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The association of Trisomy 13 and 18 and hospital discharge outcomes among neonates in California: A retrospective cohort study

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Abstract

Background: Despite Trisomy 13 and 18 being among the most fatal congenital anomalies, limited information exists about resource utilization and factors associated with length of stay (LOS) and total hospital charges (THC) for these anomalies.

Methods: We studied data sets of the patient discharge data set from the California Office of Statewide Health Planning and Development from 2006 to 2010, to determine differences in resource utilization for survivors and non-survivors and identify the predictors of LOS and total hospital charges. Descriptive statistics were assessed for demographic and clinical characteristics. General linear regression models were used to identify predictors of LOS and THC.

Results: Seventy-six Trisomy 13 and 115 Trisomy 18 patients were identified, for whom inpatient mortality was 27.6% and 20.9%, respectively. In patients with Trisomy 13, after adjusting for gender, ethnicity, advanced directive (DNR), insurance and co-morbidities on multivariate analysis, the provision of more than 96 h of mechanical ventilation was associated with significantly increased LOS (standard error, SE) by 18.0 ± 5.3 days and THC (SE) by $399,000 ± $85,000. In terms of insurance type, patients with private coverage had 10.8 ± 4.9 days more than patients with Medicaid. In patients with Trisomy 18, on multivariate analysis, after adjusting for gender, ethnicity, DNR, insurance and co-morbidities, more than 96 h of mechanical

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Conflict of interest

The authors have no conflict of interest to disclose.

ventilation was associated with increased LOS (SE) by 36.8 ± 6.8 days and THC (SE) by $365,000 ± $59,000.

Conclusion: Understanding predictors that are associated with longer LOS and higher THC may be associated in hospital resource allocation for this vulnerable population of infants.

Keywords

neonate; resource utilization; Trisomy 13; Trisomy 18

1. Introduction

After Trisomy 21, Trisomy 13 and 18 are the most common chromosomal abnormalities.[1] Both Trisomy 13 and 18 are associated with a range of serious and often fatal congenital defects across several systems including heart defects, trachea-esophageal fistulas as well as orofacial and central nervous system abnormalities.[2] Population-based studies in the literature have demonstrated an increasing prevalence in the diagnosis of both Trisomy 13 and 18, attributable to the increase in the number of neonates born to mothers of advanced age, increased maternal aneuploidy screening and improvements in prenatal ultrasound.[3] At the same time, a decrease in the prevalence of live birth has been reported, with estimated prevalence of 0.03 per 1000 live births for Trisomy 13 and 0.10 per 1000 live births for Trisomy 18.[4]

Although trends have moved away from a description of a universally lethal condition,[5] the vast majority of pregnancies with Trisomy 13 or 18 result in stillbirth[6] and those that do survive to birth have a median survival time of 7–10 days for Trisomy 13 and 10–15 days for Trisomy 18. Despite these poor median survival rates, some studies have found one-year survival percentages as high as 6–8% for Trisomy 18[7] and 5-year survival percentages of 9.7% and 12.3% for Trisomy 13 and 18, respectively.[5] With a shift in description of Trisomy 13 and 18 from a universally lethal condition to a more nuanced condition with variances in outcomes, the attitudes of caregivers are also undergoing a shift. There is an accompanying debate as to how appropriate it is to use medical interventions. This change is reflected in the rising number of major therapeutic procedures performed on children with Trisomy 13 and 18 over the last decade.[8] Non-intervention used to be the norm in the delivery room, but now nearly half (44%) of providers consider initiating resuscitation in an infant with Trisomy 18.[8] This situation is true even if congenital heart disease is known to be present; physicians have an obligation to treat neonatal patients to the full extent possible if there is a clear benefit to the patient. Conversely, physicians are similarly obligated to withhold treatment if it is not reasonably expected to benefit the patient.[10] For patients with Trisomy 13 and 18 who fall into the ‘grey zone,’ where it is unclear what is best for the patient, parental wishes are being used as the deciding factor.[11]

With these evolving medical considerations, parents are now being given more autonomy in the decision-making process; desires for a meaningful life and enriched family experiences have been reported as important to families.[11] Current recommendations favor a balanced approach when discussing prognosis with parents rather than a “presupposed perception of quality of life.”[9] There is more thorough involvement of families’ wishes in the decision-

making process, which encompasses decisions about comfort care and full intervention.[9,11] This increasing autonomy has led to more infants being resuscitated and treated,[12] with little evidence of improved survival, and a vigorous debate about the ethical issues surrounding these decisions.[13–17] Involving families and respecting parental autonomy in decision-making prenatally or early in the infant's care would be useful in considering the family and infant quality of life.

