RESEARCH ARTICLE

Risk factors evaluation of cerebral palsy in Hazara division Khyber Pakhtunkhwa Pakistan: A cross-sectional survey

Keramat Ullah Keramat[1], Muhammad Athar Khalily[2], Abdul Haseeb Bhutta[3], Pirzada Khattak[4], Anam Habib[5], Nimra Ilyas Bhutta[6]

Abstract

Objective: To evaluate the prevalence of risk factors of cerebral palsy in the mothers of children with cerebral palsy.

Method: The cross-sectional study was conducted in 2018 at the Helping Hand Institute of Rehabilitation Sciences, Mansehra, Pakistan, and comprised mothers of cerebral palsy children aged 1-18 years from the Hazara Division. Data was collected by using a modified form of Surveillance of cerebral palsy in Europe questionnaire regarding prenatal, natal and postal natal risk factors. Data was analysed using SPSS 21.

Results: Of the 300 children, 190(63.3%) were males and 110(36.7%) were females. The mean age of the children was 5.43±3.63 years and that of their mothers at the time of delivery was 26.16±5.11 years. Among the prenatal risk factors, anaemia was the leading factor 179(59.6%), while delayed crying 187(63.3%) was the major postnatal factor. Consanguinity was reported by 200(66.7%) mothers. Majority of the deliveries 201(67%) had taken place at hospitals.

Conclusion: Anaemia and delayed crying were the major risk factors identified in mothers and children, respectively, in the study sample.

Keywords: Cerebral Palsy, Anti-natal risk factors, Postnatal risk factors, SCPE. (JPMA 72: 1315; 2022)

DOI: https://doi.org/10.47391/JPMA.1669

Introduction

Cerebral palsy (CP) is a common neurological disorder that affects 0.2% of children.[1] The prevalence of CP in the United States ranges 3-4 per 1000 live births.[2] In 2009-16 period, the prevalence of CP in children aged 3-17 years was 3.2 per 1000.[3] The prevalence of low birth weight (LBW) and preterm in live births is significantly higher (40-100/1000).[4] Incidences of 21-24 per 1000 live births were found in a Danish research.[5] According to a study in Swabi, Pakistan, the prevalence of CP is 1.22 per 1000 live births.[6] However, country-wide statistics are not found. Zaheer et al. reported 6.9% incidence of CP children admission in a Lahore hospital out of the 6.7% paediatric neurological admissions.[7]

The disorder is associated with a huge economic cost. The US spends $1 million per CP child in a lifetime for social services, educational and health needs.[8] Similar cost is observed across the developed world.[9] Effective interventions have been used in Australia since 1990, with reported efficacy in lowering CP incidence.[10] As a result, the prevention of CP is seen to avert high economic cost.[11] To reduce the incidence of CP, the priority of risk factors needs to be determined. The common risk factors in Karachi have been reported to be birth asphyxia, kernicterus, meningoencephalitis, consanguinity, infections during pregnancy and home delivery.[12-15] In this connection, anaemia, hypertension (HTN), urinary tract infection (UTI) and prenatal haemorrhage are the major risks factors associated with the worst outcome.[16] Among these factors, anaemia appears to be the leading cause of adverse outcomes, including premature births and LBW.[17]

The prenatal risk factors under constant surveillance in Europe are diabetes mellitus (DM) HTN, anaemia, high-grade fever, thyroid problem, history of fall, bleeding, hyperemesis, premature labour, recurrent infection, UTI, amniotic fluid leakage and consanguinity.[18] Among these, risk factors, such as growth restriction, intrauterine infection, premature delivery at foetal stage,[19] placental diseases, multiple pregnancies and breech position are reported to be significantly associated with CP.[20] Factors such as obesity, congenital abnormalities, HTN,[21] type 2 DM (T2DM)[22] in births after complication, such as gestational DM (GDM), preeclampsia, and preterm[23] birth can cause neurodevelopmental changes in the foetal brain. Furthermore, maternal UTI, neonatal meningitis and sepsis have been linked with CP.[16] Direct infection involving the brain results in ischaemic responses which cause CP.[24]

Rapture of the uterine wall, placental abruption, and acute delivery due to non-reassuring foetal status, caesarean sections (CS), cousin marriages and delayed crying are conditions that are reported with strong risk association with CP.[15] A similar relation of CP is also reported with gestational age; 2/3rd babies with CP in which 96% singletons born after or at 35 weeks of gestation and 1/4th prevalence in full-term babies. Other rare risk factors associated with CP include perinatal stroke[25] and placental

[1,3-6]Helping Hand Institute of Rehabilitation Sciences, Mansehra, Pakistan; [2]Department of Pediatric Neurology, Children Hospital and Institute of Child Health, Lahore, Pakistan.

