

# Biological and Environmental Factors Associated with Developmental Coordination Disorder in Mexican Children from National Rehabilitation Institute: A Case-Control Study

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## Abstract:

**Background:** Developmental coordination disorder (DCD) significantly affects a child's ability to learn and perform everyday self-care and academic tasks. It is reported to be more prevalent in children born in an adverse prenatal environment, such as extremely low birth weight or prematurity, although the potential mechanisms have not been explicitly described. There is a screening instrument for DCD that was developed in Canada for parents, and which already has a Spanish version, is the Developmental Coordination Disorder Questionnaire (DCDQ '07). The DCDQ '07 has a sensitivity of 85% and specificity of 71%. The aim of the study was to describe the demographic characteristics of the built-in sample: age, gender, and comorbidities, as well as to determine possible clinical and socio-environmental risk factors involved in developmental coordination disorder.

**Materials and Methods:** A case-control analysis was conducted, including patients with probable diagnosis of DCD, aging between 5-11 years, from the Pediatric Rehabilitation Service. As a result of the assessment in the consultation, the Developmental Coordination Disorder Screening Questionnaire (DCDQ '07) was applied. Once applied, an analysis was made to determine biological and environmental risk factors, both in patients with suspected DCD (score between 15-46) and in those who probably did not have DCD (score between 47-75). A comparison of means was made with Student's t test and Mann-Whitney U test after proving normality with Kolmogorov-Smirnov. It was possible to apply a Linear Regression model by including the variables with  $p = 0.15$  as a maximum. With a sample of 73 patients, 44 cases of children with probable DCD and 29 controls (healthy children).

**Results:** Children with probable DCD were found to have 6.2 times more exposure to risk of preterm labor and 7.0 times more exposure to cesarean delivery; 18.2% were dystocic deliveries, versus 0% of controls; furthermore, it is noteworthy that the risk of being a child of a single mother was 6.0 times greater, and 9 times that of belonging to a dysfunctional family and having a low socioeconomic status. As expected, gestational age and birth weight were significantly lower in cases of probable DCD.

**Conclusion:** This study demonstrates that the main factors associated in Mexican children with the diagnosis of probable DCD are low Apgar score, risk of preterm labor and risk of miscarriage, relevant factors were to be born to a single mother and to belong to a dysfunctional family.

**Key words:** developmental coordination disorder, biological factors, socio-environmental factors, children

## 1.Introduction

Developmental coordination disorder (DCD) is a chronic neurodevelopmental condition that significantly affects a child's ability to learn and perform everyday self-care and academic tasks [1]. A prevalence of 5-6% is reported worldwide, according to the American Pediatric Association's 2012 report. In 2001 the United Kingdom reported a prevalence of 1-7% in children 7-8 years of age, however, in 2011 the British Dyspraxia Foundation estimates a prevalence of 1-10%. An incidence of 12.5% has been reported in children with a history of prematurity and a gender difference of 3:1 to 7:1 (male/female) [2]. Higher prevalence has been reported in children born in an adverse prenatal environment, such as extremely low birth weight or extremely premature, although the potential mechanisms have not been explicitly described [3].

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the following diagnostic criteria have been established: A. Execution of motor skills below what is expected for the chronological age, learning opportunities and use of skills, the difficulties are manifested in clumsiness, slowness and poor accuracy in the execution of skills. B. Deficits interfere with day-to-day activities, academic productivity, work, leisure and play activities. C. It begins in the early developmental period. D. Deficits are not explained by any intellectual disability visual limitations, or neurological conditions affecting movement [4]. Several studies[30, 31,32] have reported that DCD is consistent with other developmental disorders, such as attention-deficit hyperactivity disorder (ADHD), in some cases with an association of up to 50%. It has also been found to be associated with learning disabilities, such as dyslexia, specific language disorders, and autism spectrum disorder (ASD). These diagnoses are most likely to come before the assessment of DCD, and most interventions focus on such comorbidities first. In addition, only less than 25% of children with DCD are referred and diagnosed before starting school. The remaining 75% are referred during the early years of primary school. Clinical presentation at this age includes the persistence of problems seen in the preschool years, such as slow, immature, and laborious writing and difficulties copying from the blackboard [5]. Recently, DCD has been considered one of the major health problems among school-age children worldwide and often extends beyond the motor domain to include secondary mental and physical health problems. Most specialists agree that these consequences are the major problem when it comes to DCD. While some of the motor skill problems in childhood can be corrected, the mental and physical outcomes can significantly compromise the quality of life and health of this population throughout their lives [6]. It has been reported that 75% of the untreated children population will have coordination disorders in adulthood [2]. It is clear that, in late childhood and adolescence, the emotional impact of DCD can be even more severe than the primary motor difficulties they experience [7]. In this way, individuals with DCD, may present difficulties including more psychosocial issues, that are more than likely to affect quality of life. For example, adults with DCD reported significantly lower levels of satisfaction with quality of life in all domains compared to adults with normal development [7]. They also report significantly higher rates of symptoms of depression, trait and state anxiety than their peers [8]. There is a DCD screening instrument for parents, which was developed in Canada and already has a Spanish version, is the Developmental Coordination Disorder Questionnaire (DCDQ'07) [9]. The DCDQ'07 has a sensitivity of 85% and specificity of 71%, and has been adapted and validated interculturally in several countries including Italy, Colombia, China, Brazil, the Netherlands and Germany [10]. There are no studies in Mexico that addresses the biological and environmental factors that may possibly be involved in DCD. There are several review articles worldwide that only discuss biological factors related to DCD. In a review study realized by the Children's Medical Center of Shanghai, China in 2013, a higher prevalence of DCD is mentioned in children with very low birth weight or who were premature [3]. In 2016, a publication was made at the

