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Research Article

Pharmacotherapy of Stroke

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ABSTRACT

The WHO defines a stroke or CVA as a clinical condition that rapidly develops clinical signs of a central (or worldwide, in the case of a trance state) disturbing influence of cerebral capability lasting over 24 hours or that results in death for no apparent reason other than a vascular origin. Ischemic, hemorrhagic, and subarachnoid drain are the three main classifications of Cerebral Vascular Accident (CVA). A vein becomes blocked, limiting blood flow to the brain, resulting in an ischemic attack. In contrast, hemorrhagic CVA occurs when a vein crack causes blood to leak into the intracranial pit. The hemorrhagic may be referred to as an intracerebral discharge or subarachnoid drain depending on where the blood was spilled. About 60 to 80 percent of CVA's are ischemic.

The objective of our study was the documentation of pharmacotherapy of stroke. It was a prospective cross-sectional study. Convenience sampling technique was used at Ayub Medical Complex. Ethical Approval for the study was taken from the Ethical Committee of Ayub Medical Complex. The 100 Prescriptions were studied of which the detailed pharmacotherapy and demographics of patients were specifically documented.

Data shows that the 20% of stroke patients have also presented with diabetes. The steroids 27%, NSAIDS 80.3%, ACEIs 12.7%, ARBs 6.5% and anti-diabetics 18% were the classes of highly prescribed drugs while the ceftriaxone and aspirin are individual drugs with are highly prescribed to the patients with stroke. Data also shows the problems in prescriptions such as untreated symptoms or indications or missing lab parameters in almost 35% of patients.

In our study, we found that the stroke was more prevalent among males (60%) than females (40%). The cases being analyzed showed that most of the people suffering from stroke were older people (*i.e.*, 62-75 years). Several interactions were seen and they are divided into three groups according to the severity of interactions. These are 58% minor {Aspirin+prednisolone (prednisolone decreases the levels of aspirin by increasing renal clearance)}, 46% moderate {Metronidazole+atorvastatin (Using metronidazole together with atorvastatin may increase the risk of nerve damage, which is a potential side effect of both medications)} and 29% major {Ceftriaxone+Enoxaparin (Ceftriaxone increases effects of enoxaparin by anticoagulation. Avoid or use Alternative drug. Cephalosporins may decrease prothrombin time)}.

Based on our study we find the total treatment cost as per prescriptions (This cost only includes the medications charges the rest *i.e.* lab tests, bed charges etc. are not mentioned) were minimum 0-500 rs which was found to be 1% whereas the maximum cost was >4500 rs which was found in 2% cases. High Blood pressure, smoking or exposure to secondhand smoke, elevated cholesterol, diabetes, obstructive sleep apnea, cardiovascular disease, including cardiovascular breakdown, heart deserts, heart contamination, or strange heart mood, and personal or family history of stroke, heart failure, or transient ischemic attack were found to be the main causes of stroke or CVA.

Controlling high blood pressure (hypertension), reducing dietary cholesterol and saturated fat, quitting smoking, managing diabetes, maintaining a healthy weight, engaging in regular exercise, consuming alcohol sparingly can help to prevent the incidence of stroke.

Keywords: Myocardium, Inflammation, Stroke, Cerebral vascular accident

Abbreviation: CNS: Central Nervous System; CO: Cardiac Output; COPD: Chronic Obstructive Pulmonary Disease; CT: Computed Tomography; CVA: Cerebrovascular Accident; CVP: Central Venous Pressure; CVS: Cerebro Vascular System; CCB: Calcium Channel Blocker; CK: Creatine Phosphate; Cl: Chloride; Clcr: Creatinine Clearance; CLD: Chronic Liver Disease; DVT: Deep Vein Thrombosis; EC: Enteric Coated; ECG: Electrocardiogram; ECHO: Enteric Cytopathic Human Orphan; EEG: Electroencephalogram; eGFR: Estimated Glomerular Filtration Rate; ER: Emergency Room; TPA: Tissue Plasminogen Activator.

INTRODUCTION

Prologue to stroke/cerebro vascular accident

The human disorder of stroke comprises of the unexpected progress of a central neurologic shortfall whose beginning can be followed to either the blockage of a cerebral vessel (generally blood vessel) or the unconstrained burst of an intracranial supply route with resulting drain in the brain parenchyma or in the subarachnoid space (Weinberg and M.G., 2006).

Types of CVA

Ischemic stroke: Ischemic stroke happens because of blockage of the vein which restricts the blood supply to the brain (**Figure 1**).

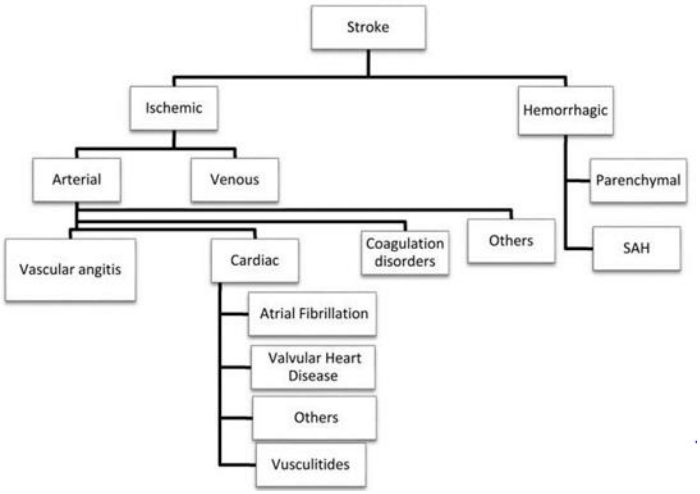

Figure 1. Types of Stroke.

Hemorrhagic stroke: A hemorrhagic stroke happens when blood from a vein unexpectedly starts bleeding into the cerebrum. Subsequently, the part of the body constrained by the harmed region of the cerebrum can't work properly (Nim, 2016) (**Figure 2**).

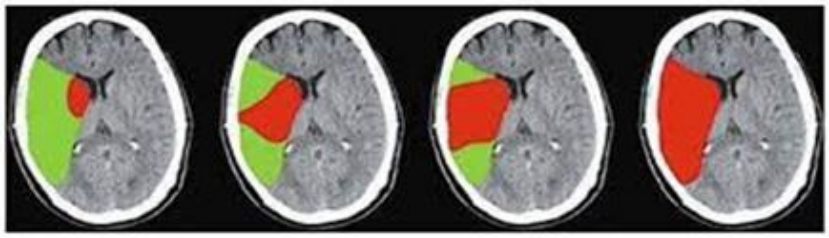

Figure 2. Hemorrhagic stroke.

Lab and additional revisions Include A total CBC, prothrombin and halfway thromboplastin times, LFT's, and kidney capability examinations might uncover an inclining cause for the drain (Nim, 2016). Lumbar cut is contraindicated in light of the fact that it might hasten a herniation disorder in affected population with a huge hematoma, and CT scan is unrivaled in identifying intracerebral discharge.

