Section A-Research paper

PHARMACEUTICAL CARE PLAN IN STROKE PATIENTS

Gopu Dharani and D.Akila Devi*

Research scholar, Department of Pharmaceutics, School of pharmaceutical sciences, VELS institute of science, technology and advanced studies, Pallavaram, Chennai.

Corresponding author, Department of Pharmaceutics, School of pharmaceutical sciences, VELS institute of science, technology and advanced studies, Pallavaram, Chennai.

Email: akilaajcp@gmail.com

Abstract

A clinical pharmacist has to have deeper understanding of medications and their therapeutic effects since the pharmaceutical treatment regimen is a continual process. The patient's healthcare outcomes are improved through pharmaceutical care plans, which also help medical practitioners avoid illness. The pharmaceutical care plan is very important in helping stroke patients discover Drug Related Problems (DRPs), which include neglected symptoms, sub-therapeutic dosages, high dosages, drug usage without a clear diagnosis, refusal to take medications, inappropriate drug choice, drug reactions, and adverse drug responses. There is significant proof that supports the clinical pharmacist's assistance in the treatment of stroke patients, and studies assessing pharmacist treatments in stroke patients have been reported in the literature. Explaining the specific evidence of pharmacist treatments on stroke patients is the goal of this study.

Keywords: *Stroke, care plan, clinical pharmacist, Drug Related Problems*

1. Introduction:

According to the World Health Organization (WHO), a stroke is a medical illness that exhibits quickly emerging clinical indications of a localized (or generalized, in the case of coma) impairment of brain activity that lasts for beyond 24hrs or causes mortality without any other obvious explanation than a vascular origin (Coupland et al., 2017). Stroke is broadly divided into subarachnoid hemorrhage, ischemic stroke, and hemorrhagic stroke. Hemorrhagic stroke occurs when a vein ruptures, causing blood to flood into the cerebral cavity, as opposed to ischemic stroke, which occurs when a vein becomes blocked, limiting blood flow to the brain (Unnithan and Mehta, 2020). Stroke is the third most common reason for disability and the 2nd largest mortal threat globally (Johnson et al., 2016). Throughout the world, ischemic strokes account for 68% of all cases, whereas hemorrhagic strokes account for 32%. (Chugh, 2019).The prevalence in the United States are slightly different, with 87% being ischemic, 10% being hemorrhagic, and approximately 3% being subarachnoid hemorrhage. In India, stroke accounts for 3.5 percent of disability-adjusted life years (DALY) (Ramesh et al., 2023; Garg et al., 2018).

According to research, the prevalence of stroke in India spans between 116 and 163 strokes per 100,000 population. As of late, ICMR has emerged with a report named "India: According to the report "Health of the Nation's States," it was the fifth most prevalent reason of disability adjusted life years (DALY) and the fourth most frequent reason for mortality in 2016.

There is ample literature evaluating pharmacist interventions in stroke patients, and the significance of a clinical pharmacist in stroke therapy is highly supported by data. The present article gives an in-depth explanation of the evidence for pharmacist interventions with stroke patients.

A clinical pharmacist needs a greater understanding of drugs along with respective therapeutic effects because creating a pharmaceutical care plan is an ever-evolving process. The patient's health outcome and the health care professionals' ability to prevent disease are both enhanced by the pharmaceutical care plan (Mossialos et al., 2015). For stroke individuals care plan assumes an extremely significant part to distinguish the Medication-Related Issues (DRPs), exploring the type and recurrence of DRPs particularly untreated signs, sub-remedial measurements, exorbitant dose, drug use without an obvious sign, inability to get drugs, inappropriate medication determination, drug connections, and unfavorable medication responses (Kanagala et al., 2016).

Three different types of ischemic stroke have been identified by the multicenter Trial of Acute Stroke Therapy (TOAST) (Adams et al., 1993):

1. Large vessel occlusion (LVO) strokes
2. Lacunar ischemic stroke
3. Cardioembolic stroke

Thrombo-embolic obstruction of the larger arteries supplying the brain, particularly the anterior cerebral, middle cerebral, internal carotid, or vertebrobasilar arteries, may result in LVO strokes (Lambert et al., 2016). The smaller or perforating capillaries that take blood to brain's inner parts are the primary cause of lacunar strokes (Wardlaw et al., 2003; Rudilosso et al., 2022; Regenhardt et al., 2019).