University of Texas at Arlington, that mentions the significant increase in DCD in children born prematurely or with extremely low weight [12]. Similarly, a 2018 study by the University of Texas Health's Division of Perinatal-Neonatal Medicine found that one-third of all preterm infants are at risk for developing DCD, being even more common than cerebral palsy [13]. The aim of our study is to identify the biological and sociodemographic factors that could be present in Mexican children with the diagnosis of DCD, as well as to inform if there are variations to what has been published internationally, to generate, strategies to detect the factors that can be modified, with the aim of carrying out an opportune intervention through a rehabilitation program.

## 2 Materials and Methods

### 2.1 Participants

A case-control type analysis was conducted, including patients with the diagnosis of probable DCD between ages 5-11 years, from the Pediatric Rehabilitation Service of the Instituto Nacional de Rehabilitación Luis Guillermo Ibarra Ibarra (National Rehabilitation Institute). Afterwards, the Questionnaire for the screening of developmental coordination disorder (DCDQ '07) was applied, where patients were divided into 2 groups: the first group, those with probable or suspected DCD, and the second group, those who probably did not have DCD. It is worth mentioning that the group of children we worked with were matched by age and schooling. Subsequently, biological risk factors were determined by an analysis, such were: age, gender, gestational age, birth weight, low APGAR at 5 minutes, presence of threatened abortion, presence of preterm delivery, type of delivery, presence of dystocic delivery, neonatal respiratory pathology, and environmental factors such as child of a single mother, family dysfunction, mental illness of parents or caregivers, age of the mother at the time of pregnancy, low socioeconomic status, presence of alcohol and drug abuse, factors that could possibly be involved in the etiopathogenesis of the disorder (Inclusion/Exclusion Criteria)[29, 31], applied to children between 5-15 years, it consists of 15 questions, which are grouped into three different factors. The first factor includes a series of aspects related to motor control when the child or an object is in motion and is called "Control during movement". The second includes aspects such as "fine motor and writing" and the third factor relates to "overall coordination". These factors are measured separately, and do not indicate that a child may have DCD. It should be noted, that when the characteristics questioned are added together, a score is established, within a range of 15 minimum and a maximum of 75, and values are also determined by age group to indicate whether DCD is suspected. From years 5 to 7 and 11 months the indication or suspicion score of DCD is 15 - 46, the score of probably no DCD is 47 - 75, for children from 8 to 9 years and 11 months the indication or suspicion score is 15 - 55 and of probably no DCD 56-75, finally, for children from 10 years to 15 years the suspicion score is 15 - 57 and 58 - 75 when there is probably no DCD [9]. DCDQ'07 has the advantage that it correlates well with some motor tests such as the MABC-2 motion assessment battery, which in turn has a highly discriminant function that makes it suitable as a screening tool [11].

A comparison of Student's t test and Mann-Whitney U means was made after proving normality with Kolmogorov-Smirnov test. It was possible to apply a non-conditional logistic regression model including variables with a significance of  $p = 0.15$  at most.

### 2.2 Sample size

For the calculation of the sample size, prematurity was taken as the main risk factor. Following the use of a formula, [33] the minimum sample of cases and controls was determined to be:

\*n = 29 cases and 29 controls.

