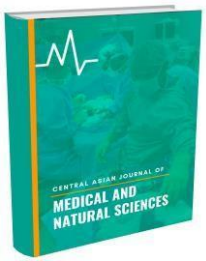

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*Article*

# Clinical and Functional Features of the Biliary Tract in Children with Cerebral Palsy

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**Abstract:** Cerebral palsy is one of the most common neurological disorders in childhood and is essentially characterized by motor impairment due to non-progressive damage to the developing brain. However, alongside neurological symptoms, children with cerebral palsy often have a range of systemic complications which can have a major impact on their general health and quality of life. Among these complications, disorders of the digestive system, including the dysfunction of the hepatobiliary tract, are still poorly studied, despite their potential clinical importance. The aim of the present study was to investigate clinical and functional characteristics of the biliary tract in children with cerebral palsy. The research included children diagnosed with cerebral palsy who were subjected to clinical evaluation, laboratory test and ultrasound examination of the hepatobiliary system. Particular attention was paid to digestive complaints, feeding characteristics and functional signs of gallbladder activity. Ultrasound assessment made it possible to evaluate the size of the gallbladder, its contractility, and the presence of bile stasis. The results of the study showed that functional disturbances of the biliary tract occur in a considerable proportion of cerebral palsy children. Hypokinetic biliary dysfunction and delayed gallbladder contraction were some of the most seen findings. These changes do not seem to have a single cause, but seem to be linked to decreased physical activity, dysfunction of the autonomic nervous system, and nutritional factors that are commonly seen in children with severe neurological impairment. The results indicate the need for thorough clinical evaluation of the hepatobiliary system in children with cerebral palsy. Early detection of biliary dysfunction is potentially a contributing factor for better diagnostic plans and more successful management of digestive complications in this vulnerable patient population.

**Keywords:** Cerebral Palsy, Biliary Tract Dysfunction, Gallbladder Motility, Biliary Dyskinesia, Hepatobiliary System, Pediatric Gastroenterology, Ultrasound Diagnostics

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## 1. Introduction

Neurological disorders that occur in early childhood tend to involve not only motor abilities but also the function of many internal organs. Cerebral palsy is one of the most common chronic neurologic conditions of childhood that is, a group of permanent disorders of movement and posture resulting from non-progressive damage to the developing brain. According to recent epidemiological studies the global prevalence of cerebral palsy is relatively constant and is around two to three cases per one thousand live births. While the main manifestations of this condition are generally linked to the inability to coordinate body movements, muscle tone abnormalities, and delayed psychomotor development, it has become increasingly recognised by clinicians that children with

cerebral palsy often have a number of systemic complications which significantly affect their overall health and quality of life [1].

Among these associated conditions, disorders of the digestive system take an important place. Children with cerebral palsy frequently exhibit feeding problems, swallowing problems, chronic constipation, gastroesophageal reflux, and disorders of intestinal motility. These problems are brought on by a combination of neurological impairment, autonomic dysfunction, decreased physical activity and sustained medication use. In many cases, gastrointestinal disorders can go unnoticed for an extended period of time because the main area of treatment is often directed towards neurological rehabilitation. Nevertheless, dysfunctions in the digestion may significantly worsen the clinical course of the disease and negatively impact the nutritional status, grow and metabolic balance [2].

One aspect that has been given less attention in pediatric research is on the condition of the hepatobiliary system in children with cerebral palsy. The biliary tract is very critical in the digestion process, especially in the processes of secretion of bile, lipid emulsification and metabolism regulation. The gallbladder and the bile ducts need to be properly functioning to allow bile to be released in a coordinated fashion into the duodenum during digestion. However, disorders in autonomic control, decreased mobility, and chronic nutritional imbalance may disturb the contractile activity of the gallbladder and cause functional biliary disorders. Such disturbances may be in the form of biliary dyskinesia or impaired evacuation of bile or the stasis of bile leading to the symptoms of abdominal discomfort, symptoms of dyspepsia and metabolic disturbances [3].

Recent clinical observations have pointed towards children with severe neurological impairment such as cerebral palsy may be especially susceptible to hepatobiliary dysfunction. The combination of impaired neuromuscular regulation, reduced physical activity and altered dietary patterns may be disruptive of the coordinated mechanisms that regulate the secretion of bile and the motility of the gallbladder [4].

In addition, long-term pharmacotherapy that may be included in the medications taken by children with cerebral palsy, such as anticonvulsant medications, may affect liver metabolism and biliary function. These are factors which support the need for careful evaluation of the hepatobiliary system in this vulnerable population. Despite the clinical importance of this issue, the state of the biliary tract function in children with cerebral palsy is not sufficiently studied. The aim of this study was to investigate the clinical and functional features of the biliary tract in cerebral palsy children.

