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ORIGINAL ARTICLE

Radiological Characteristics of Thalamic Lesions in children and their implications: an in-depth Cross-Sectional Investigation in a Tertiary Care Government Facility

MARYA HAMEED[1&2], MUHAMMAD FAZALHUSSAIN QURESHI[3], SAMRA SALMAN[3]
[1]*Head of Radiology Department, National Institute of Child Health (NICH), Karachi, Pakistan.*
[2]*Assistant Professor, Department of Radiology, Jinnah Sindh Medical University, Karachi, Pakistan.*
[3]*Department of Radiology, National Institute of Child Health (NICH), Karachi, Pakistan.*
Correspondence to Dr. Muhammad Fazal Hussain Qureshi, Email: fazalhqureshi22@gmail.com, Cell: +923001482644

ABSTRACT

Background: The thalamus' main activities are sensory processing, motor control, and consciousness regulation.
Aim: To identify connections between radiological characteristics and thalamic damage, which will help develop early diagnostic methods and improve thalamic lesion treatment.
Methods: A retrospective cross-sectional single-center study was performed in the Radiology department of the National Institute of Child Health, Karachi, Pakistan. Data was collected over 2.5 years. Non-probability consecutive sampling was utilized to acquire data. The study comprised 197 patients who met the inclusion criteria. A validated questionnaire was used to collect data regarding thalamic lesion symptoms and MRI features.
Results: The mean child age was 8.4 years, with a 3-year standard deviation. The patient population was 65.2% male and 34.3% female. The difference between the onset of symptoms and diagnosis of disease was two months on average. 45% of children experienced developmental delays. Among the most prevalent diagnoses were acute ischemia infarction, posterior reversible encephalopathy syndrome, Canavan disease, acute necrotizing encephalitis, and neurofibromatosis. MRI characteristics of thalamic lesions significantly correlated with neurological symptoms. In contrast to etiologies, MRI findings were significantly related. The Majority of the cases were bilateral, having significant results with perilesional edema, signal dropout, diffusion restriction, extra thalamic extension, basal ganglia involvement, and vascular involvement.
Conclusion: This article examines the correlation between clinical symptoms, possible causes of thalamic lesions, and imaging findings. Several large-scale investigations are needed to further settle on a clear association between MRI features and thalamic lesions in the pediatric population, as there was ample significance between the variables stated above.
Keywords: Thalamus, magnetic resonance imaging, tumors, children

INTRODUCTION

The thalamus is a crucial part of the brain that serves several essential functions, primarily related to sensory processing, motor control, and regulation of consciousness. It acts as a relay center and plays a vital role in the communication between different brain regions[1]. Some of the critical functions of the thalamus include Sensory Relay, Motor Control, Pain Perception, Regulation of Consciousness, Memory and Learning, Emotional Processing, Integration of Information, Regulation of Sensory Perception, and Relay of Motor Feedback[2].

Bilateral damage to the thalamus in children can lead to profound neurological and developmental implications. Given the thalamus' vital role in transmitting sensory inputs, regulating motor functions, and supporting overall brain activity, any impairment can have far-reaching effects. These lesions can stem from diverse factors like traumatic incidents, vascular problems, infections, tumors, metabolic irregularities, and genetic predispositions[3]. The impact of such lesions, be they unilateral or bilateral, can vary depending on factors such as specific diagnosis, lesion location, and the extent of damage. The consequences encompass sensory deficits and motor dysfunction and extend to cognitive challenges, intellectual hindrances, and developmental delays[4].

While a few case reports and literature reviews from both national and international researchers have touched upon this subject[5-7], there remains a noticeable absence of comprehensive data that could facilitate the identification of radiological connections among diverse causes of thalamic lesions and their consequential impact on daily life and functioning. Imaging has a crucial role in detecting the pattern of thalamic abnormalities but also has implications in therapies and predicted neurodevelopmental outcomes. Ultrasound (US) has emerged as a powerful screening tool for evaluatingneonates with suspected thalamic lesions. CT is often the first diagnostic imaging modality because of its easy availability. CT also answers us to evaluate nonspecific neurologic symptomsdepicting associated acute blood or calcification. However, contrast-enhanced CT does not add much advantage to imaging, and MRI with contrast administration is preferred and the modality of choice. Also, the radiation burden that CT carries can be minimized by eliminating the contrast-enhanced scan and performing an MRI instead for further evaluation. Through this paper, we will evaluate varying imaging patterns of pathologies involving thalamus, including thalamic expansion, perilesional edema, signal dropout on SWI (calcification or bleed), Diffusion Restriction, Extra Thalamic Extension, Basal Ganglia Involvement, Hydrocephalus, Vascular Involvement and Other nonspecific Indicators that can predict the future outcomes of the patient and also act as a future snapshot for the clinicians and junior radiologists.

