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ASSOCIATION OF RISK FACTORS OF CEREBRAL PALSY – A MATCHED CASE CONTROL STUDY

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ABSTRACT

Background: Cerebral palsy (CP) is one of the leading causes of childhood disability worldwide. The exact etiology of CP is poorly understood, but many risk factors are related to problems during pregnancy, labor, and delivery. The age and sex-matched control study were done to evaluate the association of perinatal risk factors with the development of CP among children in a rural area.

Methods: The study was conducted in the Division of Physical Medicine and Rehabilitation (PMR). Seventy clinically diagnosed CP children as cases and 70 children without CP as controls were included. Information regarding perinatal risk factors was collected from the parents of the children. Data were collected and statistically analyzed by using the Mc-Nemar chi-square test.

Results: The study results suggested that children with male sex (53%) had a higher incidence of CP compared to female (47%) children. Spastic diplegia (60%) was the most common subtype of CP. The significant 'p' value (< 0.01) reveals that all the perinatal risk factors are associated with the development of CP.

Conclusion: This study concluded that spastic diplegia was the most common subtype of CP. The perinatal risk factors such as preterm, low birth weight, birth asphyxia, and neonatal seizures had a significant association with the development of CP.

Keywords: Cerebral palsy, perinatal, risk factors, spastic diplegia, birth asphyxia, low birth weight.

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INTRODUCTION

Cerebral palsy (CP) is a chronic disorder of motor function resulting from a nonprogressive lesion to the immature brain [1]. Recent studies have reported that the worldwide prevalence of CP ranges from 1.5 to more than 4 per 1000 live births [2]. In India, the widespread CP has been estimated as 3 cases per 1000 live births; it is a developing country; the actual number might be higher than the probable one. Recent statistical data reveals that there are about 25 lakhs of CP children in India [3]. After the extermination of polio, CP has become one of the important causes of childhood disability [4]. CP is a chronic neurological disorder that affects the family in both aspects, psychologically and socially, which offers a great burden on the National Health System. The treatment and rehabilitation of CP need integrated management from medical and rehabilitation teams [5,6].

CP is a heterogeneous condition with multiple causes and risk factors. Still, the exact cause of CP has not been identified. Many studies proved that prenatal and perinatal events are responsible for approximately 75% of all cases of CP. Certain risk factors play a significant role in the development of CP such as prematurity, low birth weight, birth asphyxia, neonatal jaundice, epilepsy, maternal infections, perinatal adverse events, placental abnormalities, multiple gestations etc. [7-10].

The clinical spectrum of CP in our country may differ from western countries. The incidence and prevalence of CP vary significantly across different geographical zones. Literature proved that most of the children exposed to many risk factors like prematurity, birth injury, birth asphyxia during the perinatal period. Low birth weight and preterm delivery are the leading perinatal risk factors of CP[5]. Preterm babies exposed to brain damage that leads to oxygen deprivation and periventricular leukomalacia [6-11]. In olden days it was widely understood that asphyxia was the major cause of CP. Now the scenario has been changed, and recent studies proved that birth asphyxia plays a minimal role in the development of CP [12]. Studies now demonstrated that birth asphyxia contributes only 5% to 10% of CP [13]. Even though certain risk factors are responsible for the development of CP, most of the babies born with one of these risk factors but all the children would not have been developed CP. Since CP is a chronic disorder, it is vital to study and explore the causes, risk factors, and planning intervention strategies that are needed for proper understanding and management of CP [5]. Limited studies are available in focussing on the association of risk factors of CP in a rural area. This study aimed to evaluate the association of risk factors of CP among children in a rural area, which helps to frame the rehabilitation needs and primary prevention methods.

SUBJECTS AND METHODS

Study design and Settings

This age and sex-matched case-control study were conducted at the Division of Physical Medicine and Rehabilitation (PMR), Rajah Muthiah Medical College and Hospital (RMMCH), Annamalai University. The study enrolled the cases of children with cerebral palsy from the period of January 2017 to January 2018. The Institution Human Ethics Committee approved the study protocol.

Participants

The study population consists of 70 children with cerebral palsy and 70 children without cerebral palsy. Inclusion criteria for cases: Clinically diagnosed cerebral palsy, age up to 12yrs, both male and female children. Cases were included based on the clinical diagnosis of CP. Controls were selected at the same age and sex without CP and other neurological disorders. The children were recruited from the Pediatric OPD in the same institution.

Study procedure

Convenient sampling method was chosen, and face to face interview through structured proforma was used to collect the data from the parents of the children. Informed consent was obtained from the parents before collecting the data. Apart from the basic information history regarding the risk factors such as preterm, low birth weight, birth asphyxia, and neonatal seizures were collected from the parents of both groups.

Statistical analysis

Since the data is age and sex-matched, Mc-Nemar Chi-Square test has been applied to find out the association of risk factors between the cases and controls. Paired 't' test was used to find out the difference between the cases and control. The level of significance has been fixed at 0.05. SPSS version 18 has been used to analyze the data.

