Prevalence of Cleft Lip and/or Palate in Manitoban Children and the Early Childhood Caries Burden Experienced

by

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ABSTRACT:

Purpose: To examine the birth prevalence of cleft lip with or without cleft palate (CL±P), of Isolated cleft lip (CL) and of isolated cleft palate (CP) in Manitoba between January 1 2008 and Dec 31 2019. The secondary objective was to establish the burden of early childhood caries (ECC) among these children.

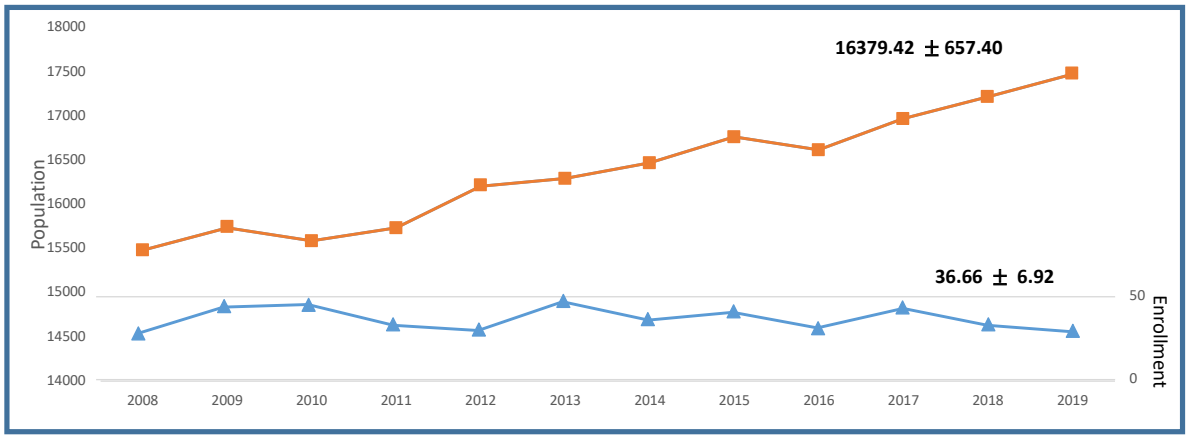
Methods: A retrospective chart review was conducted at the Manitoba Cleft Lip and Palate Program at the Health Science Centre in Winnipeg, Manitoba. Children registered between January 1, 2008 and December 31, 2019 with or without an underlying syndrome or significant medical history were included. Data was entered into a REDCap database including the following variables: sex, date of birth, postal code, type of orofacial clefting, whether GA was required to treat ECC, oral hygiene prior to treatment under GA, age at the time of GA, cost of treatment, and the type of treatment rendered. Cumulative scores of decayed, extracted, and filled primary teeth (dmft) were also calculated.

Result: The mean birth prevalence in Manitoba from 2008-2019 was 2.46 per 1000 live births for orofacial clefting, 1.33 per 1000 live births for CL±P, 0.46 per 1000 per live births for isolated CP, and 0.41 per 1000 live births for isolated CL. The orofacial clefting in Manitoba was almost 1.5 times greater than the Canadian national average. A child with any form of cleft lip and/or palate (CLP), including those who were syndromic or presented with additional medical comorbidities between 12 – 59 months were 15 times more likely to require GA to treat their ECC than a healthy child. A CLP patient who had an associated syndrome was 32 times more likely to require GA to treat ECC than their aged matched healthy counterparts, and 3.5 times more likely to require GA to treat ECC than a CLP patient who is otherwise healthy.

Conclusion: While the birth prevalence of CLP in Manitoba was relatively stable from 2008-2019, it has increased from 2 per 1000 live births in the period of 1948-1977 to 2.46 per 1000 live births. While the rates of general anesthetic (GA) to treat ECC is significantly higher, the dmft scores for CLP patients are similar to their age matched counterparts.

