

A Review On Image Segmentation Techniques In M.R.I. Brain Stroke

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Abstract

Background: A stroke is a common brain disease with many potential outcomes. The proposed review is necessary to identify an improved method for segmenting the brain stroke lesion for computer-assisted diagnosis. M.R. angiography and diffusion M.R.I. provide essential physiological information that is of great therapeutic utility in identifying patients who need immediate treatment. T2 or T2* - weighted M.R.I. is currently used to rule out intracerebral haemorrhage (ICH), Magnetic Resonance Angiography (M.R.A.) or thrombus identification, and the Diffusion Weighted Imaging (D.W.I.) and Perfusion Weighted Imaging (PWI) mismatch for penumbral identification and therapeutic determination in the diagnosis of stroke. T2 with Gradient and other common M.R.I. sequences produced the same results. Stroke mimics on M.R.I. are diagnosed using an algorithm based on Diffusion Weighted Imaging (D.W.I.), which can be abnormal or regular, followed by the results of other common M.R.I. sequences T2 with Gradient Recalled Echo weighted imaging (T2-GRE) and Fluid-attenuated inversion recovery (FLAIR). In situations of seizures (including the hippocampus), hypoglycemia, and other disorders where D.W.I. indicates the suggestive distribution of brain lesions, FLAIR is of particular value (bilateral lesions in the posterior limb of the internal capsules, corona radiata, and splenium of the corpus callosum). Parameters including cerebral microbleeds (C.M.B.s), lesion and penumbra size and position, and thrombus identification are better visualised with M.R.I.; these features assist in indicating which treatments, such as tissue plasminogen activator or thrombus ablation, should be employed (tPA).

Keywords: M.R.I., Stroke, Sequences, Brain, D.W.I., FLAIR, Perfusion.

INTRODUCTION:

Stroke is a significant cause of mortality and disability. Ischemic brain damage, brought on by a sudden drop in blood supply accounts for more than 80% of all strokes. According to the hypothesis "time is the brain," 1.8 million neurons are damaged every minute when the correct care is not received. Because of these considerations, stroke imaging is crucial and must be executed efficiently [1]. The second leading cause of death worldwide, ischemic stroke, is the most common type of stroke. Stroke lesions consist of irreparable core and penumbra tissue, representing tissue that can be saved [2]. An arterial obstruction generated by local thrombolysis or cerebral blood flow distribution (CBF) owing to thrombus,

hemodynamic factors, or embolic causes develops an ischemic stroke. When an artery closes up, blood flow to the surrounding area drops suddenly, putting the cells in a transitional state between life and death. Hyper-acute (immediately following the occurrence), acute (6 hours after the incident), sub-acute (from 24 hours), and chronic (after two weeks) are the four critical stages of a stroke lesion's temporal evolution [2,3]. The current gold standard of care is thrombolytic therapy, which involves using a tissue plasminogen activator to dissolve blood clots. This should be given within 3-4.5 hours of the onset of optimum safe function following a stroke [3]. Vascular imaging, diffusion imaging, perfusion imaging, and spectral analysis are a few examples of the multimodal imaging techniques used in clinical practice [4]. Pathophysiological processes of tissue damage and healing, such as an increase in brain oedema and the beginning of cerebral haemorrhagic transformation (H.T.), are influenced by the B.B.B.'s (Blood-Brain-Barrier) abnormalities, which vary in degree throughout the acute and sub-acute phases of stroke [4]. Magnetic resonance imaging (M.R.I.) with field strengths up to 3 Tesla (T) is an excellent imaging technique for the diagnosis of stroke, the evaluation of infarct shape, and the determination of the cause of stroke [5]. M.R.I. scans are more sensitive to ischemic lesions and can reveal subtle differences in brain tissue even in the early stages of an ischemic stroke. A high Diffusion-Weighted Magnetic Resonance Imaging (D.W.I.) signal and a low apparent diffusion coefficient (A.D.C.) signal are seen in the overall images during the early stages of myocardial infarction [6].

Magnetic Resonance Imaging:

Stroke visualisation has changed drastically due to M.R.I. developments [3]. The state-of-the-art M.R.I. system permits high-definition contrast imaging of soft tissues everywhere in the body. For example, M.R.I. uses the magnetic properties of protons, ubiquitous throughout the body, to generate a signal. A magnetic field is used in a magnetic resonance imaging machine to align the hydrogen spins along the primary domain. After radiofrequency (R.F.) pulses have modified the spins, the bulk transverse magnetisation is then measured. To begin with, early M.R.I. techniques used contrast based on four tissue characteristics: spin density, spin count per voxel, and relaxation times T1, T2, and T2*. However, M.R.I. technology has progressed since it was first developed. It is now possible to utilise M.R.I. to view and evaluate blood arteries and blood flow and track iron content, perfusion, diffusion, and oxygen saturation [3].

