Case Report

The Effect of Metabolic Disease on Language and Swallowing Skills in Children: A Case Report

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ABSTRACT

Objectives: The present research aims to highlight the impact of hyperammonemia, a common pediatric metabolic disease, on children's language and feeding skills. This research was conducted through a literature review and the presentation of a 2.5-year-old girl diagnosed with hyperammonemia.

Case Presentation: The research was conducted on a 2.5-year-old girl who had been diagnosed with a sudden-onset metabolic disorder that resulted in swallowing, speech, and language problems. The child's receptive and productive language and feeding history were obtained through interviews with her mother. Formal and informal tests were used to assess the child's language and feeding skills at two different times after the onset of symptoms.

Discussion: This study presents a new and unique case of a child with very high levels of ammonia and severe clinical manifestations of cognitive, language, and motor dysfunctions. Although the child did not receive any direct interventions during the study, a secondary assessment revealed slight improvements in some language and oral motor skills, possibly due to maturation and advice provided by rehabilitation team members.

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Highlights

- The effect of metabolic disease caused by hyperammonemia, a prevalent condition in pediatric patients, has not been widely acknowledged regarding its impact on children's language and feeding abilities.

- This article reviews previous research investigating the influence of metabolic disease caused by hyperammonemia on children's communication and feeding skills.

- Additionally, it presents a case study involving a 2.5-year-old child affected by hyperammonemia and discusses her communication and feeding skills.

- Despite differing findings from multiple studies, it seems that children with metabolic disease caused by hyperammonemia experience difficulties in language and feeding skills.

Plain Language Summary

Some children are prone to have a metabolic disease caused by hyperammonemia. This disease can cause brain injury and death. However, the impacts of the metabolic disease caused by hyperammonemia in affected children are not fully understood. This study was undertaken to review previous related studies and explore the consequences of hyperammonemia-induced metabolic disease in affected children. Additionally, a case study was presented involving a child exhibiting severe and sudden onset clinical manifestations in cognitive, language, and motor functions due to elevated ammonia levels. The aim was to emphasize the implications of this condition for speech and language pathologists. The results show that metabolic disease caused by hyperammonemia can affect language and feeding skills in children. However, a definitive link between this metabolic disorder and its effects on language and feeding skills is yet to be established, necessitating further comprehensive and well-organized research.

Introduction

Hyperammonemia is a metabolic disorder characterized by elevated ammonia levels in the bloodstream. It is a dangerous condition predominantly affecting the pediatric population that may lead to brain injury and death. It may be primary, caused by a genetic defect, or secondary, from various congenital and acquired factors, such as metabolic disorders [1-7]. Ammonia (NH_3), the primary nitrogen source, undergoes hepatic metabolism to form urea, a nitrogenous compound excreted in urine [4, 8, 9]. Consequently, abnormally high ammonia levels in the blood lead to excessive urea production, detectable through blood tests [10]. Normal levels of ammonia in the blood vary with age [11]. Plasma ammonia levels exceed 80 µmol/L in infants up to one month old and 55 µmol/L in older children. Affected newborns typically exhibit no symptoms at birth, with the age of onset ranging from hours to months after birth. Earlier clinical onset is associated with more profound enzymatic defects [12]. Age, metabolic, nutritional status, and infections affect clinical manifestations [12, 13]. Early diagnosis and prompt treatment are essential to prevent life-threatening complications like cerebral edema and cerebral hernia. Diagnostic approaches depend on the presenting symptoms [11]. The estimated incidence of this disorder in the United States is 1 in 25000 live births [14]. However, for both children and adolescents, the global prevalence data has remained obscure [15]. Individuals with metabolic syndrome and hyperammonemia are at higher risk for other conditions, including cardiovascular issues, nutritional problems, and cognitive disorders [16, 17]. Neurological problems in hyperammonemia arise due to compromised liver function, which impairs ammonia detoxification and allows toxic substances to affect brain function.

