

THE SILENT THREAT: HEART STROKE AMONG YOUNG ADULTS IN INDIA**Shaik Parveen, Afreen Sultana*, Chandana Dayaka and Katepally Pranitha**

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ABSTRACT

Stroke in young adults is an increasingly prevalent but often overlooked health issue, particularly in India, where a combination of urbanization, lifestyle changes, and rising prevalence of chronic diseases has led to a concerning rise in stroke incidence among individuals aged 18 to 45. This review article aims to explore the epidemiology, risk factors, clinical presentation, diagnostic challenges, and treatment strategies of stroke in young adults in India. We focus on the impact of modifiable risk factors such as hypertension, diabetes, smoking, and obesity, as well as the socio-economic determinants that exacerbate the condition. The article also highlights the significant delays in diagnosis and treatment, resulting from limited awareness and inadequate healthcare access in rural and underserved regions. Furthermore, we address the challenges in rehabilitation and long-term care for young stroke survivors, emphasizing the need for improved healthcare infrastructure, better post-stroke care, and public health interventions. Given the increasing burden of stroke in young adults, we advocate for comprehensive public health strategies, including awareness campaigns, better screening for high-risk individuals, and the integration of stroke prevention programs into primary healthcare systems. This review concludes by underscoring the importance of a multi-faceted approach to combat stroke in young adults in India, aiming not only to reduce the incidence but also to mitigate the long-term impact of this debilitating condition.

INTRODUCTION

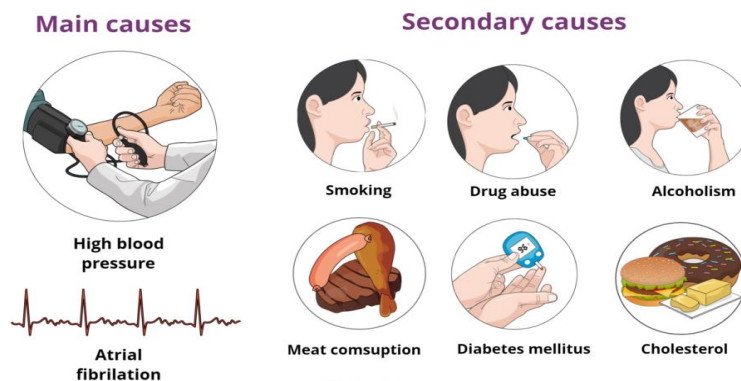
Stroke in young adults, a condition traditionally associated with older populations, has become an emerging health concern in India. The incidence of stroke in individuals aged 18 to 45 years has been rising, with a shift in risk factors, such as hypertension, diabetes, and smoking, increasingly affecting younger individuals. In India, a country with a rapidly aging population and urbanization, the increasing prevalence of lifestyle-related diseases and a lack of awareness about stroke among younger adults are significant contributors to the growing incidence. These individuals often present with severe outcomes due to delayed recognition of symptoms, improper treatment, and inadequate post-stroke rehabilitation. This review article explores the epidemiology, risk factors, clinical presentation, diagnostic challenges, and management strategies for stroke in young adults in India. It also aims to identify critical gaps in awareness, healthcare infrastructure, and public health initiatives to address this growing concern.

Etiology

Stroke in children and young adults is a relatively rare but serious condition that can result from a wide range of etiological factors, including vascular abnormalities, genetic conditions, infections, and trauma. Understanding the causes of stroke in these populations is essential for effective diagnosis, prevention, and

treatment. The etiology of stroke in children and young adults differs significantly from adults, as it often involves congenital or acquired conditions, rather than lifestyle-related risk factors such as hypertension, smoking, or diabetes. This section outlines the various causes of stroke in young individuals, with a focus on global and Indian perspectives.

