Journal of Pediatric Surgery 55 (2020) 2293–2296

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Educational level and socioeconomic status in patients born with congenital diaphragmatic hernia: A population-based study☆,☆☆,★,★★,★★★,★★★★

Carmen Mesas Burgos *, Elin Öst, Henrik Ehrén, Björn Frenckner

Department for Pediatric Surgery, Karolinska University Hospital, Stockholm, Sweden

ARTICLE INFO

Article history:
Received 25 October 2019
Received in revised form 22 December 2019
Accepted 22 December 2019

Key words:
Congenital diaphragmatic hernia
Educational level
Socioeconomic status
Income
Neurodevelopment

ABSTRACT

Background: Neurodevelopmental dysfunction is one of the most disabling outcomes for congenital diaphragmatic hernia (CDH) survivors and may have a long lasting impact in adult life.
Aim: To evaluate to which extent being born with CDH has an impact on the educational level and socioeconomic status as a proxy for neurocognitive development.
Material and methods: Nationwide, population-based prospective study of newborn children in Sweden from 1982 to 2015. School grades, highest educational level and income were assessed through Swedish public registries. Children above 15 years of age with CDH were compared with randomly selected controls.
Results: A significantly higher number of cases (17% vs 10%) did achieve neither a school nor a university degree. Among those who achieved a degree there was no difference in the highest level of education. The qualification points in elementary school did not differ, but in high school female cases had significantly lower qualification points than female controls. There were no differences in individual disposable income between cases and controls. However, males had higher income compared to females. Prematurity and a long hospital stay had a negative impact on educational level.
Conclusions: A higher proportion of children born with CDH compared to controls do not achieve a school degree. Among those who achieved a degree, the school achievements and educational level were similar to controls. Prematurity and a long hospital stay are risk factors for not achieving an educational degree.
Type of study: Prognosis study (high-quality prospective cohort study with 99% of patients followed to the study end point).
Level of evidence: Level I.
I for a prognosis study — This is a high-quality, prospective cohort study with 99% of patients followed to the study end point.

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Abbreviations: CDH, Congenital Diaphragmatic Hernia; ECMO, Extracorporeal membrane oxygenation; GA, Gestational age; ICD, International Classification of Diseases; IQR, Interquartile range; MBR, Swedish Birth Registry; NPR, Swedish National Patient Registry; PPHN, Persistent Pulmonary Hypertension of the Newborn; SD, Standard Deviation.

☆ **Financial disclosure**: Nothing to disclose.

☆☆ **Conflict of interest:** None of the authors have conflict of interest.

★ **Author's Contributions' Statement:** Dr Carmen Mesas Burgos conceptualized and designed the study, designed the data collection instruments, collected data, carried out the initial analyses drafted the initial manuscript, and reviewed and revised the manuscript. Dr Henrik Ehren och RN Elin Öst reviewed and revised the manuscript. Dr Björn Frenckner conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

★★ **Table of Contents Summary:** This study evaluates to which extent being born with CDH has an impact on the educational level and socioeconomic status as a proxy for neurocognitive development at a nationwide level. In this very comprehensive study that includes 326 individuals born with CDH and older than 15 years of age, and 1577 age-matched controls, we found that a higher proportion of children born with CDH compared to controls do not achieve a school degree, but among those who achieved a degree, the school achievements and educational level were similar to controls. Not surprisingly, prematurity and a long hospital stay are risk factors for not achieving an educational degree.

★★★ **What is Known on This Subject:** Neurodevelopmental dysfunction is common outcome for CDH survivors; as many as 20% have been described. Neuromotor dysfunction has been described early on in infancy, whereas behavioral problems are more common in older children and adolescents.

★★★★ **What This Study Adds:** Being born with CDH is associated with higher risk of not achieving a school degree, but among those who achieved a degree, the school achievements and educational level are similar to controls. Prematurity and a long hospital stay are risk factors for not achieving an educational degree. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

* Corresponding author at: Department of Pediatric Surgery, Eugeniavägen23, C11:33, Karolinska University Hospital, 17176 Stockholm, Sweden.
E-mail address: Carmen.mesas.burgos@ki.se (C. Mesas Burgos).

https://doi.org/10.1016/j.jpedsurg.2019.12.018
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Advances in past decades have led to an increased survival for babies born with congenital diaphragmatic hernia (CDH) [1, 2]. Improved survival rates, however, have also switched the focus to long-term outcomes. Neurodevelopmental dysfunction has been recognized as a common and probably most disabling outcome for CDH survivors [3, 4]. Neuromotor dysfunction has been described early on in infancy [3], whereas behavioral problems, hearing impairment and quality of life related issues are more common in older children and adolescents [5–7]. Intelligence has been described to be in the low normal range [8]. Need for ECMO, liver up, need of patch, need of oxygen at 30 days of life and right-sided defects have been described as risk factors for delayed neurodevelopment [3, 9].

