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**Research Article** 



# Clinical and Brain Imaging Findings of Children with Acute Ataxia: Ten Years of Experience at a Major Pediatric Referral Center

Mahboube Zarei <sup>1</sup>, Mahbod Issaiy <sup>2</sup>, Mahsa Asadabadi <sup>3,\*</sup> and Morteza Heidari <sup>4</sup>

<sup>1</sup>School of Medicine, Iran University of Medical Sciences, Tehran, Iran

<sup>2</sup>School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Pediatrics, Tehran University of Medical Sciences, Tehran, Iran

<sup>4</sup>Department of Pediatrics, Division of Pediatric Neurology, Children's Medical Center, Pediatrics Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran

corresponding author: Department of Pediatrics, Tehran University of Medical Sciences, Tehran, Iran. Email: mah.asadabadi@gmail.com

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#### Abstract

**Background:** Ataxia is a symptom of a wide range of disorders, which manifests as a lack of coordinated movements. It is commonly associated with cerebellar disorders.

**Objectives:** To evaluate the neuroimaging findings of children with acute ataxia (AA) and to identify the association between these findings and clinical results.

**Patients and Methods:** This cross-sectional study was conducted using the electronic medical records of patients, presenting to a major pediatric referral center over 10 years from March 2009 to February 2020. Patients were included in the study if they were younger than 18 years, were diagnosed with AA (< 30 days), and underwent magnetic resonance imaging (MRI), computed tomography (CT) scan, or both. The exclusion criteria were as follows: A history of neurological or medical disorders, explaining ataxia; pseudo-ataxia; a traumatic brain injury; severe loss of consciousness; and missing key information in the medical records (e.g., no brain imaging findings). Patient data, including the demographic data, clinical history, laboratory findings, imaging results, and in-hospital outcomes, were collected. A P-value less than 0.05 was considered statistically significant, and the confidence interval was set at 95%.

**Results:** A total of 119 patients were included in this study (51% female; mean age, 4.9 years). Clinically urgent neurological pathology (CUNP) was detected in 37 (31.09%) patients. The most common pathologies on images were tumors, acute disseminated encephalomyelitis (ADEM), and stroke. However, the most common diagnosis was acute post-infectious cerebellar ataxia (APCA) (24.4%), followed by brain tumors (16.8%) and Guillain-Barre syndrome (GBS) (15.1%), respectively. Overall, 11 variables were significantly different between patients with and without CUNP. Most notably, the duration of symptoms (P < 0.01), ophthalmoplegia (odds ratio [OR] = 13.93; 95% confidence interval [CI]: 3.5 - 54.7), focal neurologic deficit (OR = 7.26; 95% CI: 2.6 - 20.5), and fever (OR = 3.33; 95% CI: 1.1 - 9.8) were associated with a higher risk of CUNP. On the other hand, some features, such as a recent history of febrile illness (presence of fever or body temperature above 38°C in the last month)(OR = 0.36; 95% CI: 0.16 - 0.8) and hyporeflexia (P < 0.01), were associated with a lower risk of CUNP.

**Conclusion:** Acute post-infectious cerebellar ataxia was the most common diagnosis of AA in children, undergoing neuroimaging studies in our center. Nevertheless, tumor was the most common pathology detected on the images of patients with CUNP. Some pathologies might not be detected by some imaging modalities. Considering the associations identified in this study, patients with risk factors, such as a longer duration of symptoms, ophthalmoplegia, focal neurologic deficit, and fever, need to undergo another imaging modality with higher sensitivity if there are no positive findings in the initial imaging study. On the other hand, patients with protective factors, such as hyporeflexia and a recent history of febrile illness, could benefit more from other diagnostic modalities.

Keywords: Acute Ataxia, Children, Clinically Urgent Neurological Pathology, Neuroimaging, Cross-sectional Study

# 1. Background

The word "ataxia", which is derived from a Greek term, is composed of two parts, that is, "a" meaning "without" and "taxis" meaning "order" (1). Generally, ataxia refers to a disorder where motor coordination is absent. It is recognized as a threatening symptom due to uncertainties and lack of evidence on how clinicians can identify its underlying cause. Commonly, ataxia is associated with cerebellar diseases. However, it is not specific to these disorders, as many other conditions may be predisposing factors for

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ataxia, such as peripheral nerve and muscular disorders (2).

