Original Article

Outcome of acute vasculopathies in children- A case control study

N H Lonikar[1], K G Rathod[2*], A K Niswade[3], Ubaid UR Raheman[4]

[1]Consultant, Department of Pediatrician, Vishwaprayag Newborn Care, Nanded, Maharashtra, INDIA.
[2]Assistant Professor, Department of Pediatrics, Dr. Shankarrao Chavan Government Medical College, Nanded, Maharashtra, INDIA.
[3]Professor and Head, Department of Pediatrics, Government Medical College and Hospital, Nagpur, Maharashtra, INDIA.
[4]Resident, Government Medical College and Hospital, Aurangabad, Maharashtra, INDIA.
Email: kishorgrathod@gmail.com

Abstract

Introduction: Acute vasculopathy is still regarded as a rare event in childhood and therefore knowledge of diagnostics, therapy and prophylaxis is limited among general pediatricians. Besides the greater awareness, an objective increase in childhood thrombosis is due to the medical progress in the treatment of critically ill patients. The present study is an attempt to evaluate etiology, risk factors, clinical presentation and outcome of acute vasculopathy in children. It also intends to measure outcome of acute vasculopathies with or without chronic underlying disorder. **Objective:** To study clinical presentation and difference in outcome in cases of acute vasculopathies in children with and without underlying disorder. **Study Design:** Case control study. Study Period: 1 Year. Study Settings: Govt. Medical College and Hospital, Nagpur, Maharashtra, India. Data Collection: Pediatric Patients visiting Out-Patient, admitted in Pediatric Wards and Pediatric Intensive Care Units (PICU). Data Entry: was done by Microsoft Excel 1997-2003 Software. Statistical analysis: was carried out by STATA VERSION 0.8. **Results:** Hemoglobin <10 gm/dl was an independent risk factor for acute vasculopathy. There was strong co-relation between low GCS (Glasgo Coma Scale) ≤8 and MR (Modified Rankin) Scale ≥3 with poor outcome. Survival without Sequele was more in case group and survival with sequele was more in control group. Among controls coagulopathy and sickle cell disease are common predisposing factors. This study concludes poor outcome in children with acute vasculopathy who have chronic underlying disorder.

Keywords: Children, CNS, CNS Vasculopathy, Extra CNS Vasculopathy, Strokes in Children, Vasculopathy.

[*]**Address for Correspondence:**
Dr. K. G. Rathod, Assistant Professor, Department of Pediatrics, Dr. Shankarrao Chavan Government Medical College, Nanded, Maharashtra, INDIA.
Email: kishorgrathod@gmail.com

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INTRODUCTION

More than 2400 years ago, the father of medicine, Hippocrates, recognized and described stroke as the sudden onset paralysis, the earliest description of cerebrovascular vasculopathy[1]. But as Infants, children and young adults account for less than 5% of all strokes and incidence figures are sparse. The incidence of stroke in 0-14 years of age (excluding stroke related to birth, intracranial infection, and trauma) was reported as 2.52 cases /1, 00,000 per year[2]. The primary objective of this study was to find out the differences in outcomes of acute vasculopathies, predisposing factors, clinical presentation and improve outcome of patients of acute vasculopathies with or without chronic underlying disorders.

MATERIALS AND METHODS

This is a Case control study conducted over the period of 1Year. Inclusion criteria: All cases of acute vasculopathies in children of age from 1- month to 18 Years of age. Exclusion criteria : 1) Patients with chronic vasculopathies like haemangioma, cavernomas, angiosarcomas.2) Infants less than 1 month of age, as the causes of stroke and other acute vasculopathies in this age group are different as compared to other age group and 3) The patients with poor vitals, having low Glasgow coma scale scores as they cannot be evaluated further. **Case**:

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Children presenting as acute vasculopathies and **without** any chronic underlying disorder who develop Thrombosis, Embolism, Stroke, Vasculitis and DIC. **Controls:** Patients with acute vasculopathy but having chronic underlying disorders like Sickle cell disease, Congenital heart disease, Rheumatic heart disease, Nephrotic syndrome, Chronic liver disease, Inherited hematological disorders, HIV, Acute leukemia and Infective vasculitis. All patients of acute vasculopathies attending outpatient department and admitted in pediatric wards and Pediatric Intensive Care Unit (PICU) were recruited. A detailed history of present illness and a significant illness in past was recorded. On the basis of history and physical examination presumptive diagnosis of site of acute vasculopathy is made. Then these patients were subjected to relevant laboratory and radiological investigations. The patients then categorized in to cases and controls depending on the presence of chronic underlying disorder. These patients then followed up till final outcome –either up to discharge, death or up to one month of hospitalization and recorded as the final outcome of patient. The disability measurement in patients is done on the basis of modified Rankin scale[3].