Despite notable progress in understanding and identifying metabolic diseases such as hyperammonemia, limited knowledge exists regarding this population's cognitive, communicative, and oral-motor functions. A literature review reveals that most studies in this field have primarily focused on the relationship between hyperammonemia and physical symptoms of metabolic disorders in children and adolescents [5, 15, 18]. Some studies have also explored cognitive impairments in affected individuals [17, 19, 20]. Patients with hyperammonemia demonstrate difficulties in memory tasks, primarily attributed to attention and visual perception

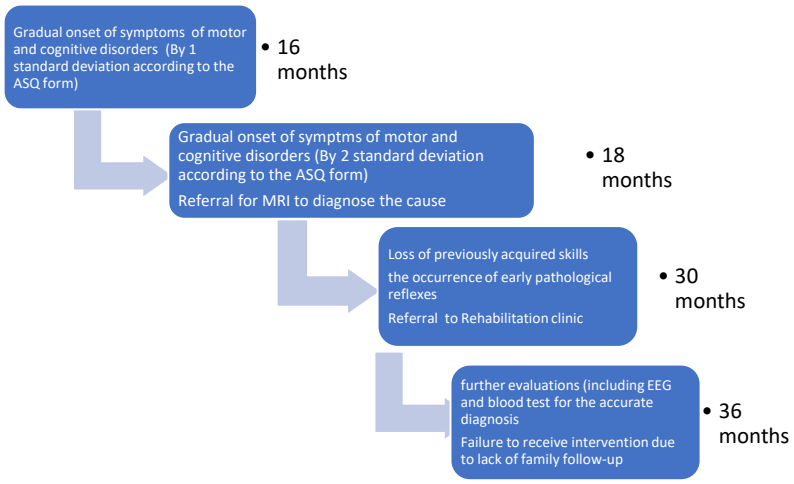

Figure 1. Case report timeline

Iranian Rehabilitation Journal

deficits [21, 22]. They also exhibit poorer performance than healthy individuals in motor functions, attention, visual perception, visual orientation, and visuoconstructive abilities [23-26]. These children seem more at risk for developmental delays and problems with receptive and expressive language [27-29].

This study presents a 2.5-year-old girl diagnosed with hyperammonemia. We investigated her receptive and expressive language problems and oral-motor and swallowing dysfunctions. Also, we hope to draw the attention of specialists and physicians dealing with individuals affected by hyperammonemia to the language, cognitive, and swallowing problems these children may experience, making early speech therapy services necessary.

Case Presentation

Patient description

A previously healthy 2.5-year-old girl was brought to a rehabilitation clinic in Mahmoudabad City, Iran, for her swallowing and communication problems that started one year ago due to a metabolic disorder. The diagnosis of metabolic disorder was made at 18 months based on clinical evidence, including the results of a blood test and magnetic resonance imaging (MRI) prescribed by a neurologist.

She was born to non-consanguine Iranian parents. According to parents' reports and the ages and stages questionnaires (ASQ), she demonstrated appropriate development for her age in various domains, including gross and fine motor skills, social and communicative abilities, as well as feeding and weight gain issues up to 14 months and family history was non-contributory (Figure 1). Following the sudden onset of symptoms at 16 months old, the child was admitted to a hospital in Mahmudabad. She was brought to the emergency care department exhibiting consistent seizure activity and an altered mental state, as indicated by a Glasgow coma scale (GCS) score of 8. She was admitted to the hospital for one week, during which her seizures were managed using intravenous lorazepam. However, following her discharge, there was a gradual decline in her previously acquired motor skills, including sitting, crawling, standing, and oral motor skills related to feeding. Additionally, she experienced a loss of babbling sounds, as well as communicative abilities, which may be attributed to central nervous system (CNS) anomalies resulting from an undiagnosed metabolic deficiency. No spontaneous recovery of these skills was observed until she visited a speech therapy clinic one year later.