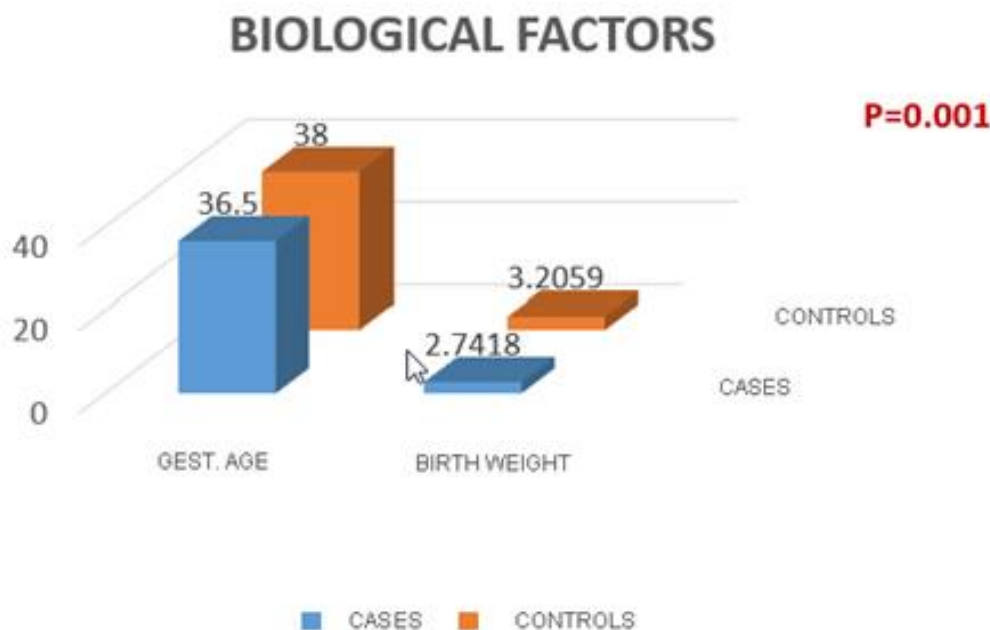
### 3 Results

We included a sample of 73 patients all of whom were male, 44 cases of children with probable developmental coordination disorder and 29 controls (healthy children). Being matched by age and gender, compared to the control group of healthy children, the children with probable DCD [whose score in the DCD test was 39.5 +/- 7.4 points against 56.8 +/- 6.3 of the controls ( $p = 0.0001$ )] differed significantly in all the variables considered as risk factors (Table 1); note that, in order to conform the matching, the percentage of children with probable DCD was 65.9% versus 69.0% of the healthy ones ( $p = 0.78$ ) respectively, and that the

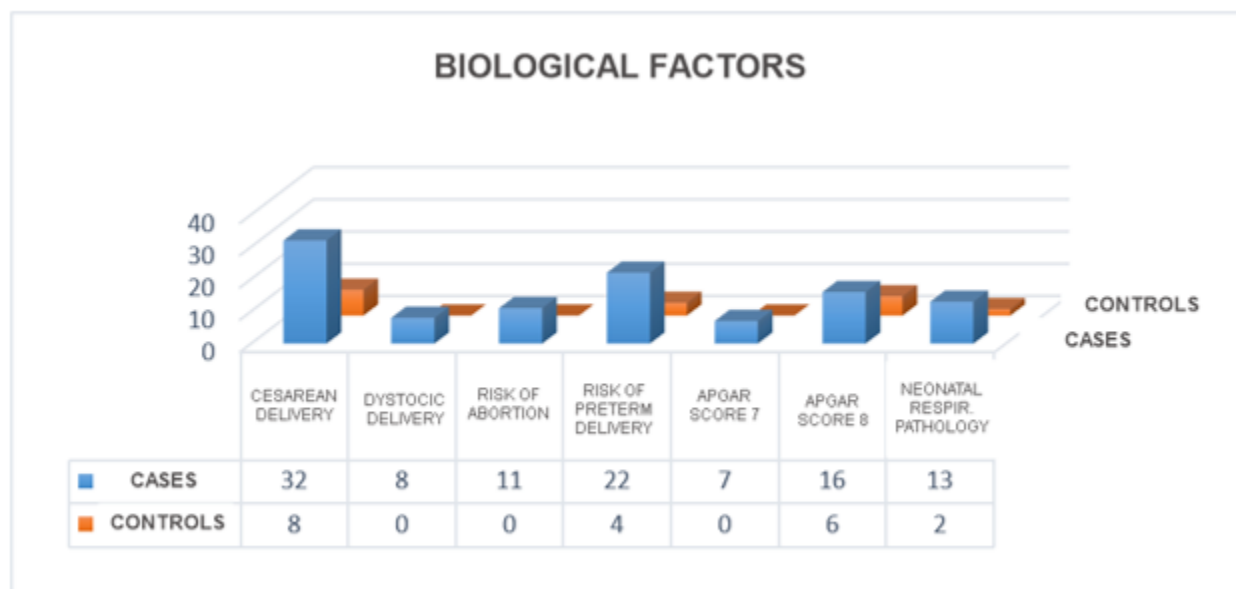
average age of one was 6.8 +/- 1.6 versus 6.4 +/- 0.9 of the other ( $p = 0.16$ ). See now that 15.9% of the children with probable DCD had Apgar at 5 minutes equal to or less than 7 compared to 0% of the healthy controls, as well as 6.2 times (CI 95% 1.8-20.9) more exposure to the risk of premature delivery and 7.0 more times (CI 95% 2.4-20.0) of birth by cesarean section; they also had 11.7 more times (CI 95% 1.4-95.6) the factor of neonatal respiratory pathology (Figure. 2). The risk of being born to a single mother was 6.0 times higher (95% CI 1.5-22.8) and, 9.3 times higher (95% CI 1.9-44.3) of belonging to a dysfunctional family, as well as 9.0 times higher (95% CI 2.6-30.4) of being of low socioeconomic status (Figure. 3).