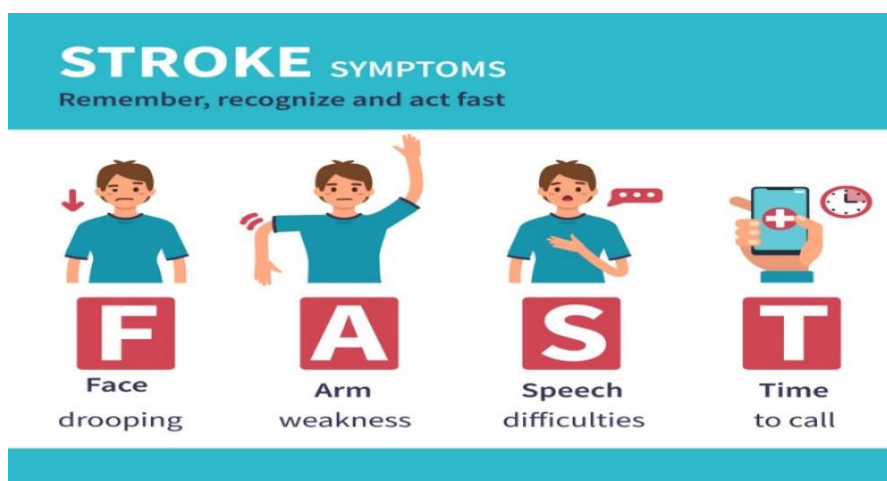
Risk factors for a **Stroke**



Global etiology of stroke in young adults

The causes of stroke in children and young adults vary according to age, genetic predisposition, and underlying medical conditions. The etiology of stroke in children and young adults is multifaceted and varies globally. While genetic and congenital conditions such as sickle cell disease, congenital heart defects, and moyamoya disease are significant contributors, infections, trauma, and emerging environmental factors also play a crucial

role. In India, the epidemiology of stroke in children and young adults is influenced by regional genetic predispositions, high rates of infections, and socio-economic factors, including malnutrition and road traffic accidents. Addressing the underlying causes through better healthcare access, early diagnosis, and preventive strategies is essential to reducing the burden of stroke in these populations.



Some Common and Well-documented etiologies include

1. Congenital and Genetic disorders

- **Arteriovenous Malformations (AVMs):** These are abnormal tangles of blood vessels that can rupture and cause hemorrhagic strokes. AVMs are often congenital and may remain undetected until a stroke occurs.
- **Sickle cell disease:** This is one of the leading causes of ischemic stroke in children, particularly in African-American children. Sickle-shaped red blood cells can obstruct blood flow in small vessels, increasing the risk of stroke.
- **Inherited thrombophilias:** Conditions like protein C or S deficiency, factor V Leiden mutation, and antiphospholipid syndrome increase the tendency for blood clot formation, leading to ischemic stroke.

- **Moyamoya disease:** This rare, progressive cerebrovascular disorder is characterized by stenosis or occlusion of the internal carotid arteries and is associated with ischemic strokes in both children and young adults.
- **Genetic disorders:** Some inherited conditions such as Down syndrome and neurofibromatosis are associated with a higher incidence of stroke in children.

2. Cardiovascular conditions

- **Congenital heart disease:** Structural heart defects, such as patent foramen ovale (PFO) or atrial septal defects (ASD), increase the risk of paradoxical embolism, which can lead to ischemic stroke in both children and young adults.

