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Stroke in Young Adults in Asia

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Abstract
Background: Stroke in young adults is a worldwide problem with long-term physical and socioeconomic implications. The largest burden of disease is expected to impact Asia. Stroke in young adults is defined broadly as strokes occurring between the ages of 18 and 49 and includes ischaemic stroke (IS) and intracerebral haemorrhage (ICH). The objective of this review was to focus on the important aspects of epidemiology, risk factors, genetic contributions, as well as evaluation, management, and outcome of stroke in young adults within the Asian context. ***Summary:*** This publication is an overview of recent literature from many countries in Asia. Population and hospital-level data offer insight into common and unique aetiologies of pre-mature IS and ICH in young adults. In young adults, prognosis and outcomes were worse in ICH compared to IS. Stroke prevention should be emphasized, while rapid access to acute stroke reperfusion and interventional therapies can benefit younger patients. More research should be performed in young adults with stroke in order to reduce the short- and long-term mortality in both stroke subtypes, improve primary as well as secondary prevention, and define further the role of next-generation sequencing for cryptogenic stroke. ***Key Messages:*** Stroke in young adults in Asia reveals the interplay between complex genetic factors, traditional risk factors, and unique aetiologies. Socioeconomic status and healthcare access are other important factors affecting the care of these patients.

Introduction

Stroke is a major cause of death and disability worldwide [1]. One important aspect of stroke in young adults is the recent increase in frequency from many parts of the world. The evidence comes not only from recent data which showed an increase in age-standardized incidence of stroke in individuals younger than 55 years in high-income countries [2] but from the GOAL initiative which reported significant differences between low-income/middle income countries and high-income countries [3]. Given that the population of Asia is approximately 60% of the world, it is expected that a significant burden of stroke will impact this continent and its younger population.

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Within the diversity of Asia, there is not only a large burden of stroke but also a large spectrum of cerebrovascular diseases and clinical management issues [4, 5]. These issues are complicated by large disparities in healthcare resources for stroke. Accordingly, the Asian Stroke Advisory Panel (ASAP) is well positioned to update this topic of stroke in young adults. The group was established in 1999 and consisted of a selected group of academic as well as clinical neurologists interested in the study of stroke in Asia [5]. Previous publications were based on important topics such as causes of early stroke mortality, stroke complications, young stroke, systems of stroke care, and consensus statement on stroke care during the COVID-19 pandemic in Asia [6]. The objective of this review was to provide an overview of the current aspects of epidemiology, risk factors, aetiology, genetic contributions, as well as evaluation, management, and outcome of stroke in young adults in Asia. 2 major subtypes of stroke, i.e., ischaemic stroke (IS) and intracerebral haemorrhage (ICH) will be covered.

Methodology

The principal investigator and participating members of the ASAP group performed a comprehensive search of PubMed for specific peer-reviewed literature on the main topic of stroke in young adults. The publications were retrieved from the literature search using the keywords and MeSH terms "stroke", "intracerebral haemorrhage", "ischaemic stroke", "young adults", "Asia" and "country" for example; "India." Boolean operators (AND, OR) refined the search.

The search strategy on PubMed returned a total of 295. Further searches by hand were undertaken from the references of these articles which produced another 25 papers. These papers did not have specific countries attached to them but included more issues related to global data on stroke in young adults. Only publications in English were selected. Publications retrieved were from January 2010 to Jan 2025. The retrieved papers were further subdivided into sections on epidemiology, stroke subtypes, aetiologies, risk factors, management, prevention, and outcome which formed the core segments of this review article. Studies were included if the publication addressed stroke in patients under the age of 50 which used data from hospital, community, or population in Asian settings.

The respective authors have selected the relevant publications as assigned and summarized the important papers. Full papers were retrieved with numerous Asian countries represented; China, India, Japan, Korea, Indonesia, Taiwan, Malaysia, Singapore, Myanmar, Sri Lanka, Bangladesh, Pakistan, and Bhutan. Other relevant publications from other parts of Asia were also included. There was a notable paucity of publications in the literature on stroke in young adults from lower income countries. Grey literature was excluded. The population covered was estimated to be approximately 85% of Asia. Due to the heterogeneity of the publications, a narrative approach was adopted and the publications were synthesized using recently published quantitative data and various qualitative topics derived from Asian publications.

