Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

# Literature Review : Relationship Between Moyamoya Disease And Cerebral Iscemic Incidents

**Muh. Fawwaz Irhadi[1], Mochammad Erwin Rachman[2], Cahyono Kaelan[3]**
[1,2,3]Fakultas Kedokteran, Universitas Muslim Indonesia
E-mail: fawwazirhadi04@gmail.com, cakaelan1@gmail.com, mochammaderwin.rahman@umi.ac.id

**Article Info**
**Keywords:**
Moyamoya disease,
stroke,
revascularization.

**ABSTRACT**
Moyamoya disease is a rare progressive cerebrovascular disorder characterized by blockage of arteries at the base of the brain, causing ischemic and hemorrhagic strokes. This condition is most common in children and adults in Asia, with the main symptoms being transient ischemic attacks (TIAs) or strokes. This study used a literature review method by collecting data from various medical journals related to the diagnosis and management of Moyamoya. Diagnosis is generally made through MRI, MRA, and DSA, with DSA being the best method to identify arterial stenosis and collateral formation. The results showed that treatment included medical therapy with aspirin and surgical revascularization procedures to improve cerebral blood flow, where direct revascularization provides faster results although technically more difficult. Early diagnosis and surgical intervention are essential to prevent disease progression.



**Corresponding Author:**
Muh. Fawwaz Irhadi
Fakultas Kedokteran, Universitas Muslim Indonesia
fawwazirhadi04@gmail.com

## INTRODUCTION

Moyamoya disease (MMD) is one of the disease rare marked with constriction progressive chronic in the arteries main the brain, especially artery distal internal carotid artery (ICA), anterior cerebral artery (ACA), and middle cerebral artery (MCA). Diseases This first described in 1957 by Takeuchi and Shimizu, who discovered bilateral hypoplasia of the arteries carotid interna. Incident disease This more common in East Asia, such as Japan and South Korea, where the incidence of MMD is higher often found in women than men. Globally, although cases in North America are relatively low, trend improvement has observed in a number of year Lastly. Interestingly, MMD often shows distribution bimodal age, with peak first at age about 5 years and peak second at age about 40 years.

In general clinical, patient with MMD usually come with associated symptoms with ischemia cerebral, such as attack ischemic temporary (TIA) or infarction cerebral. In children, seizures often become symptom early signs leading to diagnosis, while in adults, bleeding intracranial more often become presentation beginning, marked with decline sudden awareness. Occlusion vessels progressive blood loss in MMD causes hypoperfusion brain, which triggers incident ischemic. Therefore that, one of focus main study about MMD is understand How disease This related with risks and mechanisms the occurrence ischemia cerebral.

Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

Temporary The etiology of MMD is not yet known. fully understood, some study show existence influence significant genetics, especially involvement chromosomes. In addition to the factors genetics, inflammatory processes are also suspected play a role in worsening of vascular stenosis blood in MMD sufferers, which in turn increase risk ischemia cerebral. On the other hand, some study mention role important endothelial progenitor cells, which function in repair and regenerate layer vessels blood, but it seems disturbed in MMD patients. Involvement elements This highlight complexity disease this and bring up Lots question about underlying factors connection between MMD and events ischemic cerebral.

So, research This aiming For understand more in about connection between moyamoya disease and incidence ischemic cerebral. Research This will explore How factor genetics, especially involvement chromosome 17, plays a role in MMD development and its relation with ischemia cerebral. In addition, research this will also researching the possible influence of the inflammatory process to worsen constriction vessels blood, and role endothelial progenitor cells in guard health vessels blood in MMD patients. With Thus, research This expected can give outlook new about contributing factors to risk ischemia cerebral in MMD patients.

## RESEARCH METHOD

Study This done with method *literature review* use design *narrative review,* where the data used is secondary data obtained from various source articles and journals scientific. The process of searching literature focused on articles that discuss connection between *moyamoya disease* and incidence ischemic cerebral. Some of the main databases used in search literature is *Clinical Key*, Google Scholar, Gale, and *NCBI.* Keywords used in search covering *moyamoya disease, ischemic cerebral disease, risk factors of moyamoya disease, and diagnosis and treatment of moyamoya disease.* With using keywords this, it is expected can found relevant and up-to- date literature For support objective study.

