STUDY ON DRUG UTILIZATION AND PHARMACOECONOMIC STATUS OF CITICOLINE ON STROKE PATIENTS

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Abstract : The aim of present study is to evaluate the utilization of citicoline in stroke patients and its pharmacoeconomic studies. Main Objective is to interpret, evaluate and improve the prescribing administration and use of medication.To identify, measure, value and establish a link between stroke and citicoline. Methodology used prospective observational study was carried out from November 2018 to April 2019 at Rohini Super Speciality Hospital, Sri Sri Neuro Clinic Hospital, hnk, Warangal, Telengana. The data was collected from 300 patients for their demographic details and was documented and analysed.

.IndexTerms - Citicoloine, Drug utilization evaluation, NIHSS-National institute of health stroke scale, Pharmacoeconomics, Stroke

I. INTRODUCTION

DUR is a system of ongoing, systematic, criteria-based evaluation of drug use that will help ensure that medicines are used appropriately (at the individual patient level). If therapy is deemed to be inappropriate, interventions with providers or patients will be necessary to optimize drug therapy. A DUE is drug - or disease - specific and can be structured so that it will assess the actual process of prescribing, dispensing or administering, dispensing or administering a drug (indications, dose, drug interactions, etc.). DUE is the same as **Drug Utilization Review (DUR)** and terms are used synonymously.

Pharmacoeconomics is the field study that evaluates the behavior of individual, firm and markets relevant to the use of pharmaceutical products, services and programs and which frequently focuses on the cost (inputs) and consequences (outcomes) of that use.

The aim of this approach is to identify, measure, value and establish and a link between both resource consumption and outcomes so that the relative worth of selected pharmaceutical products, programs or services to the next best alternatives from selected perspectives.

Citicoline is a complex organic molecule that function as an intermediate in the biosynthesis of cell membrane phospholipid citicoline is also known as CDP – choline belongs to the group of biomolecules in living systems known as nucleotides that play an important role in cellular metabolism. [44]

- Citicoline is also known as CDP – choline and cytidine diphosphate choline.
- Citicoline is water soluble compound with greater than 90 percent bioavailability oral doses of citicoline are rapidly absorbed.
- Citicoline elimination occurs in two phases mainly via respiratory CO2 and urinary excretion.

Stroke sometimes also known as "brain attack", CVA (cerebrovascular accident), occurs when blood flow to an area in the brain is cut off. The brain cells; deprived of the oxygen and glucose needed to survive or die.

Hypertension(HTN): Also known as high blood pressure, is a long term medical condition in which the blood pressure in the arteries is persistently elevated.

Diabetes mellitus(DM): Diabetes mellitus is a chronic disease caused by inherited and / or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentration of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves.

Seizure: Uncontrolled electrical activity in the brain, which may produce a physical convulsion, minor physical signs, thought disturbances, or aa combinations of symptoms. Seizure can be caused by head injuries, brain tumor, etc.

Coronary artery disease(CAD): Is the most common type of heart disease. CAD happens when the arteries that supplies blood to heart muscle become hardened and narrowed. This is due to the buildup of cholesterol and other materials, called plaque, on their inner walls. This build up is called atherosclerosis.

REVIEW OF LITERATURE

1.Cho,h-j; Kim, y j conducted study on 'Efficacy and safety of citicoline in stroke': Drug surveillance study was carried out in 4,191 patients with a diagnosis of acute ischemic stroke. Citicoline (500-400mg/day) was administrated within less than 24 hours after acute ischemic stroke in 3,736 patients (early group) and later than 24 hours after acute ischemic stroke in 455 patients(late group) for atleast 6 weeks citicoline improved neurological, functional and global outcomes in patients with acute ischemic stroke without significant safety concerns.

2.Ryazhenov vv, Gorolekovag conducted a study on 'Pharmacoeconomics benefits of citicoline in the treatment of acute ischemic stroke in Russia': The pharmacoeconomic model was developed based on the data of meta analysis performed by A.davalos et.al. two groups of 100 patients each were included in the model. The first group received conventional therapy and the 2nd group (active treatment group). The study has demonstrated that the treatment of acute ischemic stroke with citicoline was more effective and the potential to reduce the rehabilitation expenses.

