SPASTIC CEREBRAL PALSY: A COMPREHENSIVE STUDY OF BIBLIOMETRICS, TRADITIONAL CHINESE MEDICINE SYMPTOMS ANALYSIS, AND CLINICAL INTERVENTION WITH ACUPUNCTURE AND TUINA

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By

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ABSTRACT

SPASTIC CEREBRAL PALSY: A COMPREHENSIVE STUDY OF BIBLIOMETRICS, TRADITIONAL CHINESE MEDICINE SYMPTOMS ANALYSIS, AND CLINICAL INTERVENTION WITH ACUPUNCTURE AND TUINA

WANG, XING

This research adopts an interdisciplinary approach. The first one is to summarize knowledge structure to understand the hotspots, trend, and frontier of research on spastic CP. The second one is to analyze the TCM symptom in children with spastic CP. The third one is to observe the clinical effect of acupuncture and tuina on spastic cerebral palsy. Its aim is to construct a comprehensive knowledge framework dedicated to investigating spastic cerebral palsy, with the goal of laying both theoretical groundwork and practical foundations for clinical interventions. In this study, data were gathered from 3988 publications on spastic CP retrieved from the Web of Science Core Collection (WoSCC) database spanning from January 1, 2000, to November 30, 2022. Analysis was conducted using tools such as WoSCC literature analysis wire, VOSviewer 1.6.18, CiteSpace 6.1.R4, and an online analysis platform for bibliometrics. Information from medical records of 231 eligible spastic CP cases was extracted, transformed, and analyzed. The analysis focused on general information and TCM symptoms associated with the condition. Cluster analysis and association rule analysis were employed to identify TCM core symptoms and patterns of syndrome correlations among children diagnosed with spastic CP. Treatment involved acupuncture and tuina (AT) for 83 patients and conventional rehabilitation for 85 patients, administered over a 12-week period according to the research protocol. Pre- and post-treatment assessments included the Modified Ashworth muscle tension scale (MAS), Gross Motor Function Measure (GMFM-D and GMFM-E), 6-minute walking distance measurement (6MWD), and Modified Children's Functional Independence Rating Scale (WeeFIM). The results of the study revealed key bibliometric trends over the past two decades in spastic CP, highlighting productive

countries, institutions, authors, and leading journals in the field. Noteworthy keywords and clusters included Spastic cerebral palsy, Reliability, and Gross motor function, with burst detection indicating hotspots such as management, controlled trials, and definition. The results provide potentially new directions in the study of spastic CP. TCM symptoms analysis showed the core symptoms among patients included motor dysfunction, impaired speech, delayed development, limb stiffness, and various tongue and pulse characteristics. Spastic CP should be classified as liver exuberant and spleen weakness of syndrome in TCM. After 12 weeks of treatment, both groups exhibited significant improvements in MAS scores ($p<0.01$), indicating reduced muscle tension, as well as increased scores in GMFM-D, GMFM-E, 6MWD, and WeeFIM ($p<0.01$ for all indicators), indicating enhanced gross motor function and functional independence. The AT group showed significantly superior outcomes compared to the control group ($p<0.01$ in all indicators). Furthermore, an inverse correlation was observed between children's age and treatment efficacy ($r= -0.496$, $p<0.01$ in AT group; $r=-0.540$, $p<0.01$ in control group), underscoring the importance of early intervention in CP management.

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of this thesis.

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APPROVAL SHEET

This dissertation/thesis entitled "**SPASTIC CEREBRAL PALSY: A COMPREHENSIVE STUDY OF BIBLIOMETRICS, TRADITIONAL CHINESE MEDICINE SYMPTOMS ANALYSIS, AND CLINICAL INTERVENTION WITH ACUPUNCTURE AND TUINA**" was prepared by WANG, XING and submitted as partial fulfillment of the requirements for the degree of Doctor Of Philosophy (Medical Science) at Universiti Tunku Abdul Rahman.

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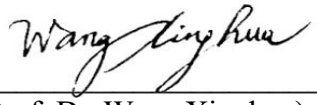

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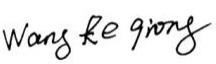

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SUBMISSION OF THESIS

It is hereby certified that WANG, XING (ID No: 21UMD00131) has completed this thesis* entitled "SPASTIC CEREBRAL PALSY: A COMPREHENSIVE STUDY OF BIBLIOMETRICS, TRADITIONAL CHINESE MEDICINE SYMPTOMS ANALYSIS, AND CLINICAL INTERVENTION WITH ACUPUNCTURE AND TUINA" under the supervision of Prof. Dr Wang Xinghua(Supervisor) and Assoc. Prof. Dr Teh Siew Hoon(Co-Supervisor) from the Department of Chinese Medicine, M. Kandiah Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman and Prof. Dr Wang keqiong (External Co-Supervisor) from Shaanxi University of Chinese Medicine, China.

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DECLARATION

I WANG, XING hereby declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UTAR or other institutions.

Wang Xing

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

CP	Cerebral palsy
TCM	Traditional Chinese Medicine
AT	Acupuncture and tuina
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
PET-CT	Positron Emission Tomography-Computed Tomography
EEG	Electroencephalogram
WoSCC	The Web of Science Core Collection
TLS	Total Link Strength
CPP	Citations per publication
TC	The total number of citations
SDT	Syndrome differentiation and treatment
LMICs	Low- and Middle-Income Countries
WFCMS	The World Federation of Chinese Medicine Societies
Tx	Treatment
MAS	Modified Ashworth muscle tension scale
GMFM D	The Gross motor function test (GMFM-88)
WL/6	The 6-minute walking distance measurement
WeeFIM	WeeFIM: Children's functional independence Rating Scale
GMFCS	Gross Motor Function Classification System

CHAPTER 1.0

INTRODUCTION

Cerebral palsy (CP) is one of the most common disabling condition during childhood. This refers to a group of permanent motor and posture developmental disorders and restricted activity syndrome that occur due to brain damage in developing fetuses or infants (Ostrander et al., 2024). Global population-based studies indicate a prevalence of CP ranging from approximately 1.5 to 4 per 1000 children (Arneson et al., 2009, Bhasin et al., 2006, Paneth et al., 2006, Johnson, 2002, Chauhan et al., 2019). In low- and middle-income countries (LMICs), the prevalence of CP is expected to be higher than in high-income countries, carrying an increased risk of severe motor impairments, poor nutritional status, and diminished health-related quality of life (Jahan et al., 2021, Jahan et al., 2022). Known risk factors include not only prenatal factors such as intrauterine infections but also perinatal factors like asphyxia and hypoxic-ischemic encephalopathy. Additionally, preterm birth, low birth weight, kernicterus, and trauma are also high-risk factors for postnatal infants and young children to develop CP (Mascarin et al., 2024, Abd Elmagid and Magdy, 2021). Despite the improvement in perinatal medical technology and advances in neonatal resuscitation techniques, the worldwide neonatal mortality rate has decreased, but the incidence of CP has not decreased. Among the different types of CP, spastic CP is the most prevalent, accounting for approximately 70% of cases (Evensen et al., 2023). The primary lesion site in spastic CP is the pyramidal system, characterized by increased muscle tone in the flexor muscles of the upper limbs, extensor muscles of the lower limbs, and adductor muscles. In later stages, tendon contractures, joint deformities, and muscle atrophy may occur, leading to significant impairment in gross motor function and severely impacting the affected child's daily life (Wahyuni, 2023). Clinical management of spastic CP poses significant challenges. Therefore, it is essential to

explore proactive and effective treatment measures to reduce muscle tone, alleviate limb spasticity, and improve gross motor function in affected children.

Although there are numerous reports on treatment methods for spastic CP, the efficacy and side effects remain a focus of research and debate. For instance, the use of neural stem cell therapy has become a hot topic in current CP treatment (Lv et al., 2023), however, the effectiveness and safety of its clinical application continue to be subjects of concern and contention among researchers. On the other hand, botulinum toxin treatment requires repeated or high-dose injections to consolidate its therapeutic effects, thereby imposing a burden on the families of affected children (Yang et al., 2023a). Modern medical rehabilitation therapies, such as physical therapy and occupational therapy, constitute the primary approaches for managing this condition. Study shows that a physiotherapy strategy that integrates personalized treatment plans, evidence-based interventions, and innovative technologies has a beneficial impact on the motor skills and functional abilities of children with cerebral palsy (Kim, 2023). Nonetheless, rehabilitation treatment is time-consuming, expensive, and exhibits slow efficacy (Fehlings et al., 2023). Furthermore, the use of certain medication to reduce muscle tone is limited due to their numerous side effects (Brunner and Götz-Neumann, 2023). Therefore, the exploration of cost-effective and efficient methods for treating spastic CP is an urgent issue currently faced by clinical practitioners.

According to previous literature reports, complementary medicine practiced in East Asia, particularly TCM, are used to treat CP widely. For instance, acupuncture and tuina(AT) methods of TCM have shown advantages and efficacy in treating spastic CP. Currently, acupuncture treatment for spastic CP includes techniques such as scalp acupuncture, body acupuncture, electroacupuncture, acupoint injection and combination of acupuncture and moxibustion and other therapies (Elken et al., 2022). Head acupuncture is known to improve cerebral blood flow and promote brain function recovery (Jin and Jin, 2023). Likewise, body acupuncture achieves therapeutic goals by unblocking meridians, harmonizing yin and yang, and regulating

internal organs. Tuina therapy, on the other hand, achieves similar therapeutic effects by stimulating acupuncture points and meridians throughout the body, thereby releasing muscle tension. However, many Western medical neurology or rehabilitation physicians currently believe that acupuncture treatment may exacerbate spasticity in patients and lead to increased muscle tone in the limbs due to the pain stimulation caused by needling. Additionally, some clinical practitioners argue that the existing literature on acupuncture treatment for spastic CP lacks quantifiable efficacy evaluation indicators and is not compelling enough. Moreover, the individualized treatment strategies inherent in acupuncture and tuina methods pose challenges to their widespread clinical application, further emphasizing the need for cautious utilization of this therapy.

Furthermore, it is important to note that terms such as CP and spastic CP are modern medical terms and do not appear in TCM. However, throughout the history of medical literature, there are numerous diseases with symptoms and etiologies similar to those of CP. This disease is generally grouped under the scope of "five lates", "five softs "and "five hards" (Wang et al., 2023b), which is mostly related to insufficient congenital endowment or improper parenting after birth. Various medical experts in different periods have different opinions regarding the differentiation and classification of these diseases, and there is no consistency standard. For example, in the book 'ChaoShi BingYuan' recorded the similar symptoms which are "delay growth of teeth", "delay growth of hair", "unable to walk in the age of several years old" and "no language ability at the age of four or five". Qian Yi also recorded in the "XiaoEr YaoZheng ZhiJue" that " When you grow up, you can't walk. Even if you can walk, your feet are thin... You don't have hair for a long time. Even if your hair grows, your hair is not black." Such as the typical symptoms of the disease. This disease is mostly identified as the problem of the "brain", and is closely related to the "liver", "spleen", "kidney" and other viscera. The book "ZhangShi YiTong. YingEr Men" points out that the cause of the disease is due to "The fetus is weak, it is caused by parents' lack of blood essence and weak kidney qi". The book "HuoYou XinShu · five

softsness” advocated that the present of the five softsness is due to: Insufficient of the father’s essence and prolonged deficiency of the mother’s blood" .In addition, the book “Baoying Sheyao · five softsness” points out that “the five softsness... Are all due to the weakness of the Qi of the five organs, it can't be nourished and topped up...”, “The source is always attributed to the stomach...”. “YiZong JinJian · YouKe ZaBing XinFa YaoJue” also mentioned that “Parents have weak Qi and blood, congenital deficiency...” “the Qi of all Yang is insufficient...” is the basic cause of the disease. This illustrates the complexity of the TCM pathogenesis and clinical patterns associated with this condition (Di and He, 2023, Jiao and Wang, 2022).

The problem statement of this study is to address the lack of comprehensive understanding and effective treatment methods for spastic CP, particularly within the framework of TCM. Nowadays, the incidence of CP remains high, with significant challenges in clinical management. Complementary medicine, particularly TCM, including AT, has shown promise in treating spastic CP. However, there is a lack of standardized method in existing literature, hindering widespread clinical application. Additionally, the terminology and classification of CP in TCM differ, posing challenges to integration into modern medical practice. Therefore, combining spastic CP with TCM syndrome types and exploring standardized interventions seems to be an option to overcome the current treatment dilemma. The study aims to comprehensively investigate spastic CP through bibliometrics, TCM symptoms analysis, and clinical interventions. The objectives include mapping global research trends, understanding TCM mechanisms, and evaluating the efficacy of standardize AT in children with spastic CP. By addressing these gaps, the research aims to provide insights for future research, treatment, and improved outcomes for spastic CP patients.

The core objective of this study was to:

1. To map out the global research trends and hotspots in the field of spastic CP. The study allowed us to identify key topic areas, innovative methodologies,

and emerging theoretical perspectives that currently dominate spastic CP research. Moreover, our analysis also highlighted crucial gaps and potential areas for future research.

2. Through the analysis of the general demographic characteristics, TCM symptoms, tongue and pulse characteristics of children with spastic CP to understand the TCM mechanism of the disease, contribute an evidence-based understanding of symptoms in spastic CP.

3. Through a Non-random, single-centered clinical study with a design specification to further explored the potential efficacy of a standardized TCM treatment -AT – in treating children with spastic CP.

CHAPTER 2.0

LITERATURE REVIEW

2.1 The Definition of CP

CP stands as the prevalent childhood disability impacting motor functionality, arising from brain injury during development. Often referred to as 'Little's disease,' it was initially characterized by William John Little in 1843. Little emphasized that spasticity is a consequence of brain damage during infancy, premature birth, or birth asphyxia (Paul et al., 2022). CP was initially delineated by Little in 1861, and over the 150 years that followed, perspectives regarding its etiology and clinical manifestations have undergone significant evolution. By 2006, CP was defined as a collection of enduring developmental disorders affecting movement and postures, resulting in restricted activity (Rosenbaum et al., 2007).

Although extensive research on CP had been conducted all over the world, it remains a complex condition, and to date, there is no universally accepted, comprehensive, and clear-cut definition. The evolution of its definition spans over a century, and it still revolves around the following three essential elements: 1 Developmental: CP results from damage to brain tissue during the growth and development process. It signifies various factors acting on immature, growing brain tissue rather than on already developed and mature brain tissue. 2 Non-progressive: The lesions and symptoms of CP are non-progressive; the condition does not worsen over time. 3 Permanent: CP is not a transient ailment; rather, it is a permanent central motor function disorder (Arpino et al., 2010, Panteliadis et al., 2015).

The intricate interplay of these developmental, non-progressive, and permanent

elements lays the foundation for a comprehensive comprehension of CP, offering insights into its etiology, progression, and the challenges faced by those affected. With these key aspects in mind, an endeavor can be made to define CP as a group of enduring central motor and posture developmental disorders that lead to restricted activity. These disorders arise from non-progressive damage to the developing brain of a fetus or an infant (Hoque, 2016). The motor impairments associated with CP are often accompanied by sensory, perceptual, cognitive, communicative, and behavioral impairments. Additionally, epilepsy and secondary musculoskeletal issues may also be prevalent among individuals affected by this condition (Pruitt and Tsai, 2009, Gunel, 2009).

2.2 The Definition of spastic CP

Spastic CP refers to non-progressive brain damage incurred during the developmental process of an immature brain, influenced by various factors (Sukhadia and Kamboj, 2024). It is the most common and widely affecting condition among CP patients, hence emerging as a focal point of scholarly interest in recent years. This condition often manifests as varying degrees of increased muscle tone and the persistence of primitive reflexes, leading to motor dysfunction, joint contractures, and impaired balance functions, thereby causing significant negative impacts on the daily lives, activities, and social participation of affected individuals (Cho and Lee, 2020, Yun et al., 2023). In Western medicine, the mechanism underlying spasticity in cerebral palsy is considered complex. It is generally believed that damage to the central nervous system results in a disruption of the central nervous system's regulation of spinal stretch reflexes, thereby intensifying these reflexes (Wahyuni, 2023, Brandenburg et al., 2023).

2.3 Prevalence of CP

The first incidence rate for CP was reported by Perlstein (1949) which is up to 4% (Perlstein, 1949). Subsequent epidemiological investigations in various countries, including the United Kingdom, Russia, Sweden, Japan, and China, corroborated Phelps' findings, suggesting a global prevalence ranging from 0.15% to 0.40%. This range indicates a consistency in reported incidence rates across diverse regions, further underlining the global health impact of CP (Downs et al., 2018, Shaunak and Kelly, 2018, Heijtz et al., 2018, Gulati and Sondhi, 2018).

2.4 Underlying Etiologies of CP

Understanding the etiology of CP is intricate, encompassing three distinct periods: pre-birth, perinatal, and post-birth (Korzeniewski et al., 2018, Rana et al., 2017). Perinatal factors stand as the primary contributors, constituting approximately 70-80% of cases. Around 20-30% of cerebral palsy cases are influenced by factors before birth, highlighting the importance of the time before birth. After birth, factors contribute to 10-20% of cases, playing a smaller but still significant role (Benfer et al., 2024). This triphasic division underscores the multifaceted origins of CP, necessitating a comprehensive approach to decipher the intricacies of its causation.

2.4.1 Prenatal Factors

The prenatal period, preceding birth, encompasses a multitude of factors that could significantly impact the potential development of CP (Sadowska et al., 2021, Upadhyay et al., 2020). These factors involve a wide array of conditions and situations, including parental habits like smoking and alcohol consumption, instances of threatened abortion, medication usage during pregnancy, exposure to harmful substances, traumatic incidents, hypertensive disorders during pregnancy, rheumatic

conditions, syphilis, diabetes, toxoplasmosis, and compromised placental functionality (Thakkar and Iyengar, 2023).

2.4.2 Perinatal Factors

Perinatal period is referring to the period before and after birth that could potentially contribute to the onset of CP (Badawi et al., 2021, Jöud et al., 2020). These include, but are not limited to, instrumental delivery methods such as forceps or vacuum extraction, breech births where the baby is positioned feet or buttocks first, prolonged or rapid labor, instances of perinatal asphyxia, premature or post-term birth, the birth of multiple infants (twins, multiples), and occurrences of kernicterus, a condition characterized by jaundice and associated with high levels of bilirubin in the blood (Tegegne, 2023). Instrumental delivery methods, such as forceps or vacuum extraction potentially leading to trauma or injury to the brain, which may increase the risk of CP. Additionally, the need for instrumental delivery may itself be indicative of underlying factors, such as fetal distress or abnormal presentation, which could also contribute to the risk of CP (Thakkar and Iyengar, 2023).

2.4.3 Postnatal Factors

The period after birth, known as the postnatal phase, encompasses a range of factors that could significantly contribute to the development of CP (Owens et al., 2020). These factors include incidents such as head trauma, intracranial hemorrhage, seizures, infections, toxic exposure, and nutritional deficiencies.

Exploring this further, it is widely acknowledged by experts that certain high-risk factors can elevate the predisposition of CP (Mendoza-Sengco et al., 2023, Bearden et al., 2016). These factors comprise prematurity, perinatal asphyxia, severe neonatal

jaundice, and low birth weight (weighing less than 2500g within the first hour after birth). CP in affected children can be attributed to one or a combination of these high-risk factors. However, it's important to note that a significant number of children with CP may not demonstrate these aforementioned high-risk factors (Gowda, 2020).

2.5 Pathological of CP

Currently, CP is primarily attributed to congenital brain abnormalities and the residual effects of perinatal brain injuries. The spectrum of congenital brain abnormalities is extensive, displaying a variety of pathological changes without distinctive features (Hirides et al., 2023). Likewise, the sequelae of perinatal brain injuries encompass numerous types, necessitating differentiation from sequelae caused by acquired brain injuries. While a substantial body of literature indicates that as many as 30% of CP cases involve copy number variations (CNVs) or single-gene mutations, definitively determining the pathogenicity of some variations remains challenging due to limited sample sizes, inadequate confirmatory studies, and the influence of genetic heterogeneity (Van Eyk et al., 2018, van Karnebeek et al., 2018). Some clinical management guidelines do not advocate for genetic testing as a routine diagnostic measure for CP. Furthermore, there is a lack of standardized and consistent operational procedures for etiological diagnosis in CP (Corbett et al., 2018). Consequently, there remains a need for further research and consensus in this area to enhance diagnostic accuracy and to guide for appropriate clinical management strategies.

2.5.1 Congenital Brain Abnormalities

Congenital brain abnormalities primarily result from disruptions in the early neural tube closure during fetal development, typically occurring after the first trimester,

causing hindrances in neuronal genesis and migration (Pooh, 2021, Adle-Biassette et al., 2018). These anomalies often manifest as multiple malformations in the gyri, particularly found in the parietal and occipital lobes. They may also involve the formation of thick gyri, often associated with heterotopia of the olivary nucleus in the medulla. Moreover, cases of polymicrogyria can arise due to various factors during the 5th to 6th month of gestation, such as exposure to carbon monoxide, cytoplasmic inclusion body disease, congenital myotonic dystrophy, and leukodystrophy. These early brain malformations usually do not exhibit distinct pathological changes and necessitate further research for comprehensive understanding (Jacobs et al., 2023).

2.5.2 Sequelae of Kernicterus

Kernicterus-induced CP typically occurs during the 5th to 6th month of pregnancy due to factors such as carbon monoxide poisoning, cytoplasmic inclusion body disease, congenital myotonic dystrophy, and leukodystrophy (Karimzadeh et al., 2020, Okoth et al., 2018). The affected areas show a decrease in neural cells, reduced myelinated fibers, hypertrophy of astrocytes, and fibrous formation. There is poor development of the corticospinal tract, with a reduced number of myelinated fibers, particularly pronounced in premature infants. Staining of the cerebral white matter reveals poor coloring (McGillivray et al., 2023). The manifestation of kernicterus-induced CP is often a choreoathetoid type, marked by involuntary, writhing movements and athetosis in addition to spasticity. The basal ganglia, especially the globus pallidus, and the hippocampus are regions frequently affected by the bilirubin toxicity in kernicterus. The damage to the brain structures impairs the motor control and coordination, resulting in the characteristic movement disorders observed in these cases. Furthermore, the severity of the CP can vary depending on the extent and location of the lesions in the brain caused by kernicterus. Advanced imaging techniques like MRI provide a clearer visualization of these brain anomalies, aiding in better understanding and management of this type of CP (Kasirer et al., 2023).

2.5.3 Postpartum Brain Injury Sequelae

CP resulting from postpartum brain injury is typically attributed to a combination of hypoxia and mechanical trauma during the birth process. The pathological manifestations involve a reduction or loss of brain cells, gliosis (an abnormal increase of glial cells), tissue degradation, and the formation of multiple cavities, often appearing in a symmetric pattern. The cortical regions are primarily affected, and in severe cases, the subcortical regions can also suffer damage. Among these, the thalamic medial dorsal nuclei are particularly susceptible to injury during the perinatal period (Novak et al., 2018, Davidson et al., 2018).

2.5.4 Spastic Brain

Brain damage resulting from spasms and convulsions ultimately leads to CP, often caused by circulatory disorders and brain edema. The pathological manifestations include ischemic and hypoxic changes, with observed gliosis in the hippocampus and thalamus (Vlasyuk and Vlasyuk, 2019). The spasms and convulsions trigger a cascade of events that disrupt blood flow and oxygen supply to the brain, leading to cellular damage and subsequent gliosis. Particularly affected regions include the hippocampus, critical for memory and learning, and the thalamus, essential for relaying sensory and motor signals in the brain (Cajigas et al., 2023).

2.6 Neurophysiological Alterations

2.6.1 Relationship Between Motor Function and Neuroanatomical Morphology

The motor impairments in CP arise from brain damage, leading to abnormalities in the functioning of the central nervous system. Based on the specific locations of the lesions, these impairments can be anatomically and physiologically categorized into three main types: damage to the pyramidal system, damage to the extrapyramidal system, and damage to the cerebellum (Ogoke, 2018). The pyramidal system is responsible for governing voluntary movements of skeletal muscles. When there is damage to the pyramidal tract, it manifests as varying degrees of impairment in voluntary movements of the limbs. On the other hand, the extrapyramidal system primarily regulates muscle tone, coordinates muscle activities, adjusts posture, and controls habitual, rhythmic movements, as well as gross motor activities. Damage to the extrapyramidal system leads to alterations in muscle tone and involuntary movements. The cerebellum plays a pivotal role in maintaining bodily equilibrium (through the vestibulospinal tract), adjusting postural reflexes (via the spinocerebellar tract), and regulating voluntary movements (through the cortico-ponto-cerebellar tract) (Takakusaki, 2017). Injury to the cerebellum results in a range of motor challenges, including balance disorders, ataxia, coordination difficulties, and disturbances in movement amplitude (Stoodley and Limperopoulos, 2016). While CP is most frequently associated with damage to the cerebral cortex, cases solely attributed to cerebellar damage are exceedingly rare. In reality, the majority of CP cases stem from damage to the cerebral cortex or basal ganglia (Bhorat et al., 2024).

2.6.2 Abnormal Postural and Movement Patterns

Movement is a sequence of continuous changes in posture, and CP involves disruptions in this seamless coordination of posture and motion. Individuals with CP face challenges in executing voluntary movements, resulting in a departure from normal functionality (O'Malley, 2022). Furthermore, they exhibit symptoms that are atypical in individuals without CP, such as abnormal muscle tension. The deviations in posture and movement observed in individuals with CP stem from factors such as

irregular muscle tension, heightened reflex activities, and conflicting neural control (Hall et al., 2023).

2.6.3 Motor Development and Regulation

Motor impairments caused by CP markedly diverge from those observed in adults with movement disorders. CP happens from early childhood brain injury, occurring before the brain reaches full maturation (Pruszczynski et al., 2016). The development of motor function is influenced by the growth of children. These children display a coexistence of postures that align relatively well with those of their non-affected peers, alongside immature and abnormal postures. CP arises from early developmental damage to the central nervous system, resulting in incomplete neurological development and, consequently, imperfect functionality. Primitive reflexes persist in these individuals, influencing the appearance of other postural reflexes and leading to abnormal coordination of movements and voluntary motor actions (Zhou et al., 2017).

2.6.4 Neurological Basis of Motor Function Rehabilitation

Lately, there has been a notable shift of the approaches in treating CP-like conditions which involving central nervous system motor impairments. This transformation has been underpinned by a deep understanding of neurophysiology and neurodevelopment. Evaluations and diagnoses now hinge on posture, reflexes, and voluntary movements, aligning with the expected trajectory of normal development. This nuanced understanding guides the selection of precise treatment methodologies aimed at curbing abnormal movements while fostering normal ones (Aisen et al., 2011). The crux of the treatment strategy lies in targeted stimulation of specific peripheral regions. Through this approach, we continually relay normative sensory stimuli from the periphery to the central nervous system. This strategic relay mechanism essentially

assists in establishing and fortifying normal motor functions, contributing to a comprehensive rehabilitation approach for individuals dealing with motor function challenges, particularly those associated with conditions like CP (Anaby et al., 2017, Trabacca et al., 2016).

2.7 Classification of CP

In 1956, the American Academy for Cerebral Palsy and Developmental Medicine (AACP) introduced a groundbreaking classification system for CP. This classification system considered the earliest and most comprehensive of its kind globally, provided a structured framework for understanding and categorizing CP. Its influence has been extensive, and it became widely adopted by countries around the world, establishing a foundational basis for research, diagnosis, and treatment of CP (Takezawa et al., 2018, Tseng et al., 2018).

2.7.1 Classification of Physiological

In the realm of physiological categorization, CP is sub-divided based on distinct motor manifestations: 1.Spasticity; 2.Athetosis: tension, non-tension, and dystonia; 3.Rigidity; 4.Ataxia; 5.Tremor; 6.Atonia; 7.Mixed; 8.Unclassified (Oh, 2019).

2.7.2 Classification of Paralyzed Body Parts

In the realm of paralyzed body parts, CP is sub-divided as follows: 1.Monoplegia: Refers to paralysis of one limb. 2.Paraplegia: Refers to paralysis of both lower limbs. 3.Hemiplegia: Refers to paralysis of the limbs on one side, either upper or lower. 4.Triplegia: Refers to the paralysis of three limbs, often involving both lower limbs

and one upper limb. 5.Quadriplegia or Tetraplegia: Refers to complete paralysis of all four limbs. 6.Diplegia: Refers to a four-limb paralysis where the lower limbs are more affected than the upper limbs, mostly seen in spastic CP. 7.Double Hemiplegia: Refers to a four-limb paralysis where the upper limbs are more affected than the lower limbs, mostly seen in choreoathetoid CP (Bevans and Tucker, 2020).

2.7.3 Classification of Etiological

The etiology of CP is a highly intricate field, involving a complex interplay of non-genetic and genetic factors. Biological and environmental influences during the prenatal, perinatal, and postnatal phases remain pivotal risk factors for CP, with the potential for interaction between individual or multiple risk factors during these critical developmental periods (Pavone and Testa, 2015, Pattar and Yelamali, 2015, Jain et al., 2015). In recent years, breakthroughs in molecular genetics, metabolomics, and proteomics have provided new opportunities for precise diagnostics and personalized treatments for CP (Xin et al., 2023). However, with these advancements comes the challenge of selecting the most appropriate diagnostic methodologies to accurately determine the etiological origins of CP.

2.7.4 Classification of Supplementary

In addition to primary classifications, supplementary classifications provide further insights into various aspects of CP: 1.Cognitive Evaluation: Assessing intellectual abilities and potential cognitive impairments (Raya et al., 2015). 2.Physical Status: Evaluating physical development, developmental stage, and fertility potentia l(Bjornson et al., 2008). 3.Spasmodic Episodes: Examining occurrences of spasms or sudden muscular contractions. 4. Posture and Behavior: Analyzing posture and behavioral patterns (Viruega et al., 2019). 5.Hand-Eye Coordination: Assessing the

coordination between hand and eye movements, including dominance of the eye, eye movements, position of the eye, gaze, convergence, grasping techniques, and dominant hand. 6.Visual Status: Sensory: Evaluating sensory aspects such as weak vision and visual field deficits. Motor: Examining motor aspects like deviation of the eyes, fixation issues, spasms, strabismus (crossed eyes), esotropia (inward deviation of the eye), exotropia (outward deviation of the eye), hypertropia (upward deviation), hypotropia (downward deviation), nystagmus (involuntary eye movements), and pseudo-paralysis (false paralysis) (Lew et al., 2015). 7.Auditory Status: Assessing aspects related to hearing, including tone and decibel impairments. 8.Language Impairment: Evaluating difficulties and impairments in language abilities (Pennington, 2008).

2.8 Clinical Manifestations of CP

In infancy, CP primarily manifests as developmental delays in motor functions, noticeable as substantial lag and stagnation compared to peers of the same age (Goin et al., 2004). Infants exhibit retained primitive reflexes that should normally diminish and a lack of expected midbrain-level and cortical balance reflexes. These challenges in reflex development are characteristic features of CP during infancy. Transitioning from infancy to early childhood, the clinical features of CP become more pronounced. Changes in abnormal postures, reflex responses, and muscle tone are readily observable. Distinctive signs of CP gradually emerge during this phase, such as a progressive increase in muscle tone (Sanger, 2015). This is evident in the flexion of upper limbs, adduction, internal rotation, crossing of limbs, tiptoeing, and impaired motor functionality. The manifestations of CP continue to evolve as the child progresses through childhood. Spasticity, involuntary movements, coordination difficulties, and other motor impairments become more pronounced. Moreover, additional challenges in speech, hearing, and vision may further compound the overall clinical picture. Each stage of development presents distinct clinical features,

emphasizing the need for tailored assessment and intervention strategies for individuals with CP (Shikako-Thomas et al., 2009).