Acute ataxia (AA) is the most common cause of childhood ataxia, accounting for 30 - 50% of all cases. It may be caused by various conditions, including post-infectious inflammatory disorders, toxins, tumors, stroke, middle-ear infections, acute disseminated encephalomyelitis (ADEM), and Guillain-Barre syndrome (GBS) (3, 4). Among these etiologies, post-infectious inflammatory disorders, which are commonly associated with varicella zoster virus, are the most prevalent ones (5). Neuroimaging can play a significant role in diagnosis and treatment planning. In some etiologies, such as stroke, tumors, and ADEM, imaging studies can represent the characteristic findings of the etiology. However, imaging studies are negative for the most prevalent etiologies, including post-infectious cerebellar disorders, GBS, and toxin ingestion (6).

# 2. Objectives

This study aimed to evaluate the neuroimaging findings of children with AA and to investigate the possible association between clinically urgent neurological pathology (CUNP) based on neuroimaging and different signs, symptoms, and laboratory test results.

## 3. Patients and Methods

#### 3.1. Study Design

This cross-sectional study was conducted on all children with AA under the age of 18 years, presenting to the emergency department of Children's Medical Center, Tehran, Iran, from March 2009 to February 2020. This center is a tertiary educational hospital, affiliated to Tehran University of Medical Sciences (TUMS), Tehran, Iran.

#### 3.2. Patient Identification

The participants were selected based on the international classification of diseases-9 (ICD-9) codes. The keywords searched in the electronic medical records were as follows: ADEM, brain tumor, encephalitis, cerebellitis, GBS, meningitis, migraine, drug poisoning, stroke, and ataxia. Subsequently, potential cases were reviewed manually.

# 3.3. Patient Population

All patients presenting with AA, who underwent magnetic resonance imaging (MRI), computed tomography (CT) scan, or both, were included in this study. On the other hand, patients with a history of neurological or medical disorders explaining ataxia (e.g., known brain mass, ataxia telangiectasia, epilepsy, and ventricular shunts), claudication or gait abnormalities due to pain or weakness (pseudo-ataxia), traumatic brain injury (TBI), and severe loss of consciousness (unresponsive patients) were excluded. Also, patients were removed if their medical records had key information (e.g., no brain imaging) missing.

## 3.4. Data Collection

The patients' electronic medical records were reviewed by the principal investigator (MI). Five variable categories were extracted: Demographic information, clinical history, laboratory findings, imaging results, and inhospital outcomes. The demographic data included age and sex. Variables extracted from the patients' clinical history included the duration of symptoms before presentation, a recent history of febrile illness (i.e., presence of fever or body temperature above 38°C in the last month), focal neurologic deficits (e.g., ophthalmoplegia), and accompanying signs and symptoms (e.g., nausea, vomiting, fever, and headache).

Moreover, laboratory findings, including electrolyte levels, white blood cell count, and the results of cerebrospinal fluid analysis and toxicology studies, were reviewed. The imaging results were extracted from the radiology reports available in the medical records. The diagnosis documented in the discharge summary was considered as the final diagnosis. Some clinical features depending on the patient's verbal communication ability, such as vertigo, were considered missing in non-verbal children. If there was no information related to a variable in the patient's medical record, it was considered missing.

#### 3.5. Definitions

In this study, AA was defined as difficulty walking/standing or truncal instability within 30 days before presentation (6). Clinically urgent neurological pathology (CUNP) was defined as any neuroimaging finding, which normally prompts a medical or surgical intervention (7, 8). Such findings mainly include ADEM, brain tumors, brain abscesses, and infarctions. Brain MRI and CT scan were considered as eligible imaging studies.

#### 3.6. Outcomes

The primary outcome of this study was determining the proportion of various causes of AA among patients. The secondary outcome was investigating the association of CUNP with different factors.

#### 3.7. Ethical Considerations

This study was approved by the Ethics Committee of TUMS, Tehran, Iran (IR.TUMS.CHMC.REC.1399.031).