Epidemiology of Stroke Subtypes in Young Adults in Asia

The global burden of IS in young adults had been described recently. The largest increases in age-standardized incidence, death and disability-adjusted life years (DALYs) rates were observed countries in the low and low-middle sociodemographic index quintiles. Affected regions in Asia include the Middle East and Southeast Asia which reported the largest increases in these metrics related to IS. The age-standardized incidence rate was also higher among young women than young men. High environmental temperature, high body mass index, and a high fasting plasma glucose contributed to the largest increases in age-standardized DALYs rates between 1990 and 2019 [7]. These changes were in tandem with the overall increase in the burden of cardiovascular diseases in young adults. There was an increase in the global age-standardized incidence rate from 126.80 per 100,000 in 1990 to 129.85 in 2019. The age-standardized prevalence rate increased from 1,477.54 to 1,645.32 per 100,000 population. In both figures, the average annual percentage changes were statistically significant [8].

Large countries in Asia such as China have reported population-based studies showing the highest age-standardized incidence of IS in the world [9, 10]. In addition, mortality rates in ICH were reported as 3.5 times greater than IS. ICH to IS ratio was 1:5 to 4 in individuals aged >75 years and this ratio increased progressively with decreasing age, reaching a ratio of 1:1.5–2.0 in young adults [11]. In 2021, the highest incidence of mortality and DALY rates were observed in young adults within Southeast Asia and East Asia. Globally, high systolic blood pressure, smoking, and ambient particulate matter pollution were identified

as the primary contributors to DALYs associated with ICH in young adults [11, 12].

On the other hand, data from a recent analysis of overall stroke epidemiology from Asia reported a trend of declining incidence, mortality, and DALYs in high-income countries from the Asia Pacific and Southeast Asia. Although there were inter- and intra-regional variations, targeted prevention in the younger age group with vascular risk factors will lead to further decreases in the overall global stroke morbidity and mortality [10].

As described in a recent review of Asian stroke epidemiology [10], many hospital-based studies have been performed across Asia. These studies provide good patient level data. From previously published data which include population-based registries, it was reported that nearly one-fifth of stroke patients admitted to hospitals in India were estimated to be under 40 years old and predominantly male [13–16]. A population-based prospective cohort performed in the Indian city of Ludhiana reported an incidence of 46: 100,000 person-years with more common risk factors such as smoking and substance abuse in younger onset stroke within the age group of 18–49. Conventional risk factors such as diabetes, hypertension, and hyperlipidaemia were also common in this age group [15].

In the context of all strokes in India, men had a higher crude and age-adjusted stroke incidence rate in Mumbai (149 per 100,000 person-years) than women (141 per 100,000 person-years) while in Trivandrum in Southern India, crude stroke incidence was higher in men after age adjustment at 143 per 100,000 person-years compared to women 128 per 100,000 person-years [13–15].

Intracerebral Haemorrhage

ICH in young patients has been described in the Global Burden of Diseases Study 2021. There has been a significant decline in global incidence but mortality was highest in Central and Southeast Asia [11]. The differential impact of increased mortality and morbidity in younger stroke patients affect patients with ICHs compared to IS [11]. Globally, risk factors of systolic hypertension, smoking, and ambient particulate air pollution are major risk factors for ICH in young adults [12].

Mortality rates in ICH range from 8.7 to 25.2%, while unfavourable outcome was reported in up to 40% of patients in the cohorts studied [17–20]. With reference to ICH in young adults, data from 2 large hospital-based studies in Taiwan and India observed that hypertension and structural causes are important aetiological factors [17, 18]. Structural vasculopathies were more prevalent in patients aged 16–30 years. In the Philippines, the most common aetiology of ICH in young patients was hypertension, while vascular lesions such as aneurysms and arteriovenous malformations were the most common aetiologies in the subgroup aged 19–29 years [19]. In Saudi Arabia, similar risk factors of ICH include hypertension and diabetes in young ICH patients from the age of 18–55 years. When stratified by age into 2 groups 18–45 and 46–55 years, worse clinical outcome was reported in the younger group (OR = 5.14; 95% CI: 1.0–26.1). This group also had a significantly higher risk factor of diabetes (OR = 4.65; 95% CI: 1.4-15.2) [20].