RESULTS

The basic characteristics of children belong to cases (children with CP), and controls (children without CP) were displayed in table 1. The mean and standard deviation of height and weight between the groups were found to be significant with the 'p' value ($p < 0.001$). The children belong to cases in CP shows the reduced height and weight when compared to the children in the control group. The observed data also shows a significant difference.

Table 1: Age distribution of population

Age (in months)	Male	Female	Frequency	Percentage
0 -12	4	4	8	11.4%
13-36	23	20	43	61.4%
37-72	5	5	10	14.3%
73-144	5	4	9	12.9%
Total	37	33	70	100%

Age distribution of observed population after age and sex-matched were displayed in table 2, which reveals that 61.4% of the children belong to the age between 13 to 36 months, i.e., most of the children belong to the age group of 1 to 3 yrs. The least number of children observed in the age groups of 73 to 144 months is observed as 5 % of the total population.

Table 2: Baseline characteristics of cases and controls

Variables	Cases		Control		t value	p value
	Mean	SD	Mean	SD		
Height (cms)	85.9	20.3	93.5	19.0	5.429	0.001
Weight(kgs)	11.3	5.5	12.9	6.0	3.874	0.001

Cases – children with cerebral palsy, Controls – children without cerebral palsy.

Table 3 displayed out of 70 cerebral palsy cases, 27 of them are preterm babies, whereas out of 70 controls only 4 of them are preterm babies. The significant 'p' value reveals that the preterm is one of the associated risk factors for CP.

Table 3: Association of Preterm and cerebral palsy

Cases/ Controls	Yes		No		Total
	Number	Percentage	Number	Percentage	
Yes	0	0.0	27	100.0	27
No	4	9.3	39	90.7	43
	4		66		70

McNemar P value<0.01

Table 4 displays the data of low birth weight, which denotes that 36 children found to be low birth weight out of 70 children in cases, and only 15 found to be low birth weight in the control group. The 'p' value found to be significant and reveals that low birth weight is also one of the associated risk factors for CP.

Table 4: Association of Low Birth Weight and cerebral palsy

Cases/ Controls	Yes		No		Total
	Number	Percentage	Number	Percentage	
Yes	9	25.0	27	75.0	36
No	6	17.6	28	82.4	34
	15		55		70

McNemar P value<0.01

In Table 5, it was noticed that out of 70 cases, 34 children had a positive history of birth asphyxia in cases, and only six children had a positive history of birth asphyxia in controls, which denotes that birth asphyxia is also one of the associated risk factors for CP.

Table 5: Association of Birth Asphyxia and cerebral palsy

Cases/ Controls	Yes		No		Total
	Number	Percentage	Number	Percentage	
Yes	5	14.7	29	85.3	34
No	1	2.8	35	97.2	36
	6		64		70

McNemar P value<0.01

Table 6 depicted the data regarding neonatal seizures, and 32 children had a positive history out of 70 children in cases-only Eleven children exposed to neonatal seizures in controls. The observed 'p' value is significant to reveal those neonatal seizures, also one of the associated factors of CP. The observed data is age and sex-matched. Mc-Nemar Chi-square test has been applied. The significant 'p' value reveals that all the perinatal risk factors are associated with the development of CP.

Table 6: Association of neonatal seizures and cerebral palsy

Cases/ Controls	Yes		No		Total
	Number	Percentage	Number	Percentage	
Yes	2	6.3	30	93.8	32
No	9	23.7	29	76.3	38
	11		59		70

McNemar P value<0.01

DISCUSSION

Cerebral palsy is one of childhood neurological disorders that impose a significant burden on families as well as society, which needs continuous care and multiple financial resources[6]. The literature revealed that the causes of CP are multiple, including various risk factors occur during the antenatal, perinatal, and postnatal period. This study aims to evaluate the association between perinatal risk factors of CP among children in and around Chidambaram town. Seventy children with CP as cases and 70 children without CP as controls of age up to 12 yrs were recruited and matched with age and sex. The history of perinatal risk factors was collected through a semi-structured questionnaire, and the Mc-Nemar Chi-square test analyzed data. In this study, it was observed that the male gender had a higher risk associated with the development of CP than the female gender. Among 70 cases, 53% of male children and 47% of female children were observed, which shows the significant difference in the association between the genders. This association was justified clearly in the study done by Hag berg et al. (2001) declared that female gender showing lower risk associated with the development of CP than the male gender [14].