Time represents a primary factor in treating an acute ischemic stroke (AIS) (Gonzalez et al., 2006; Saver, 2006). When an AIS occurs, 190,000 neurons, approximately 14,000,000 nerve connections and 12 kilometers nerve fibers are lost per minute. The brain matures roughly 3.6 years for each hour the blood supply stops (Lakhan et al., 2009; Green, 2008). Two approaches are available for treating AIS (Sacco et al., 2007). Mechanical thrombectomy and intravenous thrombolysis (Pereira et al., 2015).

After an AIS has been clinically diagnosed, the next steps must be taken.

- Verify the patient's medical stability.
- Look for neurological symptoms that can be fixed.
- Evaluate the stroke type and how to treat it.
- Find out what causes stroke.

Pharmacist interventions were identified as medicines optimisation where pharmaceutical care included medicines review, medicines reconciliation, identification and resolution of drug related problems (Pai et al., 2013; St Peter et al., 2013; Kousar et al., 2018). To allow comparison of similar outcome measures for different treatment regimens, findings have been separated into primary and secondary prevention optimisation (Al-Qahtani et al., 2022).

A person's risk of suffering a stroke can be assessed using the acronym FAST: Face—Invite the individual to smile; this will assist with distinguishing deadness or shortcoming on a side of their face. Arms: Request the individual to stretch up both of their arms; Check to see if one arm is dipping fairly low than the other. Speech: Request the individual to say a short sentence.

2. Health Care Centres

The Primary Health Centre's (PHC) role is restricted to risk evaluation, prompt diagnosis of manifestations, stabilization, and recommendation to other centers with management amenities due to the complexity of stroke treatment (Espiritu et al., 2021; Chandrashekhar et al., 2020).

- Primary prophylaxis, timely detection, and referrals for recovery process are all provided through PHC.
- Acute stroke treatment, subsequent prophylaxis and follow-up, and rehabilitative therapy are all provided through SHC.
- THC offers more sophisticated and advanced treatment of acute forms, follow-up after a stroke for procedures that allow and assist recovery, and restoration of residual damage.

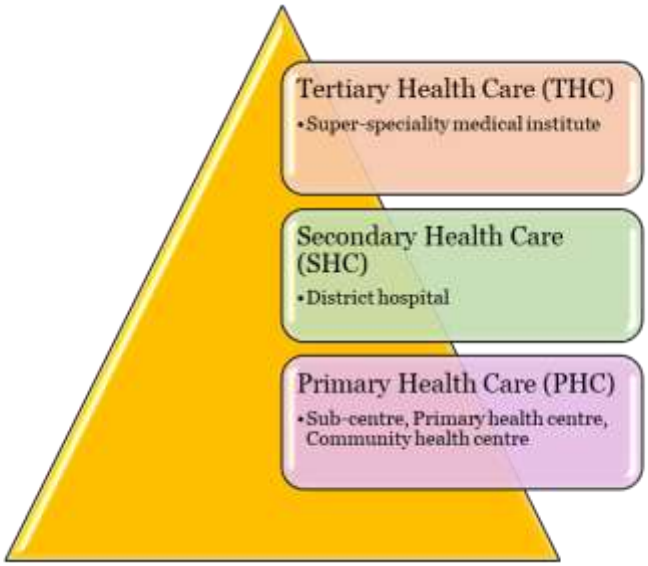

Figure 1: Health care centres for stroke patients

3. Pharmacological Therapy for Stroke

Pharmacologic treatment may be classified into two groups depending on the stroke type: stroke-specific treatment and stroke prevention. Under certain circumstances, antiplatelet medications and tPA are pharmacological options for treating initial ischemic stroke

(Bradberry et al., 2004). Regulating the individual's b.p. and intracranial pressure is the goal of Pharmacotheraputics treatment for hemorrhagic stroke (Forsyth et al., 2008; Schwarz et al., 2002).

Acute ischemic stroke (AIS) is typically treated with alteplase intravenous thrombolysis (Huang et al., 2020; Tong et al., 2016). If initiated in less than 48 hours after the commencement of an ischemic stroke, aspirin antiplatelet therapy has indeed been demonstrated to reduce the likelihood of an immediate recurrent stroke, yet fails to address the stroke itself. Clinical studies are still being conducted, however aspirin and more recent antiplatelet drugs have showed encouraging outcomes for additional early relapse prevention (Siddique et al., 2009). Unselected patients receiving low molecular weight heparin (LMWH) or unfractionated heparin (UFH) for immediate pharmacological anticoagulation in the event of an AIS did not show therapeutic advantages over antiplatelet agents (Bansal et al., 2013). The role of acute anticoagulation in specific situations with a high risk of early stroke recurrence requires additional research (Serkin et al., 2019). The strategies involved in pharmacological treatment of stroke are shown in Figure 2. A suggested list of medications covered by the NPCDCS for emergency treatment is given in Table 1.