Prevalence and incidence data: Yearly, fifteen million persons globally experience a stroke. Of these, five million passes on and additional five million are left for all period incapacitated, putting a weight on family and local area. CVA is remarkable in individuals under 40 years; when it happens, the primary cause is hypertension. Nonetheless, stroke likewise happens in around 8% of kids with sickle cell illness (Weinberg MG, 2006).

Prevalence data of Pakistan: Pakistani individuals experience the ill effects of a stroke at a somewhat more youthful age contrasted and those individuals in Western nations. An emergency clinic-built experiment revealed that out of 12, 454 successive patient entrance to clinical wards, 796 (6 4%) experienced CVA. The assessed yearly frequency of CVA in Pakistan is 250/100 000, meaning 350 000 emerging cases consistently (Nim, 2016).

A report revealed that 26% of their patients were among the stage gathering of 15-45 years. Another study showed that 34% of patients in the examinations were younger than fifty years. Syed et al. tracked down a recurrence of 28% of patients younger than 55 years who experienced a stroke early on.

Hemorrhagic stroke seems, by all accounts, to be more in Pakistan comparative with the occident. It represents 10-15% of all CVA cases in occident however there are 21% - 31% of hospitalized CVA cases in Pakistan.

Prevalence information of Abbottabad and KPK: A report series of hospitalized CVA patients at Ayub Medical Hospital, Abbottabad revealed that 46% of the male CVA cases were 61-70 years old and females were from 51-60 years of age. The average time of CVA patients was 64 years for males and 49 years for females in a report at the Post Graduate Medical Institute/Lady Reading Hospital, in Peshawar, Pakistan. Khan et. al. showed that 52% of CVA patients for their condition sequence were female with an average age of 54 years.

Out of 91 Patients with affirmed CVA on C.T check, 65 (71.42%) patients were male and 26 (28.57%) were female (M: F 2.5:1). Top CVA-inclined age 61-70 years in male (25 cases) and 51-60 patients in female (12 cases) (Chris and Pompeo, 2019).

Etiology and manifestation: Ischemic stroke rarely is the underlying indication of systemic lupus erythematosus (SLE). It predominantly influences youthful patients, particularly females, following the age and orientation example of SLE the vertebrobasilar region is lopsidedly impacted (Kramer and Jasinda, 2014).

Immunosuppressants and anticoagulant treatment is a helpful way to deal with early stroke incidence.

Signs and symptoms: Beginning is normally sudden, and there may then be almost no movement aside from that because of brain inflammation. Clinical assessment ought to constantly incorporate an assessment of the heart for murmurs and rhythm abnormalities. Auscultating over the carotid or subclavian vessels might uncover a spread yet isn't sufficiently delicate to fill in for vascular imaging.

Block of carotid Flow-Blocking of the anterior cerebral vein distal to its intersection with the foremost imparting course reasons feebleness and cortical tactile misfortune in the contralateral leg and at times gentle feebleness of the arm, particularly proximally. There might be a contralateral grasp of reflex, paratonic inflexibility, abulia (absence of inventiveness) or plain disarray. Urinary incontinency is expected; especially behavioral changes are obvious. Bilateral front cerebral dead tissue is particularly prone to cause stamped behavioral deviations and memory impairment. One-sided front cerebral vein impediment proximal to the intersection with the foremost conveying course is by and large very much endured due to the blood supply from the opposite side (Davidson, 2005).

Center cerebral vein impediment prompts contralateral hemiplegia, hemisensory loss, and homonymous hemianopia (*i.e.,* reciprocally proportional damage of eye-side in portion of the visual arenas), with the eyes, strayed to the side of the injury. If chief side of hemisphere is tangled, worldwide aphasia is likewise existing. It could be difficult to separate this clinically from blockage of the inner carotid vein. With impediment of both of these veins, there may likewise be extensive inflammation of the semi hemisphere during the initial 3 days. For instance, an infarct including one cerebral half of the hemisphere might prompt such enlarging that the capability of the additional side of the hemisphere or the rostral brainstem is upset and unconsciousness state results. Impediments of various parts of the center cerebral vein causing more restricted findings. For instance, contribution of the unrivaled partition in the prevailing half of the hemisphere prompts a prevalently expressive (Broce) aphasia and to contralateral damage of motion and damage of sensations in the arm, the visage and less significantly, the leg. Sub-par branch impediment in the prevailing half of the hemisphere creates an open (Wernicke) aphasia and a homonymous visual arena deformity.

With the inclusion of the right brain hemisphere, discourse and cognizance are saved, yet there might be a left hemi spatial disregard disorder or constructional and

visuospatial shortages may occur (Davidson, 2005). Impediment of the ophthalmic or focal retinal vein prompts unexpected visual disfunction with retinal paleness and a macular reddish spot on fundoscopic assessment. Unexpected, transient vision misfortune in one eye (amaurosis fugax) is a TIA in this blood vessel region. Patients with a cilioretinal vein (roughly 25%) may have macular saving because of collateral blood supply.

Barrier of vertebrobasilar flow-blocking of the back cerebral vein might prompt a thalamic disorder in which contralateral hemisensory aggravation happens, trailed by the improvement of unconstrained aching and hyperpathia (Davidson, 2005). There is frequently macular-saving homonymous hemianopia and at times a gentle, normally brief, hemiparesis. Contingent upon the place of the sore and the security flow, the seriousness of these shortages shifts and different shortfalls may likewise happen, including compulsory developments and alexia. Impediment of the primary vein past the beginning of its entering branches might lead exclusively to macular-saving hemianopia.

Vertebral vein impediment underneath the beginning of the front spinal and posterior inferior cerebellar arteries courses might be clinically quiet on the grounds that the flow is kept up with by the other vertebral conduit. Assuming the excess vertebral vein is innately little or seriously atherosclerotic, in any case, a shortage like that of basilar course impediment is perceived except if there is great collateral circulation from the front dissemination through the circle of Willis. Block of the posterior inferior cerebellar artery or blockage of the vertebral artery not long before it divisions to this vessel prompts the sidelong medullary disorder, portrayed by dizziness and nystagmus (vestibular core), ipsilateral spinothalamic tactile misfortune including the visage (trigeminus nucleus and tract), dysphagia (nucleus ambiguous), appendage ataxia (inferior cerebellar peduncle), and Horner condition (descending sympathetic fibers), joined with a contralateral spinothalamic loss including the appendages. Impediment of both vertebral veins or the basilar course prompts trance state with pinpoint pupils, limp quadriplegia and sensory loss, and variable cranial nerve anomalies. With halfway basilar vein impediment, there might be diplopia, visual misfortune, dizziness, dysarthria, ataxia, shortcoming or tactile aggravations in some or the appendages in general, and discrete cranial nerve paralyses. In patients with hemiplegia of pinpoint pupils, the eyes are frequently strayed to the deadened side, while in patients with a hemispheric sore, the vision usually digress from the hemiplegic side.