FIGURE 1: Live Births vs CLP enrollment in Manitoba from 2008 - 2019

■ **Live births in Manitoba from 2008 – 2019** ▲ **CLP enrollment in Manitoba from 2008 – 2019 ***



** Note the CLP graph y-axis scale is from 0-50 superimposed on the live birth scale with a y-axis from 14000 - 18000*

FIGURE 2: Percentage of children requiring GA to treat ECC, including those with additional medical comorbidities and syndromes

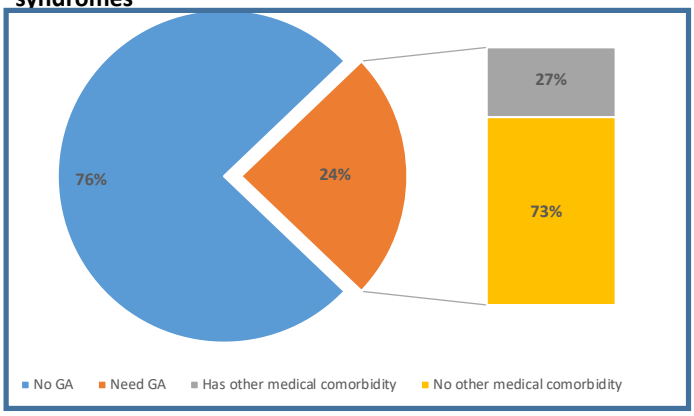


FIGURE 3: Average scores for extractions (EXO), stainless steel crowns (SSC), amalgam restoration, composite restorations, sealants and dmft (decayed, missing, filled tooth) score.

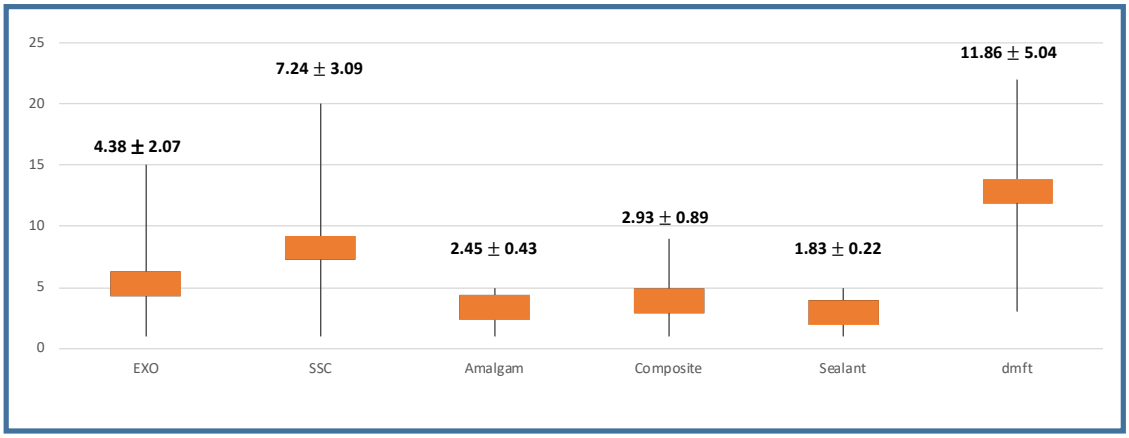


TABLE 1: Medical conditions and Syndromes experienced by Manitoba CLP patients

Medical Condition	Syndrome
Heart Disease	22q Deletion Syndrome
Respiratory Disease	Pierre Robin Sequence
Kidney Disease	FASD
Seizure Disorder	AICARDI Syndrome
Hearing Loss	Trisomy 21
Developmental Delay	Goldenhar Syndrome
GT Fed	Stickler Syndrome
Allergies	Chromosome 18p Deletion
Anemia	Ring 18 Syndrome
Autism	Dandy Walker Syndrome
ADHD/ADD	Pallister Killian Syndrome
Scoliosis	Pelizaeus-Merzbacher Syndrome
Platelet Dysfunction	

TABLE 2: Proportion of CLP patients in 12 – 59 mo age category who require GA to treat ECC/S-ECC (95% CI)

	Proportion / 1000 children
All orofacial clefting	190
CLP Only	109
CLP + Any medical comorbidity	416
CLP + Syndrome	388

INTRODUCTION:

Every year, approximately 500 children are born with orofacial clefts in Canada (Public Health Infobase 2017). Those affected require multidisciplinary surgical and non-surgical care from birth until adulthood. Without information on which to primary preventive strategies, orofacial clefts continue to pose a major challenge to the affected individuals, their families and society (Public Health Agency of Canada. Congenital Anomalies in Canada 2013 : A Perinatal Health Surveillance Report. Ottawa, 201, September 2013).