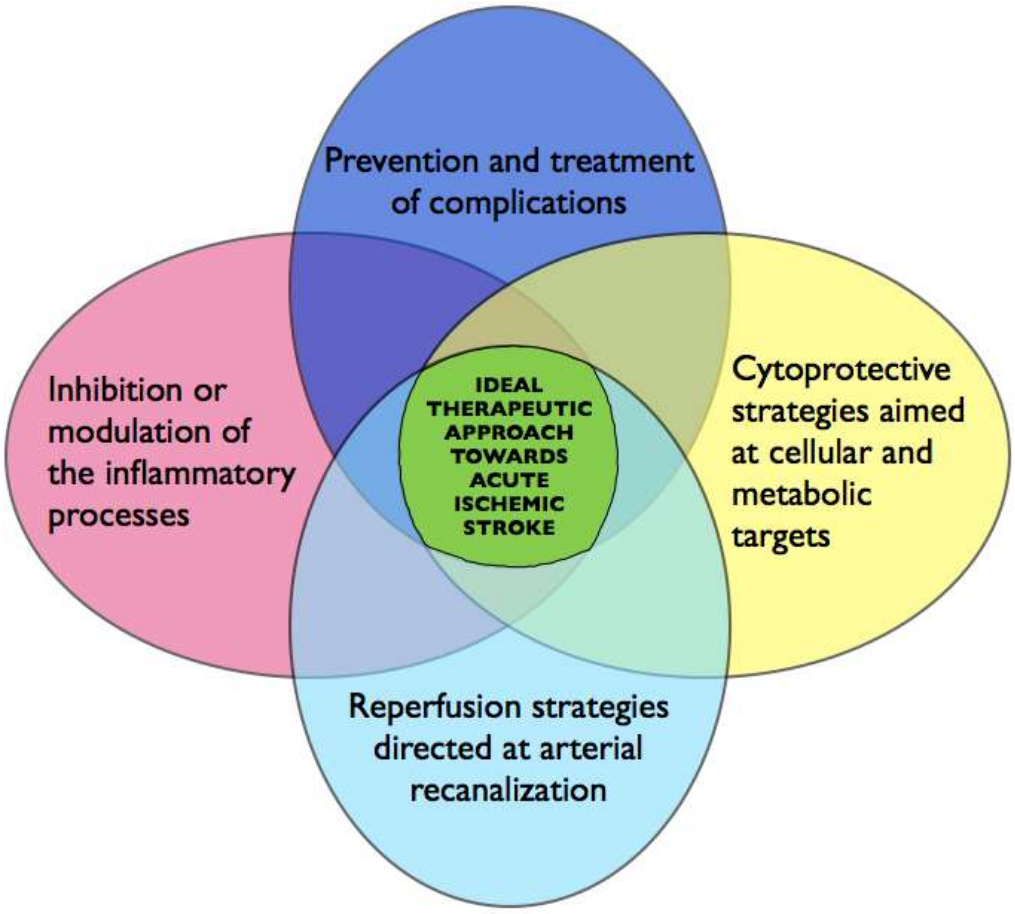

Figure 2: Therapeutic approaches towards ischemic stroke

Table 1: A suggested list of medications covered by the NPCDCS for emergency treatment

ACE Inhibitors	**Captopril, Enalapril, Lisinopril, Ramipril,**
Calcium channel blocker	Amlodipine

Diuretic	Hydrochlorthiazide, Indepamide, Frusemide, Chlorthalidone.
Mineralocorticoid receptor antagonist Beta blocker	Metoprolol, Atenolol, Labetolol
Oral hypoglycemic	Gliclazide, Metformin, Glibenclamide
Insulin	Short-, medium-, long- acting
Fibrinolytics	Streptokinase, alteplase and tenecteplase
Anti-platelet	Clopidogrel
Lipid lowering	Statins

