small vessel disease (CSVD) or due to any vascular anomaly or abnormality is comparatively much higher in those persons having developed high blood pressure which can be confirmed by performing a brain MRI [39].

Cerebral small vessel disease (CSVD) is frequent in patients with cardiovascular risk factors including arterial hypertension, and it is associated with vascular damage in other organs and the risk of stroke, cognitive impairment, and dementia which is more potent in the patients having developed uncontrolled high blood pressure [40].

Data and Methods

N.B: all methods were performed by the relevant guidelines and regulations of the affiliated institutions of authors while performing the study.

Aim of the Study

To identify the status of hypertension in people suffering from stroke or stroke-related disabilities and to assess the severity of stroke through some neurological measuring scales such as the Glasgow Coma Scale (GCS) or MRC (Medical Research Council) sum score.

Design of the Study

It is a type of cross-sectional study following a quantitative method approach. The cross-sectional method and quantitative method were chosen by the researchers because the researchers wanted to explore the number of participants at that time while conducting the study.

Two neurological tools were used to assess the severity of hypertension (High blood pressure) in the stroke patients. These tools are- the Glasgow Coma Scale (GCS) or MRC (Medical Research Council) sum score.

The Glasgow coma scale (GCS) was used to assess the participants' level of consciousness. This scale mainly assesses the participants according to the three aspects of responsiveness-Eye-opening, Motor, and Verbal Response.

MRC (Medical Research Council) sum score was another neurological tool the researchers adopted. Researchers used this neurological tool to evaluate the severity of muscle weakness of the participants. This scale was adopted to evaluate the muscle weakness of both upper and lower limbs. This scale marks the severity of muscle weakness from 0 to 5. "0" means no visible muscle movement, "1" means flickering of movement, "2" means movement with gravity eliminated, "3" means movement against gravity, "4" means movement against resistance & "5" means normal muscle power.

The researchers used the above two neurological tools for two

different purposes. The GCS score was used to assess the participants' integral consciousness, and the MRC sum score was adopted to observe the participants' muscle weakness in the upper and lower limbs.

The researchers observed the consciousness level and muscular strength of the study participants to assess the severity of hypertension in stroke patients.

Setting of the Study

The study's time period was from 04 February 2022 to 23 May 2022.

Characteristics of Participants

All participants were adults in age (between 40-60 years). They were either ischemic or hemorrhagic stroke patients.

Study Locale

This study was done in the following institutions: a) National Institute of Neurosciences & Hospital (situated at Agargaon, Dhaka), and b) Bangabandhu Sheikh Mujib Medical University (BSMMU) at Shahabag, Dhaka.

Study sampling technique: Random sampling was adopted in this study.

Sample size calculation: Respondents (hypertensive stroke patient):

$$\text{Formula } n = \frac{z^2 p}{d^2}$$

Where:

n = desired sample size

z = standard normal deviation; usually set at 1.96, which corresponds to a 95% confidence level.

p = 50% = it is estimated as it is difficult to consider about exact idea from any study.

So, $p = 0.5$

$q = 1 - p$

d = degree of accuracy required, usually set at 0.05 of the expected sample size.

So, the calculation will be

$$n = \frac{z^2 pq}{d^2} = (1.96)^2 (.5)(1-.5) \div (0.05)^2 = 384.16 \approx 385$$

However, considering financial constraints and time limitations, researchers took 130 samples. As there were financial issues (no funder for the study and all the funding of the report was done by the researchers themselves) and time limitations, the researchers had to take 130 samples to conduct the study.

Development of Research Instrument

A questionnaire was prepared before the study was conducted. The questionnaire was pre-tested among some selected respondents and was used during face-to-face interviews. After continuous effort and careful revising and discussion, an up-to-date as well as final research instrument (or questionnaire) was prepared by the authors.

Data Collection

During data collection, a pre-tested questionnaire was used. The researchers were directly engaged in data collection, data management, and data analysis.

Data Analysis

The data was analyzed by using the statistical package for the social sciences (SPSS, version-21.0). Descriptive statistics was used for the interpretation of findings.

Data Presentation and Interpretation: Data were presented using a frequency table, graph, and chart. Collected and corrected data were entered into the computer for analysis and interpretation.

Data Quality Management: Initially, data were checked for completeness and correctness to exclude missing or inconsistent data. This process was done very carefully and all of the authors were involved in this process actively.

Corrected data were then entered into the computer to run the software to obtain the results of this study.