The developmental trajectory of the brain unfolds in distinct stages and critical temporal windows, each characterized by specific neuropathological aberrations and clinical manifestations. Proficient classification and diagnosis of CP involve a thorough analysis of the child's motor and posture features, neurological signs, limb conditions, and the relevant risk factors (Hamer et al., 2011). This integrated approach allows for a nuanced understanding of CP etiology based on the different stages of brain development. For instance, spastic quadriplegia is closely tied to severe perinatal asphyxia in full-term infants, profound brain damage in preterm infants, diffuse bilateral giant cerebral hemispheres, or multiple malformations in undersized cerebral hemispheres. Spastic diplegia, a prototypical CP subtype, typically manifests after hypoxic-ischemic events or hemorrhagic brain injury in preterm infants. Hemiplegia with a dominant upper limb often presents in full-term infants with stroke or unilateral congenital brain malformations. Conversely, lower limb predominance is evident in asymmetric or unilateral periventricular leukomalacia, primarily observed in preterm infants. Non-athetoid CP typically occurs in term or preterm infants afflicted with bilirubin encephalopathy or severe hypoxic-ischemic brain injury, with infrequent instances associated with bilateral basal ganglia developmental anomalies. Spastic quadriplegia accompanied by microcephaly is commonly linked to severe asphyxia, intrauterine infections, or congenital brain malformations. Dyskinetic CP is predominantly rooted in genetic factors, including conditions such as Joubert syndrome, Dandy-Walker malformation syndrome, and incomplete cerebellar hemispheric development. Mixed CP, characterized by a blend of spasticity and involuntary movements, often coexists with multiple disabilities like epilepsy, microcephaly, visual impairment, and intellectual disabilities. This complex profile is prevalent in full-term infants or extremely premature infants with a history of severe hypoxic-ischemic brain injury (Lee et al., 2010, Chen et al., 2010, Delacy et al., 2016).

2.8.1 Spastic CP

Spastic CP, the most prevalent type of CP, predominantly affects the pyramidal system, accounting for about 70% of CP cases (Skoutelis et al., 2020, Monica et al., 2021). This type of CP is characterized by heightened stretch reflexes and continuous muscle tension, which significantly impairs motor function. The pathology of spastic CP primarily involves the pyramidal system, a crucial component of the central nervous system responsible for voluntary movement control. The heightened stretch reflexes result in increased muscle tone and exaggerated muscle contractions, leading to stiffness and difficulties in movement. The sustained muscle tension further contributes to the challenges in coordinating and executing voluntary motor actions. This type of CP often manifests as stiffness, spasticity, and jerky movements in affected muscles, particularly in the limbs (Skoutelis et al., 2020, Monica et al., 2021).

2.8.2 Athetoid CP

Athetoid CP, primarily affecting the extrapyramidal system, is a common type of CP characterized by involuntary movements, constituting about 18% of CP cases. The main feature of athetoid CP is involuntary movement, presenting as intermittent athetoid, chorea, and transient focal contractions. In this type of CP, there is a disruption in the normal control of movement, leading to uncontrollable and involuntary motions, often affecting the hands and feet (Harada et al., 2022, Seok et al., 2021).

2.8.3 Rigidity CP

Rigidity CP is associated with damage to the pyramidal tract and is also known as spastic, rigid, or contracted CP. In clinical practice, pure rigidity CP is rare and often

occurs in a mixed form. The main characteristics include consistent and uniform resistance during passive movements, bidirectional resistance during passive movements, maximal resistance during slow movements, and non-hyperactive tendon reflexes. This type of CP affects the extrapyramidal system and is marked by muscle stiffness and increased muscle tone (Bjornson et al., 2023).

2.8.4 Hypotonic CP

Hypotonic CP, also referred to as the hypotonic or flaccid type of CP, is a condition that is exceptionally uncommon i.n its pure form within clinical settings. The primary feature of this type of CP is the reduction of muscle tone. Most individuals affected by this condition are infants, and they face challenges in developing anti-gravity muscle extension, resulting in a diminished ability to engage in independent activities (Levy et al., 2020).

2.9 Diagnosis of CP

2.9.1 Early Diagnosis of CP

The definitive diagnosis of CP is typically made at the age of 1 to 2 years, or even at 5 years (Pearson et al., 2019). However, in recent years, advancements in methodology have allowed for the diagnosis or risk prediction of CP before the corrected age of 5 months (Groos et al., 2022, Harpster et al., 2021). Prior to the corrected age of 5 months, valuable tools for predicting the risk of CP include magnetic resonance imaging (MRI) at 1 month of corrected age (sensitivity 86%–89%), General Movements Assessment (GMA) by Prechtl (sensitivity 98%), and the Hammersmith Infant Neurological Examination (HINE) at 1 month of corrected age (sensitivity

90%). Beyond the age of 5 months, effective tools for predicting CP risk include MRI (sensitivity 86%–89%), HINE (sensitivity 90%), and the Child Developmental Assessment (C index 83%). Timely referral of children at high risk for CP or those diagnosed with CP to rehabilitation professionals for specific early interventions can optimize motor and cognitive plasticity, prevent secondary complications, and enhance overall prognosis (Kim et al., 2024).

With the progression of rehabilitative medicine, the early diagnosis of CP has garnered significant attention from scholars worldwide. However, there is no consensus regarding the precise timeframe defining "early diagnosis" of CP. Some scholars argue that a diagnosis made within 6 or 9 months after birth falls within the category of "early diagnosis." In recent years, there has been a proposition of "ultra-early diagnosis," indicating a diagnosis within the first 3 months after birth. CP constitutes a set of permanent syndromes involving motor and posture developmental disorders. A diagnosis of CP must adhere to defined criteria and strive to achieve localization and classification based on symptom characteristics. To facilitate early diagnosis, Vojta, after years of dedicated research, introduced the concept of Central Coordination Disorders (CCD) (Andrzejewska et al., 2021). According to his proposition, this condition can be diagnosed as early as 2 weeks after birth, allowing for the initiation of treatment during the neonatal period. This theory gained rapid acceptance among scholars globally and has been applied in many countries.

2.9.2 Diagnosis of CP

In the diagnostic process of CP, the presence of identifiable high-risk factors causing brain damage is crucial (Glass et al., 2021). Developmental neurological abnormalities associated with brain injury encompass a range of manifestations, including posture anomalies, reflex irregularities, muscle tone abnormalities, and seven specific types of posture reflex abnormalities. Moreover, the symptoms that are

indicative of brain injury, including early signs and observable clinical features, need to be considered in the diagnostic evaluation. Adherence to the three fundamental elements of CP is essential for a precise diagnosis: firstly, the brain tissue experiences damage during the growth and developmental stages (developmental); secondly, clinical symptoms subsequent to brain injury do not show a progressive pattern (non-progressive); and thirdly, the movement disorders that emerge after brain injury persist and are not transient in nature (permanent) (Jaster et al., 2022). In cases where a patient's condition does not align with these three criteria, a thorough and comprehensive examination, along with a meticulous analysis, becomes imperative. Without satisfying these criteria, a conclusive diagnosis of CP can not be established.

2.9.2.1 Testing for Non-Genetic Etiologies

Considering the necessity of differential diagnosis and the need for laboratory evidence in a minority of non-genetic cases of CP, it is recommended to conduct the following laboratory tests for children with CP (Brown et al., 2020). 1.Routine Laboratory Tests: These include standard laboratory examinations such as complete blood count, urinalysis, biochemical analysis, cardiac enzyme profile, lactate levels, ketones, and thyroid function tests. These tests are suitable for all CP patients, especially those with early hypotonia accompanied by comprehensive developmental delays. 2.Virological Testing: This is applicable for individuals with associated congenital hepatosplenomegaly, rashes, microcephaly, intracranial calcifications, and sensory impairments, suspected to have infections like toxoplasmosis, rubella virus, cytomegalovirus, or herpes simplex virus (McIntyre et al., 2013). 3.Genetic Metabolic Testing: Tests for blood and urine organic acids, amino acids, fatty acids, and other genetic metabolic disorders are suitable for infants experiencing difficulty in early feeding, metabolic disturbances, abnormal liver function, or organ involvement, along with specific odors, abnormal skin and hair, and distinct facial features. These tests are recommended for etiological differential diagnosis.

2.9.2.2 Testing for Genetic Etiologies

Genetic etiology in CP manifests in two scenarios: 1.Genetic factors cause non-progressive brain developmental abnormalities resulting in CP. 2.Genetic predisposition makes children more susceptible to brain injuries under specific circumstances, leading to CP. Genetic causes and susceptibility are closely associated with the types of CP (MacLennan et al., 2015). Although the importance and value of genetic testing in CP etiological diagnosis are increasingly recognized, routine genetic testing is not recommended in CP diagnostic guidelines. Clinicians should select appropriate testing methods based on the phenotypic characteristics of the affected children (Janzing et al., 2024).

2.9.3 Differential Diagnosis of CP

CP requires precise differentiation from transient movement disorders and developmental delays, as well as exclusion of progressive diseases such as brain tumors or encephalitis. It's crucial to distinguish CP from intellectual disabilities, brain malformations, and differentiate between hypotonic CP and progressive muscular atrophy, as well as hypotonic CP and benign congenital hypotonia, among other similar conditions (Fairhurst, 2012). Diagnosing CP involves a thorough clinical evaluation, including medical history, physical examination, neuroimaging studies, and sometimes genetic testing or metabolic screening (Monica et al., 2023).

2.9.4 Auxiliary Examinations for CP

CT, MRI are two important diagnoses for patient to rule out CP.

Computed Tomography(CT): It has been reported that 70.37% to 92.59% of CP patients exhibit abnormalities in head CT scans. Additionally, there are reports

indicating that the abnormality rate in CP CT scans is 74.7%. This suggests that approximately two-thirds of CP patients present with CT abnormalities. Common abnormalities observed in head CT scans of CP patients include cortical atrophy, ventricular enlargement (37.1%), global brain atrophy (38%), hypodense lesions (19.75%), hyperdense lesions (2.17%), cavum septum pellucidum (12.35%), cavum Vergae (8.64%), cavum veli interpositi (27.16%), septum pellucidum defects (2.17%), agenesis of the corpus callosum (2.17%), cerebral aqueduct deformities (1.23%), localized ventricular atrophy (4.94%), diffuse hypodensity of the entire brain (2.47%), cerebellar abnormalities (9.88%), cerebral fissure and gyral abnormalities, among other changes (Sadiq and Nooruldeen, 2021).

Magnetic Resonance Imaging(MRI): It can provide clear differentiation of brain cortex and white matter structures through multi-directional scans, including axial, sagittal, and coronal planes. They offer excellent visualization of areas such as the skull base, midline structures, posterior fossa, and medial aspects of the brain. MRI has a high detection rate and can reveal lesions that CT scans may not differentiate or display effectively, such as gyral abnormalities, agenesis of the corpus callosum, gray matter heterotopia, brain atrophy, white matter lesions, and more. MRI boasts a very high detection rate (Himmelmann et al., 2021, Springer et al., 2019).

Positron Emission Tomography-Computed Tomography(PET-CT): It can accurately reflect the cerebral blood flow in specific brain regions. Through this examination, epileptic lesions can be detected in CP patients with epilepsy, with a high level of concordance with EEG results. It offers high accuracy and is valuable for the differential diagnosis of CP (Wu et al., 2022).

Electroencephalogram(EEG): CP patients often suffer from conditions like epilepsy, in addition to motor function disorders. Therefore, routine electroencephalogram (EEG) examinations are recommended for CP patients to identify epilepsy in its early stages and facilitate timely treatment (Bakheet et al.,

2021).

Other Examinations: Skull X-rays, evoked potentials, electromyography, and other tests can all be used for the diagnosis and differential diagnosis of CP.

2.10 Rehabilitation Strategies for CP

The fundamental objective of rehabilitation is to employ a comprehensive range of medical, engineering, psychological, educational, and social interventions, among others, to facilitate maximal recovery and compensation for individuals with CP. This holistic approach targets their physical, psychological, social, and occupational dimensions, aiming to empower them to regain the highest possible level of functionality and adaptability. Rehabilitation endeavors to facilitate their seamless integration into society. Equipped with a robust mental and emotional framework, and possessing commendable skill sets, these individuals can actively engage with the community, thereby transforming into valued and equitable members of the societal fabric (Sarvinoz and Muzaffar, 2022).

2.10.1 Early Intervention for CP

Despite prematurity and hypoxic-ischemic brain injury being widely acknowledged as primary causes of CP, it's imperative to recognize that up to a third of children with CP do not exhibit the traditional high-risk factors. Many of these children possess potential neurogenetic or metabolic disorders, necessitating a proactive approach to identify and determine the underlying causes. This proactive approach is vital to prevent the potential consequences of delayed diagnosis, ensuring appropriate management strategies are implemented. Recent years have witnessed rapid advancements in neuroscience and genetics, presenting an opportunity for precise

diagnosis, targeted treatment, and accurate prognosis assessment for children with CP (Kwong et al., 2018). From a neurological perspective, the brains of infants and young children go through a period of fast growth and development. This stage is marked by strong compensatory brain function and a lot of adaptability. At this crucial time, offering stimulating therapies and practicing functional activities can greatly boost the brain's ability to compensate for any damage and keep growing and changing. Importantly, the younger the age of the individual, the higher the likelihood of successful motor function recovery. Early intervention, while abnormal postures and musculoskeletal configurations are still malleable and amenable to adjustments, plays a pivotal role in preventing secondary damage such as muscle spasticity and limb deformities in affected children (Damiano and Longo, 2021).

2.10.2 Integration of Rehabilitation with Daily Life

In the rehabilitation treatment of CP although physical therapists and occupational therapists play significant roles, the prevalence of CP among children and the limited number of dedicated rehabilitation professionals is a big challenge. In some countries, there are relatively few schools training specialists for this purpose. Consequently, children with CP have limited access to specialized training and therapy provided by professionals. Moreover, due to the extended duration of treatment, inpatient care throughout the entire period is often impractical. Therefore, in addition to administering systematic and structured training for CP rehabilitation, it is essential to integrate various daily life activities into the rehabilitation process. This involves educating parents, conducting family-based therapy, and incorporating rehabilitation training through daily life activities (Kim et al., 2021).

2.10.3 Adhering to Developmental Neurological Principles

In the year 1965, the world witnessed the advent of the prominent Bobath method (Zanon et al., 2019), swiftly garnering widespread acceptance among scholars globally and finding application across nations. This therapeutic approach, also acknowledged as 'Developmental Neurological Treatment,' places paramount emphasis on understanding and treating CP from the vantage points of neurophysiology and neurodevelopment. It principally involves the strategic application of Reflex Inhibiting Postures (RIP) to suppress the atypical postures and reflexes often associated with CP (Cabezas-López and Bernabéu-Brotóns, 2022). Additionally, precise adjustments at specific key points are employed to promote the establishment of normative postures and reflexes, thus facilitating the restoration of regular functionality. The Bobath method has ushered in a sense of hope, not only for the rehabilitation of CP but also for individuals grappling with various limb impairments. Its emergence in the annals of CP's developmental history is indeed revolutionary, leaving an indelible mark and achieving laudable milestones (DAR and JOHARI, 2024).

In 1966, Dr. Vojta, a renowned scholar from West Germany, pioneered the notable Vojta Induction Therapy. This therapeutic approach stemmed from Dr. Vojta's extensive research on CP treatment, initiated in 1954. Building upon the experiences of his predecessors and conducting rigorous studies and on-the-ground observations, Dr. Vojta devoted over a decade of relentless effort to develop this methodology. He stands as one of the most distinguished scholars in the world for the early diagnosis and treatment of CP. Dr. Vojta introduced the Vojta Induction Therapy, a method that involves manual stimulation of specific regions of a child's body, known as 'induction zones,' inducing reflexive turning and creeping movements (Adrian et al., 2021). These movements are part of the developmental process in young children and represent normal, coordinated movements that infants exhibit soon after birth. In children with CP, this coordination and integration ability is impaired. Through repetitive stimulation induced by the Vojta method, this functional revival can be facilitated (Ha and Sung, 2018). Dr. Vojta applied this approach to treat 207 cases of

infants below 8 months of age, achieving an efficacy rate of 96.1%. The Vojta method has gained recognition from scholars worldwide, standing as another representative school of thought in contemporary early intervention for CP (Konjen et al., 2022, Ha and Sung, 2021).

2.11 Understanding and Treatment of CP in TCM

CP, as a distinct medical condition, was not explicitly identified in ancient TCM texts. However, modern practitioners of TCM have categorized the symptoms and signs associated with CP under various classifications, including 'Wu Chi' (Five Delays), 'Wu Ruan' (five softsness), and 'Wu Ying' (Five Rigidity) (Xuemei and Duo, 2018, Xiaomin and Xinmin, 2015, Yongping et al., 2017). These classifications are based on the clinical presentation of CP. The early descriptions of 'Wu Chi' and 'Wu Ruan' can be traced back to the ancient text 'Zhu Bing Yuan Hou Lun · Xiao Er Za Bing Zhu Hou'. This text documented symptoms like 'delayed tooth eruption,' 'inability to walk at a young age,' 'delayed hair growth,' and 'delayed speech development at four or five years old' (Yongping et al., 2017). These descriptions suggest that ancient Chinese physicians had an initial understanding of CP in children. The Song Dynasty's 'Xiao Er Yao Zheng Zhi Jue · Juan Shang · Mai Zheng Zhi Fa · Za Bing Zheng' outlines the characteristic symptoms of 'Wu Chi.' It describes the difficulties in growth and walking, thin legs during ambulation, delayed tooth eruption, loose teeth upon eruption, and delayed hair growth that doesn't darken. The Yuan Dynasty physician Zeng Shi Rong furthered the understanding of CP 'Huo You Xin Shu · Wu Ruan'. He explained that CP occurs due to insufficient essence and marrow since birth, resulting in weakened tendons, bones, and muscles, accompanied by sluggishness in spirit. The invasion of the six pathogens exacerbates the condition, leading to softening of the head, neck, hands, feet, and body, which is termed 'Wu Ruan' (five softsness). During the Ming Dynasty, Lu Bo Si's 'Ying Tong Bai Wen · Wu Ruan' provided a precise definition of 'Wu Ruan,' describing it as the softness observed in the head, neck, hands,

feet, and muscles. This was further elucidated in the Qing Dynasty's 'Yi Zong Jin Jian · You Ke Za Bing Xin Fa Yao Jue', which explained the symptoms of 'Wu Ruan' in detail, encompassing softness in the head, neck, hands, feet, and flaccid muscles. The Song Dynasty's 'You You Xin Shu' elaborated on 'Wu Ruan' and also delineated the manifestations of 'Wu Ying', explaining that it is an untreatable condition characterized by a hard heart crying without tears, a hard head, hard hands, hard feet, and a hard back. In conclusion, while ancient TCM did not explicitly name CP, they contained descriptions of symptoms and manifestations that align with this condition. Over time, these descriptions were organized into classifications based on the observed presentation forms and affected body parts, providing valuable insights for modern TCM practitioners in understanding and addressing CP (Jian et al., 2023, Cheng et al., 2016).

In the Song Dynasty, the renowned pediatrician Qian Yi, in his work 'Xiao Er Yao Zheng Zhi Jue,' provided a detailed pathological understanding of this condition: 'The symptoms of Wu Chi are...due to insufficiency of parental essence and blood, weakness of kidney Qi, inability to nourish and nurture the child's body. Some manifest liver and kidney deficiencies resulting in delayed walking, some exhibit liver Qi deficiency causing clenched hands and feet, and some present liver and kidney deficiencies leading to an inability to extend the feet.' The pathology of Wu Chi is summarized as congenital insufficiency of essence and blood or weakness of kidney Qi, or liver and kidney insufficiency that fail to nourish the muscles and bones of the limbs. Zeng Shi Rong, regarding insufficiency of parental essence and blood, concluded: 'Due to the mother's prolonged blood stagnation or excessive use of tonics during pregnancy; or the father's indulgence in lust and alcohol, leading to weak Qi; or advancing age combined with delayed childbearing; or deficiencies in sun and moon energies resulting in birth; or the retention of abortifacients leading to unintended pregnancy.' 'Yi Zong Jin Jian · You Ke Za Bing Xin Fa Yao Jue' states: 'All these cases are due to insufficient inheritance, inadequate Qi and blood, weak soft bones and feeble muscles.' Chen Fu Zheng in the Qing Dynasty, in 'You You Ji

Cheng · Tai Bing Lun,' associated fetal timidity with the condition of the pregnant woman, stating: 'Fetal timidity...often arises from pregnancies in the parents' later years or from women with multiple pregnancies. Being a mature or elderly mother and late-stage pregnancies are predisposing factors. At the time of conception, the primordial essence is already exhausted, and after conception, it is difficult for Qi and blood to nurture adequately, resulting in a weak and feeble birth' (Changyu et al., 2017).

These various descriptions can be attributed to congenital factors, yet they do not disregard summaries of acquired etiology and pathogenesis (Yan and Liren, 2006). Xue Kai in 'Bao Ying She Yao · Wu Ruan' once said: 'All due to the weakness of the Qi of the five viscera, failing to nourish adequately...the root cause lies in the stomach.' This explanation elucidates the relationship between symptoms such as muscle softness and the five viscera from the perspective of the spleen and stomach being the source of Qi and blood production, the foundation of acquired conditions. Some physicians, from the perspective of righteous deficiency being invaded by pathogenic factors, have evaluated the etiology, such as: 'Whether from injury, emesis, or diarrhea, the invasion of pathogenic factors into the liver channels due to weakened Qi, leading to softening of tendons, softness of hands and feet, or softness of the neck and occiput' ('You You Xin Shu'). 'This is due to damage from emesis or diarrhea, accompanied by lack of perspiration during a febrile illness, losing the surface defense. Originally, it was not a chronic disease. Suddenly, the limbs fail to contract, thus manifesting this condition' ('Ying Tong Bai Wen') (Xiong, 2016).

In summary, TCM holds that the etiology of CP often stems from congenital deficiencies, overexertion leading to sweating or vomiting, subsequent vulnerability to external pathogenic factors, or weakness of the spleen and stomach resulting in insufficient Qi and blood, inadequate nourishment of the marrow sea, and neglect of tendons and bones. Observations and deductions regarding the predisposing risk factors for causing CP have been made in TCM, including multiple pregnancies,

inappropriate pregnancy care, and inadequate maternal constitution during pregnancy (Wang, 2012). From this, it is evident that TCM's prenatal factor analysis for CP is accurate and reliable, providing valuable insights for future generations of TCM practitioners in comprehending and addressing such diseases.

2.11.1 Acupuncture is the Main Approach for CP TCM Treatment

The TCM treatment for CP is diverse and includes various approaches such as acupuncture, tuina, Chinese herbal medicine, fumigation therapy with Chinese herbs, and topical application of Chinese herbal medicine. Additionally, acupuncture injections and acupoint application, in conjunction with pharmacotherapy, are used to treat muscle and joint contractions effectively. A study shows that TCM tuina and scalp acupuncture therapy can improve limb spasms, enhance their daily activities and quality of life (Zhu et al., 2023). Clinical study has also confirmed that scalp acupuncture can effectively treat spastic cerebral palsy, improve cerebral hemodynamics and gross motor function, reduce muscle tone and spasticity, and improve daily living abilities (Xu and Tong, 2023). Meta analysis shows that acupuncture and moxibustion combined with routine training can improve abnormal muscle tone and improve clinical treatment efficiency (Yuanjie et al., 2023). A data mining study showed that the three most commonly used acupoints for acupuncture treatment in children with CP are the foot movement sensation area, balance area, and Sanyinjiao(SP6), as well as the Taichong(LR3), motor area, Xuehai(SP10), Ganshu(BL18), Pishu(BL20), Yanglingquan(GB34), Sishencong(EX-HN1), Baihui(DU20), Fengchi(GB20), and Shenshu(BL23) ten secondary acupoints (Mou et al., 2021). Researcher conducted a survey and analysis of the treatment and rehabilitation of CP using TCM in over six hundred medical institutions across thirty provinces and cities in China. The results revealed that 77.2% of medical institutions in China offer TCM rehabilitation therapy for CP (Yubo, 2017). Among these institutions, over 80% utilize AT, and their therapeutic effects are widely recognized.

Combining TCM and Western medicine in a rehabilitation model has shown remarkable effectiveness and is currently the mainstream treatment approach.

2.11.2 Acupuncture Treatment Methods for CP

Gao Jing previously reported that the combination of scalp acupuncture with physical therapy significantly improves gross motor function and daily life abilities in spastic CP children (Gao et al., 2019). Scalp acupuncture is widely used in the treatment of CP (LI et al., 2014). Literature reviews and summaries have been conducted regarding acupuncture points on the scalp, specific techniques, and different schools of thought. Publication (Lee et al., 2019) emphasize that acupuncture treatment, with a focus on scalp acupuncture, often yields favorable outcomes. However, due to the frequent combination of scalp acupuncture with other therapies and the lack of high-quality randomized controlled trials (RCTs) comparing the different approaches, the overall quality of existing RCTs is generally low. Moreover, there is limited foundational experimental research on scalp acupuncture treatment for CP, and there is a dearth of reports regarding the mechanism and prognosis of CP. Although the main acupuncture points for scalp acupuncture in CP treatment are often Jiaoshi scalp acupuncture and Jinshi scalp acupuncture, there is inconsistency in the selection criteria for acupuncture points. The parameters and techniques for needling, including stimulation intensity, duration of needle retention, and needle insertion angle and depth, are not clearly defined. Further standardization is needed to enhance the clinical applicability and actual therapeutic efficacy of scalp acupuncture.

Jin and coworkers (Jin et al., 2018) conducted an optimization study on various operational parameters for scalp acupuncture treatment of CP. This technique focused on the aspects of electrical needle frequency, duration, intensity, and treatment frequency. The study concluded that the optimal electrical needle parameter combination was 2Hz/100Hz, with a treatment duration of 20 minutes per session,

once every other day. In another study (Wang et al., 2020a), compared the immediate effects of electrical acupuncture and manual acupuncture on the gastrocnemius muscle tone in spastic CP patients through a randomized single-blind trial. The results indicated that both approaches significantly alleviated the muscle tone in the gastrocnemius muscle, with electrical acupuncture demonstrating superior efficacy compared to manual acupuncture.

In overall, acupuncture therapy demonstrates clear efficacy in the treatment of cp, especially in improving gross motor functions, fine motor skills, speech impairments, drooling, and overall daily life capabilities. Specific acupuncture techniques utilized in the treatment include manual acupuncture, scalp acupuncture, electrical acupuncture, acupoint injections, and moxibustion, however, the principle that treatment methods should be applied according to the patient's condition based on syndrome differentiation does bring challenges to the current treatment of cerebral palsy with acupuncture.

2.11.3 Potential Mechanisms of Acupuncture in Treating CP

Currently, acupuncture for the treatment of CP remains primarily at the stage of clinical observation, although there has been some progress in experimental research. Studies have indicated (Zhang et al., 2015) that acupuncture can inhibit apoptosis of nerve cells in ischemic and hypoxic brain tissue in neonatal rats, providing a protective effect against brain tissue damage in rats subjected to ischemia and hypoxia. Additionally, the protective effect of acupuncture is more pronounced when administered at an early stage. Furthermore, research suggests that electroacupuncture treatment can enhance the expression of nerve growth factor (NGF) in the brain tissue of rats with ischemic and hypoxic brain injury, thus exerting a protective effect on brain damage. It is believed that acupuncture can release neurotransmitters such as endorphins, serotonin, and dopamine to activate nerve synapses in the central nervous

system that are usually in an unstimulated state, potentially leading to the formation of new synapses and neural circuits, ultimately reorganizing a functional neuronal network (Ji and Sun, 2019). Acupuncture at the Baihui(DU20) and Sishencong(EX-HN1) acupoints can stimulate NGF expression in the brain cortex, counteract neuronal apoptosis, improve cerebral blood circulation, reduce vascular resistance, increase blood flow velocity, and enhance cerebral tissue perfusion and oxygenation, thereby facilitating tissue repair and regeneration in the brain. Research findings (Jing et al., 2015) suggest that electroacupuncture on the motor cortex in rats with CP can promote proliferation and regeneration of neural fiber bundles in the rat's brain white matter with prolonged treatment, achieving the goal of reconstructing neural circuits to treat CP. Overall, the mechanisms of acupuncture treatment for pediatric CP are not yet fully elucidated. Potential mechanisms may include the inhibition of neuronal apoptosis, upregulation of nerve growth factor expression, reorganization of neuronal functional networks, and modulation of neurotransmitter expression, among others. These mechanisms likely result from the collective action of multiple signaling pathways, necessitating further research to establish specific mechanisms.

2.12 The Comparison of the Acupuncture, tuina and Rehabilitation in Treating CP

In the treatment of CP, acupuncture, tuina, and rehabilitation are crucial therapeutic modalities, which can assist patients in alleviating spasms, improving muscle control, and facilitating functional recovery (Wang et al., 2023a, Zhu et al., 2023, Gong et al., 2023). While acupuncture and tuina could yield some symptomatic relief in the short term, achieving more significant outcomes requires sustained adherence. Conversely, rehabilitation constitutes a protracted process necessitating ongoing engagement to progressively enhance patient functionality. However, the optimal clinical approach often entails the comprehensive integration of acupuncture, tuina, and rehabilitation, leveraging their respective strengths (Yang et al., 2023b, Casini et al., 2023). It is imperative to recognize that individual patient responses to treatment may vary,

mandating the design of personalized therapeutic regimens tailored to specific patient circumstances. The selection of appropriate treatment strategies should therefore consider patient idiosyncrasies and therapeutic efficacy, aiming to optimize treatment outcomes (Faccioli et al., 2023).

In summary, scholars worldwide are currently conducting various studies on children with CP. These studies encompass a wide range of aspects, including basic concepts, rehabilitation methods, pathogenic mechanisms, and differential diagnoses. From these studies, we can infer that TCM plays a crucial role in the diagnosis and treatment of CP, particularly spastic CP. Among TCM modalities, AT therapy have an irreplaceable role in ameliorating clinical symptoms of CP. However, the diversity in AT therapy, including varied acupuncture point selection principles and numerous prescriptions, alongside diverse techniques, and the lack of standardized criteria for evaluating efficacy across different studies, have increased the clinical application challenges. Standardizing the treatment protocol for CP is an urgent issue that needs to be addressed in pediatric TCM AT therapy. This standardization is crucial for clinical practice and will be a major focus of future research. In our study, we will analysis the hotspots and frontier of spastic CP through bibliometric study, leverage the theoretical advantages of TCM, explore and summarize the characteristic TCM symptoms of CP, and validate the efficacy of a standardized AT treatment protocol in clinical intervention for the main symptoms of spastic CP. Ultimately, we aim to develop a AT treatment method of CP that is convenient to implement and can be widely promoted.

CHAPTER 3.0

MAPPING TRENDS AND HOTSPOT REGARDING SPASTIC CP: A BIBLIOMETRIC ANALYSIS OF GLOBAL RESEARCH

3.1 Backgrounds

In recent years, the topic of spastic CP has garnered considerable attention from scholars worldwide due to its significance in the field. This increased interest has led to extensive exploration of novel treatment methods aimed at improving the condition. Noteworthy among these methods are botulinum toxin A injection which was highlighted (Kaya Keles and Ates, 2022, Gantelius et al., 2022). Stem cell transplantation has also emerged as a promising avenue in the field of neurology (Motavaf et al., 2022, Clowry, 2022). Additionally, TCM has been investigated for its potential in managing spastic CP (Niu et al., 2021, Mou et al., 2021), all of which have been presenting encouraging results. Despite the growing body of literature on these treatment approaches, it is worth noting that there remains a lack of systematic assessment and synthesis of the published studies in this particular domain. Consequently, further research and comprehensive analysis are necessary to bridge this gap in our understanding of spastic CP treatment strategies.