This research seeks to establish correlations between the radiological attributes of various conditions and the extent of resulting damage, eventually serving as crucial reference material for formulating large data model sets for generative artificial intelligence models, early diagnostic protocols and enhancing the treatment strategies for thalamic lesions.

METHODS

Study Design and Subjects*:* A retrospective cross-sectional single-center survey was performed in the Radiology department of the National Institute of Child Health (NICH), Karachi and data

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was collected from a period between 1 October 2021 and 30 July 2023. The institutional Ethical Review Committee of the Hospital exempted the study.A probability consecutive sampling technique was used to collect data.

Inclusion and Exclusion Criteria: All confirmed cases of thalamic lesions reported in the Radiology Department were eligible for participation in the study. Data of both acquired (e.g., stroke, infection) and congenital (e.g., congenital malformations) cases was included of either gender and aged between 5 years to 16 years. A totalof 197 patients were included, out of which 129 were male and 68 were female. Exclusion Criteria included all the records with incomplete information; those who were claustrophobic or patients whose parents did not consent were excluded. Data with blurred images and traumatic bleedswere also omitted.

Questionnaire and Data Collection*:* A questionnaire was designed, validated and later administered to extract information about thesigns and symptoms along with the MRI characteristics of thalamic lesions. It consisted of three parts. The first part was about the demographic parameters of the sample population (age, gender, signs and symptoms,duration of disease, diagnosis, etiology, past medical history, etc.). The othertwo parts consist of clinical and radiological characteristics, respectively. Clinical data included extensive details about neurological manifestations and effects on patients apart from general examination characteristics. Radiological characteristics included features of MRI along with varying imaging patterns, thalamicexpansion, perilesionaledema, signal dropout on SWI (calcification or bleed), diffusionrestriction, extrathalamicextension, basalgangliainvolvement, Hydrocephalus, Vascular Involvement, and other nonspecific indictors.Since no previous scales were available for this purpose, the questionnaire was constructed and approved by research team to ensure its face validity. Material for questionnaire was acquired from expert pediatric radiologists, literature reviews and data available on internet. Two authors developed the original version of questionnaire that was reviewed by a pediatric neurologist and then oneresearcherfrom the team revised it for internal clarity and validity, furthermore it was rechecked by two professionals (pediatric neurologist and radiologist) with experience in epidemiology, neurological diseases, and public health to ensure the validity and appropriate questionnaire designing to keep bias to minimum. It was tested on a sample of 25 participants to determine the reliability and Cronbach's Alpha was applied to measure the internal consistency and reliability, value of 0.7 was achieved.

Data Analysis: Data was analysed using SPSS version 25. The normality of the data was determined by Shapiro-Wilk test. The mean with standard deviation was calculated for quantitative variables while frequency and percentages for qualitative variables. Chi-Square was used to establish associations between the variables and p-value <0.05 was considered as significant at a 95% confidence interval with 5% margin of error. Fisher's exacttest were also applied according to distribution of data and p value of <0.05 was considered as significant.

RESULTS

The mean age of children was 8.4 years, with a standard deviation of 3 years. 129(65.2%) of the patients were male and 68(34.3%) were female. The average mean duration between the disease and diagnosis was two months, with a standard deviation of 2.4 months. 45% of the children had delayed developmental milestones, while 55% achieved their milestones appropriately according to their age. Only seven children have a positive past medical history, with five positive for teratology of Fallot and two for patent ductus arteriosus. A detailed list of diagnoses is given in Table 1. The most common diagnosis was Acute ischemic infract followed by PRES, Canavan disease and acute necrotizing encephalitis.

Table 1: The most common diagnosis causing thalamic lesions.

