Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

MAGNITUDE AND DETERMINE OF THE RISK FACTORS AND INCIDENCE OF THE ARTERIAL ISCHEMIC STROKE AFFECTING THE CHILDREN OF THE ZAGAZIG CITY

[1]Essam Abdallah Albakrawi,[2] Ahmed Galal Syam,[3] Ahmed Hosny Mohamed

Pediatrics Department, Faculty of Medicine, Zagazig University, Egypt.

Corresponding author: Essam A**.** Albakrawi, Email: alghaber81@gmail.com

ABSTRACT

Background: Childhood arterial ischemic stroke (AIS) differs in essential aspects from adult stroke. Pediatricians, among others, struggle with a low awareness among laypersons and physicians, resulting in delayed diagnosis, less experience in the use of thrombolysis and mechanical thrombectomy, and a time-and resource-consuming etiological clarification due to the multitude of possible risk factors. The aim of the present study was to investigate and determine the most common risk factors and causes of AIS in children.

Patients and methods: This prospective cohort study was carried out, including 24 patients admitted to Pediatric Department, Faculty of Medicine, Zagazig University. All patients were subjected to the following full history taking, proper clinical and neurological examination, and routine blood tests. All echocardiograms were reviewed by a pediatric cardiologist. Outcome of AIS treatment were followed in all patients.

Results: The variability of focal manifestation among studied patients most frequent one was hemiparesis (62.5%), followed by Speech disturbance41.7% then Facial weakness 33.3%; the least manifestation was Ataxia (16.7%) among Arterial Ischemic Stroke group. Vascular imaging artropathy subtype of AIS patients, nearly two fifths was arteropathy type,12.5%, Moyamoya, the same percent was arterial dissection. About 37.5% of arterial ischemic stroke patients were treated via anticoagulant, 29.2% by antiplatelet and one third of them was treated with both. Early outcome of treatment arterial ischemic stroke patients, 37.5% of them became normal. At late follow up period about 50% of patients became normal**.**

Conclusion: Our findings suggest that the most frequent risk factor for arterial ischemic stroke was cardiac lesion (41.7%), followed by arterioropathy (37.5%), then prothrombin disorder 29.2%; the least recorded risk factor was diabetes (4.2%). When stroke or transient ischemic attack occurs, a comprehensive survey should be performed and detailed history about the associated underlying diseases should be noted.

Keywords: Arterial ischemic stroke ; Incidence ; Pediatrics

INTRODUCTION

Pediatric arterial ischemic stroke (AIS) is an important cause of neurologic morbidity in children.Consequences can include sensorimotor deficits, language impairment, intellectual disability, behavioralproblems, and epilepsy **(1)**.

Stroke has become an increasingly recognized cause of morbidity and mortality in children. Population-based studies of arterial ischemic stroke (AIS) in children estimate an annual incidence of 2.4 per 100,000 persons with a case fatality rate approaching 4%.Hospitalizations for AIS in children have been rising in the past decade. Over 50% of survivors have persistent neurologic, cognitive or psychiatric deficits, with significant financial costs to families and society **(2).**

The rising rates of pediatric AIS hospitalization may be related in part to the increasing availability and use of better diagnostic techniques, such as Magnetic Resonance Imaging (MRI). An improving public stroke awareness and recognition of stroke symptoms may also contribute **(3).**

In spite of increased awareness of pediatric AIS, the etiology of the disease is not completely understood and its diagnostic and therapeutic procedures are still underdeveloped. It is well established

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

that identification of the multiple etiologies of childhood AIS may lead to better diagnosis, management as well as its prevention **(4)**.

Several studies from different ethnic and geographical regions have investigated the preexisting risk factors of AIS in children. According to their results, the identified risk factors were not similar in different age, ethnic, and geographical regions. Evidence indicated that most of the studies were established in Western and European countries with few studies from Asian countries **(5-7)**.

It is well established that the identification of AIS risk factors in each region is an important issue which could be used for better management, improvement of its prognosis, and prevention of its related complications. A regional study indicated that 70% of children with AIS suffered from neurological disabilities **(8)**.

Considering that better understanding of the underlying mechanisms and risk factors of AIS would be helpful for the improvement of rational management of stroke and its outcome in children as well as preventing or reducing the occurrence of its related potential disabilities, the aim of this study is to investigate and determine the most common risk factors and causes of AIS in children.

