محلة النبلين الطبية

Pattern of neurological disorders in pediatric Sudanese patients admitted to a tertiary hospital/ Khartoum; A retrospective study: January 2018 to December 2020

Asmaa Babeker Elshikh Elagib (1), Samira Ahmed Mustafa (2)

- (1) Sudan Medical Specialization Board (SMSB)
- (2) Al Neelain University / Jaafar Ibn Auf Hospital

# **Ethical Considerations:**

- The authors report no conflicts of interest in their work
- Ethical approval was obtained from Sudan Medical Specialization Board, Ministry Of Heath research department, Jaafar Ibn Auf hospital administrative authority

#### **Abstract:**

A retrospective study of records of 301 pediatric patients, one month to < 18 years of age, who presented to Jaafar Ibn Auf hospital with neurological disorders over 2 years from January 2018 up to December 2019. Male to female ratio was 1.57:1. The main objective of the study was to determine the pattern of neurological disorders in these children. Data was collected from records of patients over 6 weeks using self-structured coded data sheet. Data was analyzed using Statistical Package for Social Sciences (version 24). Results revealed the following pattern of neurological disorders: seizures disorders accounted for 92 cases (30.6%), This was followed in descending order of frequency by: cerebral palsy 57 cases (18.9%), central nervous system demyelination 38 cases

(12.6%), Guillain barre' syndrome 29 cases (9.6%), cerebrovascular disorders 15 cases (5%), CNS infections 15 cases (5%), Autoimmune encephalitis 9 cases (3%), congenital disorders 7 cases (2.3%), Brain tumors 6 cases (2%), Leukodystrophies 3 cases (1%), Muscular dystrophies 3 cases (1%), Nerve injuries 2 cases (0.7), and a variety of miscellaneous cases accounted for the rest. The main presenting features were seizure disorders in 61.3% of cases and generalized tonic/clonic seizures were the main type of seizures (53.5%), seizures with fever (51.2 %), seizures with developmental delay (29.2%). Routine and specific investigations were requested. Management included mainly the use of Anti Epileptic Drugs (AEDs), antibiotics and immune therapy, in addition to physiotherapy and neurosurgery in a minority of patients. Pattern of neurological disorders is found to be mostly similar to pattern found in previous international studies and the few documented local studies. No significant association was found between Diagnosis and parental consanguinity, but there was as significant statistical association between age and diagnosis. Prospective research work is recommended to determine the exact data regarding pattern, and to determine the true outcome regarding disability and mortality to plan for future services.

## **INTRODUCTION**

Neurological conditions in children contribute significantly to the burden of disease globally, with a high impact on morbidity and mortality <sup>(1)</sup>. The spectrum of diseases ranges from non-communicable disorders like stroke and neurodegenerative disorders to central nervous system infections <sup>(2)</sup>. Neurological disorders are defined as any disorder of the nervous system which can be Structural, biochemical or electrical abnormalities in the brain, spinal cord or peripheral nerves. which can result in a range of symptoms like paralysis, muscle weakness, poor coordination, loss of sensation, seizures, confusion, pain and altered levels of consciousness <sup>(3)</sup>. Classifying and managing these wide range of problem complexes can be problematic requiring highly specialized medical care, great use of ICU services and high consumption of resources <sup>(3)</sup>. Neurological disorders account for more than 20% of the world's disease burden with the majority of affected people living in Africa. The factors that are producing this increased burden include malnutrition, adverse perinatal conditions, malaria,

acquired immune deficiency syndrome (AIDS; human Immuno-deficiency virus HIV/AIDS), meningoencephalitis, demographic transitions, and persistent regional conflicts (4)

Neurological disorders are identified by the World Health Organization (WHO) as one of the greatest threats to global public health. WHO estimates that up to 7% of the population living in developing countries have moderate to severe disability <sup>(5)</sup>.