In order to achieve a systematic understanding of a certain field, the conventional approach has been to gradually establish it by reading a certain number of relevant and significant literature. However, in recent years, the development of literature-based bibliometric analysis methods has emerged as an important complement to traditional methods. These methods allow for the rapid extraction of key information from a large body of literature and its representation in knowledge graph (Tagorti and Kaya, 2022). As a result, they enable relatively objective, comprehensive, and

intuitive quantitative analyses of academic hotspots, evolutionary processes, research advancements, frontier trends, and other patterns within a particular academic field.

Bibliometric analysis is a valuable and widely used tool within the academic community, providing researchers with an objective and comprehensive overview of the historical development, research focus, and emerging trends within a specific research area (Subramanian et al., 2010, Singh, 2016, Davarazar et al., 2021). By employing bibliometric analysis, researchers can gain insights into the growth, impact, and interconnections of scholarly publications. In recent years, various bibliometric tools have been utilized to evaluate the landscape of different academic fields. Notable among these tools is CiteSpace (Liu et al., 2022b). Additionally, CitNetExplorer has been employed to explore citation networks (Abuín-Porras et al., 2021). Another commonly used tool, VOSviewer, has been leveraged to analyze and visualize publications (Chen et al., 2020b). HistCite has also been employed to examine citation histories and patterns within the scholarly literature (Tagorti and Kaya, 2022). The utilization of these bibliometric tools allows researchers to uncover patterns, collaborations, and influential works within a specific research field, thereby aiding in the identification of emerging trends and shaping future research directions.

This study employed various bibliometric analysis software to comprehensively assess the publications related to spastic CP research. The utilization of these tools facilitated a rigorous and objective examination of the literature in this field (Kumar et al., 2023). The primary objectives of this study were as follows:

(1) to summarize the historical features of the literature on spastic CP, thereby providing a comprehensive understanding of its progression over time. By analyzing the publication trends, citation patterns, and collaborative networks, this study aimed to uncover the key milestones, influential works, and significant shifts in research focus within the field.

(2) to identify the current hotspots within the research field, shedding light on areas of particular interest and activity. By analyzing the frequency of keywords, co-occurrence patterns, and highly cited papers, this study aimed to pinpoint the most prominent research themes, topics, and sub-disciplines within spastic CP research. This identification of hotspots would help researchers and practitioners to stay updated with the latest developments, focus their efforts on priority areas, and foster interdisciplinary collaborations.

(3) To uncover emerging trends that can guide future research endeavors and provide valuable insights for researchers in the field. By examining the growth of literature, identifying emerging keywords, and analyzing citation networks, this study sought to highlight promising avenues for future investigations. These emerging trends could encompass novel interventions, experimental techniques, or interdisciplinary approaches that hold potential for advancing knowledge and improving clinical outcomes in the treatment and management of spastic CP.

By addressing these objectives, this study aimed to make a substantial contribution to the current body of knowledge on spastic CP by conducting a comprehensive bibliometric analysis. By employing a systematic and quantitative approach, the objective was to evaluate and analyze the research landscape surrounding spastic CP. Through this analysis, a clearer and more comprehensive understanding of the overall research progress in this field can be achieved. The findings of this study are expected to have several significant implications. Firstly, they will help identify existing knowledge gaps and areas that require further investigation. By pinpointing these gaps, researchers and healthcare professionals can focus their efforts on addressing specific aspects that have received less attention or require further exploration. Additionally, the findings are anticipated to shed light on the emerging trends and areas of active research within the treatment and management of spastic CP. This understanding can serve as a valuable resource for researchers, clinicians, and policymakers in developing targeted strategies and interventions.

Moreover, the study's outcomes can potentially inspire and guide future research directions in the field, encouraging researchers to explore novel approaches, interventions, and interdisciplinary collaborations. Ultimately, by providing a comprehensive evaluation of the research landscape, this study aims to contribute to advancing knowledge, improving clinical practice, and ultimately enhancing the quality of life for individuals affected by spastic CP.

3.2 The objective of the study

To date, there has been an absence of any bibliometric analysis on consolidating the existing research on spastic CP. In this present study, we aim to execute a comprehensive bibliometric analysis pertaining to spastic CP. This endeavor is undertaken with the express purpose of encapsulating the field's knowledge framework, pinpointing its research hotspots and trend, then illuminating the frontier areas of inquiry.

3.3 Materials and methods of the study

The Web of Science Core Collection (WoSCC) is widely recognized and utilized for bibliometric analysis (Sun et al., 2022, Mu et al., 2022). It is regarded as the most authoritative, comprehensive, and systematic academic information resource, covering a vast number of disciplines worldwide (Lyu et al., 2022). In our study, we extracted publications related to spastic CP from the WoSCC database.

To retrieve relevant articles, we employed specific search terms: TS = "Cerebral palsy" and "Spastic". These terms were chosen to ensure the inclusion of literature directly related to spastic CP. The search results were then refined by applying specific criteria, including a publication date range from 1 January 2000 to 30

November 2022, the English language as the publication language, and a focus on review articles and original research articles.

By utilizing the WoSCC database and employing specific search parameters, we aimed to gather a comprehensive and up-to-date collection of publications on spastic CP. This rigorous approach ensured that our study encompassed relevant articles published within a specified timeframe and written in English, thus enabling us to perform a comprehensive analysis and generate meaningful insights into the research landscape of spastic CP.

For the analysis of publication trends and major contributors in our study, we utilized Excel 2019 (Microsoft, Redmond, Washington, USA). This software allowed us to examine the annual growth of publications and identify key contributors such as authors, institutions, countries, and journals. By analyzing these factors, we aimed to gain insights into the development and impact of research in the field of spastic CP.

To construct the knowledge network and explore various interrelationships, we employed specialized software tools. VOSviewer (version 1.6.18, Leiden University, Leiden, Netherlands) and CiteSpace (Version 6.1.R4) were utilized to visualize and analyze the collaborative network, keyword co-occurrence network, and co-citation references network. These tools enabled us to identify patterns, clusters, and important connections within the research literature.

To evaluate the strength of collaboration among researchers, we utilized the concept of Total Link Strength (TLS). This measure provided a quantitative assessment of the cooperation relationships between different authors, institutions, or countries within the field of spastic CP. Additionally, node size in the visualizations generated by VOSviewer and CiteSpace was determined based on the importance or prominence of the respective nodes. Larger nodes indicated greater significance or influence within the knowledge network.

By employing these software tools and methodologies, we aimed to gain a comprehensive understanding of the research landscape, collaboration patterns, key topics, and influential references within the field of spastic CP.

3.4 Results

3.4.1 General data

Figure 3.1 illustrates the systematic process employed for literature searching and bibliometric analysis in this study. Initially, a comprehensive search was conducted, resulting in the retrieval of 3988 relevant publications. These publications were then imported into widely used bibliometric analysis software, including VOSviewer, CiteSpace, and the Online analysis platform, to conduct further in-depth analysis. The bibliometric analysis provided valuable insights into the citation patterns and characteristics of the retrieved publications. The total number of citations (TC) across all the publications was found to be 92,603, indicating the extent of scholarly impact within the field of spastic CP research. Furthermore, the average number of citations per publication (CPP) was calculated to be 23.22. This metric reflects the average influence and visibility of each publication within the scholarly community and serves as an indicator of the significance and relevance of the research output.

The retrieval and analysis of a substantial number of publications, along with the high citation count and notable CPP, underscore the significance and scholarly attention given to the topic of spastic CP. These findings not only indicate the active research interest in this field but also highlight the importance of conducting a comprehensive bibliometric analysis to gain a holistic understanding of the research landscape.

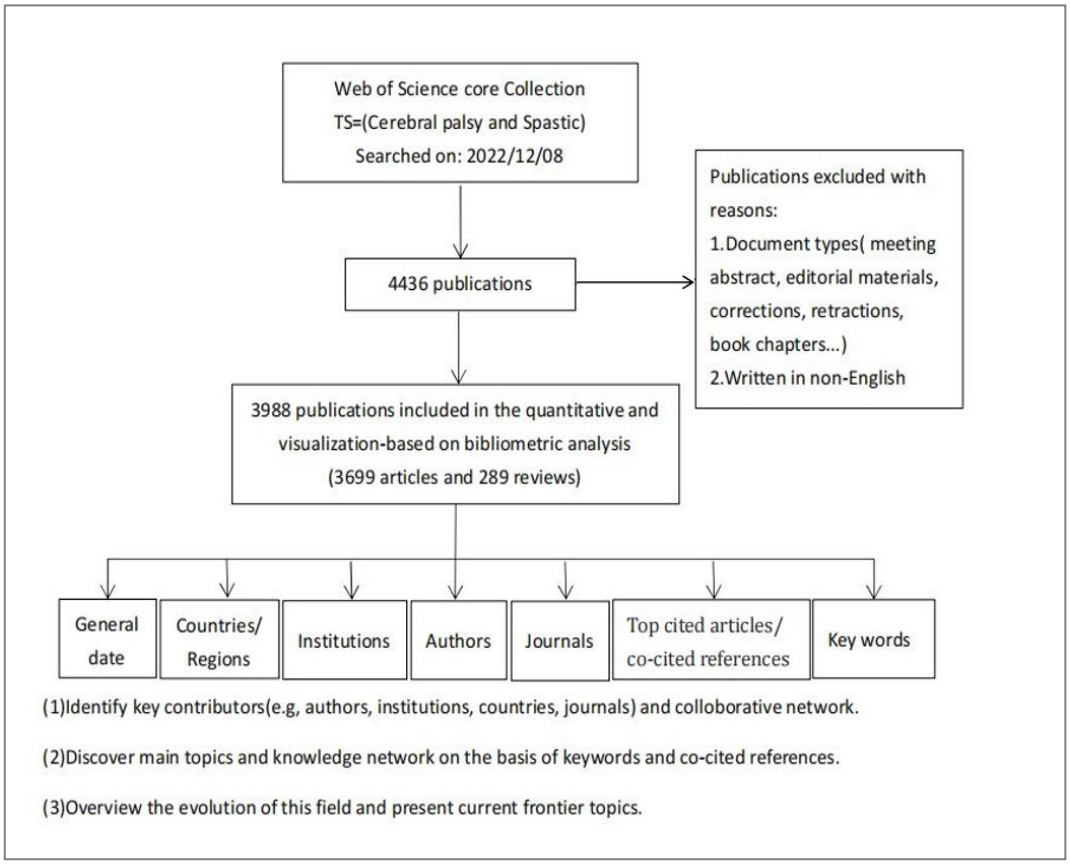

Figure 3.1: The workflow of data collection and bibliometric analysis.

3.4.2 Publication trend

The number of annual publications in the spastic CP field exhibited an upward trend and could be roughly divided into three phases. Phase I was from 2000 to 2005, with below 150 publications per year. Phrase II was from 2006 to 2015, and the number of publications steadily increased from 150 to over 250 per year. Phase III was from 2015 to 2022, the number slightly decreased in 2015 and 2016 and increased sharply after 2016 to over 300 publications per year. Figure 3.2 presents the annual output of the top three contributing countries.

Figure 3.2: Publication trend of the top three prolific countries/regions

3.4.3 Country/region and Institution contributions

Overall, a total of 3,487 institutions and 94 countries/regions contributed to this field. As depicted in Table 3.1, The USA contributed the most papers in this field (1062 publications Total citation (TC)(31220), Citations per publication (CPP)(28.788)), followed by Netherlands (356 publications, TC(9467), CPP(26.62)), Australia (290 publications, TC(9907), CPP(34.16)), implying that the contributions of the three Countries were significantly more than that of the other countries in this field, followed by England (268 publications), Canada (223 publications), South Korea (211 publications), Germany (195 publications), France (168 publications), Turkey (166 publications) and Belgium (165 publications). Figure 3.3 and figure 3.4 show the collaborative network between countries. The country/region with the highest total link strength (TLS) was the USA(520), followed by England(317), which exhibited a close mutual cooperative relationship. South Korea has(high papers(211) but low TLS(45).

Table 3.1: Top 10 most productive Countries/Regions

	Countries/Regions	Record Count	Centrality	Total citation (TC)	Citations per publication (CPP)	Total link strength (TLS)
1	USA	1062	0.12	31220	28,788	520
2	Netherlands	356	0.06	9467	26.62	269
3	Australia	290	0.00	9907	34.16	228
4	England	268	0.12	8740	32.61	317
5	Canada	223	0.04	6713	30.1	185
6	South Korea	211	0.00	3393	16.08	45
7	Germany	195	0.32	5652	28.98	253
8	France	168	0.04	3684	21.93	236
9	Turkey	166	0.04	2016	12.14	78
10	Belgium	165	0.21	4019	24.36	225

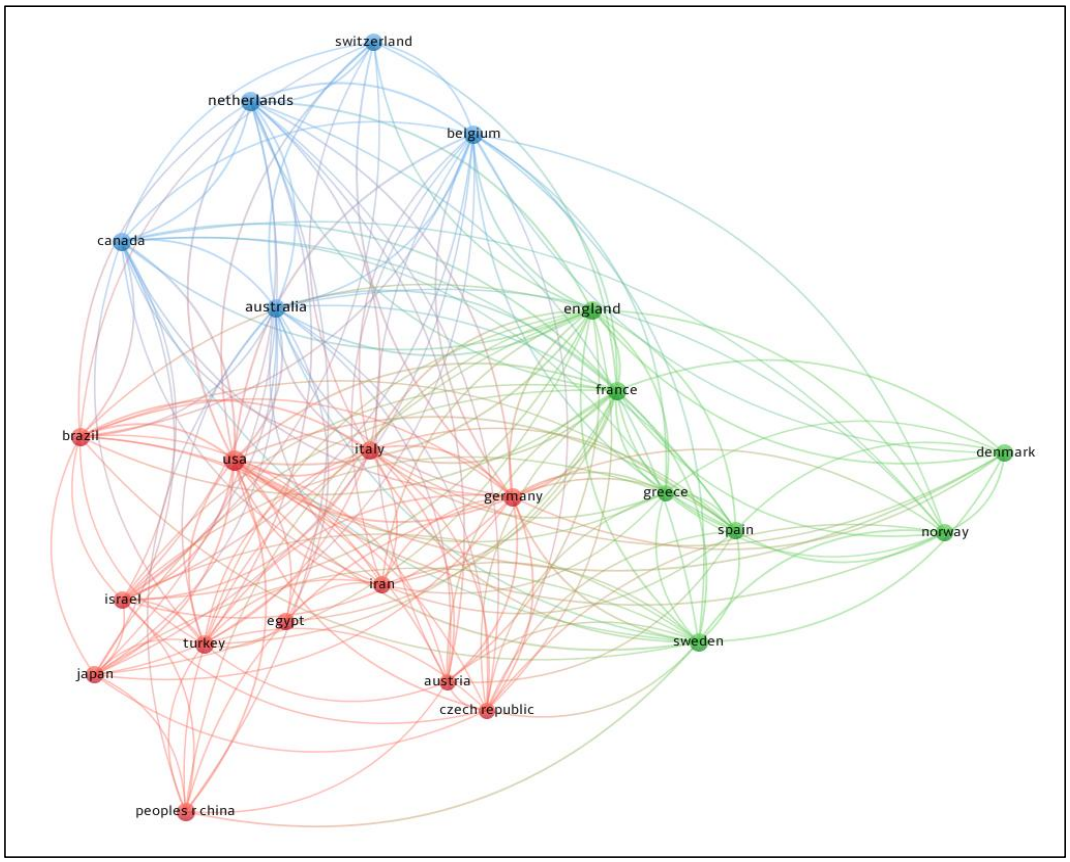

Figure 3.3: The collaboration network of Countries/Regions generated by VOSviewer

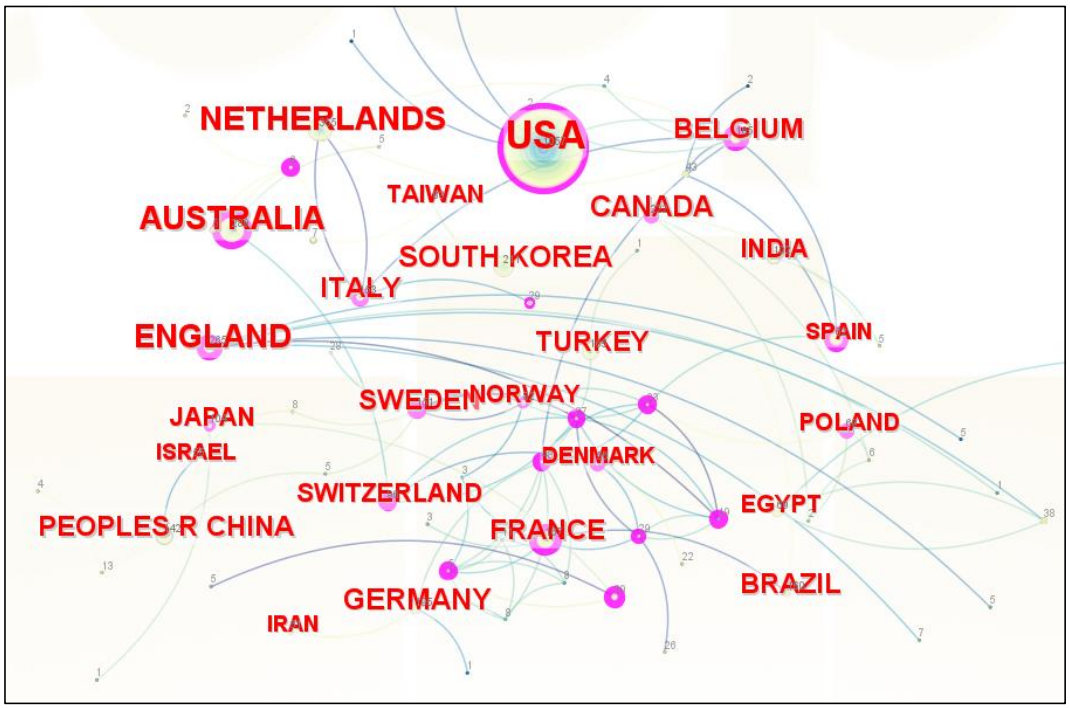

Figure 3.4: The collaboration network of Countries/Regions generated by Citespace

The institution with the most publications related to spastic CP research is listed in Table 3.2. The Kathleen Univ Leuven, with the most publications (177), TC (1421), and CPP (8.03), preceded the Vrije Univ Amsterdam and the Yonsei Univ. Additionally, in terms of CPP, the Royal Children's Hosp was at the top (16.04), with McGill Univ (11.83) and the Univ Melbourne (11.01) following closely. Figure 3.5 and figure 3.6 show weak collaborative relationships among institutions, suggesting the need for greater collaboration. The institution with the highest TLS was the Royal Children's Hosp(193), followed by Univ Melbourne(171).

Table 3.2: Top 10 most productive institutions

	Institutions	Record Count	Centrality	Total citation (TC)	Citations per publication (CPP)	Total link strength (TLS)
1	Kathleen Univ Leuven	177	0.05	1421	8.03	129

2	Vrije Univ Amsterdam	177	0.11	1213	6.85	169
3	Yonsei Univ	140	0.05	761	5.44	25
4	Royal Children's Hosp	138	0.08	2213	16.04	193
5	Shriners Hosp Children	127	0.13	1131	8.91	102
6	McGill Univ	121	0.05	1431	11.83	43
7	Washington Univ	107	0.18	694	6.49	73
8	Univ Melbourne	91	0.09	1002	11.01	171
9	Univ Hosp Leuven	82	0.01	400	4.88	84
10	Vrije Univ Amsterdam Med Ctr	74	0.05	698	9.43	55

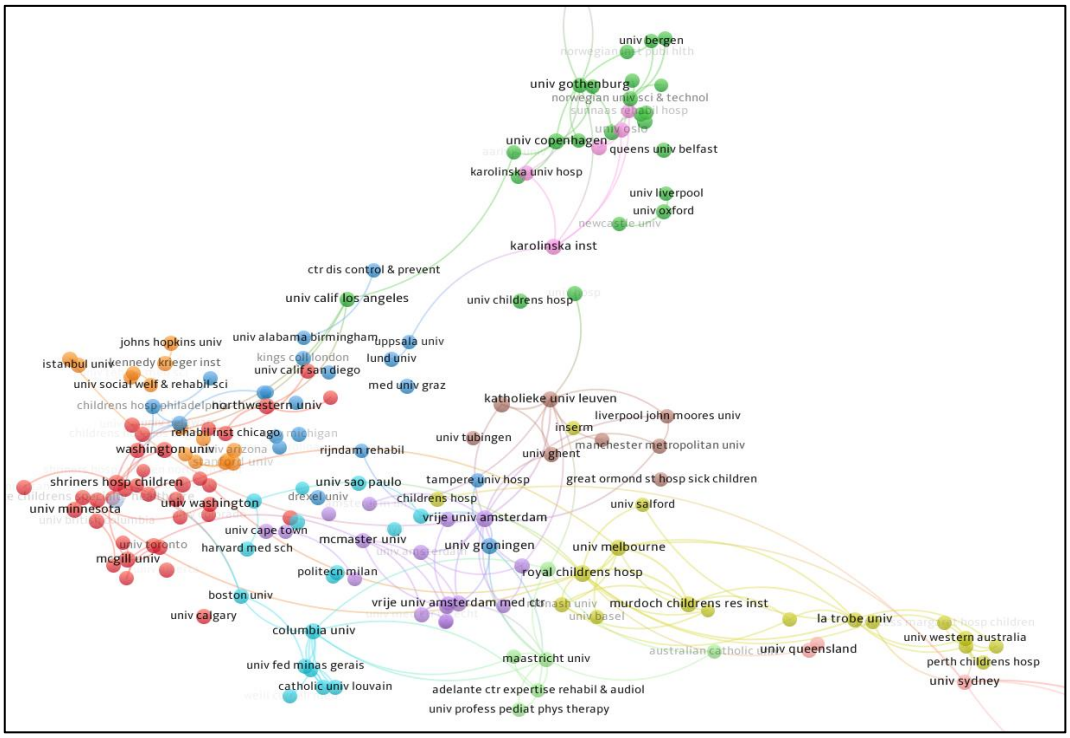

Figure 3.5: The collaboration network of Institutions generated by VOSviewer

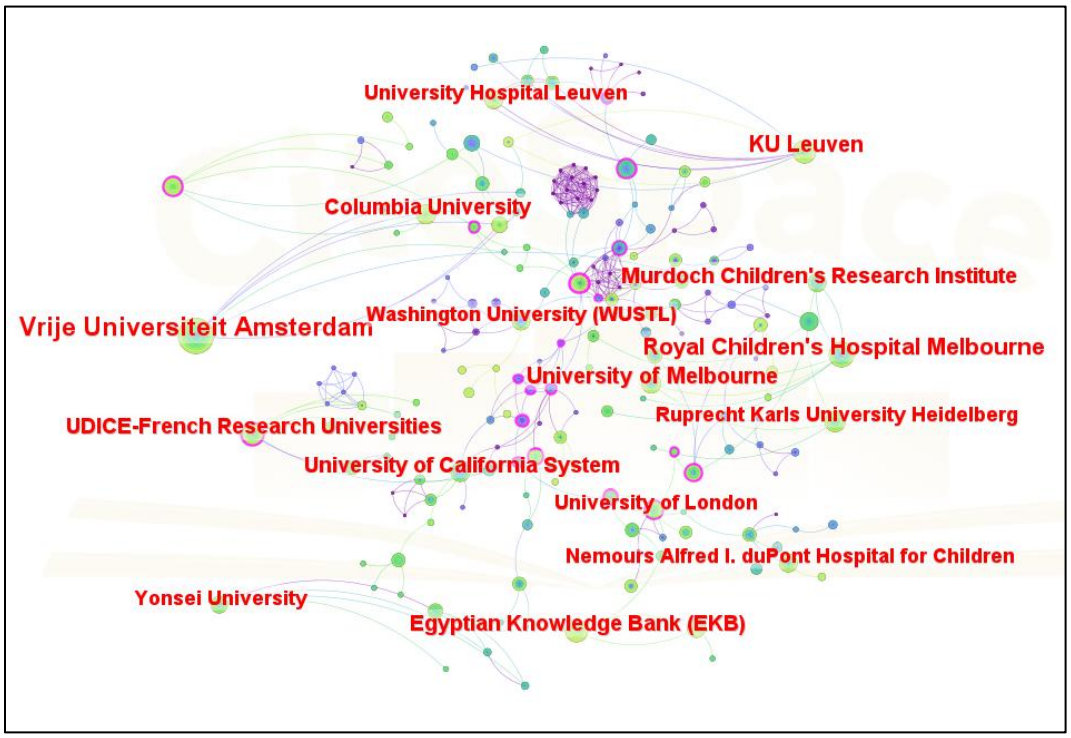

Figure 3.6: The collaboration network of Institutions generated by Citespace

3.4.4 Author contributions

The top 10 authors contributed a total of 523 publications in this field. Desloovere K with the most publications (65), TC (1309), and CPP (20.14), followed by Becher JG with publications (64), TC (1638), and CPP (25.59). Graham HK, with publications (64), has the highest TC (4042) and CPP (63.16) (Table 3.3). As shown in Figure 3.7 and figure 3.8, the top 5 authors with the largest TLS were as follows: Desloovere K (256), Molenaers G (180), Becher JG (179), Dreher T (129), and Harlaar J (104). The connections between authors from different countries are inadequate.

Table 3.3: Top 10 most productive authors

Authors	Record Count	Centrality	Total citation (TC)	Citations per publication (CPP)	Total link strength (TLS)

1	Desloovere K	65	0.01	1309	20.14	256
2	Becher JG	64	0.00	1638	25.59	179
3	Graham HK	64	0.01	4042	63.16	60
4	Miller F	57	0.00	1118	19.61	91
5	Molenaers G	51	0.00	1453	28.49	180
6	Dreher T	49	0.00	840	17.14	104
7	Gordon AM	45	0.00	913	20.29	101
8	Park ES	44	0.00	905	20.57	47
9	Wolf SI	43	0.00	684	15.91	85
10	Harlaar J	41	0.02	805	19.63	129

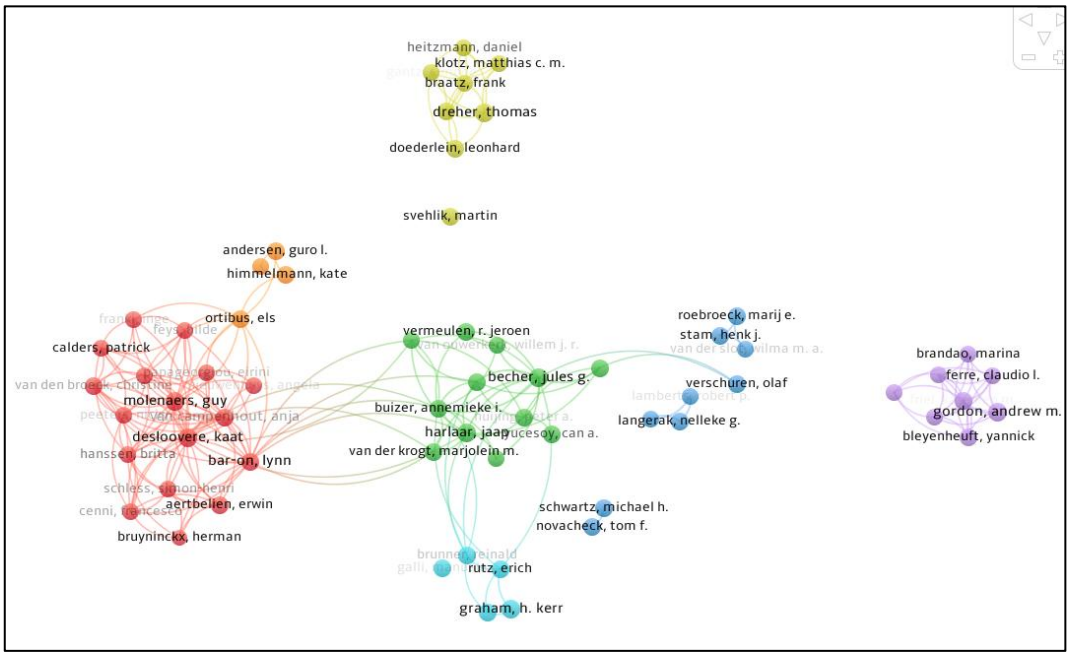

Figure 3.7: The collaboration network of Authors generated by VOSviewer

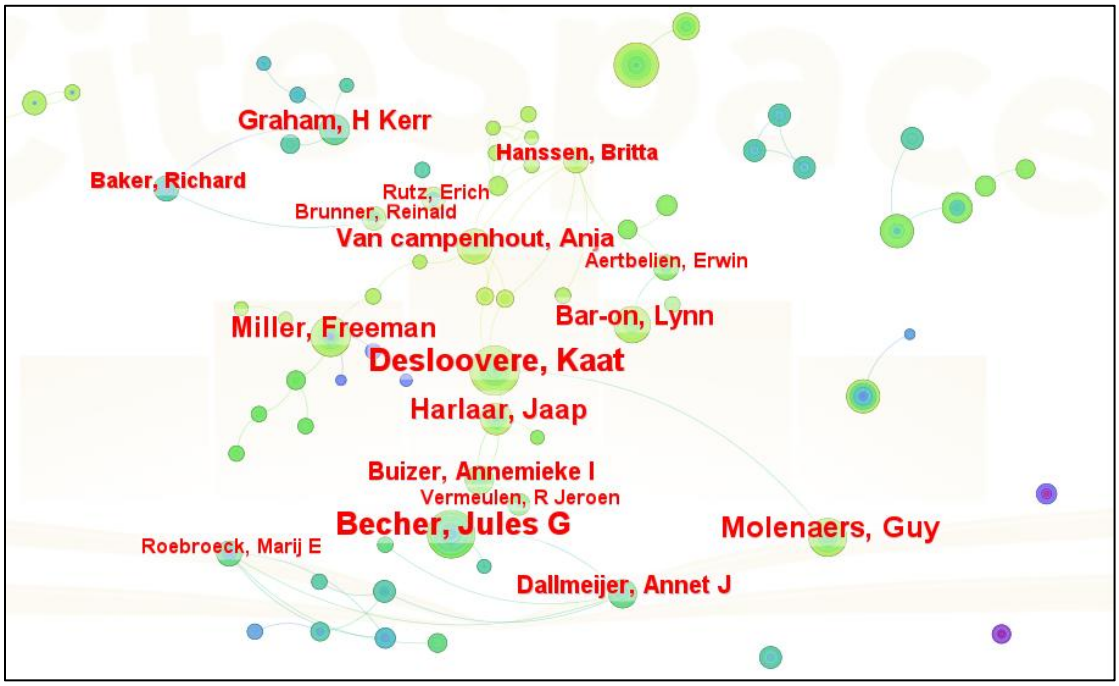

Figure 3.8: The collaboration network of Authors generated by Citespace

3.4.5 Journals contributions

Table 3.4 lists the top 10 productive journals involved in this study. DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY was the most productive journal with 418 publications in the spastic CP field， TC (5099), CPP (12.20), followed by GAIT & POSTURE (196 publications), TC (1779), CPP (9.08), JOURNAL OF PEDIATRIC ORTHOPAEDICS (137), TC (1254), CPP (9.15). RESEARCH IN DEVELOPMENTAL DISABILITIES (90), TC (502), CPP (5.58). The journals of co-citation analysis are shown in Figure 3.9 and figure 3.10. The top 5 journals with TLS were as follows: DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY (529402), JOURNAL OF PEDIATRIC ORTHOPAEDICS (165401), GAIT & POSTURE (150271), ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION (131034), and DISABILITY AND REHABILITATION (53608). We can see that most of the top journal are from USA and English.

