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A PROSPECTIVE OBSERVATIONAL COMPARATIVE STUDY ON THE EFFICACY OF ALTEPLASE VERSUS TENECTEPLASE IN ACUTE ISCHEMIC STROKE AND TO ASSESS THE CHANGES IN QUALITY OF LIFE IN THESE PATIENTS AFTER THROMBOLYTIC THERAPY- A PILOT STUDY.

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ABSTRACT:

Background: Acute ischemic stroke describes a Stroke is often referred to as a brain attack or Cerebrovascular Accident (CVA). A clot blocks a blood vessel that delivers oxygen and nutrients to the brain or bursts (or ruptures), resulting in a stroke. When this happens, brain cells in that location cannot get the blood (or oxygen) they need and perish. Alteplase and Tenecteplase are thrombolytic drugs used for ischemic stroke. Alteplase converts fibrinogen to the proteolytic enzyme plasmin, which lysis fibrin as well as fibrinogen Tenecteplase converts plasminogen to plasmin is increased relative to its conversion in the absence of fibrin. **Methods:** The study was carried out on 20 patients with AIS. The study was conducted by categorizing them into two groups, 10 patients were treated with Alteplase, and 10 patients were treated with Tenecteplase. The efficacy of Alteplase and Tenecteplase is assessed by using NIHSS and MRS. Health-related QOL of Alteplase and Tenecteplase was assessed using an SS-QOL questionnaire in patients with AIS. Anxiety and depression are assessed by HADS. The cost of both drugs is compared. **Result:** By using NIHSS and MRS it is assessed that Tenecteplase is more effective than Alteplase. The QOL in Tenecteplase patient show significant change as compared to Alteplase.

KEYWORDS: Acute ischemic stroke, Tenecteplase, Alteplase, NIHSS, MRS, SS-QOL, HADS.

INTRODUCTION

According to the World Health Organization, stroke is characterized by rapidly appearing clinical symptoms of a localized (or generalized) disruption of brain function that lasts for more than 24 hours or results in death and has no other obvious underlying cause than a vascular region[8].

Stroke is frequently referred to as brain assaults or Cerebrovascular Accidents (CVAs). A blood artery that supplies the brain with oxygen and nutrients is either blocked by a clot or bursts (or ruptures), which results in a stroke[5]. When it occurs, brain cells in that area cannot access the blood (or oxygen) they require, and they die[8].

CLASSIFICATION:

The TOAST classification denotes five subtypes of ischemic stroke[6]:

- Small vessel occlusion
- Cardio embolism
- Large artery atherosclerosis
- Stroke of other determined etiology
- Stroke of undetermined etiology

ETIOLOGY:

Risk factors for stroke that can be changed treated or medically managed[9]:

- High blood pressure
- Heart Disease
- Diabetes
- Smoking

Risk Factors for stroke that cannot be changed[9]

- Older age
- Gender
- Hereditary or Genetics
- History of prior stroke

CLINICAL FEATURES:

- Loss of balance
- Blurred vision
- Facial palsy
- Weakness
- Speech difficulty
- Loss of sensations in one half of the body[1]

DIAGNOSIS

Imaging Tests:

- Computerized Tomography
- Magnetic Resonance Imaging

Blood or Heart Tests:

- Blood Tests
- Electrocardiogram[2]

Physical Examination:

During the physical exam:

- Confusion
- Coordination and balance
- Mental Alertness
- Numbness or weakness in the face, arms, and legs
- Trouble speaking or seeing clearly will be checked accordingly[4].

TREATMENT

The initial treatment provided for stroke is antiplatelet(Aspirin), or Fibrinolytic therapy (Alteplase (Actilyse), Tenecteplase (Tenectase)) is also recommended[11].

ALTEPLASE

Alteplase is a biosynthetic version of human tissue-type plasminogen activator(t-PA). It is created using Recombinant DNA technology. It converts fibrinogen to the proteolytic enzyme plasmin, which lysis fibrin as well as fibrinogen. Intravenous Alteplase is cleared primarily by the liver with an initial half-life of fewer than 5 minutes and a terminal half-life of 72 minutes[13].

TENECTEPLASE

Tenecteplase is a recombinant, structurally modified human tissue plasminogen activator (tPA) form. In the presence of fibrin in vitro studies demonstrate that Tenecteplase conversion of plasminogen to plasmin is increased relative to its conversion in the absence of fibrin[14]. The fibrin specificity decreases the systemic activation of plasminogen and the resulting degradation of circulating fibrinogen. It has an initial half-life of 20-24 minutes and the terminal half-life is 90-130 minutes[15].

MATERIALS AND METHODS

Data source: All the relevant information regarding the study was collected from case records and direct interviews with patients and caregivers. Data from case records and caregivers were collected by using suitably designed proforma. The study was approved by the Research and Ethical Committee of Cosmopolitan Hospital, Thiruvananthapuram.

Study population: Patients were taken from the Neurology department of Cosmopolitan Hospital. Informed consent was obtained. The study was conducted for a period of 3 months.

Assessment of Efficacy: Efficacy is assessed by NIHSS and MRS scale

Assessment of QOL: Details were collected from case records of the stroke patients and direct interviews with the patients and caregivers which is been recorded in the SSQOL questionnaire

Assessment of Anxiety and Depression: Details were collected from case records of the stroke patients and direct interviews with the patients and caregivers which is been recorded in the HADS questionnaire.

Statistical Analysis: The comparison of quantitative variables between two groups was analysed by student t-test according to the nature of the data.

OBSERVATION AND RESULTS:

The proposed study, "the efficacy of Alteplase versus Tenecteplase in acute ischemic stroke and to assess the change in quality of life in these patients after thrombolytic therapy" was a prospective observational study carried out in a multispecialty tertiary care hospital. In this study, the data were collected from 20 patients diagnosed with AIS and were analyzed. Among the 20 patients selected, 10 were treated with Alteplase and 10 were treated with Tenecteplase. The study aimed to compare the efficacy of Alteplase and Tenecteplase using NIHSS and MRS, to assess the health-related quality of life using the SSQOL scale, and to assess anxiety and depression using the HADS scale. The cost-effectiveness of Alteplase and Tenecteplase was analyzed in AIS patients.

DEMOGRAPHIC DETAILS OF THE PATIENTS:

The data related to the demographic details of patients were collected and recorded.

PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON AGE:

The percentage distribution of patients based on age is shown in the following table.

Age wise distribution	Number of patients (n=20)	Percentage (%)
50-60	3	15%
61-70	9	45%
71-80	3	15%
81-90	5	25%

Table: 1 Age distribution of the study population

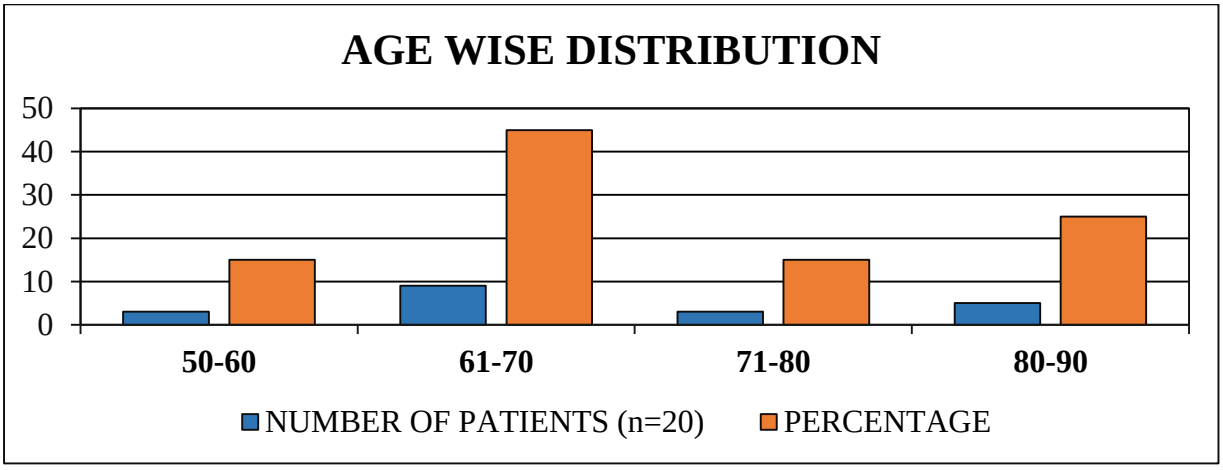

Figure: 1 Age-wise distribution of the study population

From Table 1, it was observed that out of the 20 patients with AIS,45% belong to the age group of 61-70,25% belong to the age group 81-90,15% belong to the age group of 50-60 and 15% belong to the age group of 71-80.

PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON GENDER:

The percentage distribution of patients based on gender is shown in the following table

GENDER	Number of Patients (n=20)	Percentage
MALE	12	60%
FEMALE	8	40%

Table: 2 Gender-wise distribution of the study population

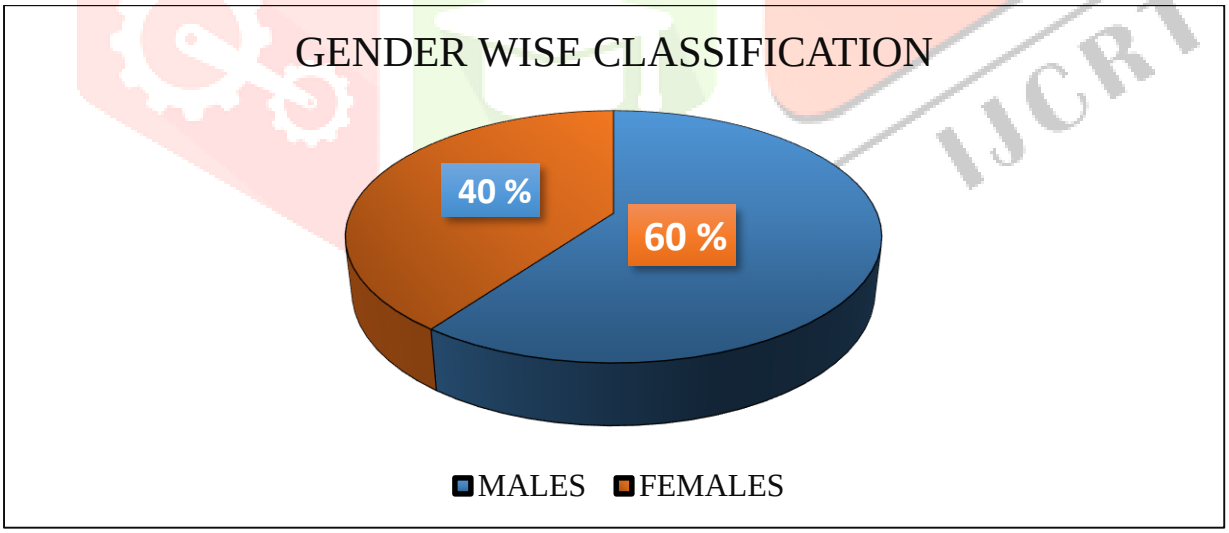

Figure: 2 Gender-wise distribution

From Table 2, it was observed that out of the total patients with AIS, 60% were female and 40% were male.

PERCENTAGE DISTRIBUTION ON STUDY GROUP:

	Groups	No of patients (n=20)	Percentage (%)
GROUP A	ALTEPLASE	10	50 %
GROUP B	TENECTEPLASE	10	50%

Table: 3 Study group distribution

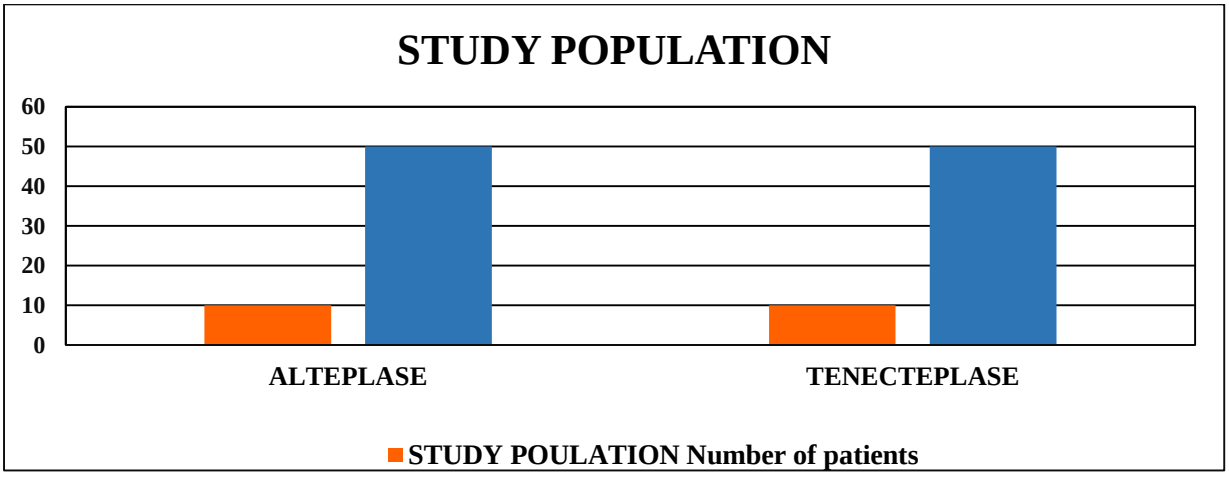

Figure: 3 Study group

From Table 3, it has been assessed that 50% of the patients were categorized in group A (Alteplase) and 50% of the patients were categorized in group B (Tenecteplase)

PERCENTAGE BASED ON SYMPTOMS OF STROKE:

The percentage based on the symptoms of stroke in both Groups A& B is shown in the following table and graph:

Symptoms of Stroke	Number of patients	Percentage (%)
WEAKNESS	16	25.0%
VISION PROBLEMS	1	1.6%
LOSS OF BALANCE	7	10.9%
DYSARTHRIA	18	28.1%
APHASIA	2	3.1%
FACIAL ASYMMETRY	15	1.6%
NUMBNESS	1	1.6%
OTHERS	3	6.3%

Table 4: Symptoms of Stroke

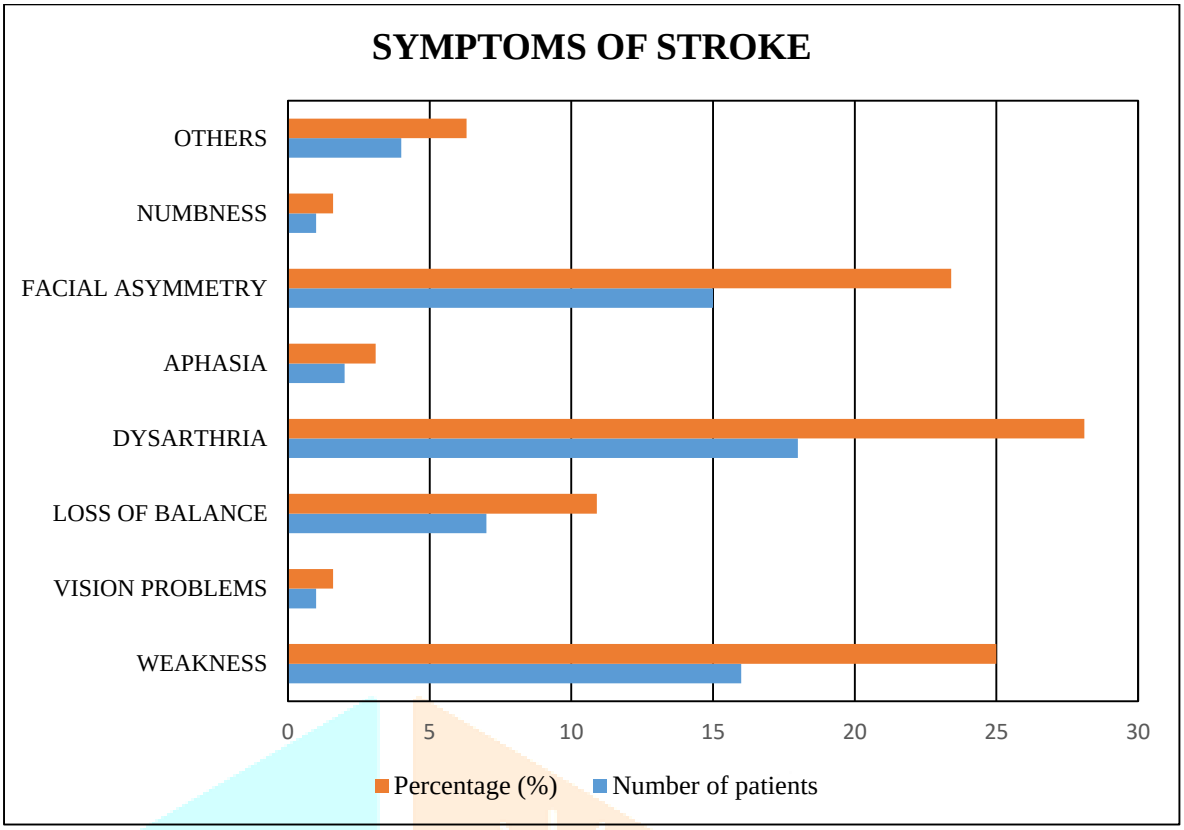

Figure 4: Symptoms of Stroke

From Table 4, it was observed from total patients from Group A &B shows that 90% of patients were having dysarthria, 80% had weakness,75% had facial asymmetry,35% had a loss of balance, 15% had other symptoms,10% had aphasia,5% had vision problems and 5% had numbness.