We hypothesize that to be born with CDH has a long lasting impact in adult life, and that patients born with CDH are at risk to reach lower educational level and it will be reflected in lower yearly income.

The aim of this study was to evaluate to which extent to be born with CDH has an impact in the educational level and socioeconomic status at a population level, as a proxy for neurocognitive development.

1. Material and methods

1.1. Study design

The study was a nationwide, population-based prospective case–control nested within a cohort of newborn children in Sweden during the observational period 1st January 1982 through 31st December 2015. The study exposure CDH and the study outcome (school grades, highest educational level and income) were assessed through linkages between registries administrated by the Swedish National Board of Health and Welfare (the Swedish National Patient Registry NPR, the Swedish Birth Registry, MBR) and Statistics Sweden (Swedish Income and Taxation Register and the Register of Education).

1.2. Registers

The Swedish National Board of Health and Welfare started the National Patient Register (NPR) in 1964, which contains prospectively collected information on all hospitals admissions in Sweden, including diagnoses according to the WHO ICD system and surgical procedures. Since 1987, 100% of the Swedish population is covered by the register.

The Medical Birth Register (MBR) contains prospective data on pregnancies and deliveries in Sweden since 1973. In 1982 a more detailed data reporting to the register was introduced, containing information of antenatal care, delivery, and medical examination of the newborn.

The risk of missing a patient using a combination of these registers has been reported as negligible [10].

Statistics Sweden administers both the Swedish Income and Taxation Register, which started in 1943, and covers all tax paying citizens, and the Register of Education, which started in 1985 and records grades for elementary school, high school and higher educational level of inhabitants between 15 and 74 years of age. It has a validity in 85% of the cases [11].

All Swedish residents are assigned a unique 10-digit personal identification number at the time of birth or immigration, which enables linkage among the different national registries and a complete follow up carried out in the present study.

1.3. Assessment of exposure and definition of cases and controls

Eligible case participants were children born with CDH during the observational period. The following codes of the International Classification of Diseases (ICD) were used to identify the diagnosis of CDH: ICD-9756.6 ICD-10 Q79.0 and Q79.1.

Using these criteria, 974 exposed cases were identified. We excluded individuals younger than 15 years of age, since the Register of Education records school information from the age of 15, or who died before 2015 (36% mortality rate, according to previous reports) [12]. Altogether, a total of 326 exposed individuals were included in the study cohort. Control participants were randomly sampled from the population register and matched for birth year and gender. A total of 5 controls per case were included ($n = 1577$).

1.4. Assessment of outcomes and covariates

The school system in Sweden consists of a compulsory 9-year elementary school ("grundskola") after which the pupils can continue to a 3 year high school ("gymnasium"). After completion of high school university studies are possible.

Highest educational level was collected from the Swedish Register of Education, and categorized in three levels: Completion of elementary school, completion of high school or completion of at least 2 years of university studies.

Qualification points in elementary school are the sum of the 16 best grades in elementary school, with a maximum value of 320 points. Qualification points in high school are the sum of the grades from all courses accomplished during a 3-year period in high school, with a maximum value of 20.0.

A subanalysis in the cases group regarding the gestational age (GA) at birth and length of hospital stay (LOS) was performed. GA at birth was categorized into 4 groups: < 35, 35–37, 38 and >38 weeks. LOS was categorized into longer or shorter than 100 days.

Individual disposable income was collected from the Swedish Income and Taxation Register, and is the sum of all income, excluding taxes, per individual and year.

A further subanalysis regarding gender and age was also performed.

1.5. Statistical analysis

The association between CDH, educational outcome and socioeconomic status was examined by Fischer's exact test and Chi-square test for categorical variables and t-test, Mann–Whitney U-test or Kruskal–Wallis for numerical variables. Linear regression was used to explore an association between gestational age and average grading. P values <0.05 were considered significant. All statistics were performed in R software version 2.38 (http://CRAN.R-project.org/package=survival).

1.6. Ethics

The regional ethical committee in Stockholm approved the study, Dnr 2013/1550–31/3.

2. Results

The proportion of cases who did not achieve either a school or a university degree (17%) was significantly higher than that of controls (10%), but among those who achieved a degree there was no difference in the highest level of education between cases and controls (Table 1).