#### 3.8. Statistical Analysis

Mean and standard deviation (SD) were calculated for continuous variables with a normal distribution, and frequency was calculated for categorical variables. Also, median and interquartile range (IQR) were measured when a continuous quantitative variable did not show a normal distribution. The data distribution of continuous variables was assessed by two-sample Kolmogorov-Smirnov test. Moreover, Pearson's chi-square and Fisher's exact tests were used to compare categorical variables. Independent samples t-test was also conducted for comparison of continuous numerical variables. Additionally, bootstrapping was performed to calculate the confidence intervals (CIs). IBM SPSS version 22 (released in 2013, IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, USA) was used for all statistical analyses. A P-value less than 0.05 was considered statistically significant.

#### 4. Results

#### 4.1. Demographic Data

After reviewing the electronic medical records of 3,810 patients, 119 cases were selected for this study. The mean and median age of the study population were 4.9 and 4 years, respectively, with an IQR of 2-7 years. Overall, 51% of the population was female. Also, the mean age of female and male patients was 4.8 and 5.1 years, respectively. A more comprehensive description of the study population is presented in Table 1.

#### 4.2. Neuroimaging Results

Thirty-one patients only underwent MRI, 64 patients only underwent CT, and 24 patients underwent both imaging modalities. Overall, 37 (31.09%) patients were diagnosed with CUNP. Fifteen patients with CUNP underwent both MRI and CT scan, 13 patients underwent only MRI, and nine patients only underwent CT scan. As shown in Table 2, the frequency of pathologies found on the images of patients with CUNP was as follows: Tumor, ADEM, stroke, meningitis, encephalitis, and acute cerebellitis, respectively. However, the most common final diagnoses were acute post-infectious cerebellar ataxia (APCA) (29/119), tumor (20/119), and GBS (18/119), respectively (Table 1).

# 4.2.1. Comparison of Patients with and Without Clinically Urgent Neurological Pathology

As shown in Table 3, the features of patients (demographic features, clinical history, laboratory findings, abnormal EEG, and length of stay in hospital) with and without CUNP were compared, and some significant differences were found. These features included the duration of symptoms, recent history of febrile illness, nausea and/or vomiting, hyporeflexia, ophthalmoplegia, headache, focal neurologic deficit, fever, serum concentrations of sodium and phosphate, and the length of hospital stay.

## 5. Discussion

This cross-sectional study was conducted on the neuroimaging findings of children with AA, admitted to a large tertiary care center over 10 years. Children with at least one neuroimaging study were recruited in this study; consequently, our results only apply to patients with brain MRI or CT scan. Nearly 31% of the study population showed CUNP on neuroimaging. The most significant factors associated with the presence of CUNP included a longer duration of symptoms, ophthalmoplegia, focal neurologic deficit, and fever. On the other hand, a recent history of febrile illness and hyporeflexia were associated with the reduced presence and observation of CUNP on imaging.

In the present study most children with AA had no clinically urgent findings on neuroimaging. Evidence suggests that APCA, as the most common etiology of AA in children (6, 8, 9), does not require further imaging workups. However, patients with the following risk factors can benefit from imaging studies: Age > 3 years, duration of symptoms > 3 days, meningeal irritation and focal neurologic signs, hyporeflexia, history of trauma, and ophthalmoplegia (7, 8, 10).

The current findings are mainly consistent with previous studies. However, since our study population was heterogeneous, only patients with neuroimaging findings were included; therefore, some differences are expected. One of the most striking differences between the present study and previous research is that hyporeflexia was not associated with AA in the current study, whereas some stud-