At the point when the little paramedian arteries emerging from the basilar course are blocked, contralateral hemiplegia and tactile shortage happen in relationship with an ipsilateral cranial nerve paralysis at the near of the injury. Impediment of any of the major cerebellar arteries produces dizziness, sickness, nystagmus, and ipsilateral appendage ataxia. Contralateral spinothalamic sensory loss in the appendages may likewise be available. Deafness because of cochlear infarct might follow impediment of the front sub-par cerebellar vein, which may likewise cause ipsilateral facial spinothalamic sensory loss and feebleness. Huge cerebellar infarct might prompt obstructive hydrocephalus, trance state, tonsillar herniation, and demise.

Pathophysiology: In thrombosis, there is a disruptive cycle that forestalls blood stream to certain parts of the cerebrum. Hazard issues incorporate atherosclerotic illness, vasculitis, or arterial partition (Martin and Carline, 2019).

Embolic occasions happen when there is a coagulation that began from some other area in the body. Most usually, the wellspring of the coagulation is the valve or cavities of the heart, for instance, when a coagulation structures inside the atria in atrial fibrillation and dislodge into the arterial vascular blood.

Other less regular reasons incorporate venous, septic, air, or fat emboli. Lacunar infarcts are normally found in the subcortical region of the mind and happen because of tiny vessel illness. The proposed system is a puncturing artery in the subcortical area that reasons the vein impediment.

Prognosis: The guess for endurance subsequently cerebral dead tissue is better compared to subsequently cerebral or subarachnoid drain. Patients getting handling with Recombinant Tissue Plasminogen Activators (rtPA) are no less than 30% bound to have negligible or no incapacity at 90 days than those not handled by this. Those handled with automatic embolectomy are likewise no less than 30% bound to accomplish movement. Harm of cognizance after a cerebral infarct suggests a less fortunate guess than in any case. The degree of the infarct oversees the potential for recovery. Patients who have had a cerebral infarct are in danger for extra CVA and for myocardial infarcts. The prophylactic estimates examined before lessen this gamble. Antiplatelet treatment (same treatment rules concerning TIA) lessens the occurrence rate by 30% among patients without a cardiac reason for CVA who are not contender for carotid endarterectomy (Sarwar, 2018).

Diagnosis: Imaging CT checking (deprived of difference) is significant in affirming that drain has happened as well as in deciding the magnitude and location of the hematoma. MRI is similarly subtle when magnetic feebleness biased groupings (like, slope reverberation) are utilized. Assuming the patient's condition allows further mediation, CT angiography, MR angiography, or cerebral angiography might be embraced to decide if an aneurysm or arteriovenous mutation is available (Kresten and Stewart, 2013). In patients below stage fifty-five with lobar

haemorrhage and no set of experiences of hypertension, contrast-enhanced MRI might show no hypertensive reason like a basic neoplasm.

Pharmacotherapy

Intravenous thrombolysis: The National Institute of Neurological Disorders and Stroke Recombinant Tissue Plasminogen Activator (NINDS rt-PA) CVA Study, a multicentre, randomised preliminary, has shown the viability of handling by intravenous rt-PA (alteplase) began in the span of 3 hours after the beginning of effects (Francis and Gron).

Other treatments

Aspirin: In two huge, randomized preliminaries, the use of aspirin (160 or 300 mg each day), started in the duration of 48 hours subsequently the start of stroke and gone on for approx. 2 weeks until release from hospital, prompted reduced steps outwards demise or dependence at release or at a semi year likely through lessening the chance of repetitive ischemic stroke.

Anticoagulant treatment: A meta-examination of six randomised preliminaries including 21,966 patients tracked down no proof that the utilization of anticoagulants (unfractionated heparin, low molecular weight heparins, heparinoids, thrombin inhibitors, or oral anticoagulants) in the intense period of CVA has any result (Dave, Kristine, and J, 2016).

Other treatments

Hypertension, a high serum glucose level, and an increased internal heat level in the main 60 minutes to days after ischemic stroke have all been related with reduced results. The impacts of the early bringing down of pulse and upkeep of normothermia and normoglycemia are presently being tried in huge, randomised preliminaries.

Emergency intravenous drug: Therapy with medications that can remove a coagulation must be given within 4.5 hours from when side effected initially began whenever given intravenously. The as soon these medicines are specified, the improved outcomes will be received. Fast treatment works to save life as well as may lessen confusions.

An Intervenous infusion of recombinant Tissue Plasminogen Activator (TPA) likewise called alteplase (Activase) or tenecteplase (TNKase) is the best quality level therapy for ischemic stroke. An infusion of TPA is normally given through a vein in the upper limb inside the initial three hours. At times, TPA can be initiated within 4.5 hours after stroke side effects began (Francis and gron).

This medication re-establishes blood flow by liquefying the blood coagulation producing the CVA. By rapidly eliminating the reason for the CVA, it might assist individuals by improving more completely from a stroke.

Management: The board is separated into acute and chronic stages, the first pointed toward limiting disability and the second pointed toward prevention of repetitive stroke. The main starting assurance is the time at which the patient was last normal; this is viewed as the hour of stroke beginning. In the event that patients get clinical consideration in the span of 6 hours of stroke beginning, a CT and CT angiogram ought to be performed to identify haemorrhage and large vessel occlusion. Intravenous thrombolytic treatment with recombinant tissue plasminogen activator (rtPA; 0.9 mg/kg to a limit of 90 mg, with 10% given as a bolus for about 60 seconds and the rest of for over 60 minutes) works on the opportunity of improvement without huge disability at 90 days from 26% to 39% whenever allowed in the span of 3 hours from CVA beginning; it is as yet viable up to 4.5 hours from CVA beginning (Dave, Kristine, and J, 2016).

Therapy ought to be started quickly; the result is straightforwardly connected with the time from CVA beginning to therapy. Intravenous thrombolysis is recognized in Europe for utilize around 4.5 hours from CVA beginning yet just for as long as 3 hours in the United States, unapproved use of approved drug is around 3 to 4.5-hour window is typical. The hazard of rtPA is haemorrhage; when given past 4.5 hours, the hazard of intracerebral haemorrhage outweighs any advantage.

Contraindications to rtPA incorporate the followings:

- Huge head injury or earlier stroke in the past 90 days.
- Side effects of subarachnoid haemorrhage.
- Arterial perforation at a noncompressible site.
- Past intracranial haemorrhage.
- Intracranial neoplasm or arteriovenous mutation,
- Current intracranial or intraspinal medical procedure.
- Dynamic inner bleeding or draining bleeding (e.g. platelets under 100,000/mcL, recent utilization of heparin with a raised aPTT, INR more prominent than 1.7, current utilization of direct thrombin or factor Xa inhibitors).
- Glucose under 50 mg/dL (2.7 mmol/L).
- Huge cerebralinjury on CT.
- Systolic strain more prominent than 185 mm Hg or diastolic tension more prominent than 110 mm Hg. The pulse ought to be brought quickly down to under 185/110 mm Hg with intravenous labetalol or nicardipine to allow rtPA is given.