Correspondence: Keramat Ullah Keramat. e-mail: karamatjee@yahoo.com

vascular pathology.[26]

To our knowledge, there is a scarcity of research on this subject in Pakistan. The current study was planned to evaluate the prevalence of risk factors of CP in the mothers of children with CP.

Subjects and Methods

This cross sectional study was conducted in 2018 at the Helping Hand Institute of Rehabilitation Sciences (HHIRS), Mansehra, Pakistan, which had registered around 2,500 CP subjects using one or more of its rehabilitation services till 2018. A sample size of 300 mothers of CP children was ascertained from the HHIRS' record from 2017 to 2018. The western estimates of CP birth occurrences range from 0.21-0.24 percent, which is three times lesser than the eastern estimates. A 10% sample size yields a sample of 300 moms with CP children.[5] Those included were mothers of CP children aged 1-18 years who had availed any of the physiotherapy, occupational therapy, speech and language pathology, or prosthetic and orthotic department services. Parents who refused to give consent, children with deceased mother, age <1 year and >18 years, children with diagnosis other than CP were excluded. Informed consent from the mothers was obtained.

Questions for data collection were mainly drawn from the Surveillance of CP in Europe (SCPE) questioner.[18] The mothers were asked a series of questions about prenatal, natal and postnatal factors. Prenatal questions included history of vaginal bleeding, DM, hypotension, HTN, human immunodeficiency virus (HIV), history of fall, premature labour, thyroid problem, recurrent infection, anaemia and high-grade fever. Postnatal questions included difficulty in feeding, delayed crying, birth canal problem (stuck), difficulty in feeding, breathing problems, cord around the neck, high-grade fever, jaundice and fits. General information, such as marriage with cousins, and demographics were also noted.

Children aged <1 year were not included because in these children, milestones are not fully developed. A panel of experts agreed on the questions in the local language that were designed for the interviewers who were final year students of the doctor of physical therapy programme.

Data was analysed using SPSS 21. Descriptive statics were expressed as frequencies and percentages. Data was split in relation to various variable and isolated comparisons were determined.

Results

Of the 300 children, 190(63.3%) were males and 110(36.7%) were females. The largest age group was 1-5 years 178(59.3)

Table-1: Distribution of children into age groups.

Age Group (years)	**n (%)**
1-5	178 (59.3)
5-10	89 (29.7)
10-15	32 (10.7)
15-18	1 (0.3)
Total	300 (100)

Table-2: History of cerebral palsy (CP) children and their mothers.

Birth history	**n (%)**
Place of Birth	
Hospital	201 (67)
Home	99 (33)
TERM	
Pre-mature	64 (21.3)
Full term	227 (75.7)
Late	9 (3)
Mode	
Vaginal	219 (73)
Caesarean	76 (25.3)
Forceps	5 (1.7)
Birth Weight	
Low birth weight	107 (35.7)
Normal	151 (50.3)
Unknown	40 (13.3)
Overweight	2 (7)
Baby's Position	
Breech	28 (9.3)
Cephalad	272 (90.7)
Child's vaccination	289 (96.3)
Maternal history	
Normal births	190 (63.3
Miscarriage	80 (26.7)
Still birth	22 (7.3)
Abortion	8 (2.7)
Mother's vaccination	251 (83.7)
Multiple birth (number of infants born at same delivery)	
Singleton	291 (97)
Twin	8 (2.7)
Triplets	1 (0.3)
Family History	
CP child in family	14 (7.8)
Consanguinity	200 (67)

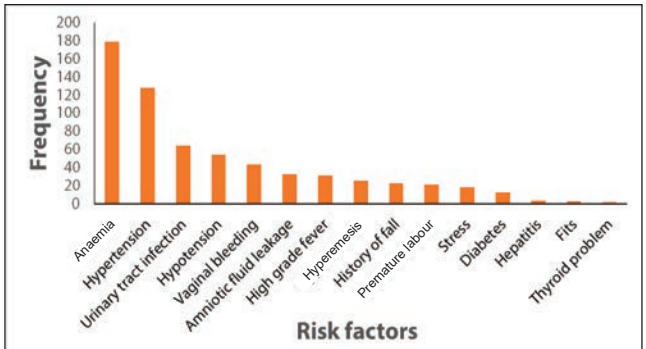

Figure-1: Prenatal Risk factors of cerebral palsy (CP).