Tissue plasminogen activator (tPA): The FDA has only authorized one IV Tissue Plasminogen Activator (tPA) medication, called alteplase, for treating Ischemic Stroke. This indication was approved once the drug's effectiveness in the NINDS rt-PA Stroke Study was established. In terms of symptomatic intracerebral hemorrhage, deaths, or a modified Rankin Scale score of 0-2 at 3 months, the Safe Implementation of Thrombolysis in Stroke-International Stroke Registry (SITS-ISTR) 3-to-4.5-hour study did not identify any variations among subjects treated in less than 3hrs as well as subjects treated in under 3 to 4.5hrs. Despite the fact that stroke survivors who qualify for IV Tissue Plasminogen Activator (tPA) must be managed in under 3hrs, the established recommendations for stroke therapy With the administration of alteplase for ischemic stroke, reports of cerebral edema, convulsions, cerebral herniation, and recurrent AIS have all been documented.

4. Optimizing drugs for Primary Prevention

The effectiveness of optimizing blood-thinners and antithrombotic medications for those who have higher chance of experiencing a stroke was the subject of three primary prevention studies (Hart et al., 1999; Ryvlin et al., 2006; Hart et al., 2007). A pharmacist consultation revealed 78 of 218 (35.6%) needed adjustments to optimize current antithrombotic therapies for individuals hospitalized at elevated stroke risks (notably AF) as per locally made evidence-based recommendations. In 60 (76.9%) of the cases, prescribing or changing preventative medications, which could be less effective but safer, was necessary to lower the chances of stroke. Similar to this, a pharmacist-led strategy to determine the likelihood of stroke in a hospital among 134 individuals with AF increased warfarin usage from 74% at admittance to 98% at discharge and produced 50 suggestions for medication modification, from which 44 (80%) were acknowledged and put into action (Jackson et al., 2011). The need for more efficient treatment was seen in 30 of the 44 cases (68 percent). 77% of the 382 suggestions for those suffering from AF to optimize their anticoagulation and antithrombotic therapy were accepted by medical doctors, as demonstrated by the clinical audit.

Men may take aspirin everyday (50-100 mg) for cardiac disease, particularly stroke prophylaxis, if their 10-yr risk is high enough (above 10%) for the improvements to exceed the concerns of therapy. A cardiovascular risk calculator might be used to determine the 10yr risk, but there is no India-specific calculator. Risk can be calculated using the WHO calculator and clinical judgment.

Aspirin should only be used when absolutely necessary because it has been associated with an higher chances of bleeding (He et al., 1998). Risk can be calculated using the WHO calculator and clinical judgment. In the coming years, risk calculators made specifically for Indians will be developed through ongoing Indian studies. Aspirin should only be used when absolutely necessary because it has been linked to an increased risk of bleeding.

Post-menopausal females, particularly those having T2DM, whose risk-to-benefit ratio is low enough for the improvements to exceed the risk involved with therapy can benefit from taking aspirin (50 mg to 100 mg daily) (Dorresteijn et al., 2011; Baill et al., 2017). Its use ought to be clinically checked in regards to draining propensity.

The therapeutic outcome will be improved by clinical pharmacist engagement in discharge planning, computerized drug order input, tracking DDIs before dosing, and patient counselling. (Mutnick et al., 1997; Alsultan et al., 2013).

As per different studies it found pharmaceutical interventions are the evidences to improve patient therapeutic outomes. Patients who are given two antiplatelets and are at a greater chance of bleeding can benefit from pharmaceutical interventions like adding omeprazole, reducing the dose of piperacillin/tazobactam from 4.5 to 2.25 g IV q 6 h in individuals whose creatinine clearance is less than 20 ml/min, raising the dosing of atorvastatin from to 40 mg for improved lessening of LDL-c Physicians have accepted 84% of the clinical pharmacist recommendations above.

The majority of ADRs, were in the WHO's "probable" category. None of the identified ADRs were "probably preventable" or "definitely preventable," and the majority were "mild" in severity. Involving a pharmacist in the evaluation of DRPs enhances patient QoL, particularly in aged polypharmacy individuals. The pharmacist's primary goal shall be on locating potential Drug Related Problem’s (Viktil et al., 2008). Mostly, the drug therapy is being altered, and these recommendations were widely accepted (Varrassi et al., 2010). It was discovered that polypharmacy may increase the likelihood of DRPs. The therapeutic outcomes are enhanced through pharmaceutical care plan for the timely diagnosis of DRPs.