Cleft lip and/or palate (CLP) are recognizable disruptions of the normal facial structure. While not a major cause of mortality in developed countries, CLP does cause considerable morbidity to affected children and imposes significant financial strains for families with an associated societal burden (Dixon, 2011). Cleft lip and/or palate are among the most prevalent congenital malformations of the orofacial structures and constitute approximately 65% of anomalies affecting the head and neck (Impellizzeri, 2019). The occurrence of CLP is influenced by complex genetic and environmental factors. While the prevalence of oral clefts varies with different ethnic backgrounds, international literature reports epidemiological indices of CLP ranging from 0.87 to 1.03 per 1000 live births (de Mourna, 2013). The prevalence at birth of CLP±CP in Canada from 1998-2007 was 0.94 per 1000 and of CP 0.70 per 1000 (Public Health Agency of Canada. Congenital Anomalies in Canada 2013 : A Perinatal Health Surveillance Report. Ottawa, 201, September 2013).

Clefts of the lip and primary palate can occur if there is any disruption in the process of cell proliferation, migration, adhesion, differentiation and/or aptoptosis before the end of the sixth

week of development. Between the sixth and tenth weeks, they cause clefts of the secondary palate (Hill, 2018). CLP is correlated with esthetic, functional, and psychological problems, and requires early interventions involving a multidisciplinary team. The patients and their family may suffer psychological effects from the burden of disease. Effective surgical treatment requires a close interprofessional collaboration between oral health, speech rehabilitation and correction of the malocclusion. Therefore, it is important to appreciate that early caries experience and premature loss of primary teeth due to caries can affect the success of surgical treatment, orthodontic treatment, and speech therapy (de Moura, 2013).

Children born with orofacial clefts may also be affected by complications early in life such as reduced fetal growth, feeding problems due to improper oral seal, swallowing and nasal regurgitation, speech difficulties due to nasal escape, hearing difficulties due to abnormalities in palatal musculature, and/or frequent ear infections (Chopra, 2014). Some sequelae of orofacial clefts can extend into adulthood, including speech and hearing disorders, disturbances of the jaw and dentition, and altered physical growth, which can impose a heavy psychosocial burden (Cook, 2016).

A healthy primary dentition with avoidance of early extractions is crucial in order to preserve space and bone adjacent to the alveolar cleft. Dental caries is a global public health problem and constitutes one of the main threat to children's oral health (Peres, 2019) (El Tantawi, 2018) (Hassloff, 2007). Patency between the oral and nasal region compromises feeding, breathing and causes the most significant morbidity in patients. Oronasal patency is also thought to disrupt the normal oral flora at a time when the teeth are erupting. Prolonged bottle-feeding to ensure adequate nutrition as well as the challenges of maintaining oral hygiene secondary to

abnormal teeth and the cleft itself, have been proposed to contribute to the increase in caries incidence in this population (Tamas, 2017).

Numerous studies have cited slow oral food clearance times, the presence of enamel defects, high mutans streptococci and lactobacilli counts and deficient oral hygiene practices as contributing factors for caries in these patients (Worth, 2017). Several case-control studies have reported that toddlers and preschool children with orofacial clefts have higher caries increments than similarly aged non-cleft or cleft-lip only control children (Karp, 2009). These studies found that 20% - 75% of cleft patients harbor caries, depending on the populations studied (Veiga, 2017) (Sunderji, 2017) (Antonarakis G. P., 2013). Likewise, the decayed-missing-filled teeth scores (dmft) for cleft subjects 6 years old and younger are noted to range from 1.3 to 9.95 teeth in several epidemiological studies (Karp, 2009). By contrast, other studies have found no difference in caries risk in patients with nonsyndromic CLP, or a lower caries risk, when compared to the general population (Hasslof, 2007) (Tannure, 2012). These inconsistencies found in different studies can be due to a variety of reasons including patients dental awareness and cultural differences, large age range, small sample size, multifactorial nature of caries, methodological differences etc. (Antonarakis G. P., 2013)

The American Academy of Pediatric Dentistry (AAPD) defines early childhood caries (ECC) as the presence of at least one decayed, missing, or filled surface (dmfs) in primary teeth in children younger than 6 years old. Severe early childhood caries (S-ECC) is an advanced form of ECC, and is at epidemic levels (AAPD Reference Manual, 2016). S-ECC is a devastating form of caries that affects the oral function of young children and can reduce their oral health related quality of life (Grant, 2019) When children with orofacial clefts develop S-ECC, the health and longevity of the