Results

This study was performed to assess as well as evaluate the effect and severity of hypertension among the participants (stroke patients). All Data were entered and analyzed by Statistical Packages for Social Science (SPSS) software version 21.0.

Table 1 shows that a major portion of stroke patients possess a GCS score of 14 (Frequency-54, percentage-41.5%). Others are as follows- score-6 (frequency-1, 0.8%), score-7 (frequency-6, 4.6%), score-8 (frequency-2, 1.5%), score-10 (frequency-1, 0.8%), score-11 (frequency-3, 2.3%), score-12 (frequency-18, 13.8%), score-13 (frequency-26, 20.0%), score-15 (frequency-19, 14.6%).

Table 2 shows that- the majority of the respondents possess an MRC score- of 3 (Frequency-70, 53.8%) in the case of the proximal portion of the upper limbs. Other scores are- MRC score- 1 (Frequency-2, 1.5%). MRC score-2 (Frequency-10, 7.7%) MRC score-4 (Frequency-48, 36.9%). In the case of the distal portion of the upper limbs, it shows that- the majority of the respondents possess an MRC score- 3 (Frequency-86, 66.2%). Other scores are as follows- MRC score- 1 (Frequency-3, 2.3%), MRC score- 2 (Frequency-23, 17.7%), MRC score- 4 (Frequency-18, 13.8%),

In the case of the proximal portion of the lower limbs, it shows that- the majority of the respondents possess an MRC score- 3 (Frequency-59, 45.4%), MRC score- 0 (Frequency-3, 2.3%), MRC

Table 1: Distribution of respondents by GCS (Glasgow coma scale) score.

GCS score	Frequency	Percent
6	1	0.8
7	6	4.6
8	2	1.5
10	1	0.8
11	3	2.3
12	18	13.8
13	26	20
14	54	41.5
15	19	14.6
Total	130	100

Table 2: Distribution of respondents by MRC sum score.

Portion of the limbs	MRC sum score	Frequency	Percentage
The proximal portion of the upper limbs	1	2	1.5
	2	10	7.7
	3	70	53.8
	4	48	36.9
The distal portion of the upper limbs	1	3	2.3
	2	23	17.7
	3	86	66.2
	4	18	13.8
The proximal portion of the lower limbs	0	3	2.3
	1	10	7.7
	2	54	41.5
	3	59	45.4
	4	4	3.1
The distal portion of the lower limbs	0	8	6.2
	1	16	12.3
	2	80	61.5
	3	26	20

score- 1 (Frequency-10, 7.7%), MRC score- 2 (Frequency-54, 41.5%), MRC score- 4 (Frequency-4, 3.1%). In the case of the distal portion of the lower limbs, it shows that- the majority of the respondents possess an MRC score of- 2 (Frequency-80, 61.5%), an MRC score of- 3 (Frequency-26, 20%), an MRC score of- 1 (Frequency-16, 12.3%), an MRC score of- 0 (Frequency-8, 6.2%),

Table 3 shows that there was a significant association between hypertension and stroke.

Table 4 shows the age groups of participants with their relative frequency.

Table 5 shows that of the total respondents, 116 (89.2%) were patients of ischemic stroke whereas subsequently, 14 (10.8%) were the patients of hemorrhagic patients.

Figure 1 shows that majority of the respondents were male (74.62%) and the rest were female (25.38%).

Figure 2 shows that, among the participants, 8.462% were primary literate, 14.62% were high school literate, 28.46% were highly educated, 23.08% were university graduates and about 25.38% were masters level educated. Figure 3 shows that most of the respondents obey Islam religion (83.08%). Hindu as well as Christian religions were subsequently 15.38% & 1.54% Figure 4 shows that, among the participants, about 20% were housewives, 0.769% were unemployed,

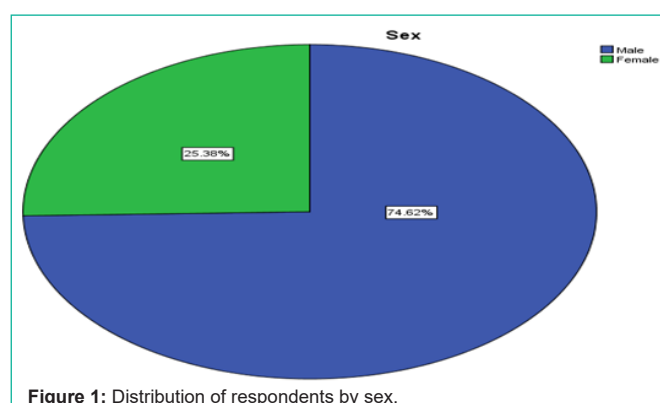


Figure 1: Distribution of respondents by sex.

