Journal of Dental Sciences 20 (2025) 118–125

Available online at www.sciencedirect.com

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journal homepage: www.e-jds.com

Original Article

The relationship between pneumonia and dental visits in patients with cerebral palsy: A nationwide registry-based cohort study in Taiwan

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Received 31 August 2024; Final revision received 22 September 2024
Available online 2 October 2024

KEYWORDS
Pneumonia;
Dental visits;
Cerebral palsy;
Cohort study;
Taiwan

Abstract *Background/purpose:* In general, improving oral health can reduce the risk of pneumonia. The purpose of this retrospective cohort study was to investigate the risk of pneumonia between cerebral palsy (CP) cohort and non-CP cohort as well as the association of pneumonia with the number of dental visits in CP patients in Taiwan.
Materials and methods: We identified 10,544 patients who were diagnosed with CP between 2010 and 2019 from the Taiwan National Health Insurance Research Database. 63,264 individuals who had never been diagnosed with CP were captured and matched in a 6:1 ratio. Cox proportional hazard regression analysis was adopted to assess the hazard ratio (HR) of pneumonia between CP cohort and non-CP cohort.
Results: Our findings demonstrated that CP cohort had 2.619-fold risk for pneumonia as compared with non-CP cohort after adjustment (95 % CI = 2.574–2.813, $P < 0.0001$). Cox regression analysis indicated that the CP group had significantly higher incidence risk of pneumonia (log rank $P < 0.0001$). Higher risks of pneumonia in CP patients were associated with younger age, and lower urbanization level. Some comorbidities as well as history of pneumonia had the higher aHR for pneumonia within 180 days prior to index date. In addition, there was a positive association with the more than two dental visits for the decrease 0.887-fold incidence of pneumonia in CP-cohort as compared with no dental visit (95 % CI: 0.799–0.984).
Conclusion: Taken together, CP patients had a higher risk of pneumonia. Dental visits are beneficial for preventing the risk of pneumonia in CP patients. The patients with CP should receive regular dental checkup.

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https://doi.org/10.1016/j.jds.2024.09.019

Introduction

Cerebral palsy (CP) is one of the most common motor and postural disorders in early childhood. The incidence of CP in high-income countries is currently about 1.6 per 1,000 individuals, while it is higher in low- and middle-income countries.[1] It arises from non-progressive lesion within immature brain and the effect is permanent.[2,3] CP often results in impaired muscle and motor function leading to physical disabilities. The clinical symptoms vary depending on the affected brain region and the extent of the injury.[4] Treatment options for CP include physical therapy and rehabilitation, wearing orthotic devices and assistive devices, medication and surgery, depending on the severity and needs of the patient.[2] Children with CP often have respiratory, musculoskeletal, nervous, and digestive system diseases that usually require hospitalization as compared to healthy individuals.[5] Pneumonia is the most prevalent respiratory complication among individuals with CP.[6] In addition, pneumonia is one of the most common hospitalization and death in CP patients.[7]

Oral cavity is a reservoir for bacteria that could lead to many systemic diseases including respiratory diseases.[8] A nationwide population survey has shown that the number of decayed and missing teeth is related to the incidence of pneumonia.[9] In addition, improving oral health was found to reduce the number of pathogenic bacteria in the mouth, decrease the severity of inflammation, and subsequently lower the risk of pneumonia in CP patients.[10] Our previous research has also indicated that patients with periodontal treatment exhibited a significantly lower risk of pneumonia than the general population.[11] Taken together, regular dental checkup is important for the prevention of pneumonia.

In Taiwan, according to the medical policy of the National Health Insurance, CP patients with catastrophic illness certificate can receive dental prophylaxis and oral hygiene instruction pre 90 days. It is very important for CP patients to improve their oral health through regular dental checkup. Previous studies have shown that the incidence of pneumonia in CP patients was significantly higher than those who in general population.[6,12] However, no research was found to explore the relationship between the risk of pneumonia and the frequency of dental visits in CP patients. The aim of this retrospective cohort study was to investigate the risk of pneumonia and the relationship regarding dental visits among CP individuals by using the National Health Insurance Research Database (NHIRD) in Taiwan.

Materials and methods

Data resources

The current study adhered to the Declaration of Helsinki and its subsequent amendments in 1964. Institutional Review Board was approved by Chung Shan Medical University Hospital (CS2-21198). Due to the use of de-identified observational data, the requirement for written informed consent was waived. This study was also complied with the guideline of Strengthening the Reporting of Observational Studies in Epidemiology for observational study.

