A Comparative Study On Quality of Life Between Thrombolysed and Non-Thrombolysed Ischemic Stroke Patients

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Abstract: Stroke is one of the leading causes of morbidity and mortality worldwide. Ischemic strokes are the most common variety of strokes caused by either thrombosis or embolism. In addition, they account for 50% – 85% of cerebrovascular accidents. Thrombolysis is used in the treatment of acute ischemic stroke. The current study examined the clinical profile and assessed risk factors, adverse events, and quality of life between thrombolytic and non-thrombotic ischemic stroke patients. A prospective observational study was conducted in a tertiary care Hospital with a sample size of 106 Ischemic stroke patients for four months. The patients were enrolled based on inclusion and exclusion criteria and were interviewed using a semi-structured questionnaire. Quality of life was assessed using Stroke specific quality of life scale (SSQOL). The results showed that the incidence of stroke is most common in the age group of 61-80 years, with a mean age of 59.9 years. Hypertension was the leading risk factor in 74.4% of cases. Speech Involvement (74.5%) was the most common presentation, followed by Hemiparesis, Altered sensorium. In our study, patients presenting to hospital >4.5hrs were higher, and the quality of life between thrombolysis and non-thrombolysis patients were nearly identical. However, there was applied statistically significant distinction in energy, mobility, self-care, vision, and work items of the SSQoL scale. We conclude that the two groups had no major variations within the primary outcome of QOL. Thus, the current study tends to expect that patients with non-thrombolytic therapy will have a worse quality of life due to the greater initial stroke severity. Therefore, medical care appears to be of more importance in achieving a higher quality of life in ischemic thrombolysis stroke patients who reply to this therapy.

Keywords: Ischemic stroke, Quality of life, Thrombolysis, Non-thrombolysis, Hemiparesis.

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Citation Dr. Vankodoth Sireesha, V. Sushma, K. Bhavitha Naga Sai, Sumaiya Sana, M. Pratibha, M. Sunil Kumar and chintalapally kanna reddy , A Comparative Study On Quality of Life Between Thrombolysed and Non-Thrombolysed Ischemic Stroke Patients.(2023).Int. J. Life Sci. Pharma Res.13(4), P61-P69 http://dx.doi.org/10.22376/ijlpr.2023.13.4.P61-P69

1. INTRODUCTION

Stroke is the second leading cause of death and a major cause of morbidity and mortality worldwide[1] According to World health organization (WHO) statistics, 15 million people suffer from stroke annually, of which approximately 5 million die and another 5 million are left permanently disabled, thereby placing a burden on the family and community. [2] Most strokes are due to blockage of an artery in the brain by a blood clot.[3] Stroke risk factors: Age is the most common, remarkable, and non-modifiable risk factor for stroke. The elderly is particularly affected by stroke. Because of future aging, it is important to pay attention to prevention and aftercare for stroke patients [4]. The most common and modifiable risk factors for stroke are Hypertension, smoking, Diabetes mellitus, hyperlipidemia, and physical inactivity[5]. Stroke has been divided into two types based on its pathophysiology [6] A) Ischemic stroke accounts for 85% of all strokes worldwide. An obstruction of blood flow frequently causes it to the brain by the hardening of the arteries. B) Hemorrhagic strokes are due to subarachnoid hemorrhage or intra-cerebral hemorrhage. They account for 15% of all strokes worldwide in which blood vessels within the brain rupture, permitting blood to leak into the brain[7]. The clinical features of ischemic stroke include Hemiparesis, Quadriparesis, Loss of Vision, Visual field deficits, Facial weakness, Dysarthria, Ataxia, Vertigo, and Altered level of consciousness [8]. Neuroimaging plays a very important role in the management of ischemic stroke. Computed Tomography is the backbone of the clinical assessment of ischemia [9]. The better outcome of early stroke management begins with recognizing stroke once it occurs. Studies demonstrate that public education concerning the signs and symptoms of stroke improves recognition.[10]. The quick algorithmic rule (Face, Arm, Speech, and Time) is the most typically used message for campaign[11]. Currently, the intervention available to improve outcomes after ischemic stroke are 1) the patient's admission to a stroke unit, 2) Aspirin within 48 hours after stroke onset, and treatment with IV tissue plasminogen activator (thrombolytic) within 4.5 hours after stroke onset[12]. This thrombolytic agent dissolves thrombi (examples include Alteplase and Tenecteplase) [13]. Of these interventions, thrombolysis is the most effective and has changed the attitude and the management towards stroke patients. However, only a small percentage of ischemic Stroke patients receive tissue plasminogen activators.[14] Lack of patient familiarity with stroke symptoms and correct response, late admission to the hospital, the narrow therapeutic window, and variances in the selection of patients for thrombolysis are the factors that contribute to this under-treatment[15]. It is important to know the difference in QOL between patients who received it and did not. The initial stroke lesion and the extent of subsequent recovery determine long-term effects.[16] Stroke affects patients' lives in many ways, both physically and through various emotional, psychological, cognitive, and socio-consequences. [17] The severity of post-stroke depicts affects the quality of life.[18] Health-Related Quality of Life (HRQOL) measures often investigate stroke's long-term impact. The most comprehensive stroke-specific HRQOL instrument measures the impact of stroke on several aspects of physical function and activities.[19] Among these instruments is the stroke-specific QOL (SS-QOL) scale, a multi-dimensional tool for various effects in post-stroke patients.[20] This study aims to assess and compare the QOL of stroke patients treated with thrombolysis to patients without thrombolytic therapy after three months of discharge from the hospital using SSQoL. It is often assessed by regular follow of the patient when discharged. It was expected that patients without thrombolytic therapy to experience worse QOL because of the greater initial severity of their stroke.