PATIENTS AND METHODS

This prospective cohort study was carried out from 1 June 2020 to 1 June 2021, including 24 patients admitted to Pediatric Department, Faculty of Medicine, Zagazig University. Approval of the ethical committee of Zagazig University was obtained before the start of patient's recruitment.

Inclusion criteria

Acute Pediatric arterial ischemic stroke is defined as an acute focal neurological deficit with the evidence of cerebral infarction in an arterial distribution on brain imaging. Patients in age between 29 days and 18 years.

Exclusion criteria:

Patients < 29 days or > 18 years and children with congenital hemiplegia.

Methods

All patients were subjected to the following:

1. Full history taking with special emphasison the onset of stroke, its clinical presentation, any history of previoussimilar attacks, or a history of a chronic systemic illness.
2. Proper clinical and neurological examination: All patients had their vitals assessed (pulse rate, bloodpressure, respiratory rate, temperature, oxygen saturation,pupils) as well as symptoms were recorded.
3. Routine blood tests incuding CBC, liver function tests, kidney function tests, RBS, PT, PTT and INR, as well as Lipid profile.
4. The available neuroradiological investigations (Brain CT, MRI, MR angiography) initially were reported by neuroradiologists. Initial brain magnetic resonance imaging/angiography was reviewed as to site(s) of infarction (right/left/bilateral, anterior circulation/posterior circulation/both), multiplicity of infarcts (single/multiple), evidence of mature infarcts at the time of index event/scan(from previous clinically silent infarction), and arteriopathy location(right/left/bilateral carotid/vertebral circulation, anterior/posterior/both circulation). A patient with multiple infarcts within a single vessel territory was considered to have multiple infarcts.
5. All echocardiograms were reviewed by a pediatric cardiologist.
6. Risk factors and defined conditions thought to be associated with childhood arterial ischemic stroke were divided into 10 categories including arteriopathies, cardiac disorders (CDs), infection, acute head-and-neck disorders, acute systemic conditions, chronic systemic conditions, prothrombotic states, chronic head-and-neck disorders and others.

Presentation and diagnosis

Clinical presentations included focal or diffuse neurological deficits as level of consciousness, seizures and non-specific systemic presentations as cardiorespiratory symptoms. Neuroimaging data incorporated classification of infarct by number, laterality, circulation (anterior or posterior), involvedbrain structures and hemorrhagic transformation.

Risk factors

Possible AIS causes were classified as 'risk factors' or 'associations' based on their strength of causation for pediatric stroke. Risk factors were selected based on high confidence in their likely causative role referencing published studies. Risk factors were then further categorized as arteriopathy,

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

cardiac, prothrombotic, acute illness, or chronic diseases. For patients with both cardiac and arteriopathy risk factors, we selected one as a primary risk factor based on individual patient details.

Treatment

Antithrombotic therapies were categorized as anticoagulant (e.g. heparins,warfarin) or antiplatelet (e.g. acetylsalicylic acid).

Outcomes

Outcome data were obtained from follow-up clinic visits when available. Neurological outcomes were collected routinelyduring clinical care and graded by the site neurologists as no deficit (normal), mild, moderate, or severe deficits.

Statistical analysis:

Data collected and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data qualitative represent as number and percentage , quantitative continues group represent by mean ± SD. Differences between quantitative independent multiple by ANOVA or Kruskal Wallis,. P value was set at <0.05 for significant results &<0.001 for high significant result.

RESULTS

The present study showed a statistically insignificant difference between patients and control as regard demographic data p>0.05 **(Table 1).**

The variability of focal manifestation among studied patientsmost frequent one was hemiparesis (62.5%), followed bySpeech disturbance41.7% thenFacial weakness 33.3% ;the least manifestation wasAtaxia (16.7%) among Arterial Ischemic Stroke group. One quarter of case had vertigo in addition one quarter of case had vomiting and nausea **(Table 2).**

The most frequent risk factor was cardiac lesion (41.7%), followed by arteriopathy (37.5%),then prothrombin disorder (29.2%);the least recorded risk factor was diabetic (4.2%) among arterial ischemic stroke group **(Figure 1)**.

Regarding Laboratory finding, there was statistically significant relation between Arterial Ischemic Stroke patients with; INR p=0.0001, Protein C p=0.0001, protein S p=0.0001. It is obvious that Ischemic Stroke patients , had lower value of protein C and protein S. They are more likely to have high value of INR **(Table 3)**.