Neurological disorders were ranked as the leading cause of disability in 2015 and were the second leading cause of death, causing 16.8% of global mortality (6). Neurological disorders contribute substantially to morbidity and mortality in children in resource-limited settings, though there is sparse data on the precise epidemiology of common neurologic disorders in these settings <sup>6)</sup>. Over the past 25 years, there has been a relative decrease in the contribution of communicable diseases to neurologic disorders in children, but the absolute contribution of these disorders in resource-limited settings remains high <sup>(6)</sup>. In a study of a tertiary children's hospital in the United Kingdom, Ramnarayan, et al. found that the primary diagnosis at death among hospitalized children was neurological in 7.0% of wards' patients and 9.3% of intensive care unit (ICU) patients. However, incidence and results by specific diagnosis were not investigated (7). In a United States tertiary pediatric ICU (PICU), Au et al. found that, regardless of primary diagnosis, neurological diagnoses were the proximate cause of death in the majority of patients (8). In the recently published International Survey of Critically Ill Children with Acute Neurologic Insults, the most common etiologies for ICU admission among children varied by region. In lower resource settings the most common etiologies were infectious, whereas in higher resource settings cardiac arrest was the most common reason for admission (9).

Most of the burden of neurological disorders occurs in the most populous parts of the world; namely Asia and Africa, There are important regional differences in the under 5 year olds. Prematurity and neonatal encephalopathy have a higher prevalence of Disability Adjusted Life Years (DALYs) per 100,000 in South Asia, compared to other regions of the world, including sub-Saharan Africa. In age group 5-14years meningitis has the largest burden in sub-Saharan Africa; while in South Asia, encephalitis is greater (mainly due to Japanese encephalitis) (10).

Recognition of the main causes of neurologic diseases in children in the developing world is important as there is often opportunity for intervention and improvement in many circumstances. Cerebral palsy, for example, is most commonly associated with preterm birth in the United States and Europe. However in many Low and Middle Income Countries(LMICs), birth asphyxia, infection, and kernicterus are more common etiologies (11, 12). Infections of the central nervous system (CNS) are relatively more common causes of acute seizures in resource-limited settings, with delay in treatment leading to prolonged seizures and higher rates of morbidity and mortality (13,14). In one study preventable infectious diseases were found to be the major causes of emergency neurologic morbidity and mortality among children five years of age and under. In that study the most common pediatric neurologic morbidities were febrile convulsion (35.1%), cerebral malaria (28.0%) and meningitis (27.0%) (15).

Considered as a major cause of disability, WHO estimated the prevalence rate of disability from neurological disorder in sub-Saharan Africa as 7.4% in Tanzania, 7.2% in Uganda, but was lower 4.6% in Kenya, and 4.7% in Rwanda (16, 17,18).

Due to late presentation and unavailability of certain diagnostic facilities in resource-limited countries including Sudan, neurology services are very challenging with a significant increase in morbidity and mortality<sup>(19)</sup>.

Diagnostic technology for neurologic disorders, such as brain imaging and electrophysiology, is often limited in Low and Middle Income Countries (LMICs) (20). Even when the technology itself exists, costs may be out of reach for most patients, and machines tend to be concentrated in a few cities and thus are not available to most patients living in rural areas (21).

The treatment period may be so long taking months to years, making room for a high rate of default from follow-up <sup>(22)</sup>. Availability of neurologic medications is even more sparse, with a few medications for neurologic disorders listed as essential medicines on the WHO model list <sup>(23)</sup>.

There is a general paucity of pediatric neurologists globally, with this being even more pronounced in low-income countries, with an average of 0.39 per 100,000 child neurologists in high- income countries versus 0.002 per 100,000 in low-income countries (24,25). Not only there are limited number

of children neurologists available, but also their geographic distribution within countries is and additional barriers to care <sup>(11)</sup>. The vast majority of all neurologists in resource-limited settings are concentrated in capital cities<sup>(26)</sup>.

Studies on the pattern of neurological disorders in children are valuable in understanding trends, characteristics and outcome of these conditions. Such studies might disclose shortage and inadequacy of resources including pediatric neurologists. Knowing the pattern and outcome might help planning, stating priorities and improving future services by the concerned health care personnel.

## Methodology

The data was collected from patients' records using self-designed structured coded data-sheet. Data was collected by the researcher over 6 weeks. The data focused mainly on the demographic characteristics, presenting symptoms and signs, diagnosis investigations and essential treatment. Total coverage was applied to cover all patients' records which fulfilled the study criteria, within the specified period. Total number of records were 301.

Data was analyzed using Statistical Package for Social Science (SPSS) version 24.

## **RESULTS**

In this study a total number of 301 patients were admitted to neurological unit at Gaffar Ibn Auf hospital during the period from January 2018 to December 2019. This number represents 9% of the total admissions to the hospital at that period.184 (61.1%) of the patients were males and 117(38.9%) were females. Male: Female ratio was 1.57: 1.