PERCENTAGE DISTRIBUTION BASED ON OTHER DISEASE CONDITIONS:

The percentage distribution based on the other disease condition of both Group A & B is shown in the following table:

Other Disease conditions	Number of patients	Percentage (%)
HYPERTENSION	15	34.1%
KIDNEY DISEASE	1	2.3%
THYROID DISEASES	1	2.3%
HEART DISEASE	7	25.9%
DYSLIPIDEMIA	7	15.9%
DIABETES TYPE2	7	15.9%
OTHERS	6	13.6%

Table 5: Other Disease Conditions

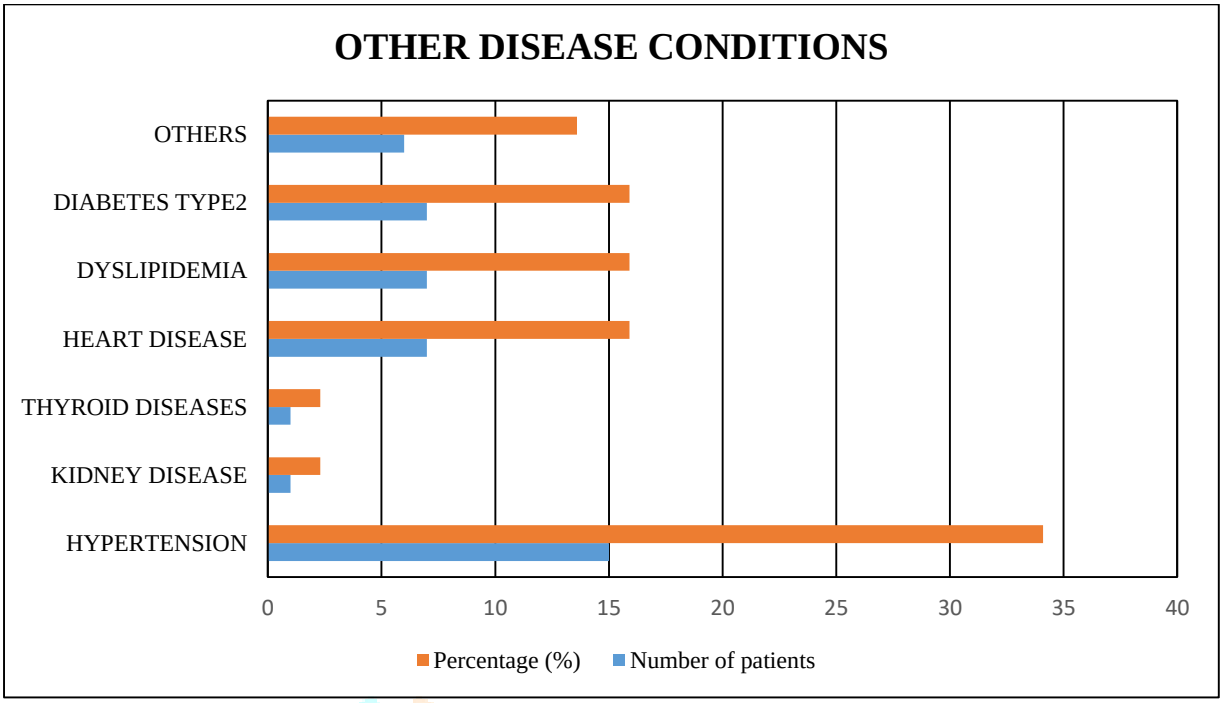

Figure 5: Other Disease Conditions

From the table no:5, it was observed that of the patient with AIS, 75% had Hypertension,35% had Dyslipidemia,35% had Heart diseases,35% had Type 2 DM, 5% had Thyroid diseases,5% had Kidney diseases, 30% had Other diseases.

ASSESSMENT OF NIHSS SCORE OF ALTEPLASE (GROUP A):

The neurological impairment at the time of admission of Group A is shown in the following table:

Neurological Impairment	Number of patients (n=10)	NIHSS score (Mean ± SD)
Minor(1-4)	2	4
Moderate(5-15)	8	7.1 ± 2.5
Severe(16-20)	0	0

Table: 6 Neurological Impairment at the Time of Admission – GROUP A

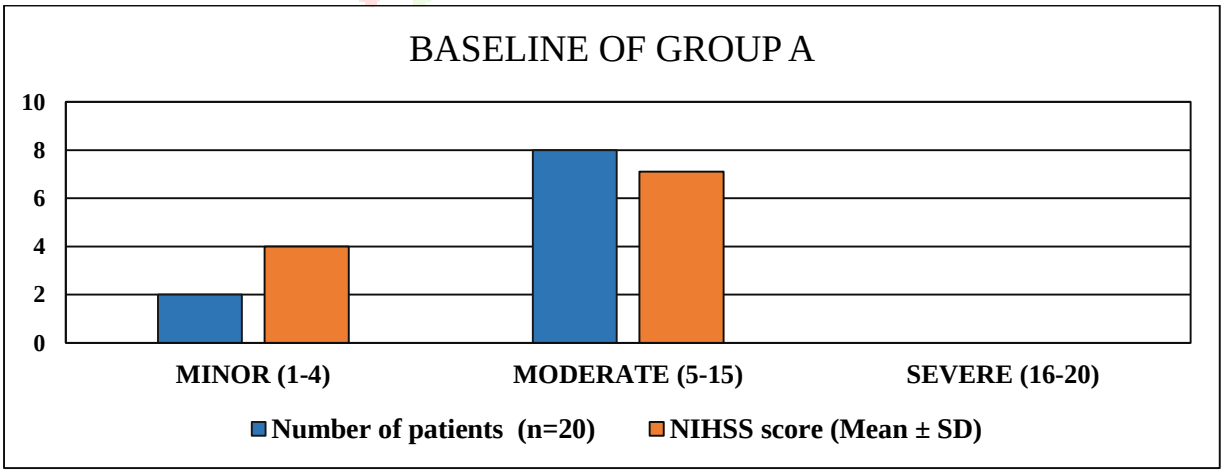

Figure: 6 NIHSS data at the time of admission – GROUP A

Table no:6 Assessment of the effect of Alteplase on the neurological impairment of the patient and the NIHSS Score of the patient. Of 10 patients about 20% had a minor neurological impairment and the NIHSS Score is 4, about 80% of patients had moderate neurological impairment and 7.1±2.5.

FIRST FOLLOW-UP ASSESSMENT OF NEUROLOGICAL IMPAIRMENT:

The neurological impairment at the first follow-up of Group A is shown in the following table:

Neurological impairment	Number of patients (n=10)	NIHSS Score(Mean ± SD)
Minor(1-4)	5	3.2 ± 0.83
Moderate(5-15)	5	5.2 ± 0.44
Severe(16-20)	0	0

Table: 7 NIHSS data at first follow-up of GROUP A

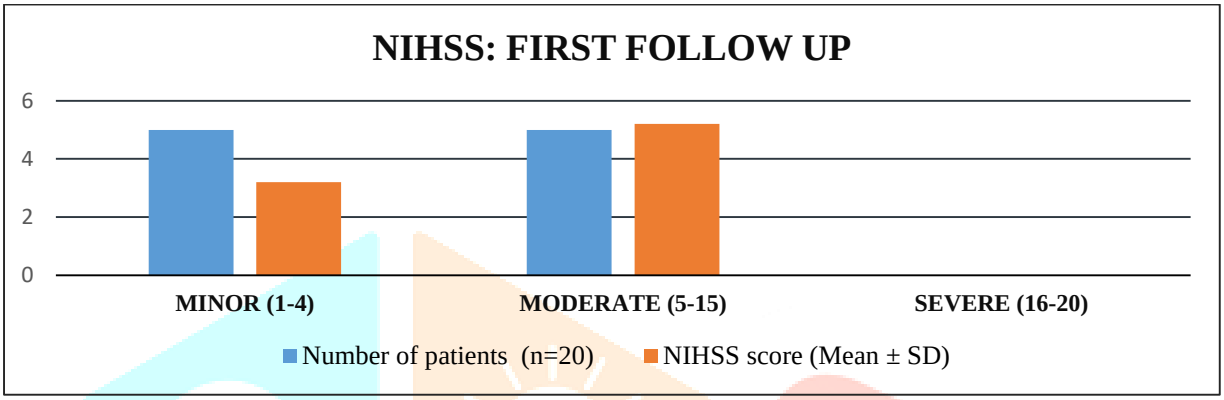

Figure: 7 NIHSS data at first follow-up of GROUP A

Table no 7, show the neurological impairment of group A at the time of the first follow up 50% of patient had a minor neurological impairment and NIHSS Score was 3.2±0.83 and 50% of patient had a moderate neurological impairment and the NIHSS score was 5.2 ± 0.44.

SECOND FOLLOW-UP ASSESSMENT OF NEUROLOGICAL IMPAIRMENT:

The neurological impairment at the second follow-up of Group A is shown in the following table:

Neurological impairment	No of patients (n=10)	NIHSS Score (Mean ± SD)
Minor(1-4)	9	2.6 ± 1.11
Moderate(5-15)	1	5
Severe(16-20)	0	0

Table: 8 NIHSS data at the second follow-up of GROUP A

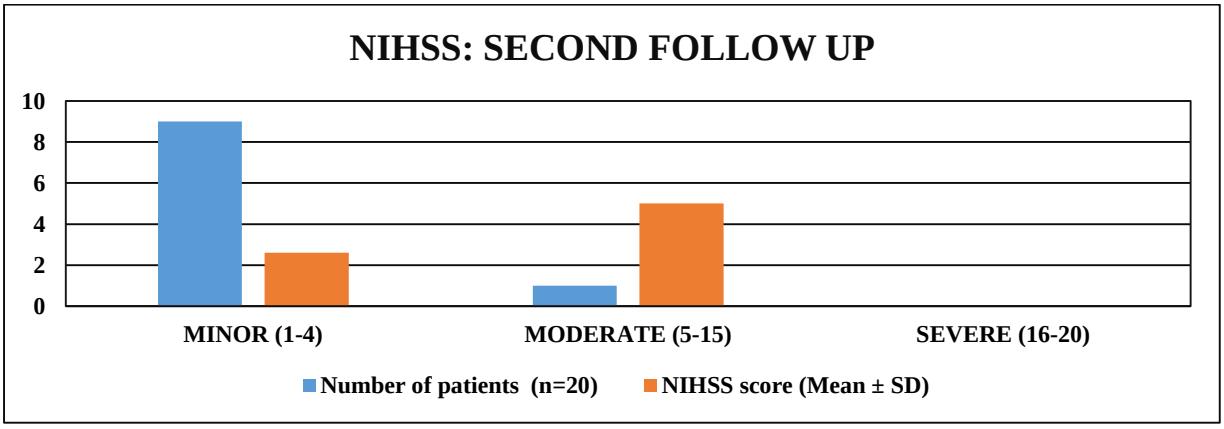

Figure: 8 NIHSS data at the second follow-up of GROUP A

Table no 8, shows the neurological impairment of group A at the time of the second-follow up 90% of patients had a minor neurological impairment and NIHSS Score was 2.6±1.11 and 10% of patients had a moderate neurological impairment and the NIHSS score was 5.

THIRD FOLLOW-UP ASSESSMENT OF NEUROLOGICAL IMPAIRMENT:

The neurological impairment at the Third follow-up of Group A is shown in the following table:

Neurological impairment	No of patients (n=10)	NIHSS Score (Mean ± SD)
Minor(1-4)	10	1.3 ± 0.7
Moderate(5-15)	0	0
Severe(16-20)	0	0

Table: 9 NIHSS data at the Third follow-up of GROUP A

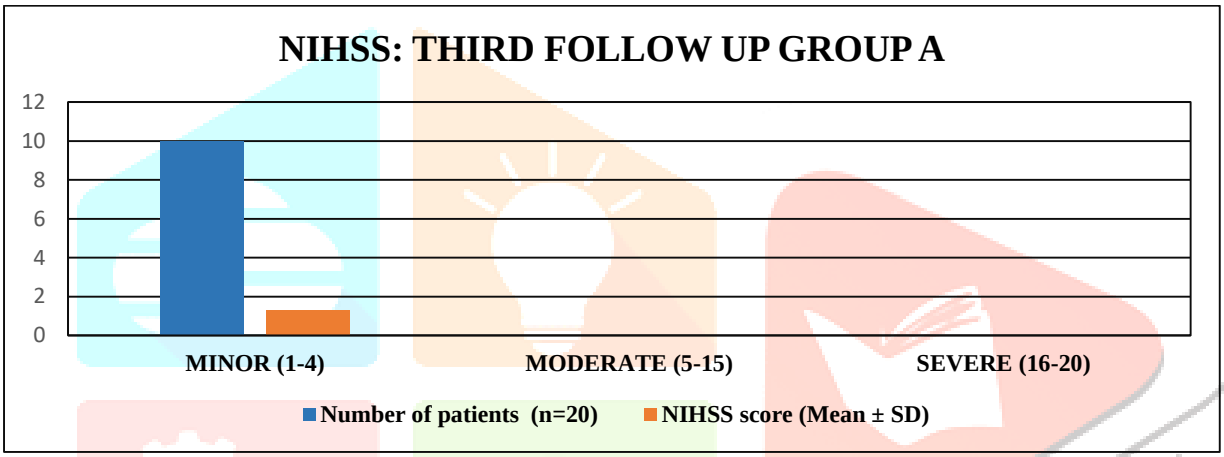

Table: 9 NIHSS data at the third follow-up of GROUP A

Table no 9, show the neurological impairment of group A at the time of the third follow up 100% of patient had a minor neurological impairment and NIHSS Score was 1.3±0.7 and 0% of patient had a moderate neurological impairment and the NIHSS score was 0.

COMPARING THE NEUROLOGICAL STATUS DURING EACH FOLLOW-UP:

The comparison of neurological improvement during each follow-up was home in the following table:

Review	NIHSS Score (Mean ± SD)
Baseline	6.5± 2.5
First follow-up	4.2 ± 1.2
Second follow-up	2.9 ± 1.2
Third follow-up	1.3 ± 0.7

Table: 10 Comparison between different follow up of group A

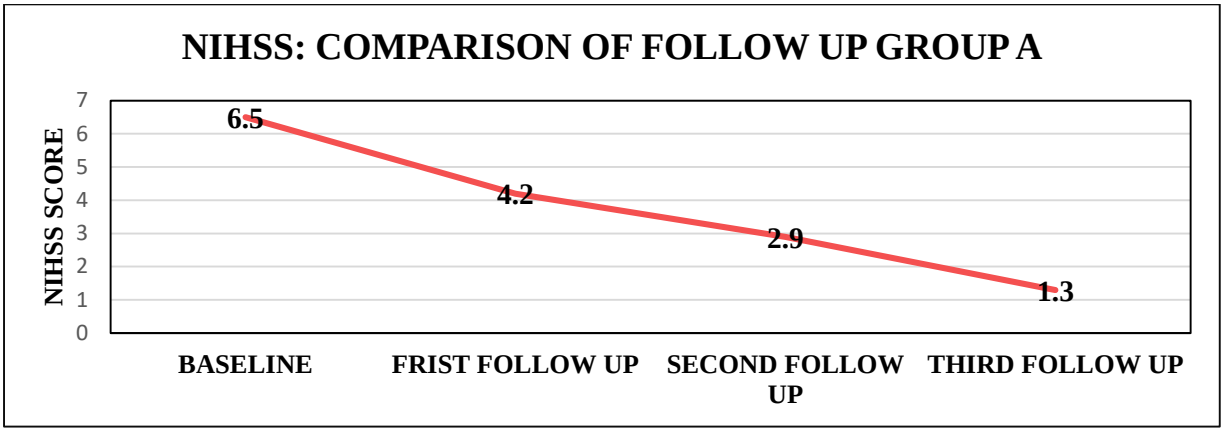

Figure: 10 Comparison of NIHSS scores at different follow up of group A

Table:10 shows, when comparing the neurological status during each follow up the baseline score was 6.5±2.5 and during the next follow-ups, the NIHSS Score decreases respectively.

ASSESSMENT OF THE NIHSS SCORE OF TENECTEPLASE (GROUP B):

The neurological impairment at the time of admission of Group B is shown in the following table:

Neurological impairment	Number of patients (n=10)	NIHSS score (Mean ± SD)
Minor(1-4)	2	4
Moderate(5-15)	7	7.5 ± 1.1
Severe(16-20)	1	16

Table: 11 Neurological impairments at the time of admission Group-B

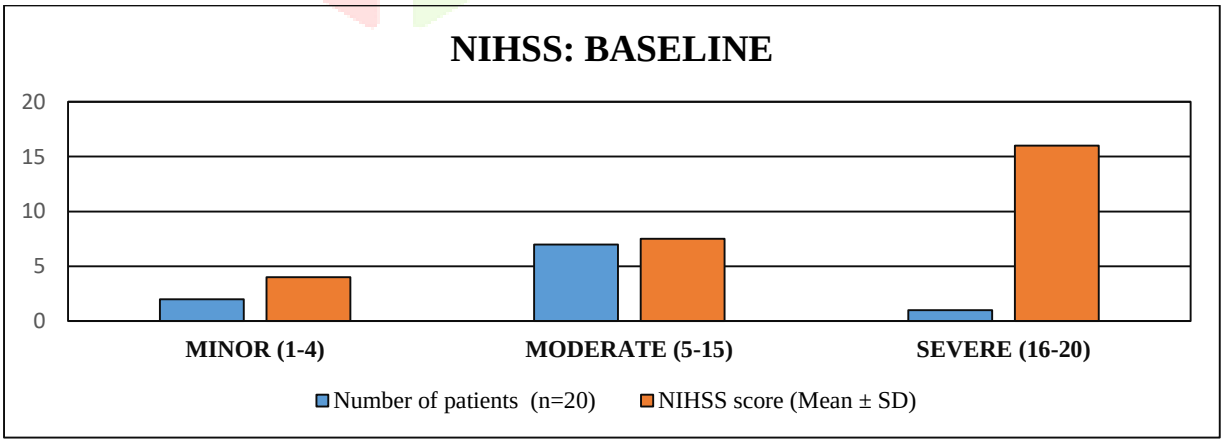

Table 11 show the neurological impairment of group B at the time of admission follow up 20% of patient had a minor neurological impairment and NIHSS Score was 4 and 70% of patient had a moderate neurological impairment and NIHSS score was 7.5±1.1and 10% of patient had a severe neurological impairment and NIHSS Score was 16.