Previous studies have examined the types of intensive care given to Trisomy 13 and 18 patients.[18] In the past, discussions of resource allocation in babies were dismissed given the infrequency of these conditions. In the current era of escalating health care costs and debates on rationing of care,[5,19] elaborating on the issue of resource utilization and allocation is increasingly relevant.

According to recent studies, 40–45% of live-born infants with diagnoses of Trisomy 13 or 18 live to be discharged from the NICU.[8] The mean hospital charges in 2003 for live-born babies were $30,021 and $39,547[20] for babies with Trisomy 13 and 18, respectively. There are limited data in the literature other than those cited above that describe health care resource utilization and predictors of length of stay (LOS) and hospital charges. Our study examines the potential differences in health care resource utilization among survivors and non-survivors of the two trisomies and possible predictors of length of hospital stay as well as total hospital charges in order to identify any factors that could improve delivery of health care.

2. Methods

We used the Patient Discharge Data dataset from the California Office of Statewide Health Planning and Development (OSHPD) from 2006 to 2010. The OSHPD includes patient demographic characteristics, diagnostic information, treatment information, disposition status, total hospital charges and expected source of payment.

Trisomy 13 and 18 patients were identified using International Classification of Diseases, ninth revision, Clinical Medication (ICD-9-CM) codes (758.1 and 758.2, respectively). Survival to discharge was determined based on OSHPD disposition codes. We included patients who were presenting with their first admission and excluded those with missing birth identification and those with multiple admissions. We extracted patients with non-missing birth ID with the first readmission. Diagnoses and procedures of OSHPD data were coded according to The International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Furthermore, patients who were utilizing inpatient resources, mainly mechanical ventilation for more than 96 h (coded as ICD-9 CM ′96.72'), were also extracted from the OSHPD database. Comorbidity information was categorized based on ICD-9-CM codes for diagnosis variables. Comorbidities were assessed including cardiovascular (745.0–745.3, 746 and 747.1–747.6), gastrointestinal (750, 751 and 756.79), genitourinary (752 and 753), musculoskeletal (754 and 755) and neurologic diseases (741–743, 756.1, 756.3 and 756.4).

For both Trisomy 13 and 18, we conducted the following statistical analyses. Descriptive statistics were assessed for demographic and clinical characteristics. Pearson's chi-square test was used to examine the univariate association of categorical variables and survival status, and Fisher's Exact Test was used when one or more cells had expected numbers less than five. Normality was tested for continuous variables. Median (25th and 75th percentiles) and Wilcoxon rank sum tests were calculated for non-normally distributed continuous variables. Analysis of variance (ANOVA) was used to assess the difference among LOS and total hospital charges stratified by year, respectively. General linear models were used to identify predictors of LOS and total hospital charges. Covariates included in the model included socio-demographics and infant characteristics such as the predisposition to mechanical ventilation and co-morbidities. We used the SAS version 9.3 software package (SAS Institute, Cary, NC, USA) for the statistical analysis. A p-value less than 0.05 was adopted as being statistically significant.

3. Results

We identified 2,523,368 neonates based on the study population from 2006 to 2010. There were 177 and 295 neonates diagnosed as Trisomy 13 and Trisomy 18. Of these, 105 and 185 patients satisfied our inclusion criteria, respectively. Among the 105 Trisomy 13 infants, 76 were identified with a first-time admission; mortality was 27.6% for first-time admission. Similarly, among the 185 Trisomy 18 infants, 115 required disposition status and mortality was 20.9%. Comorbidities, including cardiovascular, gastrointestinal, genitourinary, musculoskeletal and neurologic disorders, were assessed.