NHIRD and National Death Index Database were applied for this retrospective cohort study from January 1, 2009 to December 31, 2020. NHIRD encompasses comprehensive records including patient demographic characteristic like age, sex, urbanization level, outpatient and emergency medical visits, as well as the information on prescribed medications and medical orders. This wealth of empirical information has served as an invaluable resource for academic and clinical research in disease evaluation and risk assessment.[13—15] Disease diagnoses within NHIRD were initially based on the International classification of diseases, ninth revision, clinical modification (ICD-9-CM) until 2016. Then, the diagnostic system was transitioned to the tenth revision as ICD-10-CM.

Definition of patients diagnosed with CP

The data were captured from January 1, 2009 to December 31, 2020. In order to identify the baseline characteristics (within 180 days prior to the index date), the diagnosis of CP in this study was identified from January 1, 2010 to December 31, 2019. CP diagnosis was base on ICD-9-CM code 343 as well as ICD-10-CM code G80. In addition, the inclusion criteria required more than three outpatient visits or any admission with a CP diagnosis in order to reduce the false positive cases.[16] Moreover, CP patients were further verified by examining catastrophic illness certificate. Finally, a total 10,544 CP patients were recruited at age 2 to 70 years between January 2010 and December 2019. The index date was defined as the date of the first CP diagnosis between January 2010 and December 2019.

Definition of age and sex-matched in non-CP cohort

Non-CP individuals were matched to CP patients with a 6:1 ratio by sex, age, and the index date. A total of 63,264 individuals who had never been diagnosed with CP were identified from January 2010 to December 2019. The index date was defined as the date of cohort entry, corresponding to the first CP diagnosis of the matched CP patient.[17] The matching algorithm also verified the enrollment status on the index date, ensuring that all matched non-CP individuals were actively enrolled in NHIRD.

Assessment of pneumonia incidence and follow-up

As illustrated in Fig. 1, 10,544 patients in CP-cohort and 63,264 matched non-CP individuals were analyzed in this study. Both CP patients and their matched non-CP

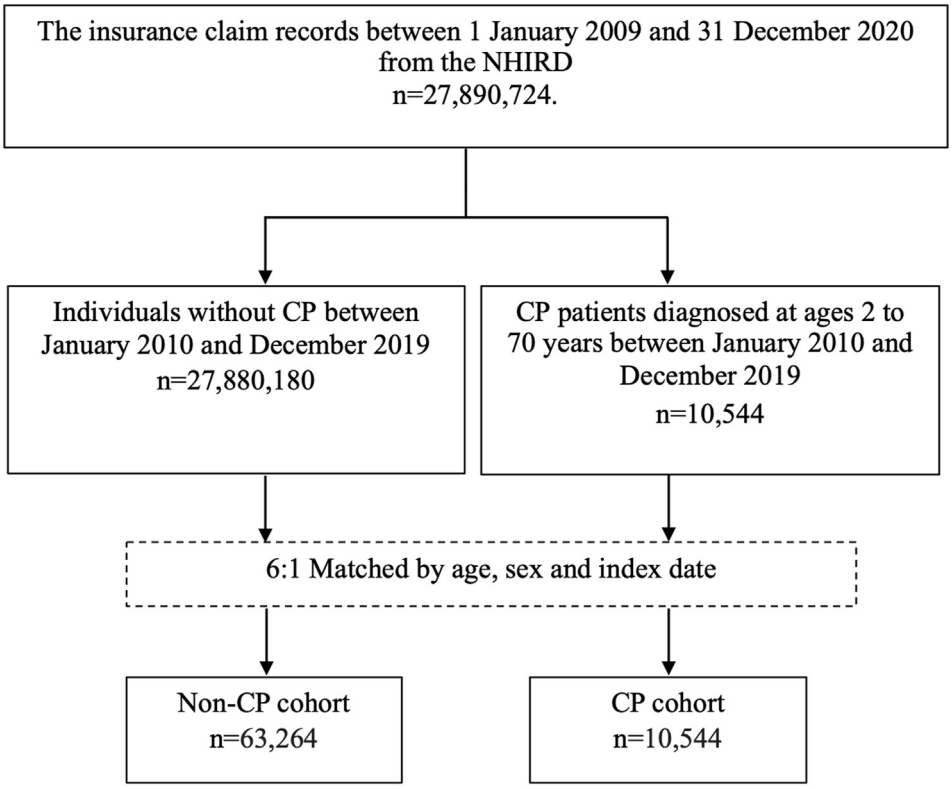

Figure 1 Flow chart of study selection procedure.