FIRST FOLLOW-UP ASSESSMENT OF NEUROLOGICAL IMPAIRMENT:

The neurological impairment at the first follow-up of Group B is shown in the following table:

Neurological impairment	Number of patients (n=10)	NIHSS score (Mean ± SD)
Minor(1-4)	**4**	**2.75 ± 0.5**
Moderate(5-15)	**6**	**6.1 ± 1.6**
Severe(16-20)	**0**	**0**

Table:12 Neurological Improvement at first follow up of Group B

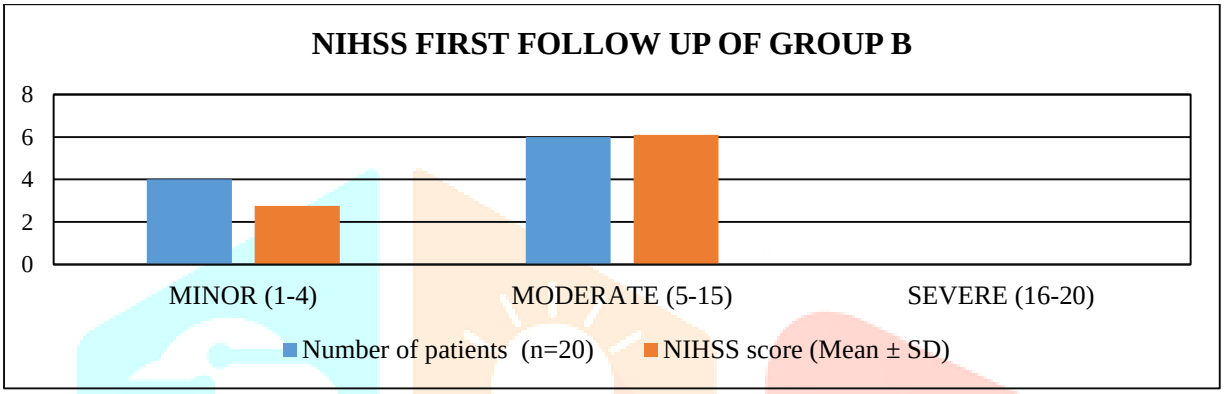

Figure:12 Neurological impairments at First follow-up of Group B

Table 12 shows the neurological impairment of group B at the time of the first follow up 40% of patients had a minor neurological impairment and the NIHSS Score was 2.75±0.5and 60% of patients had a moderate neurological impairment and the NIHSS score was 6.1±1.

SECOND FOLLOW-UP ASSESSMENT OF NEUROLOGICAL IMPAIRMENT:

The neurological impairment at the second follow-up of Group B is shown in the following table:

Neurological impairment	Number of patients (n=10)	NIHSS score (Mean ± SD)
Minor(1-4)	10	2.2 ± 1.15
Moderate(5-15)	0	0
Severe(16-20)	0	0

Table:13 Neurological Improvement at Second Follow-up of Group B

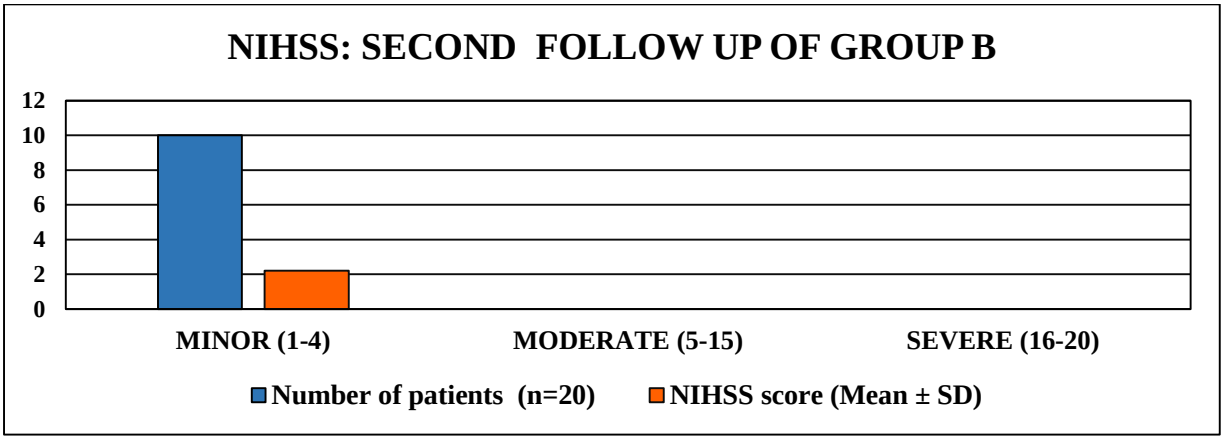

Figure:13 Neurological impairments at Second Follow-up of Group B

Table 13 shows the neurological impairment of group B at the time of the second follow up 100% of patients had a minor neurological impairment and NIHSS Score was 2.25±1.15.

THIRD FOLLOW-UP ASSESSMENT OF NEUROLOGICAL IMPAIRMENT:

The neurological impairment at the Third follow-up of Group B is shown in the following table:

Neurological impairment	Number of patients (n=10)	NIHSS score (Mean ± SD)
Minor(1-4)	10	2.2 ± 1.15
Moderate(5-15)	0	0
Severe(16-20)	0	0

Table:14 Neurological Improvement at Third Follow up of Group B

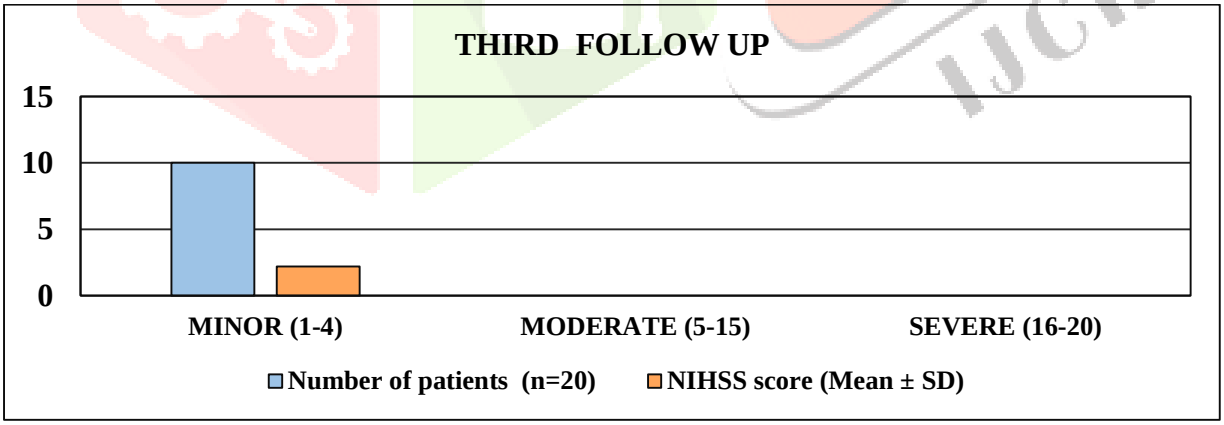

Figure: 14 Neurological Impairment at Third Follow-up of Group B

Table 14 shows the neurological impairment of group B at the time of the third follow up 100% of patients had a minor neurological impairment and NIHSS Score was 2.2±1.15.

COMPARING THE NEUROLOGICAL STATUS DURING EACH FOLLOW-UP:

The comparison of neurological improvement during each follow-up was home in the following table:

Review	NIHSS Score (Mean ± SD)
Baseline	7.7 ± 3.2
First follow-up	4.8 ± 2.03
Second follow-up	2.3 ± 1.1
Third follow-up	0.8 ± 1.8

Table: 15 Comparison of NIHSS scores at different follow up of a Group B

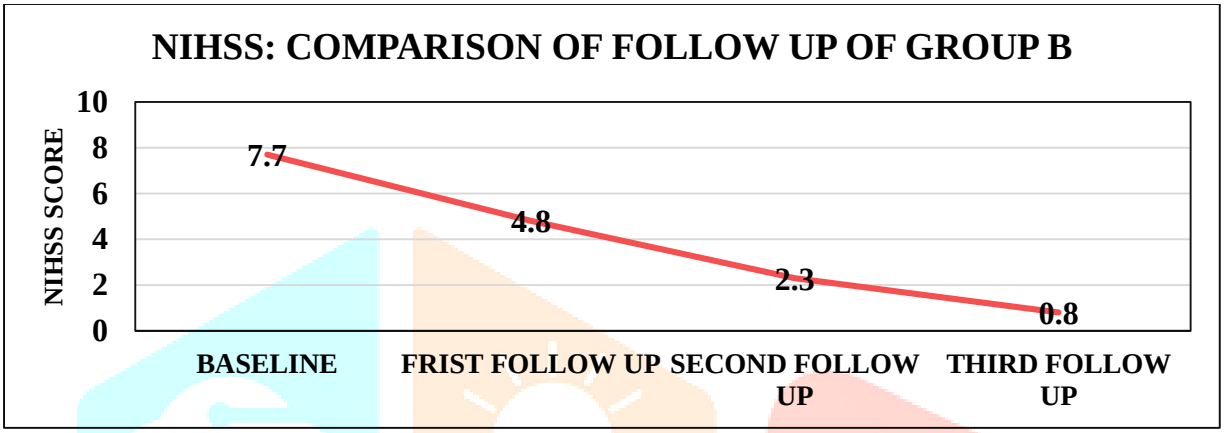

Figure: 15 Comparison of NIHSS score at different follow up of Group B

Table 15 shows, when comparing the neurological status during each follow up the baseline score was 7.7±3.2 and during the next follow-ups, the NIHSS Score decreases respectively.

COMPARISON OF NIHSS SCORE OF BOTH GROUP A & B:

GROUPS	BASELINE	END LINE
ALTEPLASE	6.5± 2.5	1.3 ± 0.7
TENECTEPLASE	7.7 ± 3.2	0.8 ± 1.8

Table: 16 Comparison of NIHSS score of both Groups

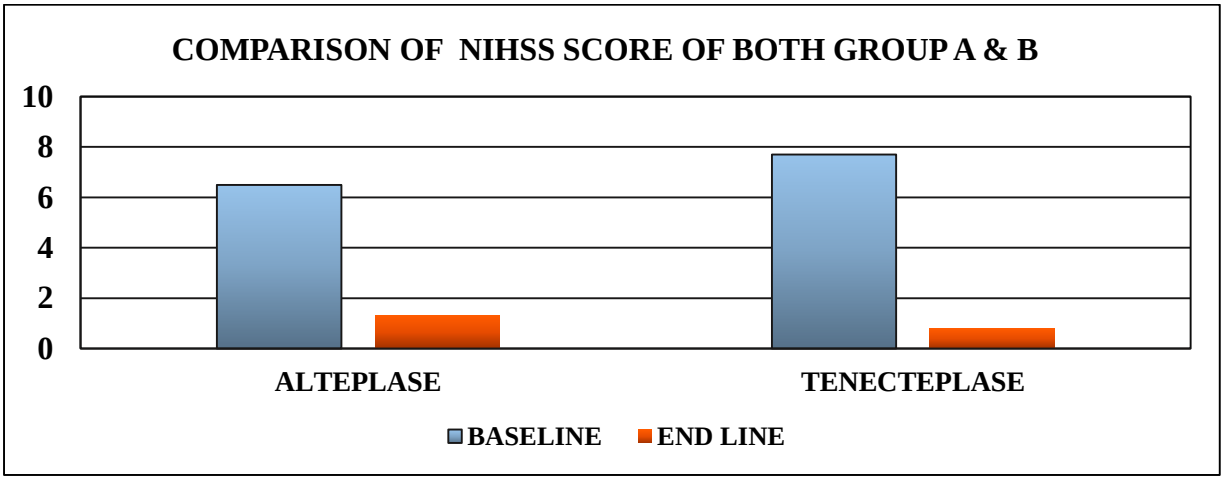

Figure: 16 Comparison of NIHSS score of both Groups A& B

Table 16, shows the comparison of NIHSS Scores of both A and B Groups. On evaluation, the NIHSS Score of Alteplase attained at the beginning was 6.5± 2.5, and end of study 1.3 ± 0.7 and the NIHSS Score of Tenecteplase attained at the beginning was 7.7 ± 3.2, and at the end of study 0.8 ± 1.8.

ASSESSMENT OF MRS SCORE OF ALTEPLASE:

MRS SCORE	Number of patients (n=10)	Percentage(%)
0- No symptoms at all	0	0%
1 -No significant disability	2	20%
2 -Slight disability	2	20%
3 -Moderate disability	4	40%
4-Moderately severe disability	2	20%
5- severe disability	0	0%
6-Dead	0	0%

Table:17 MRS Score at the time of admission -Group A

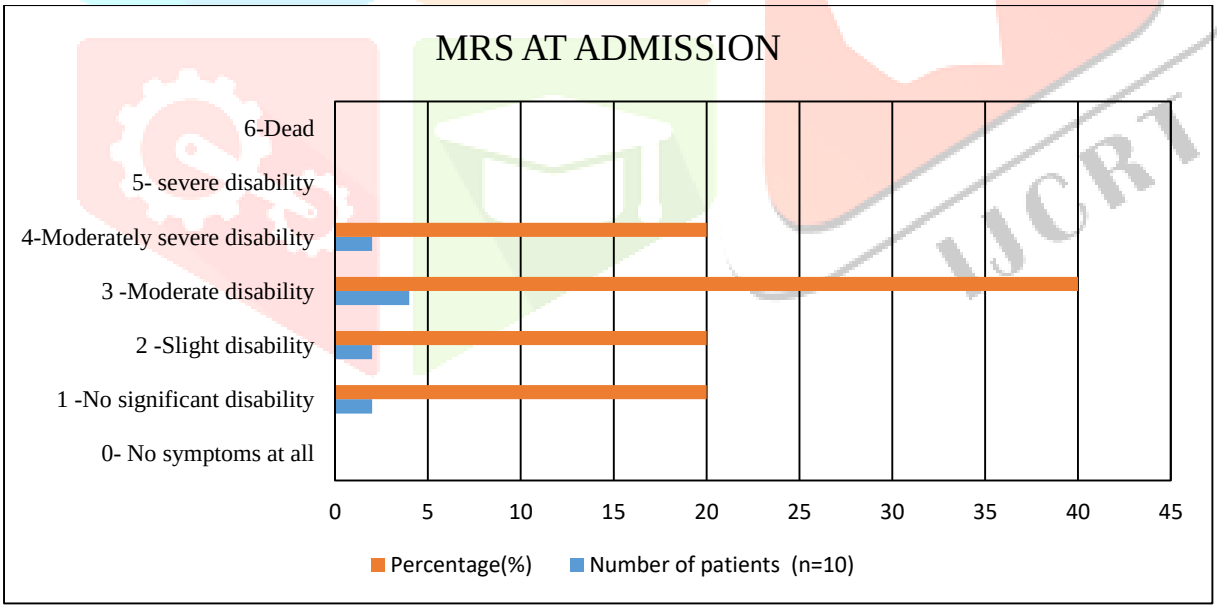

Table: 17 MRS Score at the time of admission -Group A

Table 17, shows the MRS score of group A at the time of admission, were 20% of the patient had MRS score of 1 with no significant disability, and 20% of the patients had the MRS score of 2 with slight disability, and 40% of patients had MRS score of 3 with moderate disability, and 20% of patient had MRS score of 4 with moderately severe disability.

MRS SCORE AT THE FIRST FOLLOW-UP OF GROUP A:

MRS SCORE	Number of patients (n=10)	Percentage(%)
0- No symptoms at all	0	0%
1 -No significant disability	2	20%
2 -Slight disability	6	60%
3 -Moderate disability	2	20%
4-Moderately severe disability	0	0%
5- severe disability	0	0%
6-Dead	0	0%

Table:18 MRS Score at First Follow-up of Group A

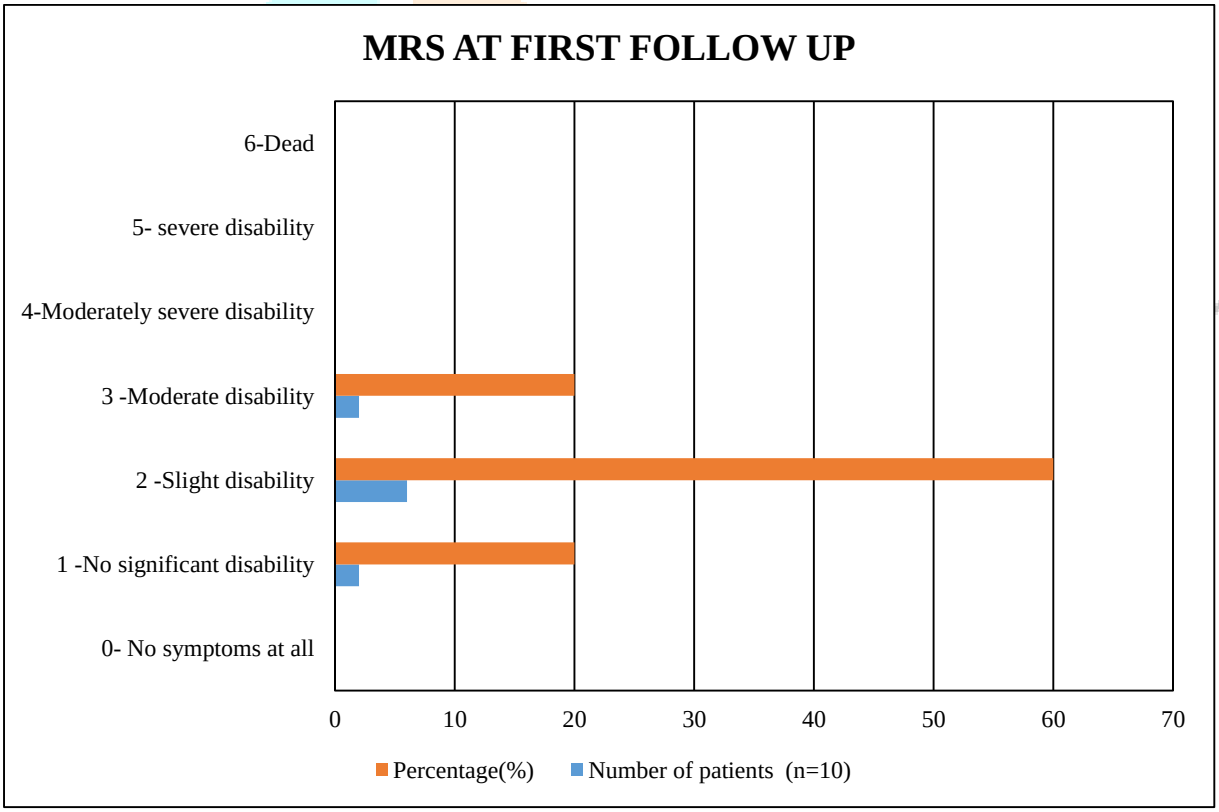

Table: 18 MRS Score First Follow-up of group A

Table 18, shows the MRS score of group A at the time of first follow up, were 20% of patients had MRS score of 1, and 60% of patients had MRS score of 2, and 20% of patients had MRS score of 3.