Stroke:

Significant death and long-term disability are caused by stroke [7]. Stroke is characterised by reduced blood flow and perfusion and can be caused by a thrombus/embolus or haemorrhage [3]. A stroke occurs when blood and nutrients ordinarily delivered to brain tissue are cut off or severely reduced, killing brain cells. Brain cells begin to deteriorate within minutes. When the brain doesn't receive enough blood, oxygen, or nutrients, proper cell activity and communication between nerve cells become impaired. The symptoms of a stroke include a sudden onset of headache, difficulty walking, trouble speaking and comprehending others, and numbness or paralysis of the face, arm, or leg. Strokes are primarily broken down into ischemic and hemorrhagic categories [7].

Ischemic Stroke:

Ischemic strokes occur when blood vessels in the brain become too narrow and blocked to deliver adequate blood and oxygen to the brain. Ischemic strokes come in two forms: thrombotic and embolic. A thrombotic stroke occurs when a blood clot forms in response to arterial plaque and obstructs blood flow to the brain. An embolic stroke occurs when a clot that has travelled via the bloodstream from another part of the body stops an artery in the brain [7].

Haemorrhagic Stroke:

A hemorrhagic stroke occurs when a blood vessel in the brain bursts and causes bleeding. Subarachnoid haemorrhage and intracerebral haemorrhage are the two subtypes [7]. An intracerebral haemorrhage occurs when blood leaks from a ruptured or bleeding artery into brain tissue. When the blood-filled sac called an aneurysm that forms on or near the brain's surface and balloons out from an artery break, it leaks into the subarachnoid space. Common risk factors for hemorrhagic stroke include hypertension, smoking, oral contraceptive use, excessive alcohol consumption, and the use of illicit drugs [7]. Most traumatic haemorrhagic strokes are caused by intracerebral haemorrhages [8]. However, these haemorrhages may originate in or disseminate to other brain regions, including the intraventricular, subdural, or subarachnoid spaces.

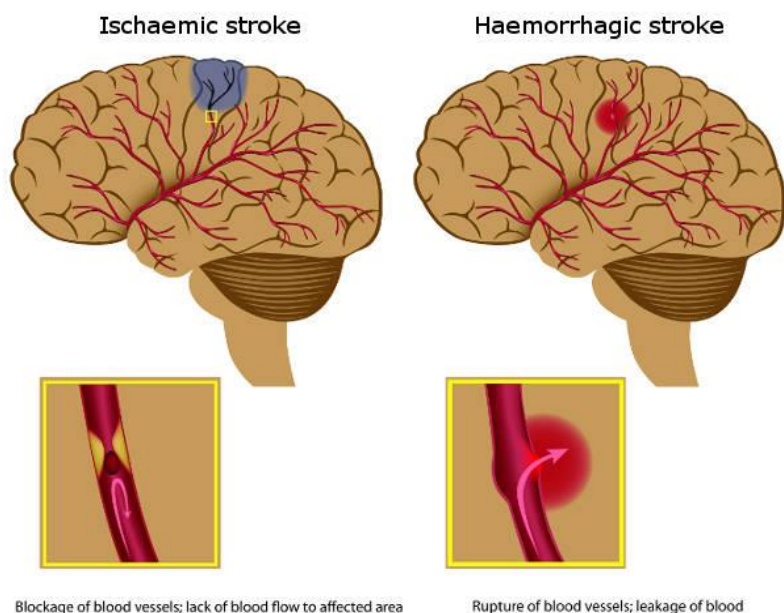


Fig: a) Ischemic Stroke and b) Haemorrhagic Stroke

Morphological Changes:

The availability of high-energy phosphates like adenosine triphosphate (ATP) is reduced, and the concentration of organic phosphates is elevated in the ischemia zone because of a lack of oxygen. Since the Na^+/K^+ channels malfunction in response to an influx of Na^+ , osmotic disruption and cytotoxic oedema occur [3]. Brains of people who die four to seven days after a stroke reveal the possibility of a stroke's extended reach across the central nervous system. These people's brains show neurological impairment both within and outside the ischemic zone [7]. Ischemia, as seen in stroke victims, causes damage to neurons, glial cells, and cerebral blood vessels. Previous research into ischemic stroke has indicated that the central ischemic region's neuronal bodies and axons undergo liquefactive necrosis [9].