Table 2: ADRs of Drugs

Drugs	**Adverse drug reaction**
Atorvastatin	Hepatotoxic, myopathy
Aspirin + dipyridamole, Cilostazol	Headache, palpitation, tachycardia
Nicardipine	Phlebitis
Warfarin	Upper gastrointestional bleeding
Hydralazine, Carvedilol	Hypotension

Table 3: Different Drug-Related Problems

Drug use without indication	**Domperidone, Ondansetron, Piperacillin + Tazobactam, Paracetamol, Tramadol, Pantoprazole**
Drug Duplication	Pantoprazole, Clopidogrel
Subtherapeutic Dose	Telmisartan, Amlodipine, Nimodipine, Metoprolol

Overdose	Rabeprazole, Ranitidine
Adverse Drug Reactions	Amlodipine-mediated constipation, insulin-caused hypoglycemia, atorvastatin-mediated myopathy
Improper drug selection	Ondansetron, Rabeprazole, Ramipril
Failure to Receive drugs	LMWH Multivitamins
Medication errors	Clopidogrel Aspirin Atorvastatin Mannitol Pantoprazole

5. Outcomes

Clinical Outcomes

Merely two trials examined clinical outcomes that did not constitute surrogate measures for the primary prevention (Bajorek et al., 2013; Lee et al., 2005). Both included the administration of anticoagulants by pharmacists, and they both conclude that clinics run by pharmacists are equivalent to pivotal trials or act as a check on bleeding and stroke risk.

Three studies (Hedegaard et al., 2014; Andres et al., 2019; Nathans et al., 2020) examined the effect of pharmacist's assistance on re - hospitalization in the context of recurrent stroke prevention. Two trials indicated statistically significant changes in favor of pharmacists' assistance in stroke health centers (Nathans et al., 2020; Andres et al., 2019), although one research did not discover a difference to control for a multi-component, pharmacist-managed, 6-month follow-up therapy (Hedegaard et al., 2014). Peripheral artery disease, myocardial infarction, and stroke rehospitalization were 9.3% (n = 24) vs. 17.2% (n = 34) p = 0.013 (Andres et al., 2019) and 5.3% (n = 94) vs. 21.3% (20/94) p = 0.001 (Nathans et al., 2020).

Patient Outcomes

The effect of a pharmacist interventions on a individual's QoL or contentment with treatment was only examined in secondary prevention trials. 286 (34.3%) of the 834 interventions that pharmacists carried out were expected to increase patient satisfaction with treatment or physical, cognitive, or interpersonal performance (Lindblad and Howorko, 2008). According to a different research, a pharmacist's assistance increased patients' confidence and improved their ability to utilize medications appropriately by around one-third of them (Hedegaard et al., 2014). Nevertheless, research of 255 individuals that had outcomes documented in two distinct studies (Hohmann et al., 2010; Hohmann et al., 2009) offered the most thorough examination. In the study's control and pharmacist intervention groups, HRQoL was comparable at the outset. After a year, neither group's overall health condition substantially changed, but the estimated HRQoL for the control group had dropped considerably in 7 out of 8 measures, whereas the intervention group's observed drop was statistically significant in just one factor (body pain). Also, as against control group, the treated group reported considerably higher levels of satisfaction and assessed the intensive counseling provided by pharmacists as being very instructive and helpful.

6. Conclusion:

Patients' health-related quality of life (HRQoL) has been shown to improve as a result of pharmaceutical care provided in hospitals, as demonstrated by different studies. Studies also indicate that men were more likely than women to suffer a stroke due to their social habits and that people between the ages of 41 and 70 are most at risk. The most severe drug interactions that were observed in this study increased the likelihood of hospitalization as well as the cost of health care. Antiplatelet agents, anticoagulants, and antihypertensives were the most common drugs to interact with one another. The use of an antihypertensive greatly increased the likelihood of ADRs. The majority of drug-related issues arise during the prescribing process and DRPs as a result of incorrect drug indication and dosage. Ageing, aphasia, a frequent occurence of comorbid conditions, polypharmacy, and the intravenous drug administration are additional factors that increase the risk of medication errors due to impaired oral intake. Patient getting certain anticoagulants, hypotensive medicine, and mix of antiplatelet agents exhibit high gamble for drug-drug interactions (DDI) or prescription blunders.