Clinical findings of the speech, language, and swallowing evaluations at 30 months of age demonstrated no sign of any vocalization other than sounds of crying and coughing. Pathological reflexes, including rooting and bite reflexes, were evident. The child was referred to a neurology center in Tehran City, Iran, for further evaluation to investigate the cause of the disorder. Electroencephalography (EEG) and MRI were performed and confirmed the existence of a metabolic disorder. Blood tests, endocrinologic evaluation, and genetic tests were performed at 36 months of age, and the cause was identified as hyperammonemia.

Clinical examinations

Assessment of language and communication

The children's language profile monitoring package (PANA) was used to assess the child's language and communicative skills. Because the child did not communicate verbally, a checklist for the pre-lingual stage (9-18 months) of PANA was completed. This checklist is completed based on the therapist's observations and the parents' reports. It contains subsections, including history (a detailed history of the child's pre- and postnatal development and family history), the child's plays (at 8 stages of symbolic play development) and gestures (at 3 levels of deictic, symbolic, and theatrical/co-speech gestures) assessed during the child's free play with the parents, the child's attention level (based on Reynell stage of attention development), and parent's reports of the child's feeding behaviors, vocalizations, intentional communicative acts and, receptive and expressive vocabularies (based on the Persian version of MacArthur-Bates communicative development inventories) [30-32]. Table 1 presents the results of evaluations at two different times: Initial assessment (A) at 18 months of age and the second evaluation (B) one year later. A single examiner conducted both evaluations. The scoring and interpretation of the child's performances were done simultaneously during the evaluation and then confirmed based on the recorded videos. Additionally, the accuracy of the scoring and interpretation of the results was confirmed by another speech therapist with at least 10 years of experience working with children with language disorders.

Finally, the interactive and communicative skills of the child were examined with the Persian version of Rossetti's infant-toddler language scale, birth to three years [33]. This valid and reliable criterion-reference test measures 6 developmental domains from birth to 36 months: Interaction-attachment, pragmatics, gestures, play, language comprehension, and language expression (Table 2).

Evaluation of oral motor and feeding skills

The facial and oral cavity muscles' structure and function were evaluated using the schedule for oral motor assessment [34], along with informal assessments performed at rest and during feeding. The results are presented in Tables 3 and 4. The most striking test results were related to the extreme movements of the jaw that caused open mouth posture and drooling, as well as the hypotension of the tongue muscles, which led to the child's feeding problems.

During one year between two evaluations, the child received no interventions, such as medication, occupational therapy, or speech therapy. This condition was due to the family's lack of follow-up.

Conclusion

While hyperammonemia is a well-known metabolic disease from the medical point of view, speech, language, cognitive, and feeding problems that affected children may experience, as well as the consequences of these disabilities on their lives and the health and social support that these children and their families require have been largely overlooked in studies. In this article, we presented a case of late-onset hyperammonemia who experienced a sudden onset of symptoms and a gradual and severe decline in cognitive, communicative, and motor functions. We aimed to highlight this disorder's clinical manifestations and consequences for speech and language pathologists. Genetic and acquired disorders can increase ammonia levels in the blood. Urea cycle disorders are the most common cause of severe ammonia elevations, leading to recurrent, progressive, or chronic neurological disorders due to the toxic effects of ammonia accumulation and subsequent neuronal death [18]. Recurrent hyperammonemia episodes can cause a variety of symptoms, including vomiting, lethargy, coma, and even death in severe cases. Survivors may experience varying degrees of developmental disabilities, which are often correlated with the number, severity, and duration of hyperammonemia episodes, as well as the stage of brain maturation.

It has been suggested that metabolic disorders in infants, particularly disorders of the urea cycle, maybe the cause of 20% of sudden infant death syndrome cases. However, the disease may remain undiagnosed in many cases, and the infant may pass away without a definite diagnosis. It is argued that some children who display various signs of autism spectrum or behavioral disorders (such as hyperactivity accompanied by screaming, self-injury, and delirium) may be among the undiagnosed cases of urea cycle disorders [35].

