

# Magnetic resonance imaging brain findings of pediatric HIV cases and its correlation with clinical and immunological stages of the disease: A study from a tertiary care center of Rajasthan

Pawan K Sulaniya<sup>1</sup>, Chandrakanta Sulaniya<sup>2</sup>, Jagdish Singh<sup>1</sup>, Kapil Garg<sup>1</sup>

From <sup>1</sup>Departments of Pediatrics, and <sup>2</sup>Obstetrics & Gynecology, SMS Medical College, Jaipur, Rajasthan, India

**Correspondence to:** Dr. Pawan K Sulaniya, Department of Pediatrics, SMS Medical College, Jaipur - 302 004, Rajasthan, India.

Phone: +91-9983225115. E-mail: [drsulaniya@gmail.com](mailto:drsulaniya@gmail.com)

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## ABSTRACT

**Objective:** To study the magnetic resonance imaging (MRI) brain findings in pediatric HIV patients and to correlate them with clinical and immunological staging. **Methods:** This study was conducted in the Department of Pediatrics of a Teaching Institute of Rajasthan. It was a prospective longitudinal study, conducted over a period of 15 months (April 2008-July 2009). Diagnosis of HIV was confirmed and classified in clinical stages and immunologic stages as per NACO guidelines. MRI brain was done in every patient. Patients with abnormal MRI brain findings were further studied and correlated with clinical findings and CD4+ cell counts. **Results:** We had total 109 HIV-positive patients registered with us; out of these, 90 were in regular follow-up. Out of these 90 patients, 16 subjects (17.78%) showed abnormal neuroimaging features on MRI brain. No case presented with abnormal MRI features in clinical Stage I and II. 4 were in clinical Stage III, and 12 were in Stage IV. No case presented with abnormal MRI in immunological Stage I and II. 5 cases (31.25%) were in immunological Stage III and 11 (68.75%) in Stage IV. Out of total 90 subjects, only 10 patients had abnormal clinical (neurological) manifestations and rested 80 patients were neurologically and developmentally normal. 6 out of 16 (37.5%) patients with abnormal MRI brain findings did not show any neurological manifestations. The most common MRI brain abnormality noted was cerebral atrophy in 7 (43.75%) cases followed by nonspecific demyelination in 31.25% cases, and ventriculomegaly, nonspecific calcification, and infarcts in 3 (18.75%) subjects each and cerebellar atrophy in 2 subjects. **Conclusions:** Our study demonstrated that abnormalities of MRI brain increases with increasing immunosuppression and advancing clinical stage. We did not found any significant correlation with age and sex with abnormal MRI brain findings. Importantly, HIV-positive children may present with only abnormal MRI brain findings without any clinical manifestation.

**Key words:** MRI brain, pediatric HIV, AIDS, Neuroimaging features

AIDS has evolved from a mysterious illness to a global pandemic which has infected tens of millions in <20 years period [1]. Every day 11,000 persons are infected with HIV globally, 1800 new pediatric cases are detected globally, and 200 new cases are detected daily in India among whom four are from Rajasthan [1-5]. In the year 2015, 86,300 new HIV cases and 10,400 new pediatric HIV cases detected and a total of 2,117,000 people are living with HIV-AIDS (PLHA) in India [6]. HIV infection in children progresses more rapidly than in adults, and some untreated children die within the first 2 years of life. This rapid progression is correlated with the higher viral burden and faster depletion of infected CD4 lymphocytes in infants and children than in adult [7,8].

HIV virus can affect each and every organ/system of the body. Central nervous system (CNS) manifestations are now recognized more frequently and as “only manifestation” of HIV/AIDS. The true incidence of CNS involvement is not known; although, it is thought to occur in the most HIV-infected children

and its incidence in children is at least 3 times more than that in adults. Neurological dysfunction in AIDS is common, occurring in as many as two-third of the children [7]. The spectrum of diseases includes HIV encephalopathy, cerebrovascular disease, progressive multifocal leukoencephalopathy (PML), opportunistic infections, and malignancies [8-13].

It is important to recognize the CNS imaging features of HIV, in particular, those of HIV encephalopathy, as this is an AIDS-defining illness. HIV encephalopathy is a common manifestation of HIV, with distinct neuroimaging features [9,10,14,15]. We planned this study to study the magnetic resonance imaging (MRI) brain findings in pediatric HIV patients and to correlate them with clinical and immunological staging.