3.1. Trisomy 13

We compared survival status with demographic variables and clinical features observed for Trisomy 13. A statistically significant difference was observed for mechanical ventilation of more than 96 h between survivors versus non-survivors ($p < 0.0001$).

After adjusting for gender, ethnicity, DNR, insurance and co-morbidities on multivariate analysis, the provision of more than 96 h of mechanical ventilation was associated with significantly increased LOS (SE) by 18.0 ± 5.3 days (Table 1). In terms of insurance type, patients with private coverage had 10.8 ± 4.9 days more LOS (SE) than patients with Medi-Cal. Charges (SE) were also significantly increased by $399,000 ± $85,000 due to more than 96 h of mechanical ventilation (Table 2).

3.2. Trisomy 18

For Trisomy 18, roughly two-thirds (66.7%) of non-survivors were Hispanic. Of the survivors, 46.2% were Hispanics. This difference was statistically significant ($p = 0.02$). We found a difference between survivors and non-survivors with respect to their advanced directive ($p = 0.02$). However, DNR status was not associated with decreased LOS or total hospital charges in the multivariate analysis. This parameter approached statistical significance in the case of total charges for Trisomy 18 cases ($p = 0.0578$). The median LOS for Trisomy 18 patients was marginally associated with survival status with 5 days for survivors and 3 days for non-survivors ($p = 0.052$).

For the multivariate analysis, after adjusting for gender, ethnicity, DNR, insurance and co-morbidities, more than 96 h of mechanical ventilation was associated with increased LOS (SE) by 36.8 ± 6.8 days (Table 3). Furthermore, the utilization of mechanical ventilation with Trisomy 18 patients was associated with increased total hospital charges (SE) of $365,000 ± $59,000, after adjusting for covariates (Table 4).

4. Discussion

The management of Trisomy 13 and 18 has changed significantly in the last several years from a strategy of almost universally withholding “futile” care for a “lethal” condition[5] to one in which physicians are giving greater consideration to parental autonomy.[10] Although discussions of this shift and subsequent increases in the level of intervention and the ethical implications of those changes are extensive in the literature,[9,14,16,17] there is a dearth of studies related to the financial implications of this change in management strategy. We found that mechanical ventilation was associated with increased length of stay and total hospital charges for neonates with either diagnosis independent of other factors.

The only discussion of hospital charges associated with Trisomy 13 and 18 is a Morbidity and Mortality Weekly Report (MMWR) Center for Center for Disease Control and Prevention report from 2007 that discusses hospital charges and in-hospital deaths of infants diagnosed with specific birth defects born in 2003.[20] This report notes a mean hospital charge of $39,547 for Trisomy 18 cases and $30,021 for Trisomy 13 cases. In our study of California infants from 2006 to 2010, we looked at differences in hospital charges for survivors versus non-survivors and found mean hospital charges of $55,000 for Trisomy 13 survivors and $92,000 for non-survivors, and $44,000 for Trisomy 18 survivors and $45,000 for non-survivors. These numbers are notably higher than the MMWR estimates, which is consistent with increasing levels of intervention. We also found a lower rate of in-hospital mortality compared with the MMWR report, which implicated 60.4% in-hospital mortality from Trisomy 13 and 56.4% in-hospital mortality from Trisomy 18.[20] We found 28% in-hospital mortality for Trisomy 13 and 21% in-hospital mortality from Trisomy 18. This change in mortality could be a reflection of increasing medical intervention for Trisomies 13 and 18.

Another interesting finding in our study was the significantly lower rate of mechanical ventilation above 96 h received by survivors vs. non-survivors of Trisomy 13. Such a difference may be expected because patients who require invasive procedures such as mechanical ventilation are expected to be sicker and therefore less likely to survive. However, this matter requires further investigation. This difference was not observed in infants with Trisomy 18. Multivariable analysis was conducted and showed that more than 96 h of mechanical ventilation was associated with increasing LOS for both Trisomy 13 and 18. The use of life-sustaining therapies such as prolonged mechanical ventilation in infants with Trisomy 13 and 18 has already generated a substantial ethical debate,[5] but this analysis attempts to augment this discussion by comparing how significantly these treatments impact LOS and total cost. Mechanical ventilation is associated with both higher cost and increased LOS, yet non-survivors had higher rates of ventilation. The associated increased cost and relative scarcity of surviving babies who received long-term mechanical ventilation prompts

the need for further investigations regarding the efficacy of mechanical ventilation as a life-sustaining measure for patients with Trisomy 13 and 18.