- **Cardiomyopathies:** Dilated or hypertrophic cardiomyopathies may predispose individuals to arrhythmias, which can result in embolic strokes.
- 3. Infections and Inflammatory disorders**
 - **Viral infections:** Conditions like varicella, influenza, or even cytomegalovirus (CMV) have been implicated in causing stroke in children through mechanisms such as vasculitis or direct infection of the cerebral vasculature.
 - **Bacterial infections:** Meningitis and encephalitis can lead to inflammation of blood vessels and contribute to stroke.
 - **Systemic inflammatory conditions:** Conditions such as lupus or vasculitis (e.g., Kawasaki disease) can result in arterial inflammation and increase stroke risk.
 - 4. Trauma**
 - **Head injury:** Blunt trauma to the head, especially in children, can result in arterial dissection or venous thrombosis, leading to ischemic or hemorrhagic strokes.
 - 5. Other causes**
 - **Idiopathic stroke:** In some cases, no clear cause of stroke is identified, and the stroke is considered idiopathic.
 - **Drug use:** Use of illicit substances like cocaine, amphetamines, or oral contraceptives (in young women) can increase the risk of stroke through mechanisms like vasoconstriction or clot formation.
- Prevalence and Etiology in young adults globally**
- In young adults (typically considered ages 18-40), stroke etiology overlaps with many of the factors seen in children, but additional causes such as lifestyle and environmental factors may also come into play:
- 1. Vascular and Cardiac risk factors**
 - **Atrial Fibrillation and Patent Foramen Ovale (PFO):** The presence of PFO increases the risk of stroke due to paradoxical embolism, especially in young adults.
 - **Hypercoagulable states:** Acquired or inherited thrombophilia, including antiphospholipid syndrome, is a significant cause of ischemic stroke in this age group.
 - 2. Substance Use and Abuse**
 - **Cocaine and Amphetamines:** These drugs are strongly associated with ischemic and hemorrhagic strokes, particularly in young adults, due to their vasoconstrictive properties.
 - **Oral contraceptives:** The use of birth control pills in young women is a well-known risk factor for stroke, particularly when combined with smoking or other predisposing factors like hypertension.
 - 3. Trauma and Dissections**
 - **Cervical artery dissection:** A common cause of stroke in young adults, this occurs when there is a tear in the wall of the carotid or vertebral arteries, often due to trauma or even spontaneous events.
 - **Head trauma:** Both accidental and sports-related head injuries can lead to stroke in young adults through mechanisms like arterial dissections or venous thrombosis.
 - 4. Genetic conditions**
 - **Moyamoya disease:** This condition, although rarer, is a significant cause of stroke in young adults and may be more prevalent in certain populations, particularly in Asia.
 - **Sickle cell disease:** Although more common in children, sickle cell disease can continue to predispose individuals to stroke through adolescence and into young adulthood.
 - 5. Infectious and Inflammatory diseases**
 - **Infectious vasculitis:** Infections like tuberculosis, malaria, and dengue are more prevalent in India and have been associated with stroke in children and young adults. Tuberculous meningitis, in particular, can cause significant cerebrovascular damage.
 - **Kawasaki disease:** A form of vasculitis, Kawasaki disease has a higher incidence in Asian populations, including in India, and can lead to ischemic strokes due to arterial inflammation.
 - 6. Genetic and Hematological disorders**
 - **Sickle cell disease:** Particularly in certain regions like central and eastern India, where sickle cell anemia is more prevalent, this condition remains a leading cause of ischemic stroke in children.
 - **Thalassemia and Other hemoglobinopathies:** These genetic disorders, which are common in India, increase the risk of thrombosis and stroke in children and young adults.
 - 7. Congenital heart disease**
 - **Patent Foramen Ovale (PFO):** There is a high prevalence of congenital heart disease in India, and PFO, in particular, is a known risk factor for stroke in both children and young adults.
 - 8. Cervical Artery Dissection and Trauma**
 - **Head Injury and Trauma:** Road traffic accidents, which are unfortunately common in India, are a major cause of cervical artery dissection and subsequent strokes in young adults.
 - **Sports injuries:** Contact sports and physical activity in young adults can lead to dissection or trauma-induced stroke.
 - 9. Malnutrition and Environmental factors**
 - **Malnutrition:** Poor nutritional status, especially during infancy, can contribute to underlying

developmental issues in the brain, making children more susceptible to strokes.

- **Environmental pollution:** Emerging evidence suggests that high levels of air pollution in urban

areas in India may contribute to the risk of cerebrovascular events, though more research is needed in this area.



Management of stroke in young adults

Stroke management in young adults involves an interdisciplinary approach focused on acute intervention, rehabilitation, and prevention of recurrent strokes. Recent advancements in medical science and technology have introduced cutting-edge treatments, including **stem cell therapy** and **AI-driven precision medicine**, offering new hope for improved outcomes.

Stem cell therapy in stroke treatment

Stem cell therapy is a promising experimental approach aimed at repairing brain tissue damaged by stroke. It involves using stem cells with the ability to differentiate into various cell types, including neurons, to regenerate lost or damaged neural connections.

