Original Article

Does Socioeconomic Status Have an Association with Cranio-vertebral Anomalies: A Step Toward Healing the Curse!

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Background: The etiological or causal factors of pediatric craniovertebral junction anomalies (CVJA) are still unknown. The disease bears a major proportion of economic and social burdens over a developing country like ours. This article aims to highlight an important modifiable factor that may prove to have a critical causal relationship with disease incidence. Materials and Methods: This is a cross-sectional, single-institutional study, wherein the socioeconomic status (SES) of all the operated pediatric patients of CVJA, between 2014 and 2019, was studied. Variables including the patient’s age, sex, residence status (rural or urban), perioperative data, length of stay, follow-up, and the time between revision surgery (if required) and clinical presentation were noted. Data regarding average household and type of family (nuclear or joint) were also enquired.

Results: Sixty-six patients (M:F 56:10) with a mean age of 13.14 ± 3.44 years were included. The mean annual family income was 11.1 ± 12.1 thousands. 43.9% belonged to joint family; according to Kuppuswami and Prasad scale, 42.4% of patients belong to lower class, while 20 patients belong to lower middle class, and 14 patients belong to the below poverty line category. Neither the SES of patient nor rural–urban background affected the surgical outcome. The mean follow-up of patients in our study was 42.3 ± 23.0 months and 83.3% had a good outcome.

Discussion: Patients operated for CVJ anomaly in the authors’ institution mainly come from the lower socioeconomic groups. The present study raises several important questions like nutritional deficiencies in reproductive age group females leading to a cascade of events as a causal factor.

Keywords: Atlantoaxial dislocation, cervico-medullary junction, Kuppuswami scale, Prasad scale, socioeconomic status, syndromic

Introduction

The craniovertebral junction anomalies (CVJA) comprise a complex clinical enigma, affecting, perhaps, the most crucial part of the body. The disease is classified according to the ICD-10 coding as ICD-10-CM M43.3.[1] The clinical presentation is variable, ranging from an incidentally detected asymptomatic patient to the crippling bed-ridden patient, in severe stages of myelopathy with respiratory compromise. Unfortunately, the pediatric age group is vulnerable and intractable, and possess a unique challenge of infixing developing cervical spine. The quoted incidence in the literature varies in geographical and genetic backgrounds, and ranges from 4% to 5% in the pediatric population.[2-5] Surgical fixation and fusion are the preferred, and sometimes the only treatment option, for symptomatic patients. Nearly a dozen

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surgical approaches have been described and validated in the literature, but still the topic remains a conundrum or most controversial and debatable.

The high morbidity and disabling problem possess a financial burden to the family, society, and country. For decades, the researchers are struggling to find a causal relationship or etio-pathological factors for pediatric CVJA. The genetic studies, nutritional supplementation, peripartum trauma, etc. have been studies for the causal relationship, but nothing substantial could be concluded to date. Our center is a tertiary care government organization, and approximately 2500 cases are operated annually, in the Department of Neurosurgery. Nearly 600 cases of CVJA have been operated in the last decade, and over the years gained, we have observed a unique fact, that majority of these children come from poor family (indirectly poor nutritional status and comparatively meager hygiene). Therefore, for this article, we proposed the null hypothesis that the CVJA (nonsyndromic) are not a disease of the poor socioeconomic status (SES) group.

MATERIALS AND METHODS

Study design
This is a cross-sectional, single-institutional study, wherein the SES of all the operated pediatric patients of CVJA was analyzed. To standardize the patients, the CVJ anomaly in our study is defined as atlantoaxial dislocation (AAD) with or without basilar impression (BI) (major criteria) and one of the three minor criteria: (a) complete or partial occipitalized C1; (b) articular mass asymmetry, and/or hypoplasia; (c) vertebral artery anomalies. The institutional ethical permission and individual consent were obtained to use personal and clinical data as per our departmental protocol.

Study population
All pediatric patients (less than 18 years age) of CVJA who underwent posterior fixation with or without trans-oral decompression (TOD) from January 2014 to July 2019 at our institution were studied. Out of 210 operated patients during the above period, 66 patients of pediatric CVJ anomaly (by our definition) were included. Of note, there was a very small set of patients, where all perioperative data were not available in the paper records. These patients \( n = 19 \) were left out of analysis for that specific variable.