Table 3: Association between Hypertension & Stroke.

Chi-Square Tests			
	Value	df	A symp. Sig. (2-sided)
Pearson Chi-Square	18.087	2	0
Likelihood Ratio	10.901	2	0.004
Linear-by-Linear Association	6.013	1	0.014
N of Valid Cases	130		

Table 4: Distribution of respondents by age.

Age groups	Frequency
40-50	57
51-60	73

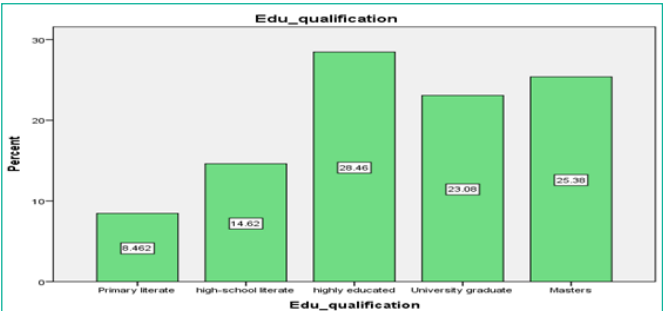


Figure 2: Distribution of respondents by education status.

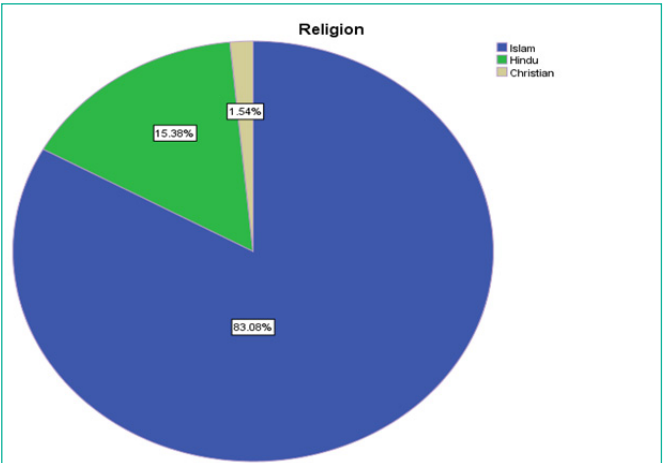


Figure 3: Distribution of respondents by religion.

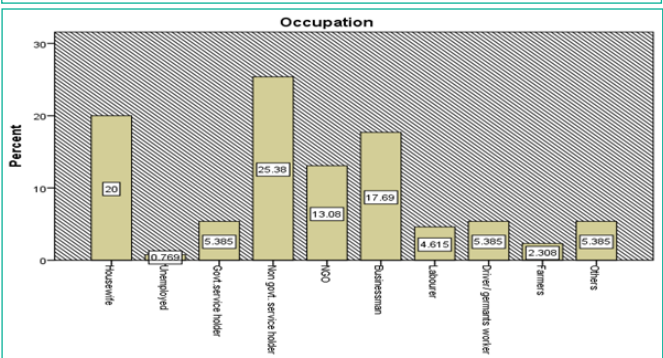


Figure 4: Distribution of respondents by working status/occupation.

5.385% were govt. service holder, 25.38% were non- govt. service holder, 13% were NGO workers, 17.69% were businessmen, 4.615% were laborers.5.385% were drivers/germants workers, 2.308% were farmers and the rest 5.385% were others.

Figure 5 shows that, among the respondents, 23.85% were unemployed and housewives (NA), 1.538% had 1000-5000tk income,

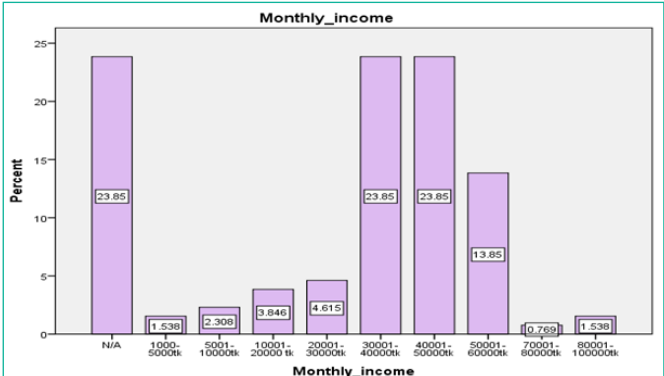


Figure 5: Distribution of respondents by income.