For Trisomy 13 patients, the multivariate analysis showed that having private insurance was associated with significantly higher total LOS but not increased total hospital charges. There are several other possible explanations for this association. It is possible that the families of patients covered by private insurance are more likely to keep their children in the hospital because they are financially more able to bear additional medical costs. In California, both public (Medicaid) and private insurance cover similar diagnoses and treatments although reimbursement to both physician and hospital may differ. Medi-Cal in California has adopted the.

All Patient Refined Diagnosis Related Group (APR-DRG) system for reimbursement practices.[20]

As a diagnosis of Trisomy 13 and 18 is no longer considered a disorder incompatible with life, paired with a shift towards longer-term therapeutic treatments, advanced directive (DNR) orders are no longer standards of care.[8,10] A DNR prohibits a physician from resuscitating a patient in the event of a cardiac or pulmonary arrest but does not address medical care given in a non-emergency setting. In some sense, it is not surprising that infants with DNR orders have lower rates of survival. This situation is due not only to the nature of the directive but also to the fact that sicker patients are more likely to be given DNR orders. Surprisingly, however, DNR status was not associated with decreased LOS or total hospital charges in our multivariate analysis (though it approached statistical significance in the case of total charges for Trisomy 18 cases; $p = 0.0578$). This finding suggests that the primary contributors to hospital charges are not the emergency life-saving services prohibited by the DNR but perhaps the more therapeutic procedures being performed on these patients.[8] Additionally, if one adopts total hospital charges as a rough proxy for the amount of medical care received, these results suggest that the patients with DNR orders are less likely to survive due to the nature of their disease rather than withholding aggressive treatment. However, more precise analysis related to the types of medical care received is necessary. The utility and effects of an advanced directive need to be further explored as well.

In terms of strengths and limitations, this large, population-based study focused on all infants in California with a diagnosis of Trisomy 13 or Trisomy 18 over a four-year period. Given the low prevalence of Trisomy 13 and Trisomy 18, such a large number of observations were required in order to observe the differences we report. The 2006–2010 timeframe is also recent enough to capture the trend towards intervention, which could be contributing to the improved survival numbers compared with those of previous reports. Our study is limited by inpatient data and does not follow patients further to observe the procedures they might have had subsequent to discharge. Additionally, the administrative dataset may lack some more granular information on predisposition to mechanical ventilation.

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Table 1

The adjusted association of length of stay and Trisomy 13 among neonates (n = 76).

Parameter	Coefficient	Standard Error	95% Confidence Interval	Significance
Intercept of model	4.2	5.1	(−5.8, 14.3)	0.4
Infant use of mechanical ventilation	18.0	5.3	(7.5, 28.6)	<0.001
Male	−0.4	3.9	(−8.3, 7.5)	0.92
Ethnicity				
Hispanic	Reference			
Non-Hispanic	3.6	4.3	(−4.9, 12.2)	0.39
Other	2.8	10.3	(−17.7, 23.4)	0.78
Use of advanced directive (DNR)	−3.1	6.3	(−15.7, 9.4)	0.62
Insurance				
Medi-Cal	Reference			
Private Coverage	10.8	4.9	(1.0, 20.5)	0.03
Other Government	12.1	6.6	(−1.0, 25.2)	0.07
Infant has comorbidities[a]	2.4	4.4	(−6.4, 11.3)	0.58

[a]Comorbidities were assessed including cardiovascular ICD9 codes (745.0–745.3, 746 and 747.1–747.6), gastrointestinal (750, 751 and 756.79), genitourinary (752 and 753), musculoskeletal (754 and 755) and neurologic diseases (741–743, 756.1, 756.3 and 756.4).

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Table 2

The adjusted association of total hospital charges and Trisomy 13 among neonates (n = 76).