Extra relative contraindications incorporate minor stroke, seizure at stroke beginning, pregnancy, significant medical procedure within the previous 14 days, GIT or urinary tract haemorrhage within the previous 21 days, and myocardial

infarction within the previous 90 days (Dave, Kristine, and J, 2016). A few randomized preliminaries have shown an improved probability of accomplishing practical freedom with the utilization of endovascular mechanical embolectomy by stent retrievers as an assistant to intravenous rtPA. Just patients with huge vessel impediment (around 20% of patients with intense ischemic stroke) are qualified for embolectomy, which should be performed in the span of 6 hours of stroke beginning.

An exemption for this time limitation might exist in patients with extreme clinical shortages and somewhat little infarct volumes (as shown by dispersion weighted MRI or perfusion CT), demonstrating a huge ischemic obscuration managable to rescue with reperfusion. A randomized preliminary examining embolectomy in such patients accomplished useful freedom in 49% of those treated somewhere in the range of 6 and 24 hours of stroke beginning contrasted with 13% of untreated patients. Early administration of a finished stroke in any case requires general strong measures. The board in a CVA maintenance unit has been displayed to further develop results, logical because of early recovery and counteraction of unexpected issues (Dave, Kristine, and J, 2016).

Throughout the intense phase, there might be checked brain inflammation and edema, with side effects and indications of expanding intracranial strain, a rising neurologic shortage, or herniation disorder. Raised intracranial strain is managed by head rise and osmotic agents like mannitol. Preservation of a sufficient cerebral perfusion burden stop further ischemia. Early decompressive hemicraniectomy (in the span of 48 hours of stroke beginning) for harmful center cerebral vein areas of dead tissue lessens mortality and works on useful results.

Attempts to bring down the blood pressure of hypertensive patients throughout the intense stage (*i.e.,* in the span of 72 hours) of a CVA should be avoided except the motive is to provide rtPA, as there is loss of cerebral autoregulation, and lower the blood pressure might cause another attack of ischemia.

In any case, assuming the systolic pressure crossed 220 mm Hg, it tends to be brought down by utilizing intravenous labetalol or nicardipine with nonstop checking to 170-200 mm Hg and afterward, following 72 hours, it should be minimized to 140/90 mm Hg. Blood pressure rise is not normally necessary in patients with absolute low blood pressure but rather upkeep of intravenous hydration is significant. Prophylactic and clinical measures are examined in the part on TIAs.

Whenever haemorrhage has been excepted by CT, aspirin (325 mg by mouth everyday) is begun quickly except if the patient got thrombolysis, in which case aspirin is started after a subsequent CT has precluded thrombolytic related discharge at 24 hours. Anticoagulant medications should begin when specified as examined in the part on TIAs. There is no benefit in postponement, and the distress toward producing haemorrhage into a formerly infarcted region is lost since there is a distant more serious danger of additional embolism to the cerebral flow in the event that treatment is held back. Active recuperation plays a significant part in the administration of patients with physical disability. Physical movement at a beginning phase will assist with forestalling contractures.

As collaboration increments and some recuperation start, dynamic developments will further develop forte and coordination. In all cases, primary assembly and dynamic recovery are significant. professional related treatment might further develop spirit and coordinated movements, while speech training might assistance in expressing aphasia or dysarthria. Due to the hazard for dysphagia succeeding CVA, admittance to diet is commonly limited till a proper gulping assessment; the top of the bed ought to be kept raised to stop aspiration. Urinary catheters ought not be set and, whenever set, eliminated within 24-48 hours (Dave, Kristine, and J, 2016).

MATERIALS AND METHODS

Study design

It was a prospective cross-sectional study.

Sampling

Convenience sampling technique was used.

Site and participant

The present study focuses on the documentation of ischemic stroke among patients hospitalized in AMC (Ayub Medical Complex) from March 2022 to July 2022.

Approval was taken from the department ethical committee. The management of stroke will be documented by patient profile. The patient profile has seven sections.

- Demographics
- Patient disease condition
- Medication on admission
- Lab test results
- Pharmacotherapy

Each section of the patient profile will be completed during the ward rounds while taking a patient history and asking for assistance from the medical staff of the ward.

Inclusion criteria

All patients admitted in ward due to haemorrhagic and ischemic stroke.

Data collection tool

PWDT (pharmacist Work-up on Drug therapy) form was modified and used for data collection.

Sample size

Sample size calculated as 96 using WHO calculator for sample size based on following assumptions.

- Standard prescription practices taken as 50%
- Absolute precision of 10%
- Confidence interval of 96 % 5

Data analysis

Data was analyzed by calculating percentages and writing detailed SOAP notes for each case.

RESULTS

Demographics

Demographic analysis is the study of a population-based on factors such as age, race, marital status and sex.

Gender wise occurrence of stroke: Figure 3 show the stroke was more prevalent among males (60%) than females (40%).

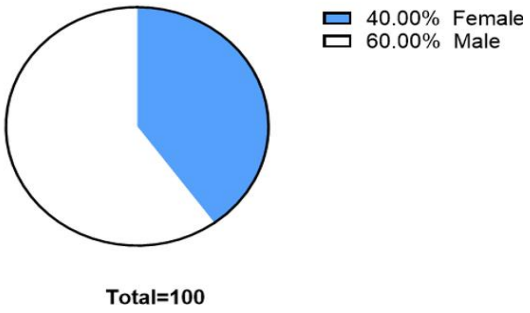

Figure 3. Gender wise occurrence of stroke.

On the basis of age distribution: Figure 3 shows age wise distribution of patients with stroke and age group range was <10->88- years out of which patients <10 years (1%), 10-23 years (1%), 23-36 years (5%), 36-49 years (13%), 49-62 years (24%), 62-75 years (31%), 75-88years (19%) and >88 years (6%). The cases being analyzed showed that most of the people suffering from stroke were older people (*i.e.,* 62-75 years).

Chief complaints: Figure 4 shows that the 67% patients were presented with headache, 49% with vision difficulty, 74% with confusion, 87% with numbness and weakness whereas 75% patients were presented with drowsiness.

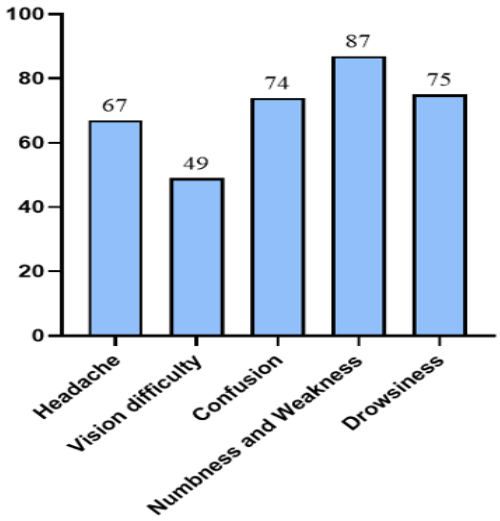

Figure 4. Chief complaints

Past medical history: **Figure 5** shows past medical history. 61% patients were presented with hypertension whereas 20% patients with diabetes.