M.R.I. Based Protocols:

Advantages: -

1. Accurate determination of the fundamental offence through D.W.I. (both detection and volume measurement)
2. Specifically for the violation of core volume delineation.
3. Capable of detecting sudden ischemia.
4. Calculating the stroke's onset time.
5. Accurate stroke diagnosis resembles.
6. Radiation absence.

Disadvantages: -

1. Restricted accessibility.

2. Greater acquisition period.
3. Workflow delays because patients had to be screened for contraindications.

D.W.I. and A.D.C. Sequences:

Studies using D.W.I. found that ischemia could be identified within 45 minutes, whereas T2 weighted imaging failed to reveal any ischemic core even three hours after the onset of the stroke. The contrast in D.W.I. is dependent on the apparent diffusion coefficient. The decreased diffusion [3]. Gives the appearance of a hyper-intense ischemic core in D.W.I. and a darker core in A.D.C. maps. A sensitive early diagnosis of ischemia is made possible by the rapid decrease in A.D.C. that can last for days. Compared to the optimal time for thrombolytic therapy [3,7], the 6-8 hours it could take for a standard M.R.I. to discover any tissue changes is unacceptable. Diffusion-weighted imaging (D.W.I.) is a type of magnetic resonance imaging (M.R.I.) sequence based on the Brownian motion of water molecules. Because of the importance of gaining reliable information from brain images, such as the location of grey matter (G.M.), white matter (W.M.), cerebrospinal fluid (CSF), and abnormal brain tissue, brain image segmentation is a crucial technique [7]. Though D.W.I. cannot differentiate between venous and arterial infarction, it may help diagnose venous thrombosis and distinguish between cytotoxic and vasogenic oedema [8]. The scan time for D.W.I. is typically reduced by using parallel imaging in addition to single-shot EPI [10]. Imaging contrast in diffusion magnetic resonance imaging is influenced by the molecular mobility of water [11].

T2 WI and FLAIR Sequences:

In the first three to eight hours after the stroke, ischemic infarction presents as a hyper-intense lesion on T2-weighted and FLAIR images. T2-weighted and FLAIR imaging is used to diagnose the severity of minor artery problems and cerebral infarctions in patients with a history of stroke or other neurological illnesses. Both subarachnoid haemorrhage and acute cerebral venous sinus thrombosis are easily detectable on FLAIR images. In the case of a hyperacute stroke, T2-weighted images can be used to detect the absence of arterial signal flow due to blocked arteries within minutes of symptom onset [11]. There may be an immediate loss of arterial signal void distal to a significant route of blockage, even though this is linked with FLAIR intravascular hyperintensities in the subarachnoid spaces. T2-Weighted Images (T2-WI) and Fluid Attenuated Inversion Recovery (FLAIR) sequences are not as sensitive as D.W.I. when exhibiting parenchyma abnormalities within the first several hours after stroke onset. Lesions that show up as hyperintense on D.W.I. but not FLAIR sequences can be employed as a second timepiece in the D.W.I. - FLAIR mismatch. This reliable M.R.I. finding indicates a stroke starts within 4.5 hours [12]. Intracranial artery thrombus occlusions may be detected by the susceptible techniques of susceptibility-weighted imaging (S.W.I.), and T2 with gradient recalled they echo weighted imaging (T2-GRE). Compared to T1 or T2 Weighted or Fluid Attenuated Inversion Recovery (FLAIR) images, T2* Weighted pictures appear more capable of detecting venous thrombosis and concomitant haemorrhage [8,12].