Diagnosis	Frequency	%age
Acute ischemic infarct patient	47	23.7%
Posterior reversible encephalopathy syndrome (PRES) c	27	13.6%
Canavan Disease	23	11.6%
Acute necrotizing encephalitis	18	9%
Neurofibromatosis Type 01 c	15	7.5%
Leigh's Disease	13	6.5%
Thalamic Gliomapt	12	6%
Dengue Hemorrhagic Encephalitispt	11	5.5%
Cerebral Venous Sinus Thrombosis c	10	5%
Atypical Viral Infection c	09	4.5%
Mitochondrial Disorders	06	3%
Basilar artery Syndrome	04	2%
Hypothalamic-ChiasmaticGlioma	01	0.5%
Wilson disease c	01	0.5%
Fahr's Disease	01	0.5%

Children presented with a variety of symptoms, including fever (reported by 65.2%), convulsions (reported by 61.6%), weakness/hemiplegia (17.7%), global developmental delay (17.2%), altered consciousness (16.2%), speech loss (6.6%), and inability to walk (reported by 3.5%). The etiology of thalamic lesions was classified into four distinct subgroups, with stroke 102(51.5%) representing the largest patient cohort, followed by congenital causes 41(20.7%), infectious causes 35(17.7%) and miscellaneous factors 19(9.6%). The most common infectious cause was dengue encephalitis as shown in figure 1 while in congenital causes Wilsons Disease was a rare find as shown in figure 2. Table 2 exemplifies the correlation between clinical examination characteristics of thalamic lesions and their respective etiologies.

Figure 1: Dengue Encephalitis, Axial sections of MR Brain with bilateral thalami showing: Swollen thalami bilaterally showing hyper-intense signals on T2W, T1W, and FLAIR images with characteristic "Double Doughnut sign" Evident as restricted Diffusion on DWI/ADC mapping and blooming in the central part of on-gradient echo sequences due to hemorrhagic residues.

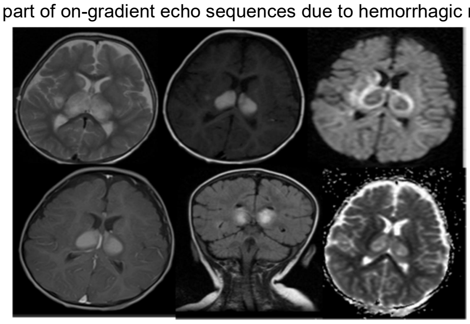
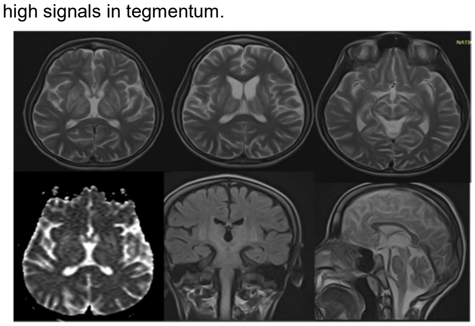


Figure 2, Wilson Disease: multi sequential imaging of MRI brain of a 10-year-old child demonstrate diffuse increased signal intensity in bilateral putamen and Thalami and midbrain giving the "face of a giant panda" showing high signals in tegmentum.



In order to further explore the relationship between MRI findings they were compared to etiologies. Majority of the cases were bilateral having significant results with perilesional edema, signal dropout, diffusion restriction, extra thalamic extension, basal ganglia involvement and vascular involvement (Table 3).

Our study observed that 120(60.5%) of the participants exhibited no evidence of thalamic expansion. In comparison, 39.5% had a thalamic and extra thalamic extension, with most common in basal ganglia followed by midbrain and pons, frontal-parietal-temporal lobe, temporal lobe, lateral ventricle, front-parietal-occipital lobe, frontoparietal region, subcortical region, optic chiasma, frontotemporal lobe, centrum ovale, occipital lobe, Sylvian fissure, parietooccipital lobe and periventricular area.

Table 2: Relationship between clinical examination features of thalamic lesions and etiology.