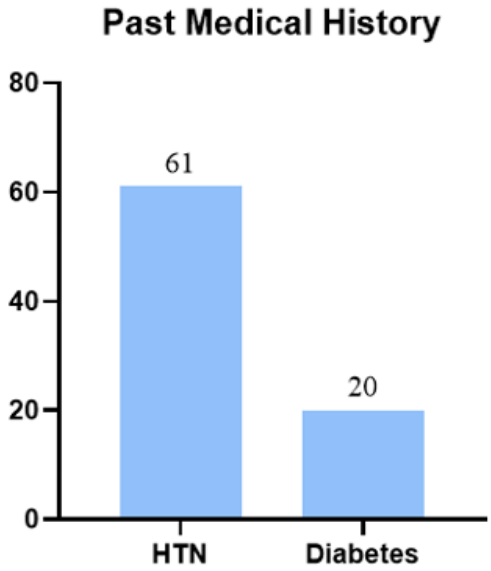

Figure 5. Past medical history.

Blood pressure: **Figure 6** shows blood pressure. 153 patients were having elevated systolic blood pressure *i.e.,* 150 mm Hg.

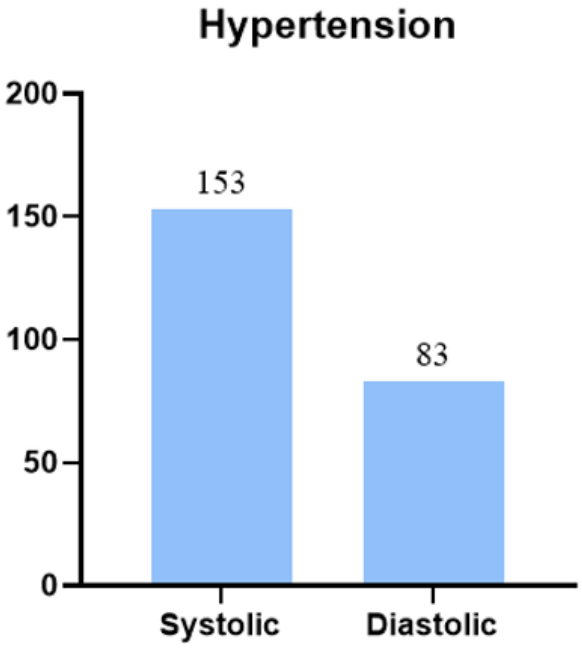

Figure 6. Blood pressure.

Classes of drugs: **Figure 7** shows classes of drugs prescribed. Steroids and NSAIDS were highly prescribed drugs to the patients with stroke.

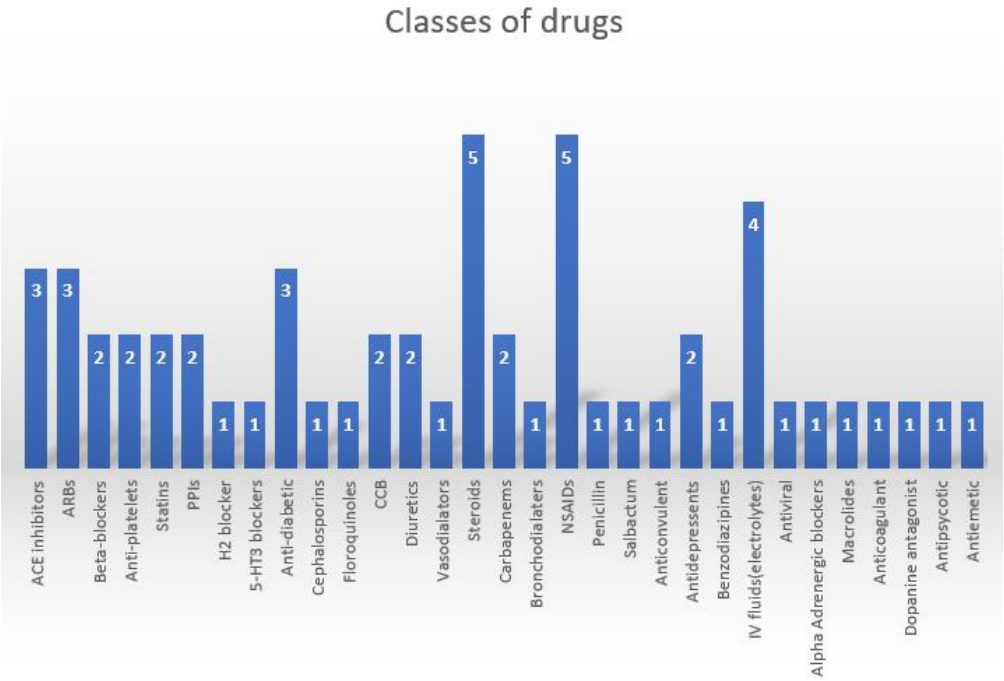

Figure 7. Classes of drugs.

Drugs: **Figure 8** shows ceftriaxone was highly prescribed drug in stroke patient. Whereas second most prescribed drug was aspirin.

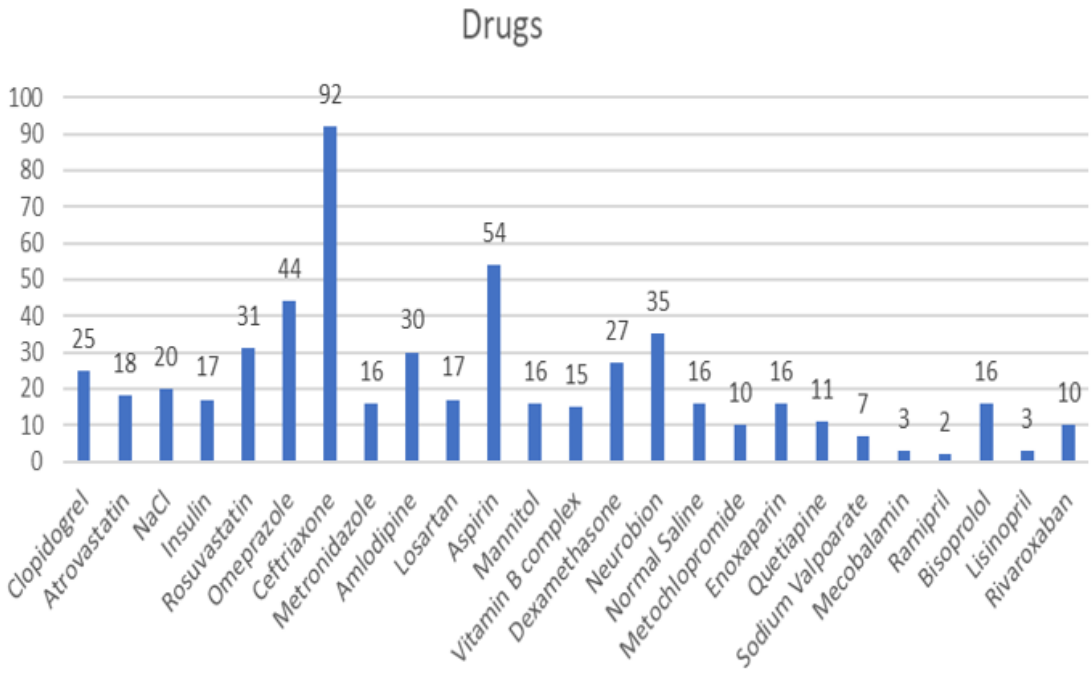

Figure 8. Drugs prescribed to stroke patient.