3.Wayne M. clark, Benjamin j, Williams, Kenneth, Richard. M, 'A randomized efficacy trial of citicoline in stroke patients':

The current trail was randomized, double-blind, efficacy trail in 394 patients comparing placebo with citicoline for 6 weeks the result of the study indicate that citicoline was safe. Post hoc analyses indicate that there may be a sub group of patients with moderate to severe strokes who would benefit.

4.Bart M Demaerschark, Ha –Mill Hwang, Grace Leung : US Cost burden of ischemic stroke; studies focus on the long term and indirect expenditures are essential to assess the impact of new treatments on total stroke costs. Overall, the high costs associated with stroke clearly indicate there is as imperative need for effective preventive therapy , early critical care , and rehabilitation , which in turn will reduce the national expenditure for stroke related health care services .

5.Markidak, J Cole JW, Cronin CA ,Merino JG Phipps MS, Wozniak MA et.al; Risk of Ischemic stroke in young men ;Stroke: 2018: The strong dose-response relationship between the number of cigarettes smoked daily and ischemic stroke among

young men. Although complete smoking cessation is the goal, even smoking fewer cigarettes may reduce the risk of ischemic stroke in young men.

6.Appelros et al., 'Sex differences in stroke epidemiology' : Male stroke incidence rate was 33% higher and stroke prevalence was 41% higher than the females, with large age bands and between populations.

7.Kenneth S. Yew and Eric Cheng-2009 conducted a study on Acute Stroke Diagnosis ; Stroke can be categorized as ischemic stroke, intracerebral hemorrhagic stroke, and subarachnoid hemorrhagic stroke . The most commonly presenting type of stroke is ischemic stroke with weakness on one side

OBJECTIVES

- To study the demographic data of stroke patients.
- To evaluate the utilization of citicoline in stroke pts.
- To evaluate the overall cost of citicoline use.
- To assess the relation between cost of treatment and outcome.
- In assessment of economic consequences of drug utilization.
- Priorities of populace
- Drug price control
- Lack of specific product patents and the relatively limited spread of the concept of health insurance.
- It evaluates the affordability of the right medtication to the right pt at the right time, comparing two drugs in the same therapeutic class or drugs with a similar mechanism of action.
- Creating guidelines (criteria) for appropriate drug utilization.
- Evaluating the effectiveness of medication therapy.
- Enhancing responsibility/accountability in the medicine use process.
- Controlling medicine cost
- Preventing medication related problems, for example adverse drug reactions, treatment failures, over-use, under-use, incorrect doses and non-formulary medicine use.
- Identifying areas in which further information and education may be needed by health-care providers.

METHODOLOGY

Study site: Rohini multispeciality hospital, Sri Sri Neuro Clinic.

Study Design: Observational prospective study

Study period:6 months (Nov 2018 to April 2019)

Sample Size: 300 patients

Study Criteria:

- **Inclusion criteria:**

1. Stroke patients (Ischemic stroke, hemorrhage stroke)
2. Patients of all ages (adults and gediatrics)
3. Patients of either sex
4. Only inpatients
5. Patients both newly diagnosed and old cases of stroke.
6. Patients with other co-morbidites (DM, HTN, OLD CVA, CAD,OTHER'S)

- **Exclusion criteria:**

1. Pregnancy
2. Pediatrics and below age group 30 years
3. Patients with severe disability.

Study Procedure:

- Patients who meet the above study criteria are enrolled into the study.
- All necessary information is collected from various sources.
    1. **Patients:** data that can be controlled includes demographic details (age, gender, address, occupation), weight, recent weight changes, height, chief complaints, physical activity, social history, family history, past medical history and past medication history. From weight and height data. BMI is calculated to assess the weight status.
    2. **Patient case-sheet:**General examination, Vital signs, lab data (culture test, WBC count, ESR, C-Reactive Protein). Current medications, Provisional and Final diagnosis.
- Cost of each dose of medication, lab parameters, materials used during treatment (syringe, catheters, needles, feeding tubes), cost of room stay (per day).
- The above data will be documented in the data collection form.
- By collecting the above data, the medications prescribed based on the lab parameters can be assessed.

RESULTS

Table.1:GENDERWISE DISTRIBUTION OF STROKE PATIENTS:

Gender	STROKE	CONFIDENCE INTERVAL
Male	216	5.08
Female	84	5.08

Table.1 shows that out of 300 prescriptions , 72% of stroke patients were males and 28% of them were females.