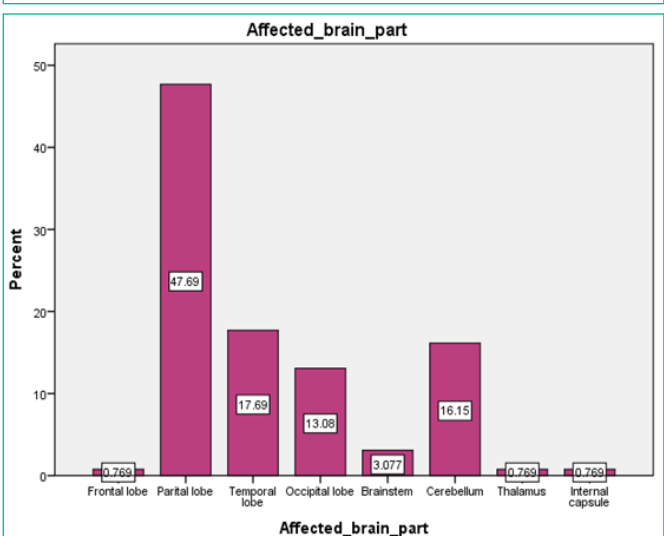


Figure 6: Distribution of stroke respondents according to the affected parts of the brain.

Table 5: Distribution of respondents by stroke types.

Stroke Types	Frequency	Percent
Ischemic	116	89.2
Hemorrhagic	14	10.8
Total	130	100

2.308% had 5000-10000tk income, 3.846% had 10001-20000 taka income, 4.615% had 20001-30000 taka income, 23.85% had 30001-40000tk and subsequently 40001-50000 taka income, 0.769% had 70001-80000 taka income and the rest 1.538% had 80001-100000 taka income.

Figure 6 shows that the most affected parts of the brain were the parietal lobe (47.69%). The percent of the rest parts were as follows- Frontal lobe- 0.769%, Temporal lobe- 17.69%, occipital lobe- 13.08%, Brainstem- 3.077%, Cerebellum- 16.15%, Thalamus & internal capsule- 0.769

Discussions

This study was conducted in two selected hospitals in Bangladesh by the researchers.

These hospitals are the National Institute of Neurosciences and Hospital, Dhaka, and Bangabandhu Sheikh Mujib Medical University. (BSMMU)

We measured the GCS score because this parameter shows how effectively any stroke patient can respond to the researcher's question

as well as guidance. The normal GCS score is- 15/15, but in almost all of the cases of stroke patients, this score has been found below 15. Especially, while assessing the GCS scores in the case of patients of hemorrhagic stroke, this score was found significantly lower (7/15 or 9/15 or 10/15, etc) than the scores found in the patients of ischemic stroke. This signifies the severity of the hemorrhagic stroke patients.

We also adopted the measurement of the Medical Research Council (MRC) sum score because this neurological parameter gives significant information about motor or muscle/limb weakness. Upper and lower limbs were divided into four quadrants by the researchers while assessing this score.

Before doing it, the researchers divided both the upper and lower limbs into two portions.

While performing this neurological process or approach, the researchers divided the upper and lower limbs (upper limb means "hand" and lower limb means "legs") into proximal and distal portions to conduct their work and get the outcome.

The researchers considered the arms of both hands as a proximal portion of the upper limbs and forearms with wrists of the both hands as distal portions of the upper limb. Similarly, they considered the thighs of both legs as the proximal portion of the lower limbs and knees and ankles with the foot as the distal portion of the lower limbs.

While performing the research, the researcher found some interesting events. Although all of the study participants were stroke participants, many of their GCS scores were well. A vast portion (Frequency-54, Percent- 41.5%) of the participants possessed a good GCS score (14/15). Their muscular strength was poor, and many of them were confined to the hospital bed but their consciousness level was very good along with their responsiveness (Eye response, Muscle and verbal response) to the questions and asking of the researchers. From this observation, the researchers got a preliminary idea that the GCS score may even remain good in case of strokes due to hypertensive causes.

However, the researchers found some notifiable findings while performing the MRC sum score of the participants. In the case of upper limbs, most of the patients possess (frequency-70, percentage-53.8%) an MRC score of 3 out of 5, on the other hand, a majority number of patients (frequency-86, percentage-66.2%) possess an MRC score of 3 out of 5 in case of distal portion of the upper limbs.