Mechanism of action

- **Neurogenesis:** Stem cells promote the formation of new neurons to replace those lost during a stroke.
- **Angiogenesis:** They stimulate the growth of new blood vessels to improve blood flow in damaged areas of the brain.
- **Anti-Inflammatory effects:** Stem cells reduce inflammation in the brain, creating a favorable environment for recovery.
- **Secretion of growth factors:** They release trophic factors that support neural repair and protect surviving neurons.

Types of stem cells used

1. Mesenchymal Stem Cells (MSCs)

- Derived from bone marrow, adipose tissue, or umbilical cord, MSCs are widely studied for their neuroprotective and anti-inflammatory properties.

2. Neural Stem Cells (NSCs)

- These cells are directly derived from neural tissue and have a high potential to integrate into damaged brain regions.

3. Induced Pluripotent Stem Cells (iPSCs)

- Reprogrammed from adult cells, iPSCs can differentiate into any cell type, including neurons, providing a personalized treatment option.

Current status

- Stem cell therapy is still in experimental stages, with clinical trials ongoing to assess safety, efficacy, and optimal delivery methods (e.g., intravascular, intrathecal, or direct brain injection).
- Challenges include potential risks of immune rejection, tumor formation, and ethical considerations.

AI in Stroke Rehabilitation

Artificial Intelligence (AI) is transforming stroke rehabilitation by providing advanced tools for personalized and efficient recovery processes. AI-driven technologies combine data analysis, machine learning, and interactive systems to enhance both physical and cognitive rehabilitation.

Robotic-Assisted Rehabilitation Systems

- **Functionality**
 - Robotic devices provide targeted, repetitive training to improve motor recovery in stroke patients.
 - Examples include exoskeletons for gait training and robotic arms for upper limb exercises.

- **Benefits**

- Ensure consistency and accuracy in therapy sessions.
- Enable intensive rehabilitation in both clinical and home settings.
- Monitor progress and adjust therapy in real time.

AI-Driven Virtual Reality (VR) Tools

- **Interactive cognitive therapy**

- VR-based systems simulate real-life environments where patients can practice daily activities, improving cognitive and motor skills.
- Examples: Simulated shopping or cooking tasks.

- **Physical therapy**

- Patients interact with virtual objects or games to perform targeted movements, making therapy engaging and motivating.

- **AI Integration**

- Tracks patient performance and customizes VR environments to suit individual needs.

Benefits of AI in rehabilitation

1. Data-Driven insights

- AI analyzes patient data to predict recovery trajectories and identify barriers.

2. Personalized therapies

- Custom-tailored programs maximize the efficacy of rehabilitation.

3. Enhanced accessibility

- Virtual tools allow for remote rehabilitation, bridging gaps for patients in underserved areas.

Prevention Strategies

1. AI-Powered risk prediction

AI is transforming stroke prevention through tools that analyze large datasets to identify individuals at risk. By integrating data from wearable devices, genetic testing, and electronic health records, AI provides precise and actionable insights.

- **How it works**

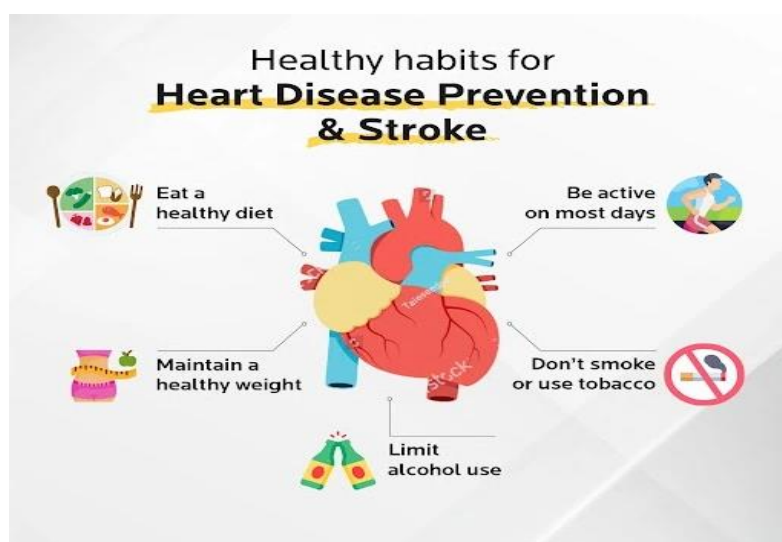
- Wearable devices (e.g., smartwatches) monitor vital signs like heart rate, blood pressure, and oxygen levels in real time.
- Genetic testing identifies predispositions to clotting disorders or other stroke-related conditions.
- AI models analyze data to predict the likelihood of a stroke and recommend preventive measures.