In filtering references, criteria inclusion set including among others published references in period 2018 to 2023. Articles only research originating from from journal national, journal international, *Clinical Key, NCBI,* and citation lecturers used. In addition, the literature included to in study This must in a way special discuss about *moyamoya disease* and its relation with incident ischemic cerebral, for ensure that topics discussed in accordance with focus study.

On the contrary, the criteria exclusion covers journal that is not available in form *full text* or not can accessed in a way full. This is done so that the literature used in study can studied in a way deep and comprehensive, without There is limitation access that can be hinder the analysis process. With existence criteria inclusion and exclusion this, research can more directed and focused on quality sources tall as well as relevant with topics studied.

Stages search literature involves a search process beginning with the keywords that have been determined, followed with filtering reference based on criteria inclusion and exclusion. Articles that meet the condition Then under review in a way deep For analyzed and synthesized in frame reach objective research. This flow ensure that only articles that meet the requirements standard academic and relevance topics used in study This.

Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

## RESULTS AND DISCUSSION

### Research Results

| No. | Journal ( Year) rise ) | Title | Method | Writer | Results | Conclusion |
|---|---|---|---|---|---|---|
| 1. | Journal of Child Neurology (2017) | Moyamoya Disease in Children: Results From the International Pediatric Stroke Study | Descriptive research | Sarah Lee, Michael J. Rivkin, Adam Kirton, Gabrielle deVeber, Jorina Elbers | A total of 173 children of 14 countries suffering moyamoya disease, or about 8% of the total 2,133 children with ischemic stroke in *the International Pediatric Stroke Study* (IPSS). The majority of strokes involved part circulation anterior (82%), and circulation anteroroposterior ( 13%). Symptoms obtained such as hemiparesis is the most common symptoms appeared in 137 patients (79%), difficult speaking to 85 patients (49%), sick headache in 82 patients (47%) and seizures in 53 patients (30%). Stroke recurrence occurred at least once in 35/173 patients (20%). | This study provide important data about events and descriptions moyamoya disease in samples international children who suffer from stroke. Incident stroke recurrence is at least 20%, almost half from they experience relapse many times. |
| 2. | Journal of Stroke and Cerebrovascular Diseases (2020) | The disease presentation of Moyamoya | Cross-sectional | Shambaditya Das, Souvik Dubey, Mrinal Acharya, Ritwik Ghosh, Subhankar Chatterjee, | Of the total 76 patients with an angiographic diagnosis of Moyamoya Angiopathy (MMA), 36 (47.4%) were patient | Moyamoya is common causes of stroke neglected at age young. Research India's largest revealed that |