(Table 1). The mean age of the children was 5.43±3.63 years and that of their mothers at the time of delivery was 26.16±5.11 years.

Consanguinity was reported by 200(66.7%) mothers. Majority of the deliveries 201(67%) had taken place at hospitals (Table 2).

Among the prenatal risk factors, anaemia was the leading factor 179(59.6%) (Figure-1), while delayed crying 187(63.3%) was the major postnatal factor (Figure-2). A

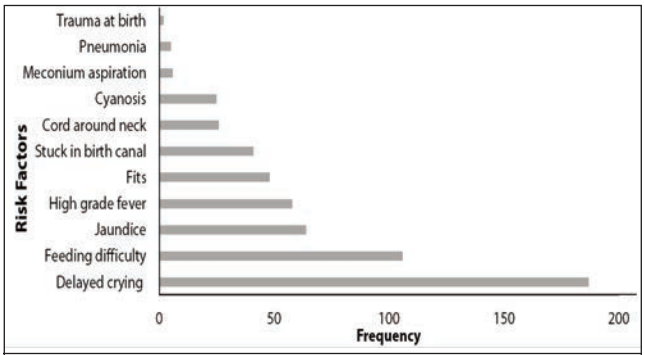

Figure-2: Intra-natal and postnatal risks factors of cerebral palsy (CP).

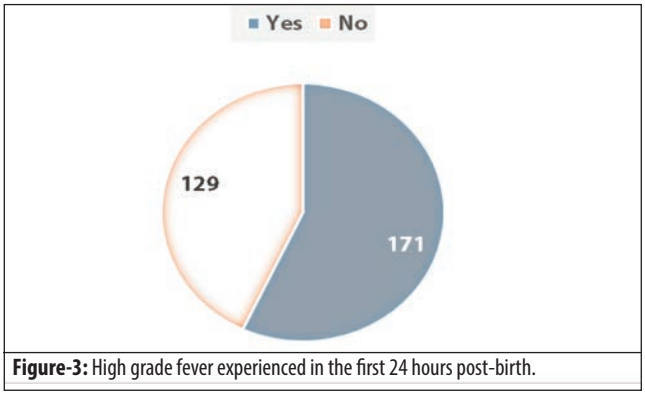

Figure-3: High grade fever experienced in the first 24 hours post-birth.

Table-3: Natal and postnatal risks factors at hospital-based versus home-based deliveries (n=300).

Risk factors		Hospital base deliveries n (%)	Home base deliveries n (%)
Delayed Crying	Yes	123 (61.2)	64 (64.6)
	No	78 (38.8)	35 (35.4)
Difficulty in Feeding	Yes	46 (22.9)	21 (21.2)
	No	155 (77.1)	78 (78.8)
High Grade Fever (child)	Yes	36 (17.9)	22 (22.2)
	No	165 (82.1)	77 (77.8)
Jaundice	yes	45 (22.4)	19 (19.2)
	No	156 (77.6)	80 (80.8)
Fits	Yes	29 (14.4)	19 (19.2)
	No	172 (85.6)	85 (85.8)
Shoulder Dystocia	Yes	17 (8.5)	24 (24.2)
	No	184 (91.5)	75 (75.8)
Cord around the neck (Nuchal cord)	yes	20 (10)	6 (6.1)
	no	181 (90)	93 (93.9)

Table-4: Major risk factors in relation to intra-natal and postnatal presentations of cerebral palsy (CP) children.

Risk Factors	Responses	Anaemia n=179 n (%)	Hypertension n= 128 n (%)	Hypotension n=54 n (%)
Delayed Crying	Yes	121 (67.6)	84 (65.4)	33 (61.1)
	No	158 (32.4)	44 (34.6)	21 (38.9)
Difficulty in Feeding	Yes	43 (24)	29 (22.7)	11 (20.4)
	No	136 (76)	99 (77.3)	43 (79.6)
High Grade Fever	Yes	35 (19.6)	19 (14.8)	14 (25.9)
	No	144 (80.4)	109 (85.2)	40 (74.1)
Jaundice	yes	38 (21.2)	31 (24.2)	12 (22.2)
	No	141 (78.8)	97 (75.8)	82 (77.8)
Fits	Yes	32 (17.9)	19 (14.8)	9 (16.7)
	No	147 (82.1)	109 (85.2)	45 (83.3)

total of 171(57%) CP children had high-grade fever within the first 24 hours of their life (Figure-3).