MRS SCORE AT THE SECOND FOLLOW-UP OF GROUP A:

MRS SCORE	Number of patients (n=10)	Percentage(%)
0- No symptoms at all	1	10%
1 -No significant disability	6	60%
2 -Slight disability	3	30%
3 -Moderate disability	0	0%
4-Moderately severe disability	0	0%
5- severe disability	0	0%
6-Dead	0	0%

Table:19 MRS Score at Second Follow-up of Group A

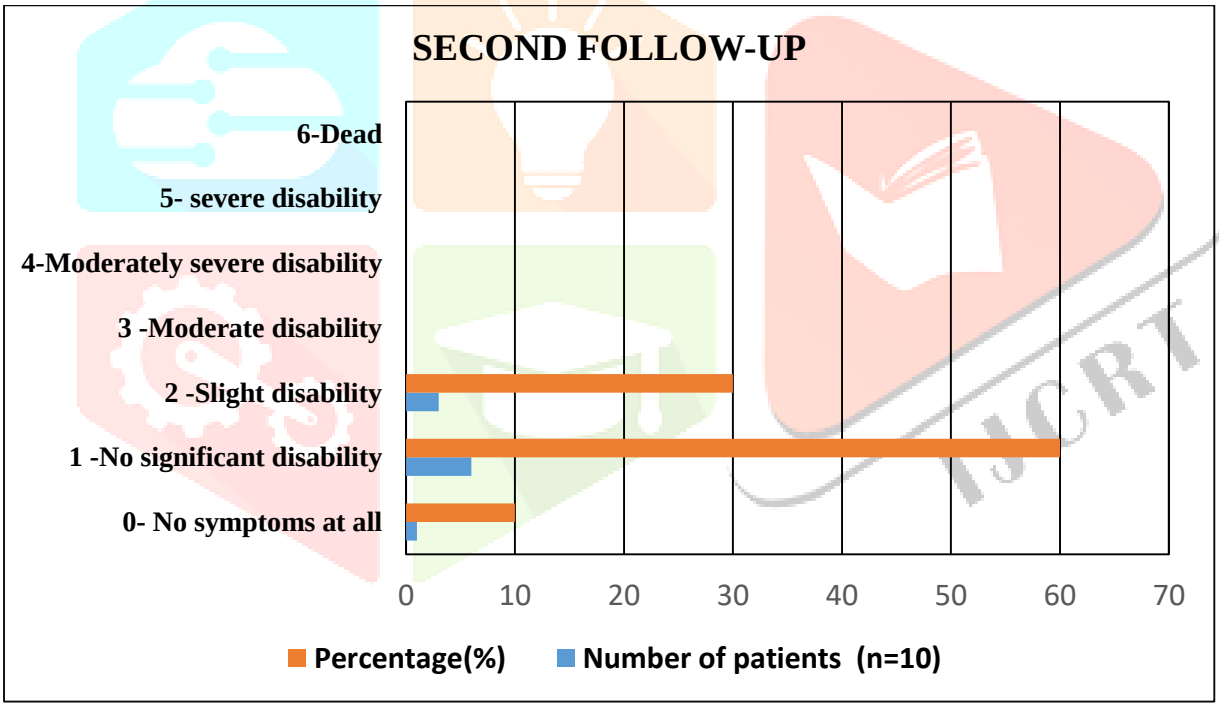

Figure:19 MRS Score at Second Follow-up of Group A

Table 19, shows the MRS score of group A at the second follow up, were 10% had MRS score of 0 with no symptoms, and 60% had MRS score of 1 with significant disabilities, and 30% had MRS score of 2 with slight disability.

MRS SCORE AT THE THIRD FOLLOW-UP OF GROUP A:

MRS SCORE	Number of patients (n=10)	Percentage(%)
0- No symptoms at all	3	30%
1 -No significant disability	6	60%
2 -Slight disability	1	10%
3 -Moderate disability	0	0%
4-Moderately severe disability	0	0%
5- severe disability	0	0%
6-Dead	0	0%

Table:20 MRS Score at third Follow-up of Group A

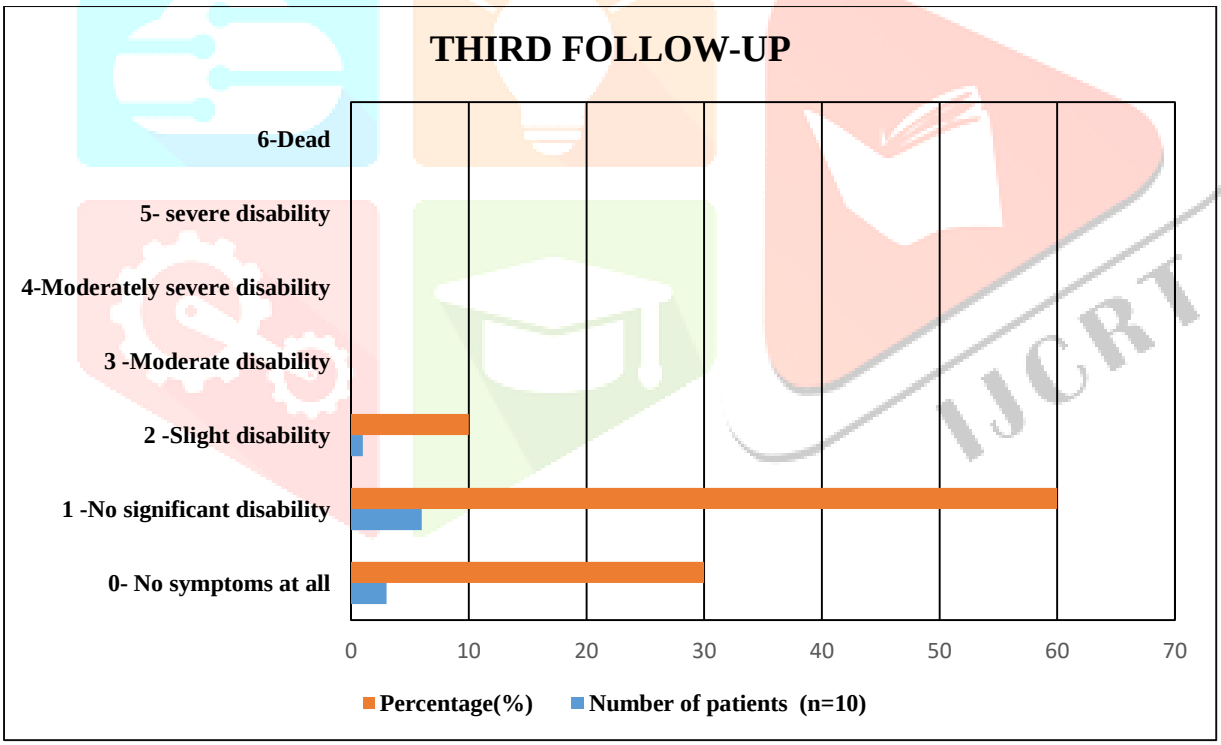

Figure:20 MRS Score at Third Follow-up of Group A

Table 20, shows the MRS score of group A at the third follow up, were 30% of patients had MRS score of 0, and 60% of patients had MRS score of 1, were 10 % of patients had MRS score of 2.

COMPARING THE MRS SCORE DURING EACH FOLLOW-UP OF GROUP A:

Review	MRS Score (Mean ± SD)
Baseline	2.6 ± 1
First follow up	2 ± 0.6
Second follow up	1.2 ± 0.6
Third follow up	0.8 ± 0.6

Table: 21 Comparison of MRS scores at different follow up of a Group A

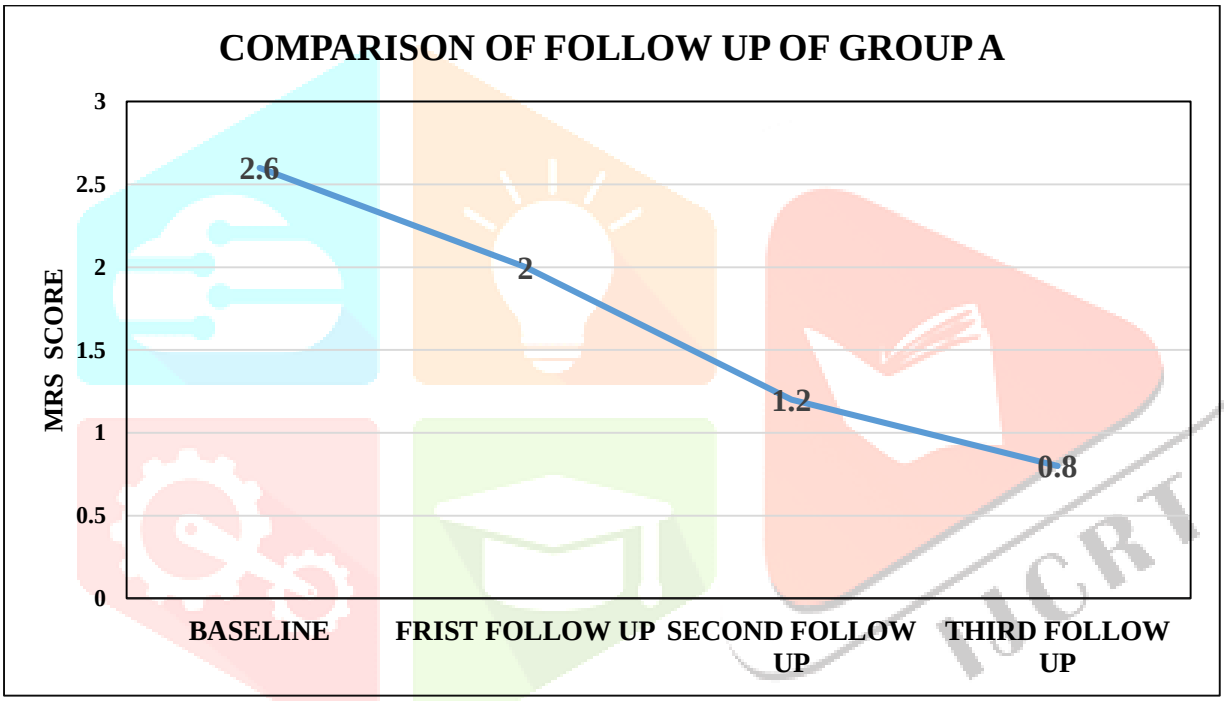

Figure: 21 Comparison of MRS scores at different follow up of a Group A

Table 21, shows the comparison of the MRS score between each follow ups of group A, where the MRS score is 2.6±1 at baseline, however, it drops with the successive follow-ups.

ASSESSMENT OF EFFECT OF TENECTEPLASE:

MRS SCORE AT TIME OF ADMISSION OF GROUP B:

MRS SCORE	Number of patients (n=10)	Percentage (%)
0- No symptoms at all	0	0%
1 -No significant disability	1	10%
2 -Slight disability	1	10%

3 -Moderate disability	5	50%
4-Moderately severe disability	3	30%
5- severe disability	0	0%
6-Dead	0	0%

Table: 22 MRS Score at the time of admission -Group B

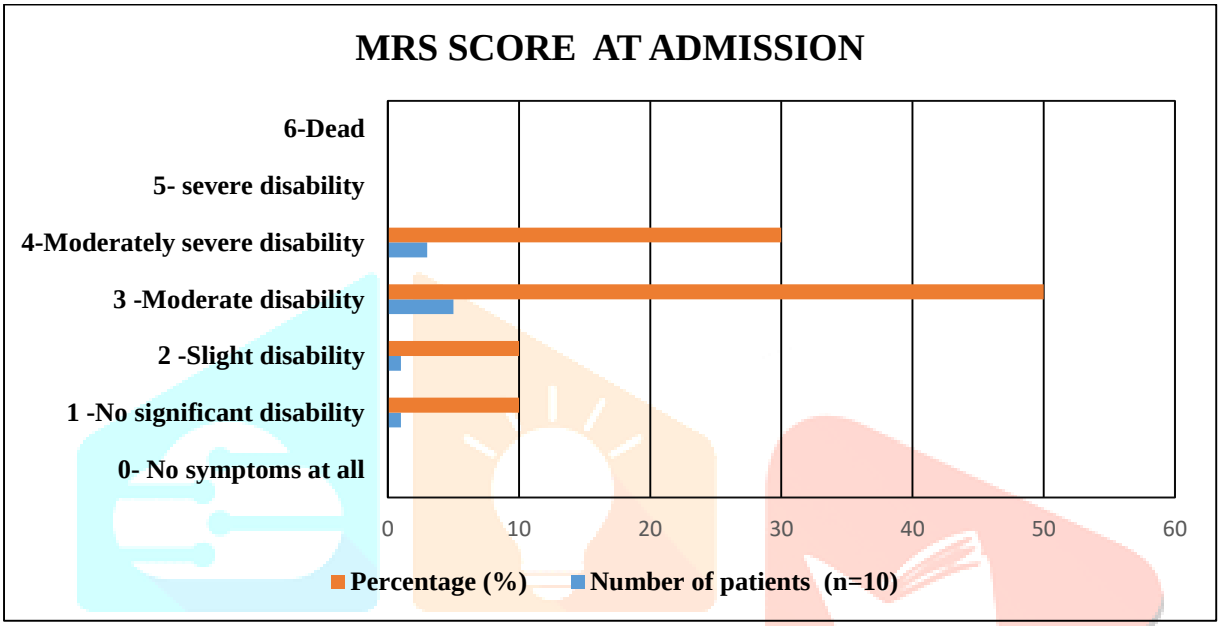

Table: 22 MRS Score at the time of Admission-Group B

Table 22 shows, the assessment on effect of Tenecteplase at the time of admission using MRS score, were 50% of patients had MRS score of 3, and 30% of patients were having MRS score of 4, and 1% of patients had MRS score of 2, and 10% of patients had MRS score of 1.

MRS SCORE AT THE FIRST FOLLOW-UP OF GROUP B:

MRS SCORE	Number of patients (n=10)	Percentage(%)
0- No symptoms at all	0	0%
1 -No significant disability	6	60%
2 -Slight disability	3	30%
3 -Moderate disability	1	10%
4-Moderately severe disability	0	0%
5- severe disability	0	0%
6-Dead	0	0%

Table:23 MRS Score at First Follow-up of Group B

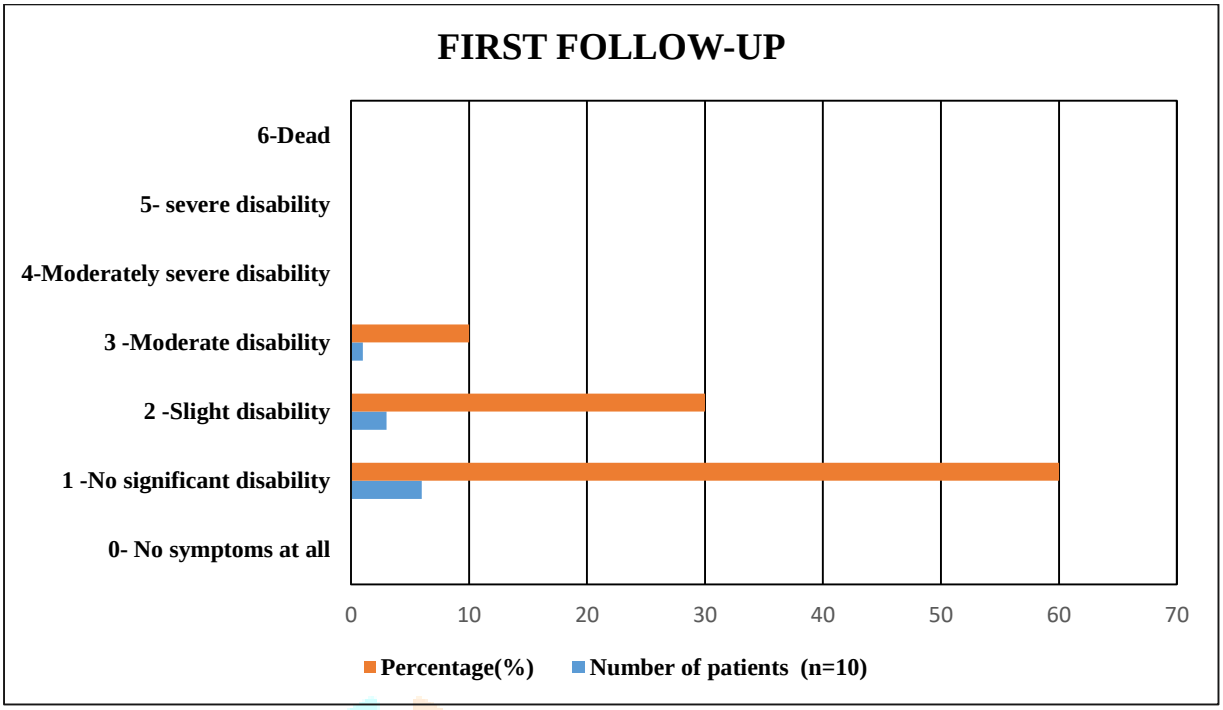

Table: 23 MRS Score First Follow-up of Group B

Table 23, shows the initial follow-up for group B using the MRS score. Were 60% had MRS score of 1, and 30% had an MRS score of 2, and 10% had an MRS score of 3.