Clinical pharmacist engagement in discharge planning would improve the curative result, and so will computerized drug order input, tracking DDIs before dosing, and patient counselling. An individual's health-related quality of life (HRQoL) is more likely to deteriorate if they do not get enhanced pharmacological therapy. The individual's HRQoL is clearly improved by the pharmacological treatment.

References

Adams HP Jr, Bendixen BH, Kappelle LJ, et al., 1993. 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*, *24*(1):35-41. doi:10.1161/01.str.24.1.35

Al-Qahtani, S., Jalal, Z., Paudyal, V., Mahmood, S. and Mason, J., 2022, November. The Role of Pharmacists in Providing Pharmaceutical Care in Primary and Secondary Prevention of Stroke: A Systematic Review and Meta-Analysis. In *Healthcare* (Vol. 10, No. 11, p. 2315). MDPI.

Alsultan, M.S., Mayet, A.Y., Khurshid, F. and Al-Jedai, A.H., 2013. Hospital pharmacy practice in Saudi Arabia: Drug monitoring and patient education in the Riyadh region. *Saudi Pharmaceutical Journal*, *21*(4), pp.361-370.

Andres, J., Stanton-Ameisen, O., Walton, S. and Ruchalski, C., 2019. Pharmacists' impact on secondary stroke prevention. *Journal of Pharmacy Practice*, *32*(5), pp.503-508.

Baill, I.C. and Castiglioni, A., 2017. Health maintenance in postmenopausal women. *American family physician*, *95*(9), pp.561-570.

Bajorek, B.V., Krass, I., Ogle, S.J., Duguid, M.J. and Shenfield, G.M., 2005. Optimizing the use of antithrombotic therapy for atrial fibrillation in older people: a pharmacist□led multidisciplinary intervention. *Journal of the American Geriatrics Society*, *53*(11), pp.1912-1920.

Bansal, S., Sangha, K.S. and Khatri, P., 2013. Drug treatment of acute ischemic stroke. *American Journal of Cardiovascular Drugs*, *13*, pp.57-69.

Bradberry, J.C., Fagan, S.C., Gray, D.R. and Moon, Y.S., 2004. New perspectives on the pharmacotherapy of ischemic stroke. *Journal of the American Pharmacists Association*, *44*(2), pp.S46-S56.

Chandrashekhar, Y., Alexander, T., Mullasari, A., Kumbhani, D.J., Alam, S., Alexanderson, E., Bachani, D., Wilhelmus Badenhorst, J.C., Baliga, R., Bax, J.J. and Bhatt, D.L., 2020. Resource and infrastructure-appropriate management of ST-segment elevation myocardial infarction in low-and middle-income countries. *Circulation*, *141*(24), pp.2004-2025.

Chugh, C., 2019. Acute ischemic stroke: management approach. *Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine*, *23*(Suppl 2), p.S140.

Coupland, A.P., Thapar, A., Qureshi, M.I., Jenkins, H. and Davies, A.H., 2017. The definition of stroke. *Journal of the Royal Society of Medicine*, *110*(1), pp.9-12.

Dorresteijn, J.A., Visseren, F.L., Ridker, P.M., Paynter, N.P., Wassink, A.M., Buring, J.E., van der Graaf, Y. and Cook, N.R., 2011. Aspirin for primary prevention of vascular events in women: individualized prediction of treatment effects. *European heart journal*, *32*(23), pp.2962-2969.

Espiritu, A.I. and San Jose, M.C.Z., 2021. A Call for a Stroke Referral Network Between Primary Care and Stroke-Ready Hospitals in the Philippines: A Narrative Review. *The Neurologist*, *26*(6), pp.253-260.

Forsyth, L.L., Liu□DeRyke, X., Parker Jr, D. and Rhoney, D.H., 2008. Role of hypertonic saline for the management of intracranial hypertension after stroke and traumatic brain injury. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, *28*(4), pp.469-484.

Garg, R. and Davalagi, S., 2018. Behavioral Risk Factors for Non-Communicable Diseases among Adult Population: A Cross Sectional Study from Urban Slums of Central Karnataka, India. *National Journal of Community Medicine*, *9*(03), pp.220-224.

Gonzalez, R.G., 2006. Imaging-guided acute ischemic stroke therapy: from "time is brain" to "physiology is brain". *American Journal of Neuroradiology*, *27*(4), pp.728-735.