2. MATERIALS AND METHODS

2.1. Study design

It is a Prospective Observational study in the Department of NEUROLOGY in KIMS Hospital, Secunderabad, for four months, i.e., from January 2022 to April 2022. Around 106 ischemic stroke subjects were observed and assessed for the quality of life of ischemic stroke patients during the study period.

2.2. Inclusion criteria

All patients of ischemic stroke of either sex, aged ≥ 18 years (including the recently diagnosed patients and patients with a history of ischemic stroke).

2.3. Exclusion criteria

1. Patients below 18 years of age. Patients with alternative varieties of stroke-like ICH, SAH, and Post-traumatic incidents.
2. Pediatrics, pregnant and lactating women.
3. Patients who are not co-operative.
4. Patients with neurological and psychological disorders (Alzheimer's, Parkinson's, schizophrenia).

2.4. Collection of data

The study's nature, type, or purpose was explained to participants. The socio-demographic details of the patient were composed using a data collection form. The patients were presented with the standard questionnaires, SSQoL, to measure the health-related quality of life. It contains domains and questions gleaned from several conversations with stroke survivors. Mobility (6 items), energy (3 items), upper-extremity functions (5 items), work/productivity (3 items), mood (5 items), self-care (5 items), social role (5 items), family role (3 items), vision (3 items), language (5 items), thinking (3 items), and Personality is the domains (3 items). Each SSQoL questionnaire requires patients to respond based on the preceding week. It is a self-report measure with 12 domains and 49 items. It takes approximately 10-15mins to complete the SSQoL scale. Each item shall be scored with the following key as show in the table 1.

Table 1: SSQoL Scale Each Item Score			
			SCORE
Total help	I couldn't do it at all	Strongly agree	1
A lot of help	A lot of trouble	Moderately agree	2
Some help	Some trouble	Neither agree nor disagree	3

| A little help | A little trouble | Moderate disagree | 4 |
| No help needed | No trouble at all | Strongly disagree | 5 |

The QoL was assessed using the SSQoL questionnaire scale, and the scoring was done according to the response given by post-stroke patients or the patient's representative.

