Original Article

Neurological manifestations of HIV positive pediatric patients - a cross-sectional study

Rathod K G[1*], Sutay N R[2], Ubaid UR Raheman[3], Suroshe B B[4]

[1]Associate Professor, Department of Pediatrics, Dr. Shankarrao Chavan Govt. Medical College, Nanded, Maharashtra, INDIA.
[2]Professor and HOD, Department of Pediatrics, Grant Medical College, Mumbai, Maharashtra, INDIA.
[3]Resident, [4]Assistant Professor, Department of Pediatrics, Government Medical College, Aurangabad, Maharashtra, INDIA.
Email: kishorgrathod@gmail.com

Abstract

Introduction: acquired Immunodeficiency Syndrome (AIDS) is a disease of 21st century, one of the youngest and most studied disease of all times. Extent of this problem is rapidly growing in children. True incidence of CNS involvement is not known although it is thought to occur in most HIV infected children and its incidence is at least 3 times than that in adults. It has been estimated that at least 40% of children with AIDS will have or will present with at least one neurological abnormality. **Objective**: to find the prevalence of neurological manifestation and study neurological manifestations in HIV positive pediatric patients. **Study design**: a cross sectional study. **Study period:** 1st January 1999 to 31 December 2004. **Study settings**: Grant Medical College and Sir J. J. group of Hospitals, Mumbai. **Data collection:** data collected from pediatric ward indoor case papers. **Dataentry:** was done by doing MS office- Microsoft Excel- 1997-2003 software. **Statistical analysis:** Statistical analysis was carried out with the help of statistical measures, such as percentages, proportion and using SPSS software. **Results:** A total of 200 HIV positive pediatric patients were admitted in wards during the study period of which neurological involvement was in 48 (24%) patients, prognosis is bad once there is Central Nervous System (CNS) involvement. Mortality is 3 times as compared to Non-CNS involvement. Commonest presentations were convulsions 23 (56%) and altered Sensorium 11 (23%). Generalized cerebral atrophy was most common findings on neuro-imaging.

Keywords: AIDS, HIV, Neurological Manifestations, Pediatric HIV.

[*]**Address for Correspondence:**
Dr. Rathod K. G., Associate Professor, Pediatrics, Dr. Shankarrao Chavan Govt. Medical College, Nanded, Maharashtra, INDIA.
Email: kishorgrathod@gmail.com
Received Date: 20/11/2015 Revised Date: 26/12/2015 Accepted Date: 14/01/2016

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	DOI: 18 January 2016

INTRODUCTION

The study was undertaken to study the neurological manifestation of Human Immunodeficiency Virus (HIV) infection in children. The manifestations of HIV infection in children are different from those in adults. The reasons for this phenomenon could be: 1) the immune system of the perinately infected young infant is immature. This may allow widespread seeding into various organs. 2) Some organs like brain may be susceptible to the effects of the virus in a manner different from that observed in adults. 3) The pattern of opportunistic infections in children is different from those in adults. CNS involvement is one of the common systems but there is scanty data about pediatric patients.

Objectives

To find the prevalence of neurological manifestations in HIV positive pediatric patients. To study various neurological manifestations in HIV positive pediatric patients admitted in the pediatric ward of a tertiary care centre.

Neurological Manifestations

HIV infection in children can present with CNS manifestations. Their frequency depends on the stage of HIV infection. For identifying these problems and relating them to HIV infection, the physician should have a high index of suspician. Availability of facilities to conduct neuro-psychiatric and neurodevelopmental examinations also help in making an early diagnosis. It has been estimated that at least 40% of children with AIDS will have or will present with at least one

How to site this article: Rathod K G, Sutay N R, Ubaid UR Raheman, Suroshe B B. Neurological manifestations of HIV positive pediatric patients - a cross-sectional study. *MedPulse – International Medical Journal* January 2016; 3(1): 80-83. http://www.medpulse.in (accessed 24 January 2016).

neurological abnormality. Encephalopathy is the clinical picture caused by encephalitic lesions of these young patients. However, lesions can affect any portion of the nervous system leading to myelitis, pheripheral neuropathy[3]. HIV cause immune-suppression and provides an oppurtinity for micro-organisms to cause opportunistic infections. These infections may lead to neurological abnormalities. Tuberculous meningitis, cytomegalovirus (CMV) encephalitis, and others are classical examples of such a mechanism; include encephalitic vascular strokes, neoplasia of the nervous system, peripheral neuropathy and myopathy. HIV encephalopathy may present early in HIV/AIDS disease, but its incidence increases with progression of the disease. Its evolution is variable; there may be progressive.