| | | | | |
|---|---|---|---|---|
| | angiopathy in Eastern India | Avijit Hazra, Durjoy Lahiri, Samya Segupta, Subham Chatterjee, Goutam Das, Niladri Sarkar, Biman Kanti Ray, Markus Kraemer | children and 40 (52.6%) were patient adults. In addition, 4/36 (11.11%) were patient child with MMS and 10/40 (25%) were patient mature with MMS. There is no history family with MMA among 76 patients. first in children is 1-11 years, in adults age 12-60 years. Weakness motor settled (FMW) to be the most common symptoms complained (68.5%), as symptom main until at the time of final diagnosis, followed by seizures (31.5%) which became more symptoms general appear in children, and symptoms neurological repetitive such as ischemic stroke, TIA, and hemorrhagic stroke. Correlation positive found between Suzuki stadium and delay in the diagnosis indicating that the diagnosis was delayed cause symptom more disease severe and worse prognosis bad. | MMA can also have diverse non- motor symptoms others. Therefore that, introduction early is challenge for doctor Because symptom the beginning that is not specific become challenge in diagnosis. |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3. | Journal of Stroke and Cerebrovascular Diseases (2021) | Moyamoya Disease and Syndrome: A National Inpatient Study of Ischemic Stroke Predictors | Retrospective cohort | Unda SR, Antoniazzi AM, Miller R, Klyde D, Javed K, Fluss R, Holland R, De la Garza Ramos R, Haranhalli N, Altschul DJ | In two years study consecutively (2016 & 2017) from the *National Inpatient Sample* database, research This find that there are 2,323 patients take care stay with a diagnosis of Moyamoya, with 1655 (71.2%) being *Moyamoya Disease* (MMD) and 668 (28.8%) patients *Moyamoya Syndrome* (MMS). The most common condition found on MMS is anemia cell disease sickle cell (559, 83.7%), neurofibromatosis type 1 (27, 4%), Down syndrome (74, 11.1%) and therapy radiation cranial (13, 1.9%). Among moyamoya spectrum, MMD patients were found own higher rates of ischemic stroke, hemorrhagic stroke and TIA tall compared to with MMS patients. However, stroke subtypes were similar in both cohort where ischemic stroke is the largest. In addition, the factor the risk of ischemic stroke in MMD is also | Distribution presentation neurological clinical features in MMD and MMS are similar, but MMD patients have it level higher incidence of stroke tall compared to with MMS. |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | increased along increase age, lipidemia and smoking status, whereas on MMS hypertension is the only one factor risk independent of ischemic stroke. | |
| 4. | Journal of Neurology (2024) | Moyamoya disease in Southeast Asians: genetic and autopsy data, new cases, systematic review, and meta -analysis of all patients from the literature | Retrospective analysis and systematic review | Daniel Strunk, Peter Bauer, Kathy Keyvani, Rolf R. Diehl, Roland Veltkamp, Peter Berlit, Sven G. Meuth, Lars Timmermann, Jan Claudius Schwitalla, Markus Kraemer | The results of the analysis of 32 Southeast Asian patients with MMD found 3 patients among them originate from Indonesia. MMD more Lots occurs in women compared to man with ratio 1.6 : 1. Average age 20-40 years, ischemic cerebral become better conditions often happened, and not obtained patients who have inspection genetics positive For p.R4810K variant of the RNF213 gene. In the results autopsy 1 patient postportem is also obtained description MMD histology with thickening layered on laminate internal elastic and fibrocellular, proliferation cell smooth muscle of the intima, fibrin deposits in the wall vessels blood and | The clinical and histopathological manifestations of MMD in Southeast Asia are similar to those in Caucasians. in Europe. The MMD genotype in Southeast Asia is different from most patients in East Asia. |

Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | degeneration tunica media. In addition, study This state that demographics and presentation MMD clinical in Southeast Asia is not different with description disease in the Caucasus Europe. | |
| 5. | Cureus Journal of Medical Science (2020) | Moyamoya : An Update and Review | Clinical Research | Berry JA, Cortez V, Toor H, Saini H, Siddiqi J | Findings histologically in MMD obtained progressive stenosis condition with an internal elastic lamina that is not regular, narrowing of the lumen, hyperplasia tunica media, intimal thickening, and degeneration vacuolar in cells smooth muscle in the tunica media. Progressive stenosis cause decline perfusion to parenchyma brain and causes ischemic and compensation vascular with develop circulation collateral (angiogenesis), blood vessels more blood small start enlarged, and hypertrophied become more seen on examination *Diagnostic Cerebral Angiogram* (DCA). In addition, the incidence of | MMD is disease chronic and progressive with Handling surgery that must be done under consideration for patient symptomatic For repair flow hemodynamics to the area that is physiological not enough perfusion, especially in the ICA, proximal MCA, and proximal ACA regions parenchyma brain. In patients children, early diagnosis and intervention surgery required For prevent infarction cerebrovascular irreversible. |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | ischemic stroke more Lots happens to children compared to hemorrhagic stroke. | |
| 6. | Journal of Neurology (2022) | The angiographic presentation of European Moyamoya angiopathy | Descriptive study | Sara Pilgram-Pastor, Rene Chapot, Markus, Kraemer | Study This state that at the stage of the Suzuki stadium which is more high (IV-VI) bleeding intracranial more often happen compared to the Suzuki stadium which is more low (I-III). Data in the United States in children found 54% with Suzuki I–III and 46% with Suzuki IV–VI while in Korea, the disease This appear For diagnosed at the stage Early Suzuki disease, 72% were diagnosed at stages I–III and 28% at stages IV–VI. This can relate with data in Japan and Korea that children more Lots affected by TIA and ischemic stroke and in adults at risk more tall experience bleeding intracranial. | Study observational the biggest about angiography in Caucasian, European MMA patients compared to with Asian data shows similarity clinical in both. |
| 7. | Stroke (2020) | Modifiable Risk Factors Associated With Moyamoya Disease | Case Control Study | Peicong Ge, Qian Zhang, Xun Ye, Xingju Liu, Xiaofeng Deng, Jia Wang, Rong Wang, | Based on results studies prospective with 138 MMD patients and 138 patients Healthy as control obtained that factor risk like | Improvement index mass body and homocysteine associated with higher risk of MMD high. On the other hand, increased albumin and |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | Yan Zhang, Dong Zhang, Jizong Zhao | improvement body mass index (BMI) and hyperhomocysteine can increase risk MMD events. On the other hand, HDL levels are high and albumin is low can lower MMD risk. MMD patients with history hypertension (44 patients, 31.8%) was found more Lots compared to group control (9 people, 6.6%). Research it also states that rare RNF213 mutation detected in ±40% of MMD patients in China, and there are connection between RNF213 mutation with disorders of fat metabolism. | high-density lipoprotein cholesterol tall correlated with higher risk of MMD low. Next increase homocysteine associated with higher prevalence of unilateral MMD high. Attention more need given at risk that can modified, because matter This can help We find causes, prevention events and knowing therapy new. |
| 8. | Molecular Medicine (2022) | Moyamoya disease is emerging as an immune-related angiopathy | Systematic review | Caroline Asselman, Dimitri Hemelsoet, Denzel Eggermont, Bart Dermaut, and Francis Impens | In 2011, two studies independent in Japan Finally identify RNF213 as the MMD gene on 17q25.3 which is also known as mysterin. In both study mentioned, the p.(R4810K) variant of RNF213 was found dramatically increase MMD risk is higher than 100 times. Although Thus, the numbers risk and frequency a very big | Addition study required For more explain connection between RNF213, infection, immunity, and arterial stenosis progressive on MMD. With method this, MMD can become evaluation For see response vascular related immunity and the fundamental processes that connect immunity mobile with disease vascular. |

Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | career the only ~0.5% of carrier heterozygotes p.(R4810K) develop MMD, where matter This show very low penetrance. In contrast, homozygous RNF213 p.(R4810K) carriers own >78% chance for developing MMD, which also clinical more severe. Other results in the study This get that RNF213 was found as an important modulator in lipotoxicity. | |
| 9. | Journal of Pediatric Neurosurgery (2022) | Absence of the RNF213 p.R4810K variant may indicate a severe form of pediatric moyamoya disease in Japanese patients | Retrospective study | Shoko Hara, Maki Mukawa, Hiroyuki Akagawa, Thiparpa Thamamongood, Motoki Inaji, Yoji Tanaka, Taketoshi Maehara, Hidetoshi Kasuya, and Tadashi Nariai | From a total sample of 129 patients with MMD, it is obtained results >80% of them own positive RNF 213 variant. Patient with RNF213 positive and homozygous own tendency more clinical heavy from heterozygous. Additionally, patients with RNF213 negative genotype p.R4810K has description more infarction small. Patient without The p.R4810K variant has results good surgery compared to with patient with | Absence RNF213 p.R4810K variant is thought to be is a new biomarker For identification degrees moyamoya disease in children. With patient focused children, we found matter That No existence RNF213 p.R4810K variant may be a new biomarker For identification patient with disease critical presentation clinical pediatric moyamoya disease. |

Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | Variants heterozygous (76.5% vs 92.2%). | |
| 10. | StatPearls (2024) | Moyamoya Disease | Descriptive study | Rupareliya C, Lui F. | Aspirin with a dose of 50-100 mg is recommended in a way conventional has used between patient Moyamoya disease for prevent further strokes continued. Headache and seizures usually handled with treatment symptomatic use drug analgesics and antiepileptics. In addition, revascularization surgery is the only one treatment main for MMD with hemodynamics cerebral deterioration For repair flow blood cerebral and prevent further strokes carry on. | MMD is abnormality relatively neurological rare and important For remember that No There is treatment curative For Moyamoya disease. Early diagnosis moyamoya disease is accompanied by intervention proper surgery very much important Because therapy medical only act as prevention secondary and not stop development disease. Education patient about change style life is highly recommended. |

Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

## Discussion

### Moyamoya Disease (MMD) and Moyamoya Syndrome (MMS)

Moyamoya Disease (MMD) is a abnormality cerebrovascular idiopathic chronic characterized by stenosis of the arteries around circle of Willis, which triggers formation vessels blood abnormal collaterals. In contrast, Moyamoya Syndrome (MMS) is condition secondary that occurs as response to pathology others. Research by Unda SR et al. (2021) on the National Inpatient Sample database showed 2,323 patients treated with a diagnosis of Moyamoya, of which 1,655 (71.2% ) were MMD and 668 (28.8%) were MMS. MMS was the most frequent caused by red cell anemia sickle cell (83.7%), neurofibromatosis type 1, down syndrome, and therapy radiation cranial. Another study by Shambaditya Das et al. (2020) in India found Of the 76 Moyamoya angiopathy patients, 14 were MMS, with children and adults as sufferer, where the condition like thalassemia and atherosclerosis dominate.

Research by Sarah Lee et al. (2017) on data from 4,024 International Pediatric Stroke Study (IPSS) patients found 173 children suffering from moyamoya, about 8% of 2,133 children with ischemic stroke. Most of patient originate from the United States, Canada, and Europe, although moyamoya is more often found among Asian descent, especially Japan. Gonzalez Nestor et al. (2023) added that highest prevalence of moyamoya located in Asia, especially Japan, although the diagnosis in the United States has increased. Analysis The latest by Daniel Strunk (2024) shows No There is difference significant in demographics and presentation clinical between Southeast Asian and Caucasian patients Europe, showing global spread of disease This.

### Moyamoya Disease (MMD) through Clinical and Genetic Features

Lots of research in 64 years final has reviewing MMD, but reason Certain Not yet known. Genetic factors, inflammation immunity, and some other factors are considered related with MMD. Research by Berry JA et al. (2020) explains that stenosis in MMD is caused by a mechanism besides atherosclerosis and inflammation. MMD histology shows progressive stenosis with an internal elastic lamina that is not regular, intimal thickening, and degeneration tunica media, causing decline perfusion brain. Postmortem studies by Daniel Strunk et al. strengthen findings This with show existence thickening of the elastic lamina and proliferation cell smooth muscle in the tunica intima. In addition, the formation of microaneurysm found, which explains height incident bleeding in adult MMD patients.

Study about endothelial progenitor cells (EPCs) show that MMD patients have more many EPCs in circulation compared to patient atherosclerotic. Abnormal activity of factors growth trigger proliferation cell smooth muscle and angiogenesis in MMD. Berry JA et al. stated that dysfunction cell former colony endothelial (ECFC) may play a role in MMD, with disturbance significant on ECFC mitochondria which affects consumption oxygen. Mutations in the RNF213 gene are now also thought to as factor genetics important. Zhang Qian et al. (2020) found that about 40% of MMD patients in China have RNF213 mutation variant p.R4810K, which is also associated with anomaly metabolic like obesity and dyslipidemia. Research by Shoko Hara et al. (2022) supports findings this, with more of 80% of MMD patients who are positive RNF213 variant, and showed that homozygous more critical compared to heterozygous. Mutation This

Jurnal Eduhealth
Volume 15 , Number 04, 2024, DOI 10.54209/eduhealth.v15i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

found in a way significant increase MMD risk, although its penetration low, indicating the need factor addition For trigger disease.

Although reason definitely MMD not known, some factor risk known. In Asia, MMD is more common in Japan, Korea, and China. Women have more MMD incidents tall compared to man with ratio of 1.6:1, as seen in the study of Daniel Strunk et al. involving 11 MMD patients, of which 8 were women. RNF213 mutations associated with MMD found bother fat stabilization, indicating existence connection with fat metabolism. Research by Roy et al. shows that RNF213 is working as regulator integrity endothelium brain, where RNF213 depletion causes improvement permeability barrier blood-brain and increased secretion cytokines proinflammatory.