Clinical Examination Features	Etiology								Chi-Square p-value
	Stroke		Congenital		Infective		Others		
	Yes	No	Yes	No	Yes	No	Yes	No	
GPE	65	37	21	20	24	11	19	00	0.003*
Respiratory Exam	52	50	10	31	13	22	18	01	0.000*
Abdominal Exam	73	29	28	13	25	10	19	00	0.052
Cardiovascular Examination	52	48	01	40	13	22	18	01	0.452
Cranial Nerve	102	00	40	01	34	01	18	01	0.001*
Changes in sensory perception (e.g., touch, temperature, pain)	98	04	40	40	32	03	19	00	0.001*
Alterations in motor control or coordination since the thalamic lesion?	83	19	38	03	33	02	19	00	0.003*
Has the thalamic lesion affected your ability to perform daily activities that involve sensory or motor skills (e.g., dressing, eating, writing)	36	18	38	03	22	02	01	00	0.003*
Attention: Is there any difficulty in sustaining attention or switching between tasks after the thalamic lesion?	82	20	38	03	33	02	19	00	0.002*
Memory: Is there any effect on the memory of the patient?	06	96	04	37	00	35	00	19	0.180
Language: Are there any alterations in language abilities (e.g., speaking, understanding, reading, writing) following the thalamic lesion?	26	76	19	22	10	25	01	18	0.008*

Table 3. Relationship between MRI features of thalamic lesions and etiology.

MRI Features	Etiology				Chi-Square p-value
	Stroke	Congenital	Infective	Others	
Unilateral	37	08	06	01	0.007*
Bilateral	65	33	29	18	
Thalamic Expansion	74	25	20	18	0.135
Perilesional Edema	26	25	09	00	0.018*
Signal dropout on SWI (Calcification or bleed)	29	15	14	01	0.042*
Diffusion restriction	21	15	14	00	0.002*
Extra thalamic extension	18	12	15	01	0.004*
Basal Ganglia Involvement	20	12	13	01	0.018*
Hydrocephalus	08	06	01	00	0.134
Vascular Involvement	27	15	15	00	0.007*

*Significant p-value

Table 4. Relationship between MRI features of thalamic lesions and neurological symptoms.

MRI Features	Symptoms					
	Changes in sensory perception (e.g., touch, temperature, pain)	Alterations in motor control or coordination since the thalamic lesion?	Difficulty to perform daily activities that involve sensory or motor skills (e.g., dressing, eating, writing)	Difficulty in sustaining attention or switching between tasks after the thalamic lesion?	Is there any effect on the memory of the patient?	Are there any alterations in language abilities (e.g., speaking, understanding, reading, writing) following thalamic lesion?
Unilateral	0.007*	0.017*	0.016*	0.010*	0.075	0.116
Bilateral						
Thalamic Expansion	0.001*	0.394	0.699	0.481	0.013*	0.031*
Perilesional Edema	0.000*	0.010*	0.010*	0.019*	0.372	0.292
Signal dropout on SWI (Calcification or bleed)	0.006*	0.201	0.04*	0.147	0.049*	0.000*
Diffusion restriction	0.000*	0.000*	0.069	0.123	0.031*	0.001*
Extra thalamic extension	0.001*	0.001*	0.001*	0.002*	0.580	0.000*
Basal Ganglia Involvement	0.000*	0.002*	0.001*	0.004*	0.035*	0.192
Hydrocephalus	0.021*	0.129	0.344	0.049*	0.000*	0.203
Vascular Involvement	0.079	0.000*	0.423	0.169	0.124	0.004*

*****Significant p-value

DISCUSSION

The thalamus is a multifaceted anatomical entity that plays a crucial role in several cognitive, motor, and sensory functions. Thalamic pathologies can be categorized into many classifications, including neoplastic, metabolic, congenital, vascular, and infectious. The utilization of multimodal magnetic resonance imaging (MRI), encompassing morphologic sequences, diffusion-weighted imaging, vascular and perfusion imaging, and spectroscopy, proves to be valuable in both diagnosing and managing various medical disorders. Computed tomography (CT) also assumes a significant role and frequently serves as a valuable adjunct to magnetic resonance imaging (MRI) in lesion with calcification and hemorrhages but caters a very limited variety of tumors.(8)Thalamic lesions presented with generalized symptoms of any neurological disease including fever, convulsions, weakness/hemiplegia, global developmental delay, altered consciousness, speech loss, and inability to walk with no significant association with etiology or any specific sub type of tumors[9].