Table 1. Descriptive Statistics of the Patients									
Variables	$\textbf{Mean} \pm \textbf{SD}$	Percentage (positive No./total No.)	95% CI	Median	IQR				
Demographics									
Age (y)	$4.9\pm3.4$	-	4.3 - 5.6	4	2-7				
Sex, female	-	51.3 (61/119)	43-60.5	-	-				
Clinical history									
Duration of symptoms (d)	6.1±7.1	-	4.8 - 7.5	3	1-10				
Recent febrile illness <sup>a</sup>		61.5 (72/117)	52.1-70.1	-	-				
Drug misuse		4.3 (5/117)	0.9 - 8.5						
Varicella infection <sup>b</sup>	-	10.1 (12/119)	5 - 16	-	-				
Vertigo		17.6 (21/119)	10.9 - 24.4						
Otalgia	-	3.4 (4/119)	0.8 - 6.7	-	-				
Nausea or vomiting		50.4 (57/113)	41.6 - 59.3						
Nystagmus		8.2 (8/97)	3.1 - 14.4		-				
Dysarthria	-	14.3 (17/119)	8.4 - 21						
Altered state of consciousness	-	8.5 (10/117)	3.4 - 13.7	-	-				
Hyporeflexia		20.6 (20/97)	12.4 - 28.9						
Ophthalmoplegia	-	12.7 (14/110)	6.4 - 19.1	-	-				
Meningeal irritation <sup>c</sup>		5 (6/119)	1.7 - 9.2						
Torticollis	-	1.7 (2/115)	0 - 4.3	-	-				
Headache		21 (25/119)	13.4 - 28.6		-				
Focal neurologic deficit		19.3 (21/109)	11.9 - 26.6	-	-				
Fever <sup>d</sup>		14.2 (16/113)	8 - 21 2						
Pach <sup>e</sup>		10.7(12/112)	E 4 17						
Laboratory	-	10.7 (12/112)	5.4-17	-	-				
Corrum magnacium (mg/dI)	21+02			21	10.22				
Sorum codium (mEc/L)	2.1 ± 0.3	-	2-2.2	2.1	1.9 - 2.3				
Serum phosphorus (mg/dL)	139.3 ± 3.1	-	138.0-140	140	137-141				
Imaging	4.8 ± 0.8	-	4.0-5	4./	4.2 - 5.3				
CUND present		211/27/10)	227 205						
MBL CIND:	•	31.1 (37/119)	22.7-39.5	-	-				
MRI, CUNP+	-	41.9 (13/31)	25.9 - 59.4						
CI, CUNP+	-	13.8 (9/05)	/.1-23./	-	-				
Einal diagnosis	-	65.2 (15/23)	44.9 - 82						
		76(0/10)	24 126						
	-	7.0 (9/19)	3.4 - 12.0	•	-				
APCA	-	24.4 (29/119)	16.8 - 31.9	-	-				
	-	4.2 (5/119)	0.8 - 8.4						
Acute cerebellitis	-	7.6 (9/119)	3.4 - 12.6		-				
Encephantis	-	4.2 (5/119)	0.8-8.4						
Meningitis	-	3.4 (4/119)	0.8-6.7		-				
Science	-	4.2 (5/119)	0.8 - 8.4						
Seizure	-	0.8 (1/119)	0-2.5	-	-				
	-	16.8 (20/119)	10.1 - 23.5		-				
Guillain-Barre syndrome	-	15.1 (18/119)	9.2 - 21.8	-	-				
Other etiologies	-	11.8 (14/119)	6.7 - 17.6						
Length of hospital stay (d)	74±61		6.3-8.6	6	3.5 - 10				

Abbreviations: ADEM, acute disseminated encephalomyelitis; APCA, acute post-infectious cerebellar ataxia; 95% CI, 95% confidence interval; CUNP, clinically urgent neurological pathology; CT, computed tomography; IQR, interquartile range; MRI, magnetic resonance imaging. <sup>a</sup> Positive history of febrile illness in the past 30 days. <sup>b</sup> Documented varicella infection in the past 30 days. <sup>c</sup> One of the nuchal rigidity, Kernig's, or Brudzinski' signs in the physical examinations. <sup>d</sup> Documented body temperature > 38°C upon admission. <sup>e</sup> Any signs of skin rash at presentation, including papules, macules, vesicles, pustules, and nodules.

Fable 2. The Imaging Findings of Patients with CUNP							
Count	Imaging (CT/MRI)	Imaging findings	Final diagnosis				
3	CT	Medulloblastoma	Tumor				
2	Both	Posterior fossa tumor	Tumor				
1	CT	Posterior fossa tumor	Tumor				
1	MRI	Posterior fossa tumor	Tumor				
3	Both	Pontine glioma	Tumor				
2	MRI	Pontine glioma	Tumor				
2	СТ	Choroid plexus tumor	Tumor				
1	MRI	Choroid plexus tumor	Tumor				
1	MRI	Ependymoma	Tumor				
1	Both	Cerebellar tumor	Tumor				
1	MRI	Suprasellar tumor	Tumor				
1	MRI	Pilocytic astrocytoma	Tumor				
2	Both	Left cerebellar stroke	Stroke				
1	MRI	Basilar and carotid dissection	Stroke				
1	CT	Cerebellar stroke	Stroke				
1	СТ	ICH	Stroke				
5	Both	ADEM	ADEM				
4	MRI	ADEM	ADEM				
1	MRI	Mastoiditis	Meningitis				
1	Both	Encephalitis	Encephalitis				
1	Both	Brain stem encephalitis	Others				
1	СТ	Acute cerebellitis	Acute cerebellitis				