counterparts were followed from the index date until the first diagnosis of pneumonia, with censoring occurring at withdrawal from insurance, death, or the end of the study period on December 31, 2020. Pneumonia was identified by ICD-9 codes 480—486, 507—507.8, or ICD-10 codes J12-J18 in any outpatient visit, emergency department visit, or hospitalization after the index date. The validation of pneumonia diagnoses within NHIRD demonstrated a sensitivity of 92.3 % and good inter-observer agreement for hospitalized pneumonia cases.[18]

Study covariates and factors associated with pneumonia

For sociodemographic characteristics, index year, sex, age, the index date of pneumonia, and urbanization level were included in this study. Comorbidities were assessed within 180 days prior to the index date including diabetes mellitus, hypertension, ischemic stroke, hemorrhagic stroke, liver cirrhosis, osteoporosis, gastroesophageal reflux disease (GERD), asthma, chronic obstructive pulmonary disease (COPD), dysphagia, scoliosis, seizure disorder, chronic ulcer of the skin, intellectual disability, and attention deficit hyperactivity disorder (ADHD).

We also compared the history of pneumonia within 180 days prior to the index date between the study cohorts. The frequency of dental visit before index date was included in the analysis as the utilization of dental care also affected the probability of diagnosis with dental diseases. Dental visits, defined by ICD-9 codes ranged from 520.x to 529.x, were categorized by the frequency of three levels: no visit, 1—2 visits, and more than 2 visits.

Statistical analysis

SAS version 9.4 (SAS Institute Inc, Cary, NC, USA) was utilized for all statistical analyses in this study. Descriptive analyses were employed to outline the distributions of demographic data, history of pneumonia, frequency of dental visits, and comorbidities between CP cohort and non-CP cohort. In the large sample size study, even small differences between groups can yield statistically significant results. The absolute standardized difference (ASD) was calculated to estimate the differences at baseline characteristics between CP and non-CP cohorts. An ASD value of less than 0.1 was defined as indicating balanced characteristics among the study cohorts.[19]

Incidence density of pneumonia was defined as the number of new pneumonia cases during a given person-time in each cohort. 95 % confidence intervals (95 % CI) were calculated using a normal approximation to the Poisson distribution. Multivariable Cox regression models were used to estimate adjusted hazard ratios (aHRs) for pneumonia. The Kaplan—Meier method and the log-rank test were used to compare the cumulative probability of pneumonia between CP and non-CP cohorts.

Results

This study included 10,544 CP patients and 63,264 matched non-CP individuals. Table 1 outlines the distribution of baseline characteristics including demographics, history of pneumonia, dental visits, and comorbidities in both CP and non-CP cohorts. Among CP patients, about individuals

Table 1 Baseline characteristics among study groups.