Drug related problems: **Figure 9** shows drug related problem. Out of such problems, untreated symptoms or indications or missing lab parameters were reported in 35% of patients.

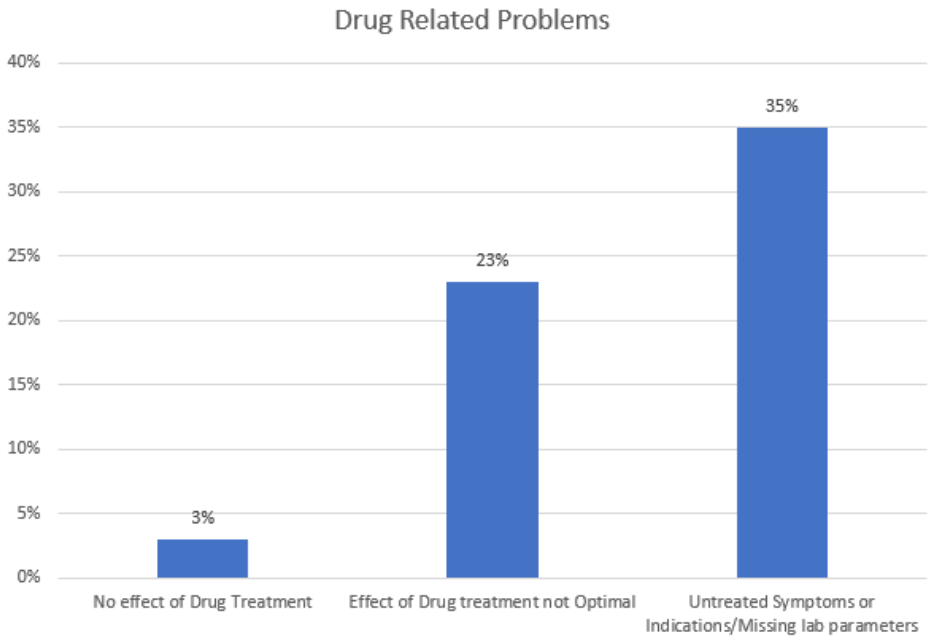

Figure 9. Drug related problems.

Dose frequency: **Figure 10** shows dose frequency. 283 drugs were given as OD, 164 drugs as BD, 74 drugs as TDS whereas only 65 drugs were given as a STAT.

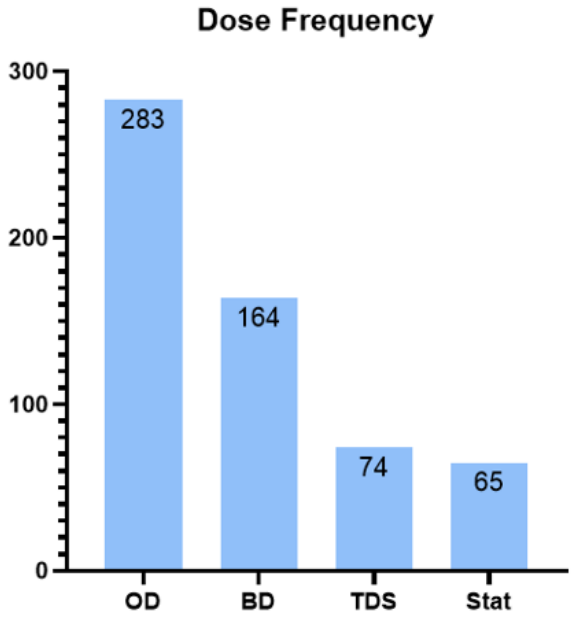

Figure 10. Dose frequency.

Route of administration: The route of administration was divided into six groups, *i.e.,* group 1 Per-oral (P/O), group 2 parenteral, group 3 inhalational, group 4 subcutaneous, group 5 nasogastric and group 6 Intramuscular. Percentages are given below **Figure 11**.

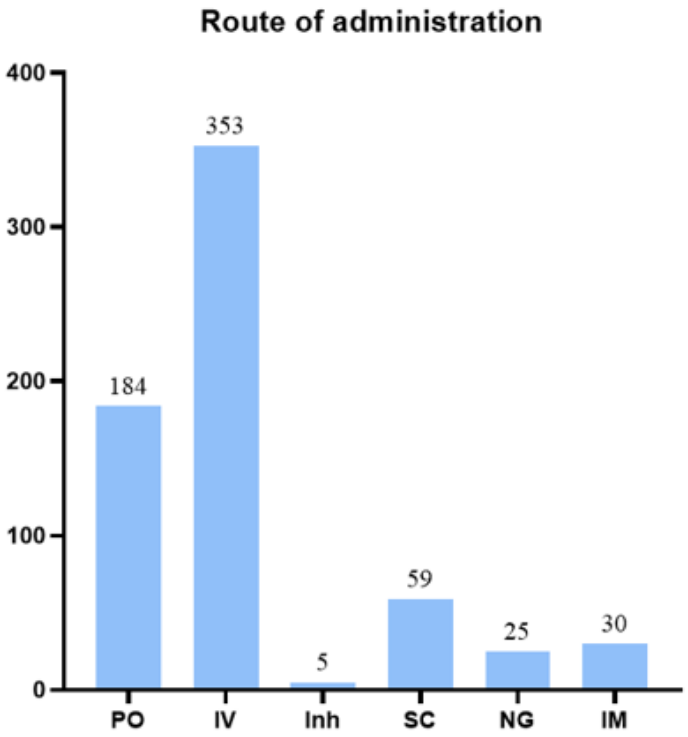

Figure 11. Route of administration.

Total cost: **Figure 12** shows total cost. The minimum cost is 0-500 which is 1% whereas the maximum cost is 1000-1500 which is 23%.

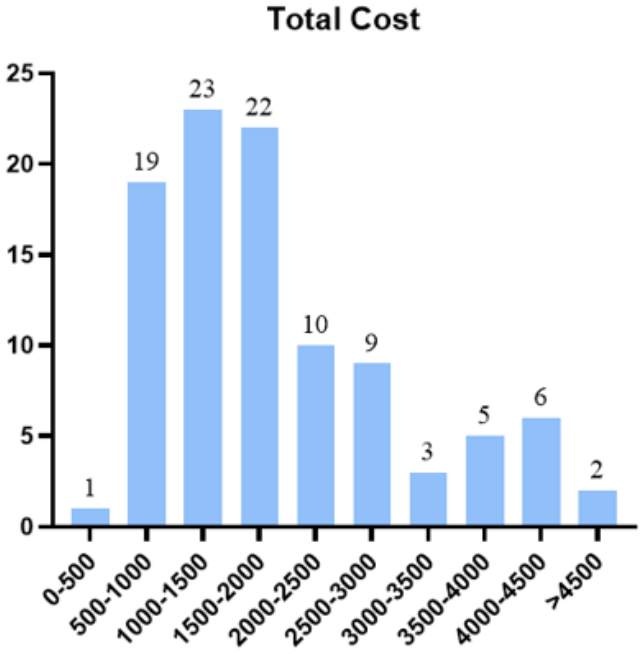

Figure 12. Total cost.