Abbreviations: ADEM, acute disseminated encephalomyelitis; CT, computed tomography; CUNP, clinically urgent neurological pathology; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging.

ies found it to be a risk factor. This discrepancy may be attributed to the relatively large number of patients with GBS in our study, as they naturally do not have positive findings on the brain MRI or CT scan. Similarly, a recent history of febrile illness possibly suggests a viral infection and indicates APCA, which is not visible in neuroimaging.

Most previous studies support neuroimaging if a patient has a focal neurologic deficit, signs of increased intracranial pressure, marked asymmetry of ataxia, longer duration of symptoms (e.g., > 3 days), or older age (e.g., > 3 years) (7, 8, 10, 11). The UpToDate currently suggests neuroimaging for patients with an altered state of consciousness, focal neurologic signs, cranial neuropathies, marked asymmetry of ataxia, suspicion of a mass lesion, or positive history of trauma (12). However, none of the mentioned studies discuss when neuroimaging results should be suspected. Generally, some pathologies may not manifest in some imaging modalities. Considering the associations discovered in this study, a reevaluation of patients using another more sensitive imaging modality is necessary if the patient has no CUNP in the first imaging study, but has at least one of the following signs and symptoms: A longer duration of symptoms, ophthalmoplegia, focal neurologic deficit, or fever at presentation.

The present study had some limitations. First, it only included patients with neuroimaging studies; therefore, the results cannot be generalized to all children with AA. Second, the used imaging modalities were not consistent; therefore, comparison of these two modalities is flawed. Third, AA was defined as ataxia occurring within the last 30 days of presentation. Consequently, our population may have more life-threatening etiologies compared to other studies, thereby overstating the prevalence of CUNP. Fourth, since data collection was only performed by two people in this study, the population may be subject to selection bias. Fifth, this retrospective study had all the lim-