**Demographic data**: Children in the age group 1-5 years accounted for 120 cases (39.9%). Age group 6-12 years accounted for 104 cases (34.6%). Enrolled children from 1 month to below 1 year accounted for 38 cases (12.6 %) and age group 13 -17 years accounted for 39 cases (13%). Most patients were from Khartoum state (40.5%). Other states are represented to a lesser extent; Gazeira state (11.3%), kordofan state (9.6%), North state (8.3%), Darfur state (8%), White Nile state (6%),

River Nile (4.3%), kassala (4.3%), Sinnar (3%) Port-Sudan (1.7%), Blue Nile (1.7%) and only (1.3%) are from AL Gadarif.

Most patients (89%) were of moderate socioeconomic status, (10%) were of low socioeconomic status and (0.3%) were of high socioeconomic status.

Regarding the pattern of neurological disorders of these patients: seizures disorder constituted the largest group which accounted for 92 cases (30.6%), This was followed in descending order of frequency by: cerebral palsy which accounted for 57 cases (18.9%), central nervous system demyelination 38 cases (12.6), Guillain barre syndrome 29 cases (9.6%), cerebrovascular disorders 15 cases (5%), CNS infections 15 cases (5%), Autoimmune encephalitis 9 cases (3%), congenital disorder 7 cases (2.3%), Brain tumors 6 cases (2%), Leukodystrophies 3 cases (1%), Muscular dystrophies 3 cases (1%), Nerve injuries 2 cases (0.7), and a miscellaneous group which accounted for 23 cases (7.6%).

(figure 1).

Family history of related condition were found in only(10.6%) of cases though, parental consanguinity was positive in (64%) of cases.

The study revealed no significant association between neurological diagnoses and parental consanguinity; using Chi square test (P- value 0.984) (table 5).

In this study it was found that the most common **presenting symptom** of admitted children was seizures (61.3%); and the common type of seizures was generalized tonic clonic (53.5%), focal (4.6%), myoclonic (1.7%), Salam attack (Infantile spasm) (1.7%) and Atonic seizure (0.3%). The second common presenting symptom was fever (51.2%), followed in descending order by developmental delay (29.2%), weakness (22.9%), headache (6.6%), abnormal movement (5%), developmental regression (4%), visual disturbance (3.3%), aphasia (2.3%), Decreased level of consciousness (1.3%), abnormal behavior (0.6%), head lag (0.6%), urine retention (0.6%), and sensory disturbance (0.3%). (table1).

**Investigations** done for patients enrolled in the study were the routine investigations done for all admitted patient in any unit in the hospital like: complete blood count, renal function tests, liver function tests, urine and stool analysis, blood film for Malaria parasites, Chest X-ray, cultures and microbiology ...etc. Specific investigations done for patients with neurological disorders included:

Neuroimaging studies performed for children enrolled in the study included: MRI Brain was the most commonly requested (52.5%) of which (23.6%) were normal, (7%) showed Brain atrophy, Cerebral infraction was seen in (3.7%), Hypoxic ischemic encephalopathy in (3.3%) and other finding represent (12.7%). Next common neuroimaging study requested was CT Brain (19.9%), and the reported findings were Brain atrophy (7.6%), Hydrocephalus (1.7%), and other finding (3.3%). (.7.3%) of the CT Bran were normal. MRI spine was the third common imaging requested (9.3%) and the reported findings were: Transverse myelitis (5%), Normal (3.7%), and other disorders (0.6%). MRA/MRV were requested in (2.7%) of admissions of which (1.3%) were normal and (1.4%) were abnormal. Cranial ultrasound was done for 2 patients (0.7%) and the result show cerebral infraction in one and hydrocephalus in the other (table 2).

*Neurophysiology*: the most common study requested was EEG (34.2%) and the report was normal in (2.3%) of cases, generalized epileptiform discharge (24.2%), Hypsarrhythmia (2%) and other finding (6%). Nerve conduction study (NCV)was done in (11.3%) and reported as: acute axonal polyneuropathy (9%), normal (1.3%), and other (1%), Visual Evoked Potential was done in (3.6%) of admissions of which (3.3%) was reported as abnormal. Electromyogram (EMG) was done for (1.3%) of patients of which (0.7%) were normal. (table 3).