Green, A.R., 2008. Pharmacological approaches to acute ischaemic stroke: reperfusion certainly, neuroprotection possibly. *British journal of pharmacology*, *153*(S1), pp.S325-S338.

Hart, R.G., Benavente, O., McBride, R. and Pearce, L.A., 1999. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. *Annals of internal medicine*, *131*(7), pp.492-501.

Hart, R.G., Pearce, L.A. and Aguilar, M.I., 2007. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Annals of internal medicine*, *146*(12), pp.857-867.

He, J., Whelton, P.K., Vu, B. and Klag, M.J., 1998. Aspirin and risk of hemorrhagic stroke: a meta-analysis of randomized controlled trials. *Jama*, *280*(22), pp.1930-1935.

Hedegaard, U., Kjeldsen, L.J., Pottegård, A., Bak, S. and Hallas, J., 2014. Multifaceted intervention including motivational interviewing to support medication adherence after

stroke/transient ischemic attack: a randomized trial. *Cerebrovascular diseases extra*, *4*(3), pp.221-234.

Hohmann, C., Klotz, J.M., Radziwill, R., Jacobs, A.H. and Kissel, T., 2009. Pharmaceutical care for patients with ischemic stroke: improving the patients quality of life. *Pharmacy world & science*, *31*, pp.550-558.

Hohmann, C., Radziwill, R., Klotz, J.M. and Jacobs, A.H., 2010. Health-related quality of life after ischemic stroke: the impact of pharmaceutical interventions on drug therapy (pharmaceutical care concept). *Health and quality of life outcomes*, *8*(1), pp.1-7.

Huang, B., Qian, F., Fan, X., Guan, S., Zheng, Y., Yang, J. and Xu, F., 2020. Efficacy and safety of intravenous thrombolysis with alteplase for treating acute ischemic stroke at different time windows: a protocol for systematic review and meta-analysis. *Medicine*, *99*(52).

Jackson, S.L., Peterson, G.M., 2011. Stroke risk assessment for atrial fibrillation: hospital-based stroke risk assessment and intervention program. *J Clin Pharm Ther., 36*(1):71-9. doi: 10.1111/j.1365-2710.2009.01156.x. PMID: 21198722.

Johnson, W., Onuma, O., Owolabi, M. and Sachdev, S., 2016. Stroke: a global response is needed. *Bulletin of the World Health Organization*, *94*(9), p.634.

Kanagala, V.S., Anusha, A., Rao, B.S., Challa, S.R., Nalla, K.S. and Gadde, R.S., 2016. A study of medication-related problems in stroke patients: A need for pharmaceutical care. *Journal of Research in Pharmacy Practice*, *5*(3), p.222.

Kousar, R., Murtaza, G., Azhar, S., Khan, S.A. and Curley, L., 2018. Randomized controlled trials covering pharmaceutical care and medicines management: a systematic review of literature. *Research in Social and Administrative Pharmacy*, *14*(6), pp.521-539.

Lakhan, S.E., Kirchgessner, A. and Hofer, M., 2009. Inflammatory mechanisms in ischemic stroke: therapeutic approaches. *Journal of translational medicine*, *7*(1), pp.1-11.

Lambert, S.L., Williams, F.J., Oganisyan, Z.Z., Branch, L.A. and Mader Jr, E.C., 2016. Fetal-type variants of the posterior cerebral artery and concurrent infarction in the major arterial territories of the cerebral hemisphere. *Journal of investigative medicine high impact case reports*, *4*(3), p.2324709616665409.

Lee, P.Y., Han, S.Y. and Miyahara, R.K., 2013. Adherence and outcomes of patients treated with dabigatran: pharmacist-managed anticoagulation clinic versus usual care. *American Journal of Health-System Pharmacy*, *70*(13), pp.1154-1161.

Lindblad, A.J. and Howorko, J., 2008. Integration of a pharmacist into a stroke prevention clinic team. *Canadian Journal of Hospital Pharmacy*, *61*(6).

Mossialos, E., Courtin, E., Naci, H., Benrimoj, S., Bouvy, M., Farris, K., Noyce, P. and Sketris, I., 2015. From "retailers" to health care providers: transforming the role of community pharmacists in chronic disease management. *Health policy*, *119*(5), pp.628-639.

Mutnick, A.H., Sterba, K.J., Peroutka, J.A., Sloan, N.E., Beltz, E.A. and Sorenson, M.K., 1997. Cost savings and avoidance from clinical interventions. *American Journal of Health-System Pharmacy*, *54*(4), pp.392-396.