Table 1: Modified Rankin scale

Score	Clinical features
0	No symptoms
1	No significant disability, despite symptoms; able to perform all usual duties and activities
2	Slight disability; unable to perform all previous activities but able to look after own affairs without assistance
3	Moderate disability; requires some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requires constant nursing care and attention
6	Death

Statistical Methods

Categorical variables are expressed in percentages. Categorical data is analyzed by performing Chi Square statistics. Mann Whitney U test is performed to compare difference of alteration of level of consciousness, involvement of cortex among cases and controls. Univariate analysis for hemoglobin, hematocrit, Modified Rankin scale. Individual Odd`s ratio with 95% confidence interval estimated on the basis of results of univariate analysis, then performed multivariate logistic analysis to allow evaluation of independent role of variables like hememoglobin, hematocrit with occurrence of acute vasculopathy. Pearson correlation is performed to see the strength of association between poor GCS and outcome (by recording Modified Rankin scale). P value <0.05 is taken as statistical significance. All statistical analysis is performed by using STATA VERSION 0.8.

OBSERVATIONS AND RESULTS

Table 2: Characteristics of patients of vasculopathy

		Cases n=38(%)	Controls n=40(%)	p value
Age Distribution	1 Mon- 4 Y 11 Mon	20 (52.6)	24 (60)	0.806
	5 Yr- 9yr 11 Mon	10 (26.3)	9 (22.5)	
	10 yr – 18 Yr	8(21.0)	7 (17.5)	
Sex Distribution	Male	22 (57.8)	21 (52.5)	0.656
	Female	16 (42.1)	19 (47.5)	
Vasculopathy	CNS	25 (65.7)	30 (75)	0.459
	Extra CNS	13 (34.2)	10 (25)	
Hemoglobin (gm %)	< 8	6 (15.7)	18 (45)	0.017
	8-10	15 (39.4)	12 (30)	
	>10	17 (44.7)	10 (25)	
Hematocrit (%)	<30	13 (34.2)	7 (17.5)	0.129
	30-40	20 (52.6)	22 (55)	
	>40	5 (13.1)	11 27.5)	
Survival Trends	Survival without sequele	31 (81.5)	22 (55)	0.034
	Survival with sequele	5 (13)	10 (25)	
	Death	2 (6)	8 (20)	
Modified Rankin Scale for Disability Measurements	0	13 (34.2)	10 (25)	0.001
	1	12 (31.6)	2 (5.0)	
	2	6 (15.8)	2 (5.0)	
	3	2 (5.3)	16 (40)	
	4	1 (2.6)	1 (2.5)	
	5	2 (5.3)	1 (2.5)	
	6	2 (5.3)	8 (20.0)	

Table 3: Characteristics of patients having CNS vasculopathy

		Cases n=25 (%)	Controls n=30(%)	p value
Frequency of Seizures	No seizures	11 (44)	10 (33.3)	0.009
	Single Episode	10 (40)	4 (13.3)	
	Multiple Episodes	4 (16)	16 (53.3)	
Cranial Nerve Palsies	Optic	0	2 (6.6)	0.514
	Oculomotor	2 (8)	5 (16.6)	
	Facial	8 (32)	16 (53.3)	
	Glasso-pharyngeal	0	3 (10)	
Speech Impairment	Global Aphasia	4 (16)	6 (20)	0.068
	Motor Aphasia	5 (20)	3 (10)	
	Sensory Aphasia	0	1 (3.3)	
	Dysarthria	0	7 (23.3)	
Motor Deficit	Hemiparesis	23 (92)	26 (86.6)	0.017
	Quadriparesis	2 (8)	2 (6.6)	
	Monoparesis	0	2 (6.6)	
Sites of CNS Vasculopathy	Cortex	15 (60)	17 (56.6)	0.572
	Subcortical White matter and Corona Radiata	6 (24)	6 (20)	
	Internal Capsule and Basal Ganglia	3 (12)	4 (13.3)	
	Thalamus	0	1 (3.3)	
	Brainstem	0	1 (3.3)	
	Cerebellum	1 (4)	0	