Neurochemistry: CSF analysis results and Enzymes assay reports: non was recorded

Genetic studies: no results were recorded

Regarding **treatment** of the study patients only (4%) of patients needed *Intensive care*. *Physiotherapy* was recommended in (45.8%) of patients.

*Drug treatment*: Anti -Epileptic Drugs (AEDs) were used in (62.1%) of studied patients, Sodium Valproate being the most common drug used (28.2%), followed by Levetiracetam (20.9%),

Benzodiazepines (18.6%) phenobarbital (13%) and other antiepileptic (27.2%). Antibiotics were used in (35.9) of admitted children; Ceftriaxone being the most commonly used (29.9%), followed by vancomycin (17.9%), and then other antibiotics (9.3%). Steroids were used in (29.2%) of admitted patients, and Intravenous immunoglobulin (IVIG) in (26.2%) of studied patients. (table 4).

The study revealed significant association between age and diagnosis, using Chi square test (p-value 0.000). (table 6).

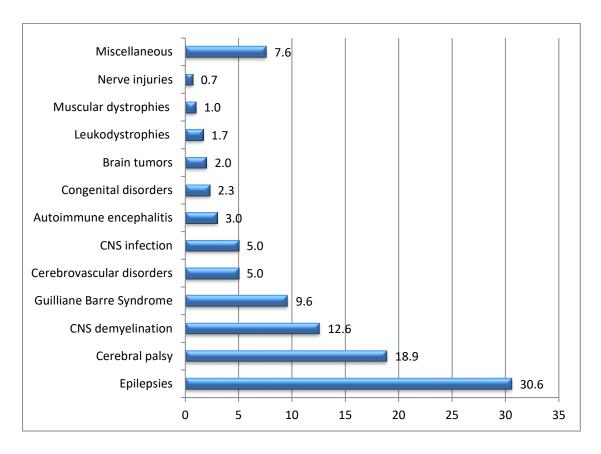


Figure 1: Spectrum of neurological disorders of study population admitted to Gaffar Ibn-Auf Pediatric Hospital during January 2018 to December 2019 (n=301)

Table 1: Presenting symptoms of neurological disorders of children admitted to Gaffar Ibn-Auf Pediatric Hospital during January 2018 to December 2019 (n=301)

Symptom	Subgroups	Frequency	Percentage
Fever	Yes	154	51.2
	No	147	48.8
Seizure	Yes	185	61.3
	No	117	38.9
Seizure type	GTC	161	53.8
	Focal	13	4.6
	Myoclonic	5	1.7
	Alsalm spasm	5	1.7
	Atonic	1	0.3
Developmental delay	Yes	88	29.2
	No	213	70.8
Sensory disturbance	Yes	1	0.3
	No	300	99.7
Headache	Yes	20	6.6
	No	281	93.4

Weakness	Yes	69	22.9
	No	232	77.1
Abnormal movement	Yes	15	5.0
	No	286	95.0
Others	Developmental regression	12	4.0
	Visual disturbance	10	3.3
	Aphasia	7	2.3
	Decreased consciousness	4	1.3
	Abnormal behavior	2	0.6
	Head lag	2	0.6
	Urine retention	2	0.6

Table 2: Neuro-imaging used for diagnosed neurological disorders of children admitted to Gaffar Ibn-Auf Pediatric Hospital during January 2018 to December 2019 (n=301)

Imaging	Findings	Frequency	Percentage
Cranial		2	0.7
ultrasound			
	Cerebral infraction	1	0.3
	Hydrocephalus	1	0.3
CT Brain		60	19.9
	Brain atrophy	23	7.6

	Normal	22	7.3
	Hydrocephalus	5	1.7
	Cerebral infraction	4	1.3
	Brain tumor	3	1.0
	Cerebral calcifications	1	0.3
	Cerebral hemorrhage	1	0.3
	Hypoxic ischemic encephalopathy	1	0.3
MRI Brain		158	52.5
	Normal	71	23.6
	Brain atrophy	21	7.0
	Cerebral infraction	11	3.7
	Hypoxic ischemic encephalopathy	10	3.3
	Acute disseminated encephalomyelitis	7	2.3
	Brain tumor	6	2.0
	Agenesis of corpus callosum	4	1.3
	Cerebral ischemia	4	1.3
	Encephalitis	4	1.3
	White matter disease	4	1.3
	Hydrocephalus	3	1.0
	Periventricular leukomalacia	3	1.0