Variables	CUNP (n = 37)		No CUNP (n = 82)				
	Mean ± SD (95% CI)	Percentage (positive No./total No.)	Mean ± SD (95% CI)	Percentage (positive No./total No.)	OK (95% CI)	P-value	
Demographics							
Age (y)	4.2 ± 3.1 (3.3 - 5.2)	-	5.3 ± 3.5 (4.6 - 6)	-	-	0.12	
Sex, female	-	59.5 (22/37)		47.6 (39/82)	1.62 (0.74 - 3.5)	0.23	
Clinical history							
Duration of symptoms (d)	11.1 ± 9.7 (7.9 - 14.4)	-	3.9 ± 4 (3.1 - 4.8)	-	-	< 0.001	
Recent febrile illness	-	44.4 (16/36)	-	69.1 (56/81)	0.36 (0.16 - 0.8)	0.01	
Drug misuse	-	0 (0/36)	-	6.2 (5/81)	-	0.32	
Varicella infection	-	2.7 (1/37)		13.4 (11/82)	0.18 (0 - 1.4)	0.10	
Vertigo		21.6 (8/37)		15.8 (13/82)	1.46 (0.5 - 3.9)	0.45	
Otalgia	-	2.7 (1/37)	-	3.7 (3/82)	0.73 (0.1 - 7.3)	1.00	
Nausea or vomiting	-	64.7 (22/34)	-	44.3 (35/79)	2.3 (1 - 5.3)	0.047	
Nystagmus		9.4 (3/32)	-	7.7 (5/65)	1.24 (0.3 - 5.6)	1.00	
Dysarthria	-	13.5 (5/37)	-	14.6 (12/82)	0.91 (0.3 - 2.8)	0.87	
Altered state of consciousness		5.6 (2/36)	-	9.9 (8/81)	0.54 (0.1 - 2.7)	0.72	
Hyporeflexia	-	0 (0/22)	-	26.7 (20/75)	-	0.01	
Ophthalmoplegia		35.5 (11/31)		3.8 (3/79)	13.93 (3.5 - 54.7)	< 0.001	
Meningeal irritation	-	8.1 (3/37)	-	3.7 (3/82)	2.32 (0.4 - 12.1)	0.37	
Torticollis		2.9 (1/35)	-	1.3 (1/80)	2.32 (0.1 - 38.2)	0.52	
Headache	-	32.4 (12/37)	-	15.9 (13/82)	2.55 (1-6.3)	0.04	
Focal neurologic deficit		42.4 (14/33)		9.2 (7/76)	7.26 (2.6 - 20.5)	< 0.001	
Fever	-	25 (9/36)	-	9.1 (7/77)	3.33 (1.1 - 9.8)	0.02	
Rash	-	2.8 (1/36)	-	14.5 (11/76)	0.17 (0 - 1.4)	0.10	
Laboratory findings							
Serum magnesium (mg/dL)	2.1±0.3(2-2.2)	-	2.1± 0.3 (2-2.2)	-	-	0.90	
Serum sodium (mEq/L)	138.3 ± 3.2 (137.3 - 139.4)	-	139.8 ± 2.9 (139.1 - 140.4)	-	-	0.02	
Serum phosphorus (mg/dL)	4.3±0.6(4-4.6)	-	$4.9\pm0.8(4.7\text{-}5.1)$	-	-	0.01	
WBC, leukocytosis <sup>a</sup>	-	45.5 (15/33)	-	32 (24/75)	1.77 (0.8 - 4.1)	0.18	
CSF analysis, abnormal <sup>b</sup>		17.4 (4/23)	-	17.9 (5/28)	0.97 (0.2 - 4.1)	1.00	
Urine toxicology, positive <sup>c</sup>	-	20 (1/5)	-	12 (3/25)	1.83 (0.2 - 22.4)	0.54	
EEG							
EEG, abnormal <sup>d</sup>	-	20 (1/5)	-	31.6 (6/19)	0.54 (0 - 5.9)	1.00	
Outcomes							
Length of hospital stay (d)	$11 \pm 7.8 (8.6 - 13.7)$	-	$5.8 \pm 4.3(5 - 6.8)$	-	-	< 0.001	

#### Table 3. Comparison of Patients with and Without CUNP

Abbreviations: CUNP, clinically urgent neurological pathology; CSF, cerebrospinal fluid; EEG, electroencephalogram; OR, odds ratio; WBC, white blood cells. <sup>a</sup> Leukocytosis is defined as > 10,000 WBC/µL. <sup>b</sup> CSF analysis is considered abnormal if it is outside these ranges: Protein, 20 - 40 mg/dL; glucose, 45 - 80 mg/dL; and WBC count, 0 - 20 cells/µL (1 - 4 years), 0 - 30 cells/µL (< 1 year), 0 - 10 cells/µL (> 5 years). <sup>c</sup> Any positive finding of a substance in urine. <sup>d</sup> Any findings other than normal wave patterns.

itations attributed to this type of design, such as lack of follow-up. Finally, the study population was too small to reveal other significant associations; therefore, more extensive studies or meta-analyses are suggested in the future.

In conclusion, APCA was the most common cause of AA in children undergoing neuroimaging studies in our center. As some pathologies might not be detected using some imaging modalities, patients with risk factors, such as a longer duration of symptoms, ophthalmoplegia, focal neurologic deficit, and fever, who have no positive findings on initial imaging, should undergo further imaging with higher sensitivity. On the other hand, patients with hyporeflexia and a recent history of febrile illness might benefit more from other diagnostic modalities.

#### Footnotes

**Authors' Contribution:** M. Z. and M. I. were responsible for the acquisition, analysis, and interpretation of data and drafting the manuscript. M. A. and M. H. supervised the study.

**Conflict of Interests:** The authors declare that they have no conflicts of interest.

Ethical Approval: This study was ap-Ethics Committee proved bv the of TUMS. Tehran, (IR.TUMS.CHMC.REC.1399.031) Iran (https://ethics.research.ac.ir/IR.TUMS.CHMC.REC.1399.031).

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