Clinical Presentation

Non progressive encephalopathy (static encephalopathy): Delay in psychomotor development, Microcephaly, Signs of pyramidal tract dysfunction (Paresis, Hypertonia, Hyper-reflexia), Cognitive deterioration (delay in speech, intellectual delay). Progressive encephalopathy: Clinical manifestations described as above, but with a progressive course, psychomotor regression, Characterized by triad of symptoms impaired brain growth, progressive motor dys-function and loss or plateau of developmental milestones.

1. Pheripheral neuropathy C1) inflammatory polyneuropathy (a phase with few symptoms of AIDS), Progressive paresis with areflexia. C2) Distal sensory polyneuropathy (in more symptomatic phases of AIDS, related to HIV infection or to neurotoxic drugs), Paresthesias or pain, chiefly in the distal zones of the lower limbs, Alterations of the Achillis reflex (hypo or areflexia) and decrease in vibration sensations.
2. Myopathy (from HIV) Proximal paresis and myalgia, Elevated levels of serum CPK.
3. Cytomegalovirus (CMV) infection, Manifestations similar to progressive HIV encephalopathy, Radicular Pain, Hypo-esthesias/paresthesias, and Areflexia of the deep tendon reflexes.

- Toxoplasmosis, abscess, strokes, neoplasia. Seizures: acute or subacute onset of neurological focal signs, Changes in mental status, intracranial hypertension.
- Cryptococcus, candida and Mycobacterial infections. Presents with manifestations similar to those described for abscess. Signs of meningeal irritation.

Pathology

Brain- pathological features noted are atrophy, gliosis, and microglial foci of necrosis with or without infiltrate around them, loss of myelin, vacuolation and perivasculitis, vascular and parenchymal calcification, characteristic multinucleated giant cells in the parenchyma and perivascular location. The multi-nucleated giant cells are probably derived from mononuclear cells. These lesions are related to HIV, which has been demonstrated in the brain by electron micropathy and in situ hybridization[4,5]. Stoler and colleagues[6] have localized the virus by in situ hybridization to macrophages, microglia, and giant cells and less commonly to glial cells and neurons. The relationship of HIV infection to mononuclear cells in the brain to encephalopathy is not clear. Release of neurotoxic substances by the inflammatory cells may be one of the mechanisms of injury to brain. It is possible that the resultant damage and atrophy to the brain may not be completely repairable in terms of morphologic structures even after anti HIV therapy is given. Besides the primary lesions of HIV infections, related to two other categories such as involvement in opportunistic infections and foci of necrosis are also seen in the lympho-reticular system and brain.

Spinal Cord

Vacuolar myelopathy due to swelling within myelin sheaths characterized by vacuolar degeneration and the presence of lipid laden macrophages, particularly in the lateral and posterior columns of thoracic spinal cord, were observed in two children. Pathogenesis of vacuolar myelopathy is not clear. It may be related directly to HIV or to sequele of HIV infection such as metabolic abnormalities secondary with the chronic debilitating disease process of AIDS, or it may be related to both HIV and its sequel[7].

Diagnosis

Neurological examination must be a part of the clinical evaluation of all children infected with HIV and should be complemented with neuro-psychological testing and cranial computerized tomography (CT) scanning. Cerebral atrophy and occasionally calcification of the basal ganglia characterized the HIV encephalopathy. Asymptomatic children should be evaluated annually for the presence of neurological abnormalities. Symptomatic HIV infected children should be evaluated more frequently, at least twice a year. If new symptoms appear, especially those not consistent with HIV encephalopathy, then it is recommended that these patients be evaluated with the help of additional investigations such as examination of the cerebro-spinal fluid and by magnetic resonance imaging (MRI).

MATERIALS AND METHODS

It is a cross sectional study of children diagnosed as pediatric HIV infection. Two hundred patients admitted

in a tertiary care centre in Mumbai were included from Jan. 1999 to Dec. 2004.