Multiple sclerosis	2	0.7
Brain mass	1	0.3
Encephalomalacia	1	0.3
Gliosis	1	0.3
Hemimesencephaly	1	0.3
Neuromyelitis optica	1	0.3
Posterior reversible encephalopathy syndrome	1	0.3
Sturg Weber syndrome	1	0.3
Tolosa hunt syndrome	1	0.3

CT, Computerized tomography

Table 2 (Cont.): Neuro-imaging used to diagnose neurological disorders of children admitted to Gaffar Ibn-Auf Pediatric Hospital during January 2018 to December 2019 (n=301)

Imaging	Findings	Frequency	Percentage
MRI Spine		28	9.3
	Transverse myelitis	15	5.0
	Normal	11	3.7
	Sacrococcgeal dysgenesis	1	0.3
	Spinal Schistosoma	1	0.3
MRA/MRV		8	2.7

Normal	4	1.3
Brain tumor	1	0.3
Cerebral infraction	1	0.3
Gliosis	1	0.3
Narrowing of internal carotid artery	1	0.3

MRI, Magnetic resonance imaging; MRI, Magnetic resonance imaging; MRA, Magnetic Resonance Angiography; MRV, Magnetic Resonance Venography

Table 3: Neuro-physiology studies used to diagnose neurological disorders of children admitted to Gaffar Ibn-Auf Pediatric Hospital during January 2018 to December 2019 (n=301

EEG		103	34.2
	Generalized epileptiform discharge	73	24.2
	Normal	7	2.3
	Hypsarrhythmia	6	2.0
	Myoclonic epilepsy	4	1.3
	Focal seizure discharge	4	1.3
	Focal with generalization	4	1.3
	Left frontocentral spike and slow wave	1	0.3
	Multifocal seizure	1	0.3
	Subacute sclerosing panencephalitis	1	0.3
	Encephalitis	1	0.3

	Encephalopathy	1	0.3
Nerve conduction study		34	11.3
study	Acute axonal polyneuropathy	25	9.0
	Normal	4	1.3
	Conginetal hypomyelinism	1	0.3
	Hereditary sensory motor neuropathy	1	0.3
	Severe bilateral peroneal motor axonal neuropathy	1	0.3
EMG		4	1.3
	Normal	2	0.7
	Duchenne muscular dystrophy	1	0.3
	Muscular dystrophy	1	0.3
VEP		11	3.6
	Prolonged P100	6	2.0
	Normal	1	0.3
	Conduction dysfunction of both eyes	2	0.6
	Optic nerve axonal neuropathy	1	0.3
	Primary optic atrophy	1	0.3

EEG, electroencephalogram; EMG, Electromyography; VEP, Visual Evoked Potential

Table 4: Treatment of neurological disorders received by the children admitted to Gaffar Ibn-Auf Pediatric Hospital during January 2018 to December 2019 (n=301)

Treatment	Subgroups	Frequency	Percentage
		131	43.5
		88	39.2
		79	26.2
		138	45,8
		130	45,0
	Baclofen, Aspirin, Anti-hypertensives,	50	16.6
	plasmapheresis, Mannitol,and others		
	in deceasing frequency		

## **Discussion**

9% of admissions to Jaffar Ibn Auf hospital during the study period were admitted to the neurological unit. This is similar the result reported by Moreau (2013) in USA whose study showed that (10.7%) of children were admitted with neurological disorders (27).

Children in the age group (1-5years) were the most commonly admitted children, representing 39.9% of neurological admissions, with male predominance (male 61.1% and females 38.9%). Male to female ratio was 1.57: 1. This is consistent with the result of a study reported by Frank-Briggs (2009), in Nigeria in which The age group (1-5 years) accounted for the most affected age group constituting 87.7%, and male: female ratio of 1.5:1 (28). It is also similar to a study done by Mohie El –Din T. Mohamed in Egypt (2015) which found male predominance; with male to female ratio 1.26: 1 (29). It was found that (40.5%) of admissions were from Khartoum state (the capital) and this is similar to result found by Inaam N Mohamed et al. (2015) in outpatient clinic in Sudan in which (65%) of patients were from Khartoum (30).