Table 3.4: Top 10 most productive journals

	Journals	Impact factor(2002) /Country	Record Count	Centrality	Total citation (TC)	Citations per publication (CPP)	Total link strength (TLS)
1	DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY	3.8 ENGLAND	418	0.95	5099	12.20	529402
2	GAIT & POSTURE	2.4 IRELAND	196	0.03	1779	9.08	150271
3	JOURNAL OF PEDIATRIC ORTHOPAEDICS	1.7 USA	137	0.60	1254	9.15	165401
4	RESEARCH IN DEVELOPMENTAL DISABILITIES	3.1 ENGLAND	90	0.00	502	5.58	42446
5	ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION	4.3 USA	86	1.02	852	9.91	131034
6	JOURNAL OF CHILD NEUROLOGY	1.9 USA	71	0.03	329	4.63	49891
7	JOURNAL OF	1.1	70	0.00	433	6.19	25025

8	PEDIATRIC ORTHOPAEDICS-PART B DISABILITY AND REHABILITATION	USA 2.2 ENGLAND	67	0.10	405	6.04	53608
9	CLINICAL BIOMECHANICS	1.8 ENGLAND	55	0.03	378	6.87	34570
10	PEDIATRIC PHYSICAL THERAPY	1.6 USA	51	0.07	127	2.49	40300

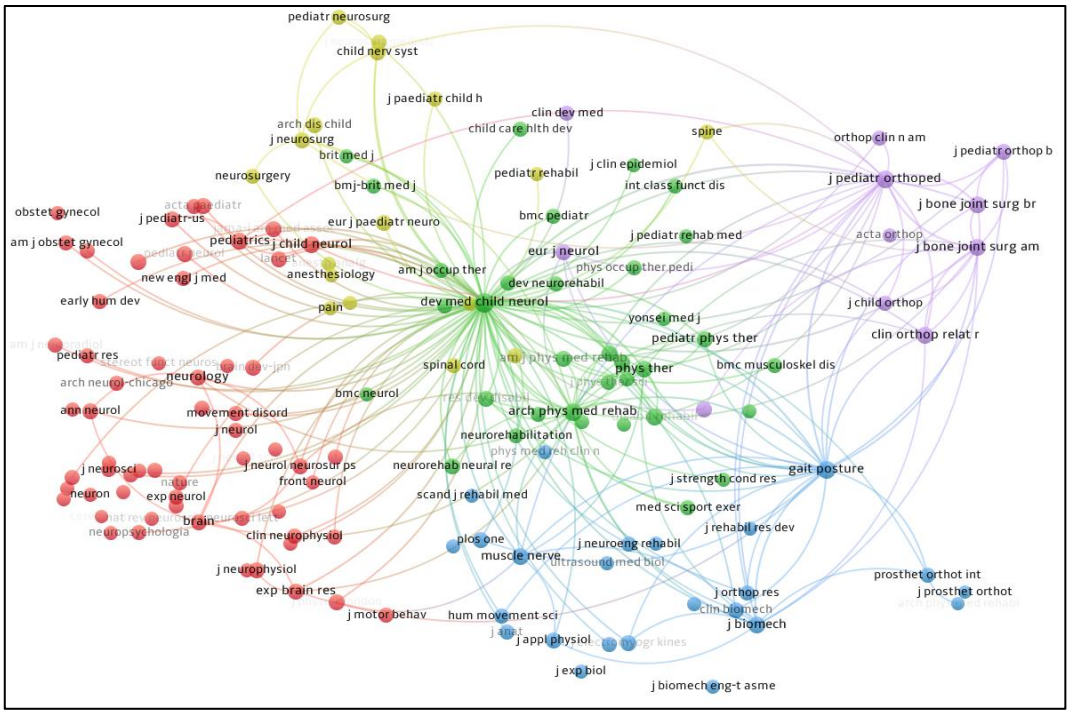

Figure 3.9: The co-citation of journals generated by VOSviewer

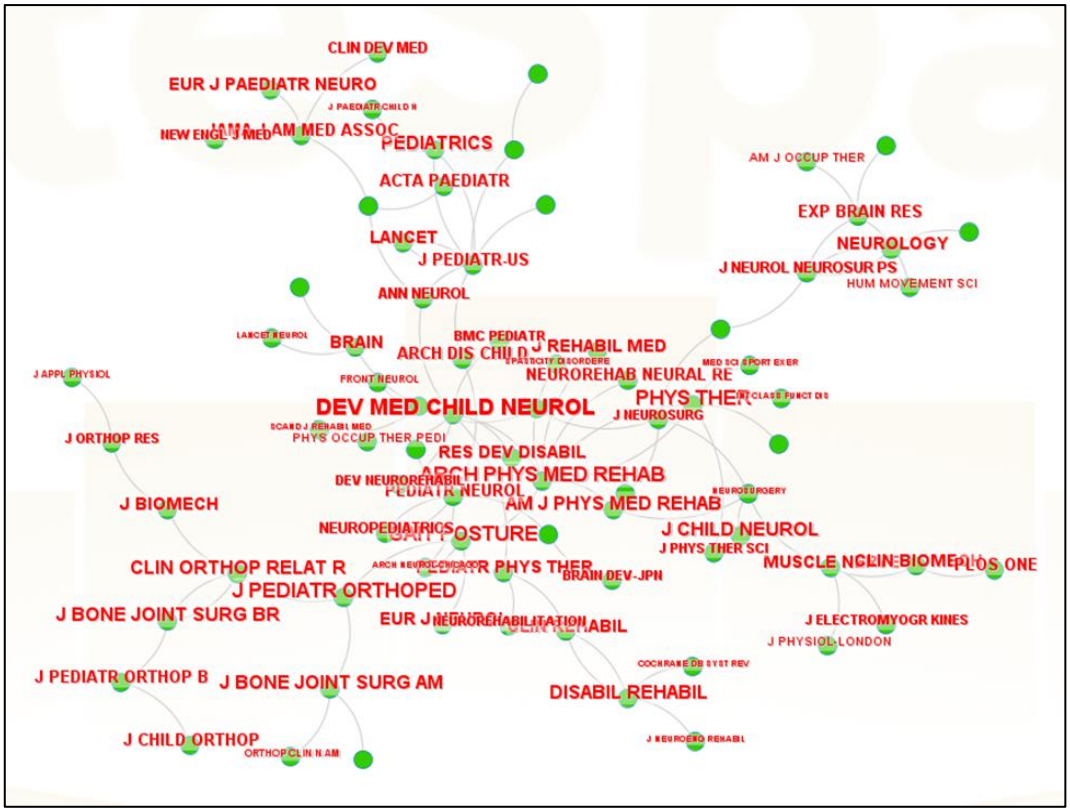

Figure 3.10: The co-citation of journals generated by Citespace

3.4.6 Analysis of high-cited references

The characteristics of publications are summarized in Table 3.5. The most-cited reference, "The epidemiology of cerebral palsy: Incidence, impairments and risk factors," was published in the DISABILITY AND REHABILITATION and authored by Odding, E in 2006. The second most-cited reference, “Classification and definition of disorders causing hypertonia in childhood," was published in PEDIATRICS and authored by Sanger, TD, in 2003. The third most-cited reference, "Use of a Low-Cost, Commercially Available Gaming Console (Wii) for Rehabilitation of an Adolescent with Cerebral Palsy," was published in the PHYSICAL THERAPY and authored by Deutsch in 2008. The top three most highly cited articles discussed the epidemic characteristics of CP (Odding et al., 2006), the definition and characteristics of hypertonia (Sanger et al., 2003), and the low-cost rehabilitation game machine for

cerebral (Deutsch et al., 2008). It could be noted that the top ten highly cited articles were all published before 2010, which shows that there are not many breakthroughs in the research of spastic CP in this decade.

Table 3.5: Top 10 highest cited references

	Title	Source Title	Total Citations (TC)	Publication Date	First Author
1	The epidemiology of cerebral palsy: Incidence, impairments and risk factors	DISABILITY AND REHABILITATION	569	2006	Odding, E
2	Classification and definition of disorders causing hypertonia in childhood	PEDIATRICS	443	2003	Sanger, TD
3	Use of a Low-Cost, Commercially Available Gaming Console (Wii) for Rehabilitation of an Adolescent With Cerebral Palsy	PHYSICAL THERAPY	374	2008	Deutsch
4	Chorioamnionitis and cerebral palsy in term and near-term infants	JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION	369	2003	Wu, YW
5	Changing panorama of cerebral palsy in Sweden. VIII. Prevalence and origin in the birth year period 1991-94	ACTA PAEDIATRICA	362	2001	Hagberg, B

6	Spastic movement disorder: impaired reflex function and altered muscle mechanics	LANCET NEUROLOGY	349	2007	Dietz, Volker
7	Models of white matter injury: Comparison of infectious, hypoxic-ischemic, and excitotoxic insults	MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES RESEARCH REVIEWS	341	2002	Hagberg, H
8	Neurobiology of hypoxic-ischemic injury in the developing brain	PEDIATRIC RESEARCH	339	2001	Johnston, MV
9	Practice parameter: Diagnostic assessment of the child with cerebral palsy - Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society	NEUROLOGY	291	2004	Ashwal, S
10	The changing panorama of cerebral palsy in Sweden. IX. Prevalence and origin in the birth-year period 1995-1998	ACTA PAEDIATRICA	287	2005	Himmelmann, K

3.4.7 Analysis of keywords

Table 3.6 shows the top 10 keywords (including Author Keywords and Keywords plus) co-occurrence frequencies. The word that came up most often was cerebral palsy (2465), followed by children (1197), reliability (685), gross motor function (558), spastic diplegia (442), gait (349), management (313), classification (303), Spastic cerebral palsy (286) and gait analysis (240). The top ten keyword clusters were selected for analysis and listed in figure 3.11, figure 3.12 and 3.13. They were as follows: coordination, management, botulinum toxin, upper extremity, prevalence, gait analysis, strength, surgery, spastic cerebral palsy, and cerebral palsy.

Table 3.6: Top 10 keywords co-occurrence frequencies

	Keyword	Frequency	Centrality	Total link strength (TLS)
1	Cerebral palsy	2465	0.00	15053
2	Children	1197	0.02	10178
3	Reliability	685	0.06	5894
4	Gross motor function	558	0.13	4684
5	Spastic diplegia	442	0.09	3555
6	Gait	349	0.12	4572
7	Management	313	0.58	2415
8	Classification	303	0.04	2672
9	Spastic cerebral palsy	286	0.11	1678
10	Gait analysis	240	0.37	1961

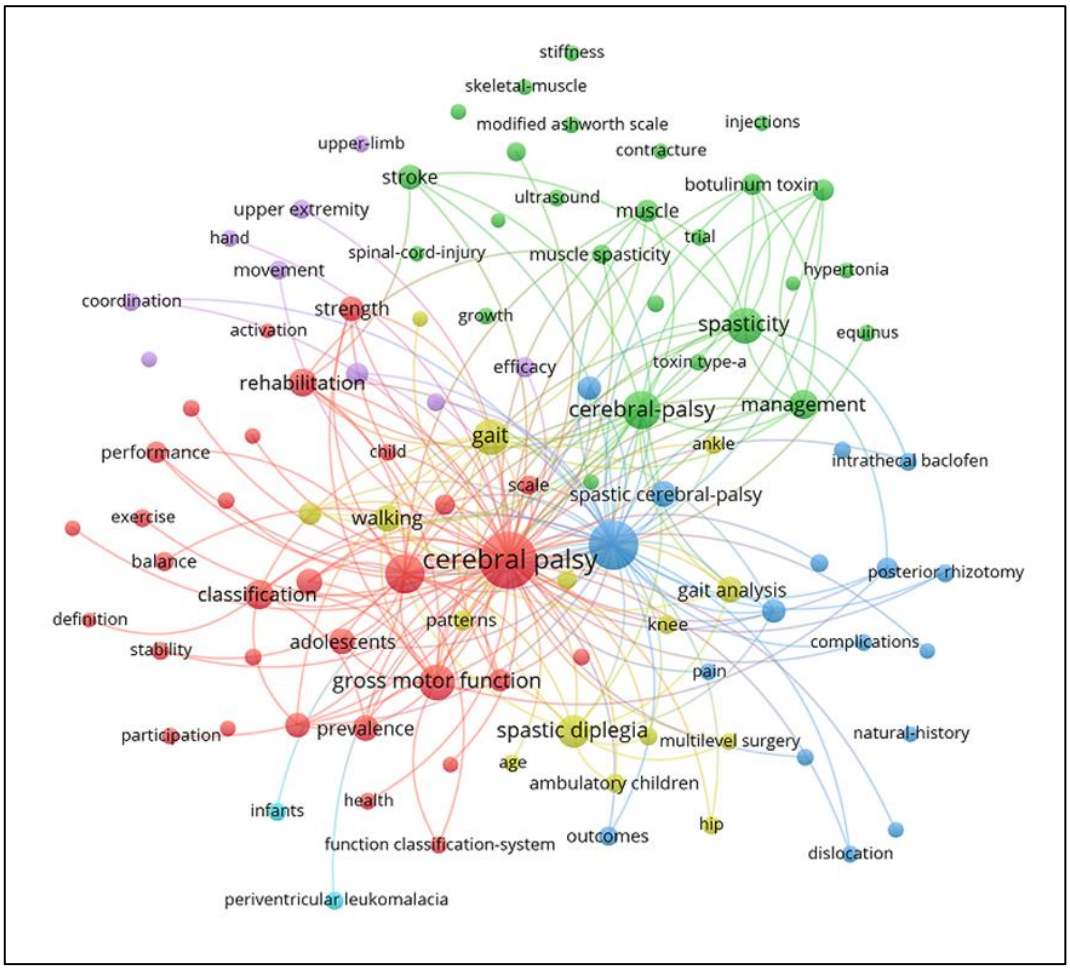

Figure 3.11 : The network of keywords generated by VOSviewer

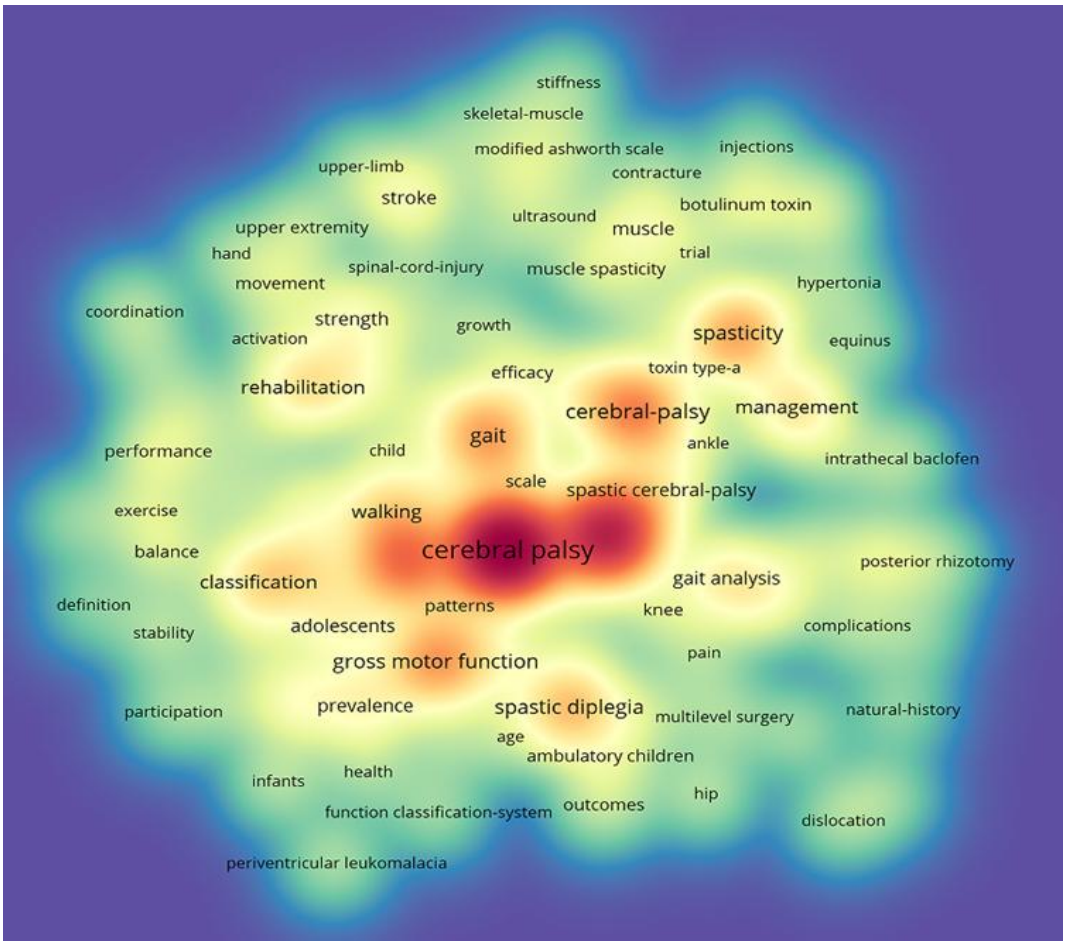

Figure 3.12: The density of keywords generated by VOSviewer

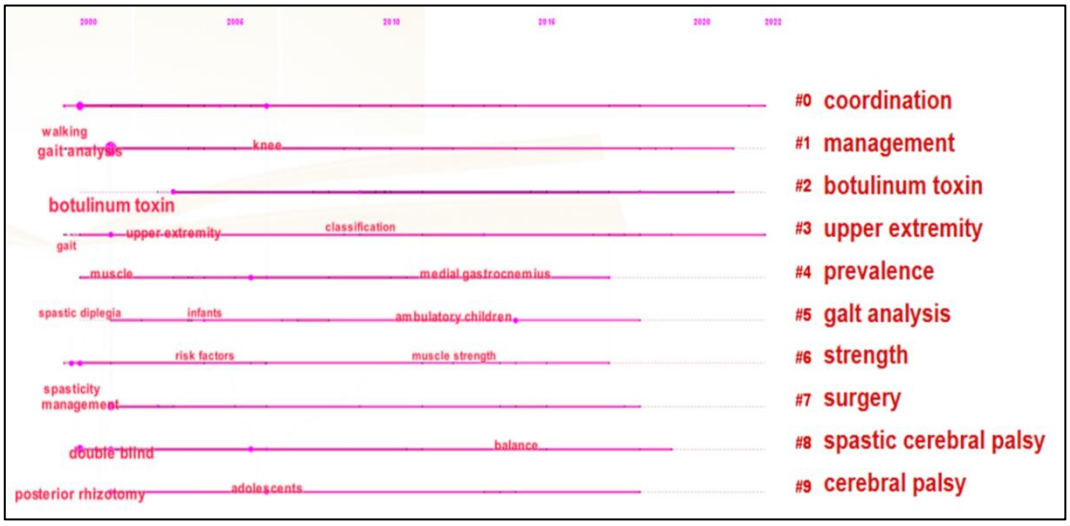

Figure 3.13: The cluster of keywords generated by citespace

3.4.8 The burst of Keywords

Figure 8 shows the top 25 keywords in terms of burst detection. From 2000 to 2011, management, double blind, trial, periventricular leukomalacia, natural history, muscle, origin, and disability were commonly cited, with burst strengths reaching 19.66, 18.37, 16.99, 15.23, and 13.25, respectively. From 2012 to 2022, randomized controlled trial, definition, gastrocnemius muscle, interrater reliability, and morphology were commonly cited, with the burst strength reaching 12.07, 11.25, 10.29, 10.26, and 9.29 respectively.

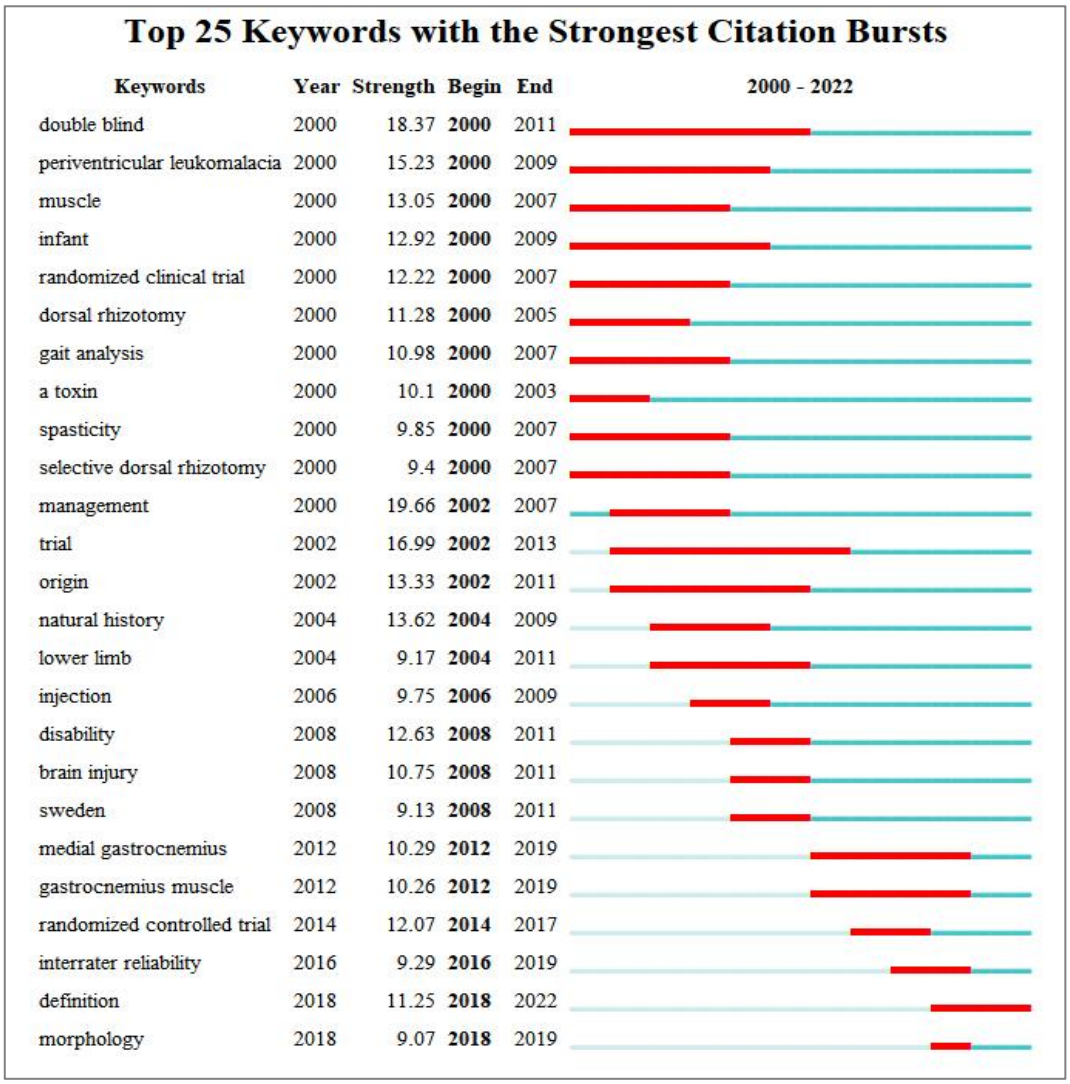

Figure 3.14: Top 25 keywords in terms of burst detection

3.5 Discussion

To the best of our knowledge, this was the first bibliometric study on spastic CP to provide a comprehensive review of the developing trends of research in this field. According to the WoSCC database search, 3988 publications were identified from 1 January 2000 to 30 November 2022. The temporal and spatial distribution, author and institution contributions, and top journal were assessed by employing WoSCC literature analysis wire, VOSviewer, CiteSpace, and online analysis platform for bibliometrics. In addition, keyword analysis, cluster analysis, and burst hotspot analysis were used to identify the currently hot research areas and frontiers of research in spastic CP.

The publication trend can reflect the development speed and research progress. The number of studies related to spastic CP has steadily increased over the past twenty years, with approximately four times as many publications in 2020 as in 2000. This indicates that this field is a hot topic and will continue to attract increased attention in the future. Specifically, from 2000 to 2005, the relatively small amount of publications in this period indicates that the study of spastic CM is in its infancy. From 2006 to 2015, because a large number of researchers began to publish their study on spastic CP, the number of publications showed steady growth, then sharply increased after 2016.

According to the top countries/regions, institutions, authors, and journals in Table 1-4. The USA not only contributed the highest number of publications, total citation but also was the most cooperative country because spastic CP has been studied more intensively than in other countries, followed by the Netherlands, which was the second most publications and cooperation. In contrast, Australia had the largest number of citations per publication, which suggest that the USA, Netherlands, and Australia were the most influential countries in spastic CP. Western countries and

regions have shown close cooperation, but A relatively low total link strength in South Korea has urged researchers to strengthen research further. Besides, in terms of institutions, nearly all of the top 10 institutions are from the top countries/regions with the most published papers, suggesting the good academic ability of the country in this field. Kathleen Univ Leuven and Vrije Univ Amsterdam were the most productive institution.

Regarding total citations and citations per publication, the highest is Royal Children's Hosp. Desloovere K, who was the top productive author. Graham HK has the highest total citation and citations per publication. At the same time, Molenaers G has an advantage in cooperation. This indicates that these institutions and authors have tremendous influence in spastic CP fields, which can be selected for research cooperation. With respect to journals that published spastic CP studies, our data suggested that DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY had the largest number of publications, total citations, citations per publication, and total link strength. Although ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION was not in the top five largest number of publications, its co-citation was well.

Cluster analysis illustrates the direction of research hotspots in spastic CP, whereas burst detection explains the evolution of relevant hotspots over time. In this study, we combined the most cited references, top keywords, keywords clusters, and the burst of Keywords, the research frontiers, and hotspots of spastic CP were found to be as follows:

(1) Definition of CP, epidemiological characteristics. Among the most-cited references, four explored these contents in spastic CP, especially there were two articles describing the changing panorama of CP in Sweden (Hagberg et al., 2001, Himmelmann et al., 2005). Similar research has been carried out by Swedish scientists (Himmelmann et al., 2010, Himmelmann and Uvebrant, 2014). The

keyword of classification is the top eight words. The word of definition was a red bar from 2018 to 2020 in terms of burst detection, revealing that the topic still is a hotpot in this field.

(2) Mechanisms of spastic CP. Chorioamnionitis and CP in term and near-term infants published in the PHYSICAL THERAPY and authored by Wu, YW in 2003, which pointed that risk factors of CP infants were as a possible role of chorioamnionitis (Wu et al., 2003). Hagberg, H discussed ischemia-reperfusion and/or infection-inflammation were important factors of white matter damage (WMD) (Hagberg et al., 2002). The intrinsic vulnerability of specific cell types and systems might be more critical in determining the final pattern of damage and functional disability (Johnston et al., 2001). The point of view was published in PEDIATRIC RESEARCH, authored by Johnston, MV, in 2001. Keywords of periventricular leukomalacia were red bar from 2000 to 2009 in burst detection, indicating that could be a reason for spastic CP.

(3) Standard for clinical studies. Keywords of double blind randomized clinical trial and randomized controlled trial were highlighted in 2000-2001, 2000-2009, and 2014-2017, respectively, indicating that clinical trials had been a hotspot in the research of spastic CP for a long time. From the keywords clusters, we could note that many new treatments had been introduced into the treatment of spastic CP, such as botulinum toxin and surgery. De Beukelaer N assessed medial gastrocnemius (MG) growth in children by 3D-freehand ultrasound prior to and six months post-BoNT-A injections suggesting that re-injections should be postponed at least beyond half of a year (De Beukelaer et al., 2022). Miyanji F studied the effect of surgery-related complications on clinical outcomes, concluding surgery in patients with CP leads to a significant improvement in health-related quality of life (HRQo) (Miyanji et al., 2018).

(4) Spastic CP diagnosis and treatment management, efficacy evaluation, etc. the American Academy of Neurology and the Practice Committee of the Child Neurology Society reported the Practice parameter: Diagnostic assessment of the child with CP

in NEUROLOGY (Ashwal et al., 2004). Among the important keywords and clusters, management, classification, and management revealed the contents of diagnosis and treatment management. Gross motor function, interrater reliability, gait analysis and coordination revealed the contents of efficacy evaluation. More specifically, the efficacy evaluation included more details, such as the upper limbs and gastrocnemius muscles. Research of Elvrum AG pointed out that the Both Hands Assessment (BoHA) provides valid measures of hand use as suggested by its high correlation with other activity-based measures of hand function (Elvrum et al., 2022). The research result of Boulard,C presented changing muscle and joint stiffness in children with CP as the effectiveness of interventions (Boulard et al., 2021). Trionfo A (Trionfo et al., 2023) introduced pain management(lumbar plexus nerve blocks，LPN) for children who underwent hip reconstruction and the results showed that LPN was an effective pathway.

3.6 Conclusions

Research on spastic CP has experienced significant growth, particularly over the past five years. Notably, high-income countries such as the USA, Netherlands, Australia, and England have made substantial contributions to the literature in this field. Recent studies have focused on various aspects of spastic CP, including reliability, gross motor function, spastic diplegia, gait analysis, standardized management, clinical trials, and efficacy evaluation.

In light of the advancements in research, there is a growing recognition of the need for new treatment methods, precise interventions, and reliable efficacy evaluation in the study of spastic CP. With this in mind, we propose exploring the symptoms characteristics and their correlation rules in spastic CP using TCM. By leveraging the unique perspective and interventions offered by TCM, we believe that

integrating TCM into the study of spastic CP can provide valuable insights and potentially open up new directions for intervention strategies. This interdisciplinary approach holds promise in advancing our understanding of spastic CP and improving the quality of life for affected individuals.

3.7 limitation

There are inevitably several limitations to our study. First, the publications were only searched from the WoSCC database, which may lead to incomplete literature. Other databases such as Cochrane Library and Google Scholar. Scopus and PubMed may produce slightly different results. Nevertheless, the Web of Science database is the most popular and widely recognized database for bibliometric analyses. Second, we excluded non-English publications, which may lead to biased results. Finally, some bias during the selection of publications may not be avoided. For example, the same institution may have used different names at different periods, although two people were assigned to review the initial results.

CHAPTER 4.0

ANALYSIS OF TCM SYMPTOMS IN CHILDREN WITH SPASTIC CP

4.1 Background

Studies (Chen et al., 2023, Liu et al., 2022a, Liao et al., 2017) have shown that TCM plays an important role in the treatment of spastic CP. especially, the efficacy of AT for spastic CP has been repeatedly verified by many studies (Ji and Sun, 2019, Jianyi et al., 2023), however, according to the characteristics of "TCM syndrome differentiation and treatment", the effective of treatment on children is closely related to whether the syndrome differentiation is accurate (Di et al., 2023). TCM clinicians or acupuncturists often decide individualized treatment measures according to the individual symptoms of children with spastic CP in the clinic, which improves the pertinence of treatment to a certain extent, but often makes it difficult to promote treatment experience. Therefore, it is urgent to explore the characteristics of spastic CP TCM symptoms and their association rules (Xiaowei et al., 2023, Yan, 2022, Zhou et al., 2023).

