

EVALUATING RISK FACTORS, CLINICAL AND THERAPEUTIC PROFILE OF STROKE PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: According to the World Health Organization, stroke is the second leading cause of death for people above the age of 60 years, and the fifth leading cause in people aged 15–59 years old. This study mainly aims to evaluate the prevalence of risk factors, clinical features, pattern of drugs prescribed, and severity of stroke among patients.

Methods: A cross-sectional study was carried out in a tertiary care teaching hospital on 210 patients for a period of 6 months. Patients aged 18 years and above were included in the study. The severity of stroke was assessed using National Institute of Health Stroke Scale (NIHSS).

Results: The majority of the patients were under the age group of 61–70 years (31%). The incidence of ischemic stroke (81%) was more common compared to hemorrhagic stroke (19%). Males (66%) are prone to stroke compared to females (34%). The most common risk factor was hyperlipidemia (29%) followed by hypertension (17%). Antihypertensives (28%) were most commonly used drugs followed by antihyperlipidemics (23%). Most of the prescriptions were prescribed with 4–6 drugs per prescription (62%). Moderate stroke (69%) was most commonly observed in patients. A total of 147 drug-drug interactions were observed. Among 147 drug-drug interaction, the most commonly observed drug-drug interaction was aspirin with metformin (15%).

Conclusion: The present study emphasizes on the need to identify risk factors and providing awareness among the patients by a pharmacist in minimizing the disease burden. Early identification of risk factors and pattern of therapy based on therapeutic guidelines plays a crucial role in qualitative patient care.

Keywords: Prescribing patterns, Risk factors, Stroke.

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INTRODUCTION

A stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause [1]. Stroke is one of the leading causes of death worldwide [2]. Stroke was found to be second leading cause of death among the age group of above 60 years simultaneously it was the fifth leading cause of death among the age group of 15–59 years old people [3]. Ischemic stroke was a major type of stroke compared to hemorrhagic stroke [4]. Worldwide, about 20 million people suffer from stroke every year out of this 5 million will die and 15 million will survive, of this 5 million who survived will be paralyzed by the stroke. The Indian National Commission on Macroeconomics and Health has stated that the number of stroke cases increases from 1 million in 2000 to 1.6 million in 2015 [5]. There are certain risk factors that results in the development of stroke. Risk factors for ischemic stroke are age and sex, family history, hypertension, hypercholesterolemia, diabetes mellitus, and lifestyle factors [6]. Risk factors for intracerebral hemorrhage include age, hypertension, anticoagulant therapy, intracranial vascular malformations, and substance abuse [7]. The common risk factors are diabetes, high blood pressure, smoking, and obesity [8].

The clinical presentation of stroke was highly variable depending on the region of brain that has been injured. The patient may complain of weakness on one side of the body, inability to speak, loss of vision, vertigo, or falling. Ischemic stroke is not usually painful, but patients may complain of headache, and with hemorrhagic stroke, it can be very severe [9]. Patients usually have multiple signs of neurologic dysfunction, and the specific deficits are determined by the area of the brain involved. Hemiparesis occurs commonly. Patients with vertigo and double vision

are likely to have posterior circulation involvement. Aphasia is seen commonly in patients with anterior circulation strokes. Patients also may suffer from dysarthria, visual field defects, and altered levels of consciousness. Some patients can present with visual disturbances, urinary incontinence, swallowing difficulties, and emotional problems [10]. The drugs involved in the management of stroke were thrombolytics, anticoagulants, antihypertensive (angiotensin changing enzyme inhibitors, angiotensin II receptor blockers, and diuretics), blood lipid-lowering agents (statins), antiplatelet medication (aspirin and clopidogrel), and cerebral activators. Hence, it is often difficult for the physicians to create the choice of drug to be prescribed among different patients. According to the American Heart Association guidelines, tissue plasminogen activator, antiplatelets, anticoagulants, antihypertensives, and lipid-lowering agents were used to treat ischemic stroke, whereas osmotherapy, neuromuscular relaxants, neuroprotection, neurorestoration therapy, refusion therapy, and calcium channel blockers are used to treat hemorrhagic stroke.