PWI Special Sequence for Stroke Imaging:

To evaluate the microcirculation of the brain's capillary network, PWI can be used [13]. Injecting a contrast agent into a vein causes it to travel via cerebral veins and affect the local magnetic field, resulting in rapid attenuation of signal strength in the surrounding brain tissue due to the contrast's paramagnetic action. Patient selection based on PWI-DWI mismatch has been used in various clinical trials focusing on acute stroke therapy. Previous investigations of imaging-based thrombolysis failed to find any advantages because they relied too heavily on PWI – D.W.I. mismatch [13]. Superior perfusion maps can only be attained with a scanning method optimised for low picture noise and good contrast sensitivity. This approach also has to ensure that the entire bolus passage is recorded with enough temporal resolution [14]. D.S.C. MR Perfusion (Dynamic Susceptibility Contrast-Enhanced MR Perfusion), also known as bolus-tracking M.R.I. or perfusion-Weighted imaging, involves taking a series of T2 or T2* M.R. images to trace the initial distribution of a bolus of a gadolinium-based contrast agent within brain tissue. The susceptibility effect of the paramagnetic contrast agent causes signal degradation in the signal intensity-time curve [15]. Serial T1-Weighted images are taken before, during, and after the administration of an extracellular, low molecular weight M.R. contrast medium for D.C.E. MR Perfusion, also known as "permeability" M.R.I. Such as a gadolinium-based contrast agent. The resulting signal intensity-time curve reflects various factors, including tissue perfusion, artery permeability, and extravascular-extracellular space [15].

Magnetic Resonance Angiography:

The main cerebral arteries are visible on M.R.A., which can be performed with or without contrast agents. In most cases, this is done to check for blockages and impaired blood flow [3]. The most widely used technique for non-contrast M.R.A. is called time-of-flight (T.O.F.) imaging. 3D TOF MRA [11]. The gold standard for evaluating cerebral blood arteries. M.R.A. seems to be a promising approach for assessing stenosis in large extracranial veins, but its sensitivity decreases for smaller intracranial arteries. Time-of-Flight may overestimate the amount of stenosis [16] If full or partial signal gaps develop in regions of high and turbulent flow. Traditional stroke treatments have long included using Time-of-Flight (T.O.F.) magnetic resonance imaging (M.R.A.) to evaluate the health of the arteries in the head and neck. Despite its hopeful outcomes, T.O.F. – M.R.A. suffers from significant limitations such as spin saturation and phase dispersion because of sluggish turbulent flow. The slowing of blood flow downstream of a clot or thrombus might cause a false positive rate to rise and an overestimation of stenosis in the artery to be reported. Most significantly, the acquisition time is lengthy, typically between 5 and 7 minutes [17]. Many experts believe that Contrast-Enhanced MR Angiography (C.E. – M.R.A.) provides more accurate imaging of the shape and degree of stenosis in the extracranial vasculature than Time-of-Flight Angiography (T.O.F. -M.R.A.). Despite its potential benefits, C.E. – M.R.A. has not been widely used in acute stroke therapy [17]. People with pacemakers, specific metallic implants, allergies to M.R. contrast chemicals, or extreme claustrophobia cannot use this approach, as with all M.R.I. imaging methods [18].

Epilepsy:

One of the most common stroke mimics is epilepsy. Some warning signs of a stroke include a severe headache, uncontrollable jerking movements, incontinence, and postictal confusion. In the absence of symptoms, however, it may be challenging to distinguish partial-characteristic seizures from genuine A.I.S. [12]. Epilepsy is a chronic condition characterised by recurrent episodes that are not the result of a recent systemic or neurological insult [19-25]. An isotropic T1-weighted volumetric acquisition (3D) with voxels measuring 1 mm or 1.5 mm in size is recommended as part of M.R.I. epilepsy protocols to reconstruct images in any plane. T2 weighted or Fluid-Attenuated Inversion Recovery (FLAIR) images are essential for qualitatively assessing the signal strength. Detection accuracy for anomalies using FLAIR imaging sequences was 97% [26-33].

Conclusions:

In terms of worldwide morbidity and mortality, stroke is a significant contributor. The evaluation of people having an acute stroke has advanced considerably with the help of state-of-the-art imaging technologies. The patient is selected by going against the norm of time-based stroke treatment. Ischemic stroke research has a lot of room for improvement, as does the development of new, more accurate models and more effective treatments in general, but it faces specific challenges. Significant progress has been made in assessing acute stroke patients utilising state-of-the-art imaging. Using cutting-edge imaging, clinicians can rethink the standard practice of selecting patients for stroke treatment based on elapsed time. Every new patient experiencing seizures should be referred for an M.R.I. using a specialised epilepsy protocol. It may be necessary to employ multiple mismatch metrics (DWI-FLAIR mismatch and PWI-DWI mismatch) and data from various M.R.I. sequences (i.e., D.W.I., FLAIR, GRE, and PWI) to determine whether or not thrombolysis should be indicated using magnetic resonance imaging (M.R.I.).