Nathans, A.M., Bhole, R., Finch, C.K., George, C.M., Alexandrov, A.V. and March, K.L., 2020. Impact of a pharmacist-driven poststroke transitions of care clinic on 30 and 90-

day hospital readmission rates. *Journal of Stroke and Cerebrovascular Diseases*, *29*(4), p.104648.

Pai, A.B., Cardone, K.E., Manley, H.J., Peter, W.L.S., Shaffer, R., Somers, M. and Mehrotra, R., 2013. Medication reconciliation and therapy management in dialysis-dependent patients: need for a systematic approach. *Clinical Journal of the American Society of Nephrology*, *8*(11), pp.1988-1999.

Pereira, V.M., Yilmaz, H., Pellaton, A., Slater, L.A., Krings, T. and Lovblad, K.O., 2015. Current status of mechanical thrombectomy for acute stroke treatment. *Journal of Neuroradiology*, *42*(1), pp.12-20.

Ramesh, S. and Kosalram, K., 2023. The burden of non-communicable diseases: A scoping review focus on the context of India. *Journal of Education and Health Promotion*, *12*(1), p.41.

Regenhardt, R.W., Das, A.S., Ohtomo, R., Lo, E.H., Ayata, C. and Gurol, M.E., 2019. Pathophysiology of lacunar stroke: history's mysteries and modern interpretations. *Journal of Stroke and Cerebrovascular Diseases*, *28*(8), pp.2079-2097.

Rudilosso, S., Rodríguez-Vázquez, A., Urra, X. and Arboix, A., 2022. The potential impact of neuroimaging and translational research on the clinical management of lacunar stroke. *International journal of molecular sciences*, *23*(3), p.1497.

Ryvlin, P., Montavont, A. and Nighoghossian, N., 2006. Optimizing therapy of seizures in stroke patients. *Neurology*, *67*(12 suppl 4), pp.S3-S9.

Saver, J.L., 2006. Time is brain—quantified. *Stroke*, *37*(1), pp.263-266.

Schwarz, S., Georgiadis, D., Aschoff, A. and Schwab, S., 2002. Effects of induced hypertension on intracranial pressure and flow velocities of the middle cerebral arteries in patients with large hemispheric stroke. *Stroke*, *33*(4), pp.998-1004.

Serkin, Z., Le, S. and Sila, C., 2019. Treatment of extracranial arterial dissection: the roles of antiplatelet agents, anticoagulants, and stenting. *Current Treatment Options in Neurology*, *21*, pp.1-10.

Siddique, A., Butt, M., Shantsila, E. and Lip, G.Y.H., 2009. New antiplatelet drugs: beyond aspirin and clopidogrel. *International journal of clinical practice*, *63*(5), pp.776-789.

St Peter, W.L., Wazny, L.D. and Patel, U.D., 2013. New models of CKD care including pharmacists: improving medication reconciliation and medication management. *Current opinion in nephrology and hypertension*, *22*(6), p.656.

Tong, X., Liao, X., Pan, Y., Cao, Y., Wang, C., Liu, L., Zheng, H., Zhao, X., Wang, C., Wang, Y. and Wang, Y., 2016. Intravenous thrombolysis is more safe and effective for posterior circulation stroke: data from the Thrombolysis Implementation and Monitor of Acute Ischemic Stroke in China (TIMS-China). *Medicine*, *95*(24).

Unnithan, A.K.A. and Mehta, P., 2020. Hemorrhagic stroke.

Varrassi, G., Müller-Schwefe, G., Pergolizzi, J., Orónska, A., Morlion, B., Mavrocordatos, P., Margarit, C., Mangas, C., Jaksch, W., Huygen, F.J.P.M. and Collett, B., 2010. Pharmacological treatment of chronic pain–the need for CHANGE. *Current medical research and opinion*, *26*(5), pp.1231-1245.

Viktil, K.K. and Blix, H.S., 2008. The impact of clinical pharmacists on drug□related problems and clinical outcomes. *Basic & clinical pharmacology & toxicology*, *102*(3), pp.275-280.

Wardlaw, J.M., Sandercock, P.A., Dennis, M.S. and Starr, J., 2003. Is breakdown of the blood-brain barrier responsible for lacunar stroke, leukoaraiosis, and dementia?. *Stroke*, *34*(3), pp.806-812.