Nowadays, many scholars have made relentless efforts in researching spastic CP (Yang and Wang, 2023, Sun et al., 2023, Houjun et al., 2023, Wang et al., 2022), especially in the context of TCM syndrome differentiation. Spastic CP etiology, affected areas, pathogenesis, and TCM syndrome differentiation and treatment of spastic CP were discussed in numerous study. Since spastic CP is a refractory and lifelong disease, the clinical manifestations of affected children are often complex. When applying TCM methods for syndrome differentiation and treatment, there may be different opinions and approaches, lacking unified standards in the standardization of syndromes.

Currently, research on the distribution of symptoms in spastic CP often relies on simple frequency statistics, focusing on symptoms distribution, but lacks deeper data mining to explore the regularities of syndromes.

Data mining (Mamasidiqova et al., 2023, Yang et al., 2020, Hwang et al., 2020) is the process of extracting implicit, previously unknown but potentially valuable information and knowledge from large, incomplete, noisy, vague, and random real-world application data. It is a decision support process primarily based on artificial intelligence, machine learning, pattern recognition, statistics, databases, visualization techniques, and other related fields. Through highly automated data analysis and inductive reasoning, data mining uncovers hidden patterns, helping decision-makers make informed and accurate decisions.

R language (Vargas and Mesa-Fúquen, 2021, Charalampopoulos, 2020, Team, 2020) is an open-source programming language for data analysis and statistics, offering extensive capabilities in data processing, visualization, and statistical analysis. It finds widespread application across various domains, including data mining in TCM symptoms analysis. TCM medical records typically encompass substantial textual descriptions, numerical data, and categorical information (ZHENG et al., 2023, Wang et al., 2020b). R language's data processing tools can be employed to cleanse and preprocess this data, ensuring data quality while extracting essential features from the raw data. Moreover, R language provides a wealth of statistical analysis and machine learning tools suitable for constructing syndrome pattern recognition models. These models can be utilized for classifying different TCM symptoms, performing clustering analyses (Bouveyron et al., 2019), or conducting association rule mining (Mokkadem et al., 2023) to reveal patterns and regularities among distinct syndromes. Simultaneously, R language's visualization (Patil, 2021) facilitate the visualization of relationships, distributions, and trends among TCM syndromes.

The objective of this research is to employ data mining technology such as R language within TCM research. This endeavor aims to assist researchers in systematically organizing and investigating the patterns and attributes of TCM symptoms across extensive medical records. By discerning evidence-based medical information, the ultimate goal is to enhance the effectiveness of clinical interventions and establish a standardized treatment protocol rooted in this knowledge. This, in turn, will enable the realization of the therapeutic potential inherent in TCM.

4.2 The Objectives of the Study

The aim of this study is to conduct a cross-sectional medical record investigation, based on a Structured Integrated Electronic Medical Record System for Clinical and Research Purposes, as well as hospital information systems. Employing data mining techniques and drawing from multidisciplinary approaches encompassing TCM, Computer science, Evidence-Based Medicine and Big data analytics, this study endeavors to explore general information on children with spastic CP. It also aims to investigate the characteristics of TCM symptoms, including clinical symptoms, tongue manifestations, and pulse conditions, with the ultimate goal of laying a foundation for further clinical research on the TCM diagnostic patterns related to this condition. This research seeks to establish and strengthen the knowledge structure that provides guidance for the development of targeted TCM treatments based on symptoms characteristics in order to guide clinical practice in TCM.

4.3 Subject of the study

This study primarily conducted a comprehensive TCM symptoms investigation. It focuses on the medical records of children patients diagnosed with spastic CP who underwent treatment at Xi'an Encephalopathy Hospital Affiliated to Shaanxi

University of Chinese Medicine, during the period spanning from October 2021 to September 2022. The study seeks to delve into the intricacies of TCM symptoms and their manifestations in this specific group of patients, shedding light on the potential applications of TCM principles in the context of CP management.

Xi'an Encephalopathy Hospital Affiliated to Shaanxi University of Chinese Medicine stands as a prominent establishment in the field of CP research and treatment. It boasts a range of national-level accolades, including its designation as a National Clinical Key Specialty in Pediatrics, recognition as a Key Discipline in Pediatric by the State Administration of Traditional Chinese Medicine, and the honor of being named a Key Research Laboratory for Cerebral Palsy by the same administration.

One of the hospital's significant strengths is its electronic medical record system (Hathaliya et al., 2019), which seamlessly integrates clinical practice with research endeavors. In terms of patient care, the hospital annually serves over 1,200 children patients with CP. Over the past decade, it has cared for several thousand children affected by this condition, amassing a wealth of experience in TCM-based diagnosis, treatment, and rehabilitation. This extensive experience, coupled with a vast patient database, positions the hospital perfectly to meet the rigorous demands of the research. The insights gleaned from this institution promise to make significant contributions to the advancement of CP management and treatment.

4.4 Criteria for Inclusion and Exclusion of Medical Record

4.4.1 Inclusion Criteria

4.4.1.1 Patients must fall within the age range of 4 to 14 years.

4.4.1.2 Patients must have received a medical diagnosis of spastic CP during their first or second hospital admission.

4.4.1.3 The TCM diagnosis must align with the diagnostic criteria for conditions characterized by the "Five Chi," "Five Ruan," and "Five Ying" patterns as specified in TCM diagnostic standards.

4.4.1.4 The admission information must be complete, including demographic information and essential clinical content within the medical records. Additionally, the medical records must include key elements such as the chief complaint and current symptoms as recorded during admission.

4.4.1.5 Detailed documentation of TCM symtoms and tongue-pulse manifestations during admission is required.

These inclusion criteria are established to ensure the comprehensive and rigorous collection of medical record data for the study, adhering to both Western and TCM diagnostic standards, and allowing for a robust analysis of pediatric spastic CP cases.

4.4.2 Exclusion Criteria

4.4.2.1 Medical records of patients with concomitant severe organic diseases affecting vital organs such as the heart, liver, or kidneys are excluded.

4.4.2.2 Medical records of patients with severe malnutrition, severe epileptic seizures, or primary hematological disorders are excluded.

4.4.2.3 Medical records lacking comprehensive TCM diagnostic information or

missing symptoms details are excluded.

These exclusion criteria are established to maintain the integrity and relevance of the medical records considered for the study, ensuring that cases with specific coexisting conditions or insufficient TCM diagnostic information are not included.

4.5 Methodology of the study

The data included in this study primarily originates from the electronic medical record system and hospital information system, both integrated into clinical research within the hospital setting. Subsequent to a patient's discharge following inpatient treatment, general information and relevant TCM symptoms, comprising clinical manifestations, tongue appearance, and pulse condition, were extracted from the hospital information technology database, within a specific time frame, for children diagnosed with spastic CP. In cases where the aforementioned information was missing, efforts were made to extract the corresponding details from structured textual segments, such as "patient characteristics" in the initial medical records or "admission conditions and diagnostic progress" in the discharge summary. In the event of persistent data gaps, those particular cases were excluded from statistical analysis.

This research approach ensures a comprehensive dataset collection, combining both clinical and TCM aspects, for a comprehensive analysis of spastic CP children's profiles. It adheres to established academic practices and data handling standards in medical research, guaranteeing the integrity and accuracy of the study's findings.

The data utilized in this study was extracted from the medical record system of Xi'an Encephalopathy Hospital Affiliated to Shaanxi University of Chinese Medicine. Following the formulation of a data extraction plan, and in compliance with hospital medical record management and medical ethics regulations, preliminary data retrieval

was conducted by hospital information department engineers. This process included a thorough self-audit of data accuracy and textual structuring, leading to necessary corrections and removal of invalid data. During the research period, instances where patient medical records were incomplete due to hospital system upgrades necessitated the cross-reference and supplementation of information through the examination of physical paper records. Subsequently, all data underwent preprocessing before being imported into Excel files, facilitating comprehensive data preprocessing tasks, such as data cleansing and terminology standardization. These measures aimed to explore distinctive patterns and distribution of TCM symptoms among children with spastic CP. For a visual representation of the research process please refer to Figure 4.1.

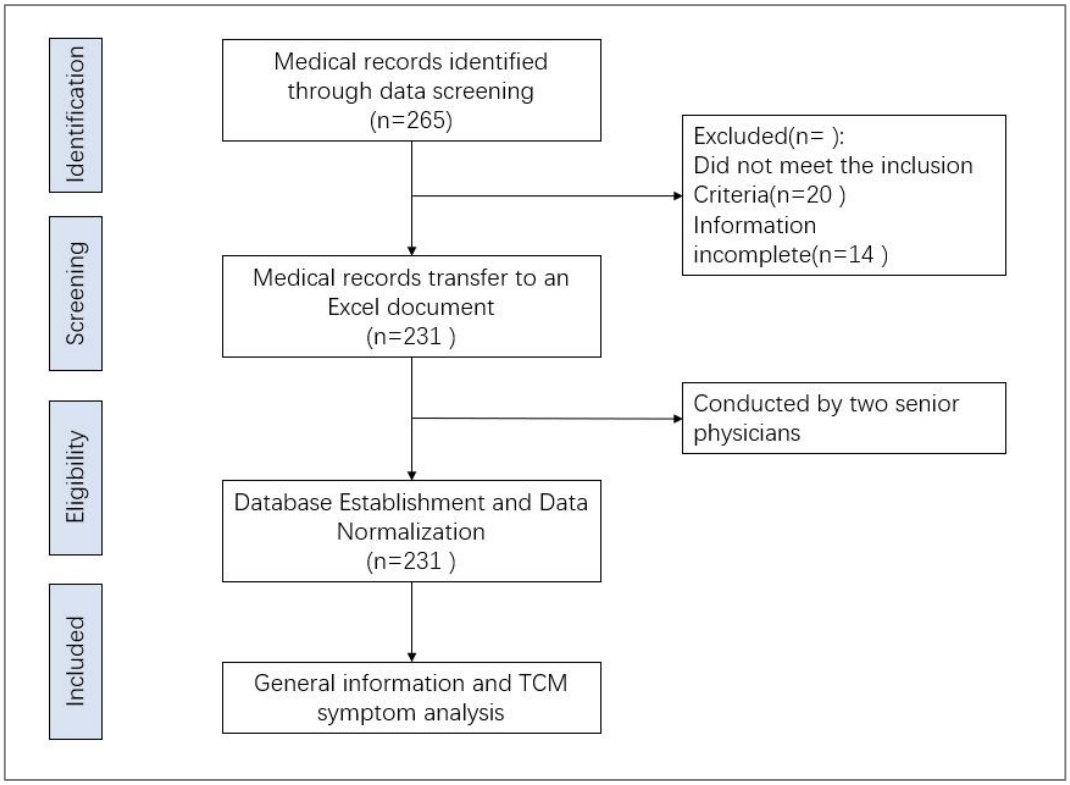

Figure 4.1: The flowchart of the TCM symptoms analysis study

4.5.1 Data Preprocessing of Medical Records

In research on data mining of TCM symptoms, achieving a substantial sample size is generally essential to maintain the study's accuracy. We included as much data as

possible that meet the inclusion. After extracting data from medical records pertaining to pediatric patients diagnosed with spastic CP, the pertinent information details were systematically organized into an Excel file. This data transformation adhered to a specific protocol: when a patient exhibited a particular characteristic, it was represented as "1" in the file; conversely, if the patient did not manifest the specified characteristic, it was denoted as "0." This data structuring methodology was primarily implemented to streamline subsequent statistical analysis. Upon the completion of all data transformations, a senior-level physician meticulously verified the information. Following this verification process, the dataset would undergo cluster analysis, focusing on the various symptom elements. This analytical approach aimed to uncover and delve into the distinctive characteristics of TCM symptoms among children diagnosed with spastic CP. This rigorous data preprocessing adheres to established academic practices, ensuring data accuracy.

4.5.2 Principles of Data Standardization Processing

The standardization of symptoms information is based on the International Clinical Practice Guidelines of Traditional Chinese Medicine in Cerebral Palsy published by the World Federation of Chinese Medicine Societies (WFCMS) In the process of standardizing clinical data related to spastic CP, the following principles are adhered to: reasonableness, accuracy, consistency, and completeness, in accordance with academic conventions.

4.5.2.1 Reasonableness

In the realm of clinical diagnosis and treatment data, elements, characteristics, concepts, and relationships, even after standardization, must remain contextually sensible within their specific linguistic contexts. This principle ensures that

standardized terms and concepts align logically with their usage in clinical practice.

4.5.2.2 Accuracy

Standardized clinical data, especially when expressed in standardized TCM terminology, should precisely reflect the original intended meaning of the data. This principle emphasizes the importance of maintaining the fidelity of clinical information during the standardization process.

4.5.2.3 Consistency

Synonyms or variant terms within clinical data should be standardized to a uniform nomenclature. For terms of the same class with similar structural forms and related conceptual content, a consistent approach to standardization is maintained. This minimizes ambiguity and enhances the clarity of the standardized data.

4.5.2.4 Completeness

This principle underscores the importance of preserving the semantic integrity of standardized terms or phrases. It is crucial that standardized terminology retains its original and essential meanings, ensuring that no crucial nuances are lost in the process.

These principles collectively form a robust framework for the standardization of clinical data in the context of spastic CP research. Adhering to these principles ensures that the standardized data remains reliable, interpretable, and consistent, thus facilitating meaningful analysis.

4.5.3 Bias Mitigation of the data

To mitigate bias, the amalgamation of semi-structured textual data with meticulously organized medical records proves instrumental in achieving precise and all-encompassing extraction of both general patient information and data pertaining to TCM symptoms. This strategic approach effectively safeguards against the inadvertent incorporation of extraneous content from the medical records system, thereby mitigating the impact of confounding variables that do not align with the research objectives.

4.5.4 Data Entry and Statistical Analysis Procedures

In the realm of data management, we adopted a meticulous approach to data collection and entry by employing a dual-entry method. This dual-entry process was instrumental in upholding the integrity and precision of the data. Following this, a comprehensive data validation protocol, including rigorous verification and logical consistency checks, was applied to ensure the highest data quality standards were met.

Turn to the statistical analyses, we used the software of IBM® SPSS® Statistics version 22 (Statistical Product and Service Solutions Statistics, I.B.M., Inc., Armonk, NY, USA) (Morgan et al., 2019). Continuous data was represented in the form of mean values accompanied by their respective standard deviations (x(_)±s), while categorical data found expression through the presentation of percentages (%).

In the sphere of R programming, we leveraged the versatility of the R programming language and the software of R studio (Gandrud, 2018). Our pursuits included clustering analysis and association rule analysis, both executed with precision. To determine the most fitting number of clusters, we engaged the "clusGap" function, a robust tool for this purpose. Data processing was facilitated through the utilization of various R packages, including but not limited to "pheatmap," "arules,"

"arulesViz," and "RColorBrewer."

For the intricate task of association rule mining, we placed our trust in the apriori algorithm, initially setting the support threshold at 0.05 and the confidence level at 0.8. Of course, we remained flexible in adjusting these thresholds when the research objectives necessitated such modifications. We harnessed the data visualization capabilities within the R programming language. These tools empowered us to craft visually compelling representations of the data, thereby enhancing our ability to grasp and interpret the research findings more effectively.

4.5.5 Ethical Approval Statement

This research focused on the analysis of electronic medical records for children with spastic CP in the hospital. It specifically concentrated on extracting and examining general patient demographics, including factors like gender, age and living area, alongside TCM symptoms. It is essential to note that the study did not delve into individual patients' detailed personal information, it was deemed exempt from the hospital's ethics review process. This exemption highlights the research's commitment to ethical considerations, privacy safeguards, and its alignment with the hospital's ethic management, ensuring that patient confidentiality remained paramount throughout the study.

4.6 Results

4.6.1 Demographic Information

Among the 231 cases of spastic CP children involved in this study, there were 128

male patients, accounting for 55.41%, and 103 female patients, accounting for 44.59%. There were 122 urban patients, making up 55.41%, and 109 rural patients, accounting for 55.41%. Table 4.1 and figure 4.2 present the data of gender and residential distribution of included patients.

Table 4.1: Gender and residential distribution of included patients

	Numbers	Percent(%)
Male	128	55.41 %
Female	103	44.59 %
Urban	122	52.81 %
Rural	109	47.19 %

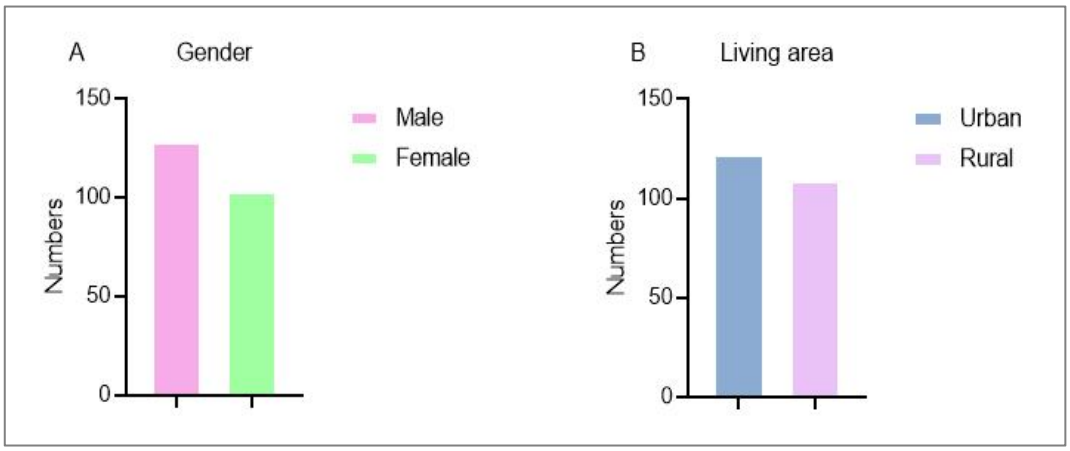

Figure 4.2: A Gender distribution of included Pediatric Patients. B Residential distribution of included Pediatric Patients

Among the 231 cases of patients in the study, the age distribution was most concentrated at 4 years old, with 42 cases, accounting for 41.35%. Following that, the second-highest concentration was observed at 5 years old, with 27 cases, representing 40.35% of the total. Subsequently, there were 26 cases at 8 years old, making up 11.26%, and 24 cases at 6 years old, constituting 10.39%. The least prevalent age groups were 13 years old and 14 years old, each having only 9 cases, with a corresponding proportion of 3.90%. Table 4.2 and figure 4.3 show the age distribution of the patients in the study.

Table 4.2: Age distribution of the patients in the study

Age of the child	Numbers	Percent(%)
4	42	18.18 %
5	27	11.69 %
6	24	10.39 %
7	21	9.13 %
8	26	11.26 %
9	22	9.52 %
10	19	8.23 %
11	18	7.79 %
12	14	6.06 %
13	9	3.90 %
14	9	3.90 %

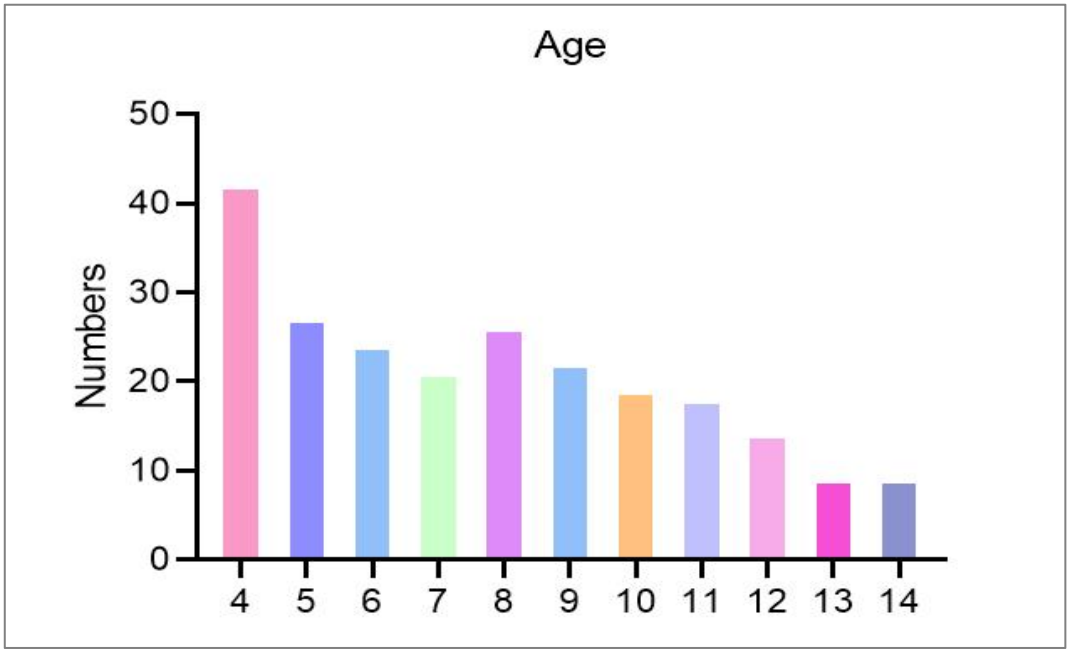

Figure 4.3: Distribution of the patients in the study

Among the 231 cases of patients with spastic CP in involved in the study, the distribution of disease duration is most concentrated within the range of 12 to 24 months, with 70 cases, accounting for 30.30%. Following that, the second-highest

distribution is observed within the 6 to 12 months range, with 55 cases, representing 23.46%. The least prevalent distribution is found in the less than 3 months range, with 25 cases, constituting 11.65%. Table 4.3 and figure 4.4 show the length of the disease.

Table 4.3: The length of the disease in the study

The length of the disease	Frequency	Percent(%)
< 3 months	25	10.82 %
3—6 months	28	12.12 %
6—12 months	55	23.81 %
12—24 months	70	30.30 %
< 24 months	53	22.9 4%

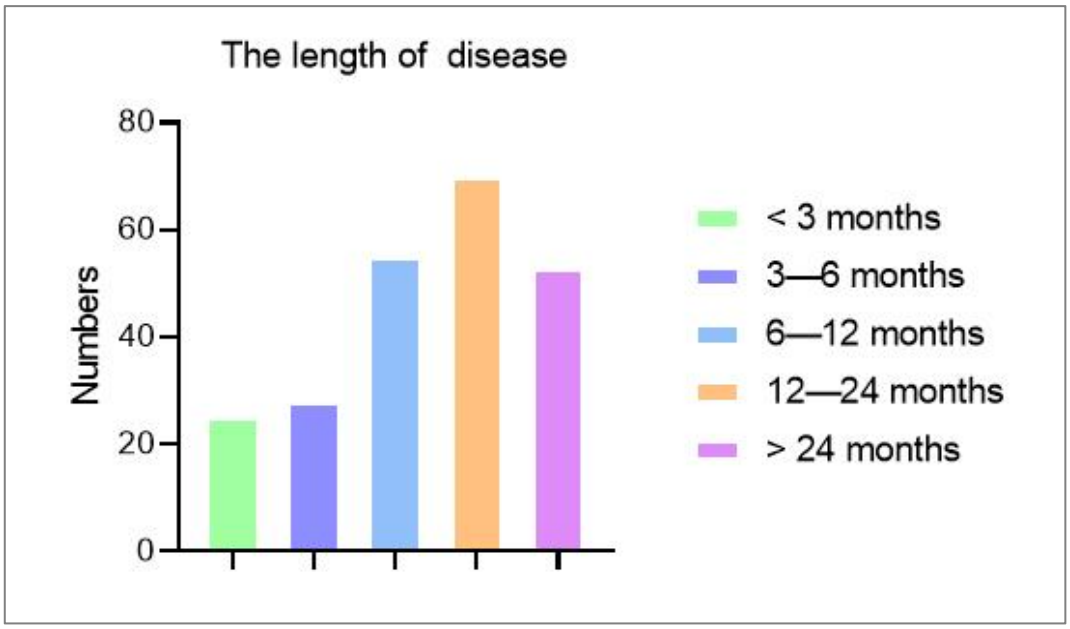

Figure 4.4: The length of the disease in the study

4.6.2 Analysis of High-Risk Factors for the Onset of Spastic CP Patients

We conducted an analysis of medical records from 231 spastic CP patients included in the study, examining their medical history, personal history, maternal prenatal anomalies, delivery methods, neonatal medical history, family history, and significant

medical events. Additionally, we performed statistical assessments of early developmental anomalies and delivery methods. Please refer to table 4.4 for detailed information.

Table 4.4: High-Risk Factors for the Onset of Spastic CP in Children

Classification	High-risk factors	Numbers	Percent(%)
Neonatal Diseases	Neonatal asphyxia and history of treatment	146	63.20 %
	History of premature birth in neonates	115	49.78 %
	History of low birth weight in neonates	114	49.35 %
	Pathological jaundice in neonates and history of treatment	47	20.35 %
	Neonatal aspiration pneumonia	2	0.87 %
	Neonatal hyperbilirubinemia	1	0.43 %
	Neonatal sepsis	1	0.43 %
Maternal Prenatal Illness and Medication History	Maternal history of medication use during pregnancy (Upper respiratory tract infections)	11	4.76 %
	Maternal history of threatened miscarriage and medication use	8	3.46 %
	Pregnancy-induced hypertension	7	3.03 %
	Advanced maternal age	6	2.59 %
	Abnormal emotional state during pregnancy	4	1.73 %
	Maternal history of medication use during pregnancy (for anemia, neurological conditions, nutritional deficiencies, high fever, others)	2	0.87 %
	Intermittent shortness of breath during	1	0.43 %

	pregnancy		
	Maternal history of hyperthyroidism during pregnancy	1	0.43 %
	Trauma	1	0.43 %
Delivery Method	Full-term pregnancy (natural delivery)	79	34.20 %
	Full-term pregnancy (cesarean section)	32	13.85 %
	Preterm birth (natural delivery)	39	16.88 %
	Preterm birth (cesarean section)	76	32.90 %
	Post-term pregnancy (natural delivery)	0	0
	Post-term pregnancy (cesarean section)	4	1.73 %
	Unknown	1	0.43 %
Birth situation	Umbilical cord around the neck	12	5.19 %
	Abnormal fetal positioning	11	4.76 %
	Premature rupture of membranes	2	0.87 %
	Rapid fetal heart rate	1	0.43 %
	In Vitro Fertilization	1	0.43 %
	Placenta previa	1	0.43 %
Amniotic Fluid situation	Amniotic fluid leakage	3	1.30 %
	Insufficient amniotic fluid	3	1.30 %
	Contaminated amniotic fluid	2	0.87 %
	Excessive amniotic fluid	1	0.43 %
Environmental Pollution Exposure History	History of environmental pollution (methanol)	2	0.87 %

Among the subgroup of pediatric patients presenting with early developmental anomalies, a noteworthy 146 cases (constituting 63.20%) had a documented history of neonatal asphyxia, along with corresponding therapeutic interventions. Additionally,

115 cases (equivalent to 49.78%) were marked by a history of premature births, and an additional 114 patients (accounting for 49.35%) had records of being born with low birth weight. It is also worth highlighting that 47 cases (comprising 20.35%) of these patients exhibited a history of neonatal pathological jaundice, coupled with the requisite treatments. In contrast, the occurrence of other conditions in this specific cohort of patients appeared to be relatively less frequent.

In our thorough examination of maternal prenatal illness and medication history within the observed children with spastic CP, we have identified several notable risk factors. Foremost among these is the maternal medication history during pregnancy, with a notable focus on cases related to upper respiratory tract infections, which afflicted 11 individuals, constituting 4.76% of the total. Following closely, we find the history of threatened miscarriage alongside the associated medication usage, ranking as the second most prevalent factor, impacting 8 cases, which accounts for 3.46% of the cohort. In the third position, there were 7 instances (3.03%) where mothers experienced pregnancy-induced hypertension during their gestational period. It is important to emphasize that other contributing factors also play a role. For instance, cases where the mothers were of advanced maternal age numbered 6 (2.59%). Additionally, there were 4 cases (1.73%) marked by abnormal emotional state during pregnancy. Furthermore, we observed maternal medication history during pregnancy for various conditions, including anemia, neurological conditions, nutritional deficiencies, high fever, and other ailments. In the same vein, maternal experiences of intermittent shortness of breath during pregnancy, a history of hyperthyroidism during pregnancy, and incidents of maternal trauma during pregnancy were also documented.

In our comprehensive exploration of the impact of delivery methods on children with spastic CP outcomes, we meticulously analyzed all the 231 cases, unveiling intriguing patterns. Among those born at full term pregnancy, a substantial 79 cases (34.20%) entered the world through natural delivery, while 32 cases (13.85%) were delivered via cesarean section. Delving into the preterm category, comprising 115

cases, a nuanced picture emerged. Within this group, 39 infants were brought into the world through natural delivery, representing 16.88%, whereas an overwhelming 76 infants arrived via cesarean section, accounting for 32.90% of this subgroup. It is worth highlighting that we also encountered 4 instances (1.73%) of post-term pregnancies, every one of them involved non-natural delivery methods.

Regarding the birth situation within the 231 spastic CP patients, we conducted a thorough analysis. Among them, 12 cases (5.19%) displayed the presence of umbilical cord around the neck, while 11 cases (4.76%) were associated with abnormal fetal positioning. Additionally, other noteworthy anomalies included premature rupture of membranes, which manifested in 2 cases (0.87%). Furthermore, specific instances were observed in smaller proportions, such as rapid fetal heart rate, occurrences involving in Vitro Fertilization, and instances of placenta previa, each accounting for only 1 case (0.43%). This detailed examination sheds light on the diverse obstetric factors potentially contributing to CP in these patients.

Some noteworthy findings were revealed when examing the amniotic fluid. Specifically, within all the 231 patients with spastic CP, we noted that only 3 cases, constituting a modest 1.30% of the total, were afflicted with amniotic fluid leakage. Similarly, an equivalent proportion of 3 cases (1.30%) exhibited insufficient amniotic fluid. Furthermore, we identified 2 cases (0.87%) with evidence of amniotic fluid contamination. A rare occurrence, excessive amniotic fluid, was documented in just one case (0.43%), underscoring its infrequency within this patient population.

Lastly, we observed that, in terms of a history of environmental pollution exposure, 2 cases of pediatric patients had a history of methanol exposure, accounting for 0.87% of the total patient population.

4.6.3 Analysis results of TCM symptoms in Spastic CP Patients

Upon conducting an exhaustive examination of TCM symptoms within the patient included in the study, particularly focusing on the top 30 symptoms, we unearthed important and multifaceted trends. Among this extensive group, which comprised well 231 cases, a remarkably consistent profile emerged. The majority of these patients presented with a cluster of symptoms, encompassing symptoms of 'Motor dysfunction', 'Impaired speech', 'Delayed development', and 'Limb stiffness'.

Furthermore, we observed that a significant proportion, exceeding 120 cases, exhibited a wide spectrum of TCM symptoms and tongue-pulse characteristics. These encompassed features such as 'Thin and white tongue coating', 'Rigidity in the limbs', a tongue named 'Pale red tongue', a pulse named 'Rapid and thready', 'Intellectual impairment', 'Stiff neck, and 'Light fingerprint patterns'.

Additionally, it is noteworthy that specific TCM symptoms were particularly prevalent within this cohort of spastic CP patients. Over 90 cases displayed clinical features including 'Timid and easily startled', 'Muscle wasting', 'Stunted growth', 'Dull expression', 'Delayed response', 'Fatigue and weakness', 'Phlegm rales in the throat', 'Susceptibility to colds', 'Cyanosis of the fingertips', 'Spontaneous perspiration', 'Frequent and clear urination', 'Poor appetite', 'Diarrhea', 'Restlessness and insomnia', 'Slow movement of limbs', 'Dry and brittle hair.' Notably, clinical symptoms of 'Irritability and easy anger', 'Pale or dull complexion' were also relatively common, each being observed in over 80 cases. For an even more detailed breakdown of these findings, we recommend referring to the table 4.5 and figure 4.5.