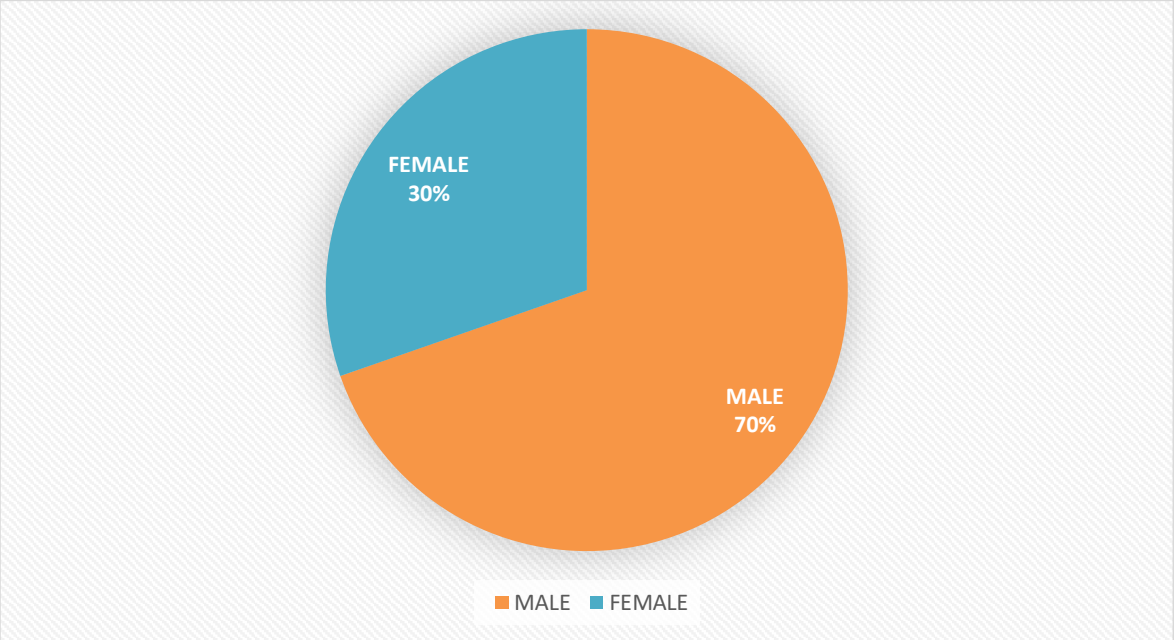

Fig 1: Gender wise distribution of stroke patients.

Table 2.DISTRIBUTION OF STROKE PATIENT'S AMOUNG DIFFERENT AGE GROUP'S:

AGE	STROKE	CONFIDENCE INTERVAL
30-65	196	5.44
GREATER THAN 65	104	5.38

Table 2 shows that out of 300 prescriptions, 36.3% of patients were between 30-65, and 34.6% were above 65years