## MATERIALS AND METHODS

This prospective longitudinal study was conducted in the Department of Pediatrics of a Teaching Institute of Rajasthan

over a period of 15 months. Approval from the Institutional Ethics Committee and written consent from the parents was obtained before recruitment. All confirmed HIV-positive children from 6 months to 18 years of age, who were registered in HIV clinic, were included in the study. Infants and children who were HIV-exposed but have an indeterminate status of HIV infection were excluded from the study. Children having pre-existing neurological abnormality not related to HIV infection such as congenital brain anomalies, CNS infections (other than HIV), perinatal asphyxia, meningitis, encephalitis, or meningoencephalitis were also excluded from the study.

Diagnosis of HIV was confirmed, and all cases were classified into clinical staging and immunologic staging as per NACO guidelines [16]. MRI brain was done in every patient. Patients with abnormal MRI brain findings were further studied and correlated with clinical findings and CD4+ cell counts. A complete history, examination, and anthropometry were recorded in the predefined pro forma. Every child was critically examined for abnormal neurological signs and confirmed by senior consultants if abnormality detected. Relevant lab investigations (e.g., cerebrospinal fluid (CSF) examination, CSF viral markers, Tuberculosis, and cultures) were also done to evaluate abnormal neurological features to confirm the diagnosis. All the data collected were analyzed using Z-test-correlation. Medcalc software was used for analysis of data.

## RESULTS

A total of 109 HIV-positive cases were registered in HIV clinic of our hospital, out of these 90 confirmed HIV-positive children regularly attending outdoor clinics or admitted in pediatric wards met the inclusion criteria. Out of these 90 patients, 16 (11 boys and 5 girls) cases (17.77%) had abnormal MRI brain findings and remaining 74 (52 boys and 22 girls) cases had normal MRI brain. All children with abnormal neuroclinical features were also having abnormal neuroimaging features (10/10). Unexpectedly, 6 out of 80 (7.56%) neuroclinically normal cases of HIV were having abnormal neuroimaging findings. This indicates the subclinical effect of HIV virus on brain (Table 1).

Out of total 90 subjects, only 10 patients were neuroclinically abnormal, rest 80 were neurologically and developmentally normal. All 10 cases who presented with abnormal neurologic features showed abnormal MRI brain features also. As per NACO guidelines, all cases who had presented with CNS manifestation were included in clinical Stage IV. Children with CNS related opportunistic infections (3 cases) were excluded from this study; hence, HIV disease related neurological manifestations were only taken into consideration. One important finding noticed was that there were 6 subjects (7.5% of total 80) who had shown abnormal MRI brain changes but no neuroclinical manifestations. Regarding clinical stage wise distribution of cases with abnormal MRI brain features, no case presented with abnormal MRI features in clinical Stage I and II while 4 cases were in Stage III and 12 were in Stage IV. Out of these, 12 were male, and 4

were female children (Table 2). On immunological stage wise distribution, no case presented with abnormal MRI brain features in “no immunosuppression” and “mild immunosuppression.” 5 cases (31.25%) were in “advance-immunosuppression” and 11 (68.75%) were in “severe-immunosuppression” as per NACO guidelines (Table 2) [16].

## DISCUSSIONS

In <3 decades, HIV infection has become a global problem. Children also have not been left unaffected. Neurological dysfunction in AIDS is common, occurring in as many as 80% of the children [7,15,16]. The spectrum of diseases includes HIV encephalopathy, cerebrovascular disease, PML, opportunistic infections, and malignancies. Opportunistic CNS infections are extremely rare in pediatric AIDS patients compared with adults [16-21].

The incidence of CNS involvement in perinatally infected children is 50-90% in developing countries but lower in developed countries, with the median onset at 19 months of age. This may range from subtle developmental delay to progressive encephalopathy with loss or plateau of developmental milestones, cognitive deterioration, impaired brain growth resulting in acquired microcephaly, and symmetric motor dysfunction. Encephalopathy may be the initial manifestation of the disease or may present much later when severe immune suppression occurs. With progression, marked apathy, spasticity, hyperreflexia, and gait disturbance may occur, as well as loss of language, oral, fine, and/or gross motor skills. The encephalopathy may progress intermittently, with periods of deterioration followed by transiently stable plateaus. Older children may exhibit behavioral problems and learning disabilities. Associated abnormalities identified by neuroimaging techniques include cerebral atrophy in up to 85% of the children with neurologic symptoms, increased ventricular size, basal ganglia calcifications, and, less frequently leukomalacia [7,8,14].