Concerning vascular imaging artropathy subtype of AIS patients, nearly two fifths was arteropathy type,12.5%, Moyamoya, the same percent was arterial dissection **(Table 4)**. About 37.5% of arterial ischemic stroke patients were treated via anticoagulant, 29.2% by antiplatelet and one third of them were treated with both **(Table 5)**.

Regarding early outcome of treatment arterial ischemic stroke patients, 37.5% of them became normal **(Figure 2)**. At late follow up period about 50% of patients became normal **(Figure 3)**.

Table (1): Demographic data, of Arterial Ischemic Stroke patients & controls

variables	Studied groups			
	Arterial Ischemicstroke group (n=24)	Control group (n=24)	χ^2	p
Age Mean± SD Median(range)	7.21±5.02 6(1-17)	7.12±4.82 6(1-16)	U=0.072	0.942
Sex Females males	 10(41.7%) 14(58.3%)	 8(33.3%) 16(66.7%)	0.36	0.55
Residence Rural Urban	 14(58.3%) 10(41.7%)	 11(45.8%) 13(54.2%)	0.75	0.38

χ^2 Chi square test, U=Mann-Whitney U, P>0.05 insignificant

Table (2) : Frequency of focal and nonspecific manifestations among Arterial Ischemic Stroke group

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

variables	Manifestations (n.24)			
	yes		no	
	n.	%	n.	%
Historysimilar attack	2	8.3%	22	91.7%
focal symptoms				
hemiparesis	15	62.5%	9	37.5%
Facialweakness	8	33.3%	16	66.7%
Speech disturbance	10	41.7%	14	58.3%
Visual disturbance	7	29.2%	17	70.8%
Ataxia	4	16.7%	20	83.3%
parasesia	6	25.0%	18	75.0%
nonspecific symptoms				
headache	4	16.7%	20	83.3%
vertigo	6	25.0%	18	75.0%
Vomiting and nausea	6	25.0%	18	75.0%
Decreaseconsciousness	1	4.2%	23	95.8%
convulsion	3	12.5%	21	87.5%

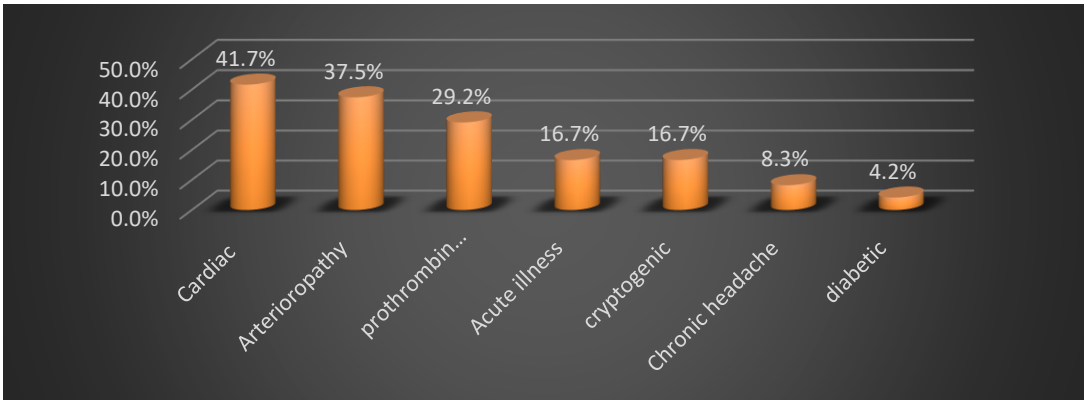

Figure (2): Percent of risk factors among Arterial Ischemic Stroke group

Table (3): Comparison between arterial ischemic stroke patients and control group regard laboratory finding

	Arterial Ischemic Stroke patients	Control	t	p
CBCs				
HB	12.85±1.16 12.8(10.4-15.3)	12.77±1.18 12.8(10.4-15.3)	0.247	0.806
PLT	294.08±68.3 286(179-432)	298.25±67.93 293.5(179-432)	0.21	0.83
WBCs	7.35±2.51 6.7(4.6-13.6)	7.3±2.49 6.7(4-13.6)	U=0.053	0.958
Liver enzyme				
ALT	23.33±5.69 23(15-34)	23.17±5.55 23(15-32)	0.103	0.92
AST	23.79±5.36 24(16-37)	21.79±4.75 21(15-31)	1.36	0.178
Kidney function				