The National Institute of Health Stroke Scale (NIHSS) is used to evaluate the severity of stroke which helps us to determine the appropriate treatment and predict patient outcomes. The scale is made up of 11 different elements. The score for each ability is a number between 0 and 4, 0 for normal functioning and 4 for completely impaired. The severity of stroke is categorized as no symptoms (0), minor stroke (1–4), moderate (5–15), moderate to severe (16–20), and severe (21–42) [11]. A clinical pharmacist can play a major role in identification of risk factors and their effects among stroke patients which can be modified by performing patient counseling regarding lifestyle modifications. Another important role of clinical pharmacist is to access the drug interactions in the prescriptions and updating the physicians regarding

the interactions will help in providing better treatment outcomes and improves patient's quality of life.

METHODS

Study design

This was a cross-sectional study.

Study site

The study was performed at General Medicine Department both male and female wards in Sri Venkateswara Ramnarayan Ruia Government General Hospital (SVRRGGH) tertiary care teaching hospital, Tirupati.

Study duration

This study duration was 6 months.

Sample size

A total of 210 cases from both male and female wards of general medicine were included in the study.

Study criteria

Inclusion criteria

- Male and female patients of age more than 18 years were included in the study.
- All patients who were diagnosed (confirmed either clinically or radiologically) to have stroke were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

- Age ≤18 years.
- Pregnant or lactating women.
- Seropositive patients.

Ethical approval

Ethical approval was obtained by the Institutional Ethical Committee Sri Padmavathi School of Pharmacy SPSP/2019-2020/PD03 and permission obtained from the head of the Department of General Medicine of SVRRGGH, Tirupati.

Method of data collection

This cross-sectional study was carried out in SVRRGH after obtaining the permission of institutional review and ethical committee, Sri Padmavathi School of Pharmacy, Tiruchanoor, Tirupati, A.P, India. All the patients (more than 18 years) who were diagnosed with stroke admitted in the general medicine in-patient ward of SVRRGGH are included in the study. The patient diagnosed with stroke along with other comorbidities was also considered for the study. The data were collected from the patient's case records and other relevant information was collected from patients and patient's caretaker by verbal consent. Patients who are willing to participate were asked to sign the informed consent form. The National Institute of Health Stroke Scale (NIHSS) was used to categorize the severity of stroke among the study population. The risk factors and symptoms of stroke were documented and evaluated. The drugs prescribed among patients were evaluated. The drug-drug interactions were assessed using Micromedex software app. The data were collected from the patient's case records regarding patients demographics, chief complaints, history of present illness, medical history, general examination, signs, symptoms, final diagnosis, and drug therapy.

RESULTS

Out of 210 patients, highest no. of patients was under the age group of 61–70 years (65, 31%) followed by 51–60 years (49, 23%).

Table 2 indicates that the incidence of stroke was more common in males 138 (66%) compared to females 72 (34%).

The prevalence of ischemic stroke 171 (81%) was found to be greater as compared to that of the hemorrhagic stroke 39 (19%).

Out of 210 patients, 171 patients suffered with ischemic stroke, and 39 patients suffered with hemorrhagic stroke. Out of 171 ischemic stroke patients, 113 (66%) were male and 58 (34%) were female, among 39 hemorrhagic stroke patients, 25 (64%) were male and 14 (36%) were female.

Among 210 patients, the most common risk factors associated with the stroke was hypercholesterolemia 170 (29%) followed by age 103 (18%) and hypertension 100 (17%).

Among 210 patients, 20 (10%) patients were alcoholic, 13 (6%) patients were smokers, 50 (24%) patients were having both habits, and 127 (60%) patients does not have any habit.

Table 1: Age-wise distribution of stroke patients

S. No.	Age (years)	No. of patients	Percentage
1.	18–30	3	1
2.	31–40	20	10
3.	41–50	35	17
4.	51–60	49	23
5.	61–70	65	31
6.	71–80	29	14
7.	81–90	9	4
	Total	210	100

Table 2: Gender-wise distribution of stroke patients

S. No.	Gender	No. of patients	Percentage
1	Male	138	66
2	Female	72	34
	Total	210	100

Table 3: Prevalence of types of stroke among patients

S. No.	Type of stroke	No. of patients	Percentage
1	Ischemic	171	81
2	Hemorrhagic	39	19
	Total	210	100

Table 4: Gender-wise distribution of different types of stroke

Gender	Types of stroke			
	Ischemic	Percentage	Hemorrhagic	Percentage
Male	113	66	25	64
Female	58	34	14	36
Total	171	100	39	100