Several studies have reported cases of acute hyperammonemia in individuals with late-onset inborn errors of metabolism, including previously healthy children, adolescents, and adults [36-38]. Early diagnosis and aggressive management to reduce ammonia levels in the bloodstream are essential to prevent serious complications, such as increased glutamate concentrations in the CNS, cerebral edema, increased intracranial pressure, irreversible brain damage, and psychomotor retardation [9, 35,

Table 1. The results of evaluation of language and communicative skills based on child's language PANA: Pre-lingual stage

Section			Results
Section 1: History	Family history		The parents were monolingual speakers of Persian and reported no history of speech and language problems in the family. The mother did not have any specific disease and did not take any medication during the pregnancy. The length of pregnancy was 40 weeks, and the baby's birth weight was 3 kg. Parents reported no physical or developmental concerns in the prenatal, natal, and post-natal period from birth to the onset of the symptoms.
	History of motor-speech development		ASQ shows the child had age-appropriate motor, social, and communicative development.
	Social, behavioral, and emotional status of the child and her family		Normal
Section 2: Observations and parents' reports	Target of evaluation	Assessment A	Assessment B
	Gestures and intentional communicative acts	No sign of any intentional communicative acts The absence of any form of gestures being utilized	No sign of any intentional communicative acts The absence of any form of gestures being utilized
	Vocal signals	Crying with high frequency. (Semivowels: The dominant vocalization pattern in 0-2 months old infants)	Crying with variation prosody and high frequency. Aimless vocalization: Semivowels (the dominant vocalization pattern in 0-2 months old infants)
	Auditory condition	Normal (reported by an audiologist)	Normal
	The child's level of attention	Level 1 (0-1 years old): transient attention	Level 2 (1-2 years old): Paying attention to her favorite activity
	Cognitive and behavioral development	Aggression, physical orientation, and touching others The child does not know how to use routine objects	Aggression, physical orientation, and touching others. The child does not know how to use routine objects.
	Receptive and productive vocabulary (based on the Persian version of MacArthur-Bates communicative development inventories	No sign of reception or production of words	No sign of reception or production of words

A: Initial evaluation (18 months of age); B: Secondary evaluation (30 months of age). Iranian Rehabilitation Journal

39, 40]. These complications can lead to various communication impairments, especially in younger children.

Motor and cognitive problems are common clinical symptoms of hyperammonemia, regardless of the underlying cause. For example, Petel et al. found these symptoms in patients with Reye syndrome [20]. Monfort et al. also showed that hyperammonemia is a major contributor to neurological alterations in patients with minimal or clinical hepatic encephalopathy, who have varying degrees of cognitive impairment [17]. A study in rats by Hernandez-Rabaza et al. reveals that hyperammonemia triggers neuroinflammation and increases GABAergic tone in the cerebellum, contributing to cognitive and motor impairment in hepatic encephalopathy [19].

Consistent with the studies that have shown that different types of metabolic disorders, including hyperammonemia, can affect cognitive and motor systems, the case presented in this study experienced acute symptoms, including seizures followed by gradual loss of motor speech as well as other communicative skills. Also, due to the weakness of the oral muscles, she was not able to suck and move his tongue and had difficulty in feeding and swallowing (Table 3). It must be noted that hyperammonemia should be considered in the differential

Table 2. Child's profile of communication and interaction based on the Rossetti infant-toddler language scale: Birth-three

Chronological Age (m)	Interaction-attachment	Pragmatic	Gesture	Play	Perception	Expression
0-3	*	*	-	*	-	-
3-6	*	*				
6-9	*					
9-12						
12-15						
15-18						
18-21						
21-24						
24-27						
27-30						
30-33						
33-36						

*The results were the same in both A and B evaluations.

Iranian Rehabilitation Journal

diagnosis of encephalopathy and seizures, particularly when MRI results show symmetrical damage to the insular and cingulate cortices on both sides of the brain [40].

Some studies have documented the occurrence of motor impairments such as dystonia, ataxia, tremor, spasticity, orofacial dyskinesia, hyperkinesia, and myopathies as a result of metabolic disorders [41-43], as in our study, this child also showed signs of motor impairments such as myopathy and tremors.