Study parameters
Variables including the patient’s age, sex, residence status (rural or urban), and clinical presentation were noted. Other parameters studied included surgery (initial and revisions), perioperative data, length of stay, follow-up, and the time between revision surgery (if required). Data regarding average household and type of family (nuclear or joint) were enquired. The local demographics was obtained from the Ministry of Home Affairs, Office of the Registrar General and Census Commissioner data reports. Mean annual household incomes were adjusted to the value of the Indian National Rupee (INR), for the year 2018. SES was inferred from dissemination area income levels by linking the patients’ postal codes with Statistics Indian Census 2011 data. Kuppuswami and Prasad scale was used for stratification of the patients on the grounds of SES. For the sake of comparison, we grouped lower middle class and upper middle class together (Group A) and compared with the second group of below poverty line (BPL) and lower class (Group B).

Exclusion criteria
Patients with any syndromic association or underlying metabolic pathology were excluded. We also excluded the patients with a history of trauma or infective etiopathogenesis for CVJ anomaly.

Statistical analysis
Univariate analysis was performed using \( \chi^2 \) and Student’s \( t \)-tests with SPSS 22.0 (IBM, New York). Pearson’s \( \chi^2 \) test or Fisher’s exact test were used where appropriate to evaluate associations between bi-variant variables. A significant \( P \)-value of \(<0.05\) was considered statistically significant. Multivariate logistic regression models were used to estimate odds ratios of CVJ anomaly while adjusting for baseline variables. We have not adjusted for race because this variable was not available in the patients’ charts. Logistic regression was done to evaluate the relationship between SES and surgical outcome, first using univariate regression, followed by multivariate regression, adjusting for age and type of surgery as these factors have been shown to affect the surgical outcome.

RESULTS

Study population
In our study, 66 patients (M:F = 56:10) with a mean age of 13.14 \( \pm \) 3.44 years (range 4 to 18) were included. The mean duration of symptoms before surgery was 21.97 \( \pm \) 19.15 days. The median Nurick grade did not change from preoperative (3 \( \pm \) 1.7) to the last follow-up (3 \( \pm \) 1.3), but the requirement of anti-spasticity drugs, neck pain, and self-care improved. Majority of our patients \( n = 62, 93.9\% \) had irreducible type of AAD. Twenty-nine (43.9\%) patients had partial occipitalized atlas while 25 patients (37.8\%) had complete occipitalization of the atlas. Radiologically, 35 patients (53.0\%) had
asymmetrical atlantoaxial joints, so the included patients belong to a surgically difficult subset of patients. Moreover, 30 patients (45.5%) had torticollis and 14 patients (21.2%) had vertebral artery anomaly. Additionally, Chiari malformation was present in seven patients (10.6%) and basilar invagination was present in 38 patients (57.6%). [Table 1] summarizes the clinical features and profile of all the included patients in our series.

Study parameters

The mean average-family income of all the included patients was 11.1 ± 12.1 thousands (range 2 to 70) [median 8 ± 7.2 IQR]. Twenty-nine patients (43.9%) in our study belonged to joint family and 48 patients (72.7%) belonged to a rural region. According to Kuppuswami and Prasad scale, majority of our patients (n = 28, 42.4%) belonged to lower class, while 20 patients belong to lower middle class, four patients belong to upper middle class, and 14 patients belong to “BPL category” [Table 2]. For the sake of further comparison, we grouped lower middle class and upper middle class together (Group A, n = 24 patients) and compared with the second group of BPL and lower class (Group B, n = 42 patients). Nineteen patients in Group A showed improvement compared to 36 patients in Group B (P = 0.78). Similarly, 41 patients of rural background compared to 14 patients in urban background had postoperative improvement (P = 0.71). Neither SES of the patient nor rural–urban background affected the surgical outcome.

Surgical procedure

Majority of patients (n = 26, 39.4%) underwent TOD and posterior fixation (C1-lateral mass with C2-pars), while 16 (24.2%) patients underwent occipital plate with C2-pars and C3 lateral mass fixation. Fourteen patients (21.2%) underwent C1-lateral mass with C2-pars with spacer placement (Goel and Harm’s technique). Other procedures included TOD only (n = 1), long segment (C1-C6) fixation (n = 2), C1 arch wiring (Jain’s technique) in two patients, occipital plate with C1-lateral mass and C2-pars in four patients, whereas, in one patient, posterior C1–C2 fixation was done initially, but needed TOD after 2 months for persistent myelopathy. (This patient had type I BI.)