An observational single-centre study conducted in Taiwan [17] reported that ICH was more prevalent in patients aged 16–30 than in those aged 31–45 (54.8% vs. 36.8%). In this younger age group, structural vasculopathy (e.g., arteriovenous malformation, cavernoma) was the most common etiologic subtype in patients aged 16–30 years ($p < 0.001$), whereas hypertensive ICH was the most common subtype in patients aged 31–45 ($p < 0.001$). Within the same study cohort, the most common stroke subtype was classified as determined causes by TOAST criteria. Hyperlipidaemia, diabetes, and cigarette smoking were more common risk factors for infarction than ICH. Familial stroke patients whose first- or second-degree relatives had a stroke by age 80 years ($n = 104$, 15.5%) had more infarctions than those without a family history of stroke.

In multivariate analyses, initial stroke severity, and infarction type were important predictors of favourable outcomes (modified Rankin scale 0–2) after 3 months. At the 1-year follow-up, patients with ICH and SAH had worse functional outcomes and survival rates than those with infarction consistent with larger population-based studies [17].

In another hospital-based study based in India with 404 patients, the aetiology of ICH was hypertension in 320 (79.2%), vascular malformation in 17 (4.2%), coagulopathy in 16 (4%), cerebral venous sinus thrombosis in 9 (2.2%), and cryptogenic in 37 (9.2%) of all the patients. The patients with cryptogenic ICH were younger, had better Glasgow Coma Scale (GCS) on admission, and had good outcome compared to those with known aetiology. The most common locations of ICH were basal ganglia and thalamus (71.3%). 102 (25%) patients died, 161 (39.9%) had poor outcome and 141 (34.9%) had good outcome. Hypertensive ICH patients had frequent death or disability ($p < 0.001$). On multivariate analysis, low GCS score ($p < 0.001$), large ICH ($p = 0.01$), and high leucocyte count on

admission (p = 0.03) were significantly related to the 1-month mortality [18].

In less developed economies such as Myanmar, hospital cases and registries showed higher proportions of ICH (49%) compared to IS (43%) [10, 21]. ICH, fever, and GCS <9 were recognized as poor prognostic factors [20]. On the other hand, data for stroke in young adults have not been described in the literature in Bhutan, another low-middle-income country (LMIC) in South Asia and this was consistent with many LMICs in Asia from another recent review in Asia [10]. International efforts have been taken to improve stroke services and related systems of care across Bhutan [22]. Overall, low- and middle-income countries at a hospital level have data consistent with larger population-based studies which report the pattern of increased ICH as an important contributing factor for poor outcomes and higher stroke burden in LMICs.

Genetic Risk Factors

Stroke is a heterogeneous disorder and genetic contributions to the clinical manifestations of stroke in young adults have been better understood in the past decade. Monogenic disorders affecting the large and small cerebral vasculature found in Asia are important considerations in the evaluation of young patients with IS. This section covers the common aetiologies of IS and the relevant genetic background.

Intra-cranial atherosclerosis (ICAS) is one of the most common causes of stroke in Asia [5]. Risk factors for atherosclerotic large vessel disease include systemic vascular risk factors such as diabetes mellitus, dyslipidaemia and cigarette smoking. The condition has been described more commonly in Asia from many hospital-based studies on stroke in young adults [23–26], while ICAS was less commonly described among young patients from outside Asia, indicating that ICAS was less common [27].

ICAS also increases the risk of recurrent stroke and vascular dementia. The development of ICAS is complex and impacted by multiple genetic, biological, and environmental factors [28]. More recent literature discussed the genetic contributions to ICAS which include variants in adiponectin Q (*ADIPOQ*), apolipoprotein E (*APOE*), phosphodiesterase 4D (*PDE4D*), methylenetetrahydrofolate reductase (*MTHFR*), lipoprotein lipase (LPL), α-adducin (*ADD1*) genes, angiotensin-converting enzyme (ACE), and other genes related to renin-angiotensin-aldosterone system [28–30].

Differences in the distribution of antioxidants and pro-inflammatory molecules in intra-cranial versus extra-cranial arteries can explain the predisposition of Asian patients in developing ICAS at a younger age. This underlying problem may be accelerated by the presence of conventional risk factors [30]. A recent study on atherosclerotic mouse models reported the importance of structural differences between intra- and extra-cranial vessels to explain these differences [31]. Another contributing factor includes the level of insulin resistance which appears to influence the differences between intra- and extra-cranial atherosclerotic burden in Asian patients [32].

