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Morbidity, mortality and resource utilization among neonates with Down syndrome admitted to NICUs

[1]Mary A Woodward, [2]Connie Williams, [3]Abhay K Lodha, [4]Prakesh S Shah, [5*]Sandesh Shivananda and Canadian Neonatal Network Investigators*

[1]Division of Neonatology, Department of Pediatrics McMaster University Hamilton, Ontario

[2]Assistant Professor Division of Neonatology, Department of Pediatrics McMaster University Hamilton, Ontario

[3]Associate Professor, Section of Neonatology, Department of Pediatrics & Community Health Sciences, University of Calgary,Calgary, Alberta

[4]Professor, Department of Paediatrics, University of Toronto, Ontario, Canada Department of Pediatrics, Mount-Sinai Hospital, Toronto, Ontario, Canada Maternal-Infant Care Research Centre, Mount Sinai Hospital, Toronto, Ontario, Canada Prakeshkumar.

[5*]Corresponding author: Dr. Sandesh Shivananda MD. FRCPC, M.Sc. Assoc. Professor, Neonatology, 4500 Oak Street. Room No. 1R-19, BC Women's Hospital and Health Centre,Vancouver, British Columbia, Canada V6H 3V4

[1]woodwm@mcmaster.ca
[2]willico@mcmaster.ca
[3]Abhay.Lodha@albertahealthservices.ca
[4]Shah@sinaihealthsystem.ca
[5*]sandesh.shivananda@cw.bc.ca

ABSTRACT

Background: Down syndrome (DS) is the most common chromosomal disorder in humans. Though single-centre studies indicate high morbidity among neonates with DS admitted to NICUs, there is lack of outcome and resource utilization data at the national level.

Aim: The aim of this study was to determine the survival, morbidity and support received in Canadian NICUs by neonates with DS.

Methods. A retrospective cohort study on neonates with DS admitted to the NICUs participating in the Canadian Neonatal Network between 2010 and 2015 was conducted. Data on characteristics, prevalence of congenital malformations, resource utilization and outcomes during hospital stay were collected.

Results. 654 neonates (0.8 % of NICU admissions) with DS were identified during the study period. 25 (4%) of the neonates had a SNAP-II score of >20. 77% of neonates received intravenous fluid, 53% antibiotics, 66% oxygen, and 29% mechanical ventilation. The mortality rate was 4%, late-onset sepsis 2%, and intraventricular hemorrhage grade ≥3 6% of neonates.

Conclusions. Neonates with DS admitted to NICUs have significant morbidity, mortality and resource needs.

Key words: Down syndrome, mortality, morbidity, resource utilization, NICU

Abbreviations

NICU: Neonatal Intensive Care Unit
DS: Down syndrome
CNN: Canadian Neonatal Network
G tube: Gastrostomy tube
O2: Oxygen
CPAP: Continuous positive airway pressure
iNO: inhaled nitric oxide
PRBC: Packed red blood cells

Introduction

Down syndrome (DS) is the most common chromosomal disorder with a reported incidence of 1 in 800 births (1, 2). In Canada, the birth rate of DS neonates has remained stable averaging 14.1 per 10,000 live births between 1998 and 2007 (3). Pediatric patients with DS have twice the hospital admission rates, longer hospitalization and experience wide range of illness than the general pediatric population (4, 5).

Families with children with DS experience considerable stress and seek out medical information that allows them to adapt and cope with the situation (6). The American Academy of Pediatrics states, "the primary goal of the antenatal consultation is to provide parents with information that will aid their decision making" (7, 8). However, the current AAP guideline "Clinical Report—Health Supervision for Children With Down Syndrome" does not provide specific information on estimated risk of admission to NICU and possible outcome for neonates admitted to NICU(9), perhaps because there is lack of information on morbidity, mortality and resource utilization among neonates with DS admitted to level III NICUs (3).