	Non-CP cohort	CP cohort	*P* value	ASD
N	63264	10544		
Index year			1.0000	
2010	48130 (76.08 %)	8024 (76.10 %)		0.0005
2011	4603 (7.28 %)	767 (7.27 %)		0.0001
2012	2588 (4.09 %)	430 (4.08 %)		0.0006
2013	1785 (2.82 %)	298 (2.83 %)		0.0003
2015	1478 (2.34 %)	245 (2.32 %)		0.0008
2016	1149 (1.82 %)	192 (1.82 %)		0.0004
2017	1116 (1.76 %)	187 (1.77 %)		0.0007
2018	844 (1.33 %)	141 (1.34 %)		0.0003
2019	820 (1.30 %)	135 (1.28 %)		0.0014
Sex			1.0000	
Male	36438 (57.60 %)	6073 (57.60 %)		<0.0001
Female	26826 (42.40 %)	4471 (42.40 %)		<0.0001
Age at index date			0.6498	
2-9	15542 (24.57 %)	2587 (24.54 %)		0.0007
10-19	22703 (35.89 %)	3844 (36.46 %)		0.0119
20-39	20170 (31.88 %)	3305 (31.34 %)		0.0116
40-69	4849 (7.66 %)	808 (7.66 %)		0.0001
Urbanization level			<0.0001	
1 (high)	17626 (27.86 %)	2775 (26.32 %)		0.0347
2	20070 (31.72 %)	3369 (31.95 %)		0.0049
3	12054 (19.05 %)	1933 (18.33 %)		0.0185
4	8181 (12.93 %)	1514 (14.36 %)		0.0416
5	1206 (1.91 %)	199 (1.89 %)		0.0014
6	2222 (3.51 %)	424 (4.02 %)		0.0267
7 (low)	1905 (3.01 %)	330 (3.13 %)		0.0069
Co-morbidity (−180 days to +0 days)				
Diabetes mellitus	481 (0.76 %)	92 (0.87 %)	0.2241	0.0125
Hypertension	777 (1.23 %)	150 (1.42 %)	0.0970	0.0170
Ischemic stroke	49 (0.08 %)	90 (0.85 %)	<0.0001	0.1142
Hemorrhage stroke	18 (0.03 %)	102 (0.97 %)	<0.0001	0.1337
Liver cirrhosis	30 (0.05 %)	8 (0.08 %)	0.2331	0.0115
Osteoporosis	238 (0.38 %)	180 (1.71 %)	<0.0001	0.1314
GERD	362 (0.57 %)	242 (2.30 %)	<0.0001	0.1453
Asthma	2125 (3.36 %)	553 (5.24 %)	<0.0001	0.0930
COPD	2622 (4.14 %)	970 (9.20 %)	<0.0001	0.2036
Dysphagia	15 (0.02 %)	129 (1.22 %)	<0.0001	0.1528
Scoliosis	175 (0.28 %)	385 (3.65 %)	<0.0001	0.2450
Seizure disorder	192 (0.30 %)	3816 (36.19 %)	<0.0001	1.0493
Chronic ulcer of skin	23 (0.04 %)	86 (0.82 %)	<0.0001	0.1199
Intellectual disability	123 (0.19 %)	1366 (12.96 %)	<0.0001	0.5328
ADHD	439 (0.69 %)	167 (1.58 %)	<0.0001	0.0839
Pneumonia (−180 days to +0 days)	755 (1.19 %)	1033 (9.80 %)	<0.0001	0.3845
Dental visit (−180 days to +0 days)			<0.0001	
No visit	42833 (67.71 %)	6611 (62.70 %)		0.1052
1−2 visits	15311 (24.20 %)	3043 (28.86 %)		0.1057
>2 visits	5120 (8.09 %)	890 (8.44 %)		0.0126

ASD: absolute standardized difference.
GERD: gastroesophageal reflux disease.
COPD: chronic obstructive pulmonary disease.
ADHD: attention deficit hyperactivity disorder.
−180 days to +0 days: 180 days prior to the index date.

Table 2 The risk of pneumonia after index date.

	Non-CP cohort	CP cohort	*P* value
N	63264	10544	
Person-months	6630349	757993	
Pneumonia case	11144	5069	
Rate[a] (95 % CI)	1.68 (1.65—1.71)	6.68 (6.51—6.87)	<0.0001
Crude HR (95 % CI)	Reference	3.610 (3.492—3.732)	<0.0001
Adjusted HR[b] (95 % CI)	Reference	2.691 (2.574—2.813)	<0.0001

HR: hazard ratio.
[a] The incidence rate of pneumonia, per 10000 person-months.
[b] Adjusted by demographic characteristics, comorbidities, history of pneumonia, and dental visits.

57.60 % were male. The age distribution within CP cohort was as follows: 24.54 % in aged 2—9 years, 36.46 % in aged 10—19 years, 31.34 % in aged 20—39 years, and 7.66 % in aged 40—69 years, respectively. The higher comorbidities were found in CP cohort expect for diabetes mellitus, hypertension, and liver cirrhosis as non-CP cohort. The prevalence of previous pneumonia was higher in CP cohort (9.80 %) as compared to 1.19 % in non-CP cohort ($P < 0.0001$). The CP cohort also exhibited a higher frequency of for dental visits more than two times ($P < 0.0001$).

As shown in Table 2, there were 5,069 pneumonia cases after CP diagnosis with an incidence rate of 6.68 per 10,000 person-months in CP cohort (95 % CI: 6.51—6.87, $P < 0.0001$). In non-CP cohort, they were 11,144 pneumonia cases with an incidence rate of 1.68 per 10,000 person-months (95 % CI: 1.65—1.71, $P < 0.0001$). In addition, the aHR for pneumonia in CP cohort was 2.691-fold than non-CP cohort after adjusting for demographics, history of pneumonia, dental visits, and comorbidities within 6 months prior to the index date (95 % CI = 2.574—2.813, $P < 0.0001$).