MRS SCORE AT THE SECOND FOLLOW-UP OF GROUP B:

MRS SCORE	Number of patients (n=10)	PERCENTAGE (%)
0- No symptoms at all	9	90%
1 -No significant disability	0	0%
2 -Slight disability	1	2%
3 -Moderate disability	0	0%
4-Moderately severe disability	0	0%
5- severe disability	0	0%
6-Dead	0	0%

Table:24 MRS Score at Second Follow-up of Group B

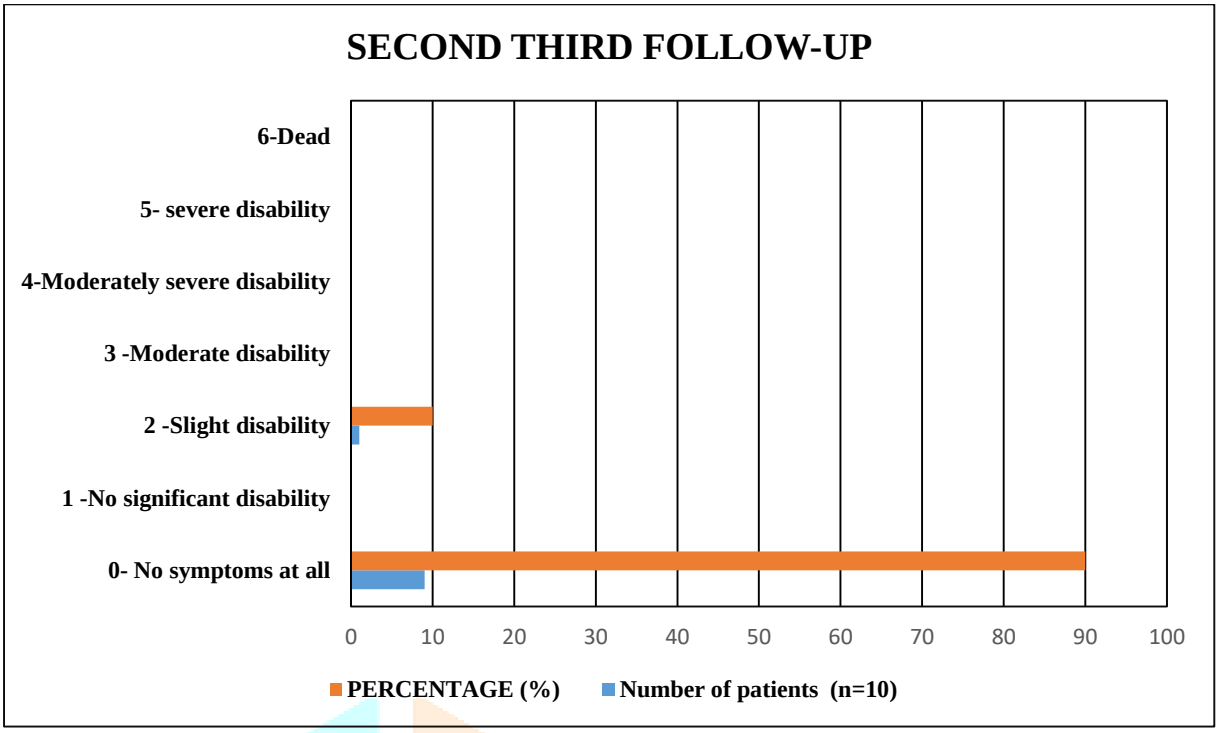

Figure:24 MRS Score at Second Follow-up of Group B

Table 24 shows the second follow-up of group B using MRS score, were 90% had an MRS score of 0 were free of symptoms of stroke, and 10% had an MRS score of 2 which is with slight disability.

MRS SCORE AT THE THIRD FOLLOW-UP OF GROUP B:

MRS SCORE	Number of patients (n=10)	MRS score (Mean ± SD)
0- No symptoms at all	9	90%
1 -No significant disability	0	0%
2 -Slight disability	1	10%
3 -Moderate disability	0	0%
4-Moderately severe disability	0	0%
5- severe disability	0	0%
6-Dead	0	0%

Table:25 MRS Score at Third Follow-up of Group B

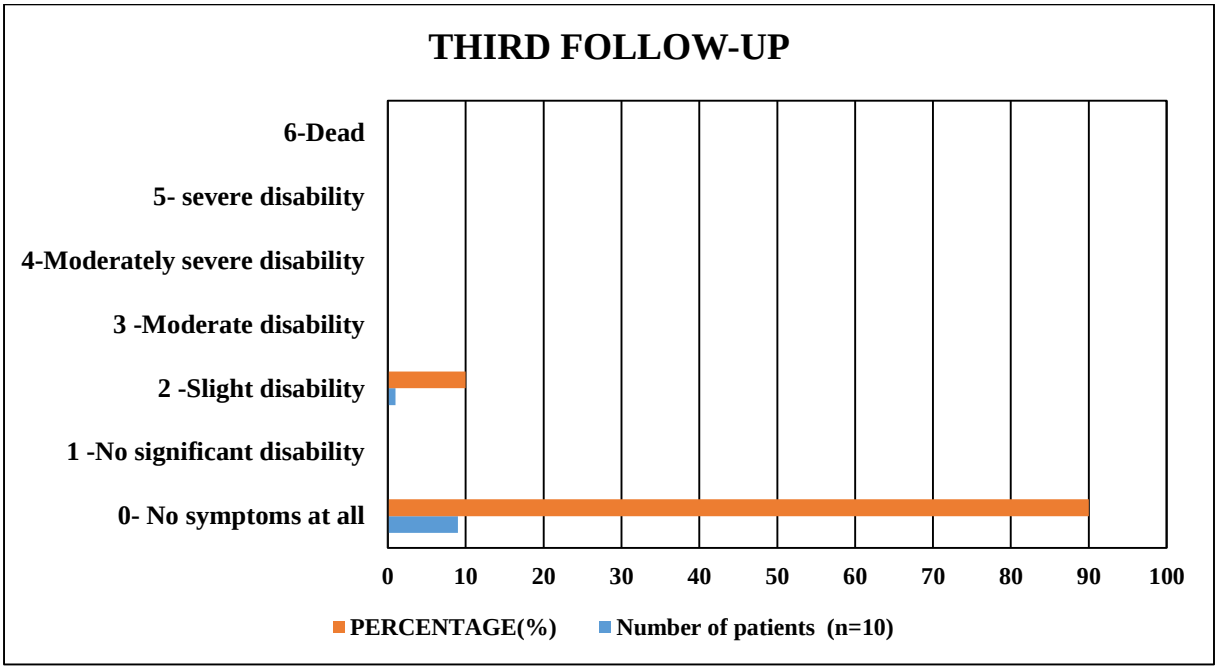

Figure:25 MRS Score at Third Follow-up of Group B

Table 25 shows, the third follow-up of group B using MRS score, where 90% had MRS score of 0 with free of symptoms, and 10% had an MRS score of 2 with a slight disability, which indicates a good improvement in patients of group B.

COMPARING THE MRS SCORE DURING EACH FOLLOW-UP OF GROUP B:

Review	MRS Score (Mean ± SD)
Baseline	3 ± 0.9
First follow-up	1.5 ± 0.7
Second follow-up	0.2 ± 0.6
Third follow-up	0.2 ± 0.6

Table: 26 Comparison of MRS scores at different follow up of a Group B

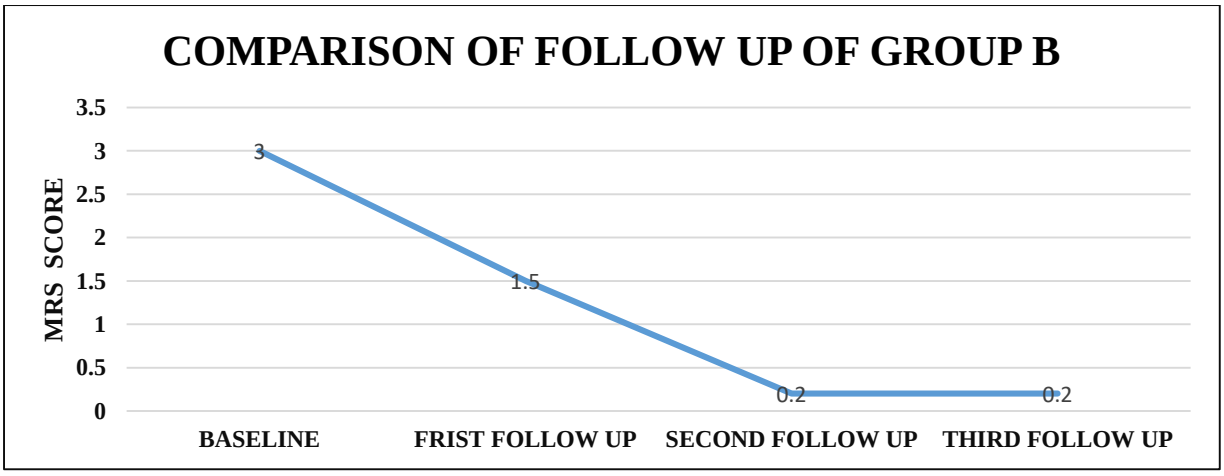

Figure: 26 Comparison of MRS scores at different follow up of a Group B

Table 26 shows using MRS scores each follow-up from group B was compared to each other were it shows MRS score of 3±0.9 and the scores declines during further follow ups respectively

COMPARISON OF MRS SCORE OF BOTH GROUP A & B:

GROUPS	BASE LINE	END LINE
ALTEPLASE	2.6 ± 1	0.8 ± 0.6
TENECTEPLASE	3 ± 0.9	0.2 ± 0.6

.

Table: 27 Comparison of MRS score of both Groups

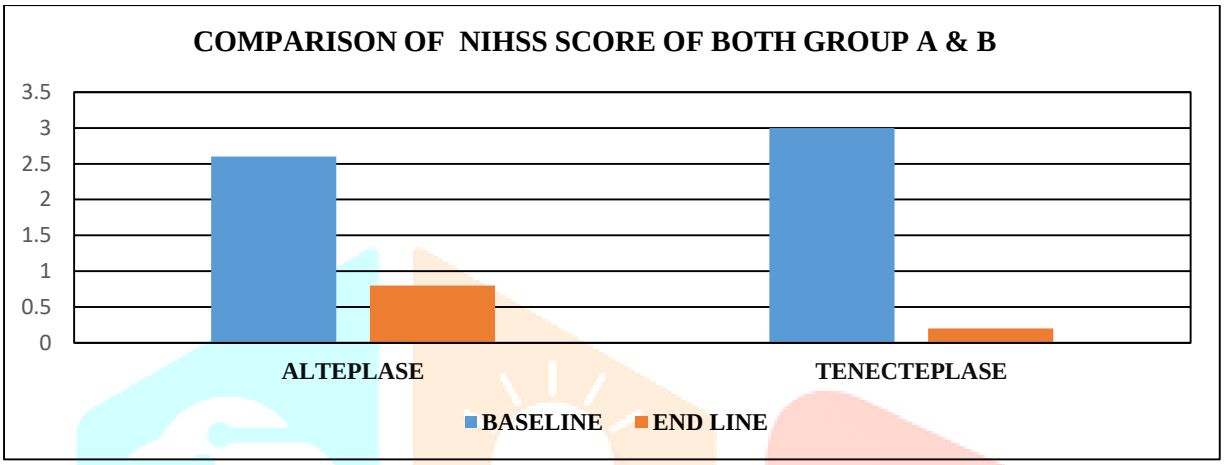

Figure: 27 Comparison of MRS score of both Groups

Table 27 shows the comparison of the MRS score of both groups A and B. On assessment, the MRS Score of Alteplase obtained at the beginning was 2.6± 1 and at the end of the study the score obtained was 0.8± 0.6 and the MRS Score of Tenecteplase obtained at the beginning was 3 ± 0.9 and at the end of the study the score obtained was 0.2 ± 0.6.

ASSESSMENT OF QUALITY OF LIFE OF ALTEPLASE BY USING STROKE-SPECIFIC QUALITY OF LIFE SCALE (SS-QOL):

Review	MRS Score (Mean ± SD)
First follow up	65.3 ± 12.4
Second follow up	119.9 ± 20.3
Third follow up	153.7 ± 37.3

Table: 28 Comparison of SS-QOL score of Group A

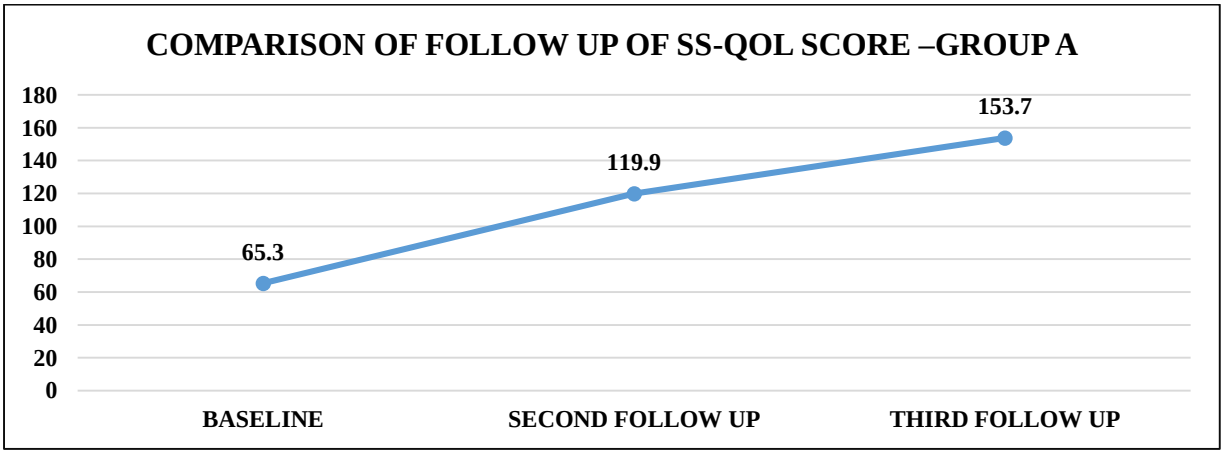

Figure: 28 Comparison of SS-QOL score of Group B

Table 28 shows, the assessment of the follow-up of the quality of life of Alteplase by using the Stroke Specific Quality of Life Scale (SS-QOL). In the initial follow up the score was 65.3 ± 12.4 and increased in the subsequent follow-ups to 119.9 ± 20.3 and 153.7 ± 37.3.

ASSESSMENT OF QUALITY OF LIFE OF TENECTEPLASE BY USING STROKE-SPECIFIC QUALITY OF LIFE SCALE (SS-QOL):

Review	MRS Score (Mean ± SD)
First follow up	101.9 ± 24
Second follow up	160.9 ± 17.5
Third follow up	210.7 ± 10.6

Table: 29 Comparison of SS-QOL score of Group B

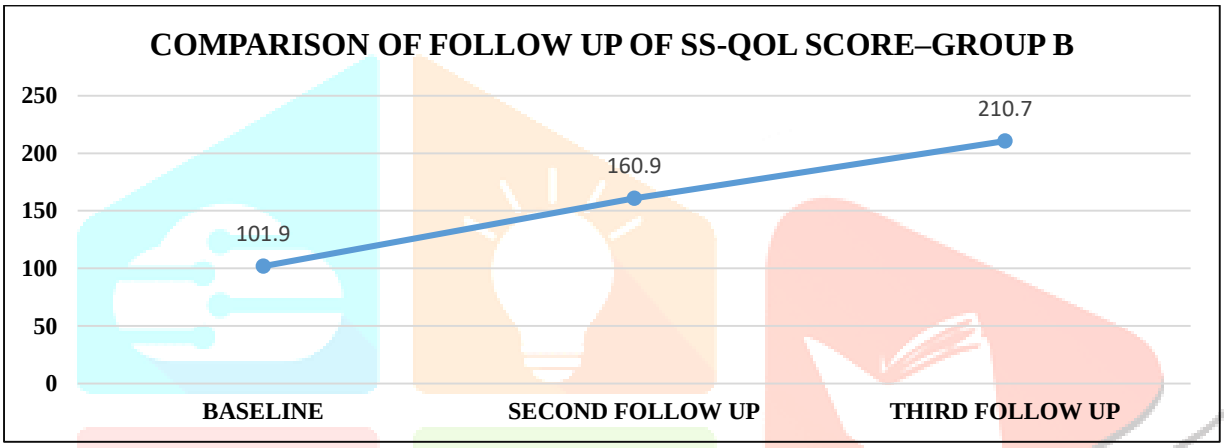

Figure: 29 Comparison of SS-QOL score of Group B

Table 29 shows, the assessment of the follow-ups of quality of life of Tenecteplase by using Stroke Specific Quality of Life(SS-QOL). In the initial follow up the score was 101.9±24 and increases in the subsequent follow ups160.9 ± 17.5 and 210.7 ± 10.6. The observed difference was $p<0.001$ which is statistically significant($p<0.05$).

COMPARISON OF SS-QOL SCORE OF BOTH GROUPS A & B

GROUPS	BASELINE	END LINE
ALTEPLASE	65.3 ± 12.4	153.7 ± 37.3
TENECTEPLASE	101.9 ± 25	210.7 ± 10.6

Table: 30 Comparison of SS-QOL score of both Groups

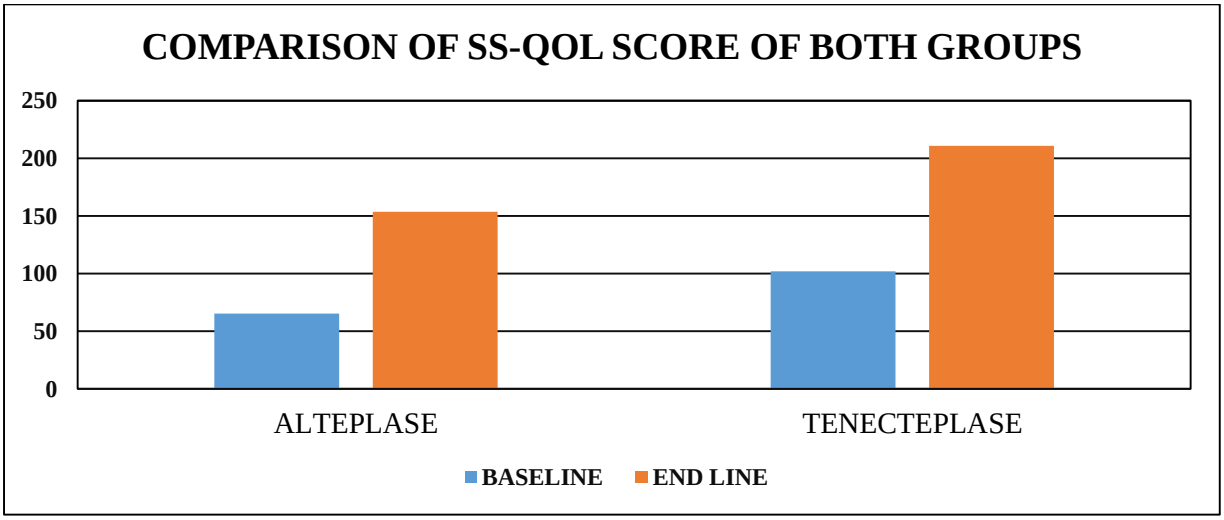

Figure: 30 Comparison of SS-QOL score of both Groups

Table 30 shows the comparison of SS-QOL of groups A and B. On assessment, the score of SS-QOL for group A obtained at the beginning was 65.3±12.4 and at the end of the study the score obtained was 153.7± 37.3, and for group B the score obtained at the beginning was 101.9±25 and at the end of the study the score obtained was 210.7±10.6.