3.   STATISTICAL ANALYSIS

The score values of the patients after QoL estimations were carried out using Statistical Package for Social Sciences (SPSS) Software. The collected data were entered using Microsoft Excel and were examined using SPSS. The demographical details were calculated using descriptive statistics. To compare the QoL between the thrombolysis and non-thrombolysis ischemic stroke patients, SPSS 20 for windows was used for statistical analysis. Statistical significance was set at P value< 0.05 (2-sided). These P- values are presented as an indication of the strength of the evidence. We used the independent t-test using the mean and the standard deviation.
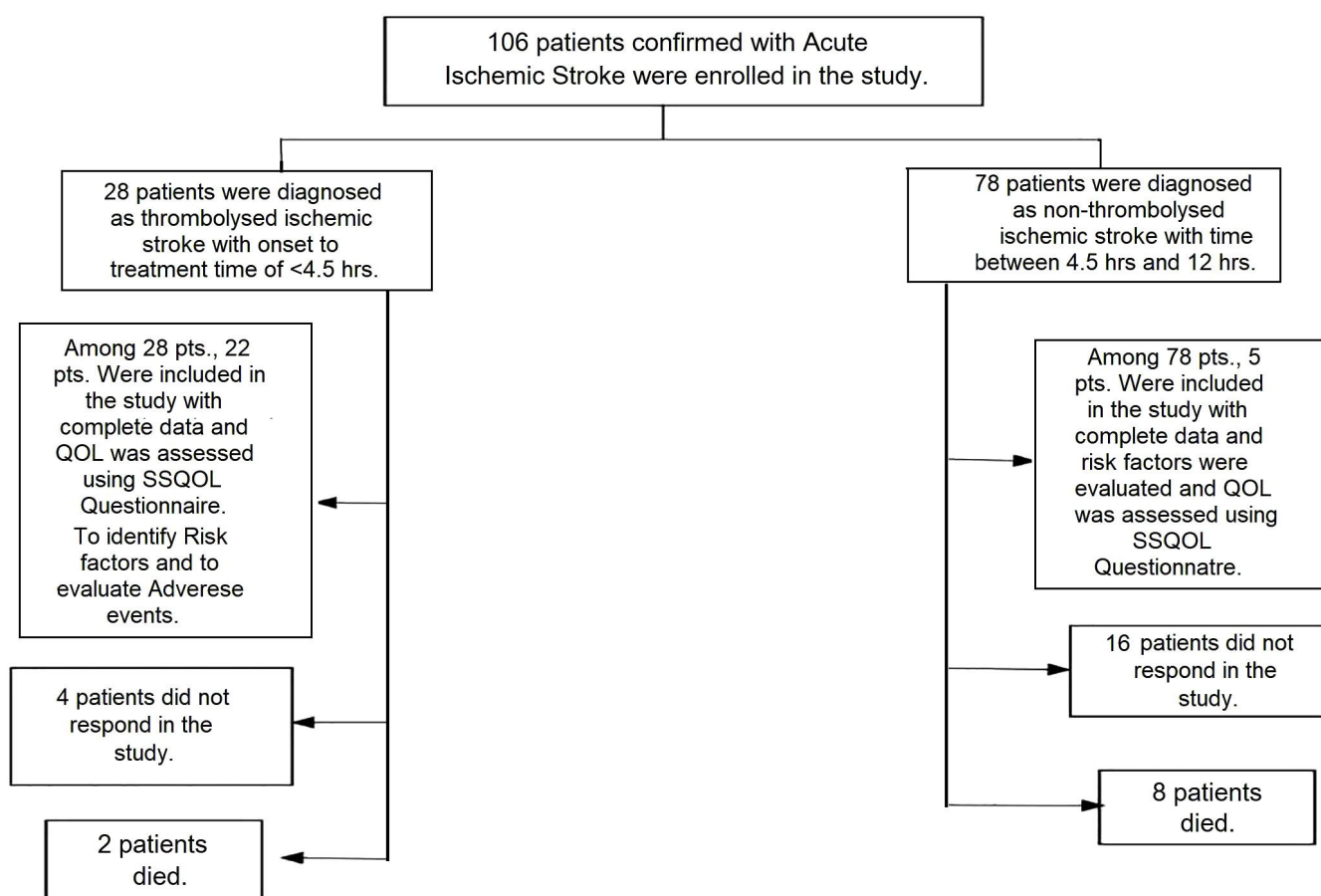
4.   RESULTS

Fig.1.Patient's flow chart
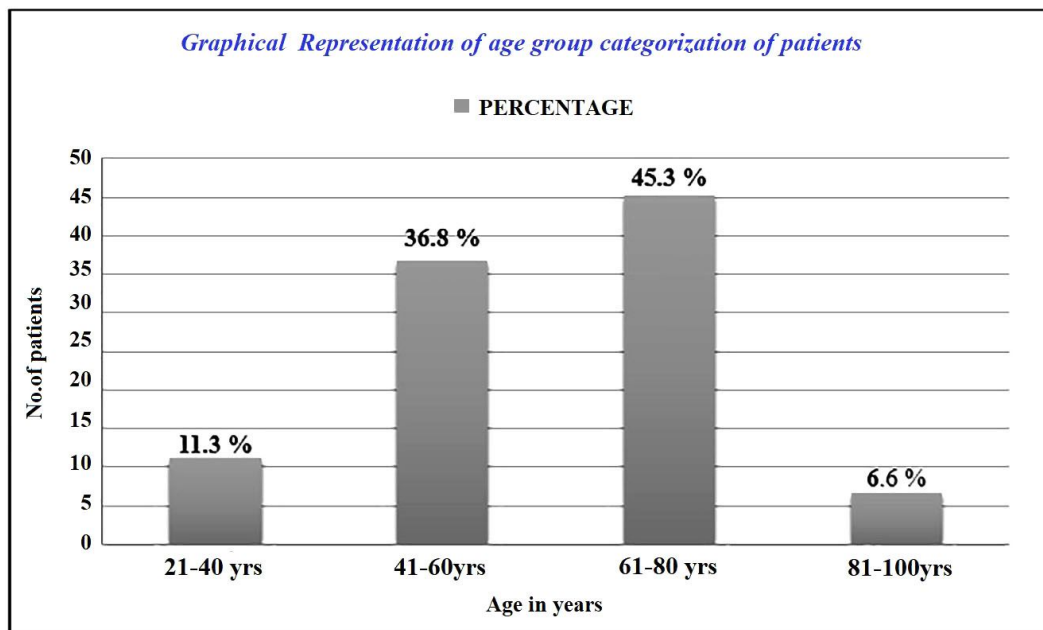
4.1. Incidence of Age among Patients