An important risk factor for non-atherosclerotic large vessel disease in young adults such as moyamoya disease (MMD) and more commonly found in Asia is ring finger protein 213 (RNF213). This was identified as a susceptibility gene for East Asian patients with MMD with a higher prevalence of RNF213 pR4810K variant [33]. It is also recognized that this gene variant is associated with progressive ICAS [34].

Monogenic causes of stroke affecting cerebral small vessels such as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) are more commonly reported in Asia which features 4 common NOTCH3 gene missense mutations: p.R141C, p.R182C, p.R544C, and p.R75P. The average age of presentation of the first 2 mutations occur a decade earlier (between the ages of 43 and 45), while men and women were equally affected and up to half of the clinical presentations include strokes [35, 36].

Neuroimaging on MRI classically showed numerous white matter lacunar infarcts and diffuse white matter hyperintensity seen on T2-weighted and FLAIR sequences. The confluent extent of disease in younger adults and the involvement of anterior temporal lobe white matter, external capsule, and corpus callosum strongly favour the diagnosis of CADASIL [35]. Scattered microhaemorrhages, on gradient-echo or susceptibility-weighted sequences, are frequent, some leading to ICHs [36–39]. ICH and cerebral microbleeds in CADASIL have been described as more common in East Asian populations than in the population of white European ancestry due to the East Asian-specific NOTCH3 p.R75P mutation [40].

In a multi-centre study in China, targeted next-generation sequencing utilizing a customized gene panel of 531 genes applied to samples from young-onset cryptogenic stroke reported pathogenic variants in the Notch3 receptor (NOTCH3), protein kinase AMP-activated noncatalytic subunit gamma 2 (PRKAG2), and ryanodine receptor 2 (RYR2). Genes associated with cardiogenic diseases were most frequently found (53.3%)

followed by small vessel disease and coagulation disorders in descending order. There is a promising role for targeted NGS in the evaluation of cryptogenic strokes. Further research is required in larger studies from relevant populations in Asia [41].

In addition, recent developments of polygenic risk scores quantified the relationship between genetic risk derived from genome wide association studies' (GWAS) datasets and lifestyles on the differential development of early- and late-onset coronary artery disease, IS, and ICH in a large cohort of East Asians. The findings indicate that in those with high genetic risk and unfavourable lifestyle when compared to subjects with low genetic risk and a healthy lifestyle, the hazard ratios (HRs) of early-onset CAD, IS, and ICH were 6.62, 3.34, and 6.53, respectively. In this study, early onset was defined as vascular events under the age of 60 [42].

From the Indian sub-continent which has numerically the largest population in Asia, four genetic polymorphisms have been identified which confers greater risk of ISs. These occur in *ACE I/D*, *IL10*, and *MTHFR* genes [43]. Other genetic risk factors for stroke include associations with single nucleotide polymorphisms (SNPs) of novel phosphodiesterase 4D (PDE4D) [44, 45].

A substantial number of studies observed large variations in the proportion of IS subtypes among young adults. Most studies used the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria for stroke subtyping. The studies documented larger proportions of large artery atherosclerosis (LAA) and small vessel occlusion with percentages ranging from 8 to 29.8% and 17.4 to 32.8%, respectively, in Asia [46–50]. Recently, the use of International Paediatric Stroke Study (IPSS) risk factors was proven to be useful to further reflect the heterogeneous risk factors and possible stroke aetiologies beyond the use of TOAST criteria [46].

Despite the distinct classification of the various stroke subtypes, silent cerebrovascular disease co-exist in young patients with a first episode of clinical stroke, manifesting in the form of silent brain infarctions and white matter hyperintensities at frequencies of 14.5% and 8.75%, respectively. The presence of these lesions was related to hypertension and homocysteine levels [49].

Modifiable Risk Factors

Hypertension remains the main risk factor globally, regionally, and nationally in young adults for cardiovascular diseases including IS [8, 50]. In addition, other conventional risk factors feature prominently in a large majority of published stroke studies. Increased prevalence of multiple risk factors including hypertension, diabetes, tobacco smoking, alcohol consumption, obesity, lack of physical activity, and high ambient pollution leads to a high stroke burden in Asia, particularly in young adults [7–9].