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Creat	**0.91±0.18 0.87(0.6-1.21)**	**0.88±0.17 0.87(0.5-1.21)**	**0.585**	**0.561**
RBS	**114.21±18.11 109(89-178)**	**109.92±21.09 106.5(80-178)**	**0.756**	**0.453**
INR	**1.55±0.48 1.41(1.03-2.5)**	**1.05±0.11 1.05(0.87-1.3)**	**4.99**	**0.0001 (S)**
Lipid profile				
Cholesterol	**153.5±7.44 153(143-176)**	**146.25±19.47 151.5(112-176)**	**1.73**	**0.095**
TG	**124.75±6.97 125(112-134)**	**122.83±11.92 125(99-143)**	**1.07**	**0.292**
HDL	**44.83±3.11 45(39-51)**	**47.46±7.13 46(37-65)**	**1.65**	**0.108**
LDL	**105.58±5.14 105.5(96-119)**	**101.54±10.28 100.5(77-118)**	**1.72**	**0.092**
Serology				
Protein C	**83.38±19.07 87.5(48-109)**	**118.33±19.04 122.5(83-144)**	**6.35**	**0.0001 (S)**
Protein S	**78.48±23.34 86.5(42-105)**	**115.46±23.32 123.5(79-142)**	**5.49**	**0.0001 (S)**
CRP	**9.58±5.42 7.6(3.1-22.5)**	**9.75±4.99 8(4-21)**	**U=0.37**	**0.7**

Data presented by Mean± SD, t test of significant U =Mann-Whitney U test, (S)=significant p<0.05

Table (4): Frequency of vascular imaging artropathy subtypeamong arterial ischemic stroke group (n=24)

variables	**vascular imaging artropathy subtype (n.24)**			
	yes		**no**	
	n.	**%**	**n.**	**%**
Arteropathytype	**10**	**41.7%**	**14**	**58.3%**
Moyamoya	**3**	**12.5%**	**21**	**87.5%**
Arterialdissection	**3**	**12.5%**	**21**	**87.5%**
vacuities	**1**	**4.2%**	**23**	**95.8%**
Postvaricella	**1**	**4.2%**	**23**	**95.8%**
Sicklecell	**1**	**4.2%**	**23**	**95.8%**
unspecified	**1**	**4.2%**	**23**	**95.8%**

Table (5): Frequency of treatment of arterial ischemic stroke patients (n=24)

variables	**treatment (n.24)**			
	yes		**no**	
	n.	**%**	**n.**	**%**
anticoagulant	**9**	**37.5%**	**15**	**62.5%**
antiplatelet	**7**	**29.2%**	**17**	**70.8%**
Both	**8**	**33.3%**	**16**	**66.7%**