Fig. 2. Graphical representation of age group categorization of patients (both thrombolysis and non-thrombolysis) in percentages using descriptive statistics

As shown in fig.2, out of a total of 106 patients, 12 Patients were in the age group between 21- 40 years, 39 patients were in the age group between 41- 60 years, 48 patients were in the age group between 61-80 years and only 07 patients were between 81-100 years. The age range was from 21 to 100 years. In this study, the youngest patient was 27 years old, and the oldest was 93. The incidence of cerebrovascular accidents is maximum in those between 61-80 years of age group, which comprises 45.3% of total patients, and stroke patients aged ≤ 40 comprised 11.3 % of all patients.

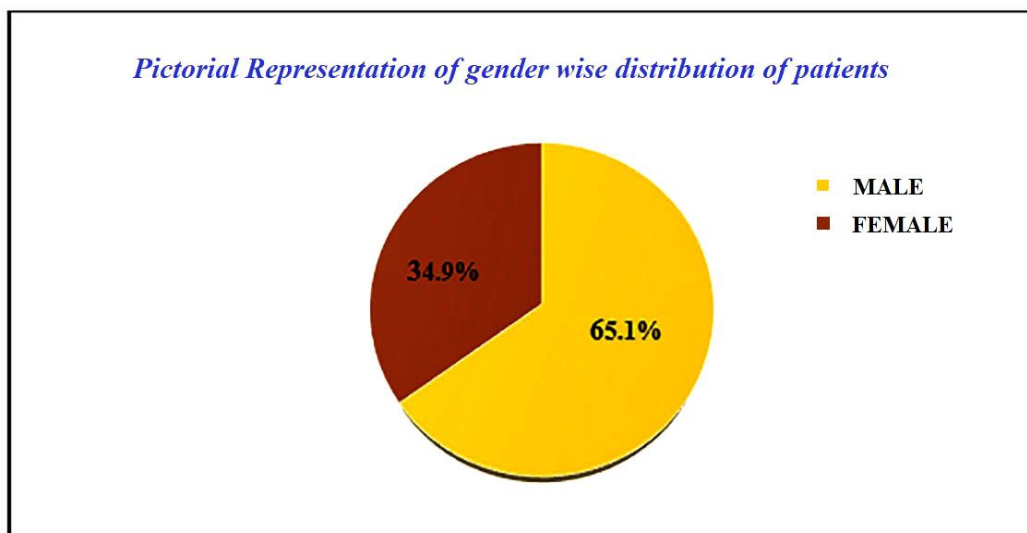## 4.2. Gender-Wise Distribution of Patients

Fig. 3: Pictorial representation of gender-wise distribution (both thrombolysis and non-thrombolysis) of patients in percentages using descriptive statistics

As shown in fig.3, out of 106 patients, males are about 69 (65.1%), and females are about 37 (34.9%). Therefore, the male-to-female ratio in the present study was 1.86:1. From the above observation, the incidence of ischemic stroke was more common in males (65.1%) than in females (34.9%).