Drug-drug interaction: Several interactions were seen and they are divided into three groups according to the severity of interactions. These are 58 % minor, 46 % moderate and 29% major (**Figure 13 and Table 1**).

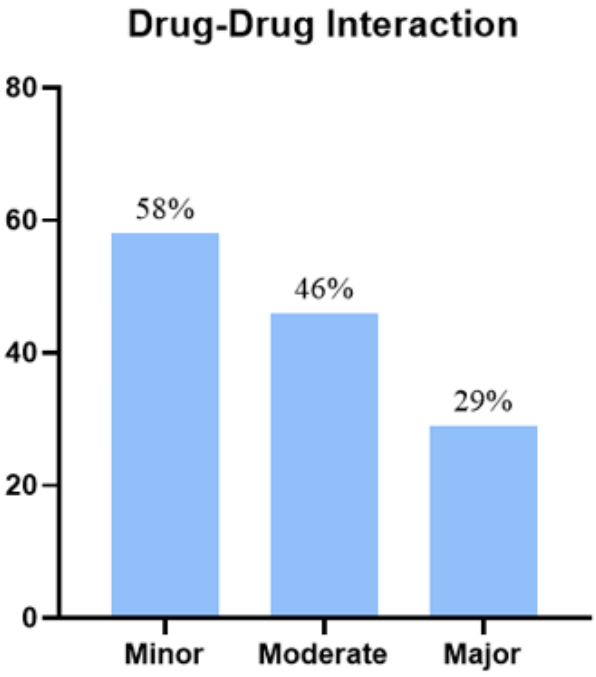

Figure 13. Drug-drug interactions.

Table 1. Drug-drug interactions.

Severity	Drug interaction	Result
Minor	Aspirin+Prednisolone	Prednisolone decreases levels of aspirin by increasing renal clearance.
	Omeprazole+Mecobalamin	Omeprazole decreases absorption of mecobalamin
	Dexamethasone+Omeprazole	Dexamethasone will decrease the effect of omeprazole by affecting hepatic enzymes
	Levetiracetam+Paracetamol	Levetiracetam decreases acetaminophen concentration by hepatic metabolism that may result in increased hepatotoxic metabolites
	Furosemide+Thiamine	Furosemide decreases levels of thiamine by increasing renal clearance
	Dexamethasone+Amlodipine	Dexamethasone decreases level of Amlodipine by affecting CYP3A4.

Moderate	Metronidazole+Atorvastatin	Using metronidazole together with atorvastatin may increase the risk of nerve damage, which is a potential side effect of both medications
	Aspirin+Dexamethasone	Using aspirin together with dexamethasone may increase the risk of side effects in the gastrointestinal tract such as inflammation, bleeding, ulceration, and rarely, perforation. Dexamethasone can also decrease the activity of aspirin.
	Aspirin+Valsartan	Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) may attenuate the antihypertensive effects of angiotensin II receptor antagonists.
	Ceftriaxone+Furosemide	Ceftriaxone increases toxicity of furosemide by pharmacodynamic synergism. Increased risk of nephrotoxicity.
Major	Hydrocortisone+Moxifloxacin	Increased risk of Tendon rupture
	Aspirin+Enoxaparin	Increased toxicity by pharmacodynamic synergism. Increased anticoagulation effect.
	Rivaroxaban+Clopidogrel	Avoid concurrent administration of clopidogrel with rivaroxaban unless benefit outweighs the risk of increased bleeding.
	Ceftriaxone+Enoxaparin	Ceftriaxone increases effects of enoxaparin by anticoagulation. Avoid or use Alternative drug. Cephalosporins may decrease prothrombin time.
	Captopril+Furosemide	Pharmacodynamic synergism. Risk of acute hypotension, renal insufficiency.

DISCUSSION

The most important findings of this study were the extremely high Occurrence of observed potential drug-drug interactions in patient receiving care in Intensive care unit regard-less of severity. Two classes of medications that were most frequently linked to pDDIs were Cardiovascular drugs and Non-Steroidal Anti-Inflammatory drugs (NSAIDs). Moreover, about one-sixth of the patients received prescriptions for medications whose concurrent use were possibly contraindicated, and prevalence of these combinations was noticeably greater than those passed away (Dave, Kristine, and J, 2016). The amount of prescribed medications and the use of antipsychotic medications were found to be the main contributors to exposure to potentially contraindicated drug-drug interactions. The causes of the occurrence of pDDI/pCDDI in severe ill patients with Acute Ischemic stroke are possibly improper prescription due to their long-term hospital stay, commonly with parenteral drug, in addition typically age of the patients as well as any major comorbidities, such as cardiovascular. Such a health problem frequently calls for taking several medications at once, which raises the risk of drug interactions.

Patients are vulnerable for various harmful drug-drug interactions and their well-known adverse effects, including death, because these numerous combinations typically comprise drugs with varied pharmacokinetics and pharmacodynamics and a small therapeutic index.

Other studies have revealed various incidence of potential drug-drug interactions in the CCU ranging from 49.3% to 91.3%, through online drug-drug interactions checker. There are, however, few studies investigating prevalence in neurological ill patients. The studies of just 89 of these patients, the prevalence of potential drug-drug interactions at time of discharge from a general neurology

department was 71%, whereas it ranged from 60% to 88.5% in patients who had suffered an ischemic or hemorrhagic stroke (Chris and Pompeo, 2019). With regard to antimicrobial medications, CCU patients showed the highest prevalence of potential drug interactions, 98% for very significant interactions, and patients with Chronic Kidney Disease (CKD), 96%. Since a significant link between length of stay and pDDI has been demonstrated, a greater number of potential drug-drug interactions were anticipated in patients since our sample comprised of patients who were admitted in hospital for last seven days. In accordance with the findings of other research, we documented potential drug-drug interactions exposure throughout the patient's stay rather than only at admission or discharge. Moreover, in certain research, the potential drug-drug interactions rate was only assessed during a particular day of hospitalization or with a single prescription per patient, which may have contributed to the lower pDDIs incidence in these studies.