Surgical outcome and follow-up

The mean follow-up of patients in our study was 42.3 ± 23.0 months (range 6 to 83). Fifty-five patients (83.3%) had a good outcome with either improvement in Nurick grade, improvement in cervical pain, or decrease in the requirement of anti-spasticity drugs. Nine patients (13.6%) had no change in the postoperative course. At the last follow-up, 46 patients (69.7%) had a good outcome and 12 patients remained unchanged as compared to the preoperative clinical situation. Therefore, four patients who deteriorated in the postoperative period also improved in long-term follow-up. Six patients (9.1%) had prolonged postoperative ICU stay, with tracheostomy required in five patients (7.6%). There was one death in our study; the patient had severe basilar invagination, underwent TOD and posterior fixation, had prolonged ICU stay, and subsequently developed pneumonia, and died of septicemia. The patient belonged to the BPL category and rural background.

Discussion

A curse for the undeveloped or developing countries

We performed a PubMed search of all the major studies related to CVJA in the last 5 years and found that most of the studies are reported from the developing or poor countries. The reported cases of CVJA from western literature are scattered and mostly of syndromic association. Hence, we observed that this spectrum

| Parameters                  | Number of patients |
|-----------------------------|--------------------|
| Mean age (in years)         | 13.14 ± 3.44 (4 to 18) |
| Gender (Male:female)        | 56:10              |
| Family type                 |                    |
| Nuclear                     | 37                 |
| Joint                       | 29 (43.9%)         |
| Socioeconomic group         |                    |
| Group A                     | 24                 |
| Group B                     | 42                 |
| Other anomalies             |                    |
| Occipitalized atlas         |                    |
| Partial                     | 29                 |
| Complete                    | 25                 |
| Absent atlas                | 7                  |
| Joints anomaly              |                    |
| Symmetrical                 | 31                 |
| Asymmetrical                | 35                 |
| Torticollis                 | 30                 |
| Vertebral artery anomaly    | 14                 |
| Chiari malformation         | 7                  |
| Platybasia                  | 4                  |
| Postoperative status        |                    |
| Improve                     | 55 (83.3%)         |
| Deteriorate                 | 2                  |
| Same                        | 9                  |
| Tracheostomy                | 5                  |
| ICU stay of more than 7 days| 6                  |
| Follow-up status            |                    |
| Improve                     | 46                 |
| Deteriorate                 | 8                  |
| Same                        | 12                 |
Effect of SES of the family on pediatric CVJ anomaly

The average annual family income of the included patients was 11.1 ± 12.1 thousands (range 2 to 70). These values itself validate our contention. The current average family income is significantly less than the family income of a middle class family which we are supposing to have a better nutritional and hygienic life as compared to families with poor family income. None of our patients belong to the upper class! and 42 patients (63.6%) belonged to the BPL and lower class. Out of the remaining 30% of patients, the majority belonged to the lower middle class. Thus, the operated patients in our center are mainly from poor SES. Henceforth, this poor SES has the following roles in euthenics of these anomalies: (a) Lack of some essential food element in the females of reproductive age group (antepartum malnutrition), (b) lack of proper ante-natal care, (c) peripartum taboos, (d) traumatic home deliveries by quacks, and (e) immediate postpartum care-related issues.[8] The difference between rural vs urban family was not significant; however, the total number of patients was less for a conclusive statistical analysis. Interestingly, on retrospective analyses of residence, we identified some places near the river Ganges with more prevalence and further conducting a soil and water analysis.

Triggering effect

We believe that an unknown factor, arising because of the poor SES, is probably triggering the somite formation and assimilation around the 7th week of intrauterine or peripartum life.[9] It seems that the steps of embryogenesis of CVJ are closely inter-related and affected by the one another, and that is why most of our patients exhibit a combination of the anomalies like AAD with occipitalized C1 in 89%, 53% has asymmetrical atlantoaxial joints, and 21.2% had vertebral artery anomaly.

Realizing a major issue: its time to re-think the cost issue

The average cost of treatment including preoperative work up and hospital expenses with instrumentation charges is around 80,000 INR, excluding the postoperative stay. The postoperative stay was variable as some patients are discharged in the stipulated duration of 5–7 days while the remaining remain admitted for a prolonged period of time owing to the need for ventilator support and critical care. 94% of the time, we used one or more of the Indian made instrumentation systems ranging in cost from 25,000 to 40,000 INR. This assumes importance as the international implants come with a significantly higher cost and there is a need to further refine our indigenous implants to best suit our patients.