4.3. Clinical Features of Patients

Table 2: Frequency and percentage of clinical presentation of stroke patients (both thrombolysis and non-thrombolysed)		
Predominantly Presenting Clinical Features	**No. of Ischemic Patients (both thrombolysed and non-thrombolysed)**	**Percentage [%]**
Speech Involvement	79	74.5
Right Hemiparesis	54	50.9
Left Hemiparesis	55	51.9
Giddiness	18	17.0
Right UMN palsy	29	27.4
Left UMN palsy	24	22.6
Headache	13	12.3
Altered Sensorium	30	28.3
Gait Disturbances	29	27.4
Numbness	9	8.5
Urinary incontinence	9	8.5
Blurred Vision	4	3.8

In our study, as shown in Table 2, the most common clinical presentation found for both thrombolysis and non-thrombolysis ischemic stroke patients was speech involvement which was about 74.5%, followed by both left Hemiparesis (51.9%) and Right Hemiparesis (50.9%). Various other clinical features observed were altered sensorium (28.3%) then by Gait disturbances (27.4%), Right UMN palsy (27.4%), Left UMN palsy (22.6%), Giddiness (17.0%), Headache (12.3%), Numbness (8.5%), and Urinary Incontinence (8.5%) and last was blurred Vision (3.8%).

4.4. Prevalence of Risk Factors in Patients

In our study, as shown in fig.4, the most common modifiable risk factor for ischemic stroke was Hypertension at 77.4%, followed by Diabetes (60.4%), Past H/O of CVD (21.7%), Past H/o of CAD (17.9%), Dyslipidemia (15.1%) Alcohol (13.2%), Hypothyroidism (11.3%) and last risk factor was smoking (8.5%) among these patients. Only 3.8% of the total patients were without any comorbidities.
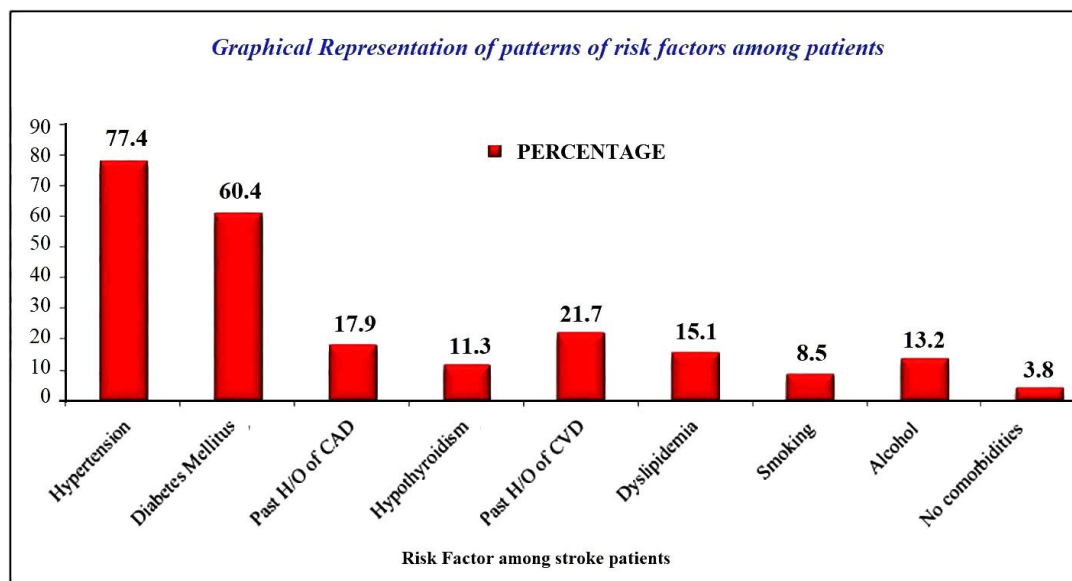

Fig 4: Graphical Representation of patterns of risk factors among patient

4.5. Time of Presentation to Hospital

Table 3: Time of Presentation of the ischemic patients to the Hospital		
Time of Presentation	**No of Patients**	**Percentage**
< 4.5 HRS	28	26.4
>4.5 HRS	78	73.6
TOTAL	106	100

In our study, as shown in Table 3, 106 patients were diagnosed with ischemic stroke. Based upon the time of a presentation to the hospital after the onset of symptoms, the patient was included as thrombolysis patients, i.e., who were admitted to the

hospital within 4.5 hours, and as the non-thrombolysis patients, i.e., who were admitted to the hospital after 4.5 hours and within 24 hours and they did not receive any thrombolytic therapy. As a result, thrombolysis patients were 28 (26.4%), and non-thrombolysis patients were 78 (73.6%). Therefore, from the above table, non-thrombolysis ischemic stroke patients were more in number than thrombolysis ischemic stroke patients.