The etiology of thalamic lesions was classified into four distinct subgroups, withstroke representing the largest patient cohort, followed by congenital causes, infectious causes and miscellaneous factors. The data regarding prevalence and epidemiology is scanty, only case reports, pictorial essays and series have been reported so far[10,11]. This study is first in South Asia to highlight the prevalence along with radiological features of thalamic lesions. This study aims to bridge this gap by conducting an exhaustive evaluation of thalamic lesions on magnetic resonance imaging within the largest pediatric tertiary care facility in Karachi[12]. Furthermore, etiologies were further analyzed using chi square to compare the clinical findings that revealed significant relationship with abnormal general physical examination features and neurological examination showing signs of effected sensory perception, motor control, memory, language and attention. These findings are consistent with previously published literature[13].

In order to further explore the relationship between MRI findings they were compared to etiologies. Majority of the cases were bilateral lesions with significant association with perilesional edema, signal dropout (calcification or bleed), diffusion restriction, extra thalamic extension, basal ganglia involvement and vascular involvement as shown in Table 3. These relationships have never been explored before in large sets of primary data;only case series and literature reviews has described these associations[14,15]. One of the objectives behind this study is to raise awareness among radiologist regarding the intricate interaction between the pathophysiology of disease and possible MRI findings. This will not only help the trainee radiologist to understand the gist of disease and intricate MRI characteristics but also will be help to establish literature for future research and training purposes.

The clinical features for the disease are correlated with the MRI findings to understand the complex physiology of brain and their implication as physical symptoms[16]. Patients exhibiting symptoms related to sensory perception showed positive significance with laterality of lesion, thalamic extension, perilesional edema, signal dropout, diffusion restriction, extra thalamic extension, basal ganglia involvement and hydrocephalus. While the conducted in 2023 evaluated the MRI findings of sensory stimulation in healthy population through MRI and to explore the pathophysiology behind it and explains the MRI features that can be potentially disturbed in disease which are similar to the one discussed in our results[17]. Literature was searched to explore this relationship further but only one study related to schizophrenia was found that correlated the MRI features with sensory perception and was supportive of our data[18]. Another study explored these neurological connections with physical manifestation in an animal model and showed promising results somewhat similar to our findings[19]. Motor coordination and skills were also compared with MRI findings and were significantly associated withlaterality of lesion, perilesional edema, diffusion restriction, extra thalamic extension, basal ganglia involvement and vascular involvement. A study done 2013 in compared the normal motor functions of thalamus and compared with parkinsonism in adults and the normal pathways elaborate on the tentative MRI findings[20]. These findings were identical to a study conducted to understand the MRI findings in children with developmental delay[21]. These findings indeed show it is a developing area in terms of pediatric neurology and need extensive research on large scale to make concrete conclusions.

Furthermore, children's attention difficulties were also accessed and were significantly associated with laterality of lesion, perilesional edema, extra thalamic extension, basal ganglia involvement and hydrocephalus. These findings were supported by literature studied in thalamic lesions and their association with attention difficulties[22,23]. Memory and communications skills were significantly associated with thalamic expansion, signal dropout, diffusion restriction, basal ganglia involvement, hydrocephalus and vascular involvement. The relationship between learning and memory skills has been explored extensively in structures other than thalamus but data related to thalamus is limited and one of the earliest study was done in 2001 that concluded lesions in the thalamus not only affect declarative memory but also interfere with nondeclarative motor skill learning; these findings are supportive of our results[24].

Limitation of study includes limited number of patients, lack of available literature in regards to thalamic lesions their implication and association with MRI findings specially in terms of pediatrics population. Our recommendations would include to conduct county level studies with large set of data to make concrete conclusions. Because once the pathophysiology and MRI features are co related it will not only enhance the training of radiologist but will also provide future prospective of amalgamation of artificial intelligence in the field of radiology.

CONCLUSION

This article is the first one its kind the evaluate the complex interplay between the clinical features, etiologies of thalamic lesions and MRI characteristics. Ample significance was found between the aforementioned variables that demand a number of large-scale studies to further decide on conclusive relationship between MRI features and thalamic lesions of pediatrics population.

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