In the current study, epilepsy/seizure disorders were the most common neurological disorders, affecting (30.6%), of patients. This result is similar to result reported by Moreau (2013) in which seizures account for (53.9%), and also to result obtained Inaam N Mohamed et al. (2015) in which childhood epilepsies accounted for (47.8%) (30). Epilepsy/seizure disorders were also shown by an Egyptian study (2015 to be the most common neurological disorder, occurring in (30.22%) of patients (29), and a Nigerian study (2009) in which most frequent Pediatric neurological disorders were epilepsy (24.6%) (28).

Cerebral palsy was the second most common neurological conditions in this study representing 18.9%%. This high percentage may reflect the fact that prenatal and perinatal medical care in our country still need to be developed. This result is in agreement with the previous studies done by Mohie El –Din T. Mohamed (2015) who found CP to represent (19.4%) <sup>(29)</sup> and also by Inaam N Mohamed et al. (2015) who found CP to represent (19.1%) <sup>(30)</sup>. On the other hand, Okafor and Lagunju (2009), reported that cerebral palsy was the second commonest neurological disorder but with higher percentage 36%, <sup>(31)</sup>.

Congenital anomalies were found to be (2.3%), and this is inconsistent with the result obtained by Inaam N Mohamed et al. (2015) who reported that congenital anomalies represented  $(6.2\%)^{(30)}$ , This may be explained by the limited number of admissions or by patients being or referred to general units or other specialties.

In the current study, the most common presenting symptom of admitted children was seizures' disorder (61.3%), this is similar to the finding of Moreau et al, who found that in (53.9%) of patients the presenting symptom is a seizures (27).

Generalized tonic/clonic seizures (GTCS) was the predominant seizure sub-type on the current study as it constituted (3.5%) of patients. This finding is consistent with results reported by Okafor and Lagunju, Frank and Alikor, and Mohie El –Din T. Mohamed, and is inconsistent with the finding of Kotsopoulos et al., who found that focal seizures are more common in their studied children than GTCS (31,28,29,32). This difference may be explained by that focal seizures may remain unnoticed and that patients seek medical attention only when they develop secondary generalization or their focal seizures evolved to generalized tonic/clonic seizure.

Regarding neurological conditions who needed PICU care were (4%). This is inconsistent with the findings of Moreau et al, who found that (30.6%) of their admissions needed intensive care <sup>(27)</sup>, and also inconsistent with the general knowledge that PICU admission among patients with neurological disorders are more than other subspecialties. This could be explained by the limited capacity and limited facilities of PICU in our hospital and so most patients needing intensive care are treated in the ward.

As far as investigations of neurological disorders are concerned, most necessary investigations were performed but no recorded were found regarding results of CSF analysis, genetic studies or enzyme assays. This may be explained by incompleteness of records or by the fact that most patients with CNS infections are seen in general pediatric units or by unavailability or unaffordability of these specific investigations.

Regarding drug treatment antiepileptic drugs(AEDs) were the most commonly used, and among these sodium valproate was the commonest constituting (28.2%) of the drugs used; this was similar

to the result obtained by Badrelddin A. Abass et al (2013) who reported that his result is expected as sodium valproate is commonly used in most types of seizure disorders <sup>(33)</sup>.

Long term outcome was difficult to assess in our study because of high rate of patients' default from follow-up and incompleteness of records, but as mentioned cerebral palsy was the second leading cause of neurological problems, and 45.8 % of admissions required physiotherapy.

From the results of the study it was **concluded** that

The pattern of neurological disorders was found to be mostly similar to the pattern found in previous studies both local and international. Seizures disorders were the most common followed by cerebral palsy.

No statistical association was found between Diagnosis and parental consanguinity, but there is significant statistical association between age and diagnosis.

To ensure completeness of records computerized records are **recommended** to keep all the patients' data in one place.

Prospective research work is recommended to determine the exact pattern and the true outcome regarding disability and mortality of pediatric neurological diseases to plan for future services.

The high frequency of cerebral palsy makes research work regarding health education, preventive measures and advanced neonatal care a priority to facilitate early diagnosis and proper management to prevent complications.

In view of the serious consequences of pediatric neurological disorders, and to avoid delay in diagnosis and treatment, pediatric neurologists should be available in general hospitals especially in our country where specialized neurological hospitals are lacking.

It is recommended that neurology unites in tertiary hospitals should be properly equipped, with high facilities and appropriate resources and should have highly qualified and experienced staff.

Specialization related to all aspects of pediatric neurology: intensive care, nursing, physiotherapy, laboratory, imaging and also collaboration with other specialties like neurosurgery should be encouraged

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