Inclusion Criteria: Children more than 18 months of age up to 12 years of age with ELISA positive for HIV were included in the study.

Exclusion Criteria: Children below 18 months of age, diagnosed of HIV infection confirmed by positive ELISA test were excluded from the study as their HIV status cannot be confirmed by PCR due to financial constrains. The study was approved by Institutional Ethics Committee. The informed consent was obtained from Parents / Guardian before interviewing. Demographic details, clinical features at presentation with special reference to detailed neurological system, diagnostic information, management status were recorded in the protocol. The presumed mode of transmission was arrived after history and HIV serological status of parents. Results of investigations included complete blood counts, serum chemistry, cerebro spinal fluid examination including microscopy for bacteria, AFB, fungus specially Cryptococcus neoformans neuro-imaging were recorded. CD4/CD8 counts were not done due to financial constraints. All patients meriting hospitalization were admitted in the pediatric ward and treated by the concerned admitting unit. Children with tuberculosis were treated with anti-Koch's treatment. Prophylaxis with co-trimoxazole was advised according to available guidelines. The data was entered in Microsoft Office Excel Spreadsheets and analyzed by SPSS software. P value for significance was calculated.

OBSERVATIONS AND RESULTS

Clinical Presentations: the clinical presentations in HIV infection is diverse and depends on exposures to different infections. The common presenting features in our study were:

Table 1: Clinical Presentations

Sr. No.	Clinical presentations	% (n)
1	Convulsion	56.3% (27)
2	Altered Sensorium	23% (11)
3	Delayed milestones	8.3% (4)
4	Headache	6.25% (3)
5	Involuntary movements	4% (2)
6	Gait disturbances	4% (2)
7	Aphasia	2% (1)
8	Diplopia	2% (1)

Table 2: SIGNS

Sr. No.	Signs	% (n)
1	Thrush	18.7% (9)
2	Hepatomegaly	33.3% (16)
3	Splenomegaly	4% (2)
4	Hepatospenomegaly	27% (13)
5	Pallor	46% (46)
6	Lymphadenopathy	31.2% (31)
7	Focal neurological deficit	6.2% (3)
8	Neck stiffness	14.6% (7)
9	Deep tendon reflexes – Brisk	20.8% (10)
10	Deep tendon reflexes – Depressed	6.2% (3)
11	Deep tendon reflexes – Absent	2% (1)

Table 3: Neuroimaging In our study, total 11 patients were subjected to Neuro-imaging:

Sr. No.	Impression	% (n)
1	Generalized atrophy	54% (6)
2	Infarct	27% (3)
3	Tuberculoma	18% (2)
4	Encephalomalacia	9% (1)
5	Hydrocephalus	9% (1)
6	Calcification	9% (1)
7	Encephalitis	9% (1)
8	Meningeal cyst	9% (1)

Table 4: Clinical diagnosis

Sr. No.	Clinical diagnosis	%(n)
1	Convulsion ↓ Investigation	8.3% (4)
2	Tuberculous Meningitis	18.75% (9)
3	Tuberculoma	2% (1)
4	Hemiparesis	2% (1)
5	Paraparesis	2% (1)
6	Encephalopathy	14.6% (7)
7	Encephalitis	6% (3)
8	Developmental Delay	4% (2)
9	Status Epilepticus	2% (1)

OUTCOME:

Out of 48 patients with neurological manifestations, 69% (33) discharged, 23% (11) Died, 4% (2) took discharge against medical advice and 4% (2) Absconded.

Table 5: Clinical Diagnosis in Patients died: Total 11 patients Died

Sr. No.	Clinical Diagnosis	Number (n)	Percentage %
1	Tuberculous Meningitis	2	18
2	Status Epilepticus	1	9
3	Convulsion ↓ Investigation	1	9
4	Encephalopathy	1	9
5	Encephalitis	1	9