Table 4.5: High-Frequency Distribution of TCM Symptoms in Spastic CP Patients

Name of Symptoms	Numbers	Percent(%)	Name of Symptoms	Numbers	Percent (%)
Motor dysfunction	231	100 %	Delayed response	103	44.59

(运动障碍)			(反应迟钝)		%
Impaired speech (言语不利)	224	96.97 %	Fatigue and weakness (神疲乏力)	102	44.16 %
Delayed development (发育迟缓)	218	94.37 %	Phlegm rales in the throat (喉间痰鸣)	100	43.29 %
Limb stiffness (肢体拘挛)	207	89.61 %	Susceptibility to colds (易感冒)	99	42.86 %
Thin and white tongue coating (苔薄白)	195	84.42 %	Cyanosis of the fingertips (指纹青紫)	99	42.86 %
Rigidity in the limbs (手足硬)	169	73.16 %	Drooling (口角流涎)	98	42.42 %
Pale red tongue (舌质淡红)	162	70.13 %	Spontaneous sweating (自汗)	97	41.99 %
Rapid and thready pulse (脉细数)	151	65.37 %	Frequent clear urination (小便清长)	94	40.69 %
Intellectual impairment (智力低下)	139	60.17 %	Poor appetite (食少纳差)	93	40.26 %
Stiff neck (头项硬)	137	59.31 %	Diarrhea (便溏)	93	40.26 %
Light fingerprints	120	51.95	Restlessness and	91	39.39

(指纹淡)		%	insomnia (夜寐不安)		%
Timid and easily startled (胆小易惊)	115	49.78 %	Slow movement of limbs(手足徐动)	90	38.97 %
Muscle wasting (肌肉消瘦)	110	47.62 %	Dry and brittle hair (毛发干枯)	90	38.97 %
Stunted growth (身材矮小)	108	46.75 %	Irritability and easy anger (烦躁易怒)	86	37.23 %
Dull expression (神情呆滞)	105	45.45 %	Pale or dull complexion (面色少华或无华)	81	35.06 %

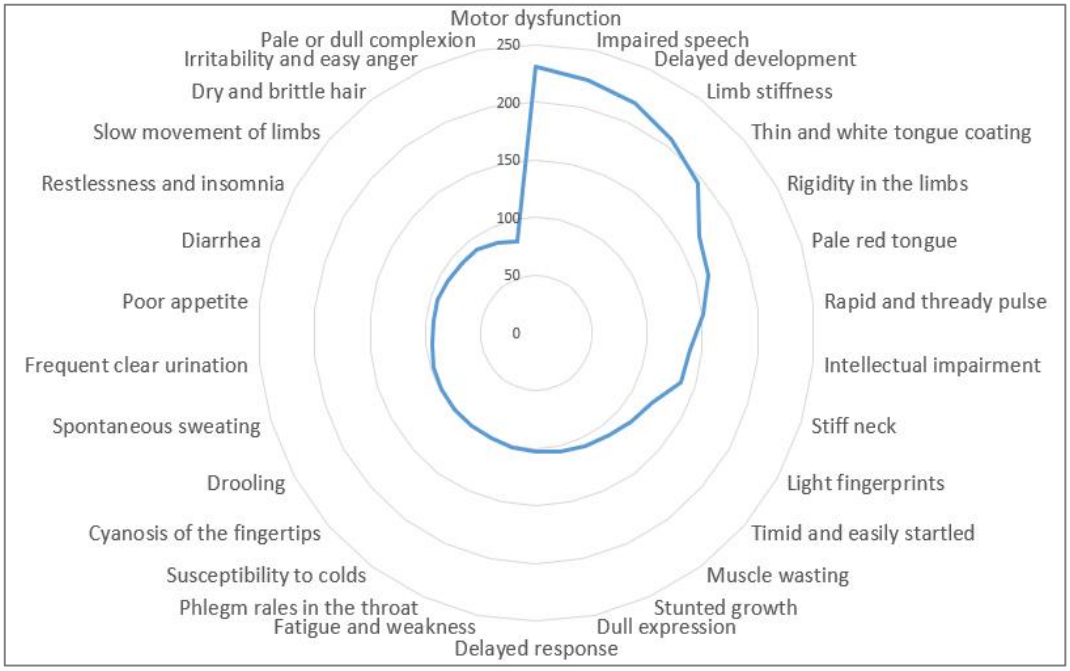

Figure 4.5: Radar Chart of High-Frequency TCM Symptoms in Spastic CP Patients

4.6.4 Cluster Analysis results of the high-frequency TCM symptoms on spastic CP patients

In our study of high-frequency TCM symptoms in spastic CP patients, we employed rigorous analytical methods. Utilizing the R Studio software, we conducted a comprehensive cluster analysis focusing on the top 30 frequently occurring symptoms. To determine the optimal number of clusters, we employed the 'clusGap()' function, resulting in a discernible peak at four clusters, indicating the attainment of the most suitable clustering solution. This outcome is visually represented in figure 4.6. Subsequently, we proceeded to perform a cluster analysis encompassing all identified TCM symptoms in the patients. Employing the 'pheatmap()' function, we visualized the clustering outcomes. Notably, our analysis unveiled that high-frequency TCM symptoms in spastic CP patients could be effectively categorized into four distinctive clusters, as demonstrated in figure 4.7. Within these clusters, the first group stands out as comprising the core TCM symptoms commonly associated with spastic CP patients, while the remaining clusters encompass non-core TCM symptoms in the patients. This comprehensive analysis enhances our understanding of the intricate TCM patterns observed in these patients.

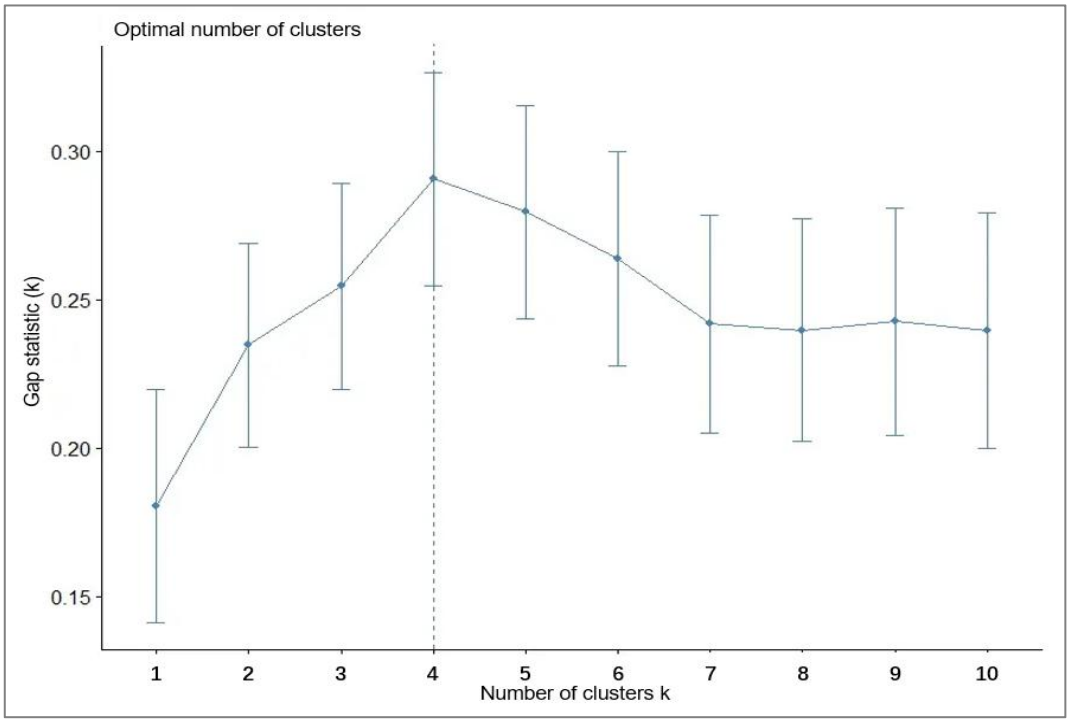

Figure 4.6: The result of optimal cluster number

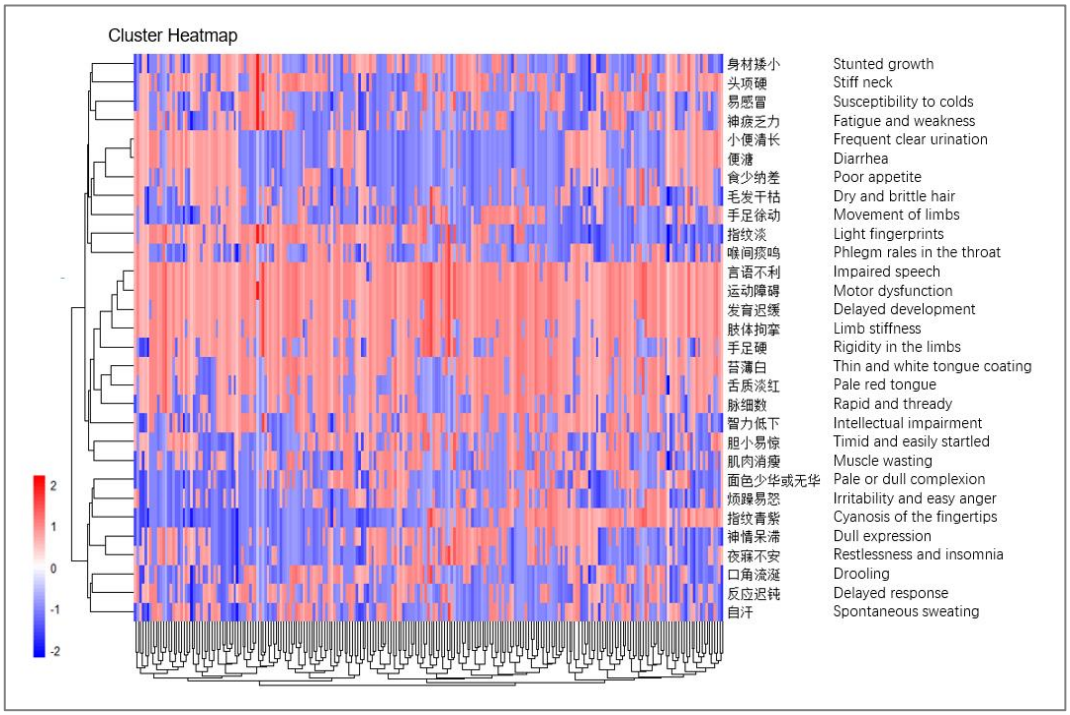

Figure 4.7: The cluster analysis result of TCM symptoms in spastic CP patients

The TCM symptoms observed in the study could be divided into four categories as follows:

The first category, characterized by a constellation of symptoms including ‘Motor Dysfunction’, ‘Impaired speech’, ‘Delayed development’, ‘Limb stiffness’, ‘Rigidity in the limbs’, ‘Intellectual impairment’, ‘Timid and easily startled’, ‘Muscle wasting’, and ‘Pale or dull complexion’, was identified as the core set of symptoms associated with this spastic CP patients. Additionally, these individuals typically exhibited a tongue with ‘Thin and white tongue coating’, ‘Pale red tongue’, and a ‘Rapid and thready pulse’.

The second category of TCM symptoms encompassed behavioral traits such as ‘Irritability and easy anger’, ‘Dull expression’, ‘Restlessness and insomnia’, ‘Drooling’, ‘Delayed response’, ‘Spontaneous sweating’, and ‘Cyanosis of the fingertips’.

Moving on to the third category, patients in this group predominantly displayed signs of ‘Poor appetite’, ‘Dry and brittle hair’ ‘Slow Movement of limbs’, ‘Light fingerprints’, ‘Phlegm rales in the throat’, ‘Frequent clear urination’, and ‘Diarrhea’.

Lastly, the fourth category was characterized by TCM symptoms such as ‘Stunted growth’, ‘Stiff neck’, ‘Susceptibility to colds’, and a persistent state of ‘Fatigue and weakness’.

These detailed categories help provide a deeper understanding of TCM symptoms patterns observed within the spastic CP. In accordance with the cluster analysis results, we can summarize that the main characteristics of TCM symptoms in spastic CP patients primarily revolve around motor dysfunction and limb stiffness. Simultaneously, patients exhibit signs of weakness, such as persistent fatigue and weakness, susceptibility to colds, and delayed development, which are attributed to both congenital and acquired deficiencies. It is believed that the pathogenesis of this condition in TCM is driven by excessive liver qi and weakened spleen qi, with an imbalance where the strong liver qi dominates and overcomes the weaker spleen qi. In terms of TCM syndrome differentiation, it should be classified as a pattern characterized by liver exuberant and spleen weakness.

4.6.5 Association Rule Analysis results of the high-frequency TCM symptoms on spastic CP patients

In this section of our study, we conducted an in-depth association rule analysis, focusing our attention on the 30 most high frequently occurring TCM symptoms among the cohort of 231 spastic CP patients that that we included in our research. This comprehensive analysis entailed the development of a robust modeling framework using R Studio. To ensure the extraction of meaningful insights, we strategically employed the Apriori algorithm with specific parameter configurations.

Our approach involved setting a minimum support threshold at 0.1 and a minimum confidence threshold at 0.8, which effectively guided the entire association rule analysis process. It's worth emphasizing that 'support' (Sup) in this context quantifies the probability of both the left-hand set of symptom or symptoms combinations and the right-hand set of symptoms occurring concurrently when represented by the '=>' symbol. Conversely, 'confidence' (Con) signifies the probability of the right-hand set of symptom manifesting when the left-hand set of symptom or symptoms combinations combinations is observed, denoted by the '=>' symbol.

To gain a comprehensive understanding of the interplay between symptoms, we meticulously ranked and analyzed the top 20 contributing association rules within our research. These rules were meticulously generated, using the most frequently encountered symptoms as the anchor in the left-hand set. The culmination of our analysis is thoughtfully presented in table 4.6 and figure 4.8, where we meticulously arrange the association rules characterizing spastic CP symptoms in a descending order, meticulously organized by support values. It is of paramount importance to underscore that, throughout this ranking process, the association rules consistently demonstrated remarkable levels of confidence, all surpassing the significant threshold of 0.8.

Table 4.6: Association rules for high-frequency TCM symptoms in spastic CP patients

	Lhs	Rhs	Support	Cofidence
1	Motor dysfunction (运动障碍)	Impaired speech (言语不利)	0.9695652	0.9695652
2	Motor dysfunction (运动障碍)	Delayed development (发育迟缓)	0.9434783	0.9434783
3	Delayed development	Impaired speech	0.9173913	0.9723502

	(发育迟缓)	(言语不利)		
4	Impaired speech (言语不利)	Delayed development (发育迟缓)	0.9173913	0.9461883
5	Delayed development (发育迟缓)	Limb stiffness (肢体拘挛)	0.8956522	0.8956522
6	Limb stiffness (肢体拘挛)	Impaired speech (言语不利)	0.8695652	0.9708738
7	Impaired speech (言语不利)	Limb stiffness (肢体拘挛)	0.8695652	0.8968610
8	Limb stiffness (肢体拘挛)	Delayed development (发育迟缓)	0.8521739	0.9514563
9	Delayed development (发育迟缓)	Limb stiffness (肢体拘挛)	0.8521739	0.9032258
10	Rigidity in the limbs (手足硬)	Thin and white tongue coating (苔薄白)	0.8434783	0.8434783
11	Delayed development, limb stiffness (发育迟缓，肢体拘挛)	Impaired speech (言语不利)	0.8260870	0.9693878
12	Impaired speech, limb stiffness (言语不利，肢体拘挛)	Delayed development (发育迟缓)	0.8260870	0.9500000
13	Delayed development, impaired speech (发育迟缓,言语不利)	Limb stiffness (肢体拘挛)	0.8260870	0.9004739
14	Thin and white tongue coating	Impaired speech	0.8173913	0.9690722

	(苔薄白)	(言语不利)		
15	Impaired speech (言语不利)	Thin and white tongue coating (苔薄白)	0.8173913	0.8430493
16	Impaired speech (言语不利)	Delayed development (发育迟缓)	0.8130435	0.9639175
17	Thin and white tongue coating (苔薄白)	Pale or dull complexion (面色少华或无华)	0.8130435	0.8617512
18	Delayed development, thin and white tongue coating (发育迟缓,苔薄白)	Impaired speech (言语不利)	0.7869565	0.9679144
19	Impaired speech (苔薄白，言语不利)	Delayed development (发育迟缓)	0.7869565	0.9627660
20	Delayed development, impaired speech (发育迟缓，言语不利)	Thin and white tongue coating (苔薄白)	0.7869565	0.8578199

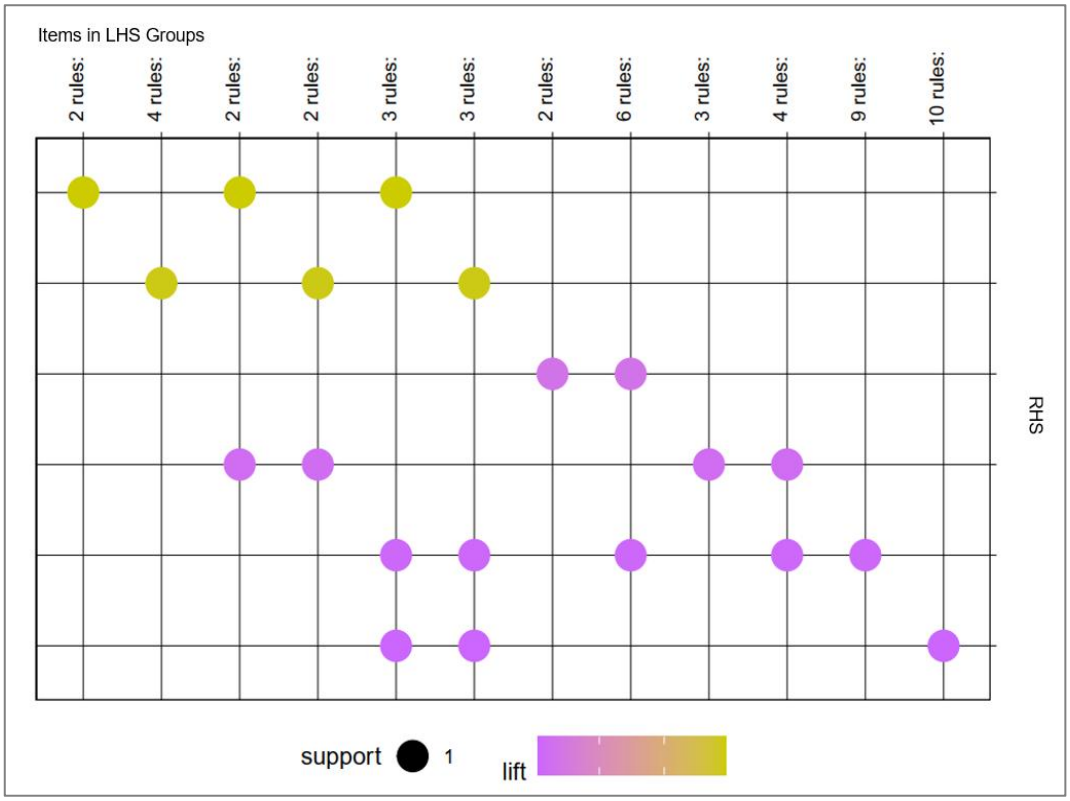

Figure 4.8: The visualization for high-frequency TCM symptoms in Spastic CP

As we delve into the rich insights encapsulated in Table 12, an intriguing narrative unfurls. When 'Motor dysfunction' takes the lead in the left-hand set, it forges a strong association with the primary TCM symptoms of 'Impaired speech' and 'Delayed development.' Similarly, when 'Delayed development' hold sway as the keystone in the left-hand set, we discern a robust and profound link with 'Impaired speech' and 'Limb stiffness,' reaffirming the symbiotic nature of these clinical phenomena. This intricate web of associations paints a vivid picture of the nuanced interplay among these symptoms. Moreover, our analysis unveils additional layers of compelling association rules. Notably, 'Impaired speech' and 'Delayed development' 'Limb stiffness' and 'Impaired speech,' as well as 'Delayed development' and 'Limb stiffness,' all manifest as a cohesive network, characterized by its robustness and profound interdependence. This intricately woven tapestry of symptoms, unified by their strength and coherence, collectively shapes the fundamental symptoms profile that typifies individuals living with spastic CP.

Furthermore, it is worth directing our attention to the robust associations observed between tongue and pulse characteristics and other TCM symptoms in spastic CP patients. Notably, certain correlations stand out prominently, signaling significant clinical relevance. Among these correlations, we find the strong associations between 'Thin and white tongue coating' and 'Impaired speech' , 'Thin and white tongue coating' and 'Pale or dull complexion' , as well as 'Delayed development' , 'Thin and white tongue coating' and 'Impaired speech'.

These associations are not merely coincidental but are underpinned by robust levels of support and confidence. They shed light on 'Thin and white tongue coating' as the most prevalent tongue and pulse characteristic among individuals afflicted with spastic CP. Simultaneously, it becomes evident that 'Pale or dull complexion' is a relatively common facial feature observed among spastic CP patients. This is similar as the diagnosis of the syndrome pattern characterized by liver exuberant and spleen weakness adds further credence to these findings.

4.7 Discussion

Within the scope of this study, a comprehensive analysis of patient general demographics reveals differences in terms of both gender distribution and urban-rural distribution among children diagnosed with spastic CP. Nonetheless, the ratios remain relatively even, with a minor male predominance and a slight urban bias, specifically, there are slightly more male than female and slightly more urban than rural patients. This observation aligns with earlier epidemiological studies in China and other Countries (Goldsmith et al., 2023, Andromeda et al., 2023, Zhakupova et al., 2023, Feng et al., 2022, McIntyre et al., 2022). In relation to male children being slightly more affected, we consider this could be attributed to the biological vulnerability in males, believed to be based on multiple factors, ranging from potential differences in

brain organization to the influence of genetic conditions or female hormones that might mitigate the impact of brain injury (Romeo et al., 2016). Moreover, urban-rural disparities appear to be influenced more by factors such as affordability of medical costs and caregivers' perspectives.

CP is a complex developmental disorder characterized by motor and postural impairments (Paul et al., 2022), often originating in early childhood and persisting throughout an individual's lifetime (Handsfield et al., 2022). It significantly impacts movement, muscle tone, and motor skills due to damage to the developing brain, which can occur during pregnancy, childbirth, or shortly after birth. The incidence of CP is multi factorial, influenced by a range of variables. Notable factors include premature birth, complications during birth, and the overall health of the mother during pregnancy (Liew and Zhuo, 2023, Khan et al., 2022). Our study delved into these factors, shedding light on critical elements associated with spastic CP. The research highlighted the significance of a history of (Goldsmith et al., 2023, Daou et al., 2022) neonatal asphyxia and subsequent treatments, premature birth, low birth weight in neonates, neonatal pathological jaundice, and specific medical interventions during the neonatal period as substantial risk factors for spastic CP. Moreover, maternal prenatal conditions, including medication use during pregnancy, maternal history of threatened miscarriage, history of certain medications, pregnancy-induced hypertension, emotional disturbances during pregnancy, and advanced maternal age, were identified as frequent contributors to the incidence of spastic CP. Prenatal care that addresses these risk factors can play a pivotal role in reducing the incidence of CP and improving outcomes for both the mother and the child. When examining the mode of delivery revealed a higher prevalence of preterm births and cesarean section among children with CP. Conversely, cases involving in situation amniotic fluid and exposure to environmental pollutants were remarkably rare among children diagnosed with spastic CP, suggesting a need for further research to comprehend these intriguing correlations fully. Understanding these factors comprehensively is crucial for devising preventive strategies and enhancing the quality of care for individuals with spastic CP.

According to the TCM theory, CP is often attributed to deficiencies in vital essence and energy, leading to impaired brain development (Li et al., 2022). The disorder is thought to involve disharmony in organs such as the liver, spleen, and kidneys. However, the diagnosis and treatment of TCM are often a dynamic and personalized process (Jiao and Wang, 2022). TCM practitioners approach treatment through a holistic lens, aiming to restore yin and yang balance in the body. But different academic system and professional orientations can lead to varying syndrome differentiation conclusions, such as organ-based differentiation(Zang Fu), defense-qi nutrient, and blood differentiation(Wei Qi Ying Xue), six meridian differentiation(Liu Jing), and three-Jiao differentiation (Matos et al., 2021a, Liu et al., 2021). This rich tapestry of theories enriches the scope of clinical diagnosis and treatment in TCM but also poses challenges in organizing, summarizing, communicating, and learning knowledge of diagnosis and treatment in TCM. Therefore, this study does not use TCM syndrome types as the classification basis for children with CP. Instead, it chooses spastic CP diagnosed in Western medicine as the inclusion criteria for the study. Through the integration of data mining techniques, evidence-based medicine theory, computer technology, and TCM theory, it explores the characteristics of TCM symptoms in the included patients diagnosed with spastic CP. It aims to summarizes the clinical symptom characteristics of the corresponding population, understands their clinical differentiation patterns, and ultimately provides guidance and standardization for clinical TCM intervention for this disease. Subsequently, we hope that the research in the next phase can enhance the clinical treatment efficiency of spastic CP through TCM intervention(such as AT), seeking to ameliorate the patients' conditions and mitigate the burden on families and society. By amalgamating TCM principles with modern medical approaches, a comprehensive and effective strategy can be formulated to manage CP, potentially augmenting the quality of life for affected individuals and their families.

Syndrome differentiation and treatment(SDT) (Dou et al., 2021, Ma et al., 2019)

is one of the fundamental and paramount therapeutic principles in TCM. It entails TCM practitioners continuously collecting experiences from effective medical cases of predecessors and their own practice. By aggregating these experiences, TCM practitioners identify common phenomena, contemplate shared pathogenic mechanisms, and summarize effective treatment methods and prescriptions. Building upon this foundation, practitioners then apply these identified patterns to clinical practice and continually validate the reliability of the derived principles through ongoing clinical verification and validation. The significance of SDT transcends theoretical understanding—it is deeply rooted in pragmatic clinical application. TCM practitioners implement these derived patterns and principles in the tailoring treatments to individual patients. Through continuous application and validation in clinical scenarios, practitioners not only reaffirm the efficacy of identified patterns but also contribute to the evolution and expansion of the vast tapestry of TCM knowledge (Zhang and Li, 2021, Deng et al., 2018).

This study is a cross-sectional investigation conducted in a non-interventional setting, focusing on exploring clinical characteristics and TCM symptom distribution in children with spastic CP. A comprehensive analysis was carried out on 231 medical records, involving data extraction, cleansing, mining, and summarization. The research unearthed prevalent TCM symptoms shared among the majority of patients, typified by ‘Motor dysfunction’, ‘Impaired speech’, ‘Delayed development’, and ‘Limb stiffness’. Furthermore, over half of the patients exhibited similar symptoms such as ‘Thin and white tongue coating’, ‘Rigidity in the limbs’, ‘Intellectual impairment’, ‘Stiff neck’, and ‘Light fingerprints’ with ‘Pale red tongue’ and ‘Rapid and thready pulse’, These findings shed light on specific TCM patterns observed in both tongue and pulse manifestations, contributing valuable insights into the diagnostic and therapeutic approaches for spastic CP within the realm of TCM. The study provides a foundational understanding to aid further research and to refine tailored treatments for affected individuals, potentially improving their overall quality of life.

Among the top-ranking combinations of symptoms, patterns emerge wherein 'Motor dysfunction' intertwine with 'Impaired speech', 'Motor dysfunction' coexist with 'Delayed development', and 'Impaired speech' are accompanied by 'Delayed development'. These association rules provide critical insights into the intricate interplay of symptoms, allowing for a more nuanced understanding of the condition. Upon analysis of clustering and high-frequency TCM symptoms, a central framework of core symptoms for children diagnosed with spastic CP materializes. This foundational framework comprises important symptoms like ‘Motor Dysfunction’, ‘Impaired speech’, ‘Delayed development’, ‘Limb stiffness’, ‘Rigidity in the limbs’, ‘Intellectual impairment’, ‘Timid and easily startled’, ‘Muscle wasting’, and ‘Pale or dull complexion’. These core symptoms encapsulate the key clinical manifestations that define spastic CP in the context of TCM. In addition to the core symptoms, there exist non-core symptoms that, while noteworthy, don't hold the same level of important in characterizing spastic CP. These include manifestations such as ‘Irritability and easy anger’, ‘Dull expression’, ‘Restlessness and insomnia’, ‘Drooling’, ‘Delayed response’, ‘Spontaneous sweating’, ‘Cyanosis of the fingertips’, ‘Poor appetite’, ‘Dry and brittle hair’ ‘Slow Movement of limbs’, ‘Light fingerprints’, ‘Phlegm rales in the throat’, ‘Frequent clear urination’, ‘Diarrhea’, ‘Stunted growth’, ‘Stiff neck’, ‘Susceptibility to colds’, and a consistent state of ‘Fatigue and weakness’. Although these non-core symptoms provide valuable clinical insights into the overall health and state of the individual with CP, they are not as pivotal as the core symptoms in characterizing the condition. By addressing the core symptoms that play a central role in spastic CP, healthcare practitioners can design treatment method that encompass a holistic approach striving for enhanced therapeutic outcomes and improved quality of life for affected individuals.

Based on the core and non-core clinical symptoms observed in the study, the TCM perspective attributes the pathogenesis of these symptoms to an exuberant of liver Qi, weakness in spleen Qi, and the dominant and overpowering nature of liver Qi

over the weaker spleen. This categorization aligns with TCM syndrome differentiation as the "liver exuberant and spleen weakness" pattern. In TCM theory, the liver is believed to govern the body's tendons and fascia, playing a vital role in storing and regulating blood. On the other hand, the spleen is responsible for managing the body's muscles, controlling the processes of digestion and absorption, and serving as the fundamental source for Qi and blood generation. When the liver exerts dominance and overpowers the spleen, especially when the spleen is weak, its functionality diminishes. This weakening leads to compromised digestion and absorption processes, resulting in a deficiency of Qi and blood generation. Consequently, insufficient blood storage in the liver and its impaired ability to regulate blood volume lead to the muscles losing their nourishment from Qi and blood. This deficiency manifests as stiffness in the limbs, neck rigidity, and difficulty in swallowing, often referred to as the "internal wind" phenomenon or the "five Ying" concept in TCM, characterized by involuntary muscle spasms and rigidity. When the child's limbs are stimulated, the muscle spasms intensify. Hence, By addressing the imbalance and strengthening the spleen while regulating liver Qi, practitioners aim to restore equilibrium in the body, ultimately ameliorating the symptoms and enhancing the overall well-being of children with spastic CP.

4.8 Conclusion

This research employed an interdisciplinary methodologies, integrating data mining techniques, evidence-based medicine, computer technology, big data mining， and TCM. The comprehensive approach was aimed at conducting an in-depth investigation of medical records, delving into the population characteristics, and identifying disease risk factors in children diagnosed with spastic CP. The ultimate objective was to explore and understand the clinical TCM symptoms prevalent in these young patients.

By utilizing advanced statistical methods such as frequency analysis, cluster analysis, and association rule analysis, the study initially identified and summarized the core and non-core TCM symptoms observed in children diagnosed in spastic CP. This foundational work not only provided a robust theoretical foundation but also supplied evidence rooted in evidence-based medicine. Informed by the core symptoms and TCM theories applicable to the pediatric population, the study suggests the feasibility of standardized TCM treatment, such as AT, as a viable intervention for children with the disease. It is noteworthy that standardized TCM interventions often exhibit strong generalizability and broad applicability, making them promising avenues for clinical application. Looking ahead, the clinical interventional research in the subsequent phase, built upon the insights derived from this study, is expected to bring tangible benefits to a larger cohort of children grappling with spastic CP.