- **Benefits**

- Early identification of at-risk individuals.
- Continuous, real-time monitoring for high-risk patients.
- Alerts to healthcare providers for timely interventions.

2. Lifestyle intervention programs

Technology-enabled lifestyle intervention programs aim to reduce stroke risk by promoting healthy behaviors and adherence to preventive measures.



- **Key features**

- **Mobile health applications**

- Track physical activity, dietary habits, and medication adherence.
- Provide reminders for blood pressure monitoring or medical check-ups.

- **Behavioral economics principles**

- Utilize incentives (e.g., rewards for consistent exercise) to encourage positive behaviors.
- Gamification elements make lifestyle changes engaging and sustainable.

- **Telehealth counseling**

- Regular virtual consultations with healthcare professionals to guide behavior change.

- **AI-Powered insights**
 - AI evaluates user behavior and provides tailored advice to optimize health outcomes.
- **Examples of focus areas**
 1. **Hypertension management:** Encouraging regular monitoring and medication adherence.
 2. **Dietary improvements:** Promoting a heart-healthy diet rich in fruits, vegetables, and whole grains.
 3. **Smoking Cessation and Stress management:** Providing personalized strategies to quit smoking and manage stress effectively.

Impact of prevention strategies

1. **Improved awareness:** Patients gain better understanding and control of their health.
2. **Reduced risk factors:** Systematic management of modifiable factors such as hypertension and diabetes.
3. **Cost-effectiveness:** Preventing strokes reduces long-term healthcare expenses and disability-related costs.

CONCLUSION

In conclusion, stroke in young adults is an emerging public health issue in India, exacerbated by rising prevalence of risk factors such as hypertension, diabetes, and smoking. Despite advancements in medical care, the lack of awareness about stroke symptoms and prevention, especially in rural areas, significantly affects timely diagnosis and treatment. To address this issue, a multi-pronged approach involving enhanced public health campaigns, better diagnostic capabilities, and targeted healthcare policies is necessary. Additionally, improving access to rehabilitation services and post-stroke care for young stroke survivors will be critical in reducing the long-term disability and improving the quality of life for these individuals. Addressing stroke in young adults is not just a medical challenge but a societal one, demanding attention from policymakers, healthcare professionals, and the general public alike. Innovations such as stem cell therapy, AI-driven rehabilitation tools, and technology-based prevention strategies are revolutionizing stroke care. These advancements promise better functional recovery, improved quality of life, and significant reductions in stroke incidence, making them integral components of future stroke management and prevention frameworks.