Childbirth history was compared between those that took place in hospitals and homebased deliveries. Delayed crying was mentioned by 123(61.2%) mothers in the former group compared to 64(64.6%) in the latter group (Table 3).

Intra-natal and postnatal cases were compared with respect to major prenatal risk factors, including anaemia 179(59.6%), HTN 128(42.6%) and hypotension 54(18%) (Table 4).

Discussion

The current study aimed at evaluating the risk factors of CP and its demographics. Anaemia, HTN, and hypotension were found more prevalent prenatal risk factors in mothers of CP children at the time of their pregnancies. It has been previously reported that anaemia is prevalent up to 75% among pregnant women at Faisalabad[27] in the general population. The adverse outcomes in association with anaemia in the third trimester are reported and predicted.[28]

Male children with CP were more (63.3%) than female (36.75) in the current study which is consistent with earlier Australian and Japanese studies.[29,30] Similar results of gender-based prevalence in Pakistan has also been reported.[31] Males are more prone to CP than females, suggesting a relationship with Y chromosomes that are more sensitive to mutations than the X chromosomes.[32]

Mothers aged 40 years and above are at a higher risk factor for CP.[33] The mean of age of mothers in the current study, in contrast, was 26.16±5.11 years, with only 5 mothers aged >40 years. Since anaemia was a common factor and the mothers in the sample were from poor socioeconomic class, therefore, mothers' age may not have been of significance.

Among the prenatal determinants in the current study,

anaemia was more prevalent (59.75%). The high prevalence of anaemia during pregnancy is quite common in the general population in Pakistan[28] and our findings are similar to the findings of Minocha et al. who reported the major risk factors as anaemia, maternal infections, HTN and antenatal haemorrhage.[17,34] The prenatal risk factors probably lead to natal and postnatal complications and adverse outcomes, including damage to the neonatal brain.[17,28] Further analysis in relation to the prenatal risk factors (Table 4) revealed a higher percentage of delayed crying, kernicterus, difficulty in feeding, and fits which indicate an association and higher risk. Similar factors are identified previously in the local population.[14,15]

Vaginal bleeding was the 4th highest factor in the current study (14.3%) among the antenatal hazards (14.3%). Mothers in the 2nd and 3rd trimesters are reported with higher risks if they were anaemic and that increased the likelihood of preterm deliveries with LBW.[28]

High-grade fever in the first 24 hours of life is an important predictor of CP and other complications. In the current study, 19.3% mothers reported high-grade fever in their children within 24 hours post birth; higher in-home based deliveries (22.2%) than the hospital deliveries (17.9%).

The fall during pregnancy was 7.3%, preterm labour 7%, stress 6%, DM 4%, hepatitis 1%, fits 0.7% and thyroid issue in 0.3%. Trauma in relation to Pakistan has previously been reported as a major risk factor found in CP cases (5%).[12]

The majority (67%) of the births took place in hospitals and 61.2% of the mothers reported delayed crying of the child at the time of birth. Meconium aspiration, prenatal risk factors, breech presentation, shoulder dystocia and preeclampsia could be the possible reason, but the number was sufficiently high and future studies should investigate the factors that lead to such a high proportion of delayed crying.

Consanguinity in mothers was 66% which is relatively high and may be a possible risk factor in the Hazara division. A complex genetic inheritance or multifactorial inheritance of CP has been proposed[35] and seems to be true in relation to the current study since cousin marriages were in high proportion.

Neonatal jaundice increases the risk of CP. A 20% of CP children are reported with neonatal jaundice.[36] Neonatal jaundice was one of the major factors in postnatal cases. The bilirubin-mediated brain damage is called kernicterus and causes hyperbilirubinaemia. It is neurotoxic and can cause brain damage. In Pakistan, 13% CP cases are associated with kernicterus.[37]

One of the major limitations of the current study is the recall bias since the questions were asked about their pregnancy experience of 1-18 years ago. However, motherhood experience is unique and most of the experiences during the pregnancies are not forgettable, and, therefore, the information gathered from the mothers may be close to reality without prejudice. Also, the CP children were grouped according to age and age group 1-5 years was the largest, meaning that for mothers the experience was not too old. The second limitation was the absence of Appearance-Pulse-Grimace-Activity-Respiration (APGAR) score. Ideally, much of the information regarding the postnatal complication could have been extracted from these scores. Records of the birth history were found to be poorly documented and, therefore, could not be accessed for the selective age group of patients in the local hospitals. Thirdly, mothers of children with CP enrolled at HHIRS belonged to the poor socioeconomics class (30%) since the institute offer incentivised treatment for their children. Therefore, the sample may not be truly representative of the community. The strength of the study is its large sample size.