4.6. *Adverse Events among Ischemic Stroke Patients*

Table 4: Adverse Events of both thrombolysed and non-thrombolysed		
Adverse Event	No.of Patients	Percentage [%]
Bleeding	41	38.3
Headache	31	29.2
Fever	29	27.4
Constipation	24	22.6
Irritation	23	21.7
Sleep Disturbances	21	19.8
Pedal Edema	12	11.3
Vertigo	09	8.5

The study observed eight adverse drug events from 106 ischemic stroke patients (both thrombolysis and non-thrombolysis patients). As shown in Table 4, the most common adverse event was bleeding for about 41 patients (38.7%), followed by headache for 31 patients (29.2%), 29 patients (27.4%) with fever, 24 patients (22.6%) with constipation, 23 patients (21.7%) with irritation, 21 patients (19.8%) with sleep disturbances, 12 patients (11.3%) with pedal edema and last was vertigo for 9 patients (8.5%)

4.7. STROKE SPECIFIC QUALITY OF LIFE [SSQol] SCORE IN PATIENTS WITH ISCHEMIC STROKE

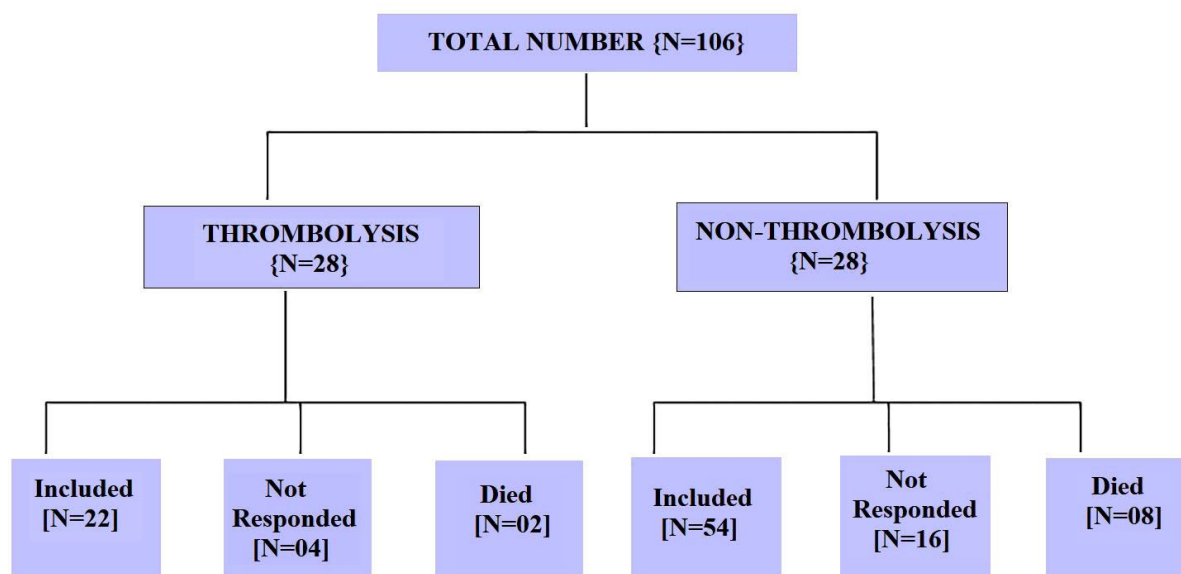Out of 106 patients, 28 are thrombolysis, and 78 are non-thrombolysis.

Table 5: SSQoL Score in Patients With Ischemic Stroke			
Items	Thrombolysis	Non-Thrombolysis	P Value
	MEAN	MEAN	
Energy	3.77	2.87	**0.025***
Family Role	3.59	3.17	0.231
Language	3.73	3.31	0.288
Mobility	3.73	2.83	**0.033***
Mood	3.09	3.07	0.965
Personality	3.45	3.15	0.435
Self-care	3.45	2.70	**0.046***
Social Role	2.50	2.65	0.680
Thinking	3.23	3.26	0.933
Upper Extremity Function	3.23	3.19	0.916
Vision	3.86	2.96	**0.025***
Work	3.50	2.57	**0.032***

As shown in Table 04, the interaction effects between the group and the changes in activity concerning the SS-QoL are given to know to what extent these variables mediate the difference between the two treatment modalities. There are statistically significant differences, i.e., p-value (<0.05) in Energy (p-0.025), Mobility (p-0.033), Self-care(p-0.046), Vision (p-0.025), Work (p-0.032) items between thrombolysis and non-thrombolysis ischemic patients. No significant difference was observed in other items such as family role (p-0.231), Language (p-0.288), mood (p-0.965), personality (p-0.435), social role (p-0.680), thinking (p-0.933), and upper extremity function (p-0.916). By comparing the mean scores of each health item in the SS-QoL scale between the two groups, thrombolysis patients have a significantly better quality of life than non-thrombolysis ischemic stroke patients.