Parameter	Coefficient	Standard Error	95% Confidence Interval	Significance
Intercept of model	6.4	8.2	(−10.0, 22.9)	0.44
Infant use of mechanical ventilation	39.9	8.5	(22.9, 56.9)	<0.0001
Male	−5.5	6.5	(−18.6, 7.7)	0.41
Ethnicity				
Hispanic	Reference			
Non-Hispanic	4.1	7.1	(−10.2, 18.4)	0.57
Other	0.3	16.5	(−32.7, 33.3)	0.99
Use of advanced directive (DNR)	−3.1	10.6	(−24.3, 18.2)	0.77
Insurance				
Medi-Cal	Reference			
Private Coverage	15.0	9.0	(−3.0, 33.0)	0.1
Other Government	11.4	10.5	(−9.6, 32.5)	0.28
Infant has Comorbidities[a]	1.4	7.5	(−13.5, 16.3)	0.85

[a]Comorbidities were assessed including cardiovascular ICD9 codes (745.0–745.3, 746 and 747.1–747.6), gastrointestinal (750, 751 and 756.79), genitourinary (752 and 753), musculoskeletal (754 and 755) and neurologic diseases (741–743, 756.1, 756.3 and 756.4).

Table 3

The adjusted association of Length of Stay (LOS) and Trisomy 18 among neonates (n = 76).

Parameter	Coefficient	Standard Error	95% Confidence Interval	Significance
Intercept of model	13.2	5.6	(2.2, 24.2)	0.02
Infant use of mechanical ventilation	36.8	6.8	(23.2, 50.4)	<0.0001
Male	3.2	4.7	(−6.1, 12.4)	0.51
Ethnicity				
Hispanic	Reference			
Non-Hispanic	−1.1	4.7	(−10.5, 8.2)	0.81
Other	4.0	12.7	(−21.2, 29.1)	0.76
Use of advanced directive (DNR)	−8.9	5.9	(−20.6, 2.8)	0.13
Insurance				
Medi-Cal	Reference			
Private Coverage	−7.9	5.1	(−18.1, 2.2)	0.12
Other Government	−9.2	8.3	(−25.7, 7.2)	0.27
Self Pay	−8.1	14.1	(−36.0, 19.8)	0.57
Other Payer	−3.3	24.2	(−51.3, 44.7)	0.89
Infant has comorbidities[a]	−1.6	4.9	(−11.4, 8.2)	0.74

[a]Comorbidities were assessed including cardiovascular ICD9 codes (745.0–745.3, 746 and 747.1–747.6), gastrointestinal (750, 751 and 756.79), genitourinary (752 and 753), musculoskeletal (754 and 755) and neurologic diseases (741–743, 756.1, 756.3 and 756.4).

Table 4

The adjusted association of total hospital charges and Trisomy 18 among neonates (n = 76).

Parameter	Coefficient	Standard Error	95% Confidence Interval	Significance
Intercept of model	10.3	4.8	(0.9, 19.8)	0.03
Infant use of mechanical ventilation	36.5	5.9	(24.7, 48.3)	<0.0001
Male	2.7	4.0	(−5.3, 10.6)	0.51
Ethnicity				
Hispanic	Reference			
Non-Hispanic	3.0	4.1	(−5.2, 11.2)	0.47
Other	6.8	11.7	(−16.4, 30.0)	0.56
Use of advanced directive (DNR)	−9.6	5.0	(−19.5, 0.3)	0.05
Insurance				
Medi-Cal	Reference			
Private Coverage	−6.8	4.6	(−16.0, 2.3)	0.14
Other Government	−8.2	6.6	(−21.3, 5.0)	0.22
Other Payer	0.04	19.1	(−38.0, 38.0)	0.99
Infant has Comorbidities[a]	−0.7	4.1	(−8.9, 7.5)	0.87

[a]Comorbidities were assessed including cardiovascular ICD9 codes (745.0–745.3, 746 and 747.1–747.6), gastrointestinal (750, 751 and 756.79), genitourinary (752 and 753), musculoskeletal (754 and 755) and neurologic diseases (741–743, 756.1, 756.3 and 756.4).