Table 5: Distribution of risk factors among stroke patients

S. No.	Risk factors	No. of patients	Percentage
1.	Hypercholesterolemia	170	29
2.	Age	103	18
3.	Hypertension	100	17
4.	Alcohol	70	12
5.	Smoking	63	11
6.	Diabetes mellitus	51	9
7.	Cardiac diseases	20	4

Table 6: Distribution of social habits in stroke patients

S. No.	Social habits	No. of patients	Percentage
1.	Only alcoholic	20	10
2.	Only smoker	13	6
3.	Both	50	24
4.	None	127	60
	Total	210	100

Table 7: Distribution of clinical manifestations among study population

S. No.	Clinical features	No. of patients	Percentage
1.	Slurring of speech	87	23
2.	Weakness on left side	72	19
3.	Weakness on right side	63	16
4.	Deviation of mouth	47	12
5.	Altered sensorium	45	12
6.	Vomiting's	24	6
7.	Giddiness	23	6
8.	Headache	16	4
9.	Loss of consciousness	6	2

Table 8: Topographic distribution of stroke

S. No.	Altered areas	No. of patients	Percentage
1.	Cerebellar	29	19
2.	Parietal lobe	19	12
3.	Frontoparietal lobe	19	12
4.	Corona radiata	18	11
5.	Thalamus	17	11
6.	Capsuloganglionic region	12	8
7.	Lentiform nucleus	9	6
8.	Temporal lobe	8	5
9.	Pons	7	4
10.	Middle cerebral artery	6	4
11.	Tempoparietal lobe	5	3
12.	Occipitoparietal lobe	2	3
13.	Basal ganglia	2	1
14.	Corpus callosum	2	1

Table 9: Different categories of drugs prescribed to patients

S. No.	Category of drugs	Frequency	Percentage
1.	Antihypertensive	205	28
2.	Hypolipidemic	169	23
3.	Antiplatelets	152	21
4.	Antibiotics	110	15
5.	Antidiabetics	61	8
6.	Antiepileptic	35	5
7.	Anticoagulants	4	0

Table 10: Distribution based on antiplatelet therapy

S. No.	Drugs	Frequency	Percentage
1.	Aspirin	127	84
2.	Clopidogrel	8	5
3.	Aspirin + clopidogrel	17	11
	Total	152	100

Among 210 patients, the most common clinical manifestation was slurring of speech 87(23%) followed by weakness on the left side 87 (19%).

Among 210 patients, the most commonly effected area is cerebellar 29 (19%) followed by parietal lobe 19 (12%) and frontoparietal lobe 19 (12%).

Among 210 patients, the most commonly prescribed category of drug are antihypertensives 205 (28%) followed by hypolipidemics 169 (23%) and antiplatelets 152 (21%).

Out of 210 patients, most of the patients were prescribed with aspirin 127 (84%) followed by aspirin with clopidogrel 17 (11%).

Among all antihypertensive drugs (205), the most commonly prescribed drugs were calcium channel blockers 91 (44%) followed by diuretics 75 (37%).

Table 11: Distribution based on antihypertensive drugs

S. No.	Drugs	No. of patients	Total	Percentage
	Calcium channel blockers			
1.	Amlodipine	85	91	44
2.	Nimodipine	5		
3.	Verapamil	1		
	Beta-blockers			
4.	Metoprolol	9	15	7
5.	Atenolol	6		
	Alpha + beta-blockers			
6.	Labetalol	6	6	3
	Alpha-blockers			
7.	Prazosin	2	2	1
	At-1 antagonist			
8.	Telmisartan	4	6	3
9.	Losartan	2		
	Ace inhibitors			
10.	Enalapril	10	10	5
	Diuretics			
11.	Mannitol	61	75	37
12.	Furosemide	14		
	Total	205	205	100

Table 12: Distribution based on antidiabetic therapy

S. No.	Drugs	Frequency	Percentage
1.	Metformin	28	46
2.	Glimepiride	12	20
3.	Plain insulin	12	20
4.	Glibenclamide	5	8
5.	Human mixtard	3	5
6.	Voglibose	1	1
	Total	61	100