Infections are uncommon but recognized risk factors for stroke in young adults within Asia. These include tuberculous meningitis, dengue (IS and ICH) neurocysticercosis (ICH, IS, SAH) and snakebites (IS, ICH). Other studies from Sri Lanka, India, and Taiwan have revealed numerous under-recognized risk factors for IS which include betel consumption and scorpion stings [5, 50–52].

Acute IS is a common complication in young patients with TB meningitis. Among the numerous risk factors for acute IS include age >35, hypertension, diabetes, smoking, meningeal enhancement, and hydrocephalus. The percentage of TB meningitis patients complicated by IS was approximately 20.4–67% depending on the geographical location of the study [53–55]. Smaller blood vessels such as perforators and distal cortical branches were involved in AIS in these TB meningitis cases. This is further affected by co-existing conventional risk factors and the pro-inflammatory milieu which contribute to vasculitis and atherothrombosis [54, 55].

Lesser known risk factors include evidence that herpes zoster infection increases the risk of stroke/transient ischaemic attack. A meta-analysis on IS cases post-herpes zoster infection reported increased risk of IS in age groups younger than 40 years compared to age groups 40–59 and greater than 60 years, respectively [56]. This observation was also detected by a study conducted on the Korean Health Insurance Database which found a gradual decrease with age in the risk of IS after herpes zoster infection [57]. The role of infection can also be seen in rheumatic heart disease as an immunological complication of streptococcal pharyngitis. In Asia, rheumatic heart disease is an important cause of stroke and remains under-recognized and under-treated. Several studies have confirmed the significant contribution of RHD in causing IS in young adults [58]. Other risk factors in Asia include the increased risk of IS in patients with systemic lupus erythematosus compared to the general population as reported from a study utilizing the Korean National Health Insurance database [59].

In a population of young patients with nasopharyngeal carcinoma from a National Health Research

Insurance Database in Taiwan, who were followed up for 7 years, IS incidence rates were twice higher in patients who received radiotherapy, radiotherapy/chemotherapy, and without radio/chemotherapy in comparison to control group (13.8, 12.8 and 12.6 versus 6.07 per 1,000 person-years, respectively). The age strata with highest risk were 20–39-year-old patients who had both radiotherapy/chemotherapy (HR 14.7, 95% confidence interval 9.24–23.4). Hypertension, diabetes, hyperlipidaemia, and increased alcohol intake further increased the risk with HRs ranging from 2.4 to 9.3 [60].

Ethnicity and Socioeconomic Factors

A study in China reported that there was significant stroke burden with increased incidence in young and middle-aged adults living in the setting of a rural environment with low income and educational background [61]. On the other hand, ethnicity was another important determinant of age of first onset of stroke as reported in a study comparing South Asians living in the UK and India with white British patients. South Asians experienced stroke 19.5 years and 7.2 years earlier than their white British counterparts in a highly statistically significant manner [62]. These examples underscore how socioeconomic factors affect the age of stroke onset with the complex interplay of genetic factors and the environment.

In many parts of the world, despite government initiatives and strategic planning for stroke detection, prevention, and management, there are significant challenges on the ground. In many LMIC countries, there is a rural-urban divide, exacerbated by the limited access to education and healthcare, making it challenging for people to recognize stroke symptoms and risk factors. Resource limitations also lead to insufficient acute care and preventive efforts while further highlighting healthcare disparities [14, 51].

Outcome and Long-Term Follow-Up

The National Mortality Surveillance System in China explored temporal trends and reported that the age-standardized mortality rate from IS and ICH increased by 11% from 2005 to 2020 [63]. As described earlier, in-hospital mortality rates from ICH range from 8.7% to 25% [17–20]. Another study reported that the prediction of stroke recurrence in young adults can be estimated with a nomogram utilizing the risk factors of hypertension, diabetes, smoking, as well as the stroke classification of small vessel disease and large artery atherosclerosis. Conversely, a longer duration of formal education (>12 versus 0–6) was inversely correlated with recurrent stroke [64].

There were a few studies on short-term follow-up at 1 year on young adults with IS in Asia. These studies [65, 66] found good functional outcome (modified Rankin scale 0–2) in 76.3–84.3% of patients with a relatively low recurrence of 2.5–7.9% at 1 year among young IS patients. Mortality rate was 1.7–3.7%. Baseline stroke severity, age, and male gender predicted a poor 1-year functional outcome.