Further studies should focus on the case-control design for risk association of factors identified in the current study. Stress has been the vital risk factor reported, but a firm conclusion can be reached since it was reported by 18 mothers and without much understanding of the concept of stress.

Conclusion

Anaemia, HTN, UTI and vaginal bleeding were the major prenatal risk factors. The most common postnatal risk factors of CP were birth asphyxia, jaundice and high-grade fever. Majority of the CP children had vaginal delivery mode. Consanguinity was prevalent in the mothers of CP children.

Disclaimer: None.

Conflict of interest: The person who signed the IRB letter is also co-author of the study.

Source of Funding: None.

References

1. Smithers-Sheedy H, McIntyre S, Gibson C, Meehan E, Scott H, Goldsmith S, et al. A special supplement: findings from the Australian Cerebral Palsy Register, birth years 1993 to 2006. Dev Med Child Neurol 2016; 58: 5-10
2. Boyle CA, Boulet S, Schieve LA, Cohen RA, Blumberg SJ, Yeargin-Allsopp M, et al. Trends in the prevalence of developmental disabilities in US children, 1997–2008. Pediatrics 2011; 127: 1034-42.
3. McGuire DO, Tian LH, Yeargin-Allsopp M, Dowling NF, Christensen DL. Prevalence of cerebral palsy, intellectual disability, hearing loss, and blindness, National Health Interview Survey, 2009-2016. Disabil Health J 2019; 12: 443-51.