Table 13: Distribution based on antiepileptic therapy

S. No.	Drugs	No. of patients	Percentage
1.	Phenytoin	21	60
2.	Diazepam	10	28
3.	Lorazepam	2	6
4.	Valproic acid	1	3
5.	Carbamazepine	1	3
	Total	35	100

Table 14: Distribution based on antibiotic therapy

S. No.	Drugs	No. of patients	Percentage
1.	Ceftriaxone	88	80
2.	Cefixime	3	3
3.	Cefoperazone + sulbactam	1	1
4.	Azithromycin	2	2
5.	Amoxicillin + clavulanic acid	8	7
6.	Piperacillin + tazobactam	5	4
7.	Meropenem	1	1
8.	Ciprofloxacin	2	2
	Total	110	100

Out of 61 antidiabetic drugs, the most commonly prescribed drug was metformin 28 (46%) followed by glimepiride 12 (20%) and plain insulin 12 (20%).

Out of 35 antiepileptic drugs, the most commonly prescribed drug was phenytoin in 21 (60%) patients followed by diazepam 10 (28%).

Out of 110 antibiotic drugs, the most commonly prescribed drug was ceftriaxone in 88 (80%) patients and the least prescribed drugs were cefoperazone + sulbactam in 1 (1%) patient and amoxicillin + clavulanic acid in 1 (1%) patient.

Out of 210 patients, antihyperlipidemic was prescribed to 168 (80%) patients.

Out of 210 patient's, enoxaparin was prescribed to 4 (1.90%).

Of all miscellaneous drugs, the most commonly prescribed drugs were pantoprazole 166 (41%) followed by optineuron 80 (20%) and B complex 66 (16%).

Out of 210 prescriptions, 131(62%) contain 4–6 drugs, 62 (30%) contain 4–6 drugs, 12 (6%) contain 10-12 drugs, 4 (2%) contain 1-3 drugs, and 1 (0%) contains ≥13 drugs, respectively.

Among 210 patients, 144 (69%) patients have moderate stroke, 33 (16%) patients have minor stroke, 24 (11%) patients have moderate-to-severe stroke, and 9 (4%) patients have minor stroke.

Out of 147 drug-drug interactions, the major drug-drug interactions were found to be 91 (62%) followed by moderate drug-drug interactions 50 (34%) and minor drug-drug interactions were 6 (4%).

Out of 147 drug-drug interactions, the most frequently observed drug-drug interactions were with antiplatelet therapy among them the most commonly observed were aspirin with metformin (23, 15%) followed

by aspirin with clopidogrel (17, 11%) and clopidogrel with atorvastatin (17, 11%).

DISCUSSION

Stroke is one of the leading causes of high morbidity and mortality worldwide. Stroke was found to be second leading cause of death among the age group of above 60 years simultaneously it was the fifth leading cause of death among the age group of 15–59 years old people. In the present study, 210 were analyzed.

In the present study, the incidence of stroke was maximum in the age group of 61–70 years (65, 31%) followed by 51–60 (49, 23). It may be due to chronic diseases such as hypertension, diabetes, and hyperlipidemia which

Table 19: Classification using National Institute of Health Stroke Scale

S. No.	Severity	No. of patients	Percentage
1.	Minor	33	16
2.	Moderate	144	69
3.	Moderate-severe	24	11
4.	Severe	9	4
	Total	210	100