DISCUSSION

Our study included 200 patients, of these 118 were males and 82 were females. Prevalence of neurological manifestations according to our study is 24%. In one study 14% patients fulfilled the criteria for HIV encephalopathy. In one study by B. Bhandari and Suresh Goyal 9% patients presented with HIV encephalopathy[8]. In one study by Shirin Mullan, 31% patients presented with neurological complications. Age at presentation children might present at any age but incubation period with perinately acquired infection is much shorter than

incubation period in other transmission. In our study, 40% patients were between 2- 5 years, 47% between >5-10 years and 13% between 10-12 years. Sex Distribution in our study 62.5% were males and 37.5% were females. In various studies it has been shown that there is no preponderance for any sex. In our study male to female ratio was 1.6:1. In a study by Udgirkar VS, Tullu MS, Bavdekar S 75% (6) patients presented with convulsion, 50% (4) altered Sensorium, 25% (2) delayed milestones, 25% (2) with Aphasia and 12.5% (1) with gait disturbance which is in consistent with our study. Table 1. In the same study Signs were 87.5% (7) presented with Brisk deep tendon reflexes, 75% (6) patients presented with focal neurological deficit and 12.5% (1) presented with depressed Deep tendon reflexes. Table 2. Neuro-imaging 62.5% patients were presented with generalized atrophy, 37.5% patients presented with infarct and 37.5% were presented with hydrocephalus and 25% were presented with Calcification[9]. Cerebral atrophy is common in up to 85% of children with neurologic symptoms, increased ventricular size, basal ganglia calcification. Six to 10 % of patients from large clinical series have been affected by infarct both hemorrhagic and non-hemorrhagic[10]. Overall mortality in general is 11.5% but in Neurology group it is 23% i.e. double and in non-Neurology group it is 8%. So the mortality in neurology group is 3 times than in non neurology group. Being a manifestation of advanced disease, encephalopathy increases the risk of death 28 fold[11], over half of the patients succumb to the illness within 3 years of the diagnosis and the median survival rate in patients with HIV encephalopathy is about 11 months from the diagnosis[12].

CONCLUSIONS

Prevalence of neurological involvement in HIV positive pediatric patients is 24%. Prognosis is bad once there is CNS involvement. Mortality is 3 times as compared to other system involvement. Neurological manifestation can be the FIRST presentation in HIV positive children. Commonest neurological manifestations are convulsions 56% and altered Sensorium 23%. Tuberculous CNS infections mainly Tuberculous Meningitis and Tuberculoma are found in 21% patients. Generalized cerebral atrophy was commonest findings in neuro-imaging of these patients.

REFERENCES

1. Tarchieu M, Le Cheriadec J, Persoz A, Meyer L, Blanche S, Mayaux MJ: HIV – 1 related encephalopathy in infants compared with children and adults, French Pediatric HIV infection study and the SEROCO group: Neurology. 2000; 54: 1089-95.
2. Kaplan JC: Pathogenesis of infection with HIV: NEJM. 1987; 317:278.
3. Share LR: Pathology – AIDS encephalopathy: Human Pathol.1986; 17: 271.
4. Share LR: multinucleated giant cells and HTLV- III in AIDS encephalopathy: Human Pathol.1985; 16: 760.
5. Share LR: HTLV III infection in brain of children and adults with AIDS encephalopathy:Science. 1985; 227: 177.
6. Stoler MH: HTLV—III infection of CNS, A prelimenory in situ analysis: JAMA. 1986; 256: 2360.
7. Petito CK: Vacuolar myelopathy pathologically resembling subacute combined degeneration in patients with AIDS: NEJM.1985; 312: 874.
8. Bhandari B, Goyal S: Pediatric AIDS, Quality care in Pediatrics.1997; 2(1).
9. Udgirkar VS, Tullu MS, Bavdekar S: Neurological Manifestations of HIV infection:Indian Pediatrics. 2003; 40: 230-234.
10. Ram Yogev, Ellen Gould Chadwick, Acquired immunodeficiency syndrome (Human Immunodeficiency Virus). In: Richard E. Behrman, Robert m. Kligman, Hal B. Jenson(ed). Nelson Textbook of Pediatrics, 17 edn: WB Saunders; 2004.pg 1114-15.
11. Lauter M, Scott GB:Medical management of HIV disease in children:PCNA. 2000; 47: 127-153.
12. Grubman M, Oleske J: HIV infection in infants, children and adolescents. In: AIDS and other manifestations of HIV infection: Ed Wormser GP, 3rd edn, Philadelphia: Lippincott- Raven Publishers; 1998, pg. 349-371.

Source of Support: None Declared
Conflict of Interest: None Declared