ASSESSMENT OF HOSPITAL ANXIETY AND DEPRESSION SCALE (HADS) IN GROUP A:

ASSESSMENT OF ANXIETY IN GROUP-A AT FIRST FOLLOW-UP:

HADS SCOREC	Number of patients (n=10)	ANXIETY score (Mean ± SD)
Normal (0-7)	0	0
Borderline (8-10)	0	0
Abnormal (11-21)	10	15 ± 1.4

Table: 31 Assessment of Anxiety at First Follow-up in Group A

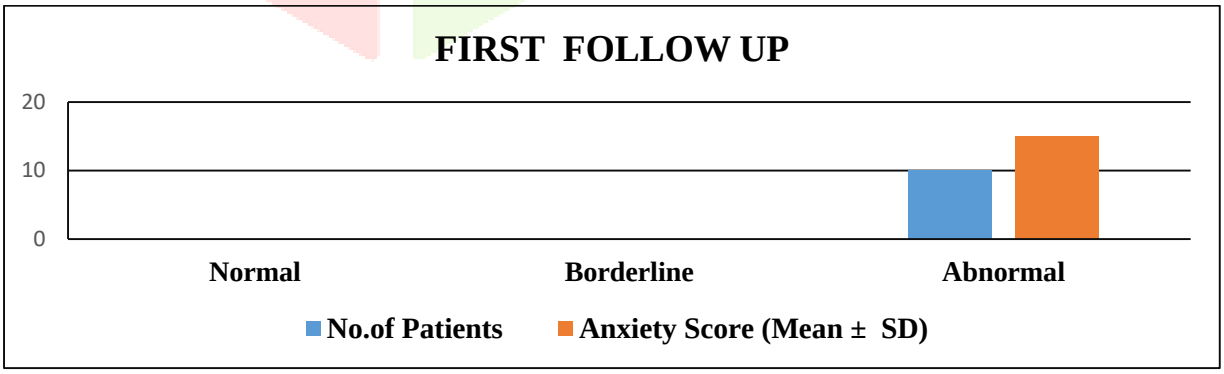

Figure: 31 Assessment of Anxiety at First Follow-up in Group A

From table 31, it has been observed, the initial follow-up of anxiety levels in group A using the HADS scale. Where 100% of the patients had an anxiety score of 15 ± 1.4 during the initial follow-up.

ASSESSMENT OF ANXIETY IN GROUP-A AT SECOND FOLLOW-UP:

HADS SCORE	Number of patients (n=10)	ANXIETY score (Mean ± SD)
Normal (0-7)	0	0
Borderline (8-10)	1	10
Abnormal (11-21)	9	11.8 ± 1.3

Table: 32 Assessment of Anxiety at Second Follow-up in Group A

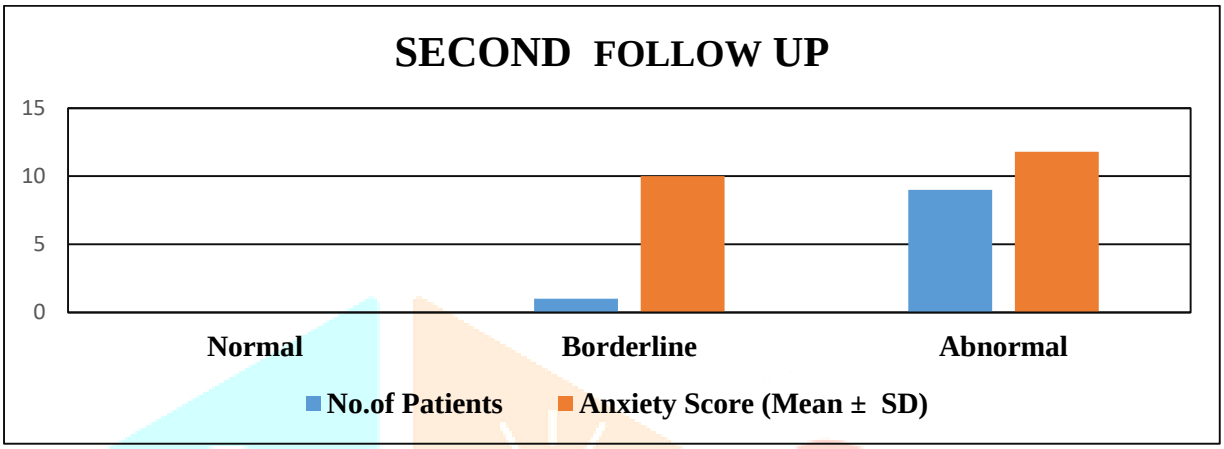

Figure: 32 Assessment of Anxiety at Second Follow-up in Group B

From table 32, it shows the assessment of anxiety level in group A at the second follow up where 90% of patients had an anxiety score of 11.8 ±3, indicating a high degree of anxiety, and 10% had a borderline anxiety score of 10 which shows a slight improvement in the second follow up when compared with first follow up.

ASSESSMENT OF ANXIETY IN GROUP-A AT THIRD FOLLOW-UP

HADS SCORE	Number of patients (n=10)	ANXIETY score (Mean ± SD)
Normal (0-7)	8	5.75 ± 1.5
Borderline (8-10)	2	8
Abnormal (11-21)	0	0

Figure: 33 Assessment of Anxiety at Third Follow-up in Group A

From Table 33, at the third follow-up, the level of anxiety in group A was evaluated and it was observed that 80% of the patients had an anxiety score of 5.75±1.5 and 20% of the patients had an anxiety score of 8 which, when compared to the earlier assessments, shows that the group A patients have improved more.

COMPARISON OF ANXIETY SCORE IN GROUP A:

Review	ANXIETY Score (Mean ± SD)
First follow up	15.8 ± 1.4
Second follow-up	11.7 ± 1.4
Third follow-up	6.2 ± 1.6

Table: 34 Comparison of Anxiety in Group A

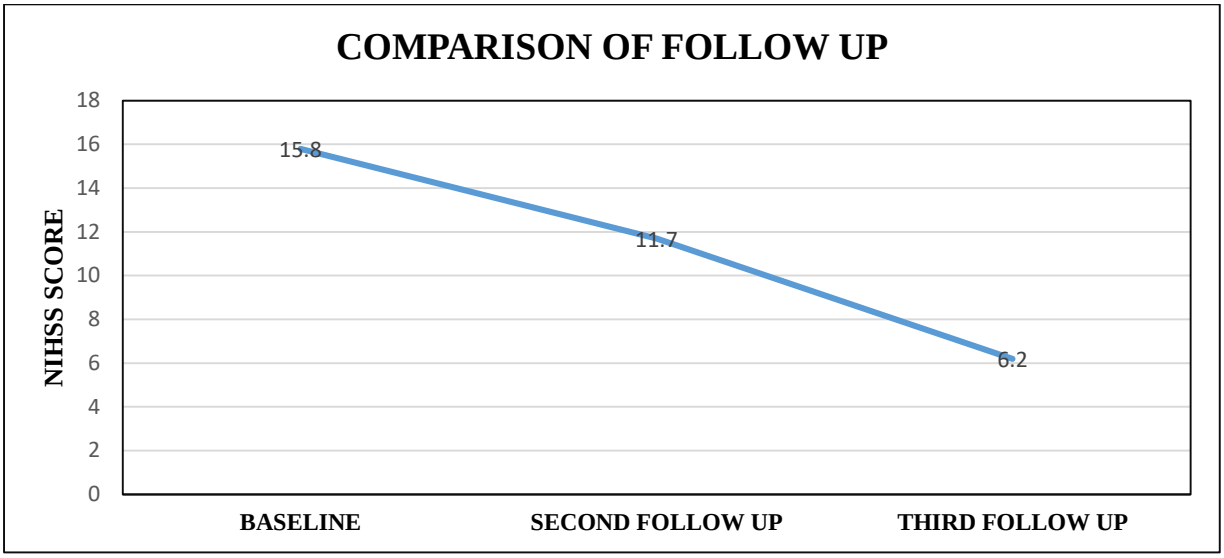

Figure: 34 Comparison of Anxiety in Group A

From Table 34, observations on the comparability of the anxiety score in group A were made in accordance with the reviews. The initial review shows an anxiety score of 15.8±1.4 and further declining in the subsequent follow-ups.

ASSESSMENT OF DEPRESSION IN GROUP-A AT FIRST FOLLOW UP:

HADS SCORE	Number of patients (n=10)	DEPRESSION score (Mean ± SD)
Normal (0-7)	0	0
Borderline (8-10)	0	0
Abnormal (11-21)	10	17.7 ± 2.5

Table: 35 Assessment of Depression at First Follow-up in Group A

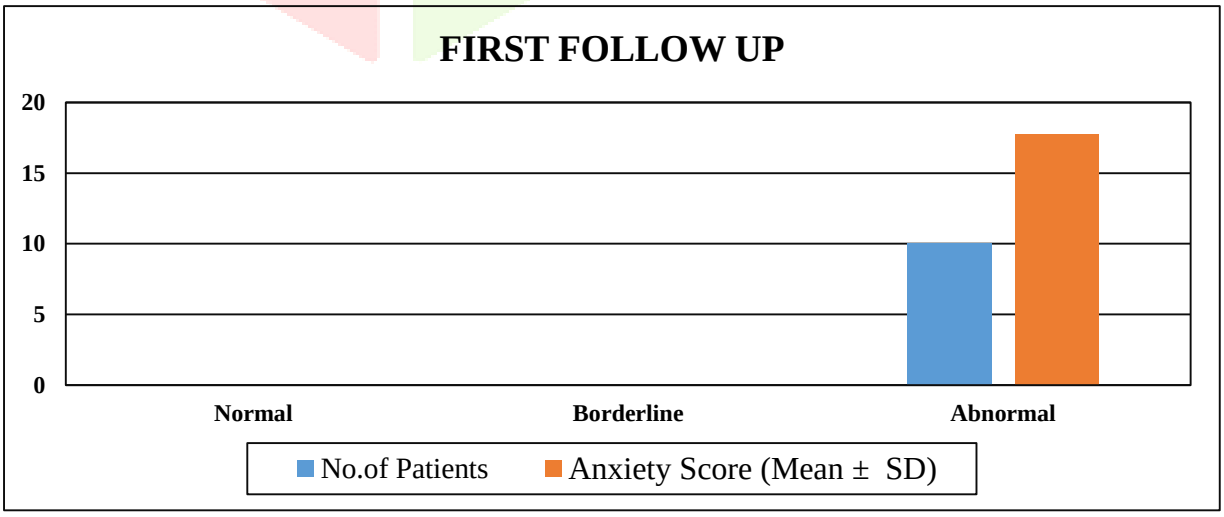

Figure: 35 Assessment of Depression at First Follow-up in Group A

Table 35 displays the evaluation of depression in group A at the first follow-up. Where it has been observed that 10% of the patient had a depression score of about 17.7±2.5.

ASSESSMENT OF DEPRESSION IN GROUP -A AT THE SECOND FOLLOW-UP

HADS SCORE	Number of patients (n=10)	DEPRESSION score (Mean ± SD)
Normal (0-7)	0	0
Borderline (8-10)	4	9.75 ± 0.5
Abnormal (11-21)	6	12.3 ± 1.9

Figure: 36 Assessment of Depression at Second Follow-up in Group A

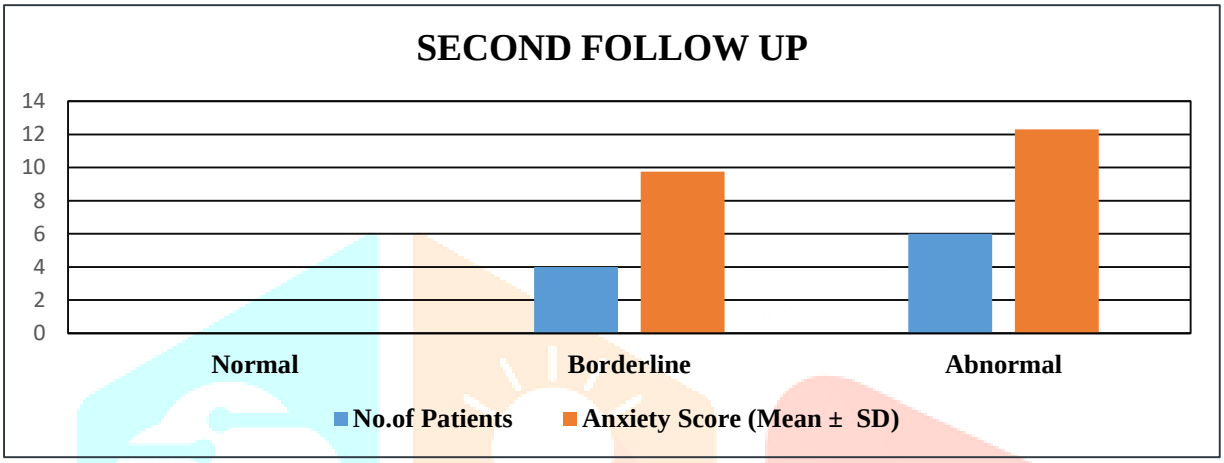

Figure: 36 Assessment of Depression at Second Follow-up in Group A

From Table 36, an assessment of depression in group A at the second follow-up was noted, where it was observed that about 60% of patients were having a depression score of 12.3±1.9 and about 40% of patients were having a depression score of 9.75±0.5.

ASSESSMENT OF DEPRESSION IN GROUP -A AT THE THIRD FOLLOW-UP:

HADS SCORE	Number of patients (n=10)	DEPRESSION score (Mean ± SD)
Normal (0-7)	8	4.1 ± 2.1
Borderline (8-10)	2	8
Abnormal (11-21)	0	0

Figure: 37 Assessment of Depression at Third Follow-up in Group A

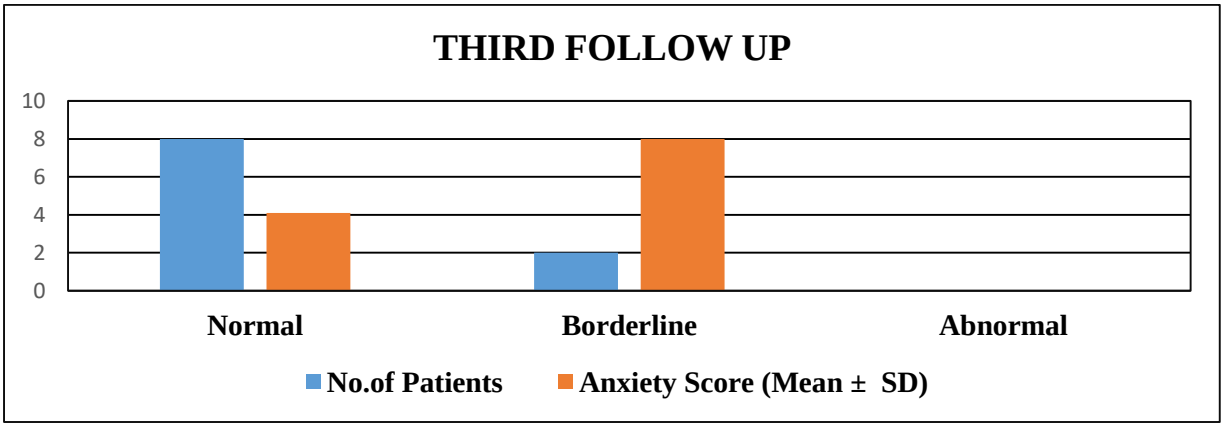

Figure: 37 Assessment of Depression at Third Follow-up in Group A

From Table 37, the third follow-up of depression in group A has been evaluated. This shows 80% of patients had a depression score of about 4.1±2.1 and 20% of patients had a depression score of 8 which shows improvement in these patients.

COMPARISON OF DEPRESSION SCORE IN GROUP A:

Review	DEPRESSION Score (Mean ± SD)
First follow up	17.7 ± 2.5
Second follow-up	11.3 ± 2
Third follow-up	4.9 ± 2.4

Table: 38 Comparison of Depression in Group A

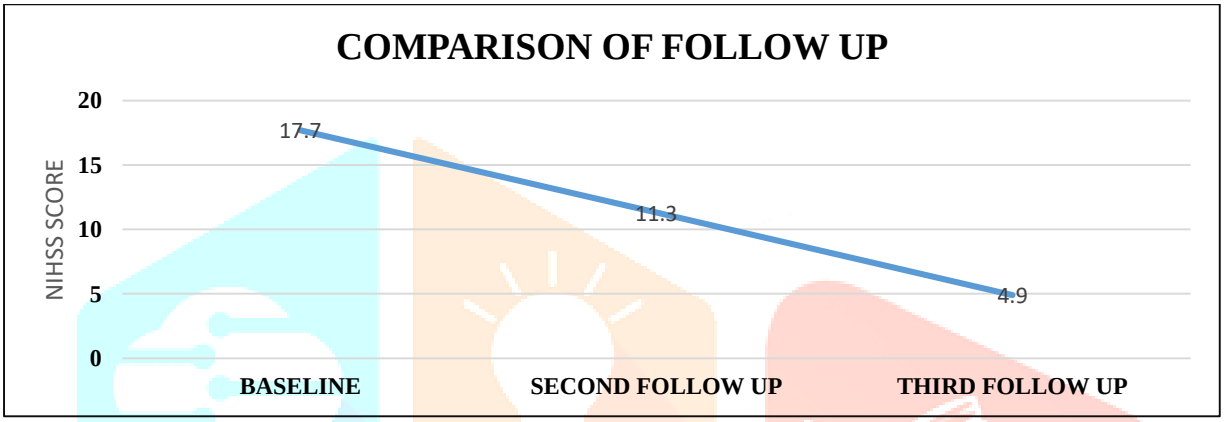

Figure: 38 Comparison of Depression in Group A

Table 38 shows the comparison of depression between three reviews of group A where it demonstrates the increased score in the initial follow-up and decline in the further follow-ups and shows the betterment in those patients. The observed difference was $p<0.001$ which is statistically significant($p<0.05$).