Table 20: Classification based on severity of drug-drug interactions

S. No.	Drug-drug interactions	Frequency	Percentage
1.	Major	91	62
2.	Moderate	50	34
3.	Minor	6	4
	Total	147	100

Table 21: Distribution of drug-drug interactions

S. No.	Drug-drug interactions	Frequency	Percentage
1.	Aspirin + Metformin	23	15
2.	Aspirin + Clopidogrel	17	11
3.	Aspirin + Glimepiride	10	6
4.	Aspirin + Furosemide	10	6
5.	Aspirin + Phenytoin	6	4.5
6.	Aspirin + Atenolol	4	3
7.	Aspirin + Metoprolol	2	2
8.	Aspirin + Glibenclamide	2	2
9.	Aspirin + Insulin	2	2
10.	Aspirin + Diclofenac	1	0.7
11.	Aspirin + Labetalol	1	0.7
12.	Aspirin + Valproate sodium	1	0.7
13.	Clopidogrel + Amlodipine	17	11
14.	Clopidogrel + Atorvastatin	16	10
15.	Clopidogrel + Enoxaparin	1	0.7
16.	Clopidogrel + Phenytoin	1	0.7
17.	Phenytoin + Atorvastatin	13	8
18.	Atenolol + Metformin	2	2
19.	Phenytoin + Paracetamol	2	2
20.	Glibenclamide + Atenolol	2	2
21.	Ciprofloxacin + Metronidazole	1	0.7
22.	Sucralfate + Furosemide	1	0.7
23.	Metronidazole + Ondansetron	1	0.7
24.	Diclofenac + Telmisartan	1	0.7
25.	Diazepam + Phenytoin	4	3
26.	Diazepam + Tramadol	1	0.7
27.	Phenytoin + Carbamazepine	1	0.7
28.	Paracetamol + Carbamazepine	1	0.7
29.	Enalapril + Losartan	1	0.7
30.	Enalapril + Furosemide	1	0.7
31.	Phenytoin + Nimodipine	1	0.7
	Total	147	100

Table 15: Details of antihyperlipidemic drugs prescribed to the patients

S. No.	Drug category	No. of patients	Percentage
1.	Atorvastatin	168	80

Table 16: Details of anticoagulant drugs prescribed to the patients

S. No.	Drug category	No. of patients	Percentage
1.	Exoxaparin	4	1.90

Table 17: Distribution based on miscellaneous drug therapy

S. No.	Drugs	Frequency	Percentage
1.	Proton-pump inhibitor		
	Pantoprazole	166	41
	Vitamin supplements		
2.	Optineuron	80	20
3.	B complex	66	16
	Analgesics		
4.	Paracetamol	40	10
5.	Tramadol	1	0
6.	Diclofenac	1	0
	Antiemetic		
7.	Ondansetron	15	4
	Anti-amebic		
8.	Metronidazole	16	4
	Calcium supplement		
9.	Calcium	22	5

Table 18: Distribution of drugs per prescription

S. No.	Drugs per prescription	No. of patients	Percentage
1.	1-3	4	2
2.	4-6	131	62
3.	7-9	62	30
4.	10-12	12	6
5.	>12	1	0
	Total	210	100

was common in aged people. These findings were similar to the study done by Shaik Afzar Pasha *et al.* (2017) [12], Jaladi Himaja *et al.* (2017) [13], Sanjay V. Patne *et al.* (2016) [14], and Chirayu V. Vaidya *et al.* (2014) [15].

In the overall study population (240 patients), the incidence of stroke was more common in males (138, 66%) compared to females (72, 34%). Males are more prone to HTN, DM, smoking, and alcohol than females. These findings were similar to the study conducted by Sridhar Srimath Tirumala Konduru *et al.* (2017) [16].

Among the study population, the most common type of stroke was ischemic stroke (171, 81%) compared to hemorrhagic stroke (39, 19%). This explains that the prevalence ischemic stroke was more than hemorrhagic due to pathophysiological changes in blood supply to brain. These findings correlate with the study done by Himaja *et al.* (2017) [13], Patne *et al.* (2016) [14], Vaidya *et al.* (2014) [15], and Konduru *et al.* (2017) [16]. The present study revealed that males are more prone to ischemic stroke compared to hemorrhagic stroke because of smoking, which leads to free radical formation that reduces oxygen supply. These findings correlate with the study of Konduru *et al.* (2017) [16].

In the present study out of 210 patients, hyperlipidemia (170, 29%) was most common risk factor followed by age (103, 18%) and hypertension (100, 17%). It may be due to increased cholesterol levels which may lead to plaque formation that results in decreased blood supply to brain. These findings were similar to the study done by Raghuvanshi *et al.* (2014) [17]. According to the present study, the patients who neither drink alcohol nor smoke (127, 60%) are more in number compared to the patients who drink alcohol and smoke (50, 24%). These findings were similar to the study done by Singh *et al.* (2018) [18].

In the present study, most of the patients were presented with the symptoms like slurring of speech (87, 23%) followed by weakness on the left side (72, 19%) similar to the study done by Vurumadla *et al.* (2015) [19]. This is because the cerebellar region (29, 19%) was most commonly effected area which involved in coordinating voluntary movements such as speech, posture, and balance. These findings were in contrast to the study conducted by Patne *et al.* (2016) [14] because in their study thalamus was most affected area.