No differences were found in the qualification points in elementary school between male and female CDH cases nor was there any difference between cases and controls in both genders. In high school female cases had significantly lower qualification points than female controls. Female controls had higher qualifications points than male controls. In male cases there was no difference compared to male controls (Table 2).

There were no differences in individual disposable income between cases and controls (Table 1). However, males had higher income compared to females. In the control group this difference was significant.

The proportion of cases who did not achieve any educational degree was 38% among children with a GA shorter than 35 weeks compared to 22% with a GA of 35–37 weeks and 12% for those with GA of 38 weeks or more (Table 3). This difference was highly significant. For cases who

Table 1
Educational level and annual income for cases and controls.

	Cases	Controls	p-value
n	326	1577	
Age group			
15–20 years *n* (%)	119 (37)	569 (36)	
21–25 years *n* (%)	123 (38)	599 (38)	
26–30 years *n* (%)	76 (23)	368 (23)	
31–40 years *n* (%)	8 (2.5)	41 (2.6)	
No degree *n* (%)	54 (17)	161 (10)	0.001*
Highest level of education			0.904
Elementary school *n* (%)	69 (25)	372 (26)	
High school *n* (%)	135 (50)	682 (48)	
University *n* (%)	68 (25)	362 (26)	
Qualification points elementary school, mean (SD)	203 (62)	212 (68)	0.214
Qualification points high school, mean (SD)	12.0 (5.4)	12.6 (5.2)	0.115
Individual disposable income in SEK (median [IQR])	150,300 [114,500–205,100]	154,400 [108,150–217,900]	0.430

A significantly lower proportion of cases achieved a school or university degree compared to controls. Among those achieving a degree there was no difference in the highest level of education. No difference in school grades or annual income was seen. Chi-square *p < 0.05.

achieved a degree neither the highest level of education nor qualification points differed with different GA.

Long hospital stay had a negative impact in educational level. Seven out of 13 cases with LOS > 100 days did not achieve an educational degree, which are significantly higher compared to patients with shorter hospital stay (Table 4). There was no difference in the median LOS between boys and girls, but significantly more girls had a LOS > 100 days.

3. Discussion

This is the first study to show at a national, population-based level the educational and socioeconomic status of patients born with CDH, as a proxy for neurocognitive development. Not surprisingly, more children born with CDH will not achieve any educational degree compared with controls. However, at a population level, for those children who make it throughout school, we found no difference in the highest educational level achieved, or in the qualifications points in elementary school or high school between cases and controls. Overall, school performance of patients born with CDH is similar to age and gender matched controls.

Previous reports have shown than CDH patients born before 38 weeks GA are at higher risk of neurodevelopmental delay [13]. This correlates very well with our finding that only 38% of cases born before 35 weeks of gestation achieved an educational degree. On the other hand, 88% of term babies with CDH reached a school or university degree, which is almost the same as in the control group (10%). Among children with CDH who reached a degree the highest level of education was the same as in the control group.

It is not surprising that longer hospital stay (>100 days) is a risk factor for poor school performance, since these patients will represent a more severely ill population. Despite representing the sickest cohort, almost half of them reached an educational degree.

From the socioeconomic perspective, being born with CDH did not lead to a lower economic status, since there were no differences in

Table 2
Educational level and annual income for cases and controls subdivided by gender.

	Cases Male	Controls Male	Cases Female	Controls Female
n	188	918	138	659
Age group				
15–20 years *n* (%)	72 (38)	348 (38)	47 (34)	221 (34)
21–25 years *n* (%)	67 (36)	328 (36)	56 (41)	271 (41)
26–30 years *n* (%)	47 (25)	231 (25)	29 (21)	137 (21)
31–40 years *n* (%)	2 (1.1)	11 (1.2)	6 (4.3)	30 (4.6)
No degree *n* (%)	26 (14)[a]	70 (7.6)	28 (20)	91 (14)
Highest level of education				
Elementary school *n* (%)	43 (27)	230 (27)	26 (24)	142 (25)
High school *n* (%)	82 (51)	435 (51)	53 (48)	247 (43)
University *n* (%)	37 (23)	183 (22)	31 (28)	179 (32)
Qualification points elementary school, mean (SD)	202 (61)	208 (68)	206 (67)	220 (71)
Qualification points high school, mean (SD)	12.2 (4.9)	11.8 (5.2)	11.6 (6.1)	13.6 (4.9)[b]
Individual disposable income SEK, median [IQR]	159,250 [123,325–220,375]	162900[c] [112,425–233,750]	137,100 [105,900–193,650]	143,800 [104,525–197,525]

No difference among cases between genders regarding educational level, school grades or annual income was seen.
[a] A significantly higher proportion of male patients did not achieve any degree compared to male controls. For females this difference did not reach statistical significance.
[b] Female controls achieved significantly higher grades in high school compared to both female cases and male controls.
[c] However, male controls had a significantly higher annual income than female controls.