4. Streja E. Maternal Risk Factors for Congenital Cerebral Palsy: UCLA; 2012.
5. Ravn SH, Flachs EM, Uldall P. Cerebral palsy in eastern Denmark: declining birth prevalence but increasing numbers of unilateral cerebral palsy in birth year period 1986–1998. Eur J Paediatr Neurol 2010; 14: 214-8.
6. Ahmad A, Akhtar N, Ali H. Prevalence of cerebral palsy in children of District Swabi, Khyber Pakhtunkhwa - Pakistan. Khyber Med Univ J 2017; 9: 88-91.
7. Zaheer A, Rashid A, Chishty Al. Neurological Disease Spectrum and Associated Factors for Morbidity and Mortality among admitted Children. Pak Pediatr J 2009; 33: 24-9.
8. Kancherla V, Amendah DD, Grosse SD, Yeargin-Allsopp M, Braun KVN. Medical expenditures attributable to cerebral palsy and intellectual disability among Medicaid-enrolled children. Dev Disabil Res Rev 2012; 33: 832-40.
9. Oskoui M, Coutinho F, Dykeman J, Jette N, Pringsheim T. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. Dev Med Child Neurol 2013; 55: 509-19.
10. Reid SM, Meehan E, McIntyre S, Goldsmith S, Badawi N, Reddihough DS, et al. Temporal trends in cerebral palsy by impairment severity and birth gestation. Dev Med Child Neurol 2016; 58: 25-35.
11. Shih ST, Tonmukayakul U, Imms C, Reddihough D, Graham HK, Cox L, et al. Economic evaluation and cost of interventions for cerebral palsy: a systematic review. Dev Med Child Neurol 2018; 60: 543-58.
12. Bangash AS, Hanafi MZ, Idrees R, Zehra N. Risk factors and types of cerebral palsy. J Pak Med Assoc 2014; 64: 103-7.
13. Khan AA, Ahmad K, Ayaz SB, Ayyub A, Akhlaq U. Cerebral Palsy in Pakistani Children: A Hospital Based Survey. Cukurova Med J 2014; 39: 705-11.
14. Majeed R, Memon Y, Majeed F, Shaikh NP, Rajar UD. Risk factors of birth asphyxia. J Ayub Med Coll Abbottabad 2007; 19: 67-71.
15. Omar N, Kokab F. Intellectual disability among special children and its associated factors: A case control study, Lahore Pakistan. J Pak Med Assoc. 2019; 69: 684-9.
16. Haider G, Zehra N, Munir AA, Haider A. Risk factors of urinary tract infection in pregnancy. JPMA 2010; 60: 213-6.
17. Vural T, Toz E, Ozcan A, Biler A, Ileri A, Inan AH. Can anaemia predict perinatal outcomes in different stages of pregnancy? Pak J Med Sci 2016; 32: 1354-9.
18. Surveillance of Cerebral Palsy in Europe. Surveillance of cerebral palsy in Europe: A collabouration of cerebral palsy surveys and registers. [Online] [Cited 2019 Oct 28]. Available from: URL: https://www.researchgate.net/publication/299009506_Surveillance_of_cerebral_palsy_in_Europe_A_collabouration_of_cerebral_palsy_surveys_and_registers.
19. Korzeniewski SJ, Slaughter J, Lenski M, Haak P, Paneth N. The complex aetiology of cerebral palsy. Nat Rev Neurol 2018; 14: 528-43.
20. O'Callaghan ME, MacLennan AH, Gibson CS, McMichael GL, Haan EA, Broadbent JL, et al. Epidemiologic associations with cerebral palsy. Obstet Gynecol 2011; 118: 576-82.
21. Pan C, Deroche CB, Mann JR, McDermott S, Hardin JW. Is prepregnancy obesity associated with risk of cerebral palsy and epilepsy in children? J Child Neurol 2014; 29: NP196-201.
22. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. JAMA 2009; 301: 636-50.
23. Xiao D, Qu Y, Huang L, Wang Y, Li X, Mu D. Association between maternal overweight or obesity and cerebral palsy in children: A meta-analysis. PloS one 2018; 13: e0205733.
24. Rellosa N. Infectious Etiologies of Cerebral Palsy. Cerebral Palsy 2018:1-10.
25. Nelson KB. Causative factors in cerebral palsy. Clin Obstet Gynecol 2008; 51: 749-62.
26. Ray JG, Redelmeier DA, Urquia ML, Guttmann A, McDonald SD, Vermeulen MJ. Risk of cerebral palsy among the offspring of immigrants. PloS one 2014; 9: e102275.
27. Anjum A, Manzoor M, Manzoor N, Shakir HA. Prevalence of anaemia during pregnancy in district Faisalabad, Pakistan. Punjab Univ J Zool 2015; 30: 15-20.
28. Mahmood T, Rehman AU, Tserenpil G, Siddiqui F, Ahmed M, Siraj F, et al. The Association between Iron-deficiency Anaemia and Adverse Pregnancy Outcomes: A Retrospective Report from Pakistan. Cureus 2019; 11: e5854.
29. Reid SM, Meehan E, Gibson CS, Scott H, Delacy MJ; Australian Cerebral Palsy Register Group. Biological sex and the risk of cerebral palsy in Victoria, Australia. Dev Med Child Neurol 2016; 58: 43-9.
30. Toyokawa S, Maeda E, Kobayashi Y. Estimation of the number of children with cerebral palsy using nationwide health insurance claims data in Japan. Dev Med Child Neurol 2017; 59: 317-21.
31. Ahmad A, Akhtar N, Ali H. Prevalence of cerebral palsy in children of District Swabi, Khyber Pakhtunkhwa - Pakistan. Khyber Med Univ J 2017; 9: 88-91.
32. MacLennan AH, Lewis S, Moreno-De-Luca A, Fahey M, Leventer RJ, McIntyre S, et al. Genetic or other causation should not change the clinical diagnosis of cerebral palsy. J Child Neurol 2019; 34: 472-6.
33. McIntyre S, Morgan C, Walker K, Novak I. Cerebral palsy—don't delay. Dev. Disabil. Res. Rev 2011; 17: 114-29.
34. Minocha P, Sitaraman S, Sachdeva P. Clinical spectrum, comorbidities, and risk factor profile of cerebral palsy children: A prospective study. J Pediatr Neurosci 2017; 12: 15-8.
35. Schaefer GB. Genetics considerations in cerebral palsy. Semin Pediatr Neurol 2008 Mar; 15: 21-6.
36. Gladstone M. A review of the incidence and prevalence, types and aetiology of childhood cerebral palsy in resource-poor settings. Ann Trop Paediatr 2010; 30: 181-96.
37. Palsi PÇS. Cerebral Palsy in Pakistani Children: A Hospital Based Survey. Çukurova Med J 2014; 39: 705-11.