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

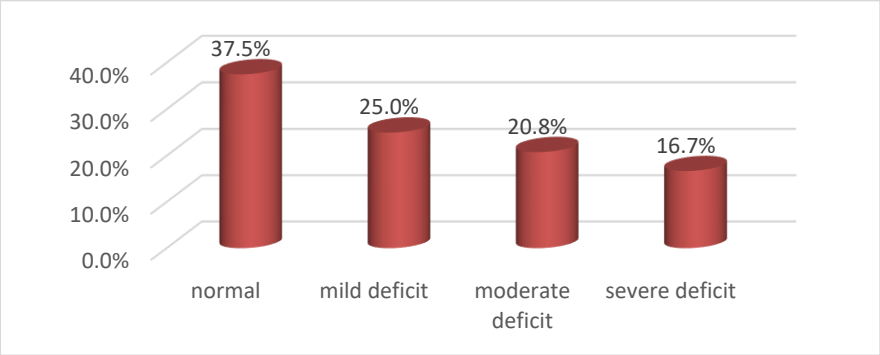

Figure (2): Percent of early outcome of arterial ischemic stroke patients

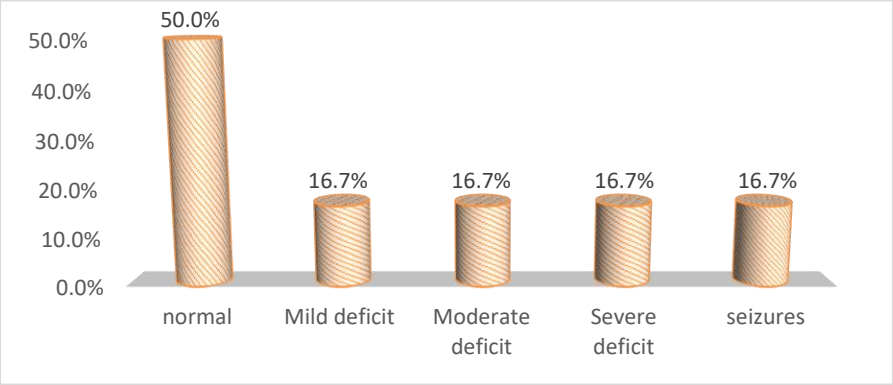

Figure (3): Percent of delayed outcome of arterial ischemic stroke patients

DISCUSSION:

The overall population burden of cerebrovascular disease in the young may be underestimated, since clinically silent infarcts and white-matter changes have been shown to be prevalent even in young stroke patients **(9).**

Recent evidence suggests that traditional vascular risk factors are highly prevalent in young adolescent and children stroke populations with distinct demographic characteristics, yet the strength of association of these risk factors has received scarce attention. On the contrary, there are also young patients and children without traditional risk factors, while these individuals may harbor other conditions with only weak or uncertain association with the stroke alone. These conditions often represent a risk factor that may be strictly young-age specific, more prevalent in younger than older patients, or more prevalent among young people and children in the population (**10,11).**

So, we aimed in this study to investigate the incidence and determine the most common risk factors and causes of Pediatric arterial ischemic stroke in children referred to Zagazig University Hospitals.

In the present study, boys had a higher prevalence and incidence than girls, but there is no statistical significance. Also, there is no statistic significant urbanization level, and geographic location. This came in agreement with **Chiang and Cheng (12)** who found the same results.

The male predominance has been previously reported in pediatric AIS (**13,14).**This gender predominance persisted across neonatal and childhood age groups and also remains unexplained. Hormonal factors may predispose males to early thrombotic stroke (**15)**; however, further study is required to explore this area.

In the current study, the variability of focal manifestation among studied patients, most frequent one was hemiparesis (62.5%), followed by Speech disturbance41.7%, then Facial weakness 33.3%; the least manifestation was Ataxia (16.7%) among Arterial Ischemic Stroke group. One quarter of case had vertigo in addition one quarter of case had vomiting and nausea. **Chiang and Cheng, (12)** found that the most commonly associated codes related to clinical manifestations during admission were seizures (25.4%), hydrocephalus (10.8%), hemiplegia (9.9%) and hypertension (5.0%).

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

DeVeber et al. (16) found that children frequently presented with focal neurological deficits (61%) or seizures (50%) on a background of diffuse neurological deficits. Focal deficits (primarily hemiparesis) predominated in older children. Among diffuse neurological deficits, altered level of consciousness predominated, including coma in 57 older children. Non-specific presentations, observed in 49 per cent, included mainly cardiorespiratory disorders in neonates and headache, nausea, vomiting and fever in older children.

In the current study, the most frequent risk factor was cardiac lesion (41.7%), followed by arterioropathy (37.5%),then prothrombin disorder 29.2%;the least recorded risk factor was diabetic (4.2%) among arterial ischemic stroke group.

In agreement with our study, **Chung and Wong, (17)** found that In Hong Kong, cardiac disorders were identified in 42% of children with ischemic stroke, and it was the second most common cause of stroke in a Turkey study (**18).**

Also, **DeVeber et al. (16)** found that heart disorders accounted for 12–28% of pediatric ischemic stroke in North America and Europe.

Gerstl et al. (19) revealed prothrombotic states, cardiac diseases, and arteriopathies were most common. Especially, cardiac disorders are often described as a single risk factor (19/47 children), whereas coagulation problems often co-occur with other risk factors (43/56 children). Infectious diseases were seen in 19 children, of which 4 children did not show any additional risk factors. Moreover, **Medley et al. (20)**found the highest population attributable risk factors were found to be hypertension, low HDL-C, cardiovascular disease (CVD), type 1 diabetes mellitus, family history of stroke, and trial fibrillation.