## 2. Materials and Methods

The present study was conducted to assess the clinical and functional characteristics of the biliary tract of children with cerebral palsy. The study was carried out at a pediatric clinical setting where children with neurological disorders routinely undergo medical supervision as well as rehabilitation care. The observation period was 2 consecutive years and during this period, children undergoing neurological follow-up examinations were further evaluated for the presence of digestive system disorders. The study included children with an accepted diagnosis of cerebral palsy certified by pediatric neurologists based on accepted clinical criteria. Patients were selected at routine medical visits and hospital admissions in relation to neurological rehabilitation. Children with severe congenital liver diseases, hereditary metabolic disorders, or structural abnormalities of the hepatobiliary system already diagnosed by other means were excluded from the investigation in order to avoid any possible confounding factors that may influence the secretion of bile or gallbladder motility. In total, the group of examined children comprised children of different ages that exhibited different clinical forms of cerebral palsy (spastic diplegia, hemiplegia, and mixed neurological forms)[5].

During the clinical stage of the research, particular emphasis has been placed on identifying digestive complaints as reported either by parents or caregivers. Since many children with cerebral palsy have limited verbal communication, detailed interviews with parents were thought to be an important source of information. The collected data consisted of periods of abdominal discomfort, episodes of periodic nausea, changing appetite, vomiting after meals and symptoms suggestive of dyspepsia. Information on feeding patterns and dietary structure as well as the use of long-term pharmacological therapy was documented too. Anticonvulsant medications, prescribed in this patient population, were reported because of their possible impact on the liver metabolism and biliary secretion. Physical examination was performed on all subjects. Anthropometric indicators were also measured including body weight, height and nutritional status as malnutrition and limited mobility may influence gastro-intestinal physiology in children with neurological impairment. In order to get objective information on the functional state of the biliary tract, ultrasound examination of the hepatobiliary system was conducted for each participant. Ultrasonography was chosen as the main instrumental technique because it is safe, not invasive and has a high diagnostic value in pediatric settings. The examination was performed following a period of fasting to improve the visualisation of the gall bladder. Several parameters were tested, such as gallbladder size, wall thickness, presence of bile stasis and contractile function during functional testing. Dynamic observation of gallbladder contraction following a physiologic stimulus permitted the evaluation of motor activity of the biliary system, which is needed to diagnose biliary dyskinesia in children [6].

Laboratory investigations were also included in the research protocol. Blood samples were taken to determine biochemical indicators that reflect the hepatobiliary function. The parameters analyzed were serum bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase. These biochemical markers were used to assess whether functional disturbances of the biliary tract were associated with changes in the metabolism of the liver function. The laboratory procedures were performed following the standard clinical diagnostic guidelines that are widely used in pediatric practice [7].

Considering the important role that autonomic nervous system dysfunction plays in gastrointestinal motility disorders in children with cerebral palsy, clinical observations were interpreted taking into account neurological severity. The severity of motor impairment was recorded from the results of neurological examination and later the correlation between the neurological status and biliary system functioning was analyzed. Previous clinical research research shows that diminished physical and autonomic dysregulation could significantly affect the contractility of the gallbladder in neurologically impaired children, which has a reason to include neurological parameters in the analytical framework of this research. All collected data were recorded systematically and analysed following statistical methods for clinical research. Differences were regarded as statistically significant if probability value was less than 0.05. The usage of statistical analysis allowed to provide an objective interpretation of the clinical and instrumental results and identify possible associations of the severity of cerebral palsy with disorders of the functional state of the biliary tract [8].

## 3. Results

Clinical observation of children with cerebral palsy showed that disorders of the digestive system were not rare and they often expressed themselves by subtle manifestations that were not immediately recognized during the routine neurological care. During the examination period, many caregivers found persistent gastrointestinal issues for which previously general feeding problems associated with neurological impairment had been blamed. However, closer analysis of these complaints suggested that functional disturbances of the biliary system might play an important role in the development of these symptoms.