COMPARISON OF HADS SCORE IN GROUP A:

HADS	BASELINE	END LINE
ANXIETY	17.7 ± 2.5	4.9 ± 2.4
DEPRESSION	15.8 ± 1.4	6.2 ± 1.6

Table: 39 Comparison of HADS Score in Group A

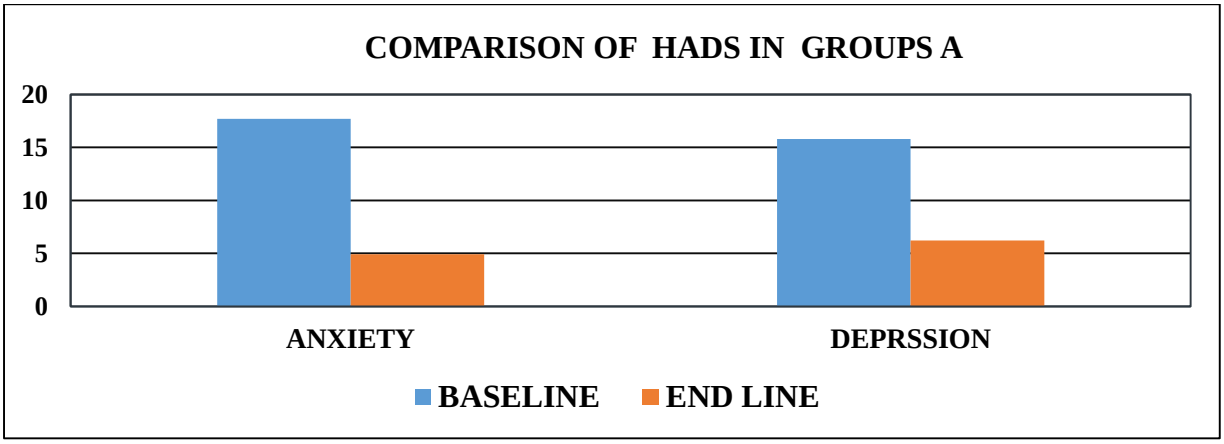

Table: 39 Comparison of HADS Score in Group A

Table 39, shows the complete comparison of HADS in group A patient, in which it was discovered that the anxiety score for group A was 17.7±2.5 at the start of the study and 4.9±2.4 at the end of the study, while the depression score was 15.8±1.4 at the start of the study and 6.2±1.6 at the end of the study.

ASSESSMENT OF HOSPITAL ANXIETY AND DEPRESSION SCALE (HADS) IN GROUP B:

ASSESSMENT OF ANXIETY IN GROUP-B AT FIRST FOLLOW UP:

HADS SCORE	Number of patients (n=10)	ANXIETY score (Mean ± SD)
Normal (0-7)	0	0
Borderline (8-10)	2	8.5 ± 0.7
Abnormal (11-21)	8	14 ± 2.9

Table: 40 Assessment of Anxiety at First Follow-up in Group B

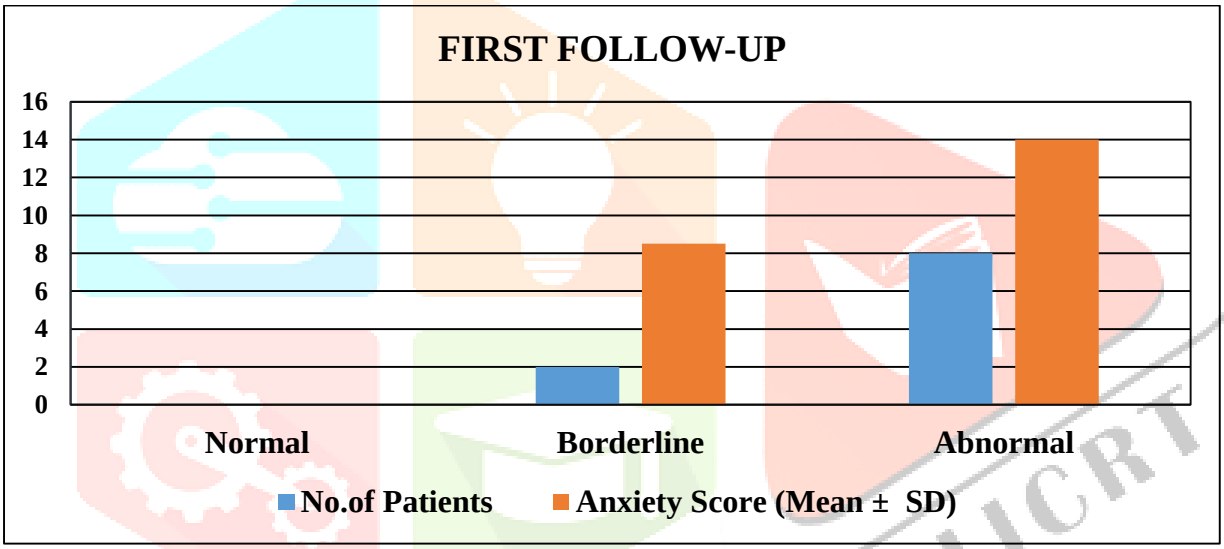

Figure: 40 Assessment of Anxiety at First Follow-up in Group B

From table 40, it shows the assessment of anxiety in group B at the first follow up where 80% of the patients had an anxiety score of 14±2.9 and 20% of the patients had a score of about 8.5±0.7.

ASSESSMENT OF ANXIETY IN GROUP B AT THE SECOND FOLLOW-UP:

HADS SCORE	Number of patients (n=10)	ANXIETY score (Mean ± SD)
Normal (0-7)	3	5.3 ± 1.5
Borderline (8-10)	3	8.6 ± 0.5
Abnormal (11-21)	4	13.2 ± 2.6

Table: 41 Assessment of Anxiety at Second Follow-up in Group B

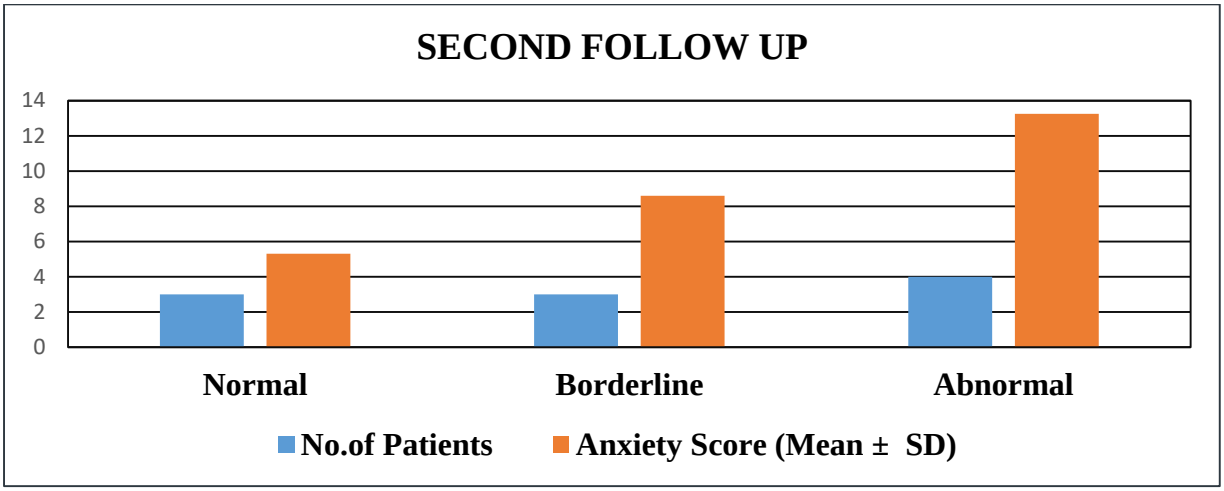

Figure: 41 Assessment of Anxiety at Second Follow-up in Group B

From table 41, it shows the assessment of anxiety in group B at the second follow up 40% of the patient had an anxiety score of 13.2±2.6 and 30% of the patient scored about 8.6±0.5 and 30% of the patient had a score of about 5.3±1.5. On evaluation, it shows a little improvement from the previous review.

ASSESSMENT OF ANXIETY IN GROUP B AT THIRD FOLLOW-UP:

HADS SCORE	Number of patients (n=10)	ANXIETY score (Mean ± SD)
Normal (0-7)	10	4.8 ± 1.9
Borderline (8-10)	0	0
Abnormal (11-21)	0	0

Table: 42 Assessment of Anxiety at Third Follow-up in Group B

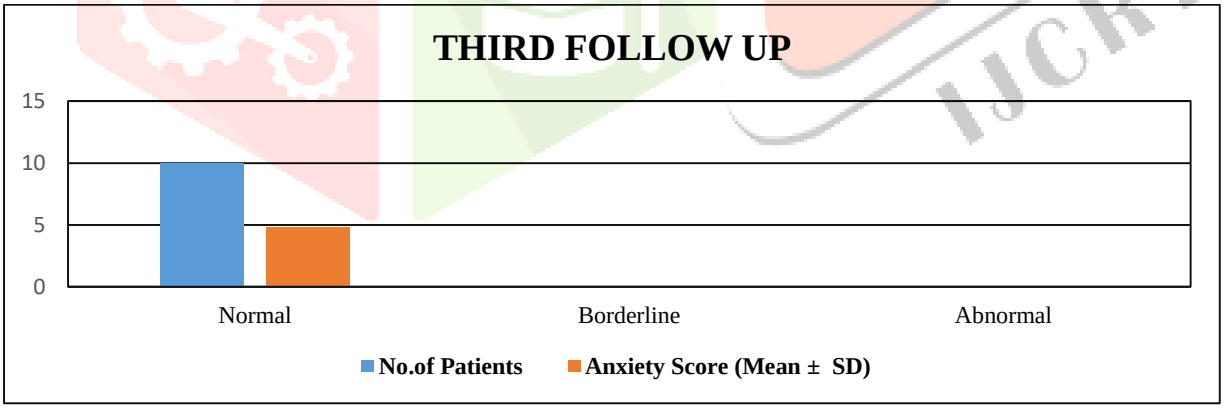

Figure: 42 Assessment of Anxiety at Third Follow-up in Group B

Table 42 shows the assessment of anxiety in group B at third follow up where 100% of the patients had a score of about 4.8±1.9 which shows a better improvement from previous two reviews.

COMPARISON OF ANXIETY SCORE IN GROUP B:

Review	ANXIETY Score (Mean ± SD)
First follow up	12.9 ± 3.5
Second follow-up	9.5 ± 3.8
Third follow-up	4.8 ± 1.9

Table: 43 Comparison of Anxiety in Group B

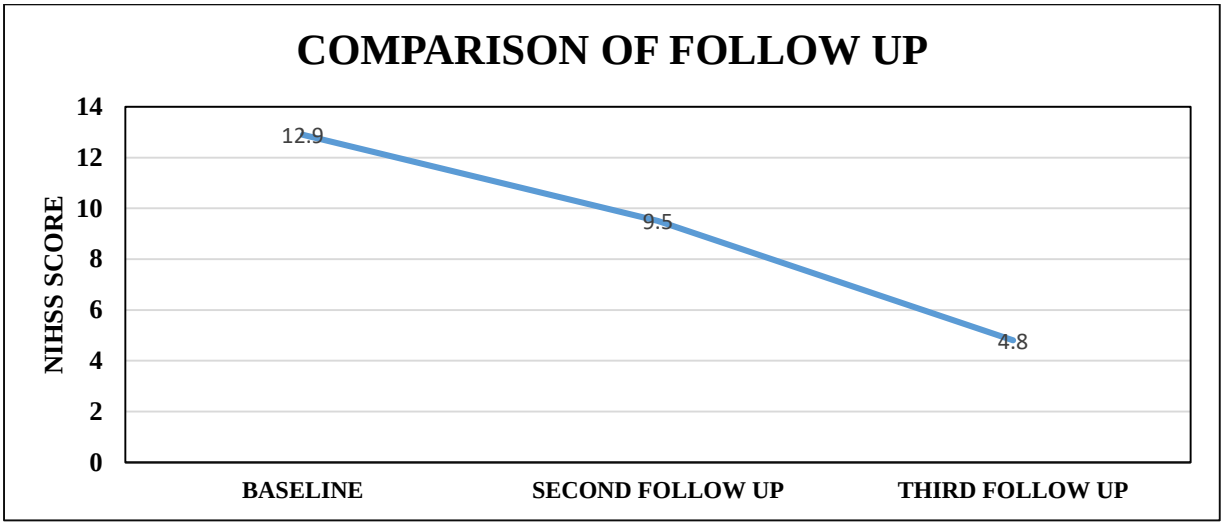

Figure: 43 Comparison of Anxiety in Group B

Table 43 shows the comparison between three follow-ups of anxiety scores in group B. On evaluation, the score shows 12.9±3.5 at the initial follow-up, and the score declines at the subsequent follow-ups. The score declining indicates the better improvement in group B patients, where the observed difference is $p<0.001$ which is statistically significant ($p<0.05$).

ASSESSMENT OF DEPRESSION IN GROUP-B AT FIRST FOLLOW UP:

HADS SCORE	Number of patients (n=10)	DEPRESSION score (Mean ± SD)
Normal (0-7)	0	0
Borderline (8-10)	2	8.5 ± 0.7
Abnormal (11-21)	8	14 ±2.9

Table: 44 Assessment of Depression at First Follow-up in Group B

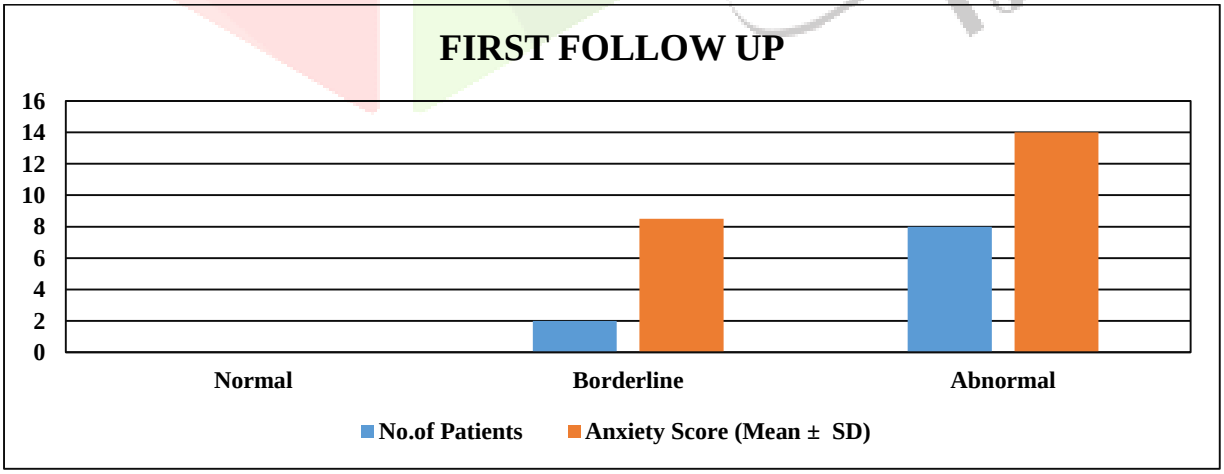

Table: 44 Assessment of Depression at First Follow-up in Group B

Table 44 shows the assessment of depression in group B at their first follow-up, where 80% of the patients had a depression score of about 14±2.9 whereas 20% of the patients had a score of 8.5±0.7. On assessment, it describes the degree of depression as borderline and in the abnormal range.

ASSESSMENT OF DEPRESSION IN GROUP -B AT THE SECOND FOLLOW-UP:

HADS SCORE	Number of patients (n=10)	DEPRESSION score (Mean ± SD)
Normal (0-7)	5	4.8 ± 1.4
Borderline (8-10)	2	10
Abnormal (11-21)	3	11.6 ± 0.5

Table: 45 Assessment of Depression at Second Follow-up in Group B

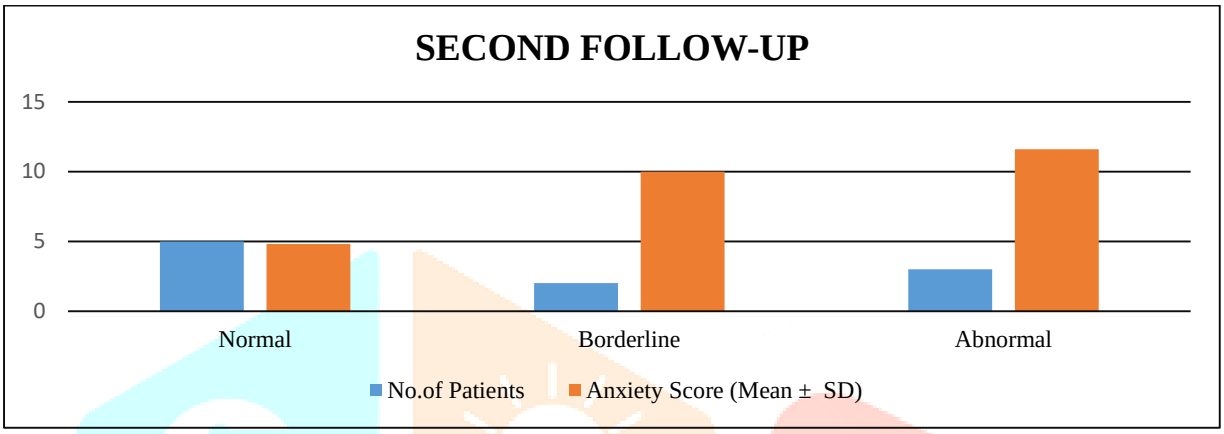

Figure:45 Assessment of Depression at Second Follow-up in Group B

Table 45 shows the assessment of depression in group B at their second follow-up. On evaluation, it shows 50% of the patients had a score of 4.8±1.4 and about 30% of the patients had a score of 11.6±0.5 and 20% of the patients had a score of 10.