References:

1. El-Koussy M, Schroth G, Brekenfeld C, Arnold M. Imaging of acute ischemic stroke. *European neurology*. 2014;72(5-6):309-16.
2. Pinto A, Mckinley R, Alves V, Wiest R, Silva CA, Reyes M. Stroke lesion outcome prediction based on M.R.I. imaging combined with clinical information. *Frontiers in neurology*. 2018 Dec 5;9:1060.
3. Rastogi R, Ding Y, Xia S, Wang M, Luo Y, Choi HS, Fan Z, Li M, Kwiecien TD, Haacke EM. Recent advances in magnetic resonance imaging for stroke diagnosis. *Brain Circulation*. 2015 Jan 1;1(1):26.
4. Chen H, Zhu G, Liu N, Li Y, Xia Y. Applications and development of permeability imaging in ischemic stroke. *Experimental and Therapeutic Medicine*. 2018 Sep 1;16(3):2203-7.
5. Madai VI, von Samson-Himmelstjerna FC, Bauer M, Stengl KL, Mutke MA, Tovar-Martinez E, Wuerfel J, Endres M, Niendorf T, Sobesky J. Ultrahigh-field MRI in human ischemic stroke—a 7 tesla study. *PLoS One*. 2012 May 31;7(5):e37631.
6. Weng L, Yao D, Wang R. Unusual images of ischemic stroke with hyperacute spontaneous recanalization: a case report. *Annals of Translational Medicine*. 2020 Aug;8(16).