Although motor disorders in children with metabolic disorders have been well-documented in the literature, there is a lack of studies documenting communication impairments in this population.

Despite the previous age-appropriate growth (based on the child's health records and ASQ results), all social, pragmatic, and language skills in the case presented in this study were severely impaired at the assessment times. She did not play in the real sense and only looked at objects temporarily (Tables 1 and 2). This clinical

Table 3. Results of Persian version of schedule for oral motor assessment [34]

Food Stuff	Oral-motor Behaviors	
	A	B
Puree	+	+
Semi-solids	-	+
Solids	-	+
Cracker	-	+
Bottle	+	+
Trainer cup	-	+

A: Initial evaluation; B: Secondary evaluation.

Iranian Rehabilitation Journal

Table 4. The results of the informal evaluation conducted to assess the structures and functions of the oral-facial region

Oral-facial Structure		Assessment Items	Observations (Initial and Secondary Evaluation)
Face		Symmetry: Normal symmetry/ droops on right side/ droops on left side	N
		Abnormal movements: None/ grimaces/ spasm	None
		Mouth breathing: Yes/no	Yes
Jaw and teeth	Assessing the functionality of the jaw while performing the action of mouth opening and closing	Range of motion: Normal/reduced	R
		Symmetry: Normal/ deviates to right/ deviates to left	N
		Movement: Normal/ jerky/ groping/ slow/ asymmetrical	Slow
		Temporomandibular joint noises: Absent/ grinding/ popping	A
		Dentition observation	
		Molar occlusion: Normal / class / class II/ class III	N
		Incisor occlusion: Normal/ overbite/ under bite/ cross bite	N
		Teeth: All present/ dentures/ teeth missing	Teeth missing
		Arrangement of teeth: Normal/ Jumbled/ spaces/ misaligned	Absence of teeth
		Hygiene	N
Lips	The client was asked to purse her lips together	Range of motion: Normal/reduced	R
		Symmetry: Normal/ droops bilaterally/ droops right/ droops left	Droops bilaterally
		Strength (press tongue blade against lips): Normal/weak	Weak
		The client was asked to create a cheek bulge and maintain it	
		Lip strength: Normal/reduced	R
		Nasal emission: Absent/present	A
Tongue		Surface color: Normal/abnormal	N
		Movement: Normal/ absent/ jerky/ spasms/ writhing/ fasciculation	A
		Size: Normal/ small/ large	N
		Frenulum: Normal/short	N
	The client was asked to protrude the tongue	Excursion: Normal/ deviates to right/ deviates to left	Not able to do
		Range of motion: Normal/reduced	R
		Speed of motion: Normal/reduced	R
		Strength (apply opposing pressure with tongue blade): Normal/reduced	R
	The client was asked to perform a tongue retraction maneuver	The client was asked to perform a tongue retraction maneuver	
		Excursion: Normal/ deviates to right/ deviates to left	Not able to do
		Range of motion: Normal/reduced	R
		Speed of motion: Normal/reduced	R