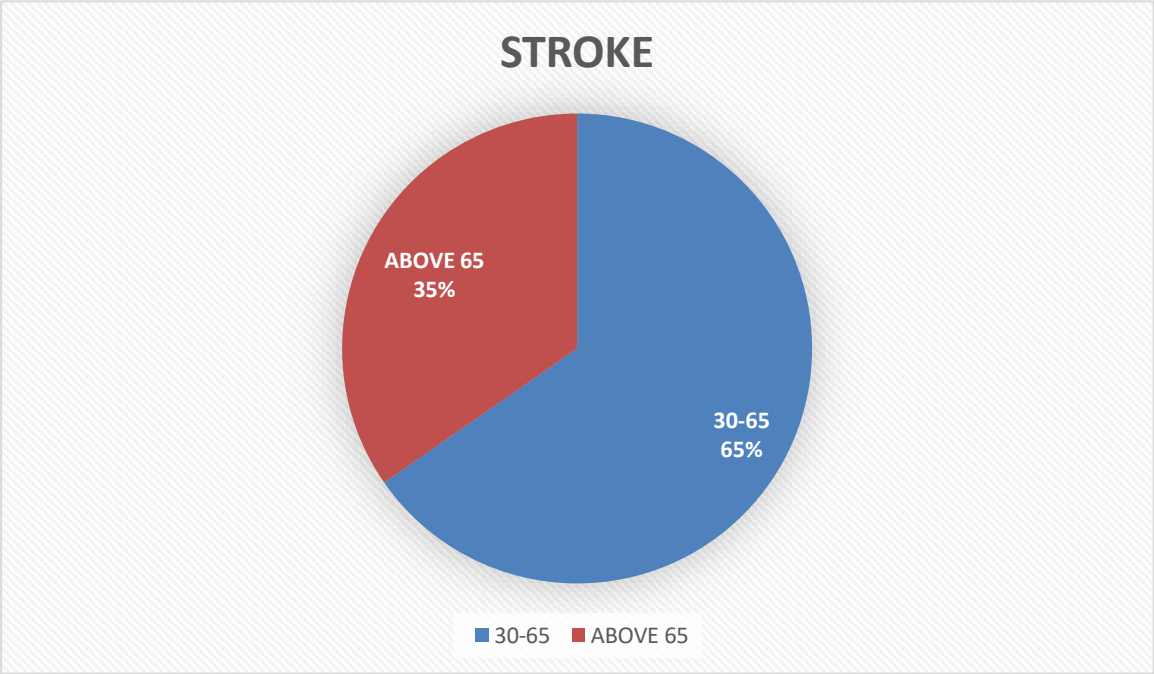

Fig 2 Distribution of stroke patient's amoung different age group's

Table 3. COMORBID CONDITIONS VS NO.OF STROKE PATIENT'S

COMORBIDITIES	STROKE	CONFIDENCE INTERVAL
HTN	224	4.93
DM	106	5.41
CAD	28	3.29
OLD CVA	6	1.58
OTHER	18	2.69

Table 3 shows that out of 300 prescriptions 74.6% of stroke patients were having hypertension, 35.3% DM, 9.3% CAD, 2% old CVA and others 6%

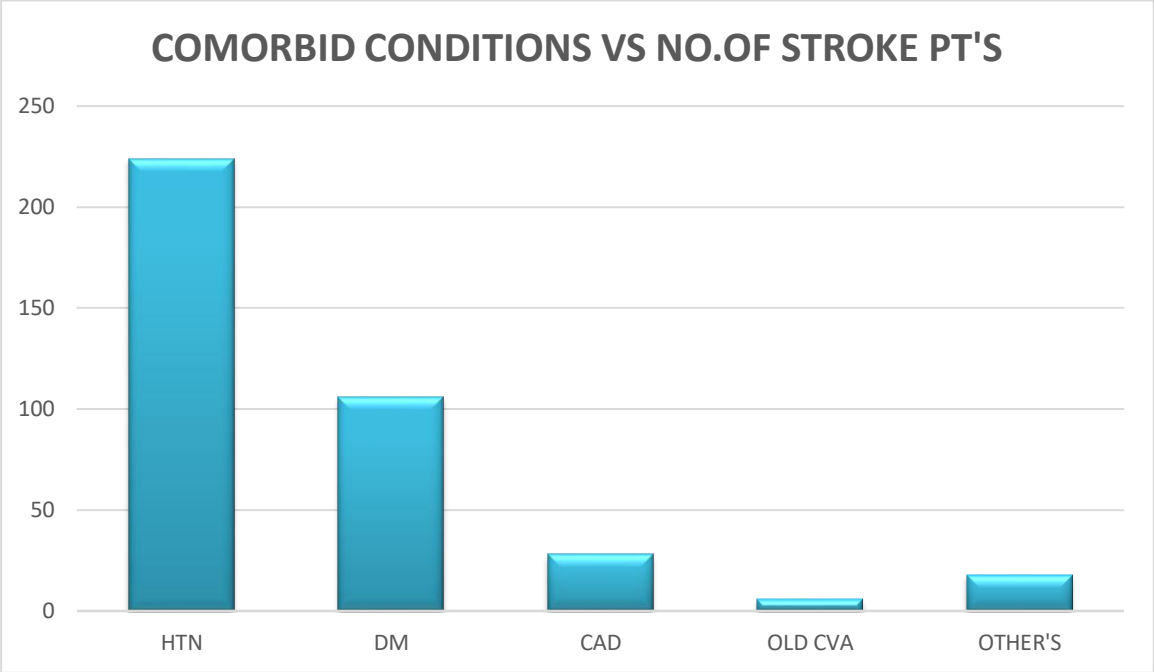

Fig 3. Comorbid conditions vs no.of stroke patient's

Table 4.TYPEWISE CLASSIFICATION OF STROKE PATIENT'S:

TYPE	STROKE	CONFIDENCE INTERVAL
HEMORRHAGIC STROKE	55	±4.38
ISCHEMIC STROKE	245	±4.38

Table 4 shows that out of 300 patients 18.33% were admitted with hemorrhagic stroke and 81.66% with ischemic stroke.