5. DISCUSSION

The present study focused on the "Clinical Profile of stroke and Comparison of Quality of Life between Thrombolysed and Non-Thrombolysed Ischemic Stroke Patients" conducted in tertiary care hospital over four months from January 2021 to April 2021. The data was collected from 106 patients using a specially designed form. In our study, the age range of ischemic stroke patients was from 21 to 100 years, almost similar to the study conducted by Punna S[21]. The incidence of stroke was maximum in the age group of 61 – 80 years, accounting for 45.3% of the total patients because of more risk factors like chronic diseases (HTN, DM), similar to the studies conducted by Sivanesan P[22]. It shows that age is considered one of the non-modifiable risk factors. The incidence of stroke with the age of ≤ 40 comprised 11.3% of all 106 patients, indicating that stroke rates are increasing among the younger population. So, there is a need to control the risk factors such as smoking, alcohol use, obesity, and lifestyle modifications in a younger population to prevent premature stroke attacks. Even these risk factors have the same impact in causing cardiovascular events, similar to the study conducted by Raghuvanshi S[23]. The patients' mean (SD) age was 59.9(15.7) years, almost similar to the study conducted by Naik M[24]. In the present study, the gender distribution of both thrombolysis and non-thrombolysis ischemic stroke patients showed the male-to-female ratio was 1.86: 1which almost resembled the results from the studies conducted by Aiyar[25]. So it can be concluded that the incidence of stroke is more common in the male sex (65.1%) than in females (34.9%), similar to the study conducted by KingslyJebasingh Y[26]. The occurrence of stroke is low among females because of the vasodilator action of estrogen, which could be the protective mechanism for a lower incidence of stroke in females[27]. Estradiol has potent effects on endothelial that promote dilation and blood flow, whereas testosterone has opposite effects indicating women are protected by estrogen[28]. Males are more predominant to have an increase in risk factors like HTN and DM than females, thus increasing the risk of developing stroke. In our society, smoking and alcoholism in the male population are high, which is not so common among females. In the present study, no cases of the female with alcoholism or smoking had been reported. Both thrombolysis and non-thrombolysis patients included in the present study showed Speech involvement as the most common clinical presentation, which was reported in 74.5 % of patients, followed by left and right Hemiparesis in 51.9% and 50.9% of patients, respectively. These findings concord with the study conducted by Aiyar et

al.[25] Altered sensorium and Gait disturbances were noted in 28.3% and 27.4% of patients. Almost three-fourths of thrombolysis and non-thrombolysis ischemic stroke patients were associated with hypertension and diabetes mellitus in our study, which are the prime risk factors for stroke, i.e.., 77.4% of patients with Hypertension and 60.4% with diabetes mellitus, were reported. The presence of a history of cerebrovascular accidents accounted for only 21.7%. The percentage of alcohol (13.2%) and smoking (8.5%) were least in the present study. Similar findings were found in data from the study as Inter heart and Inter stroke studies conducted in 22 countries, including India, by Donnell et al.[30] From various studies, it was concluded that strict blood pressure control in diabetic patients would reduce the incidence of stroke.[29] According to the AHA/ASA guidelines, CT/MRI is the standard diagnostic test for detecting different types of stroke performed at the time of admission in the ER at the study site. According to ASA/AHA guidelines, the recommended therapeutic window period for presenting stroke patients ranges from 3hrs to 4.5 hrs. The group patients with a 3-4.5 hrs therapeutic window period also had a positive primary outcome. In the present study, only 26.4% of patients presented within the window period [< 4.5hrs] and were included as thrombolysis patients and received thrombolytics, and the majority of patients, about 73.6% were presented after the window period [> 4.5hrs] and did not receive thrombolytics and were considered as non-thrombolysis patients in the present study which is approximately similar to the study conducted by Leonie de weerd[32]. About 91.5% of the patients in our study were presented with a BP < 180/110mm of Hg, and only 8.5% with BP > 180/110 mm of Hg. The mean Systolic blood pressure was 165 mmHg, and the mean Diastolic blood pressure was being 95mmHgwhich is almost similar to the study conducted by Yamini M.[31] Out of 106 patients, only nine patients needed IV anti-hypertensive drugs before the administration of tPA. In the present study, at admission, most had blood sugar levels between 140-200mg/dl (44.3%) and HBA1C between 6.0% - 9.9% (60.4%). The mean blood sugar level is 244 mg/dl, and 32.1% of patients needed correction of blood glucose levels before thrombolysis. In the study by Yamini M, the mean blood sugar level is 166mg/dl.[31] Patients included in our study had relative bleeding (38.7%) as the most commonly reported adverse drug event, followed by headache (29.2%), fever (27.4%), constipation (22.6%), Irritability (21.7%), Sleep disturbances (19.8%), pedal edema (11.3%) and vertigo (8.5%). It is concordance with the study conducted by Eby Mathew, Chandrika C[33] had also reported bleeding, headache, and pedal edema, as the major adverse events found in their study. Monitoring of ADRs in stroke patients is important. The adverse reactions were managed by withdrawing the drug that caused a reaction or by providing symptomatic treatment. The dose of the drug was reduced in cases where the drug could not be removed. In the present study, the clinical pharmacist was involved in ADR monitoring by reporting, assessing, and creating awareness of ADRs in the neurology unit. This study showed that including a clinical pharmacist in the healthcare system could help with inadequate ADR monitoring and prevention. Drugs such as thrombolytics, antiplatelets, and anticoagulants commonly used in stroke pose a high risk of causing serious hemorrhagic manifestations. ADR monitoring is highly warranted among stroke patients due to multiple risk factors like polypharmacy, prolonged therapy, medication errors, and comorbidity. Monitoring and reporting ADRs will help identify and quantify the risks associated with drug use. It