Similar studies from Singapore and Malaysia [67, 68] reported that 30–45 percent of young stroke patients do not return to work. Return to work was lower in patients with ICH. The mortality at 1 year was 5%, consistent with other more recent studies [65, 66]. On the other hand, a more comprehensive registry in Taiwan which followed up 65,097 young stroke patients with ICH and IS over 10 years, reported mortality rates of 28%, indicating an excess in pre-mature deaths after a first stroke in young Taiwanese adults [69]. Further studies are required to explore the long-term outcome of stroke in young adults in Asia.

Management

Management and prevention strategies for strokes in young adults do not differ from older stroke patients and depend on the stroke subtype. The principles of acute medical treatment for younger stroke patients are identical to older adults. The recommendations for physiological parameters such as blood pressure, temperature, glucose, and oxygenation are the same as older adults with stroke [70].

In acute IS, there was evidence that younger patients (under the age of 50) had better outcomes compared to older patients after endovascular thrombectomy in the MR CLEAN registry in Europe [71]. In Asia, in countries where these acute resources are available, studies from China reported that there were more favourable outcomes from intravenous thrombolysis in younger AIS stroke patients with less in-hospital mortality and higher odds of independent ambulation [72]. Endovascular therapy was also reported to be more successful in younger stroke patients compared to older subjects in China [73]. Multi-centre studies which included centres from Asia and Europe have reported greater success in younger subjects compared to older patients. These findings strongly support the use of thrombolysis and thrombectomy in large vessel occlusions in younger Asian patients [74].

One promising therapy is minimally invasive surgery for ICH. Recently, this improved surgical technique was proven

to be beneficial in lobar ICHs from a randomized controlled trial [75]. To our knowledge, no such studies have been performed or published in a cohort of young adults with lobar ICB in Asia, where the disease burden is highest.

Management of young adults with acute and post-stroke complications have numerous other challenges. This age-specific special population has multi-faceted issues in many segments of care. In the acute stage, there is a need for greater awareness of stroke in younger patients, leading to rapid access for specific treatment. The other important factor is the degree of diagnostic investigations that should be performed. Over a prolonged period of time, the management of stroke in young adults will include stroke prevention, rehabilitation, recovery, and adaptation which encompass the high cumulative cost of consultations, investigations, medications, assistive devices, transport, and care-giving resources. Other psychosocial factors such as the consequences of disability, loss of productive work and income, as well as altered family dynamics are other complicating factors [76, 77].

At present, there are no specific guidelines for stroke in young adults in Asia. There are applicable concepts from outside Asia with recommended best practices. Centres of excellence have longitudinal programs designated to streamline healthcare in this special population as organized in the USA [78].

The ability to adhere to these proposed best practices is dependent upon the resources available for each country. Therefore, clinical practice and the resources allocated will vary across the different countries depending on its sociodemographic index in Asia. In more developed Asian countries with greater resources such as Singapore, Japan, and Taiwan, cost and healthcare access will be less of a problem due to the presence of robust public healthcare and national insurance systems [79].

On the other hand, the availability of diagnostic equipment, rehabilitation facilities, and the lack of skilled rehabilitation, imaging, and clinical specialists are problems in low- and middle-income countries. This will have substantial impact on young adults with stroke. Possible strategies to mitigate the inadequacies include task shifting to available healthcare workers or caregivers, telerehabilitation, community-based rehabilitation services with scalable mobile and communication technologies [80].

Psychosocial issues can be addressed by peer-support groups, peer-mentoring programs, healthcare information resources in various formats, and involvement in research projects where available could help address the unique needs of this population [81]. Our review article found limited information from publications in Asia with reference to unique psychosocial issues, indicating gaps in this research area.

In the setting of limited resources, such programs can be integrated in whole or in part into rehabilitation and primary care outpatient programs with more specific input from neurologists/physicians interested in stroke in young adults. The use of stroke support groups with social and community services may also be required for re-assimilation into society.

Primary and Secondary Prevention

Pillars of primary prevention depend upon robust identification and optimization of modifiable risk factors such as smoking, diabetes, hypertension, and dyslipidaemia which are highly prevalent in young stroke populations in Asia. In secondary prevention, the best strategy is directed towards stroke aetiology and addressing detected existing and unrecognized risk factors [70, 82, 83].