Additionally, the comparatively high and varied numbers of physician who treat our patients in accordance with a prescription practice that emphasized symptom management may potentially account for the variations in pDDIs frequency between our sample and those of other research. In earlier research, the prevalence of potential drug interactions was considerably impacted by a large number of comorbidities (HTN, Hyperlipidemias, DM, CKD, Arrhythmias, Sudden cardiac death, and Seizures) (How and Su, 2011). Comparable to what we found, where a significant number of patients has cardiovascular comorbidity, a frequency of potential drug interactions was seen in patients with heart problems, up to 91.6%. Due to their frequent changed pharmacokinetic and pharmacodynamic, and compromised autoregulation systems, aged people are substantially more likely to experience potential drug-drug interactions than younger patient. They consequently have a very high probability of experiencing negative outcomes. effect. The majority of the patients in our sample were above 65 years old, which may have attributed to the increase incidence of possible drug-drug interactions. Although a research indicated a mean number of prescriptions of 17, which was close to our report's findings, the typical quantity of various medicines administered to our patients were much greater than the majority of other research. 90% of the individuals in this research experienced potential drug interactions. According to research, individuals taking two distinct medications had a 14% chance of drug-drug interactions, whereas those taking seven or more medications concurrently had an 81% chance.

The average number of prescriptions per patient grew dramatically over time, from 9 to 14, according to a sample of 100 outpatients, and as a result, there was a larger risk of dangerous possible drug-drug interactions. The high incidence of pDDI/pCDDI in our study may be related to the very high polypharmacy rates among our patients, which suggests a higher risk of prescriptions cascades (more medication prescriptions to manage adverse drug reactions. Similar to our patient sample, the majority of patients in Intensive Care Units (ICUs) get antibiotic therapy, and research has demonstrated a really high rate of possible drug-drug interactions involving antimicrobial medication, up to 48%. Ceftriaxone with Ringer's solution constituted the most typical pCDDI in our sample (which can cause intravascular precipitation of the calcium-ceftriaxone complex). Atorvastatin and azithromycin were the most often seen potentially contraindicated drug-drug interactions in our study, which we saw in 2.9% of our patients. Metoclopramide was the medicine which was most frequently implicated in potentially contraindicated drug-drug interactions, according to the data, and it was present in 25.75% of all pCDDIs in our patients (Chaw, 2017). A recent research discovered a greater likelihood of cerebral haemorrhage in people using these kinds of medications simultaneously, despite another study showing that NSAIDs and Selective Serotonin Reuptake Inhibitors (SSRIs) do not impair each other's efficacy and that the mixture should never be ignored. Similar to our study, more than 80% of all potential drug-drug interactions upon Hospitalization were accounts for by 30 pairs of possible drug interactions.

The study found that 10 Potentially Drug-Drug Interactions account for 2/3 of the overall DDI exposure duration. By properly educating the neuro physician on the drugs that cause the most of pDDIs, this is among the variables that really can assist to reduce the number of pDDIs. It is vital to monitor patients' clinical symptoms and biochemical findings since the most common potential drug-drug interactions, such as Diclofenac Sodium-Aspirin, Diclofenac Sodium-Enoxaparin, and Diclofenac Sodium-Clopidogrel, may increases the likelihood of bleeding (PT, aPTT, and INR). Aspirin-Furosemide usage together may be toxic to kidneys; hence kidney functioning must be carefully monitored. The incidence of potentially contraindicated drug-drug interactions identified in past research (2.18% in mentally ill patients and 8.2% in patients hospitalized in family medicine wards) was lower than the percentage of pCDDIs observed in our patients. In patients suffering from Chronic Kidney Disease (CKD), a comparable prevalence of potentially contraindicated drug interactions of 11.4% was noted.

Similar to the study done at the ICU, where 18 distinct potentially contraindicated drug-drug interactions were detected, our sample contained 17 different possibly contraindicated drug-drug interactions.

Moreover, individuals with Type-2 Diabetes have been shown to have a significant incidence of possible drug-drug interactions (Chaw, 2017). These factors were discovered to be strongly related to potentially contraindicated drug-drug interactions in sinuni variance decomposition

analysis because these people were treated for high blood sugar levels; however, after controlling for other independent and confounding variables, its significance was reduced. Dual antiplatelet treatment was identified as a substantial factor for potentially contraindicated drug-drug interactions, but this importance was lost in the statistical tests. The fact that somewhat more than one fifth of patients had Aspirin-Clopidogrel pDDIs is one reason for the high incidence of possible drug-drug interactions in stroke patients. The results show that prolonged dual antiplatelet therapy lowers the likelihood of a second Acute Ischemic Stroke while increasing the risk of systemic and cerebral haemorrhage in patients. Moreover, recent literature recommendations highlight the fact that patients with slight strokes should regularly take a combination of Aspirin and Clopidogrel for about 7 to 21 days to lower their risk of having another stroke (D and laura, 2009). Because the prevalence of mild strokes in our setting coincides based on the number of patients in our research in whom these interactions were detected, we conclude that compliance to this suggestion by competent prescribers may explain our results. The frequency of prescription medications and the usage of antipsychotics were the two primary variables in this study that contributed to the occurrence of potentially contraindicated drug-drug interactions. In our investigations, the most frequent factor linked to drug-drug interactions was the quantity of prescription medications (Chaw, 2017). However, under this study, we confirmed it impact on the incident of potentially contraindicated drug-drug interactions in patients with ischemic stroke, which is a move forward. Since earlier mentioned, the most of our individuals were then given prescriptions for antibiotics with a propensity to cause pCDDIs, non-steroidal anti-inflammatory medicines (NSAIDs), and cardiovascular medications. Patients who had mental comorbidities were more likely to experience potentially contraindicated drug-drug interactions (1.8%) and potentially drug-drug interactions (80.75%), perhaps as a result of the use of antipsychotic medications, which have a high risk of interactions. However, there were considerably more potentially contraindicated drug-drug interactions involving antipsychotics in our group.

The most often used antipsychotic medication, risperidone, has a high risk of interfering with other medications, including antidepressants, anticonvulsants, statins, azole-antimycotics, and antivirals (Jacky, 2010). On Contrary, information from investigational studies shows that it has a considerable impact on the occurrence of stroke in older people.

Finally, it is suggested that patients using a specific medication from the antipsychotic drug class, such as risperidone, take extreme precautions and undergo particular screening for potentially contraindicated drug-drug interactions (Chaw, 2017).

CONCLUSION

The study was conducted on 100 patients. From the results obtained we concluded that stroke was more prevalent among older people and there were many problems in pharmacotherapy of stroke. The problems identified were mostly missing lab parameters, we found that in most of the cases PT (Prothrombin Time), INR (International normalized ratio) were missing which help in measuring how quickly the blood clots. Inappropriate doses were observed in some cases where cholesterol level was not that much high, still high doses of statins were being prescribed, statins causes serious side effects mainly myopathies so these should be prescribed starting from low doses and then dose should be increased according to cholesterol level and doses should be adjusted after monitoring the control over cholesterol. CT scan was prescribed for the diagnosis of stroke in majority of the cases and it was good enough for early diagnosis and was economical as compared to MRI.

We also found that there were many major drug-drug interactions, these drug interactions need to be considered by the prescribers as these can lead to serious problems, all the major drug-drug interactions are mentioned above in results with their major side effects. Stroke has significant financial expenses, is the second highest cause of mortality throughout the globe, and causes disability. Therefore, improving therapeutic approaches and post-stroke care should be top priority for global health. Pharmacists should play their role to identify these major side effects and interactions of drugs to save the patients from any kind of serious diseases.

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