Information about neonates with DS who are admitted to level III NICUs has the potential to improve family's understanding and participation in decision-making process. Furthermore, the information can also be useful for care providers anticipating problems and preparing for resuscitation at birth as well as administrators planning to effectively care for this population. The aim of this study was to determine the morbidity, mortality and resource utilization among neonates with DS admitted to Canadian level III NICUs.

Materials and Methods

Study design:This was a retrospective non-comparative cohort study. Neonates with a clinical diagnosis of Down syndrome and admitted to tertiary NICUs participating in the Canadian Neonatal Network (CNN) between January 1, 2010 and December 31, 2015 were included. There were no exclusion criteria. Ethics approval was obtained from the local ethics board of McMaster University and Hamilton Health Sciences.

Data collection and variables

The CNN database contains data, collected by trained data abstractors, on all admissions to the 31 Canadian tertiary NICUs (10). Details of data collection and data management for CNN have been published elsewhere (11). Standard definitions provided in the CNN abstractor's manual were used for all variables and outcomes in this study (11). Data were extracted for neonatal characteristics; presence of malformations; range and duration of intensive care supports; antibiotic use; vascular catheter use; ventilation; parenteral nutrition; supplemental oxygen; inhaled nitric oxide; postnatal systemic corticosteroids; packed red blood cell transfusion; length of NICU stay; and use of technology dependent interventions at discharge (ie oxygen, continuous positive airway pressure [CPAP], tracheostomy and ventilation, ventriculoperitoneal shunt and gastrostomy tube [G tube]). Down syndrome was defined by the presence of congenital anomalies as indicated in ICD 10 coding guidelines (12).

Outcomes

The primary outcome was mortality at discharge. The secondary outcomes were morbidity (late-onset sepsis, intraventricular hemorrhage grade ≥3 (13) and necrotizing enterocolitis stage 2 or 3 (14), technology dependency at discharge/transfer from NICU, and NICU resource utilization. Technology dependency was predefined as any neonate receiving oxygen, non-invasive or invasive mechanical ventilation, gastrostomy tube, gavage feeds, ventriculo-peritoneal shunt or tracheostomy at discharge (15). Resource utilization was measured using the following indicators: median length of NICU stay, use of NICU interventions including mechanical ventilation, vascular catheters, antibiotics, oxygen days, inhaled nitric oxide (iNO), inotropes and postnatal systemic steroids and packed red blood cell (PRBC) transfusion(16).

Analysis

Neonatal characteristics and outcomes were described using frequency (%), mean (SD) or median (range), as appropriate.

Results

Out a total of 85928 neonates admitted to CNN Level III NICUs during the study period, 654 neonates with DS were identified (0.8 % of NICU admissions). The characteristics of neonates with DS are presented in Table 1. The mean gestational age of neonates was 36.4 weeks. One hundred and eighty-six neonates (28%) received positive pressure ventilation at birth, and 24 (4%) of the neonates had SNAP-II scores > 20 (Table 1).

Table 1 Characteristics of neonates with Down syndrome admitted to NICUs

Characteristics	
Number of neonates with Down syndrome	654
Gestational age (weeks), mean (SD)	36.4 (2.9)
Birth weight (grams), mean (SD)	2694 (740)
Males, n (%)	373 (57)
Caesarean section delivery, n (%)	290 (44)
Outborn, n (%)	142 (22)
Apgar at 1 minute, median (IQR)	8 (6, 8)
Apgar at 5 minutes, median (IQR)	9 (8, 9)
SNAP-II score >20, n (%)	25 (4)
Positive pressure ventilation at birth*, n (%)	186 (28)
Chest compressions at birth*, n (%)	7 (1)
Receipt of epinephrine at birth*, n (%)	2 (0.3)

*at initial resuscitation after birth

Abbreviations: SD - standard deviation; n, number in subgroup; IQR - Interquartile range; SNAP-II - Score for Neonatal Acute Physiology with Perinatal Extension-II

Neonates with DS had variable types of congenital malformations (Table 2). Congenital heart disease was the most common congenital anomaly and was observed in 548 neonates (84 %). The most common diagnosis was atrial septal defect (28%), followed by atrioventricular septal defect (25 %) and ventricular septal defect (22%). Gastrointestinal anomalies were observed in 145 neonates (22%) with duodenal malformations being the most common gastrointestinal anomaly (Table 2).