Table 4: Vessels in CNS vasculopathy

Vessel	Cases (n=25)	Controls (n=30)
Internal Carotid Artery	3(12%)	4(13.3%)
Anterior Cerebral Artery	5(20%)	5(16.6%)
Middle Cerebral Artery	15(60%)	22(73.3%)
Posterior Cerebral Artery	3(12%)	4(13.3%)
Anterior communicating	0%	1(3.3%)
Posterior communicating	0%	1(3.3%)
Basilar artery	0%	1(3.3%)
Venous sinuses	1(4%)	0%
Moya Moya disease	1(4%)	2(6.6%)
Lacunar infarct	1(4%)	0%

Table 5: vessels affected in peripheral vasculopathy

Vessel	Cases(n=13)	Control (n=10)
Brachial artery	2(15.3%)	1(10%)
Radial artery	3(23%)	1(10%)
Ulnar artery	2(15.3%)	1(10%)
Femoral artery	0%	1(10%)
Poplitial artery	0%	1(10%)
Dorsalis Pedis artery	1(7.6%)	2(20%)
Upper limb terminal branches	4(30.7%)	2(20%)
Lower limb terminal branches	4(30.7%)	2(20%)
Hepatic vein	0%	1(10%)
Renal artery	3(23%)	1(10%)
Splenic vein	0%	1(10%)

Table 6: Chronic underlying disorder identified in controls (n=40)

Sickle cell disease	12(30%)
SS	8(20%)
AS	4(10%)
Cardiac disease	4(10%)
Congenital	3(7.5%)
Rheumatic	1(2.5%)
Nephrotic syndrome	2(5%)
Infective vasculitis	8(20%)
Pyogenic meningitis	3(7.5%)
Tuberculous meningitis	3(7.5%)
Viral meningoencephalitis	2(5%)
HIV	5(12.5%)
Moya Moya vasculitis	3(7.5%)
Acute leukaemia	3(7.5%)
Coagulopathy	10(25%)

DISCUSSION

The age and sex matching did not differ significantly in both groups. High hematocrit, thrombocytosis, leukocytosis is associated with increased incidence of thrombotic complications and stroke[4]. (Table 2). Bacterial meningitis is the most common cause of intracranial arteritis in children. Stroke is a common sequel of intracranial infections in children, especially H.influenze, pneumococci, and tubercular meningitis[5]. Gulati *et al*[6] in India found that childhood stroke multiple risk factors co-exist. Mortality was 20-30% with residual neurodeficit found in > 50% cases. (Table 6) Martelle *et al*[7] and Linde *et al*[8] in their series of 50 patients with Fallots tetralogy found that stroke occurred only in patients younger than 5 years and there appeared to be relation between stroke and high hematocrit. This is co-relating with the present study. On the other hand stroke correlated with relative microcytic hypochromic anemia. (Table 2) Nagraja D *et al*[9] studied 43 children with stroke over 8 years. Hemiplegia is commonest manifestation. Middle Cerebral Artery was commonest artery involved, etiological diagnosis is possible in <50% of cases. (Table 3 and 4). The seizures of variable pattern are one of the manifestations of clinical interest in CNS vasculopathy. It occurred in 56% cases and 66.6% control group patients. Considering the neurological disease leading to vascular injury, it is expected that incidence of seizures will be more, however not happened so. The present study has shorter duration, therefore it cannot report on continued seizure activity in further life. The lower incidence of seizures is comparable to the results of study by Nagraja *et al* which reported seizures in 27% cases. (Table 3). When lesion is small or not found on angiography, unconsciousness was not a feature to manifest. Supranuclear facial nerve palsy was the frequently observed cranial nerve palsy in the present study. In this study facial nerve palsy recorded in 32% cases and 53.3% controls at the time of presentation in hospital. Facial paralysis in 62.9%was reported by Obama *et al*[10]. While at the time of measuring outcome, there was facial nerve palsy in 7.89% cases and 15% controls. Speech defect in two groups was statistically in significant. Aphasia was reported in 28.6% by Obama *et al*[9] and in 23%by Verma *et al*[10]. Hemiperesis was the frequently reported motor deficit and was found frequently in both case and control group. And there was no statistically significant difference in two (p=0.782) hemiperesis found in 92% cases and 86.6% control group patients. Obama *et al*[9] and Verma *et al*[10] have reported similar findings 97.1% hemiplegia and 86% monoplegia. (Table 3) Central Nervous System vasculopathy 60% had cerebral cortex involvement, while control group patients with CNS vasculopathy 56.6% cases recorded to have cerebral cortex involvement. The sub-cortical white matter and corona radiata affected in 24% cases and 20% control group patients. This was consistent with vascular area involved. Similar study by Chung B *et al*[11] observed that out of 11 cases with infarction involving middle cerebral artery territory, 18.2% were limited only to cortex, 27.3% were limited to sub-cortical structures such as basal ganglia or internal capsule or both,54.4%had complete middle cerebral artery involvement, with cortical and sub-cortical stroke. (Table 3). Middle cerebral cerebral artery being direct extension of internal carotid artery and its high flow dynamics, becomes victim of thrombo-embolic occlusion frequently. Present study showed similar findings. On CT angiography study, among major vessel occlusion, MCA was most commonly affected area 60% in cases and 73.3% in control group. Similar observation were found by Andre P.C. *et al*[12]. (Table 4). Vessels affected in Peripheral Vasculopathy are shown in Table 5. The study observed survival trends in the form of complete recovery, survival with sequele and death. **A**pplication of Mann Whitney u test showed significant