Risk factors that can modified for MMD including increased BMI and hyperhomocysteine, while high HDL levels and low albumin can lower MMD risk, according to Ge Pelcong's research et al. (2020). Hyperhomocysteinemia ( Hcy ) has long been recognized as factor risk of stroke and disease heart Coronary as well as found relate with improvement MMP-9 expression, which can play a role in pathogenesis of MMD.

## CONCLUSION

Moyamoya disease is abnormality cerebrovascular progressive rare marked with blockage artery at the base brain and its formation network collaterals that resemble " puffs of smoke". Condition This cause decline flow blood and increase risk of ischemic and hemorrhagic stroke. Moyamoya syndrome is often is complications from other diseases such as Down syndrome and disease cell sickle. Incident highest Moyamoya disease occurs in Asia, especially in Japan, and is more often attack Woman as well as children aged 5–9 years and adults age 30–50 years. In children, the symptoms are covering attack ischemic transient ischemic attack (TIA) or ischemic stroke, while adults often experienced a hemorrhagic stroke. For diagnosis, MRI and MRA are often used Because noninvasive, while DSA is considered as method imaging best (gold standard) for detect characteristics disease this. Treatment main covering use of aspirin for prevent stroke, as well as revascularization surgery For repair flow blood brain. Revascularization direct give results more fast, though more difficult done compared to method indirect. Early diagnosis and intervention proper surgery time is of the essence Because treatment medical only functioning as prevention secondary.

## REFERENCES

1. Gupta A, Tyagi A, Romo M, Amoroso KC, Sonia F. Moyamoya Disease: A Review of Current Literature. *Cureus.* 2020;12(8). doi:10.7759/cureus.10141
2. Zhang H, Zheng L, Feng L. Epidemiology, diagnosis and treatment of moyamoya disease (Review). *Exp Ther Med.* Published online 2019:1977-1984. doi:10.3892/etm.2019.7198
3. Zhang X, Xiao W, Zhang Q, et al. Progression in Moyamoya Disease: Clinical Features, Neuroimaging Evaluation, and Treatment. *Curr Neuropharmacol.* 2021;20(2):292-308. doi:10.2174/1570159x19666210716114016
4. Mertens R, Graupera M, Gerhardt H, et al. The Genetic Basis of Moyamoya Disease. *Transl Stroke Res.* 2022;13(1):25-45. doi:10.1007/s12975-021-00940-2