Risk Factor	DCD		p
	Cases (n = 44)	Controls (n = 29)	
Age	6.8 +/- 1.6	6.4 +/- 0.9	0.16 Student's t test
Male gender	29 (65.9%)	20 (69.0%)	0.78 square chi
Apgar 5 min			0.01 (square chi)
≤7	7 (15.9%)	0	
8	16 (36.4%)	6 (20.7%)	
9	221 (47.7%)	23 (79.3%)	
Gestational age	36.5 +/- 4.0	38.0 +/- 1.2	0.02
Weight at birth	2741.8 +/- 697.6	3205.9 +/- 282.9	0.001
Risk of abortion	11 (25%)	0	0.002 (Fisher test)
Risk of Preterm Delivery	22 (50%)	4 (13.8%)	0.002 (Fisher)
Cesarean delivery	32 (72.7%)	8 (27.6%)	0.0001 (square chi)
Dystocic delivery	8 (18.2%)	0	0.013 (Fisher)
Neonatal respiratory pathology	13 (29.5%)	1 (3.4%)	0.006
Born to a single mother	18 (40.9%)	3 (10.5%)	0.005
Family dysfunction	18 (40.9%)	2 (6.9%)	0.001
Low socioeconomic status	26 (59.1%)	4 (13.8%)	0.0001
Intellectual Functioning	97.9 +/- 5.9	95.1 +/- 5.6	0.04

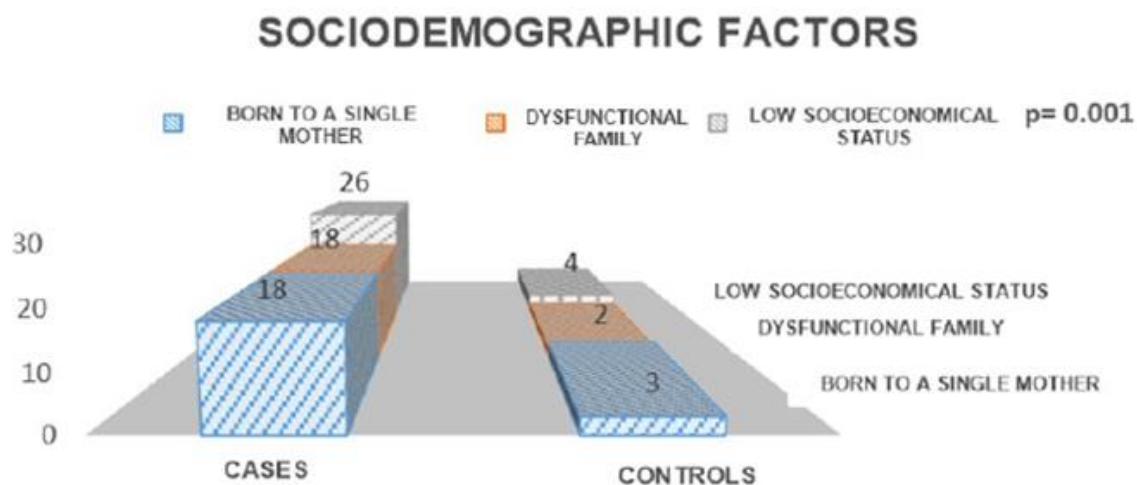
**Table 1:** Comparison of risk factors between DCD cases and controls by bivariate analysis