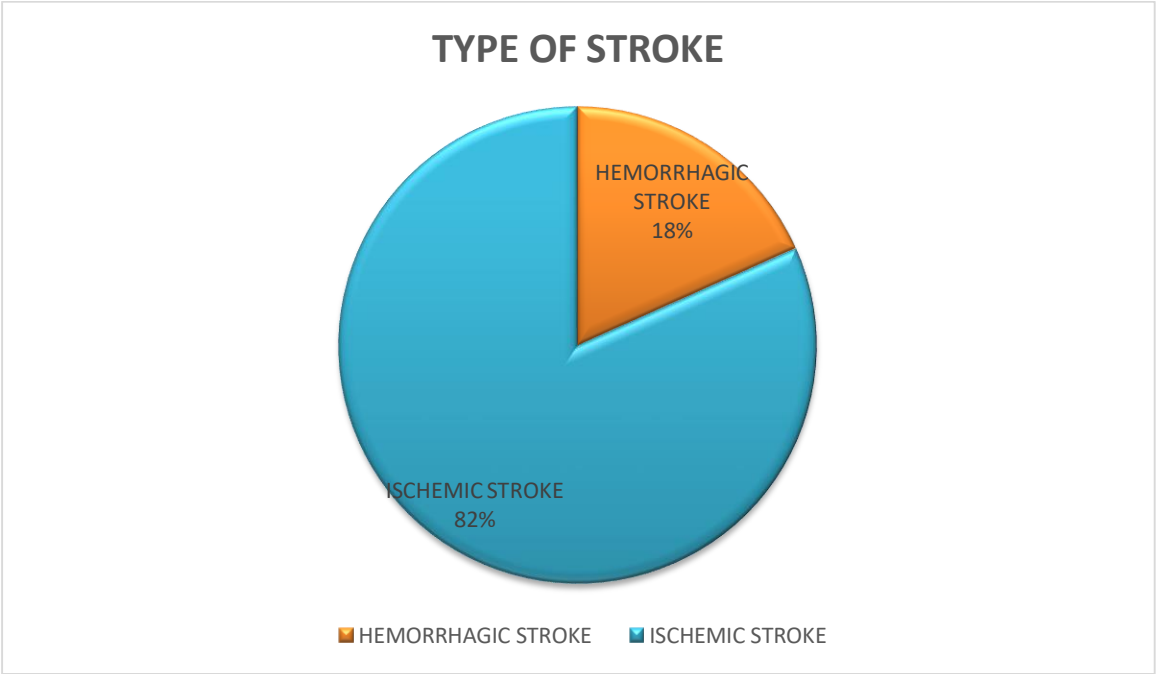

Fig 4. Typewise classification of stroke patient's

Table 5. ETIOLOGY OF STROKE:

ETIOLOGY	STROKE	CONFIDENCE INTERVAL
SMOKING	102	± 5.38
ALCOHOLIC	138	± 5.64
TOBACCO CHEWING	10	±2.02
AGE	104	±5.38

Table 5 shows that out of 300 patients 34.6% of then were smokers, 46% alcoholic, 3.3% tobacco chewing and 34.6% having age related etiology.