On the other hand, in the aspect of lower limbs, about 45.4% (frequency-59) was found to have an MRC score of 3 out of 5, and about 61.5% (frequency-80) was found to have an MRC score of 2 out of 5.

From this observation of the researchers, it was found that the motor function (muscular strength and activity) of the lower limbs (especially the distal portion of the lower limbs) was more affected than the upper limbs in case of stroke caused by high blood pressure. From the above observation, it was also noticed that a small number of participants (frequency-8, percentage-6.2%) possess an MRC score of 0 out of 5 in case of the distal portion of lower limbs whereas in the case of the proximal portion of the lower limbs, this number of participants are-3 (frequency-3, percentage-2.3%) The MRC sum

score 0 means they are unable to move this portion of the limb and from this observation, it is clear that the proximal portion of the lower limbs gets more affected than the distal portion of the lower limbs in stroke patients and this stroke is caused by the high blood pressure.

The primary aim of the researcher was to assess the consciousness level (eye-opening, muscle activity, and verbal response) and motor (muscle) function activity of stroke patients and the stroke caused by high blood pressure.

From this study, it is evident that the motor activity (especially the distal portion of the lower limb) of the stroke participants is more damaged than the consciousness level of the stroke patients caused by high blood pressure.

While performing the study, the researchers faced some potential limitations. There were some limitations during data collection for the study. Appropriate participants were difficult to find for the research. Time was not enough to cope with the real picture of the scenery and to adopt a full sample size. The authors also can not contain an estimated full sample size due to financial constraints as they did not find any suitable funders/ funding agencies while conducting the study and all costs of the research had to be carried and paid by themselves.

Conclusions

This descriptive type of cross-sectional study was done in two hospitals with 130 respondents to assess the severity of stroke and the effect of hypertension on them.

If there is consideration of the stroke types, it is said that the most prevalent stroke type is ischemic stroke. Of the 130 total respondents, 116 (89.2%) cases were found as ischemic stroke and the rest (14, 10.8%) were diagnosed as hemorrhagic stroke types. It is also obvious that the GCS score is less in the case of hemorrhagic stroke rather than in the case of ischemic stroke. So, it is obvious that hemorrhagic stroke is more severe than hemorrhagic stroke.

The severity of the stroke was assessed by GCS. It is seen that most of the respondents were found to have a GCS score of 14.

The severity of stroke could also be assessed by the MRC sum score. MRC score was done in 4 portions. These were – the MRC score in the proximal portion of the upper limb, the distal portion of the upper limb, the proximal portion of the lower limb, and the distal portion of the lower limb. Most found MRC sum score is 3 except in the distal portion of lower limbs (MRC sum score-2). MRC score 3 means- they can uplift their limbs against gravity but not against the resistance of the examiner's hand. On the other hand, MRC score-2 means there is only some flickering of contraction but there is no movement of the limbs at all. So, it is obvious that the severity of stroke is higher in the distal portion of the lower limb than in other portions.

So it is said that hypertension is one of the major risk factors in case of occurring stroke in comparison to other risk factors.

This point denotes the most affected part of the body due to the severity of the stroke. This will help the clinicians to identify the potential severe stroke patients and allow them to arrange the treatment properly and as appropriate based on the scores.

Declarations

Ethical Approval and Consent to Participate

Approval from the Ethical Review Board (ERB) of AIUB was taken.

Permission was taken from the National Institute of Neurosciences & Hospital, Agargaon, Dhaka, and also from Bangabandhu Sheikh Mujib Medical University, BSMMU.

Informed consent was taken from the respondents before enrolling in the study.

Confidentiality was maintained strictly.

During Data collection, the respondents were explained about the aim and objectives of the study.

Informed consent was taken from the respondent prior to data collection.

Respondent's dignity and respect were maintained and interviews were taken with strict privacy.

Availability of Data and Materials

During the study, the data were collected actively by the researchers from the respondents or study participants through the questionnaire method and by face-to-face interview.

The researchers used only their collected data while doing this work.

Funding

The researchers took the responsibility of funding while performing their research. The authors themselves carried out all the issues related to funding.

Author's Contribution

All authors contributed equally to perform the study and prepare the manuscript.

Dr. Sakib Tajwar conducted the study and prepared the manuscript.

Dr. Jahir Uddin Ahmed supervised everything and gave tremendous support and help in preparing the manuscript.

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