**Table 1: Various neuroclinical features in study subjects**

Neuroclinical findings	Sex		Total (16)
	Male n=11 (%)	Female n=05 (%)	
Brisk DTR	4 (36.35)	3 (60)	7
Extensor plantar	4 (36.35)	3 (60)	7
Microcephaly	2 (18.17)	3 (60)	5
Altered sensorium	1 (9.59)	3 (60)	4
Aphasia	1 (9.59)	3 (60)	4
Altered behavior	3 (27.76)	1 (20)	4
Focal neurological deficit	1 (9.59)	2 (40)	3
Developmental delay	2 (27.17)	1 (20)	3
Hemiplegia	0	2 (40)	2
Visual disturbance	0	1 (20)	1
Cerebellar dysfunction	0	1 (20)	1
Quadriplegia	1 (9.59)	0	1
No neurologic abnormality	5	1	6

DTR: Deep tendon reflexes

Table 2: MRI findings in different clinical and immunological stages

MRI findings	Clinical stage		Immunological stage		Total n=16
	3 (%)	4 (%)	Advance n=5 (%)	Severe n=11 (%)	
	n=4	n=12			
Cerebral atrophy	3 (9.09)	4 (17.39)	3 (60)	4 (36)	7
Nonspecific demyelination	1 (3.03)	4 (17.39)	1 (20)	4 (36)	5
Cortical atrophy	0	4 (17.39)	2 (40)	2 (18)	4
Ventriculomegaly	1 (3.03)	2 (8.69)	2 (40)	1 (9)	3
Nonspecific calcification	0	3 (13.04)	1 (20)	2 (18)	3
Infarct	0	3 (13.04)	3 (60)	0	3
Cerebellar atrophy	0	2 (8.69)	0	2 (18)	2

MRI: Magnetic resonance imaging

There is no pathognomonic radiologic appearance for any of the CNS disorders seen in patients with advanced HIV disease; however, several patterns are clinically helpful. Widespread white matter abnormalities without contrast enhancement or mass effect suggest either PML or HIV encephalitis. Enlarged ventricles are usually the result of atrophy (hydrocephalus ex vacuo) [14,17,18]. HIV-infected children in our study showed a variety of MRI brain changes. Out of 90 cases, 16 (17.24%) showed MRI changes and the most common abnormal feature noted was cerebral atrophy. However, Kirck and Andranikou [14] noticed that up to 76% of asymptomatic HIV-positive children are found to have at least one abnormality on computed tomography (CT). Chamberlain et al. found that 40% of the HIV-positive children have abnormal CT or MRI scans by the age of 1 year [22].

The most common findings on imaging according to the study of Kirck and Andranikou were cerebral atrophy and basal ganglia calcifications. White matter changes related to HIV itself are less common but occur more frequently than PML [14]. Generalized atrophy is seen in up to 90% of the HIV-positive children. Central atrophy is more prominent than cortical atrophy (which is usually in the frontal lobes), because of the predilection of HIV for the basal ganglia, causing necrosis [8]. Chamberlain et al. also noticed in their study that the most common abnormal neuroimaging finding was cerebral atrophy [22]. Gavin et al. found 68% of HIV-positive symptomatic children to have cerebral atrophy and 78% to have ventriculomegaly [23].

Udgirkar et al. noticed cerebral atrophy as the most common (62.24%) feature of MRI brain in their study. Encephalopathy manifests as cerebral atrophy and leukoencephalopathy seen radiologically as prominent surface markings with ventriculomegaly and signal abnormalities on MRI, respectively. Cerebral atrophy and basal ganglia calcification remain the most frequent positive findings in neuroimaging [8].

There is 100% correlation between neurological findings and MRI brain abnormality, i.e., all cases with clinical manifestations had shown definite MRI changes. The most common neurological manifestations noted were brisk deep tendon reflexes (DTR) and extensor planters in 70% cases. In a study by Udgirkar et al. [8], the most common manifestation was brisk DTR and microcephaly (87.5%), convulsions and FND in 75% cases, extensor planters in 62.5% cases, altered sensorium in 50%, followed by quadriplegia

in 50% cases. This study supports the findings of our study. The most common MRI brain features in their study was cerebral atrophy in 5 (62.5%), ventricular dilatation in 3 (37.5%), infarct in 3 (37.5%), basal ganglia calcification in 2 (25%), and cerebellar atrophy in 1 (12.5%) case. Basal ganglia calcification is unique to vertically infected children, is one of the most frequent CNS imaging findings in pediatric AIDS. The prevalence varies from 19% to 53% [12]. Our study has some limitations and due to a small number of cases significance of results is needed to be confirmed further. Multicentric, large scale studies can only give statistically significant results.

## CONCLUSIONS

The incidence of CNS involvement is still not known, in our study, was 17.45%. The chances of having MRI brain changes increases as the patient progress to higher clinical stages and decreasing CD4 cell count. Our study demonstrated that CNS abnormality can also present as “only” abnormal MRI brain findings. However, it can be a possibility that these children may present neurological manifestations later on.

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