ASSESSMENT OF DEPRESSION IN GROUP -B AT THE THIRD FOLLOW-UP:

HADS SCORE	Number of patients (n=10)	DEPRESSION score (Mean ± SD)
Normal (0-7)	9	3 ± 1.3
Borderline (8-10)	1	10
Abnormal (11-21)	0	0

Table: 46 Assessment of Depression at Third Follow-up in Group B

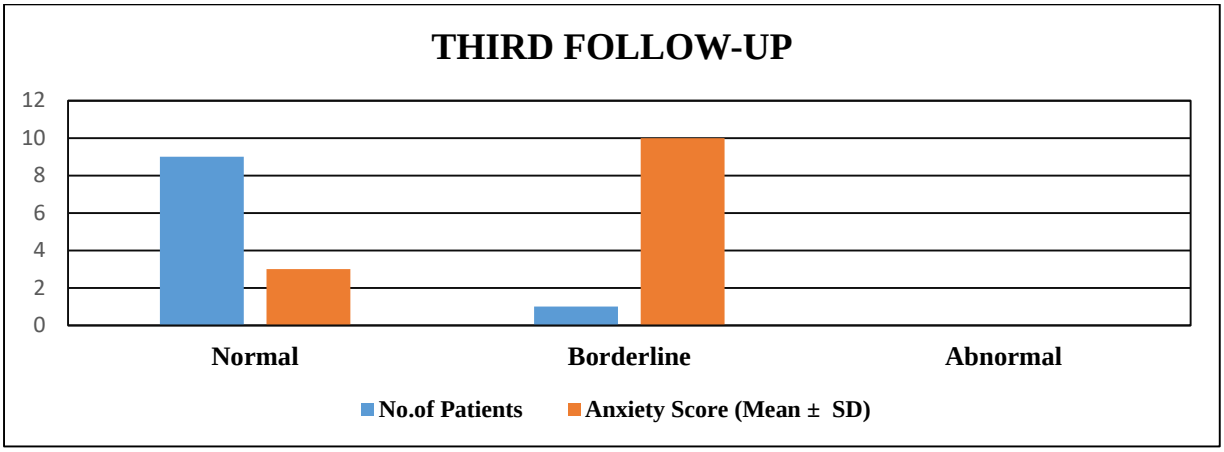

Figure: 46 Assessment of Depression at Third Follow-up in Group B

From table 46, it shows the assessment of depression in group B at the third follow up.

Where 90% of the patients had depression score of 3±1.3 and 10% of the patients had depression score of 10

COMPARISON OF DEPRESSION SCORE IN GROUP B

Review	DEPRSSION Score (Mean ± SD)
First follow up	10.9 ± 3.3
Second follow-up	7.9 ± 3.4
Third follow-up	3.7 ± 2.5

Table: 47 Comparison of Depression in Group B

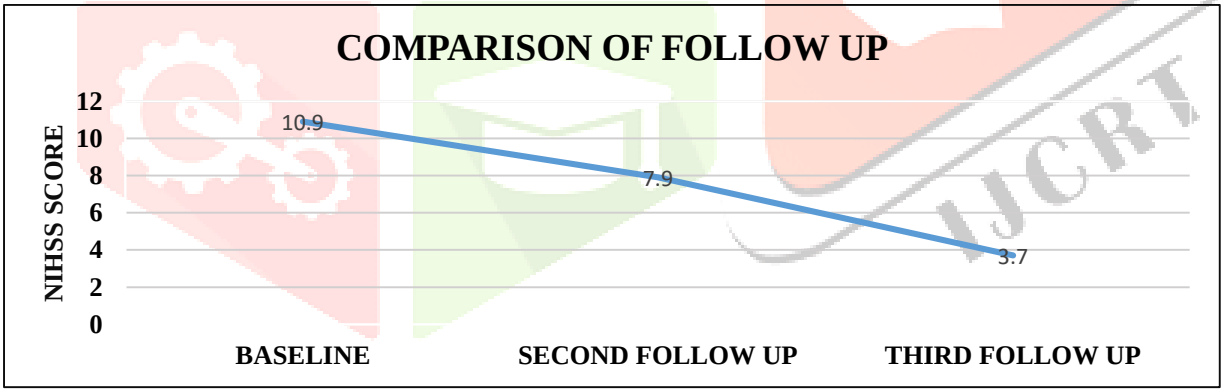

Table: 47 Comparison of HADS Score in Group B

Table 47 shows the comparison of depression scores in group B, where on evaluation the score shows 10.9±3.3 at the start of the study and 7.9±3.4 during the second follow up and declines in the third follow up of 3.7±2.5. This indicates an improvement in the third follow up when compared to the initial follow up. The observed difference is $p<0.001$ which is statistically significant ($p<0.05$).

COMPARISON OF DEPRESSION SCORE IN GROUP B:

HADS	BASELINE	END LINE
ANXIETY	12.9 ± 3.5	4.8 ± 1.9
DEPRESSION	10.9 ± 3.3	3.7 ± 2.5

Table: 48 Comparison of HADS Score in Group B

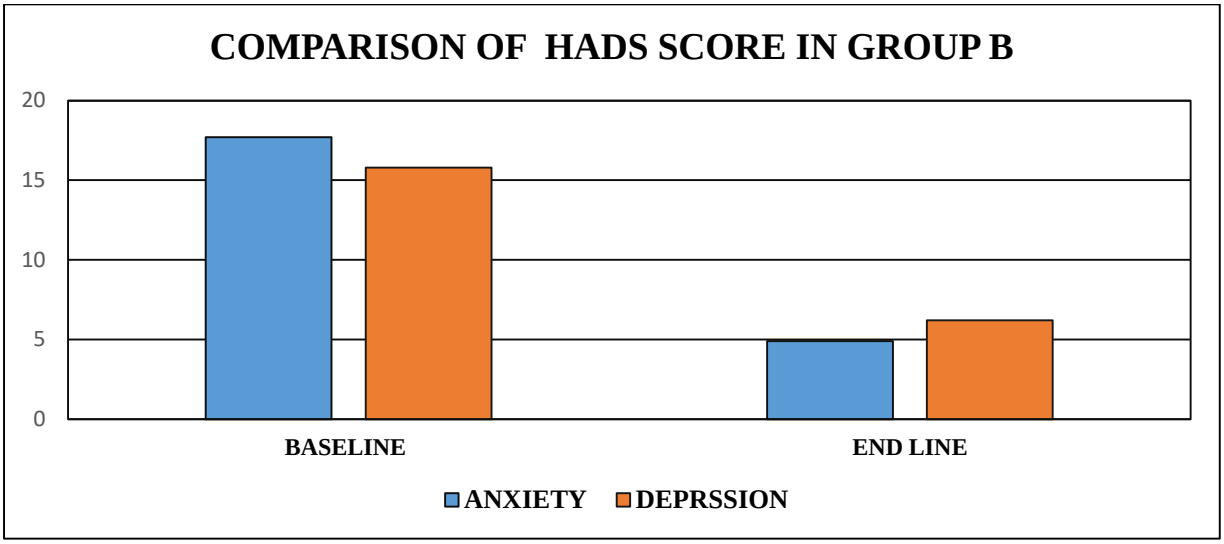

Table: 48 Comparison of HADS Score in Group B

From table 48, on evaluation it shows the comparison of the HADS score in group B, in which it was discovered that the anxiety score for group B was 12.9±3.5 at the start of the study and 4.8±1.9 at the end of the study, while the depression score was 10.9±3.3 at the start of the study and 3.7±2.5 at the end of the study.

COMPARISON OF HADS SCORE IN BOTH GROUP A & B:

GROUPS	HADS	BASE LINE	END LINE
ALTEPLASE	ANXIETY	17.7 ± 2.5	4.9 ± 2.4
	DEPRESSION	15.8 ± 1.4	6.2 ± 1.6
TENECTEPLASE	ANXIETY	12.9 ± 3.5	4.8 ± 1.9
	DEPRESSION	10.9 ± 3.3	3.7 ± 2.5

Table: 49 Comparison of HADS Score in Both Groups

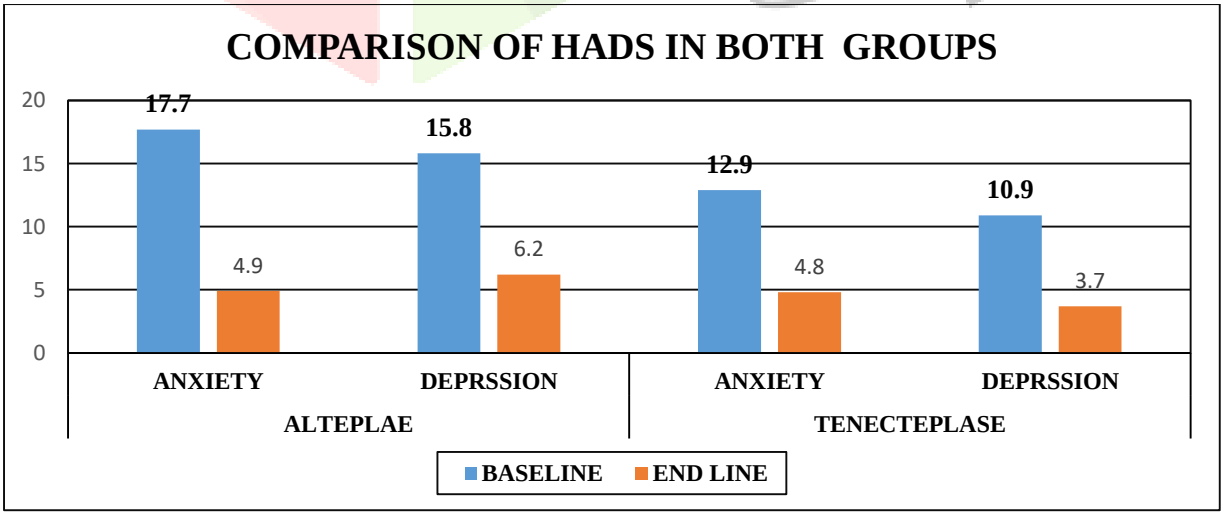

Figure: 49 Comparison of HADS Score in Both Groups

Table 49 shows the comparison of HADS score in both groups A and B. On evaluation it has been assessed that the score of HADS in group A is higher when compared to group B, HADS score in group B shows a better outcome than group A. The degree of anxiety at the start of study in group A is 17.7 ±2.5 and for group

B it is 12.9±3.5 and at the end of the study is 4.9±2.4 for group A and for group B it is 4.8±1.9. The degree of depression at the start of the study in group A is 15.8±1.4 and for group B it is 10.9±3.3 and at the of the study is 6.2±1.6 for group A and for group B it is 3.7±2.5.

COST-EFFECTIVE ANALYSIS OF ALTEPLASE AND TENECTEPLASE:

Incremental Cost -Effective Ratio (ICER)= Difference in Cost / Difference in Effectiveness

COST AND DIFFERENCE OF INTERVENTION:

	GROUP	COST PER UNIT (₹)	TOTAL COST IN 10 PATIENTS (₹)	DIFFERENCE IN INTERVENTION
COST OF INTERVENTION	ALTEPLASE	₹ 49,310	₹ 4,93,100	₹ 1,44,405
	TENECTEPLASE	₹ 34,905	₹ 3,49,050	

Table: 50 Cost difference of intervention

Table 50 shows the cost per unit of both the drugs and the total cost in each group and shows the difference in cost of intervention.

EFFECTIVENESS OF INTERVENTION

GROUP	EFFECTIVENESS (MEAN)	DIFFERENCE IN EFFECTIVENESS
ALTEPLASE	153.7	57
TENECTEPLASE	210.7	

Table: 51 Difference in Effectiveness of Intervention

Incremental Cost -Effective Ratio (ICER)= 144050 / 57

= ₹2527 per unit of effectiveness

- ALTEPLASE is ₹2527 per unit of effectiveness costlier than TENECTEPLASE
- So Tenecteplase is Less costly and has great effectiveness than Alteplase

Table 51 shows the mean effectiveness of the intervention of both groups using ICER and assessed the difference in effectiveness.On assessment, alteplase was found to be costlier when compared to tenecteplase

DISCUSSION:

This study aims to compare the efficacy of Alteplase and Tenecteplase in acute ischemic stroke and to assess the changes in quality of life in these patients after thrombolytic therapy and also to assess the cost effectiveness of both the drugs. The two drugs considered in this study are Alteplase and Tenecteplase which are thrombolytic agents used for the treatment of AIS[13].

Alteplase is a thrombolytic agent which is a FDA approved drug for use in the acute ischemic stroke, acute myocardial infarction and occluded catheters. It converts fibrinogen to the proteolytic enzyme plasmin, which lysis fibrin as well as fibrinogen.[15]

Tenecteplase is a fibrin specific tissue plasminogen activator, a thrombolytic agent for acute ischemic stroke due to its drug characteristics and ease of administration and has a longer half-life. At 0.5mg/kg, has regulatory approval to treat ST–segment–elevation myocardial infarction.

This study about 20 patients were taken, among them 10 patients are categorized in one group and given Alteplase and the remaining 10 patients were categorized into other group and given Tenecteplase. Statistical analysis was performed using student t-test and the detailed analysis was performed.[17]

In this study demonstrated that there is significant difference in the efficacy of drugs by checking the neurological conditions of all the patients using NIHSS and MRS scales. On evaluation of both the drugs Tenecteplase shows a better outcome when compared to the other drug Alteplase. The observation shows a similar to the outcome study conducted by **Steven.J.Warach et al** .In their study to test defined hypotheses about Tenecteplase versus Alteplase in routine clinical practice in which they found Tenecteplase as a non-inferiority for early indices of efficacy and reduced hospital costs compared to Alteplase as a result they found Tenecteplase as an alternative to Alteplase for ischemic stroke thrombolysis additionally shorter time from stroke onset to Tenecteplase bolus in their data was associated with a higher probability of the favorable outcome of walking independently.[25]

This study also assessed the health related quality of life in AIS patients using SS-QOL which is similar to that of the study conducted by **Williams et al**. In their study of SS-QOL assesses health related quality of life specific to stroke survivors, the scale contain 49 domains in which the score ranges from 49-245 and they found Higher scores indicate better functioning.[18]

This study also demonstrates the degree of anxiety and depression using the HADS scale in AIS patients which is similar to the study conducted by **R.Philip Snaith**, where they found that the HADS was found to perform well in assessing severity and caseness of anxiety disorders and depression in both somatic and psychiatric cases in hospital patients.[19]

The investigation also looked at the cost-effectiveness of both the drugs using ICER.

This study also showed a remarkable improvement in the QOL of AIS patients which was done by evaluating SS-QOL which was filled during the three reviews after the treatment. It was evident from the comparison that the patients had an improvement in lifestyle and mental and physical health in group A when compared to group B patients.[12]

The effectiveness of Alteplase and Tenecteplase is comparable. Significant differences were discovered between the two medicines. When compared to Alteplase, Tenecteplase acts faster and has a somewhat greater effect on the effectiveness and quality of life of patients with AIS.[16]

CONCLUSION:

From this study, it was concluded that Tenecteplase has more efficacy than Alteplase in Acute ischemic stroke. However, in patients taking Tenecteplase, there is an improvement in the social functioning when compared to that of Alteplase. By assessing both drugs' quality of life, it was found that Tenecteplase is more efficient than Alteplase. It was also found that by assessing the HADS score there is improvement in the mental health status of the patient, Tenecteplase patient shows better outcome when compared to a patient who had taken Alteplase. The cost-effective analysis of both drugs is compared using ICER.

REFERENCE:

1. Neha potla; et.al, Tenecteplase vs Alteplase for acute ischemic stroke: a systematic review. International journal of emergency medicine 2022(15:1)
2. Wardlaw J M, Murray V, Berge E et.al. recombinant tissue plasminogen activator for acute ischemic stroke: an updated systematic review and meta analysis. Lancet 2012; 379:2346-2372.
3. Kidwell C S, Jahan R, Gornbein J et.al, For the MR RESCUE Investigators. A trial of imaging selection and endovascular treatment for ischemic stroke. N Engl J Med 2013;368:914-923.
4. Parsons M, Spratt N, Bivard A, et al. A randomized trial of tenecteplase versus alteplase for acute ischemic stroke. N Engl J Med 2012; 366:1099-2007.

5. Lyden P, Shuaib A, Ng K, Levin K, Atkinson RP, Rajput A, Wechsler L, Ashwood T, Claesson L, Odergren T, Salazar-Grueso E. Clomethiazole acute stroke study in ischemic stroke (CLASS- I). Stroke. 2002;33(1):122-9.
6. Heidi Sucharew,PhD,Jane Khoury,PhD et.al, Profiles of the National Institutes Of Health Stroke Scale Items as a Predictor of patient outcome.Stroke.2013 August ; 44(8):2182-2187.
7. Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. Bull World Health Organ 1980; 58: 113–130.
8. American Stroke Association,A Division of the American Heart Association. Mayo clinic link: neurologist Robert Brown MD Ferri FF. Stroke, acute ischemic. In: Ferri's Clinical Advisor 2022. Elsevier; 2022. https://www.clinicalkey.com. Accessed Aug. 31, 2021.
9. Caplan LR. Basic pathology, anatomy, and pathophysiology of stroke In: Caplan's T, ed. Stroke: A Clinical Approach, 4th edition Saunders Elsevier; 2009:22.
10. Adams, H.P., Jr.; Bendixen, B.H.; Kappelle, L.J.; Biller, J.; Love, B.B.; Gordon, D.L.; Marsh, E.E., 3rd. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993, 24, 35–41.
11. Wolters Kluwer clinical drug information I. Lexi-drugs:Tenecteplase average wholesale price; accessed may 14,2020.
12. Parsons M, Spratt N, Bivard A, Campbell B, et.al . A randomized trial of Tenecteplase vs Alteplase for acute ischemic stroke. N England journal of medicine. 2012;366:1099-1107.
13. Campbell BCV, Mitchell PJ, Churilov L, Yassi N, Kleinig TJ,Dowling RJ, et.al. Tenecteplase versus Alteplase before thrombectomy for ischemic stroke. N Engl J Med. 2018;378:1573-1582.
14. Reeves MJ,Smith EE, Fonarow GC, Zhao X, Thompson M, Peterson ED,et.al.Variation and trends in the documentation of national institutes of health stroke scale in gwtg-stroke hospitals. Circ Cardiovascqual outcomes.2015;8:S90-98
15. Saver JL, Goyal M,Van der Lugt A, Menon BK, Majoie CB,Dippel DW, et.al.Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: A meta-analysis. JAMA.2016;316:1279-1288.
16. Tanswell P, Modi N, Combs D, Danays T. Pharmacokinetics and pharmacodynamics of tenecteplase in fibrinolytic therapy of acute myocardial infarction. Clin Pharmacokinet 2002;41:1229-45.
17. Van De Werf F, Adgey J, Ardissino D, et al. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 doubleblind randomised trial. Lancet 1999;354:716-22.
18. Parsons M, Spratt N, Bivard A, et al. A randomized trial of tenecteplase versus alteplase for acute ischemic stroke. N Engl J Med 2012;366:1099-107.
19. Kunz WG, Almekhlafi MA, Menon BK, Saver JL, Hunink MG, Dippel DWJ,et.al. Public health and cost benefits of successful reperfusion after thrombectomy for stroke.Stroke.2020;51:899-907.
20. Gao L, Moodie M, Mitchell PJ,Churilov L, Kleinig TJ, Yassi N, et.al. Cost-effectiveness of tenecteplase before thrombectomy for ischemic stroke. Stroke.2020;51:3681-3689.