The cumulative incidence curve of pneumonia is shown in Fig. 2. The average follow-up time was 71.9 months for CP cohort and 104.8 months for non-CP cohort, respectively. The cumulative incidence rate of pneumonia after 12 months was 5.1 % in non-CP cohort and 22.2 % in CP cohort, respectively. In 60 months, the cumulative incidence rate of pneumonia increased to 12.4 % for the non-CP and 39.8 % for the CP cohort. After 132-month follow-up, the cumulative incidence of pneumonia in CP patients with CP was higher than that in the control subjects (log rank test, $p < 0.0001$).

Table 3 presents the aHRs for different factors associated with the risk of pneumonia in non-CP cohort and CP cohort. Female was found to have statistical significant risk for pneumonia in non-CP cohort (aHR: 1.094, 95 % CI: 1.053—1.135). However, it was not significantly related sex difference in CP cohort. In addition, age distribution, and

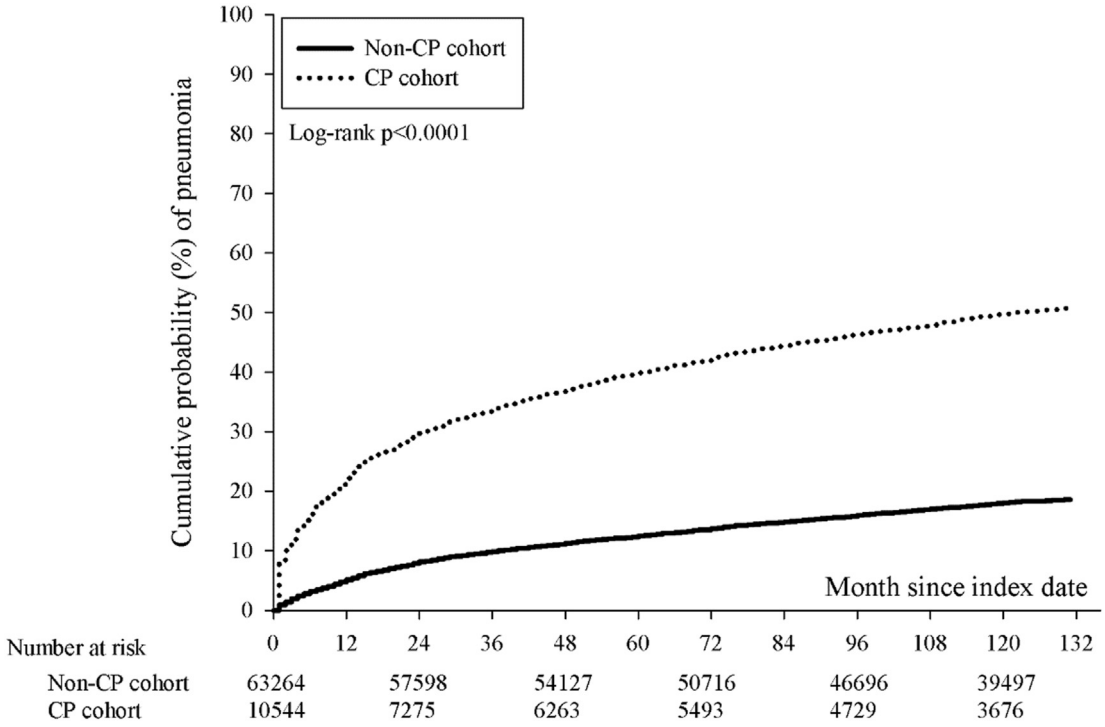

Figure 2 Cumulative incidence of pneumonia in CP and control groups.

Table 3 The hazard ratio for the occurrence of pneumonia.