Is it worth treating them surgically?

After a follow-up of 42.3 ± 23.0 months (range 6 to 83), in our study, we have found that 55 patients (83.3%) had a good outcome with either improvement in motor power, improvement in cervical pain, or decrease in requirement of anti-spasticity drugs. In the remaining patients, the majority of the patient had either no change in their status (13.6%) or showed a late improvement (3%). We had only one mortality in this group. Therefore, these patients require surgical intervention and show improvement that can further meaningfully contribute to the society.

Do the included patients represent a population-based study?

Being an apex tertiary center in the northern part of India and providing subsidized treatment and some times providing existing government aid, one may have doubt on the spectrum of patients treated at our center and the overall SES of all the patients operated

| Parameter                          | Lower class (n = 28) | Lower middle class (n = 20) | Upper middle class (n = 4) | Below poverty line (n = 14) | P value |
|------------------------------------|---------------------|-----------------------------|---------------------------|----------------------------|---------|
| Sex (male)                         | 25                  | 16                          | 3                         | 12                         | 0.643   |
| Residence (rural)                  | 19                  | 14                          | 3                         | 11                         | 0.970   |
| Family (nuclear)                   | 16                  | 12                          | 1                         | 8                          | 0.704   |
| AAD type (irreducible)             | 23                  | 20                          | 4                         | 12                         | 0.479   |
| Occipitalised atlas (partial)      | 10                  | 8                           | 2                         | 8                          | 0.648   |
| Occipitalised atlas (complete)     | 10                  | 10                          | 1                         | 4                          | 0.598   |
| Joints (symmetrical)               | 7                   | 5                           | 1                         | 3                          | 0.846   |
| Torticollis (yes)                  | 11                  | 10                          | 2                         | 7                          | 0.842   |
| Vertebral artery anomaly (yes)     | 6                   | 5                           | 0                         | 3                          | 0.999   |
| Other anomaly (ACM)                | 4                   | 2                           | 0                         | 1                          | 0.727   |
| BI (Type 1)                        | 16                  | 14                          | 0                         | 8                          | 0.068   |
upon. The CVJA registry system does not exist in our country and this present study highlights the need for the same. However, most of our patients are a complex subset of CVJA and considering the morbidity and mortalities related to this subset, most of the patients are not operated in private and/or corporate hospitals and referred to us. Therefore, we believe that our data represent the population in general. Definitely, a uniform registry system will address this very problem.

Our included patients represent a regional population of a developing country. One must understand that the correlation of poor SES and prevalence of complex CVJ anomalies may not stand true for a western or developed country. Some studies from developed countries show that the incidence of CVJ anomaly is either sporadic or syndromic.\textsuperscript{[10,11]} The cost of hospital stay and treatment is mostly beared by the government; so, the socioeconomical factors were not taken into account. To the best of our knowledge, ours is the first study highlighting these small issues. The government policies and healthcare system differ from country to country; in our case, it differs from state to state also. The percentage of national income spent on healthcare system also differs. In a western population, rich and poor may avail the same level of medical expertise, but in our country, poor people are referred to government hospitals only. This segregation may transform into a “bias” in our study. In our center, patients are referred to irrespective of their economic background but a multi-centric larger population-based study may substantiate our result in a better way.

**Limitation of the study**
The retrospective design of the study and less number of included patients limit the statistical significance. A prospective, comparative analysis may substantiate our findings in a better way; however, the rarity of the disease and stringent inclusion criteria makes it onerous. Also, as no national-level registry exists at the moment, there was also a lack of any historical control to compare our data with. The 2020 edition of ICD-10-CM M43.3 became effective on October 1, 2019.

**Conclusion**
Patients operated for CVJ anomaly in our institution mainly come from the lower socioeconomic groups. The poor SES is associated with CVJA and the present study raises several important questions like nutritional deficiencies in reproductive age group females leading to a cascade of events as a causal factor and/or compromised peripartum practices as a probable cause of this curse like pediatric anomalies. Although the statistical data did not substantiate our hypothesis, the study paved a road ahead for a standardized, prospective, larger population study.

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**Conflicts of interest**
There are no conflicts of interest.

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