In the Vascular Effects of Infection in Pediatric Stroke (VIPS) study of 355children who had arterial ischemic stroke after the neonatal period, 30%had congenital or acquired cardiac disease, 36% had definite vascular disease (arteriopathy), 10% had suspected arteriopathy, and 18% had acute fever or systemic sepsis (**21).**

The risk factors seen in older adults (hypertension, hyperlipidemia, smoking, and diabetes mellitus) were not commonly found in this age range. In comparison, in a large European cross-sectional study of 3331young adults with first-time ischemic stroke, 17% had cardioembolic disease, 13% had cervical artery dissection, 12% had small vessel occlusion, 9%had large-artery atherosclerosis, and9% had other identified causes (not dissection), followed by thrombophilias, antiphospholipid antibody syndrome, systemic vasculitis, migraine with aura, and others **(22).**

Young adults have a substantial number of potentially modifiablerisk factors that are similar to those common in older adults (**10).**

In the present study, more than one half 58.3% of arterial ischemic stroke patients had single infraction, mainly at left side 45.8%, affected mainly anterior circulation (58.3%). **Gerstl et al. (19)**found the lesion was right-sided in 42% of children and left-sided in 47% of children, and both sides were affected in 10% of children

In the current study, vascular imaging artropathy subtype of Arterial Ischemic Stroke patients nearly two fifths were arteropathy type, 12.5%, Moyamoya, the same percent was arterial dissection. **Wintermark et al. (21)** found that the most common childhood arteriopathies in their cohort of children presenting with acute arterial ischemic stroke were moyamoya disease and arterial dissection

In the present study, that 37.5% of arterial ischemic stroke patients was treated via anticoagulant, 29.2% by antiplatelet and one third of them was treated with both. This came in agreement with **DeVeber et al. (16)** revealed 30% received anticoagulant agents alone while 27% we retreated with antiplatelet agents alone. A further 18% received both treatments, usually provided consecutively.

In the present study, 37.5% of patients became normal early. After follow up period one half of them became normal. Unfortunately 16.7% had severe deficit at early follow up and still at late follow up period.

DeVeber et al. (16) found an abnormal long-term outcome (stroke-specific death or long-term neurological deficit) was documented in 69% of children. Two-thirds of children surviving stroke (67%) demonstrated neurological deficits at long-term follow-up. Neurological deficits were graded as mild in approximately half, with the remainder moderate or severe. The likelihood of abnormal outcomes was stable over the16 years of follow-up. In older children, observed deficits remained mostly stable over time with 16% demonstrating a reduction in their deficit severity, while another 8% demonstrated an increase.

CONCLUSION

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Our findings suggest that the most frequent risk factor for arterial ischemic stroke was cardiac lesion (41.7%), followed by arterioropathy (37.5%), then Prothrombin disorder 29.2%; the least recorded risk factor was diabetes (4.2%). When stroke or transient ischemic attack occurs, a comprehensive survey should be performed and detailed history about the associated underlying diseases should be noted.

No Conflict of interest.

REFERENCES:

1- **Felling, R. J., Sun, L. R., Maxwell, E. C., Goldenberg, N., & Bernard, T. (2017).** Pediatric arterial ischemic stroke: epidemiology, risk factors, and management. Blood Cells, Molecules, and Diseases, 67, 23-33.
2- **Hajek, C. A., Yeates, K. O., Anderson, V., Mackay, M., Greenham, M., Gomes, A., Lo, W. (2014).** Cognitive outcomes following arterial ischemic stroke in infants and children. Journal of Child Neurology, 29(7), 887-894.
3- **Numis, A. L., & Fox, C. K. (2014).**Arterial ischemic stroke in children: risk factors and etiologies. Current neurology and neuroscience reports, 14(1), 422.
4- **Rosa, M., De Lucia, S., Rinaldi, V., et al. (2015).** Paediatric arterial ischemic stroke: acute management, recent advances and remaining issues. Italian Journal of Pediatrics, 41(1), 1-12.
5- **Mackay MT, Wiznitzer M, Benedict SL, et al. (2011):**Arterial ischemic stroke risk factors: the international pediatric stroke study. Ann Neurol 2011; 69: 130–140.
6- **Ghofrani, M., Tonekaboni, H., Karimzadeh, P., Nasiri, J., Pirzadeh, Z., Ghazzavi, M., Yghini, O. (2018).** Risk factors of pediatric arterial ischemic stroke; A regional survey. International journal of preventive medicine, 9.
7- **Sarecka-Hujar, B., &Kopyta, I. (2020).** Risk Factors for Recurrent Arterial Ischemic Stroke in Children and Young Adults. Brain Sciences, 10(1), 24.
8- **Nasiri, J., Ariyana, A., Yaghini, O., Ghazavi, M. R., Keikhah, M., &Salari, M. (2016).** Neurological outcome after arterial ischemic stroke in children. Advanced biomedical research, 5.
9- **Fazekas, F, Enzinger, C, Schmidt, R. (2013):** MRI in acute cerebral ischemia of the young: the Stroke in Young Fabry Patients (SIFAP1) Study. Neurology; 81: 1914–1921.
10- **von Sarnowski, B, Putaala, J, Grittner, U. (2013):** Lifestyle risk factors for ischemic stroke and transient ischemic attack in young adults in the Stroke in Young Fabry Patients study. Stroke; 44: 119–125.
11- **Putaala, J, Yesilot, N, Waje-Andreassen, U. (2012):** Demographic and geographic vascular risk factor differences in European young adults with ischemic stroke: the 15 Cities Young Stroke Study. Stroke; 43: 2624–2630.
12- **Chiang, K. L., & Cheng, C. Y. (2018).** Epidemiology, risk factors and characteristics of pediatric stroke: a nationwide population-based study. QJM: An International Journal of Medicine, 111(7), 445-454.
13- **Tuckuviene, R., A.L. Christensen, J. Helgestad, S.P. Johnsen, and S.R. Kristensen. (2011):**Paediatric arterial ischaemic stroke and cerebral sinovenous thrombosis in Denmark 1994- 2006: a nationwide population-based study. Acta Paediatr; 100:543-549.
14- **Agrawal, N., S.C. Johnston, Y.W. Wu, S. Sidney, and H.J. Fullerton. (2009):**Imaging data reveal a higher pediatric stroke incidence than prior US estimates. Stroke; 40:3415-3421.
15- **Normann, S., G. de Veber, M. Fobker, C. Langer, G. Kenet, T.J. Bernard, et al. (2009):** Role of endogenous testosterone concentration in pediatric stroke. Ann. Neurol 2009; 66:754-758**.**
16- **DeVeber, G. A., Kirton, A., Booth, F. A., Yager, J. Y., Wirrell, E. C., Wood, E., Bjornson, B. H. (2017).** Epidemiology and outcomes of arterial ischemic stroke in children: the Canadian Pediatric Ischemic Stroke Registry. Pediatric neurology, 69, 58-70.
17- **Chung, C. P. (2017).** Types of stroke and their differential diagnosis. In Primer on Cerebrovascular Diseases (pp. 372-376). Academic Press.
18- **Per H, Unal E, Poyrazoglu HG, Ozdemir MA, Donmez H, Gumus H, et al. (2014):**Childhood stroke: results of 130 children from a reference center in Central Anatolia, Turkey. Pediatr Neurol; 50:595–600.

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

19- **Gerstl, L., Weinberger, R., Heinen, F., Bonfert, M. V., Borggraefe, I., Schroeder, A. S., Olivieri, M. (2019).** Arterial ischemic stroke in infants, children, and adolescents: results of a Germany-wide surveillance study 2015–2017. Journal of neurology, 266(12), 2929-2941.

20- **Medley TL, Mitef C, Andrews I, Ware T, Cheung M, Monagle P, Mandelstam S, Wray A, Pridmore C, Stojanovski B, Mackay MT (2018)** Australian Clinical Consensus Guideline: The diagnosis and acute management of childhood stroke. Int J Stroke. https:// doi.org/10.1177/1747493018799958.

21- **Wintermark M, Hills NK, deVeber GA, Barkovich AJ, Elkind MS, Sear K, Zhu G, Leiva-Salinas C, Hou Q, Dowling MM, Bernard TJ, Friedman NR, Ichord RN, Fullerton HJ, Investigators V (2014)** Arteriopathy diagnosis in childhood arterial ischemic stroke: results of the vascular efects of infection in pediatric stroke study. Stroke 45(12):3597–3605.

22- **YesilotBarlasN, Putaala J, Waje-Andreassen U, et al. (2013):**Etiology of first-ever ischaemic stroke in European young adults: the 15 cities young stroke study. Eur J Neurol;20(11): 1431Y1439. doi:10.1111/ene.12228.