4.9 Limitation

Due to limited personal resources, this study was conducted only in Xi'an City, Shaanxi Province, in the western region of China. The number of cases included in the study was also insufficient. Therefore, further research is needed in other regions or countries to verify whether spastic CP can be linked to the TCM syndrome of " liver exuberant and spleen weakness" pattern of CP, which would provide more theoretical basis for the standardization of TCM interventions in spastic CP.

CHAPTER 5.0

ACUPUNCTURE AND TUINA TREATMENT IN GROSS MOTOR FUNCTION OF CHILDREN WITH SPASTIC CEREBRAL PALSY

5.1 Background

According to the Fundamental Theories of TCM, AT is characterized by its ability to regulate Qi and blood, harmonize Yin and Yang, and strengthen the body while dispelling pathogenic factors (Lin et al., 2022, Chen et al., 2019, White et al., 2018, Organization, 2020). AT therapy involves the use of needles, moxibustion and tuina techniques applied to specific acupoints on the human body to achieve therapeutic effects (Matos et al., 2021b). According to TCM, the meridians are channels that connect the internal and external aspects of the body and play a role in adjusting the balance of Yin and Yang, promoting meridian flow, and invigorating blood circulation to dispel stasis. These meridians connect the internal organs and extend to the limbs and joints. Acupoints are specific locations on the body where the Qi of the meridians and internal organs gathers on the surface (Zhou and Benharash, 2014).

AT represents an indispensable and fundamental element within the realm of TCM and has an extensive historical legacy, spanning thousands of years of utilization in China to address a diverse range of medical conditions, including CP (Fan et al., 2010, Huang et al., 2022, Yang et al., 2021). Studies (Yu et al., 2015) had explored and demonstrated that acupuncture can effectively promote the reorganization of brain nerve cells, including improving cerebral cortex ischemia and hypoxia, reducing brain edema and lipid peroxidation, and enhancing cognitive and motor function.

AT has significant advantages in the treatment of children with CP. The efficacy of AT treatments in managing CP has been the subject of considerable studies, with a multitude of them showcasing promising results (Yan et al., 2019, LI et al., 2020, Xu et al., 2022), demonstrating more pronounced therapeutic effects compared to other rehabilitation treatments (Lang et al., 2023, Mali et al., 2023). It is a convenient, economically safe, and well-accepted therapy by a large number of patients, yielding satisfactory results. In recent years, AT therapy for CP has rapidly evolved, displaying a trend towards diversification and integration of various treatment methods. In clinical practice, commonly used techniques include scalp acupuncture, body acupuncture, electroacupuncture, tuina along meridian, and acupoint pressure, among others (Xiaofei et al., 2023).

Acupuncture therapy shows precise therapeutic effects in the treatment of pediatric CP. Among these therapies, scalp (Xueli et al., 2023, Jinpeng et al., 2021) acupuncture is based on modern medical functional localization of the cerebral cortex and utilizes the theory of visceral meridians. Principle of acupuncture reflexively increases blood supply to the cortical area, improves peripheral blood circulation, and repairs damaged cells. In addition to scalp acupuncture, other treatment methods such as body acupuncture, electroacupuncture, and aquapuncture are also applied (Yaochen et al., 2022), resulting in the best, fastest, and most significant clinical outcomes for affected children. Conventional Tuina adheres to the traditional theories of Zang-Fu organs, meridians, and muscular, aiming to achieve the goals of regulating tendons, integrating, and restoring qi, promoting blood circulation, opening the meridians, benefiting the joints, and harmonizing the Zang-Fu organs, ultimately leading to the balance of Yin and Yang. Specific acupoint Tuina (Xian et al., 2022), guided by the concept of 'tonifying the spleen and strengthening the kidneys,' applies specific techniques to certain acupoints beyond the traditional fourteen meridians and extraordinary points. This approach primarily focuses on treating deficiencies and weakness in the Zang-Fu organs. The spleen governs transformation and transportation, nourishing the brain and promoting bone health. Only when the

spleen's Qi and blood transformation function normally can the brain function properly.

A noteworthy advantage of AT treatments lies in their inherent simplicity and cost-effectiveness when compared to other therapeutic modalities, rendering them particularly advantageous in Low- and Middle-Income Countries (LMICs), where access to expensive medical interventions may be constrained (Chagas and Leite, 2023, Hamid Namaganda et al., 2023), however, the individualized nature of TCM treatment presents a distinctive challenge in promoting widespread adoption of AT for CP management. Each patient's condition is regarded as unique within the TCM framework, necessitating practitioners to carefully tailor treatment protocols to align with the specific syndrome manifested by the patient, all while adhering to the guiding principles of TCM theory.

In this study, the treatment protocol implemented is based on The World Federation of Chinese Medicine Societies (WFCMS) TCM protocol, a meticulously crafted and standardized framework. This protocol was meticulously developed through the collaborative efforts of over 50 experts hailing from seven countries and regions. Following several rounds of expert validation, it was ultimately adopted for scrutiny and endorsement at the 5th Standing Council of the 4th WFCMS, which convened in Hungary in November 2019.

The standardized and easily replicable nature of the chosen TCM protocol serves as a critical foundation for this study (Yi et al., 2023). The primary objective of this study is to ascertain the effectiveness of the AT protocol in enhancing gross motor function among children afflicted with spastic CP, as compared to the conventional rehabilitation techniques conventionally employed. By undertaking this research endeavor, we aspire to contribute valuable empirical evidence to the ever-expanding body of knowledge surrounding the efficacy of AT in managing CP. Such insights could potentially provide a valuable therapeutic option for affected children and their

families, advancing the domain of clinical practice and positively influencing patient outcomes.

5.2 The Objective of the study

The primary objective of this study was to investigate the effects of standardized AT therapy on muscle tone and gross motor function in children diagnosed with spastic CP. To achieve this, a non-randomized controlled trial design was employed. This approach allowed us to systematically observe and assess the impact of AT treatment in a controlled setting. Additionally, we aimed to compare the outcomes of standardized AT therapy with those of conventional rehabilitation methods commonly used for the clinical management of spastic CP in children.

To evaluate the efficacy of the AT therapy in reducing muscle tone and enhancing gross motor function, we utilized a battery of quantitative assessment tools. These tools included the Modified Ashworth Scale (MAS), the Gross Motor Function Measure (GMFM), the 6-Minute Walk Distance (6MWD), and the Wee Functional Independence Measure (WeeFIM). The MAS facilitated the evaluation of muscle tone, while the GMFM enabled a comprehensive assessment of gross motor skills. The 6MWD test measured the endurance and functional capacity of the participants, and the WeeFIM scale assessed their independence in various daily life activities.

By employing these standardized measurement tools, we aimed to provide robust, reliable, and objective data to support the application of acupuncture as an effective therapeutic approach in the rehabilitation of children afflicted with spastic CP. The findings from this study have the potential to contribute significantly to the body of knowledge in pediatric rehabilitation and offer practical insights for clinicians and researchers in the field.

5.3 Trial registration

The registration of this clinical trial has been documented in the Chinese Clinical Trial Registry under the identifier ChiCTR2200059823. The initial registration took place on 12 May 2022, and subsequent revisions to the registration details were made on 20 August 2023. This study initially planned to evaluate gross motor function, fine motor function and intellectual factors of children, and then adjusted to focus on gross motor function and walking ability of children.

5.4 Methods/Design of the study

5.4.1 Hypotheses

5.4.1.1 There are differences in the treatment outcomes between AT and conventional rehabilitation in children with spastic CP.

5.4.1.2 AT are more effective in improving gross motor function and alleviating associated related symptoms in children with CP.

5.4.2 Study Population

primary diagnosis of spastic CP, admitted to the Children's Ward of Xi'an Encephalopathy Hospital Affiliated to Shaanxi University of Chinese Medicine, located in Xi'an, China, between October 2021 and September 2022."

5.4.3 Design

This study is a single-center, non-randomized, clinical trial that was conducted at Xi'an Encephalopathy Hospital Affiliated to Shaanxi University of Chinese Medicine in China. The study screened all patients diagnosed with spastic CP to determine their eligibility for receiving AT treatment. The patients were divided into either the AT group or the control group depending on their guardians' decision. Both groups underwent a 12-week treatment period according to the established protocol (Wang et al., 2023c). The study adheres to the principles of the Declaration of Helsinki and good clinical practice guidelines and has obtained approval from the Research Ethics Committee (Approval No. 2021-18) of Xi'an Encephalopathy Hospital Affiliated to Shaanxi University of Chinese Medicine. Prior to participating in the trial, all participants provided written informed consent.

The schedule for enrolling, treating, and evaluating the trial is presented in Table 1, outlining the specific timelines and milestones for participant recruitment, treatment administration, and data assessment. The table provides a comprehensive overview of the trial's sequential procedures and enables a clear understanding of the study's timeline and activities. Researchers and stakeholders can refer to table 5.1 to monitor the progress and adherence to the planned schedule throughout the course of the clinical trial.

Table 5.1: The schedule for enrolling, treating, and evaluating the clinical study

	Study period		
	Screening	Before treatment	After treatment
Eligibility screening	√		
Demographic date	√		
Case data	√		
Inclusion criteria	√		

Exclusion criteria	√		
Informed consent	√		
GMFCS	√		
	Outcome assessment		
(1) MAS		√	√
(2) GMFM D		√	√
(3) GMFM E		√	√
(4) WL/6		√	√
(5) WeeFIM		√	√
Safety assessment		√	√

MAS: Modified Ashworth muscle tension scale, GMFM: The Gross motor function test (GMFM-88), WL/6: The 6-minute walking distance measurement, WeeFIM: Children's functional independence Rating Scale, GMFCS: Gross Motor Function Classification System

5.4.4 Diagnostic criteria

The diagnostic criteria for CP and the clinical classification criteria for spastic CP have been established according to the committee members' determinations in the Guidelines for Rehabilitation and Treatment of Cerebral Palsy in China (Li, 2014).

The necessary conditions for diagnosing CP include:

(1) Persistent presence of central motor disorders. In infants and young children during early brain development (immature period), there are impairments in gross motor skills such as rolling over, sitting, crawling, standing, and walking, as well as

fine motor skills, or significant growth disorders. The functional impairments are enduring and non-progressive, but not static. Mild cases may gradually improve, while severe cases may progressively require hospitalization and may ultimately result in secondary amputation and joint complications.

(2) Abnormalities in motor and posture development. This includes abnormalities in dynamic and static postures, as well as postural abnormalities during prone, supine, sitting, and standing positions, which should be evaluated based on posture development in different positions. Abnormal movement patterns occur during motor activities.

(3) Abnormal reflex development. Main manifestations include delayed disappearance of primitive reflexes, delayed or absent appearance of postural reflexes (such as protective extension reflex), and exaggerated pathological reflexes.

(4) Muscle tone and spasticity. Spastic CP is characterized by increased muscle tone, which can be assessed by examining tendon reflexes, static muscle tone, postural muscle tone, and movement-induced muscle tone. Assessment is primarily based on measurements of anatomical catch-up growth, palmar flexion angle, bilateral lower limb angle, popliteal angle, limb range of motion, joint range of motion, dorsiflexion angle, scarf sign, and heel-to-ear test, among others.

The reference conditions for CP diagnosis, although not essential, may include etiological basis of CP and cranial imaging evidence, such as MRI, CT, and B-ultrasound. Spastic lesions are primarily located in the corticospinal tract and can affect different parts of the body, with an increase in muscle tension primarily observed in flexor muscles. This increased muscle tension is characterized by an excessive increase in speed-dependent stretch response.

Clinical classification is as follows:

(1) Spastic quadriplegia: It mainly involves damage to the pyramidal tract, including injury to the cortical motor area. The characteristic feature of this type is increased stretch reflex. The muscles in all four limbs exhibit increased tone, with the upper limbs extending backward, adducting internally, and rotating internally, the thumbs adducted, the trunk flexed forward, the lower limbs adducted, rotated internally, crossed, with knee joint flexion, scissoring gait, equinovarus foot deformity, arching sitting posture, increased tendon reflexes, ankle clonus, Babinski sign, and pyramidal tract signs, among others.

(2) Spastic diplegia: This type is characterized by spasticity and more severe functional impairments in the lower limbs than the upper limbs. It is commonly seen in premature infants. The affected infants often exhibit decreased muscle tone in both lower limbs within 1-3 months. This is followed by a phase known as "hypotonia," during which the infants exhibit simultaneous stiffening and crossing of both lower limbs in a scissoring pattern when standing and their soles touch the examination surface. Finally, they enter the spastic phase, characterized by hip and knee flexion, internal rotation of the lower limbs, and a scissoring gait. Severe cases may result in an inability to walk independently.

(3) Spastic hemiplegia: This type manifests symptoms in one side of the body and is the most common form. It affects one side of the body, with the upper limb usually more severely affected than the lower limb, and the distal part more affected than the proximal part. Facial involvement is often absent. Symptoms in affected children typically become evident after 3 months and include reduced movement on the affected side, persistent clenched fist, persistent grasp reflex, flexed and pronated forearm, and circumduction gait. In some patients, the initially affected limb may exhibit decreased muscle tone before transitioning to a spastic state. This type is often accompanied by intellectual disability and epilepsy, and strabismus is common.

TCM Diagnostic Criteria of The Five Delays(Chi), five softsness(Ruan), and five hardsness(Ying).

Liver Exuberant and Spleen Deficiency syndrome: Since birth, the patient tends to rest more and move less. The neck is stiff and not flexible, and when picked up, the legs straighten and rotate inward. The limbs exhibit stiffness, spasticity, rigidity, or clumsy movements, and the muscles are lean. The patient is irritable and easily angered, with aggravation upon exposure to external stimuli, and has poor appetite and dullness. The tongue may be enlarged or thin, with a white and greasy coating or a thin coating. The pulse is weak or deep and string-like, and the fingerprints appear stagnant."

5.4.5 Inclusion criteria

5.4.5.1 Patients are diagnosed as spastic CP.

5.4.5.2 The age of the children is between 4 and 14 years old.

5.4.5.3 Able to cooperate and complete various clinical examinations and scale assessments.

5.4.5.4 The Gross Motor Function Classification System(GMFCS) of the children is between I and III.

5.4.5.5 The patient’s guardian signs the informed consent form.

5.4.5.6 No history of drug allergies.

5.4.5.7 No other hereditary diseases.

5.4.6 Exclusion criteria

5.4.6.1 Patients who do not meet the above diagnostic criteria.

5.4.6.2 Patients with other serious organic diseases of heart, liver, kidney, and other important organs.

5.4.6.3 Exclude leukodystrophy, infantile spinal muscular atrophy, spinocerebellar ataxia syndrome, and hereditary Metabolic diseases such as phenylketonuria, congenital cretinism, congenital hydrocephalus.

5.4.6.4 Patients who interrupt treatment in the medium term for non-curative effect reasons.

5.4.6.5 Patients who do not cooperate with the treatment observer.

5.4.6.6 Patients with severe visual or auditory impairments, or intellectual disabilities, which may impact the rehabilitation assessment.

5.4.6.7 Patients who undergo other treatments that may influence the evaluator's assessment of efficacy.

5.4.7 Rejection criteria

5.4.7.1 Patents who do not treated according to the study protocol after inclusion.

5.4.7.2 Patients who experience severe adverse events during the course of treatment."

5.4.8 Shedding standard

5.4.8.1 Patients who do not meet the inclusion criteria but are mistakenly included.

5.4.8.2 Patients with poor compliance (inability to come to treatment as required, children not cooperating, etc.).

5.4.8.3 Patients with irregular treatment, loss to follow-up, leading to incomplete clinical observation indicators and scale data.

5.4.8.4 Participants who cannot continue participating in the study due to sudden severe illness, serious adverse events, or complications.

5.4.8.5 Patients who withdraw from treatment on their own.

5.4.9 Grouping method

The participants were divided into two groups, namely the Acupuncture Group and the Traditional Rehabilitation Group, based on the guardians' preferences for their inclusion in the study. In the Acupuncture Group, patients received acupuncture treatments as part of their rehabilitation regimen, while the Traditional Rehabilitation Group underwent conventional rehabilitation interventions. This grouping approach allowed us to respect the preferences of the patients' guardians and explore the potential effects of acupuncture in comparison to traditional rehabilitation methods.

5.4.10 Intervention in the study

The control group.

Rehabilitation methods, through individualized training programs to promote children's head-up, rollover, sitting, climbing, standing, Walking and other gross motor functions. including Bobath, occupational therapy (OT), and physical therapy (PT), are implemented in a selective manner. Experienced rehabilitation therapists create personalized rehabilitation plans for each patient based on their age, physical quality, and motor function. The rehabilitation sessions are conducted once a day, five times a week, for a duration of three consecutive months.

The AT group：

Patients are treated with AT combined with rehabilitation therapy the same as control group.

Acupuncture treatment:

Main points of scalp acupuncture: motor area, foot movement sensation area and balance area.

Main points of body acupuncture: Ganshu(BL18), Pishu(BL20), Taichong(LR3), Taibai(SP3), Yanglingquan(GB34) and Sanyinjiao(SP6).

Acupuncture methods:

If the diagnosis is spastic diplegia or spastic quadriplegia, the body acupuncture point is bilateral; If the diagnosis is spastic hemiplegia, the body acupuncture is unilateral. Acupuncture methods: For scalp acupuncture, strong stimulation is used,

catharsis is used at Taichong(LR3) and even reinforcing-reducing method are used at other points.

The appropriate body position is chosen for the child, and the aforementioned acupoints are selected. Huatuo brand disposable stainless steel filiform needles are chosen (needle specifications are selected based on the location), and after disinfection, the needles are inserted. Acupuncture needles with a diameter of 0.35mm and a length of 25mm shall be selected. All needling procedures for the child are performed by a professional acupuncture physician with the title of associate chief physician or above, who has years of experience in pediatric acupuncture.

Tuina treatment:

Tuina includes tuina along meridians, acupoint pressure, abnormal local muscle tuina, abnormal posture correction. The principle of tuina is light and orderly, and the principle of manipulation is flexible and rigid.

Tuina along meridians: Upper limbs along the hand three yin meridians, hand three yang meridians sequence, lower limbs along the foot three yang meridians, foot three yin meridians sequence, using push method, roll method and other composite techniques.

Acupoint pressure: Compound techniques such as point, kneading and pressing were applied to the main acupoints of each meridian (Referring to acupuncture).

Abnormal local muscle tuina: Soothing techniques such as kneading and holding. Posture correction: The pulling method, shaking method and stretching method are used for the abnormal postures of the spine and limbs.

Tuina methods:

Tuina mostly adopts relaxation manipulation. The practitioner will be a registered practitioner with at least 3 years of practical experience in tuina.

The acupuncture needles shall be retained for 30 minutes, and hand-manipulating of needle shall be once every 15 minutes. Tuina operation in accordance with upper limbs, lower limbs, each limb four operations in order. 20-30 minutes each time.

The two group of treatment conducted every day with the interval of 2 days every week during the weekend. A course of treatment duration is 12 weeks.

5.4.11 Standardization of acupuncture operations

Before all studies begin, acupuncturists are required to attend training according to the study protocol. The primary objective of this training is to establish and maintain a standardization in the selection of acupuncture points and the proficient execution of needle techniques. By ensuring adherence to these standardized practices, the validity and reliability of the research findings can be enhanced.

5.4.12 Outcome measures

In this study, we conducted assessments of both primary and secondary outcomes pre- and post-treatment. The primary outcome measures encompassed the modified Ashworth muscle tension scale (MAS) as well as the Gross Motor Function Measure (GMFM-D and GMFM-E), which collectively serve as indicators for evaluating improvements in gross motor function among patients. On the other hand, the secondary outcome measures comprised the 6-minute walking distance measurement (6MWD) and the Modified Children's Functional Independence Rating Scale (WeeFIM). These secondary outcomes were chosen to gauge the extent of recovery in

terms of patients' walking ability and overall adaptability in daily living.

5.4.12.1 Primary outcomes

Modified Ashworth muscle tension scale (MAS)

The modified Ashworth muscle tension scale (MAS) holds paramount significance in clinical practice as a widely employed tool for assessing spasticity (Harb and Kishner, 2021). The MAS categorizes muscle tone into distinct levels, namely 0, 1, 1+, 2, 3, and 4. In the current study, we assigned respective point values of 0, 1, 2, 3, 4, and 5 to quantify the spasticity assessment. This quantitative approach enabled the translation of spasticity evaluation from a qualitative assessment to a more objective and measurable format. The lower the score, the lower the muscle tone of the child, indicating better function.

The Gross motor function test (GMFM-88)

The Gross Motor Function Measure (GMFM-88) test encompasses five distinct functional areas, namely: A (lying and rolling), B (sitting), C (crawling and kneeling), D (standing), and E (walking, running, and jumping). Each functional area is assigned specific point values, with scores of 51, 60, 42, 39, and 72 points respectively. However, in our study, only functional areas D and E were applied, and the scoring was adjusted based on a full score of 100 points. Consequently, higher scores on the GMFM-88 indicate better motor abilities in the specific functional areas evaluated (Te Velde and Morgan, 2022).

5.4.12.2 Secondary outcome

The 6-minute walking distance measurement(6MWD)

The 6-minute walking distance (6MWD) test represents the prevailing method employed for quantifying both walking distance and endurance among children (Fitzgerald et al., 2016). This assessment entails conducting measurements on a level treadmill, with the participant walking continuously for a pre-determined duration of 6 minutes. Subsequently, the distance covered during this specific time interval is precisely measured and recorded. The 6MWD test serves as a reliable and widely utilized means to evaluate the walking capacity and endurance of children. The longer the distance, the better the recovery of the child's walking function.

Children's functional independence Rating Scale (WeeFIM)

The Functional Independence Measure for Children (WeeFIM) is a comprehensive assessment tool specifically designed for children and adolescents between the ages of 6 months and 18 years who experience functional disabilities and developmental delays (Jang et al., 2022). This assessment encompasses a total of 18 specific items that evaluate both motor function (such as self-care, sphincter control, transfer, and walking) and cognitive function (including communication and social cognition). Each item is scored on a scale ranging from 1 to 7, representing the degree of dependence or independence, with higher scores indicating greater levels of independence. The WeeFIM assessment provides a robust reflection of an individual's daily living skills and social adaptation abilities. It has demonstrated high reliability and validity, making it a valuable tool for evaluating functional abilities and monitoring progress in children and adolescents with disabilities and developmental delays.

All the above observations were measured on two occasions: once prior to the initiation of treatment and once upon completion of the treatment. these measured were conducted by a senior rehabilitation therapist who remained unaware of the

subject grouping. This blinding method was implemented to ensure the impartiality and objectivity of the measurements, reducing the potential for bias in the evaluation process.

5.4.13 Sample size calculation

The sample size for this study was calculated by G-Power (V.3.192). The software has the capability to accommodate a wide range of clinical research designs. Additionally, its parameter configuration can prevent potential complexity that may arise from the two primary outcomes in this study. The specific parameter settings are as follows: Power 95% with a significance level of $\alpha = 0.05$. Effect size = 0.3, 67 participants would be required for each group. Considering the expected shedding rate of 20%, the sample size for each cohort should not be less than 85.

5.4.14 Statistical analysis

IBM® SPSS® Statistics version 22 (Statistical Product and Service Solutions Statistics, I.B.M., Inc., Armonk, NY, USA) was used for data analysis. Firstly, the Shapiro-Wilk test was used to check for normal distribution and the t-test to assess group homogeneity. On the other hand, t-tests for paired samples were used to measure differences between baseline and post-treatment scores, and t-tests for independent samples to test for differences between groups. Spearman correlation analysis is used to analyze the correlation between factors and efficacy. Differences between or within groups were considered significant at $p < 0.05$.

5.4.15 Blinding

In this study, AT practitioners and participants were not blinded to group assignment due to the unique nature of TCM and the difficulty of blinding participants and practitioners. It would be optimal to have those collecting the study results blinded, however, this is not possible in the current protocol. Instead, for the evaluation and data analysis of the primary and secondary study outcomes, the group members will be blinded.

5.4.16 Adherence

Health education is provided to guardians of children with CP through a WeChat group, and monthly meetings are held with them through a combined online and offline model to share their experiences of their child's development. These strategies are expected to help improve adherence.

5.5 Results

5.5.1 Demographic Information

In this study, 231 patients diagnosed with spastic CP were screened during the study period from Oct 2021 to Sep 2022 (Table 5.1). Among 231 patients, 19 did not meet the inclusion criteria, while 212 patients were eligible. Among the 212 eligible patients, 42 refused to participate in the study. 170 were assigned to the AT groups and control groups according to the decision of the guardian. Among the 85 selected participants in AT group, 2 dropped out. Results of 168 participants were included in the statistical analysis.

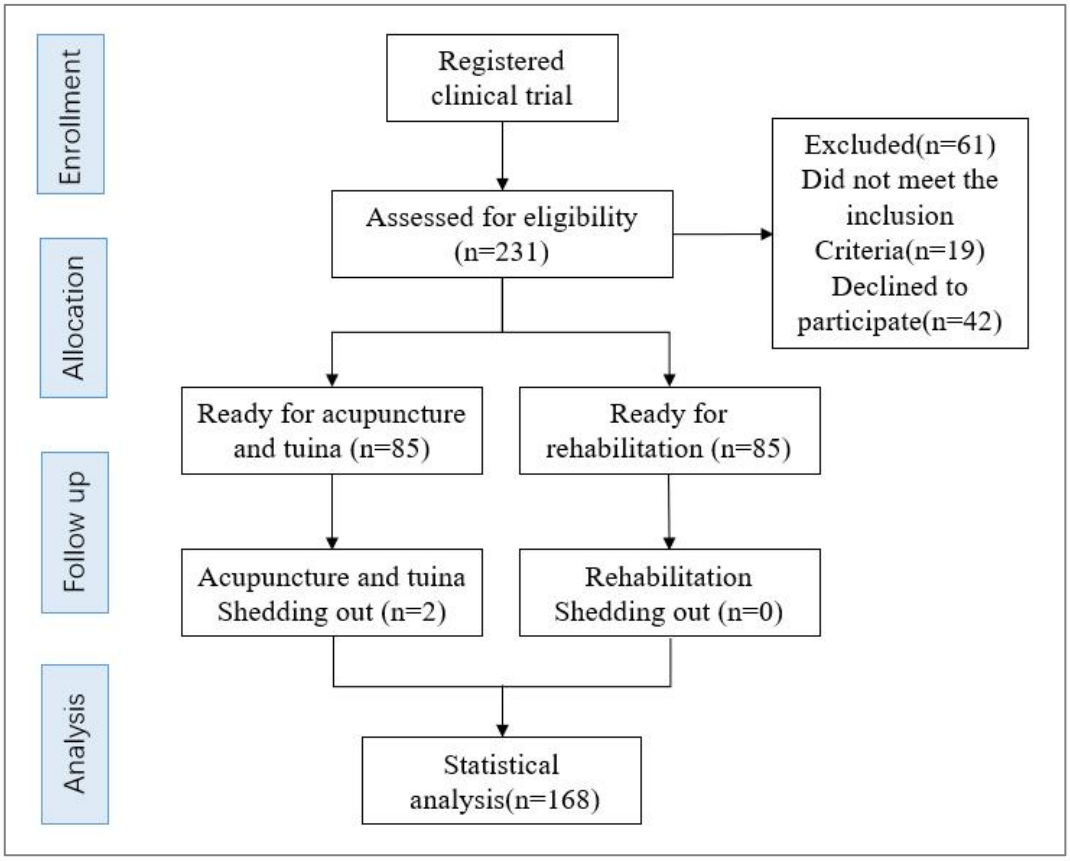

Figure 5.1: CONSORT flow chart of the clinical study

The basic characteristic of the eligible participants are listed in table 5.2. In all basic characteristic data of the two groups involved in the study, In the AT group, the average age was 7.68±3.02 years, while the control group had an average age of 7.44±2.81 years. Gender distribution was relatively balanced in both groups, with 43 males and 40 females in the AT group, and 44 males and 41 females in the control group. Among the classification of the spastic in the AT group, there were 32 cases of quadriplegia, 32 cases of diplegia, and 19 cases of hemiplegia. In the control group, there were 30 cases of quadriplegia, 33 cases of diplegia, and 22 cases of hemiplegia. Regarding the birth history of the children, it is noteworthy that in the AT group, there were 40 premature births, 51 cases with a history of hypoxia, and 44 low birth weight children. In the control group, there were 42 premature births, 48 cases with a history of hypoxia, and 40 low birth weight children. As for the Gross Motor Function Classification System in the children, in the AT group, there were 24 cases classified

as Grade I, 20 cases as Grade II, and 39 cases as Grade III. In the control group, there were 26 cases classified as Grade I, 21 cases as Grade II, and 38 cases as Grade III. Following a statistical analysis, we found that there was no difference between the two groups, including age, gender, Classification of spastic CP, birth history and Gross Motor Function Classification System (GMFCS) of the children.

Table 5.2: Characteristic of two group patients in the clinical study

Variables	Treatment group (N=83)	Control group (N=85)	*P* value
Age	7.68±3.02	7.44±2.81	0.423
Gender			0.874
Male	43	44	
Female	40	41	
Classification			0.871
Quadriplegia	32	30	
Diplegia	32	33	
Hemiplegia	19	22	
Birth history			
Premature birth	40	42	0.874
Hypoxia	51	48	0.512
Low weigh	44	40	0.440
GMFCS			0.954
I	24	26	
II	20	21	
III	39	38	

5.5.2 Primary Outcome

Effects of AT on MAS and GMFM

MAS and GMFM measurement were performed before treatment and after treatment in two groups. As shown in table 5.3 and figure 5.2(A, B, C). There was no significant difference between the two groups in the baseline of the MAS (AT group: 2.71 ± 0.65 vs Control group: 2.88 ± 0.71; p = 0.107), GMFM-D (AT group: 62.78 ± 11.53 vs Control group: 63.45 ± 9.97; p = 0.690) and GMFM-E (AT group: 42.31 ± 9.75 vs Control group: 42.51 ± 10.22; p = 0.901). The intra-group comparison of two groups revealed that the average score of MAS, GMFM-D and GMFM-E significantly changed after the treatment (p < 0.01) compared with the baseline. After treatment. The between-group comparison showed that the score of MAS of the AT group was significantly lower compared to the control group (AT group: 1.36 ± 0.48 vs Control group: 1.92 ± 0.58; p < 0.01).The score of GMFM-D and GMFM-E of the AT group was significantly higher compared to the control group (AT group:78.96 ± 7.73 and 55.61 ± 9.68 vs Control group: 72.28± 7.71 and 48.38 ± 8.87; p < 0.01).

5.5.3 Secondary outcomes

Effects of AT on 6MWD and WeeFIM

According to table 5.3 and figure 5.2 (D, E), there was no significant difference between the two groups in the baseline of the 6MWD (AT group: 142.48 ± 5.13 vs Control group: 142.66 ± 5.42; p = 0.828), WeeFIM (AT group: 70.53± 13.19 vs Control group: 68.82 ± 11.57; p = 0.374). The intra-group comparison of two groups revealed that the average score of 6MWD and WeeFIM significantly changed after the treatment (p <0.01) compared with the baseline. After treatment. The between-group comparison showed that the score of 6MWD and WeeFIM of the AT group was significantly higher compared to the control group (AT group:182.65 ± 6.53 and 97.42 ± 10.22 vs Control group: 167.32 ± 10.28 and 82.24 ± 11.68; p < 0.01).