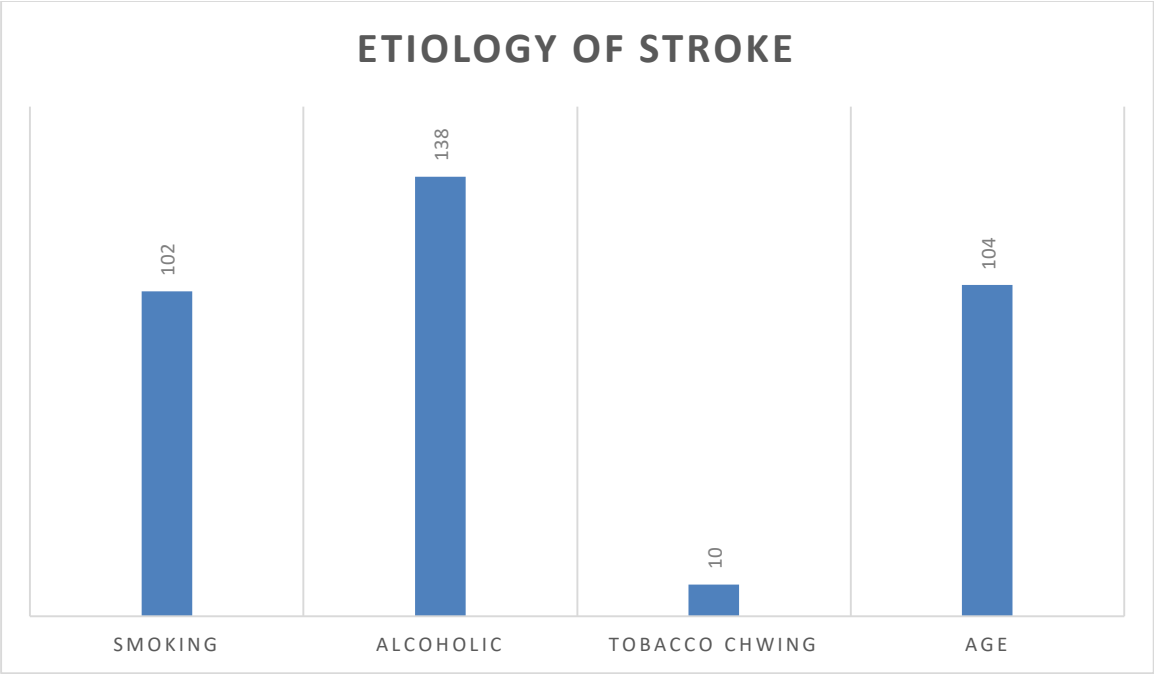

Fig 5. Etiology of stroke.

Table 6. GENDERWISE COST OF CITICOLONE:

GENDER	COST OF CITICOLINE	STANDARD DEVIATION
MALE	466,020	± 424.71
FEMALE	184,680	±400.13

Table 6 shows the cost of citicoline is 466,020 at standard deviation of ±424.71 and is females the cost is 184,680 at standard deviation of ±400.13.

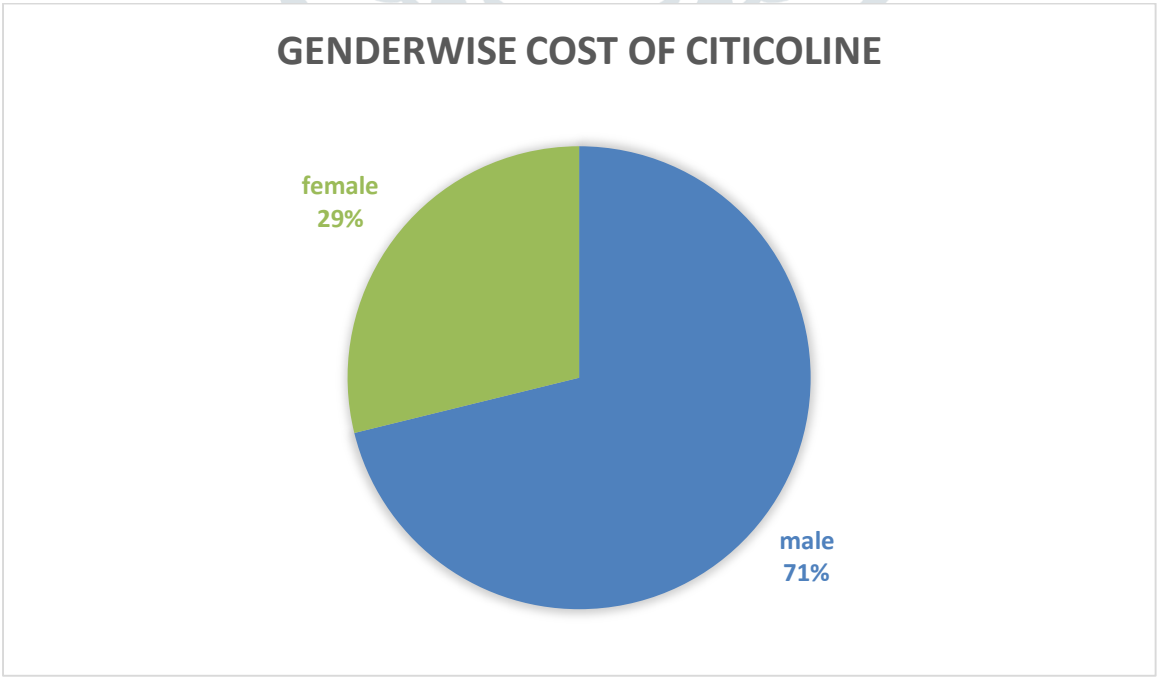

Fig 6. Genderwise cost of citicolone

Table 7. COST OF CITICOLINE BASED UPON TYPE OF STROKE:

TYPE OF STROKE	COST OF CITICOLINE
Hemorrhagic stroke	127,980
Ischemic stroke	522,720

Table 7 shows that cost for patients with ischemic stroke is more compared to hemorrhagic stroke.

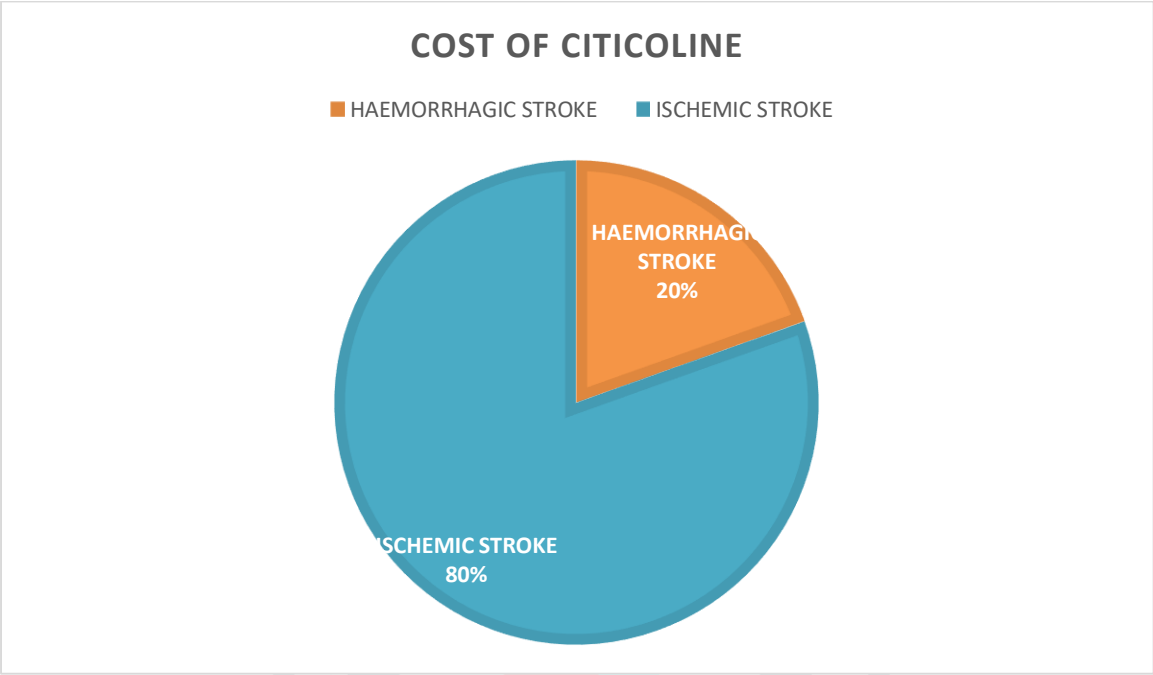

Fig 7 Cost of citicoline based upon type of stroke.

8.TOTAL COST OF CITICOLINE:

DAYS	NO.OF DAYS	COST
D2	4	4,320
D3	75	121,500
D4	133	287,280
D5	88	237,600
TOTAL		**650,700**

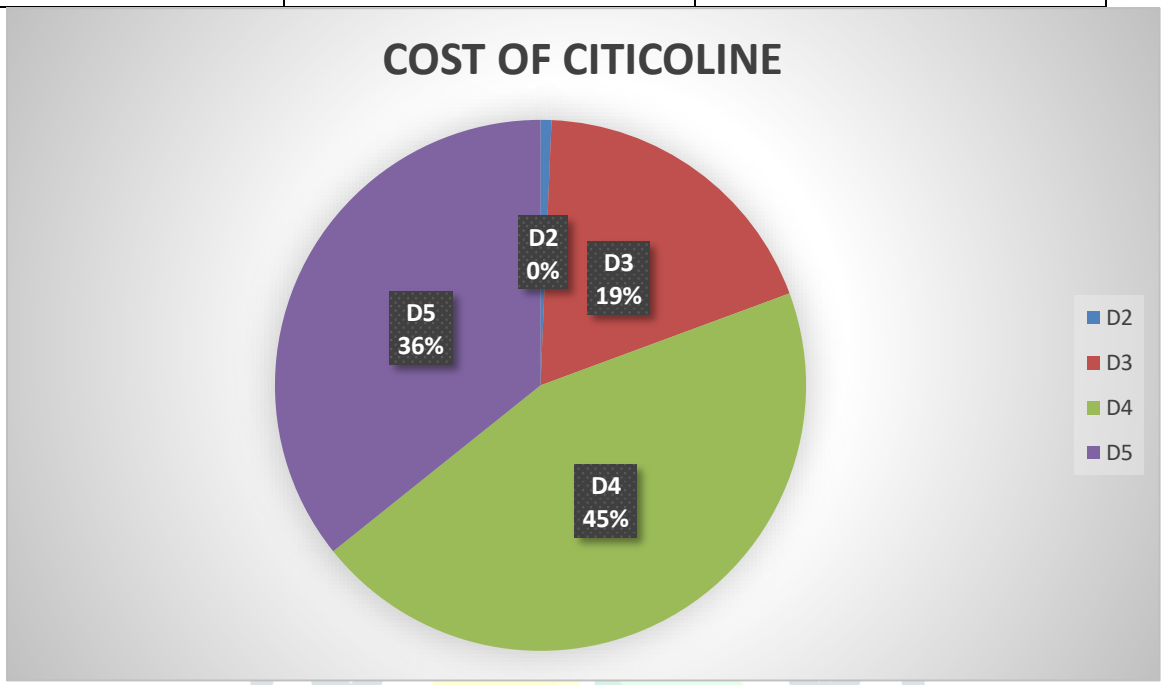

Fig 8. Total cost of citicoline

9.STROKE SEVERITY

BEFORE		AFTER	
Moderate to severe	Severe stroke	Moderate stroke	Minor stroke
104	196	64	236

Table.9 shows that out of 300 prescriptions ,in accordance with NIHSS before admission 104 patients was with moderate to severe stroke and 196 patients was admitted with severe stroke. And while discharge 64 patients were having moderate stroke and 236 were having minor stroke.

DISCUSSION

A total of 300 patients were reviewed in inpatients in Rohini Superspeciality hospital during a study period of 6 months.

In the study 81.66% of patients are reported with ischemic stroke and 18.33% with hemorrhagic stroke which is similar to study conducted by Kenneth s.yew and Eric cheng-2009 'Acute Stroke Diagnosis'.

In the study of 300 patients 216(72%) patients were male and 84(28%) were females admitted with stroke, which is similar to study done by Appelros et al. 'Sex differences in stroke epidemiology'.

In this study it shows that 102(34.5%) of patients were having habit of smoking, 138 patients (46%) were alcoholic 10 patients (3.3%) having habit of tobacco chewing which is similar to the study conducted by markidan et al. 'Risk of ischemic stroke in young men'.

Based on past medical history 224(74.6%) of patients are with hypertension, 106 (35.33%) patients are with diabetes, 28 (9.3%) of patients are with CAD, 6 (2%) are with old CVA and 18 (6%) are with other co morbidities like asthma, seizures, which is similar to study conducted by parth dhruv et al. a systemic literature review of patients with carotid web and acute ischemic stroke.

Based on severity 196 patients were admitted with severe stroke and 104 with moderate to severe stroke after the treatment with citicoline 64 patients were with minor symptoms of stroke and 236 with moderate stroke symptoms which is similar to the study conducted by Wayne M. clark, Benjamin J, Williams, Kenneth, Richard. M,:A randomized efficacy trail of citicoline in stroke patients.

Average cost of citicoline in females is 184,680, at a standard deviation of 424.71 and in males the average cost is 466,020, at a standard deviation of 400.13 which is similar to study conducted by Bart M De maerschark , Ha-mill Hwang , Grace Leung: US Cost burden of ischemic stroke.

Citicoline side effects were minimally identified , with less problematic side effects like headache, diarrhea, nausea, blurred vision, high or low blood pressure , tachycardia; which is studied by CH0,H-J; KIM J 'Conducted by study on efficacy and safety of citicoline in stroke'.

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