**Figure 1:** Comparison of gestational Age and Birth Weight between Cases and Controls



**Figure 2:** Comparison of significant biological factors between cases and controls.



**Figure 3:** Comparison of Significant socio-dermographic factors between Cases and Controls

#### 4: Discussion

This is the first study carried out in Mexico in which the main objective is to describe the demographic characteristics of the incorporated sample: age, gender, and comorbidities, as well as to determine possible clinical and socio-environmental risk factors involved in the developmental coordination disorder.

Coordination difficulties in children have been described for almost 100 years, there is increasing evidence of persistent effects in adulthood and long-term negative effects on social and physical relationships and employment. It has also been reported that children with DCD are at increased risk of overweight and obesity, which increases with age and severity of the motor disorder [6,14,15]. In the present study, consisting of a completely homogeneous sample, an analysis of the risk factors possibly involved in patients with suspected BDD was carried out using the DCDQ'07 questionnaire, making a comparison with patients who probably did not have this pathology. It was found that the percentage of children was 65.9% and that the average age was 6.8 years (+/- 1.6), which correlates to what was described in the literature above, where there is a higher prevalence in children in a proportion of 3:1, with an average

age of diagnosis between 7 and 8 years [16]. It was also determined that 15.9% of children with probable DCD had an Apgar score at 5 minutes equal to or less than 7, versus 0% of healthy controls, and that 18.2% of children with probable DCD had a dystocic birth, versus 0% of controls. These data have not been previously investigated in the literature as a risk factor for DCD, however we believe that their association is possible since they have previously been associated with perinatal repercussions that can range from minor injuries to severe brain damage. Low Apgar score has been described as an indicator of birth asphyxia, which in turn could lead to neurodevelopmental disorders [17], on the other hand, it has been described a greater percentage of newborns with low Apgar scores, both at one minute and five minutes, after a dystocic birth. Alongside, the following clinical profile of a patient at risk of suffering from dystocic delivery has been studied: a mature patient, nulliparous or low parity, medium or high height, estimated weight of the product close to or greater than 4,000 gr and who had a prolonged labor [18], these data were not considered in our study, but will be important to consider in future research. For this reason, they should be risk factors considered in children with a suspected diagnosis of DCD. Other relevant factors, which we will mention altogether due to the relationship between them, are