For instance, younger patients with IS benefit more from closure of patent foramen ovale compared to older patients as shown by a recent systematic review and meta-analysis [84]. This benefit was seen in younger patients under the age of 55 compared with older patients and in those on medical therapy for the prevention of recurrent ischaemic neurological events. Specific treatments for stroke prevention in the setting of TB meningitis are still uncertain, although a recent meta-analysis of previous trials of aspirin did not reduce mortality but significantly reduced the risk of new infarctions [85]. On the other hand, immunomodulatory drugs such as dexamethasone showed some success in reducing mortality but insignificant reduction in strokes. Immunomodulatory agents and biologics such as infliximab and adalimumab have been tested with variable success [86].

Research and Clinical Practice

Recommendations for further improvement in clinical practice in Asia for this special population include funding internal education programmes for clinicians as well as through external stroke advocacy organizations in Asia such as Asia Pacific Stroke Organization and Asian Stroke Advisory Panel (ASAP) [4, 6]. This collaborative effort will ensure that best clinical practices are implemented and

adapted for each country. National screening programs targeting the younger age groups may be another approach with the objective of improving primary prevention. These programmes can be augmented by improved access and affordability of medications in a single polypill [87] to ensure uniform compliance which can also contribute to improvement in secondary prevention [88].

The formation of community-based rehabilitation centres and involvement of primary care physicians can ensure complete longitudinal care for young adults with stroke across many parts of Asia [80]. Diagnostic and treatment gaps from lack of resources can be bridged by scalable interventions such as mobile imaging [89], digital technologies [90–93], and increased training of personnel in poorly resourced areas.

Future research for stroke in young adults in Asia can be directed towards understanding genetic contributions to the various stroke subtypes with improved epidemiological data in countries with limited resources. Other possible research areas include improving acute therapies, addressing specific conditions such as infection-related stroke and MMD while investigating longer term outcomes and improving the implementation of primary as well as secondary prevention. Investigations into the psychosocial impact of stroke in the young can also be increased in Asia, given the paucity of literature. Ultimately, the aim is to mitigate the pathophysiological and psychosocial consequences of stroke in young adults. Integrating new information with resources for patients, families, and caregivers will help strengthen the partnership between clinician and patient, leading to more specific clinical practice guidelines for this group.

In order to improve clinical practice and research, governmental grants and directives, philanthropic and corporate grants, as well as non-governmental organizations such as national stroke support groups can help in a collaborative effort with each country and its stakeholders deciding on the specific research or clinical requirements in this special population.

Conclusion

Stroke among young adults in Asia is a growing continental problem. This contribution re-visited published data from many countries across Asia and presented a contemporary overview of this topic. This review is cognizant of the relevant local literature and the ethnic composition of the various regions in Asia, given the diverse spectrum of diseases across Asia as the aetiology of stroke varies according to age strata, geographical region, background prevalence of conventional risk factors, environmental factors, as well as underlying genetic risk factors. Outcome and short follow-up studies of younger stroke patients showed low mortality and recurrence in the short term after hospital discharge but with the majority failing to return to their previous occupation. Longer term studies report pre-mature mortality. Standardized comprehensive population studies are pivotal for informed public health policies, while comprehensive data collection specifically on stroke in young adults with genetic evaluation can further enrich the understanding of the interaction of genetic versus environmental factors. Barriers to stroke care call for improved healthcare infrastructure, awareness campaigns, and support systems.

Statement of Ethics

Ethical approval was not required for this study in accordance with local or national guidelines of the respective countries. The work was done on publicly available resources.

Conflict of Interest Statement

Prof. Tsong Hai Lee and Prof. Shinichiro Uchiyama were members of the Journal's Editorial Board at the time of submission of the manuscript. The other authors have no conflicts of interest to declare.

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Author Contributions

K.S.T. conceptualized the manuscript, wrote the first draft, administered the entire project, and re-wrote the final manuscript. Co-authors T.H.L., S.U., U.K.R., P.P.L. Y.C., and N.V. searched, retrieved, and selected the relevant articles, summarized the key points, co-wrote the first draft, and were involved in reviewing and editing subsequent drafts. All authors have read, commented, and subsequently agreed to the final manuscript.

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