	Non-CP cohort aHR (95 % CI)	CP cohort aHR (95 % CI)
Sex		
Male	Reference	Reference
Female	1.094 (1.053–1.135)*	0.950 (0.898–1.005)
Age at index date		
2-9	Reference	Reference
10-19	0.314 (0.299–0.329)*	0.613 (0.571–0.658)*
20-39	0.298 (0.283–0.313)*	0.541 (0.501–0.584)*
40-69	0.340 (0.312–0.372)*	0.536 (0.472–0.608)*
Urbanization level		
1 (high)	Reference	Reference
2	1.014 (0.965–1.065)	1.097 (1.019–1.182)*
3	1.079 (1.021–1.140)*	1.126 (1.034–1.226)*
4	1.120 (1.052–1.192)*	1.256 (1.149–1.373)*
5	1.160 (1.017–1.323)*	1.285 (1.049–1.573)*
6	1.141 (1.030–1.264)*	1.327 (1.152–1.528)*
7 (low)	1.299 (1.171–1.442)*	1.341 (1.144–1.572)*
Co-morbidity (−180 days to +0 days)		
Diabetes mellitus	1.238 (0.983–1.558)	1.229 (0.919–1.644)
Hypertension	1.392 (1.152–1.682)*	1.319 (1.039–1.673)*
Ischemic stroke	1.060 (0.546–2.060)	1.099 (0.847–1.426)
Hemorrhage stroke	1.136 (0.421–3.065)	1.044 (0.817–1.333)
Liver cirrhosis	2.224 (1.188–4.163)*	1.274 (0.524–3.094)
Osteoporosis	1.354 (1.038–1.765)*	1.193 (0.976–1.459)
GERD	1.527 (1.212–1.923)*	1.442 (1.239–1.678)*
Asthma	1.221 (1.047–1.425)*	0.953 (0.823–1.104)
COPD	1.527 (1.322–1.763)*	1.693 (1.508–1.899)*
Dysphagia	4.510 (2.142–9.496)*	1.292 (1.057–1.579)*
Scoliosis	1.510 (1.093–2.087)*	1.205 (1.046–1.389)*
Seizure disorder	1.824 (1.395–2.384)*	1.467 (1.385–1.555)*
Chronic ulcer of skin	3.214 (1.728–5.979)*	1.988 (1.537–2.570)*
Intellectual disability	1.051 (0.704–1.570)	1.004 (0.925–1.089)
ADHD	1.041 (0.855–1.268)	0.801 (0.632–1.014)
Pneumonia (−180 days to +0 days)	3.671 (3.343–4.032)*	5.066 (4.675–5.490)*
Dental visit (−180 days to +0 days)		
No visit	Reference	Reference
1–2 visits	0.984 (0.942–1.027)	0.995 (0.936–1.059)
>2 visits	0.964 (0.903–1.030)	0.887 (0.799–0.984)*

*$P < 0.0001$.
HR: hazard ratio.
GERD: gastroesophageal reflux disease.
COPD: chronic obstructive pulmonary disease.
ADHD: attention deficit hyperactivity disorder.
−180 days to +0 days: 180 days prior to the index date.

urbanization level demonstrated a higher risk for the occurrence of pneumonia in both groups.

The results further stratified by comorbidities, pneumonia, and frequency of dental visit within 180 days prior to index date were represented as following. In terms of comorbidities, hypertension, GERD, COPD, dysphagia, scoliosis, seizure disorder, chronic skin ulcers and the history of pneumonia were highly associated with pneumonia in both CP and non-CP cohorts.

The correlation between the development of pneumonia and the frequency of dental visits is concerned, the aHR values in CP-cohort were 0.995-fold (95 % CI: 0.936–1.059) and 0.887-fold (95 % CI: 0.799–0.984) for the subjects with 1–2 visits and >2 visits as compared with no visit, respectively. Taken together, there was a positive association with the more than two dental visits for the decrease the incidence of pneumonia in CP-cohort. The aHRs in non-CP cohort were 0.984-fold (95 % CI: 0.942–1.027) and 0.964-fold (95 % CI: 0.903–1.030) for the subjects with 1–2 visits and >2 visits as compared with no visit, respectively. The frequency of dental visits was borderline significantly to reduce the incidence of pneumonia in non-CP cohort.

Discussion

To the best of our knowledge, this is the first nationwide population-based cohort study to report the relationship

between pneumonia and dental visits in CP patients. Similar to previous findings,[20] our results showed a higher prevalence of male patients with CP compared to female. In terms of age, CP is usually diagnosed at a very young age,[21] but with advances in medical care, most children with CP now could survive into adulthood.[22] This may partly explain why the majority of CP patients in this study were in the adolescence and young adulthood age. Our findings are in agreement with earlier studies that the higher incidence of pneumonia was found among patients with CP.[6,12,23] Recently, Hollung et al. have reported about 52 % CP patients with one or more comorbidities.[24] In this study, respiratory diseases, digestive diseases, and neurological disorders are the common comorbidities which are consistent with our findings.