gestational age and birth weight, which were significantly lower in probable cases of DCD compared to healthy children. In addition, children with probable DCD had 11.7 more times (CI 95% 1.4 - 95.6) neonatal respiratory pathology, these data are consistent with what has been published internationally, since prematurity is considered one of the main risk factors to be taken into account in patients with DCD [19]. There is a relationship between prematurity and neonatal respiratory pathology since it has been described that there are certain perinatal and postnatal factors that confer a greater risk of long-term neurodevelopmental deficits in children with prematurity, including severe intraventricular hemorrhage, periventricular leukomalacia, persistent fetal circulation, infections such as meningitis and pneumonia resulting in respiratory failure, severe respiratory distress syndrome, seizures, and very low birth weight [20]. Premature babies are born at a time when their brains are particularly susceptible to injury. Early insults during this time can adversely affect several processes involved in brain development including neuronal migration, synaptogenesis, myelination, cytological maturation, and cell receptor development [13]. There are also some articles that mention late prematurity of 34 to 36.6 weeks of gestation, which was found in several of our patients, as a risk factor for the development of DCD, language problems, attention deficit and hyperactivity, learning disorders, etc. [19]. In our opinion, we, therefore, consider it necessary to search for such factors in our clinical interrogatory of every child suspected of DCD. It is worth noting that 25% of children with probable DCD were exposed to the risk of abortion compared to 0% of controls; half of them (50%) were exposed to the risk of premature delivery compared to only 13.8% of controls, so children with probable DCD had 6.2 times (CI 95% 1.8-20.9) more exposure to the risk of premature birth, these data have not been previously associated with DCD either. However, we consider necessary to take them into account as risk factors, since there are several publications that discuss the effect on neurodevelopment of children who were subjected to periods or situations of stress. It has been studied that insults or alterations in normal fetal maturation can lead to long-lasting neurobiological diseases. The fetus is involved in a dynamic communication with the mother throughout gestation, including exchanges on biological stress markers that originate in the maternal-placental-fetal unit. One of the main signs of placental stress in pregnant primates is corticotropin-releasing hormone (CRH). This peptide plays a key role in the maturation of the fetus at the hypothalamic-pituitary-adrenal axis (HPA axis) as well as other systems, events that impact on fetal growth and maturation, such as the onset of labor [21]. In a 2008 study at Columbia University, New York, levels of maternal corticotropin-releasing hormone (CRH) in the placental and maternal cortisol were collected from plasma from 158 women at 15, 19, 25 and 31 weeks of gestation. The results indicated that maternal cortisol increases at 15, 19 and 25 weeks, and that the increase in placental CRH at 31 weeks of gestation was significantly associated with decreases in infant maturation. The findings suggest that stress hormones have effects on human fetal neurodevelopment. They have been associated with MRI abnormalities detected in newborns, including basal ganglia and white matter injuries, as well as motor alterations in children [22]. Another factor we found and believe important to mention, was that children with probable DCD had 7.0 more times (CI 95% 2.4-20.0) the risk of being born by cesarean section. As many other factors that hadn't been related to DCD, we consider important to take it into account in future research, since there are several studies where the importance of bacterial colonization of the gastrointestinal tract during delivery has been evaluated, and it has been described as an essential process that modulates the physiology and immunity of the host, an aspect that apparently does not occur when a cesarean section is performed [23]. Recently, researchers have begun to understand how and when these microorganisms colonize the gut and the early life factors that affect their natural ecological establishment. The vertical transmission of maternal microbes to their young is a critical factor in the immune and metabolic development of the host. Growing evidence also points to a role in the wiring of the gut-brain axis. This process can be altered by several factors,

including delivery method, gestational age at birth, use of antibiotics in early life, infant feeding, and hygiene practices. In fact, these early exposures affecting the intestinal microbiota have been associated with the development of diseases such as obesity, type 1 diabetes, asthma, allergies, and even neurodevelopmental disorders [24]. As previously stated, we analyzed the sociodemographic factors that may be associated with DCD. It is noteworthy that the risk of being born to a single mother was 6.0 times greater, 9.3 times greater of belonging to a dysfunctional family and 9.0 times greater of being of a low socioeconomic level in children with probable DCD. These data are very relevant since they make us suspect that there is a relationship with the disorder; although there is no research that shows association, there are some studies where psychosocial deprivation has been established as the fourth cause of global delay in development [25], this situation could lead to any of the sociodemographic factors found in our study. The relationship between socio-environmental influences, children's behavior and their mental health have been further investigated. The household environment plays a critical role in the development of appropriate coping strategies and emotional regulation for any child. Maternal age at birth may also be a relevant factor, as it has been found that families often face a variety of adverse social influences. It has been studied that premature infants born to teenage mothers are about 1.6 times more likely to develop emotional and behavioral problems than those born to mothers in their 20s or older. There is a reciprocal relationship between parenting behaviors, parental well-being, and behavior, as well as the well-being of the children [26,27,28,29,30]. In the light of this, prevention and opportune management of these factors in a multidisciplinary way is key in order to favor a better outcome on the condition; as previously mentioned, children with DCD are associated to emotional and physical health problems, which make their treatment, as well as the response to it, more complicated.

## 5 Study limitations

Within the limitations of our study, we firstly acknowledge that the sample size is small. Another aspect to consider is that to identify children with probable DCD, was used a standardized screening instrument instead of a clinical diagnosis, it is also important to remember that the DCDQ '07 instrument has a sensitivity of 85% and specificity of 71%, which could have led to a misclassification.

Finally, we consider that it would have been convenient to use a quality-of-life scale in order to determine the impact generated by the factors found in each of the children with probable DCD and whether the presence of any of them had any direct relation to the severity of the disorder.

## 6 Conclusion

In conclusion, this study highlights the importance of the timely detection of possible biological and sociodemographic factors associated with DCD from the first years of life, and also the growing need for more population-based, case-control and longitudinal studies to identify possible risk factors and early signs of DCD at an early stage, which will ultimately allow us to understand and address this condition comprehensively.

In future research it will be necessary to increase the number of enrolled children with DCD, in addition to making a clinical diagnostic confirmation based on the criteria of DSM 5, which will allow us to improve the evidence of the studies.

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