5. Tinelli F, Nava S, Arioli F, et al. Vascular remodeling in moyamoya angiopathy: From peripheral blood mononuclear cells to endothelial cells. *Int J Mol Sci.* 2020;21(16):1-22. doi:10.3390/ijms21165763
6. Fang YC, Wei LF, Hu CJ, Tu YK. Pathological circulating factors in moyamoya disease. *Int J Mol Sci.* 2021;22(4):1-12. doi:10.3390/ijms22041696
7. Dorschel KB, Wanebo JE. Physiological and pathophysiological mechanisms of the molecular and cellular biology of angiogenesis and inflammation in moyamoya angiopathy and related vascular diseases. *Front Neurol.* 2023;14. doi:10.3389/fneur.2023.661611
8. Yadav R, Pokhriyal SC, Yadav V, Idries I, Berekashvili K. The Role of Dual Antiplatelet Therapy (DAPT) vs Surgery in a Case of Moyamoya Disease: A Case Report and Review of the Literature. 2023;15(5). doi:10.7759/cureus.39694
9. Parchmont EC, Adler AC. Moyamoya Disease. *Case Study Pediatric Anesthesia.* 2019;1:164-168. doi:10.1017/9781108668736.039
10. Berry JA, Cortez V, Toor H, Saini H, Siddiqi J. Moyamoya: An Update and Review. Cureus. 2020 Oct 16;12(10 ):e 10994. doi : 10.7759/cureus.10994. PMID: 33209550; PMCID: PMC7667711
11. Unda SR, Antoniazzi AM, Miller R, Klyde D, Javed K, Fluss R, Holland R, De la Garza Ramos R, Haranhalli N, Altschul DJ. Moyamoya Disease and Syndrome: A National Inpatient Study of Ischemic Stroke Predictors. J Stroke Cerebrovasc Dis. 2021 Sep;30(9):105965. doi : 10.1016/j.jstrokecerebrovasdis.2021.105965. Epub 2021 Jul 8. Erratum in: J Stroke Cerebrovasc Dis. 2021 Dec;30(12):106150. doi : 10.1016/j.jstrokecerebrovasdis.2021.106150. PMID: 34247053.
12. Lee S, Rivkin MJ, Kirton A, deVeber G, Elbers J; International Pediatric Stroke Study. Moyamoya Disease in Children: Results From the International Pediatric Stroke Study. J Child Neurol. 2017 Oct;32(11):924-929. doi : 10.1177/0883073817718730. Epub 2017 Jul 17. PMID: 28715924.
13. Strunk D, Bauer P, Keyvani K, Diehl RR, Veltkamp R, Berlit P, Meuth SG, Timmermann L, Schwitalla JC, Kraemer M. Moyamoya disease in Southeast Asians: genetic and autopsy data, new cases, systematic review, and meta-analysis of all patients from the literature. J Neurol. 2024 Jun;271(6):3328-3339. doi : 10.1007/s00415-024-12228-0. Epub 2024 Mar 13. PMID: 38478032; PMCID: PMC11136762.
14. Das S, Dubey S, Acharya M, Ghosh R, Chatterjee S, Hazra A, Lahiri D, Segupta S, Chatterjee S, Das G, Sarkar N, Ray BK, Kraemer M. The disease presentation of Moyamoya angiopathy in Eastern India. J Stroke Cerebrovasc Dis. 2020 Aug;29(8):104957. doi : 10.1016/j.jstrokecerebrovasdis.2020.104957. Epub 2020 Jun 14. PMID: 32689603.
15. Ge P, Zhang Q, Ye X, Liu X, Deng Strokes. 2020 Aug;51(8):2472-2479. doi : 10.1161/STROKEAHA.120.030027. Epub 2020 Jul 9. PMID: 32640948.
16. Pilgram-Pastor S, Chapot R, Kraemer M. The angiographic presentation of European Moyamoya angiopathy. J Neurol. 2022 Feb;269(2):997-1006. doi : 10.1007/s00415-021-10684-6. Epub 2021 Jul 8. PMID: 34240321; PMCID: PMC8782787.
17. Hara S, Mukawa M, Akagawa H, Thamamongood T, Inaji M, Tanaka Y, Maehara T, Kasuya H, Nariai T. Absence of the RNF213 p.R4810K variant may indicate a severe form of

pediatric moyamoya disease in Japanese patients. J Neurosurg Pediatr. 2021 Oct 8;29(1):48-56. doi : 10.3171/2021. 7. PEDS 21250. PMID: 34624841.

18. Asselman C, Hemelsoet D, Eggermont D, Dermaut B, Impens F. Moyamoya disease emerging as an immune-related angiopathy. Trends Mol Med. 2022 Nov;28(11):939-950. doi : 10.1016/j.molmed.2022.08.009. Epub 2022 Sep 14. PMID: 36115805.
19. Navandhar PS, Gharde P, Shinde RK, Nagtode T. Moyamoya Disease: Advances in Diagnosis, Treatment, and Surgical Interventions. Cureus. 2024 May 7;16(5 ):e 59826. doi : 10.7759/cureus.59826. PMID: 38846195; PMCID: PMC11156423.
20. Canavero I, Vetrano IG, Zedde M, Pascarella R, Gatti L, Acerbi F, Nava S, Ferroli P, Parati EA, Bersano A. Clinical Management of Moyamoya Patients. J Clin Med. 2021 Aug 17;10(16):3628. doi : 10.3390/jcm10163628. PMID: 34441923; PMCID: PMC8397113.
21. Rupareliya C, Lui F. Moyamoya Disease. [Updated 2023 Jun 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535455/