The most common complaints were periodic abdominal discomfort, anorexia, nausea after meals, and episodic emesis. Some of the parents also described episodes of bloating and irregular bowel movements. These symptoms were especially apparent in the children with more extreme motor impairments, in which decreased mobility and sitting positions might affect digestive physiology. During physical examination slight tenderness in the right hypochondrium was noticed in part of the examined children. In most cases the liver size was still within physiological limits but functional disturbances of bile secretion could not be excluded based on clinical signs only. Ultrasound examination has added more details about the condition of the hepatobiliary system. In several children, the gallbladder showed evidence of impaired motor activity. The most common findings were delayed contraction after functional stimulation, an increase in the amount of gallbladder contents during fasting, and the presence of bile stasis. These changes are consistent with functional biliary dyskinesia, which is a condition in which there is abnormal gallbladder motility but no structural obstruction. Similar patterns of hepatobiliary dysfunction have been described in neurologically impaired pediatric populations in which the autonomic regulation of the gastrointestinal organs may be disrupted [9].

The results of ultrasound analyses showed that hypokinetic forms of biliary dysfunction were more often observed than hyperkinetic patterns. This finding may be linked to reduced physical activity and altered autonomic regulation which is commonly found in children with cerebral palsy. In addition, the misuse of anticonvulsant medications for long periods of time, and the irregular feeding schedules may be factors in the impaired contraction of the gallbladder and impaired flow of bile. Previous clinical studies have suggested that children with severe neurological disorders are at increased risk of biliary stasis which can later lead to inflammatory hepatobiliary conditions if not detected at an early stage [10].

Laboratory markers of the liver function were normal in most of the participants, although slight biochemical variations were sometimes seen. Slight elevations of the liver enzymes were found in a small proportion of the children undergoing long-term pharmacological therapy. These biochemical changes did not necessarily mean structural damage of liver but could be effect of functional stress on hepatobiliary metabolism. Researchers have observed that chronic exposure to medications and nutritional imbalance can affect the activity of liver enzymes among pediatric patients with neurological disorders [11].

When were compared children with different degree of motor impairment, a tendency towards more pronounced forms of biliary dysfunction was shown in children with severe forms of cerebral palsy. Reduced mobility, impaired swallowing, and prolonged enteral feeding practices may be a combination of factors that affect the digestive motility and circulation of the bile. These findings are consistent with earlier findings that gastrointestinal complications in children with neurological disabilities are often secondary to impaired neuromuscular control of internal organs [12].

Overall, all the results obtained suggest that functional disturbances of the biliary tract appear relatively frequently among children with cerebral palsy. Although these disorders may not always cause serious clinical symptoms, they can have a major impact on the comfort of digestion and nutritional status. Early identification of hepatobiliary dysfunction may therefore play an important role in improving comprehensive medical management of this group of patients.

**Table 1.** Clinical and Ultrasound Features of Biliary Dysfunction in Children with Cerebral Palsy

| Indicator | Number of children (n) | Percentage (%) |
|---|---|---|
| Abdominal discomfort | 21 | 46% |

| | | |
|---|---|---|
| Nausea after meals | 16 | 35% |
| Reduced appetite | 18 | 39% |
| Ultrasound signs of bile stasis | 14 | 30% |
| Hypokinetic biliary dyskinesia | 19 | 41% |
| Hyperkinetic biliary dysfunction | 8 | 17% |

The table summarizes the most commonly observed clinical and ultrasound indicators of biliary malfunction of the examined children with cerebral palsy. Functional disturbance of the biliary tract was identified in a considerable amount of the participants. Hypokinetic biliary dyskinesia was the most frequent finding and symptoms such as abdominal discomfort and decreased appetite were very common as reported by caregivers, providing evidence of the clinical relevance of hepatobiliary evaluation in this population.

## 4. Discussion

The results of the current study have shown that functional problems of the biliary tract are relatively frequent among children with cerebral palsy and may be an underrecognized part of their overall clinical presentation. Although traditionally cerebral palsy was thought of as a neurological disorder with movement and posture as its main characteristics, more and more clinical evidence is emerging that systemic physiological processes, such as digestive, are also affected to a large degree by neurological impairment. The results obtained in this study support the growing understanding that gastrointestinal and hepatobiliary dysfunctions should be considered important comorbid conditions in children with severe neurodevelopmental disorders. One of the most notable aspects that we have observed in the group of people studied has been the predominance of hypokinetic biliary dysfunction. Ultrasound results were often the presence of delayed gallbladder contraction as well as signs of bile stasis and were typical findings indicating impaired biliary motility. These results are consistent with a concept that states that autonomic nervous system dysregulation plays a major role in the pathophysiology of gastrointestinal disturbances in children with cerebral palsy. The autonomic nervous system is responsible for the coordination of the motor activity of the digestive tract, such as the gallbladder contraction and the secretion of the bile. Damage of structures within the central nervous system may therefore result in a disruption of these regulatory mechanisms and the development of functional abnormalities in the biliary tract [13].