REFERENCE

1. Schurks M, Rist PM, Bigal ME, Buring JE, Lipton RB, Kurth T. Migraine and cardiovascular disease: systematic review and meta-analysis. *BMJ*, 2009; 339: b3914. [DOI] [PMC free article] [PubMed] [Google Scholar]
2. Pezzini A, Grassi M, Lodigiani C, Patella R, Gandolfo C, Casoni F, et al. Predictors of migraine subtypes in young adults with ischemic stroke the Italian project on stroke in young adults. *Stroke*, 2011; 42: 17–21. [DOI] [PubMed] [Google Scholar]
3. Tietjen GE, Collins SA. Hypercoagulability and migraine. *Headache*, 2018; 58: 173–183. [DOI] [PubMed] [Google Scholar]
4. Swartz RH, Cayley ML, Foley N, Ladhani NNN, Leffert L, Bushnell C, et al. The incidence of pregnancy-related stroke: a systematic review and meta-analysis. *International Journal of Stroke*, 2017; 12: 687–697. [DOI] [PubMed] [Google Scholar]
5. Kuklina EV, Tong X, Bansil P, George MG, Callaghan WM. Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007. *Stroke*, 2011; 42: 2564–2570. [DOI] [PubMed] [Google Scholar]
6. Penther P Patent foramen ovale: an anatomical study. Apropos of 500 consecutive autopsies. *Arch Mal Coeur Vaiss*, 1994; 87: 15–21. [PubMed] [Google Scholar]
7. Schroeckenstein RF, Wasenda GJ, Edwards JE. Valvular competent patent foramen ovale in adults. *Minn Med*, 1972; 55: 11–13. [PubMed] [Google Scholar]
8. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc*, 1984; 59: 17–20. [DOI] [PubMed] [Google Scholar]
9. Saver JL, Mattle HP, Thaler D. Patent foramen ovale closure versus medical therapy for cryptogenic ischemic stroke, a topical review. *Stroke*, 2018; 49: 1541–1548. [DOI] [PubMed] [Google Scholar]
10. Wintzer-Wehekind J, Alperi A, Houde C, Côté J-M, Asmarats L, Côté M, et al. Long-term follow-up after closure of patent foramen ovale in patients with cryptogenic embolism. *Journal of the American College of Cardiology*, 2019; 73: 278–287. [DOI] [PubMed] [Google Scholar]
11. Jiang B, Ryan KA, Hamedani A, Cheng Y, Sparks MJ, Koontz D, et al. Prothrombin G20210A mutation is associated with young-onset stroke. *Stroke*, 2014; 45: 631–667. [DOI] [PMC free article] [PubMed] [Google Scholar]
12. Factor V Leiden thrombophilia. <https://ghr.nlm.nih.gov/condition/factor-v-leiden-thrombophilia#statistics>. Reviewed August, 2010. Accessed 1/23/2019
13. Previtali E, Bucciarelli P, Passamonti SM, Martinelli I. Risk factors for venous and arterial thrombosis. *Blood Transfus*, 2011; 9: 20–38. [DOI] [PMC free article] [PubMed] [Google Scholar]
14. Jadaon MM. Epidemiology of prothrombin G20219A mutation in the Mediterranean region. *Mediterranean Journal of Hematology and Infectious Diseases*, 2011; 3: e2011054. doi: 10.4084/MJHID.2011.054 [DOI] [PMC free article] [PubMed] [Google Scholar]
15. Protein C deficiency. <https://ghr.nlm.nih.gov/condition/protein-c-deficiency#genes>. Reviewed May, 2013. Accessed 1/23/2019.