Table 2 Congenital malformations in neonates with Down syndrome

Congenital malformations	Number with malformation (%)*
Congenital heart disease	
Atrial septal defect	186 (28)
Atrio-ventricular septal defect	161 (25)
Ventricular septal defect	145 (22)
Tetralogy of Fallot	25 (4)
Coarctation of aorta	12 (2)
Double outlet right ventricle	9 (1)
Pulmonary valve stenosis or atresia	7 (1)
Patent ductus arteriosus	1 (0)
Persistent pulmonary hypertension of the newborn	2 (0)
Congenital gastrointestinal anomalies	
Duodenal stenosis or atresia	68 (10)
Other congenital malformations of the digestive system	66 (10)
Tracheoesophageal fistula	7 (1)
Other small intestine stenosis	2 (0)
Jejunal atresia or stenosis	1 (0)
Hirschprung's disease	1 (0)
Cranial ultrasonography anomalies	10 (2)
Renal anomalies	
Hydronephrosis	21 (3)
Renal agenesis and other defects of the kidney	5 (1)
Renal cystic diseases	3 (0)

*654 total number of infants with Down syndrome

For the primary outcome, 28 neonates (4%) died before discharge. Sixteen (2.4%) neonates had late-onset sepsis, 17 (2.6%) had an intraventricular hemorrhage grade ≥3 and 17 (2.6%) had necrotizing enterocolitis. Eighty-two neonates (13%) had technology dependency at discharge or transfer from a level III NICU, 69 (11%) had supplemental oxygen, 3 (<1%) CPAP, and 14 (2%) gastrostomy tube.

Resource utilization among neonates admitted to level III NICUs is provided in Table 3

Table 3 Resource utilization in the NICU among neonates with Down syndrome

Intensive care support	Number receiving intervention, (%)	Duration of intervention* (days), median (IQR)
Initial 48 hours in NICU		
Mechanical ventilation on day 1or 2	91 (14)	N/A
Umbilical venous catheter on day 1	89 (14)	N/A
Inotrope on day 1	18 (3)	N/A
Anytime during NICU stay		
Antibiotics	345 (53)	5 (3, 9)
Vascular access		
PIV	501 (77)	4 (3, 8)
PICC	145 (22)	13 (6, 19)
UAC	62 (9)	4 (2, 8)
UVC	134 (20)	5 (3, 8)
Surgical CVL	21 (3)	16 (12, 26)
TPN use	306 (47)	8 (4, 15)
Noninvasive ventilation		
• CPAP	153 (23)	3 (2, 8)
• High flow	100 (15)	5.5 (2, 13)
• Nasal High frequency ventilation	20 (3)	4 (2, 11)
Mechanical ventilation		
• High frequency ventilation	26 (4)	4 (2, 10)
• IPPV	161 (25)	4 (2, 6)
Oxygen use	429 (66)	4 (2, 11)
Inhaled nitric oxide	31 (5)	4 (2, 7)
Inotrope use	60 (9)	3 (2, 6)
Postnatal corticosteroid use	45 (7)	4 (2, 11)
Packed red blood cell transfusion	63 (10)	N/A
Length of stay	N/A	14 (7, 30)

*Duration only calculated for those who received the intervention

Abbreviations: NICU-neonatal intensive care unit, IQR-interquartile range, N/A-not available or applicable, PIV-peripheral intravenous catheter, PICC-percutaneous inserted central catheter, UAC-umbilical arterial catheter, UVC-umbilical venous catheter, CVL-central vascular catheter, TPN-total

parenteral nutrition, CPAP-continuous positive airway pressure, IPPV-intermittent positive pressure ventilation The median length of NICU stay was 14 days. During the first two days, of neonates received mechanical ventilation and 14% received umbilical venous catheterization. One hundred and fifty three (23%) received CPAP and 161 neonates (25%) were intubated and ventilated during the entire NICU stay. Antibiotics were used in 345 (53%), oxygen in 429 (66%), and peripheral intravenous catheters in 501 (77%) of neonates.