Another major factor that could contribute to hepatobiliary dysfunction in children with cerebral palsy is decreased physical activity. Many patients with severe motor impairment remain in sedentary positions for extended periods of time, which can have a negative impact on the circulation of the gastrointestinal tract and bile. Physical movement usually stimulates the digestive processes, and causes the rhythmic contraction of smooth muscles in the gastrointestinal tract. In children with restricted mobility this physiological stimulation is diminished and it can result in stasis of the bile and inability to empty the gallbladder. Similar mechanisms have been described in past pediatric studies examining the presence of digestive complications in children with neurological disabilities [14].

Nutritional factors may also be important in the development of biliary disorders in this patient group. Feeding difficulties have been well documented in children with cerebral palsy and can result in erratic dietary patterns, lengthy feeding periods and in some cases enteral nutrition. Such conditions may affect the usual stimulation of the secretion of bile, which is normally triggered during the regular food intake. In addition to that, insufficient intake of some nutrients may affect the metabolism of lipids and the hormone control of digestion further impacting the biliary function. It has been stressed among researchers that nutritional management is a key feature of the overall management

of children with cerebral palsy because digestive disturbance can have a major impact on growth and metabolic stability [15].

Pharmacological therapy is another possible contributing factor. Many children with cerebral palsy have long-term treatment with an anticonvulsant medication because of seizure disorders. While these medications are important in the management of the neurologic condition, they may affect hepatic metabolism and bile production. Some of the anticonvulsant drugs are known to have effects on the activity of liver enzymes and potentially impact the hepatobiliary function indirectly. Although the current study could not detect serious biochemical abnormalities in the majority of patients, mild alterations in liver enzyme levels seen in some of the patients may reflect the cumulative effects of long-term pharmacotherapy [16].

It is also important to emphasise therefore that hepatobiliary dysfunction in children with cerebral palsy could remain clinically silent for long periods. The symptoms are often nonspecific and may overlap with other gastrointestinal symptoms that commonly are seen in neurologically impaired children. As a result, biliary disorders may be missed unless diagnostic evaluation for these disorders is directed. Ultrasound examination proved to be a valuable tool for this study since it offered a means of non-invasive imaging of morphological and functional activity of the gallbladder. Early identification of biliary dyskinesia may help prevent more serious problems such as chronic inflammation, gallstone formation or continued discomfort in digestion [17].

## 5. Conclusion

The present study results highlight the fact that functional disturbances of the biliary tract are relatively common in children with cerebral palsy and may be an important but frequently underestimated component of their overall clinical condition. Although cerebral palsy is basically considered a neurological disease that affects motor development and posture, the results of this research have shown that cerebral palsy may also have a considerable effect on the digestive physiology, specifically the functioning of the hepatobiliary system. Clinical observations recorded many children with cerebral palsy had symptoms coming from digestive dysfunction like loss of appetite, episodic nausea, abdominal pain, and bizarre digestive patterns. These manifestations may be nonspecific at first and hence may not always be linked to biliary tract disorders. However, the instrumental findings made by ultrasound examination suggest the presence in a significant percentage of these patients of functional abnormalities of gallbladder motility. The predominance of hypokinetic biliary dyskinesia seen in this study appears to indicate that the functional disturbances of the gallbladder in terms of contraction and stagnation of bile may be closely related to the neurological and physiological manifestations associated with cerebral palsy. Several factors seem to be involved in development of these disturbances. Reduced physical activity, autonomic nervous system (ANS) dysregulation, feeding difficulties and long-term pharmacological therapy are likely to have a combined role in the changing the normal mechanisms that regulate bile secretion and gallbladder motility. In children with significant motor impairment, extended period of immobility and unbalanced nutritional intake may further worsen the digestive dysfunction leading to functional disorders of the hepatobiliary system. Early identification of the biliary dysfunction enables clinicians to take the preventive and therapeutic measures to improve the digestive comfort and nutritional status. Timely management of hepatobiliary disturbance may help to reduce the risk of chronic digestive complications and improve the general quality of the child with cerebral palsy. In conclusion, the results of this study highlight the importance of the multidisciplinary clinical approach in the management of children with cerebral palsy. Assessment of digestive and hepatobiliary function should be thought of as a part of routine medical care for these patients. The research is therefore necessary in larger numbers of patients and over longer periods to get a better

understanding of the mechanisms that underpin biliary dysfunction and effective ways of early diagnosis and targeted treatment..

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