7. Saad NM, Noor NS, Abdullah AR. A Review on Image Segmentation Techniques for MRI Brain Stroke Lesion. *Journal of Telecommunication, Electronic and Computer Engineering (JTEC)*. 2021 Dec 31;13(4):27-34.
8. Lanni G, Catalucci A, Conti L, Di Sibio A, Paonessa A, Gallucci M. Pediatric stroke: clinical findings and radiological approach. *Stroke research and treatment*. 2011 Apr 19;2011.
9. Barthels D, Das H. Current advances in ischemic stroke research and therapies. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*. 2020 Apr 1;1866(4):165260.
10. You SH, Kim B, Kim BK, Park SE. Fast MRI in acute ischemic stroke: applications of MRI acceleration techniques for MR-based comprehensive stroke imaging. *Investigative Magnetic Resonance Imaging*. 2021;25(2):81-92.
11. Gean A. *Imaging of Ischemic Stroke, An Issue of Neuroimaging Clinics*. Elsevier Health Sciences; 2011 Jul 22.
12. Adam G, Ferrier M, Patsoura S, Gramada R, Meluchova Z, Cazzola V, Darcourt J, Cognard C, Viguier A, Bonneville F. Magnetic resonance imaging of arterial stroke mimics: a pictorial review. *Insights into Imaging*. 2018 Oct;9(5):815-31.
13. Kim BJ, Kang HG, Kim HJ, Ahn SH, Kim NY, Warach S, Kang DW. Magnetic resonance imaging in acute ischemic stroke treatment. *Journal of stroke*. 2014 Sep;16(3):131.
14. Demeestere J, Wouters A, Christensen S, Lemmens R, Lansberg MG. Review of perfusion imaging in acute ischemic stroke: from time to tissue. *Stroke*. 2020 Mar;51(3):1017-24.
15. Anzalone N, Dörfler A, Rovira À, Wintermark M, Law M. Perfusion MRI: The Five Most Frequently Asked Technical Questions.
16. Sanelli PC, Sykes JB, Ford AL, Lee JM, Vo KD, Hallam DK. Imaging and treatment of patients with acute stroke: an evidence-based review. *American Journal of Neuroradiology*. 2014 Jun 1;35(6):1045-51.
17. Nael K, Khan R, Johnson K, Martin D. Acute MR stroke protocol in six minutes. *Siemens Healthcare. Magnetom Flash*. 2013;5.
18. Birenbaum D, Bancroft LW, Felsberg GJ. Imaging in acute stroke. *Western Journal of Emergency Medicine*. 2011 Feb;12(1):67.
19. Ponnatapura J, Vemanna S, Ballal S, Singla A. Utility of magnetic resonance imaging brain epilepsy protocol in new-onset seizures: how is it different in developing countries? *Journal of Clinical Imaging Science*. 2018;8.
20. Cendes F, Theodore WH, Brinkmann BH, Sulc V, Cascino GD. Neuroimaging of epilepsy. *Handbook of clinical neurology*. 2016 Jan 1; 136:985-1014.
21. Kaluse, Prathmesh Siddheshwar, Neha Bhatt, and Nandkishor Bankar. "Study of Typhoid Fever: A Review." *Journal of Pharmaceutical Research International*, July 31, 2021, 286–91. <https://doi.org/10.9734/jpri/2021/v33i39A32172>.
22. Kamble, Shailesh D., Pawan Patel, Punit Fulzele, Yash Bangde, Hitesh Musale, and Saipratik Gaddamwar. "Disease Diagnosis System Using Machine Learning." *Journal of Pharmaceutical Research International*, June 29, 2021, 185–94. <https://doi.org/10.9734/jpri/2021/v33i33B31810>.
23. Kamble, Shweta, Anita Wanjari, Bharat Rathi, and D. Rajput. "Pharmaceutico-Analytical Study of Muktashukti Pishti and Muktashukti Bhasma and Comparative Evaluation of Their Relative Oral Bioavailability." *Journal of Pharmaceutical Research International*, June 11, 2021, 1–9. <https://doi.org/10.9734/jpri/2021/v33i31B31680>.
24. Kannao, Vaidehi. "A Case Report on Proximal Humerus Fracture and Physiotherapy Rehabilitation." *Bioscience Biotechnology Research Communications* 14, no. 6 (June 15, 2021): 120–23. <https://doi.org/10.21786/bbrc/14.6.28>.
25. Kapgate, Shreya, Ranjana Sharma, Deeplata Mendhe, and Mayur Wanjari. "A Case Report on Tuberculous Meningitis." *Journal of Pharmaceutical Research International*, December 8, 2021, 274–78. <https://doi.org/10.9734/jpri/2021/v33i53B33707>.
26. Karadbhajne, Priti. "A Case Report on Ancylostoma Duodenale Infection in Pregnant Woman." *Bioscience Biotechnology Research Communications* 14, no. 6 (June 15, 2021): 100–103. <https://doi.org/10.21786/bbrc/14.6.23>.
27. Kariya, Sakshi K., Waqar M. Naqvi, Om Wadhokar, and Pratik Phansopkar. "Sub Occipital Muscle Inhibition Technique Verses Cranial Cervical Flexion Exercise for Increasing Hamstring Flexibility in Physiotherapy Students." *Journal of Pharmaceutical Research International*, November 11, 2021, 8–13. <https://doi.org/10.9734/jpri/2021/v33i49A33295>.
28. Kashyap, Pratheek R., Rakesh Kumar Jha, and Praful Patil. "Depression Due to Polycystic Ovary Syndrome in Adolescents." *Journal of Pharmaceutical Research International*, July 28, 2021, 224–27. <https://doi.org/10.9734/jpri/2021/v33i38B32117>.
29. Kasturkar, Pooja, Jaya Pranoykumar Gawai, Tessy Sebastian, Trupti Uke, Dharti Meshram, Shabnam Sayyad, and Samuel Vanlalpeka. "Case Report on Paranoid Schizophrenia with Capgras Syndrome." *Journal of Pharmaceutical Research International*, October 25, 2021, 72–77. <https://doi.org/10.9734/jpri/2021/v33i47A32991>.
30. Katkar, Anjali. "How COVID-19 Pandemic Impacted General Population, Diagnostic Facilities and Frontline Warriors." *Bioscience Biotechnology Research Communications* 14, no. 6 (June 15, 2021): 225–30. <https://doi.org/10.21786/bbrc/14.6.47>.
31. Kawale, A., and V. Taksande. "Prevalence and Risk Factors of Anaemia among Adolescent Girls in Selected Schools." *Journal of Pharmaceutical Research International*, September 11, 2021, 210–20. <https://doi.org/10.9734/jpri/2021/v33i43B32547>.
32. Kawale, Aparna M., and Manoj Patil. "Management of Hypertension in Elderly Pregnant Women with IVF Conception: A Case Report." *Journal of Pharmaceutical Research International*, July 22, 2021, 113–18. <https://doi.org/10.9734/jpri/2021/v33i38A32065>.
33. Kediya, Anup Shivom, Anil Kalyandas Agrawal, Arvind Shridharrao Bhake, and Obaid Noman. "Malignant Phyllode Tumour with Heterologous Sarcomatous Differentiation – A Rare Case Report." *Journal of Evolution of Medical and Dental Sciences* 10, no. 4 (January 25, 2021): 240–42. <https://doi.org/10.14260/jemds/2021/52>.