In this study, both the youngest age groups and the lowest urbanization level have the highest risk of pneumonia. Our results were in agreement of previous study, pneumonia is one of the leading causes of morbidity and mortality in children.[25] There are still over 100 million cases of pneumonia occurring annually in children under 5 years.[26] Possible reasons include poor living conditions, malnutrition, and higher risk of exposure to infectious diseases, leading to higher risk in groups with low urbanization levels. Therefore, the prevention and treatment of pneumonia in children and low urbanization level areas are crucial.

Due to CP can directly affect breathing by muscle issues, respiratory diseases are one of the most common frequent reported cause of morbidity and mortality in CP.[27] In Taiwan, pneumonia (35 %) is the most common cause of acute hospitalization among young patients with CP.[28] In this study, comorbidities GERD, COPD, scoliosis, seizure disorder, and chronic skin ulcers are associated with higher risks of pneumonia in both two group. These findings are consistent with previous researches that GERD,[29] COPD,[30] and scoliosis,[31] were found to be significantly associated with a high risk of pneumonia. Chronic skin ulcers, also known as pressure ulcers, are localized skin injury caused by pressure.[32] Patients with chronic skin ulcers often have a lower functional level, leading to a relatively higher incidence of pneumonia. Moreover, dysphagia was found to be the unique comorbidity in the CP cohort that contributes to the significantly increased risk of pneumonia. Dysphagia is a very common symptom among patients with CP that leads to food aspiration and respiratory infections.[33] Therefore, early identification and treatment of dysphagia are important to prevent or delay severe respiratory diseases in CP patients.

Regular dental visit is important to maintain oral health. Compared to individuals with better oral health conditions, the risk of pneumonia is higher in individuals with poor oral health. Our results revealed that CP patients with 1—2 dental visits 180 days prior to the index date had borderline significantly decreased risk of pneumonia. Individuals with more than two dental visits 180 days prior to the index date had significantly reduced risk of pneumonia in CP cohort. Taken together, dental visits may provide protection for pneumonia in patients with CP. In Taiwan, CP patients with catastrophic illness certificate can receive dental prophylaxis and oral hygiene instruction every three months. Our findings support this policy and provide the scientific evidences. Similarly, previous studies from Spain,[34] Brazil,[35] and Saudi Arabia[36] have also recommended that regular dental care is essential to maintain oral health for CP patients. Therefore, CP patients with regular dental visits very three months, this not only helps maintain oral health but can also reduce the risk of pneumonia.

Some potential limitations should be noted regarding the use of registry databases. First, several crucial factors cannot be obtained from NHIRD. For instance, the severity of cerebral palsy is difficult to distinguish. It was unable to obtain classification systems for CP patients from the NHIRD. However, these classification systems are important factors that significantly affect prognosis. Second, we could not determine the specific type of pneumonia. Although both ICD-9 and ICD-10 codes classify pneumonia into specific types, they are often recorded simply as "pneumonia, unspecified organism." If we could obtain more precise information regarding the types of pneumonia, the results would be more beneficial. Last, since this study relied on existing database, it was difficult to prevent bias. Moreover, individuals who did not utilize NHI service were also not included in the study sample, potentially leading to an underestimation of the sample size.

In conclusion, CP patients have higher risk of pneumonia than general population. More than two dental visits within six months may lower the risk of pneumonia among CP patients. Comorbidities such as hypertension, GERD, COPD, dysphagia, scoliosis, epilepsy, and chronic skin ulcers may increase the risk of pneumonia in patients with CP. Pneumonia has a significant impact on individuals with CP. For patients with CP, regular dental checkup every 3 months are important for the oral health and may help to prevent the occurrence of pneumonia. In addition, it is important to understand patients' history of comorbidities through medical records before any medical interventions. CP is a group of undesirable neurological disorders that appear in infancy or early childhood, resulting in body movement and muscle coordination. In addition, reforming oral health care through inter-professional collaboration such as medical doctor, speech and language therapists will enable dentist to take necessary precautions to prevent aspiration during dental treatment resulted in pneumonia. Further researches on the types of dental treatment are required to reduce the incidence and mortality risk of pneumonia among individuals with CP.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

This study is supported by a grant from Chung Shan Medical University Hospital (Grant No: CSH-2022-C-047).

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