In overall study population, the most commonly prescribed category of drugs for the management of stroke were found to be antihypertensives 205 (28%) followed by other category of drugs like hypolipidemics (169, 23%) which may be due to the increased blood pressure may results in decreased blood supply to the brain or rupture of blood vessels and most commonly prescribed antiplatelet drug was aspirin (127, 84%) followed by aspirin along with clopidogrel (17, 11%). These findings were similar to the study done by Isaac *et al.* (2019) [20]. In the present study of all antihypertensive drugs, the most commonly prescribed drugs were calcium channel blockers (91, 44%) followed by diuretics (75, 37%). Among calcium channel blockers, the most commonly prescribed was amlodipine. Among diuretics, the most commonly prescribed drug was mannitol. These findings were similar to the study done by Abbasi *et al.* (2012) [21].

In the present study of all antidiabetic drugs, the most commonly prescribed drugs were metformin (28, 12%) followed by glimepiride (12, 20%) and insulin (12, 20%). These findings were contrast to the study done by Isaac *et al.* (2019) [20]. In the present study of all antiepileptic drugs, the most commonly prescribed drugs were phenytoin (21, 60%) followed by diazepam (10, 28%). It may be due phenytoin is used as prophylaxis to prevent post-stroke seizures. These findings were similar to the study done by Abbasi *et al.* (2012) [21] and Jena *et al.* (2018) [22].

In the present study of all antibiotic drugs, the most commonly prescribed drugs were ceftriaxone (88, 80%) and least commonly prescribed drug were cefoperazone + sulbactam (1, 1%) and meropenem (1, 1%). It may

be due to the major complication for the patients in the acute phase of stroke was infection that should be managed promptly. Ceftriaxone is most commonly prescribed because it is a broad-spectrum antibiotic. These findings were contrast to the study done by Jena *et al.* (2018) [22].

According to the present study out of 210 patients, atorvastatin was only the antihyperlipidemic drug prescribed to 168 (80%) patients and enoxaparin was only the anticoagulant drug prescribed to 4 (1.9%) patients. These findings were similar to the study done by Himaja *et al.* (2017) [13]. In the present study, the most commonly prescribed miscellaneous drugs were pantoprazole followed by optineuron and B complex.

In overall study population, most of the patients were prescribed with 4–6 drugs per prescription (131, 62%) followed by 7-9 drugs per prescription (62, 30%). These findings were similar to the study done by Singh *et al.* (2018) [18]. In the present study, the severity of stroke was assessed using National Institute of Health Stroke Scale. Out of 210 patients, most of the patients had experienced moderate stroke (144, 69%) followed by minor stroke (33, 16%) and a smaller number of patients had experienced severe stroke (9, 6%).

In the present study, a total of 147 drug-drug interactions were identified. Out of 147 drug-drug interactions, most of the drug-drug interactions were found to be major drug-drug interactions (91, 62%) followed by moderate drug-drug interactions (50, 34%) and minor drug-drug interactions (6, 4%). Out of 147 drug-drug interactions, the most frequently observed drug-drug interactions were with antiplatelet therapy among them the most commonly observed were aspirin with metformin (23, 15%) followed by aspirin with clopidogrel (17, 11%). These findings were similar to the study done by Bimal Sah *et al.* (2018) [23].

CONCLUSION

The study concludes with the occurrence of stroke commonly associates with increase in age and lifestyle of individuals including other risk factors. The present study accentuates the need to identify risk factors and providing awareness among the patients regarding lifestyle changes (weight management, cessation of smoking, reduce alcohol intake, and exercise) by a clinical pharmacist in minimizing the disease burden. We acknowledge, the proper risk factor management could be achieved by following the standard guidelines for treating and reducing the severity to obtain the desired prognosis (positive therapeutic outcome) of stroke. In the end, we concluded that early identification of risk factors and pattern of therapy plays a crucial role in qualitative patient care.

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AUTHORS' CONTRIBUTIONS

All the authors have prepared the conception, data collection, data analysis, interpretation, and drafting of the article and also discussed the methods, results, and contributed to the final manuscript. Mrs. P. Lakshmi supervised the whole work until the completion of manuscript.

CONFLICTS OF INTEREST

No conflicts of interest to disclose.

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