Further strengthened by many studies in India Singhi et al., (2002) reported (67.5% male out of 1000), Srivatsava et al., (1992) (65.1% male among 100), Reddy et al., (2018) (66% male out of 100) [15-17]. The study results revealed that the basic characteristics such as height and weight of the cases were found lower than the controls, which suggested that children with CP had lesser growth than the children without CP. These results strengthened by Suzan Campbell et al. (1989) stated that children exposed to early insult in gestation typically produces a proportional decrease in all anthropometric measures [18]. In this study the age distribution of cases reveals that more number of children was observed in the age of 13-36 (61%) months that is 1-3 years and less number of children in the age of 73-108 months that is 6 to 9 years (5%), similar results were found in the study by Rajkumar et al., (2018) and Makwana et al., (2017) [19-20]. Our study suggested that the observed cases of CP are younger age group; the reason for this result might be due to the inability of the parents to bring their older CP children to the institution. This might be due to older children were grown up and difficult to bring them to the hospital by the parents, probably confined within homes and

special schools with or without improved functional status.

From the results, it was observed that among 70 cases 60% of spastic diplegia, 21% of quadriplegia, 8% of hemiplegia, 5% of athetoid and 8% of hypotonic CP were observed, which indicates that this population (cases in Chidambaram town) consists of more number of spastic diplegic children and less number of athetoid children. It was noticed that almost 88% of cases belong to the spastic type of CP, which is the most common type worldwide. Further, the results supported by the studies done by Nabanita Das et al. (2016), who observed 80% of spastic cp in his research [4]. In European countries studies have been reported that 18-20% cases of quadriplegia and 41% - 55% cases of spastic diplegia were observed in their studies which is similar to this study (Bottos et al., (1999) Kavcic et al., (1998) and Johnson (2002) [21-23]. Gowda et al. (2015) reported that he observed 16% cases of spastic diplegia and 71.6% of spastic quadriplegia in their study related to the clinical profile of cp children in south India, which is in contrast to our study [24]. From the results, it was observed that there was a significant association between gestational age and the development of CP. Among the study population, 27 babies were preterm in cases, and only four were observed in controls, which may lead to perinatal brain damage and further development of CP, similar results obtained in the study done by Hai MSBA et al., (2015) [9].

In this study, there was a strong association between birth weight and development of CP; out of 70 cases, 36 children observed as low birth weight, and only 15 were found in controls. Birth weight is one of the significant predictors of an individual baby's survival and neurological impairment. The literature revealed that lower the weight higher the risk of infant mortality. It was well supported by the study done by Wilcox et al. (1983) and Johnson (2002), who found that the rate of CP was higher in low birth weight babies [22-25]. Birth asphyxia is one of the perinatal risk factors which had a significant association with the development of CP, and it was noticed that out of 70 children 34 children had a history of birth asphyxia in cases and only six exposed in controls, which was found to be independently associated with risk of developing CP. The results supported by the studies done by ozturk et al. (2006) and Erkin et al. (2007) [26-27]. The longitudinal study was done by Lagunju et al. (2009) [28] declared that birth asphyxia is the leading cause of the development of CP. Even though many old publications in 1993 and 1994 has been suggested that birth asphyxia was the leading cause of CP, early publications in 2006 reveal that birth asphyxia plays a less significant role in the development of CP.

The observed results show that among 70 cases, 32 found with the history of epilepsy, and 11 children found in controls. Neonatal epilepsy had an association with developing CP 32% of cases observed with the history of neonatal epilepsy, which is similar to the recently published study and is similar to the study done by Rajkumar et al., (2018) [22]. Strengths and Limitations: Regarding the strength of the study, this study tries to explore the association of risk factors of CP among the population in the locality and helps to identify the causes of CP, which will be useful in promoting and developing preventive strategies of CP in the same locality. It is also helpful in solving the problem of CP in a local setting to improve the available resources and provide better neonatal care services. There are some limitations to this study. The major limitations were the poor memory of the parents and the unavailability of medical records of the cases and also the relatively small number of the population included. Hence a long term follows up study with a large number of cases is needed for further comprehensive analysis of the risk factors. The present study is hospital-based and identified only cases of children with CP attending PMR OPD. There is also the possibility that some children might be missed in the community without reference. This study was a case-control study based on retrospective events that failed to explain the temporal relationship between the outcome and risk factors. This study focussed on perinatal risk factors, antenatal, and postnatal risk factors that were not considered and analyzed. Another limitation was the data were collected based on binary answers such as a yes or no and present and absent, which failed to estimate the severity and grade, especially in preterm, birth asphyxia, neonatal seizures.

CONCLUSION

This study concluded that children with male sex had a higher chance of developing CP than female children. Spastic diplegia was the most common subtype of CP. Children with CP had lesser growth than children without CP. The perinatal risk factors such as preterm, low birth weight, birth asphyxia, and neonatal seizures had a significant association with the development of CP in a rural area. From the results, it was concluded that the enhancement of neonatal care services, training of medical and paramedical staff involved in neonatal care, and proper resuscitation would go a long way in preventing the development of CP. Our study further suggests that the role of government and non-governmental organizations in the prevention of the development of cerebral palsy is also very important.

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