16. Tait RC, Walker ID, Perry DJ, Islam SIAM, Daly ME, McCall F, et al. Prevalence of Antithrombin deficiency in the healthy population. *British Journal of Hematology*, 1994; 87: 106–112. [DOI] [PubMed] [Google Scholar]
17. Antiphospholipid syndrome. <https://ghr.nlm.nih.gov/condition/antiphospholipid-syndrome#statistics>. Reviewed April 2016. Accessed 1/23/2019.
18. Holmqvist M, Simard JF, Asplund K, Arkema EV. Stroke in systemic lupus erythematosus: a meta-analysis of population-based cohort studies. *Rheumatic & Musculoskeletal diseases*, 2015; 1: e000168. [DOI] [PMC free article] [PubMed] [Google Scholar]
19. Cavallaro M, Barbaro U, Caragliano A, Longo M, Cicero G, Granata F, et al. Stroke and systemic lupus erythematosus: a review. *European Medical Journal Rheumatology*, 2018; 5: 100–107. [Google Scholar]
20. Wiseman SJ, Bastin ME, Jardine CL, Barclay G, Hamilton IF, Sandeman E, et al. Cerebral small vessel disease burden is increased in systemic lupus erythematosus. *Stroke*, 2016; 47: 2722–2728. [DOI] [PMC free article] [PubMed] [Google Scholar]
21. Leclerc D, Sibani S, Rozen R. Molecular biology of methylenetetrahydrofolate reductase (MTHFR) and overview of mutations/polymorphisms. *Madame Curie Bioscience Database*. Austin (TX): Landes Bioscience, 2000–2013. <https://www.ncbi.nlm.nih.gov/books/NBK6561/> Accessed 2/27/ 2019. [Google Scholar]
22. MTHFR gene. <https://ghr.nlm.nih.gov/gene/MTHFR#conditions>. Reviewed April, 2016. Accessed 2/27/2019.
23. Zaric BL, Obradovic M, Bajic V, Haidara MA, Jovanovic M, Isenovic ER. Homocysteine and hyperhomocysteinemia. [published online March 12, 2018] *Current Medicinal chemistry*, 2018. <http://www.eurekaselect.com/160407/article>. Accessed May 1, 2019. [DOI] [PubMed] [Google Scholar]
24. Sickle cell disease. <https://ghr.nlm.nih.gov/condition/sickle-cell-disease#statistics>. Reviewed August, 2012. Accessed 1/23/2019.
25. Verduzco LA, Nathan DG. Sickle cell disease and stroke. *Blood*, 2009; 114: 5117–5125. [DOI] [PubMed] [Google Scholar]
26. Tate J, Bushnell C. Pregnancy and stroke risk in women. *Women's Health*, 2011; 7: 363–374. [DOI] [PMC free article] [PubMed] [Google Scholar]
27. Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, et al. Guidelines for the prevention of stroke in women A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, 2014; 45: 1545–1588. [DOI] [PMC free article] [PubMed] [Google Scholar]
28. Nieuwdorp M, Stoes ES, Meijers JC, Buller H. Hypercoagulability in the metabolic syndrome. *Curr Opin Pharmacol*, 2005; 5: 155–159. [DOI] [PubMed] [Google Scholar]
29. Vykoukal D, Davies MG. Vascular biology of metabolic syndrome. *Journal of Vascular Surgery*, 2011; 54: 819–831. [DOI] [PMC free article] [PubMed] [Google Scholar]
30. DeBette S, Leys D. Cervical-artery dissections: predisposing factors, diagnosis, and outcome. *Lancet Neurology*, 2009; 8: 668–678. [DOI] [PubMed] [Google Scholar]
31. Nedelchev K, der Maur TA, Georgiadis D, Caso V, Mattle HP, Schroth G, et al. Ischaemic stroke in young adults: predictors of outcome and recurrence. *J Neurol Neurosurg Psychiatry*, 2005; 76: 191–195. [DOI] [PMC free article] [PubMed] [Google Scholar]
32. Yang L, Ran H. Extracranial vertebral artery dissection. *Medicine (Baltimore)*, 2018; 97: e0067. doi: 10.1097/MD.00000000000010067 [DOI] [PMC free article] [PubMed] [Google Scholar]
33. Terni E, Giannini G, Brondi M, Montano V, Bonuccelli U, Mancuso M. Genetics of ischaemic stroke in young adults. *BBA Clinical*, 2015; 3: 96–106. [DOI] [PMC free article] [PubMed] [Google Scholar]
34. Fabry Disease. National Organization of Rare Diseases. <https://rarediseases.org/rare-diseases/fabry-disease/> 2019. Accessed 04/29/2019.
35. Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes. <https://ghr.nlm.nih.gov/condition/mitochondrial-encephalomyopathy-lactic-acidosis-and-stroke-like-episodes#synonyms>. Reviewed December, 2013. Accessed 04/29/2019.
36. Ohama E, Ohara S, Ikuta F, Tanaka K, Nishizawa M, Miyatake T. Mitochondrial angiopathy in cerebral blood vessels of mitochondrial encephalomyopathy. *Acta Neuropathologica*, 1987; 74: 226–233. 10.1007/BF00688185 [DOI] [PubMed] [Google Scholar]
37. NOTCH3 gene. <https://ghr.nlm.nih.gov/gene/NOTCH3> Reviewed August, 2016. Accessed 04/29/2019.
38. Birkeland P, Lauritsen J. Incidence of Moyamoya disease in Denmark: a population-based register study. *Acta Neurochirurgica Suppl*, 2018; 129: 91–93. [DOI] [PubMed] [Google Scholar]