helps improve the prescriber's knowledge in identifying and minimizing preventable ADRs.

5.1. *Discussion on the role of Thrombolysis*

Our study demonstrated that thrombolysis significantly reduced the incidence of unfavorable outcomes, shown as follows. This study's main outcome was comparing the quality of life between thrombolysis and non-thrombolysis ischemic stroke patients using the SS-QOL scale. Quality of life is nearly identical in both groups except for the scales in Energy (p – 0.025), Mobility (p – 0.033), Self-care (p -0.046), Vision (p – 0.025), and Work (p – 0.032) items. Patients in the thrombolysis group have a significantly better QoL for the above scales with a statistically significant difference, i.e., $p < 0.05$. However, no significant difference was observed in other items such as Family role (p- 0.231), Language (p- 0.288), mood (p- 0.965), Personality (p- 0.435), Social role (p- 0.680), Thinking (p- 0.933), Upper Extremity function (p - 0.916). It was noted that the mean scores of each health item in the SS-QOL tool are higher in patients undergoing treatment with recombinant tissue plasminogen activator (rt-PA), which suggests additional effectiveness for treating the patients is similar to the study conducted by L De Weerd.[31] This group seems to have a better physical and psychological condition due to rt-PA treatment. To increase better QoL, brief Psychological intervention and antidepressant treatment could reduce post-stroke depression and improve functional outcomes.[34]

6. CONCLUSION

As health care providers, clinical pharmacists play a pivotal role in assessing the risk factors, adverse events, and quality of life of ischemic stroke patients. This study was conducted to learn about the clinical profile of ischemic stroke patients and also compare the quality of life of thrombolysis and non-thrombolysis ischemic stroke patients using SS-QOL among the subjects. To conclude, this study found no essential differences in quality of life between patients with or without thrombolytic therapy. But thrombolytic therapy is of great value in achieving good quality of life in ischemic stroke patients. Therefore, thrombolytic therapy positively but indirectly affects patients' QOL, especially in the first months after stroke. If aftercare is more specific, the quality of life can be improved further for both groups. It needs further investigation in stroke patients. Performing exemplary and extensive research studies on stroke and its quality of life could improve individual patients' health outcomes.

7. LIMITATIONS

This study has several limitations. Firstly, study groups were relatively small because of the selection criteria; due to this, there is no significant difference between the QoL of thrombolysis and non-thrombolysis ischemic stroke patients. Therefore, we may need to study a larger group of patients to detect a significant improvement in QoL after thrombolysis. In addition, a short follow-up time of 1 month we have hindered the evaluations of long-term neuro disabilities.

8. AUTHORS CONTRIBUTION STATEMENT

Sireesha, Sushma, Sumaiya, and Bhavitha have designed and planned the conceptualization framework and methodology of the study and also carried out the data collection for the implementation of the study. They also performed the statistical analysis and contributed to interpreting the results. Bhavitha, Pratibha, and Sunil carried out the literature search required for the study. Sireesha, Prathibha, and Sunil took the lead and wrote the manuscript with input from all authors. Sireesha and Pratibha supervised the writing and editing of the project. All authors provided critical feedback and helped to shape the research, analysis, and manuscripts.

9. CONFLICT OF INTEREST

Conflict of interest declared none.

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