Table 5.3: Changes in efficacy measures of AT and control groups in the clinical study

Efficacy indicators	AT group			Control group			*p*-value for Difference between Group
	Before TX	After TX	*P*-value	Before TX	After TX	*P*-value	
MAS	2.71 ± 0.65	1.36 ± 0.48	p < 0.01	2.88 ± 0.71	1.92 ± 0.58	p < 0.01	p < 0.01
GMFM D	62.78 ± 11.53	78.96 ± 7.73	p < 0.01	63.45 ± 9.97	72.28± 7.71	p < 0.01	p < 0.01
GMFM E	42.31 ± 9.75	55.61 ± 9.68	p < 0.01	42.51 ± 10.22	48.38 ± 8.87	p < 0.01	p < 0.01
6MWD	142.48 ± 5.13:	182.65 ± 6.53	p < 0.01	142.66 ± 5.42	167.32 ± 10.28	p < 0.01	p < 0.01
WeeFIM	70.53± 13.19	97.42 ± 10.22	p < 0.01	68.82 ± 11.57	82.24 ± 11.68	p < 0.01	p < 0.01

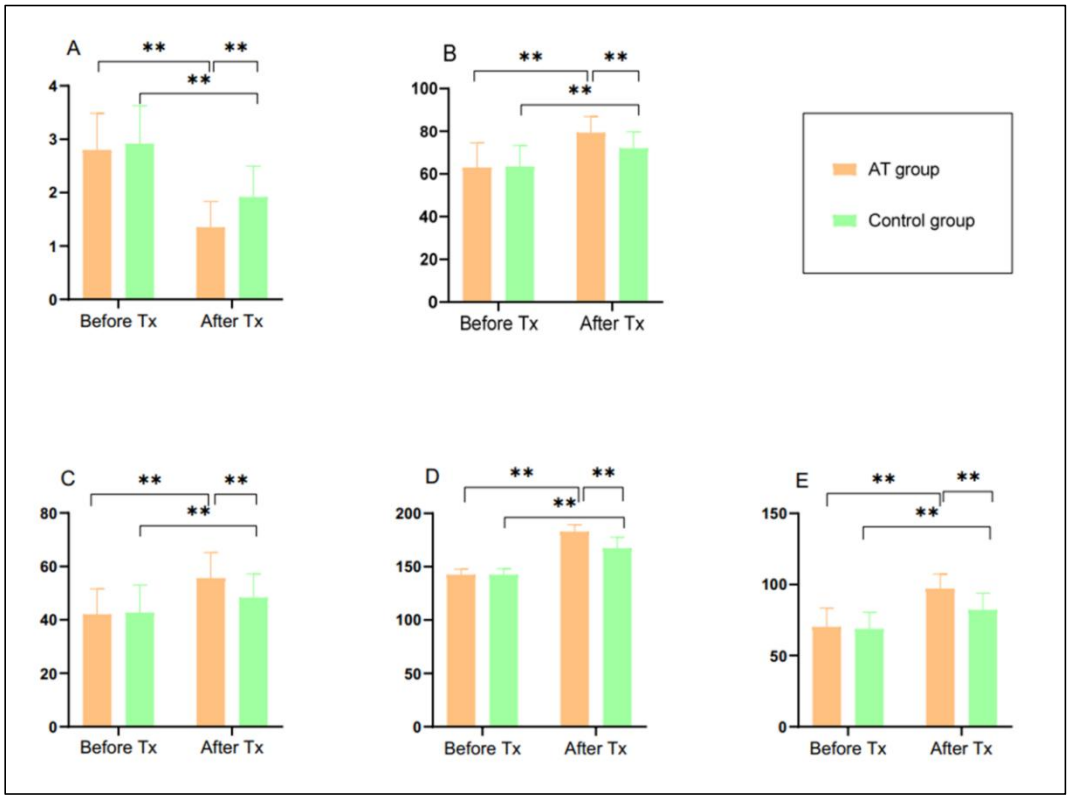

Figure 5.2: A: Average MAS scores in two groups during the treatment periods; B: Average GMFM-D scores in two groups during the treatment periods; C: Average GMFM-E scores in two groups during the treatment periods; D: Average 6MWD in two groups during the treatment periods; E: Average WeeFIM scores in two groups during the treatment periods. Abbreviations: Tx, treatment. ** means p<0.01

5.5.4 Correlation between basic characteristic and efficacy improvement rate

The 6MWD can reflect the overall recovery of the child, we use score of 6MWD after treatment minus score of 6MWD before treatment)/ score of 6MWD before treatment to represent the efficacy improvement rate. After spearman correlation analysis, it was found that children's age was negatively correlated to the efficacy. Other information is no relevant to the efficacy, as shown in table 5.4 and figure 5.3.

Table 5.4: Correlation between basic information and efficacy improvement rate

		Treatment group	Control group
Age	r value	-0.496**	-0.540**
	p value	<0.01	<0.01
Gender	r value	0.017	0.056
	p value	0.875	0.613
Premature birth	r value	-0.175	-0.035
	p value	0.109	0.750
Hypoxia	r value	-0.037	-0.018
	p value	0.735	0.870
Low weigh	r value	-0.128	0.061
	p value	0.249	0.582
Classification	r value	-0.033	0.008
	p value	0.765	0.941
GMFSC	r value	0.003	0.016

	p value	0.980	0.886

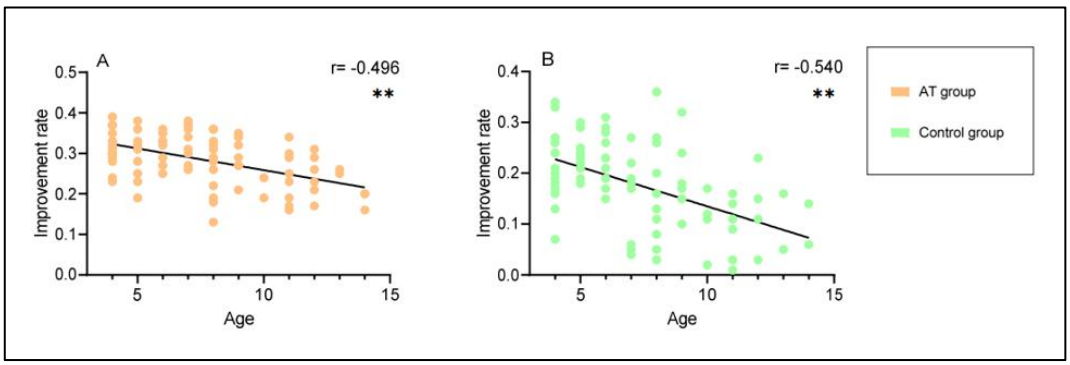

Figure 5.3: Correlation between age and clinical improvement rate in two groups

5.5.5 Adverse events

In the course of this study, it is noteworthy to state that no patients encountered any unfavorable responses, including severe adverse events or any other adverse occurrences.

5.6 Discussion

This study represents an initial phase of research conducted at a single medical center. It adopts a non-randomized clinical approach aimed at assessing the impact of AT therapy on the gross motor function of children diagnosed with spastic CP.

Spastic CP refers to a group of syndromes characterized by abnormal central nervous system development leading to increased muscle tone and hyperactive tendon reflexes in the limbs (Burgess et al., 2022). Clinically, spastic CP is classified based on the predominant motor syndrome, which includes spastic hemiplegia, spastic diplegia, and spastic quadriplegia (Te Velde et al., 2019). This condition results in

reduced muscle strength, limited joint movement, and impaired motor function. Furthermore, it also inhibits the coordination of synergistic and antagonistic muscles during movement, thus affecting balance control and causing gross motor dysfunction (Więch et al., 2020, Nashner et al., 1983). At the same time, it is observed that these patients with spastic CP experience an increase in muscle tone, accompanied by muscle spasms that can lead to tendon contraction and joint rigidity, ultimately progressing into joint deformities. Common deformities associated with this condition include abnormal development of the hip joint (hip subluxation, dislocation) and spinal abnormalities (lumbar lordosis, spinal scoliosis, etc.) (Xiaohong and Xiaoye, 2020). These deformities present substantial impediments to rehabilitation training for the affected children, substantially diminishing their mobility and overall quality of life (Gang et al., 2023). Therefore, that the early prediction and intervention to reduce the incidence of deformities constitutes a focal point and challenge in children with spastic CP. Clinically, the management of spastic CP aims to reduce muscle tone in the affected muscle groups, improve joint range of motion, and enhance walking ability in affected children. According to the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY), the therapeutic objectives for CP management have evolved from treating injury and disability to promoting health, mobility, and participation in daily life (Illum et al., 2016, Mukhtiar et al., 2020). In this study, we aimed to restore gross motor function related to spastic CP using simple and cost-effective TCM (AT) methods.

Several studies had demonstrated that acupuncture is an effective method to reduce muscle tone in spastic muscle groups, improve joint mobility, and enhance gross motor function and walking ability in children with CP (Li et al., 2018, Xu et al., 2022). As reported by Dian and team, the acupuncture group exhibited a significant reduction in the Modified Ashworth Scale score compared to the control group ($p = 0.003$) (Putri et al., 2020). Similarly, YH Ji investigated the therapeutic impact of acupuncture combined with repetitive transcranial magnetic stimulation for the

management of spastic CP in children with spleen-kidney deficiency and observed an improvement in cerebral hemodynamics and motor function (Ji and Sun, 2019). In contrast to prior studies on acupuncture for CP, this study employs standardized acupuncture treatment, which eliminates the need for varied treatments based on the child's condition. This standardized approach provides a promising avenue for applying acupuncture to enhance gross motor function and walking ability in children with CP living in low- and middle-income countries. Scalp acupuncture targets the motor area, foot movement sensation area, and balance area, which can alleviate neurological dysfunction and improve motor function and daily living ability in stroke patients, as evidenced by functional magnetic resonance imaging studies (Zanardi et al., 2016, Cui et al., 2013). The key acupoints employed in this study are Ganshu(BL18), Pishu(BL20), Taichong(LR3), Taibai(SP3), Yanglingquan(GB34) and Sanyinjiao(SP6). These acupoints have been shown to regulate muscle contracture, muscle weakness, posture abnormalities, etc (Mou et al., 2021), and stimulate brain electrical activity. Additionally, they increase the secretion of neurotransmitters and improve blood circulation in brain tissue, thereby improving clinical efficacy. Moreover, the therapeutic effects of these acupoints correspond to the TCM concept of spastic CP mostly belonging to the syndrome of liver exuberance and spleen deficiency (Ma et al., 2013).

Recovery of motor function is a multifaceted process that involves several factors such as muscle tone, strength, endurance, sensation, and coordination (Francisco and McGuire, 2012). As a kind of peripheral intervention, Tuina is a passive mechanical therapy that is a cost-effective adjunct therapy. A study by J Chen revealed that Tuina massage effectively improves motor function and reduces spasticity in stroke survivors (Chen et al., 2023). In addition, Tuina has demonstrated efficacy in improving gross motor function in children, especially in the sitting position (Liu and Cen, 2013). A retrospective study demonstrated that the Rougan Tongdu Tuina combined with point-pressing massage therapy in the neonatal period

could significantly improve the neurodevelopment of children (Geng and Yang, 2021). In our study, the acupoints of tuina are similar to those of acupuncture, but we utilize tuina therapy along the meridians which the acupoints belongs to. In addition to relieving spasticity, meridian stimulation can also expand blood vessels, promote circulation, activate cells, and restore damaged functions (Jia et al., 2019, Chen et al., 2021). These therapeutic effects have been substantiated through additional scholarly studies, reinforcing their credibility and applicability. Notably, Tuina therapy has shown promising results in alleviating inflammation and modulating the expression of inflammatory cytokines in the hippocampus of young rats afflicted with CP (Qi et al., 2018, Xiantao et al., 2012). Furthermore, Tuina therapy exhibits the potential to stimulate excitability within the central nervous system, fine-tune signaling pathways, and regulate the release of neurotransmitters. These intricate mechanisms collectively play a pivotal role in promoting neural regeneration and repair processes, enhancing muscle blood circulation, and optimizing metabolic activities. Consequently, these effects demonstrate significant promise in individuals grappling with CP (Rui, 2020). Moreover, Tuina therapy effectively boosts the synthesis rate of skeletal muscle proteins, promoting improved localized blood circulation and mitigating excessive fibrous tissue proliferation within muscle fibers. These beneficial effects contribute to the restoration of muscle morphology and aid in sustaining a relaxed muscle state, thereby augmenting blood flow and enhancing oxygen supply to muscle tissues (Mahmood et al., 2020, Jing et al., 2019).

This study utilized MAS, GMFM88, 6MWD, and WeeFIM as evaluation indicators to assess the effectiveness of AT therapy in improving gross motor function in children with spastic CP. Following 12 weeks of treatment, both the AT and control groups exhibited decreased MAS scores, improved GMFM scores, 6MWD, and WeeFIM scores. The reduction in dystonia, improved walking ability, and increased functional independence were observed in both groups, suggesting that both AT treatment and rehabilitation training can effectively improve gross motor function in

children with spastic CP, which is consistent with previous studies. Systematic reviews have also indicated that acupuncture is a promising and safe therapy for CP (Hu et al., 2022, Tang et al., 2021). Additionally, integrative medicine rehabilitation (IMR) has been shown to be effective and safe for treating motor dysfunction, language disorder, and social-emotional disorders in children with CP (Lee et al., 2020). However, it is important to note that the AT group, which received a combination of AT therapy based on rehabilitation, demonstrated better improvement in all indicators than the control group, which only underwent rehabilitation training. These findings confirm the specific efficacy of AT therapy. The mechanism of this therapy is based on the theory of medicine theory, which suggests that AT can promote the activation of the motor cortex and repair damage, effectively relieving muscle spasm in the limbs and improving the function of the gross motor nerve (Chen et al., 2023). This theory has been supported by multi-modality MRI combined with dynamic electroencephalogram analysis (Chen et al., 2020a). Another study (Zixuan et al., 2021) showed acupuncture can improved expression of nerve growth-related proteins, enhancement of ATPase activities, and regulation of the brain microenvironment. Stimulation through AT can be more effective in promoting the activation of deep spinal stabilizing muscles (Wright, 2021), increase muscle strength, and improve movement control, so that children can obtain more muscle strength and exercise opportunities for limb movement control required for effective movement, thus improving the movement function of the trunk and lower limbs of the children to a greater extent, improving their gross motor function, further improving the static and dynamic balance ability of sitting and standing, and improving their walking ability. Meanwhile, our results indicate that younger children had a better response to AT treatment, suggesting that they have a greater potential for neuroplasticity and functional recovery and children with CP should be treated as soon as possible.

5.7 Conclusion

Spasticity is a primary concern in CP, particularly the spastic type. How to decrease muscle tension and relieve spasticity represents a focal point and a challenging aspect of CP rehabilitation training. In this study, standardized AT techniques were employed in the treatment approach. This was aimed at preventing the issue of treatment plans becoming too personalized due to the physician's individual experiences, thereby addressing concerns regarding poor generalizability. In evaluating the effectiveness of the treatment, beyond the use of conventional assessment tools such as the MAS and GMFM, additional emphasis was placed on functional recovery and social adaptability. This was achieved by introducing assessment indicators like 6MWD and WeeFIM. This shift broadened the focus from the gross motor function of the children with spastic CP to their overall functional recovery. It also helped in mitigating the limitations associated with previous efficacy indicators, which were often criticized for being singular and subjective. As a result, the study design became more convincing. Additionally, the study's results provided evidence for the effectiveness and safety of acupuncture and massage therapy in treating spastic CP in children.

5.8 Limitation

It is important to note that our study has some limitations. First, the sample size was relatively small, which may limit the generalizability of our findings. Second, our study found the relationship between age and treatment efficacy. the reason that other factors involved have no relationship maybe is the sample size too. To recruit more children with CP to participate in this study, we decided not to limit our selection to randomized controlled trials (Wang and Kattan, 2020). Despite the limitations inherent in our study, we believe that the use of standardized AT techniques for the treatment of spastic CP has shown significant efficacy. We acknowledge that there is room for improvement in certain aspects of our study due to our limited personal

resources. Nonetheless, our findings confirm the initial hypothesis of the study design, which suggested that a standardized AT protocol could effectively enhance the gross motor function of children with spastic CP. Furthermore, the efficacy of this standardized protocol was found to surpass that of traditional rehabilitation treatment. At the same time, the findings suggest that there is potential for future research to explore the effectiveness and mechanisms of AT techniques in improving motor function and overall quality of life for children with spastic CP and highlight the importance of considering individual differences in age when evaluating the efficacy of treatments for children. By doing so, healthcare providers may be better able to tailor treatments to individual needs and maximize their efficacy. Future studies with larger sample sizes and more comprehensive data collection may further refine our understanding of these relationships and provide insights for clinical practice.

CHAPTER 6.0

RESULTS OF THE STUDY

6.1 Discussion of The Study

This comprehensive study blends various interdisciplinary research methodologies and theories, encompassing TCM, Evidence-based medicine, Bibliometrics, and Computer science. Together, they construct an expansive knowledge framework dedicated to the study of spastic CP. This framework not only illuminates current research hotspots and offers predictions for future research directions but also delves into the patterns of disease symptoms and the clinical intervention system of TCM. This collaborative effort greatly aids in the in-depth integration of diverse data sources, facilitating the establishment of a networked structure housing disease-relevant information. This, in turn, provides substantial and robust support for further research endeavors. Ultimately, this initiative lays a solid foundation for a comprehensive understanding of spastic CP, underpinning future research in this domain.

6.1.1 Exploring the Applications of Bibliometrics in Spastic CP Research

Bibliometrics, a quantitative study of literature characteristics, citation relationships, publication trends, and research directions, stands as a valuable discipline for academic exploration. In this study, our focus was on articles related to spastic CP, published in the English language between 2000 and 2022, within the Web of Science Core Collection(WOSCC) database. Employing advanced bibliometric tools such as Citespace and VOSviewer, we meticulously analyzed and quantified the dynamics of research in this particular domain. Our findings distinctly underscore the dominant

influence and close collaborative partnerships among well-developed Western nations, prominently represented by the United States, the Netherlands, Australia, and the United Kingdom, in the sphere of spastic CP research. This collaborative trend is also notably reflected in the concentration of prolific research institutions and authors. Conversely, nations with emerging economies, particularly those low-and middle-income countries (LMICs), must intensify their efforts and investments in this critical research area. We do acknowledge a potential limitation in our study, rooted in the exclusive selection of English-language publications and the utilization of the WOS core collection, which might introduce a certain level of bias in our analysis.

Turning our focus to the evolving research focal points concerning spastic CP over distinct time periods, from 2000 to 2022, a discernible trajectory unfolds. This trajectory begins with grasping the concept of the related disease, advances to an in-depth exploration of disease mechanisms, progresses further into conducting insightful clinical studies, and culminates in a comprehensive approach to managing the disease across the entire lifespan. The current landscape is witnessing a surge of ingenuity in clinical management, in-depth investigations into disease mechanisms, innovative intervention strategies, and refined evaluation methodologies integrated seamlessly into spastic CP research. This infusion of innovation brings forth a wealth of inspiration and contemplation for clinical practitioners and researchers, fueling progress and advancements in this critical domain.

6.1.2 Revealing the Relationship Between Spastic CP and Liver Exuberant and Spleen Weakness Type CP through R Language Analysis

In the realm of TCM, understanding the syndrome differentiation of spastic CP involves an in-depth examination of symptomatic expressions and characteristic features within the TCM theoretical framework. This facet of study necessitates a combination of clinical practice and the collection of extensive medical data.

Thorough organization and analysis of these data reveal prevalent symptoms among CP patients. Additionally, employing methodologies like cluster analysis and association analysis unveils commonalities and discrepancies among patients with spastic CP, allowing for a quantitative understanding of symptom distribution patterns. This, in turn, lays a scientific foundation for devising personalized treatment strategies. For example, different CP types of TCM manifest distinct TCM syndrome patterns; certain patients may prominently display symptoms related to phlegm-dampness obstruction, while others may primarily present symptoms linked to compromised qi and blood circulation. Employing cluster analysis and association analysis allows for a more precise classification of syndrome patterns in pediatric patients.

R language stands as a widely used tool for statistical computation and data analysis. When harnessing the potential of R language to explore TCM symptoms, it is imperative to ensure the availability of high-quality research data and to ascertain the accuracy and reliability of the model in uncovering TCM syndrome patterns. Additionally, various visualization libraries can be harnessed to present the results of the exploration, aiding medical professionals in comprehending the findings and making informed clinical decisions. In our research endeavor, we leveraged the hospital's electronic medical record system and integrated knowledge from TCM theory. Through the application of R language for clustering, association rule algorithms, and visualization, we conducted a preliminary exploration and summarized the clinical symptomatic characteristics of children with spastic CP. Furthermore, we delved into the correlation between spastic CP and the liver exuberant spleen weakness type of CP.

Upon analysis of clustering and high-frequency TCM symptoms, a central framework of core symptoms and non-core symptoms for children diagnosed with spastic CP materializes. Based on the core and non-core clinical symptoms observed in the study, the TCM perspective attributes the pathogenesis of these symptoms to an

excess of liver Qi, weakness in spleen Qi, and the dominant and overpowering nature of liver Qi over the weaker spleen. This categorization aligns with TCM syndrome differentiation as the " liver exuberant and spleen weakness" pattern. In TCM theory, the liver is believed to govern the body's tendons and fascia, playing a vital role in storing and regulating blood. On the other hand, the spleen is responsible for managing the body's muscles, controlling the processes of digestion and absorption, and serving as the fundamental source for Qi and blood generation. When the liver exerts dominance and overpowers the spleen, especially when the spleen is weak, its functionality diminishes. This weakening leads to compromised digestion and absorption processes, resulting in a deficiency of Qi and blood generation. Consequently, insufficient blood storage in the liver and its impaired ability to regulate blood volume lead to the muscles losing their nourishment from Qi and blood. This deficiency manifests as stiffness in the limbs, neck rigidity, and difficulty in swallowing, often referred to as the "internal wind" phenomenon or the "five Ying" concept in TCM, characterized by involuntary muscle spasms and rigidity. When the child's limbs are stimulated, the muscle spasms intensify.

6.1.3 Distribution of Gender and Age in Pediatric Cases and Its Influence on Diagnosis and Treatment Outcomes in Spastic CP

Understanding the demographic landscape, encompassing gender and age distribution, holds significant relevance in the diagnosis and treatment efficacy of spastic CP. It's imperative to emphasize the nuanced and intricate nature of this relationship, shaped by individual variabilities, underlying causes, and the severity of the condition.

In the realm of spastic CP, gender typically doesn't exert a direct influence on diagnosis or treatment efficacy. Nevertheless, research hints at a slightly higher incidence of CP in male patients. This may be attributed to males' heightened susceptibility to specific risk factors during early fetal development. However, it's

vital to emphasize that the success of clinical rehabilitation hinges more on the individual disease profile of the child than their gender. In our study, the gender distribution among pediatric cases aligns with this observed characteristic.

Age plays a crucial role in the context of CP diagnosis and treatment. Typically diagnosed in childhood, CP necessitates a nuanced approach as individuals age. Early intervention and treatment are paramount for enhancing the quality of life and functional recovery of CP patients. Early initiation of treatment capitalizes on the brain's neuroplasticity and the developmental potential of the pediatric nervous system. Our clinical research has notably established an inverse relationship between a child's age and clinical effectiveness, irrespective of the treatment type. This is likely due to the rapid development of neural connections and adaptability within the brains of younger children. Their heightened neural plasticity enables adaptation, repair of damaged areas, and even the establishment of novel neural connections. Timely intervention can facilitate brain reorganization, paving the way for the establishment of new neural pathways, ultimately aiding children in refining their motor skills and overall functionality.

Moreover, early treatment allows healthcare professionals to tailor treatment plans based on specific developmental stages. These plans encompass a spectrum of therapies, including physical therapy, occupational therapy, speech therapy, acupuncture, and massage therapy. These targeted therapies address the motor, sensory, and cognitive dimensions of a child's development, effectively promoting improvements in motor skills and overall functionality. In summary, the clinical approach should optimize the brain's neuroplasticity to drive substantial advancements in movement and functionality.

6.1.4 Selection of Efficacy Indicators Stands Out in Clinical Research on Spastic CP

CP is a common neurodevelopmental disorder in children, with spastic CP being the most prevalent subtype. Previous clinical efficacy studies on spastic CP have primarily focused on the improvement of patients' motor function and social adaptability. Specifically, researchers in clinical trials on spastic CP often use indicators such as muscle tone, muscle strength, and joint mobility for observation. However, with the socio-economic development and evolving understanding of rehabilitation concepts, the emphasis in the rehabilitation of children with cerebral disorders like CP has shifted towards functional recovery and enhancement of quality of life. This includes assessing the stability and coordination of movements such as walking and running, as well as the independent performance of daily life activities like dressing, washing, brushing teeth, and eating, aiming to minimize the adverse effects of the disease on the patient's daily life and social interactions.

Due to this shift in rehabilitation focus, when selecting efficacy indicators for clinical trials, compared to traditional measures like MAS, GMFM, FMFM, and WeeFIM, this study introduced a walking capacity test indicator commonly used for adults in the later stages of cardiovascular and cerebrovascular diseases, namely the 6-minute walk distance (6MWD). This indicator provides an objective measurement of the child's movement ability and endurance over a specific time period. With a longer testing duration, it reflects the patient's endurance and functional level in daily life. It simulates common activities in daily life, such as walking, offering insights into the movement ability requirements the child may face in daily activities.

By mitigating the subjectivity often associated with traditional scales, particularly in clinical trials, using the 6MWD as an observational indicator for intergroup efficacy comparisons enhances objectivity and evidentiary strength. In summary, the 6-minute walk test, being a simple, objective, and widely used assessment indicator, can provide critical insights for the rehabilitation treatment of CP patients. Healthcare professionals can comprehensively understand a patient's

rehabilitation progress through the 6MWD, allowing for timely adjustments to treatment plans to maximize the improvement of the patient's functionality and social adaptability, ultimately enhancing the patient's quality of life.

6.1.5 Standardized AT Therapy: A Key to Replicable Clinical Study

AT, as the most representative TCM treatments and rehabilitation methods, have been extensively validated for their effectiveness and safety in the treatment of spastic CP through numerous clinical trials. To ensure the stability of clinical efficacy, the field of AT for spastic CP is constantly being explored, expanded, and updated. Whether it's the flexible selection of acupoints based on TCM diagnosis and treatment theory, acupoint injection combined with a combination of Chinese and Western medical treatment methods, or interventions like acupuncture and electroacupuncture guided by modern neurophysiology knowledge, modern TCM practitioners widely apply AT techniques in clinical practice, primarily in conjunction with modern rehabilitation treatment plans. This approach holds significant clinical, societal, and economic value. However, the diversity of acupuncture point selection, numerous prescriptions, and varying tuina techniques in spastic CP acupuncture therapy and tuina have also brought about challenges, making it difficult to achieve the desired therapeutic effects.

In our study, we adopted the AT therapy for treating spastic CP as suggested by the World Federation of Chinese Medicine Societies. This protocol, based on scientific study, clinical study, modern medical theory, and the characteristics of spastic CP in children, provides clear treatment principles and procedures, offering scientific guidance and standardization for AT therapy. Prior to commencing any treatment, standardized training is provided to the physicians involved in administering the therapy, covering acupoint selection, needling, and tuina techniques. This ensures the consistency and replicability of all intervention methods. Following a 12-week treatment period, the outcomes met the expected therapeutic goals and

surpassed those of traditional rehabilitation treatments. Additionally, defined indications and contraindications in this protocol mitigate the risk of misdiagnosis, preventing adverse reactions or complications resulting from inadequate clinical experience or incorrect selections by clinicians. Moreover, the absence of any unsafe incidents related to AT in this study directly affirms the safety of this therapeutic approach.

Furthermore, due to the high uniformity of clinical frequent TCM symptoms among spastic CP patients, the proposed protocol in this study adheres to standardized processes, from acupoint selection and operating techniques to treatment duration. This standardization facilitates ease of dissemination and training, enabling more practitioners to learn and master the techniques, ensuring the quality and safety of AT procedures, ultimately benefiting a larger number of patients.

6.2 Findings

(1) The number of studies related to spastic CP has steadily increased over the past twenty years. This indicates that this field is a hot topic and will continue to attract increased attention in the future.

(2) Studies about spastic CP in developing countries should be enhanced.

(3) Finding a new treatment method, precise intervention, and reliable efficacy evaluation could be helpful and potentially new directions in developing the spastic CP study.

(4) The main characteristics of TCM symptoms in spastic CP patients primarily revolve around motor dysfunction and limb stiffness. Simultaneously, patients exhibit signs of weakness.

(5) In terms of TCM syndrome differentiation, spastic CP should be classified as a pattern characterized by liver exuberant and spleen weakness.

(6) There are differences in the treatment outcomes between AT and conventional rehabilitation in children with spastic CP.

(7) AT are more effective in improving gross motor function and alleviating associated related symptoms in children with CP.

(8) AT can regulate qi and blood, unblock meridians, and play a role in inhibiting the liver, supporting the spleen and relaxing muscles.

(9) The sooner a child with CP receives treatment, the better the curative effect.

6.3 The innovative aspects of this study

(1)Interdisciplinary Approach: This study adopts an interdisciplinary approach aimed at delving into spastic CP, including understanding its research hotspots, trends, and frontiers, analyzing TCM symptoms, and observing the clinical effects of acupuncture and tuina on spastic cerebral palsy. This interdisciplinary method aids in constructing a comprehensive knowledge framework to provide both theoretical and practical foundations for clinical interventions.

(2)Integrated Use of Bibliometric Analysis and Medical Record Data: The study combines analysis of 3988 publications on spastic cerebral palsy with the extraction and analysis of medical record data from 231 eligible cases. This comprehensive use of data helps in a thorough understanding of the disease.

(3)TCM Symptom Analysis: Through TCM symptom analysis, the study reveals core symptoms among children with spastic CP, including motor dysfunction, impaired speech, delayed development, and limb stiffness. Furthermore, TCM classifies spastic CP as liver exuberance and spleen weakness syndrome, establishing a connection between Western medical disease and TCM syndrome patterns, thereby guiding standardized TCM interventions.

(4)Clinical Effects of Standardized Acupuncture and Tuina Treatment: The study results indicate significant improvements in muscle tension, overall motor function, walking distance, and functional independence after 12 weeks of acupuncture and tuina treatment. Compared to rehabilitation, the acupuncture and tuina group shows more significant treatment effects, emphasizing their importance in managing spastic cerebral palsy.

(5)Correlation between Age and Treatment Effects: The study finds a negative correlation between children's age and treatment effects, highlighting the crucial importance of early intervention in managing spastic cerebral palsy.

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APPENDIX A

LIST OF PUBLICATIONS

1.Wang, X., Teh, S.H. & Wang, Xh. Knowledge mapping of spastic cerebral palsy. A bibliometric analysis of global research (2000–2022). *Ital J Pediatr* 50, 9 (2024).

2.Wang X, Pang F, Du XG. Analysis of Traditional Chinese Medicine Symptoms in Children with Spastic Cerebral Palsy: A Data Mining Study. *J Multidiscip Healthc.* 2024;17:913-922

3.Wang X, Pang F, Du X G. Analysis of Traditional Chinese Medicine Symptoms in Children with Spastic Cerebral Palsy, a Protocol for Data Mining[J]. *Journal of Multidisciplinary Healthcare*, 2023: 3143-3149.

4.Wang X, Teh S H, Du X G, et al. Acupuncture and Tuina Treatment for Gross Motor Function in Children with Spastic Cerebral Palsy: A Monocentric Clinical Study[J]. *Neuropsychiatric Disease and Treatment*, 2023: 1875-1886.

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