Table 3
Influence of gestational age at birth in educational levels in cases with CDH.

	Gestational age at birth				p
	<35	35–37	38	+38	
n	29	63	43	167	
Female, *n* (%)	13 (44)	26 (41)	21 (49)	66 (40)	0.718
No Degree *n* (%)	11 (38)	14 (22)	5 (12)	20 (12)	0.0007
Highest level of education					0.224
Elementary school *n* (%)	7 (40)	10 (20)	7 (18)	40 (27)	
High school *n* (%)	8 (44)	31 (63)	18 (47)	69 (46)	
University *n* (%)	3 (17)	8 (16)	13 (34)	38 (25)	
Qualification points elementary school, mean (SD)	193 (64)	201 (66)	146 (60)	216 (60)	0.121
Qualification points high school, mean (SD)	10.2 (5.7)	11.5 (5.5)	12.4 (4.9)	12.0 (5.6)	0.659

No difference in the level of education or grading in elementary or high school in at any GA. Chi-square *p < 0.05.

Table 4
Influence of length of hospital stay (LOS) on level of education in CDH cases.

	Length of hospital stay			p
	Median LOS (IQR)	≤ 100 days	> 100 days	
n		297	13	
Female, *n* (%)	24 (12–66)	121 (41)	*9 (6.9)	0.049*
Male, *n* (%)	26 (11–54)	176 (59)	4 (2.2)	
No Degree *n* (%)		43 (14)	*7 (54)	0.0015*
Highest level of education				
Elementary school *n* (%)		61 (24)	[a]	
High school *n* (%)		128 (50)	[a]	
University *n* (%)		65 (26)	[a]	

LOS was available in 310 cases.
[a] Figures are too small to be disclosed.
* $p < 0.05$.

annual income between cases and controls. However, males, both cases and controls, had higher income than females. With the information available from the specific registers it was not possible to analyze the reasons for this. Firstly, the number of cases over 20 years of age is fairly small and secondly, the proportion of patients in different occupations and the level of occupation were not available.

Advances in neonatal intensive care have led to an increased survival for severe CDH, but with a cost of increasing morbidities [2]. Neurodevelopmental disorders have been described to be as high as 20% at discharge, according to the data published by the CDH Study Group, and are related to the severity of the condition [14]. These results are in line with the results of our study, with 17% of the children born with CDH not able to achieve any school degree. Previous studies have shown that neurodevelopmental outcome in preschool age in children born with CDH is normal [4, 15, 16], even though neurofunctional outcome may be delayed [9, 16]. We have previously shown that children born with congenital diaphragmatic hernia adjust well and show no behavioral or emotional problems compared to the standard population [17]. Neurological development has gained great focus during the past decades, and it has been implemented in all serious multidisciplinary follow up programs [16–18].

A strength of the present study is the robustness and completeness of the data, covering the entire population at a national level and high validity, with a negligible risk of missing a patient using a combination of the registers [11]. The number of patients included over a 33-year period corresponds with a yearly frequency of approximately 30 new patients, and is in accordance with the expected incidence of 3/10000 live born [12].

A big limitation of the study though is that the population presented corresponds to the cohort born between 1982 and 2000 including the earlier period, when gentle ventilation, preoperative stabilization and ECMO had not yet been introduced. From 1990 the results improved with a higher survival to hospital discharge [19–22] which has led to a new group of survivors with a more pronounced morbidity [7, 23, 24]. Thus, the survivors from the first part of the study period represent a, somehow, "healthier" cohort compared to the patients who are managed today and who survive with more frequent comorbidities. Another limitation of the present study is that it is unknown how much extra support at school was needed for the CDH children in order to perform as their peers. Also, information of known risk factors, such as defect size and liver position is not available in these nationwide registries, and it is not possible to correlate the results of this study with the severity of the condition other than to adjust for gestational age and LOS as proxy.

Summarizing, CDH is a severe condition in the neonatal period, and a significantly higher proportion of children born with CDH compared to controls will not achieve a school degree. However, among those who are able to achieve a school degree, the school achievements and educational level are similar to age and sex-matched healthy controls. Prematurity and a long hospital stay are risk factors for not achieving an educational degree. Gender seems to be a more significant risk factor for income inequities than being born with CDH.

This may be valuable information when counseling parents of CDH babies.

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