difference of outcomes. Death rate was significantly higher in control group 8 (20.0%) as compared to case group2 (5.3%). Higgins *et al*[13] reported that 23% of their patients died during the immediate infarct period. Keidan *et al*[14] in their study found that 17.7% succumbed to an acute event. This study also showed that presence of chronic underlying disorder, children presenting with a generalized neurological disorder, namely alteration in level of consciousness and those with hemorrhagic infarction have a statistically significant risk of immediate post infarction death and associated with poor outcome. In our study, patients presenting poor level of consciousness as measured by applying Glasgo Coma Scale had poor outcome as demonstrated by Pearson correlation (p value 0.008). The measurement of outcome depending on underlying disorder showed worse outcome in controls.

SUMMARY

Seizures of varying pattern were one of the manifestations of clinical interest. The difference between occurrence and frequency between two groups is observed, both occurrence of seizures and recurrence of seizures are common among control group. There are no difference recorded two groups for loss of consciousness as recorded by applying Glasgow coma scale. Consistent with CT evidence of location of infarct and vessel occlusion, supra-nuclear facial nerve palsy was frequently observed cranial nerve palsy. Hemiperesis was the commonest motor deficit. There no difference observed in pattern of motor deficit. (P value 0.782). Higher values of M.R. scale in controls are more and associated with poor outcome. Hemoglobin <10 is independent risk factor for occurrence of acute Vasculopathy (P value is 0.017). Sickle cell disease and Coagulopathy are among the common predisposing causes of acute Vasculopathy. Cortex was frequently observed site of infarct in both cases and controls. (Mann Whitney U test=0.572) this was consistent with the vascular area involved. On CT Angiography, Middle Cerebral Artery was the commonest vessel involved in both case and control group 60% cases and 73.3% control. The outcome measurement with Modified Rankin scale showed number of patients having poor outcome i.e. MR scale ≥3 are 26(65%) in control group while in case group patients having poor outcome i.e. MR scale≥3 are 7(18.6%) only and application of Mann Whitney u test showed significant difference of outcomes. A significant association exists between MR Scale and GCS (p value - 0.008). Death rate was significantly higher in control group as compared to case group.

CONCLUSIONS

Chronic underlying disorders are common predisposing factors for acute vasculopathy. Hemoglobin <10 gm/dl is independent risk factor for acute vasculopathy. In both cases and controls, poor level of consciousness (GCS≤8) is associated with poor outcome. Pearson correlation reveals strong association between low GCS and MR scale score ≥3 i.e. poor outcome. Survival without sequele was more in case group 31patients (81.5%) as against control group 22 patients (55%).survival with sequele was more in control group;10 (25%) patients as against 5 (13%) patients of case group. Death rate was high in control group; 8 (20%) patients as against 2 (6%) case group patients. These results reveals that outcomes are poor in control group i.e. those having chronic underlying disorder as compared to those not having chronic underlying disorder, as measured with application of M.R. scale. Among controls coagulopathy and sickle cell disease are common predisposing factors. Thus this study concludes poor outcome in children with acute vasculopathy who have chronic underlying disorder.

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