Discussion

This multicentre, national study describes the mortality, morbidity and resource utilization among neonates with DS admitted to Level III NICUs. The mortality, morbidity and technology dependency at discharge were 4%, 2-6% and 13% respectively. To date, this is the first study to describe the spectrum of illness and outcomes among neonates with DS admitted to level III NICUs in Canada.

We found identifying a comparison group for the study population extremely challenging. While planning for the study, we explored many comparison groups including late preterm neonates admitted to a NICU, term neonates admitted to a NICU, all neonates admitted to a NICU, and all neonates with DS but not admitted to a NICU. However, we realized that neonates with DS admitted to level III NICUs are a unique population who can present with a spectrum of conditions, congenital anomalies and severity of illness during the neonatal period. The closest population for comparison is probably all neonates with DS, but not admitted to a NICU. Since such data was not available at the national level, we chose a non-comparative study design.

We compared mortality, morbidity, and spectrum of congenital anomalies in our study population, with previous studies. The mortality rate observed in our study is similar to previous studies from the Netherlands and United Kingdom where the mortality rate was 1.6-3% (17, 18). Reported factors associated with higher mortality patients with DS included prematurity, low birth weight, and presence and severity of structural anomalies (19, 20). However, limited sample size precluded us from performing a similar analysis in our study.

We observed cardiac malformations in 84% of neonates with DS, which is higher than the prevalence of 22-56% previously reported in population based studies (21-24). We believe that the DS neonates admitted to level III NICUs constitute a subset of the whole DS population who had more illness to begin with or were meticulously screened with echocardiography resulting in a higher observed rate of cardiac malformations.

The median length of NICU stay was 14 days in our study, which was higher than the 11 days reported in a study from Mann from 122 NHS units in England (18). Similarly, the proportion of neonates who received endotracheal intubation and ventilation was higher in our study than the study from Mann (25% vs. 11%) (16). We speculate that inclusion of neonates with DS admitted to both level III NICUs and level II nurseries in Mann's study with possible lower acuity of patients may explain the observed differences. In general, the high need for intravenous fluid, ventilation, antibiotics and length of stay observed in our study is consistent with previous reports (16, 18). A high proportion of neonates receiving supplemental oxygen and intravenous fluid in our study may reflect the potential presence of pulmonary hypertension with delay in resolution of pulmonary vascular resistance and challenges with oral feeding (6, 25) Our study results indicate that neonates with DS and admitted to a level III NICU have considerable mortality, morbidity and length of stay. During their NICU stay, these neonates receive

a significant amount of intensive care supports. Given the significant number of neonates born annually with DS, practices and policies related to care of these neonates have the potential to have a large impact on resources. We believe that information from our study will be useful to the stakeholders, hospital administrators, and financial strategists who plan services for this population. Moreover, our study results could be used by pediatricians and neonatologists when called to counsel a family whose fetus has been identified at increased risk of DS and help families prepare for a long hospital course, often involving mechanical ventilation, surgery, prolonged need for parenteral nutrition and vascular access (9). The current focus of antenatal counseling for women with a fetal diagnosis of DS is on developmental delay and the challenges of independent living, but information on the likelihood of admission to the NICU and outcomes of infants with DS admitted to NICU is limited (9). Our study provides objective data for caregivers and families to anticipate higher morbidity, prolonged hospitalization and possible need for complex planning at discharge.