Oral-facial Structure		Assessment Items	Observations (Initial and Secondary Evaluation)
Tongue	The client was asked to move the tongue tip to the right	Excursion: Normal/ incomplete/ groping	Not able to do
		Range of motion: Normal/reduced	R
		Strength (apply opposing pressure with tongue blade): Normal/reduced	R
		The client was asked to move the tongue tip to the left	
		Excursion: Normal/ incomplete/ groping	Not able to do
		Range of motion: Normal/reduced	R
		Strength (apply opposing pressure with tongue blade): Normal/reduced	R
	The client was asked to move the tongue tip up	Movement: Normal/ incomplete/ groping	Not able to do
		Range of motion: Normal/reduced	R
	The client was asked to move the tongue tip down	Movement: Normal/ incomplete/ groping	Not able to do
		Range of motion: Normal/reduced	R
	Observation of quick movements of the tongue from side to side	Rate: Normal/ reduced/ slows down progressively	Slows down progressively
		Range of motion: Normal/reduced on left/reduced on right	Reduced bilaterally
Pharynx		Color: Normal/abnormal	N
		Tonsils: Absent/ normal/ enlarged	N
Hard and soft palates		Color: Normal/abnormal	N
		Rugae: Normal/ very prominent	N
		Arch height: Normal/ high/ low	N
		Arch width: Normal/ narrow/ wide	N
		Growths: Absent/present	A
		Fistula: Absent/present	A
		Cleft: Absent/present	A
		Symmetry at rest: Normal/ lower on right/ lower on left	N
		Gag reflex: Normal/ absent/ hyperactive/ hypoactive	N
		The client was asked to produce the vowel sound /ɑ/	
		Symmetry of movement: Normal/ deviated to right/ deviated to left	Lack of response, no movement
		Posterior movement: Present/ absent/ reduced	A
		Lateral movement: Present/ absent/ reduced	A
		Uvula: Normal/ bifid/ deviated to right/ deviated to left	N
		Nasality: Normal/hypernasal	N

Abbreviations: N: Normal; A: Absent; R: Reduced.

profile of performances indicates severe impairments in intellectual and cognitive abilities and damage to adaptive and communicative skills resulting from likely irreversible damage to the central nervous system. Although there were slight improvements in the child's oral-motor and language skills over time, even without direct interventions, the progress was insignificant. It could be attributed to natural maturation and or advice provided to the mother by the rehabilitation team.

Tiwari et al. retrospectively reviewed 392 case records of children with different inborn metabolic disorders. They reported that some children had communication impairments, such as delayed development of speech and language, language impairment associated with autism, hearing loss, or mental retardation, and speech and language problems associated with attention-deficit/hyperactivity disorder. Other studies have also reported communication disorders such as autism [35] and mental retardation [42, 44-46] as the general clinical presentation of metabolic disorders in children. However, there is currently a lack of research on the range of communication impairments in children with early or late-onset hyperammonemia. The oral-motor and communicative impairment observed in our case may be linked to seizures and nerve damage caused by hyperammonemia rather than being directly caused by the disorder. More studies are needed to determine the full range of communication impairments in children with hyperammonemia.

Despite the increasing awareness of metabolic disorders globally, diagnostic laboratory tests to identify some life-threatening metabolic disorders have not yet been added to the list of disorders that are screened for in newborns in Iran. Due to the limited time between the onset of initial symptoms and the onset of irreversible brain damage, rapid and effective diagnosis and treatment are critical. In the absence of mandatory screening tests that can increase the likelihood of receiving timely diagnosis and necessary services, paying particular attention to clinical symptoms is paramount for the early identification of at-risk children. General developmental delay or a decline in acquired developmental skills, including feeding and communication skills, can be the first sign in some affected children. So, attention to these signs can be crucial in the early identification of affected children, in providing adequate medical care and attention, and in reducing the extent of potential damage. Furthermore, considering the potential motor, cognitive, and communicative difficulties of children presenting with hyperammonemia, referral for a comprehensive assessment of speech, language, and communicative abilities can be a crucial step in reducing the impact of the disease on the quality of life of affected children and their families. Yet, it is possible that some parents may be unaware of the importance of screening for communication-related impairments, or physicians can sometimes miss communication disorders during routine examinations. Conducting further studies aimed at identifying the types of communication problems that individuals presenting with early- or late-onset hyperammonemia may experience and the impact that these problems have on their lives can help increase awareness of professionals who work with these children and their families, and providing appropriate and necessary services.

Conclusion

Metabolic disease caused by hyperammonemia is a rare and devastating disorder that affects all aspects of life for both the child and their family caregivers. Children and adolescents with hyperammonemia are at higher risk for other diseases, including nutritional problems and cognitive and communicative impairments. Therefore, it is crucial to pay attention to the rehabilitative evaluation and treatments following the onset of the disorder, or even slight declines in the cognitive and communicative skills that could be the first signs of a metabolic disorder.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

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