The strengths of this study are that it is a multi centre, national-level study including level III NICUs using standard definitions to abstract data. The limitations of the study include lack of relevant details to describe the full spectrum of DS e.g. thyroid function, hematological function, feeding issues etc., These data were not available from the database; therefore, they could not be ascertained. Finally, determinants of mortality, morbidity and technology dependency at discharge could not be determined due to inadequate sample size.

Conclusion

Neonates with DS admitted to level III NICUs have significant morbidity, mortality and resource needs. Future population-based studies should consider including all neonates with antenatal or postnatal diagnosis of DS to determine the predictors of NICU admission.

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Appendix

Canadian Neonatal Network Investigators

Prakesh S Shah, MD, MSc (Director, Canadian Neonatal Network and site investigator), Mount Sinai Hospital, Toronto, Ontario; Jaideep Kanungo, MD, Victoria General Hospital, Victoria, British Columbia; Joseph Ting, MD, B.C. Women's Hospital and Health Centre, Vancouver, British Columbia; Zenon Cieslak, MD, Royal Columbian Hospital, New Westminster, British Columbia; Rebecca Sherlock, MD, Surrey Memorial Hospital, Surrey, British Columbia; Wendy Yee, MD, Foothills Medical Centre, Calgary, Alberta; Jennifer Toye, MD, Royal Alexandra Hospital, Edmonton, Alberta; Carlos Fajardo, MD, Alberta Children's Hospital, Calgary, Alberta; Zarin Kalapesi, MD, Regina General Hospital, Regina, Saskatchewan; Koravangattu Sankaran, MD, MBBS, and Sibasis Daspal, MD, Royal University Hospital, Saskatoon, Saskatchewan; Mary Seshia, MBChB, Winnipeg Health Sciences Centre, Winnipeg, Manitoba; Ruben Alvaro, MD, St. Boniface General Hospital, Winnipeg, Manitoba; Amit Mukerji, MD, Hamilton Health Sciences Centre, Hamilton, Ontario; Orlando Da Silva, MD, MSc, London Health Sciences Centre, London, Ontario; Chuks Nwaesei, MD, Windsor Regional Hospital, Windsor, Ontario; Kyong-Soon Lee, MD, MSc, Hospital for Sick Children, Toronto, Ontario; Michael Dunn, MD, Sunnybrook Health Sciences Centre, Toronto, Ontario; Brigitte Lemyre, MD, Children's Hospital of Eastern Ontario and Ottawa General Hospital, Ottawa, Ontario; Kimberly Dow, MD, Kingston General Hospital, Kingston, Ontario; Ermelinda Pelausa, MD, Jewish General Hospital, Montréal, Québec; Keith Barrington, MBChB, and Anie Lapoint, MD, Hôpital Sainte-Justine, Montréal, Québec; Christine Drolet, MD, and Bruno Piedboeuf, MD, Centre Hospitalier Universitaire de Québec, Sainte Foy, Québec; Martine Claveau, MSc, LLM, NNP, and Marc Beltempo, MD, Montreal Children's Hospital at McGill University Health Centre, Montréal, Québec; Valerie Bertelle, MD, and Edith Masse, MD, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, Québec; Roderick Canning, MD, Moncton Hospital, Moncton, New Brunswick; Hala Makary, MD, Dr. Everett Chalmers Hospital, Fredericton, New Brunswick; Cecil Ojah, MBBS, and Luis Monterrosa, MD, Saint John Regional Hospital, Saint John, New Brunswick; Julie Emberley, MD, Janeway Children's Health and Rehabilitation Centre, St. John's, Newfoundland; Jehier Afifi, MB BCh, MSc, IWK Health Centre, Halifax, Nova Scotia; Andrzej Kajetanowicz, MD, Cape Breton Regional Hospital, Sydney, Nova Scotia; Shoo K Lee, MBBS, PhD (Chairman, Canadian Neonatal Network), Mount Sinai Hospital, Toronto, Ontario.

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