primary dentition and the success of future cleft care interventions can be jeopardized. S-ECC must be treated aggressively to prevent declines in oral function and cosmetic outcomes, as well as to promote optimal surgical outcomes in the future (Karp, 2009). According to the AAPD, "Children with known risk factors for S-ECC should have care provided by a practitioner who has the training and expertise to manage both the child and the disease process. In some children where preventative programs are not successful, areas of demineralization and hypoplasia can rapidly involve the dental pulp, lead to infections and possibly life-threatening facial space involvement. Such infections may result in medical emergency requiring hospitalization, antibiotics, and extraction of the offending tooth" (AAPD, 2016). Extracting teeth in the cleft site during the preadolescent period can result in widened cleft widths and reduced bone volume before alveolar bone grafting is completed. In addition, soft tissue remodeling can also be problematic as oronasal fistulae can become patent or increase in size after tooth extraction. Early tooth extractions in cleft patients can impact mastication as a result of marked malocclusion and interarch crossbite. Reasons to restore carious teeth with intracoronal restorations or stainless steel crowns include maintenance of arch length, control of the vertical dimension of occlusion and stable anchorage for orthodontic appliances (Karp, 2009).

Age appropriate behavior patterns coupled with an extensive history of orally focused surgery and examination can make cleft patients orally defensive. This behavior pattern can limit the ability to perform restorative and surgical dental procedures without sedation or general anesthesia. Moderate and deep forms of sedation, as defined by the AAPD, may be contraindicated for these patients. This is because head and neck anomalies could jeopardize

resuscitation efforts in a medical emergency. For these patients, dental surgery under general anesthesia (GA) is an common option for treatment of ECC (Karp, 2009).

The current model for treating children with orofacial clefts involves the collaborative efforts of multiple specialists and health care professionals including but not limited to orthodontists, plastic surgeons, pediatric dentists, maxillofacial surgeons, ear nose & throat (ENT) surgeons, speech pathologists and prosthodontists. There is little information on the oral health status of children with oral clefts in Canada. The oral health facilities vary considerably, and the clinical management of orofacial anomalies involves considerable resources. In Manitoba, the costs for dental restorations and orthodontic treatment are covered by the Manitoba Cleft Lip and Palate Program (MCLPP) up to the year in which the patient reaches their 25th birthday. In order to be accepted into the program, the patient needs to be a resident of Manitoba, maintain a good oral hygiene regimen at home, and present at least once a year to a dentist for an oral health exam and assessment.

There is significant literature reporting on the etiological factors for CLP. In addition, much is written on the outcomes of CLP patients relating to the surgical interventions that the patients undergo. However, the current body on both the incidence of CLP, as well as knowledge on caries prevalence in Canadian children with CLP is sparse. In the light of the global decline in caries in children, it is important to evaluate the incidence of CLP in Manitoba, along with the current burden of caries among these children.

The primary objective of this study was to examine the birth prevalence of cleft lip with or without cleft palate (CL±P), Isolated cleft palate (CP) and of isolated cleft palate (CP) in

Manitoba between January 1, 2008 and December 31, 2019. The secondary objective was to establish the prevalence of CLP in Manitoba during that time period and to examine the burden of caries among these children. Of particular interest is the ratio of children requiring a GA for treatment of ECC.

METHODS:

This retrospective chart review was approved by the University of Manitoba's Health Research Ethics Board and the Health Sciences Centre in Winnipeg, Canada. Children born in the province of Manitoba with confirmed orofacial clefting are registered at birth (children can also be registered on relocation to Manitoba) through the MCLPP and are periodically followed by the Craniofacial team, which includes the Graduate Pediatric Dentistry Clinic.

Inclusion criteria for this review included children registered with the MCLPP between January 1, 2008 and December 31, 2019. Children in the MCLPP presenting with an underlying syndrome or significant medical history were also included. Children who were stillborn, did not survive beyond the perinatal period, or relocated outside the province of Manitoba were excluded.

All patient information was retrieved through a direct search of MCLPP registry, MCLPP billing records, the craniofacial team charts, and electronic patient dental charts in the Dentrix software (Henry Schein One, American Fork, Utah) used by the Children's Hospital Dental Clinic. All relevant findings from each initial and periodic comprehensive exam were noted. Data were entered into a REDCap database including the following variables: sex, date of birth, postal

code, type of orofacial clefting (i.e. CL, CP, submucous cleft (SMC), alveolar notch (AN), forme fruste (FF), bifid uvula (BU) commissural cleft (CC)), and whether GA was required to treat ECC. For children who were treated for ECC under GA at the Graduate Pediatric Dental Clinic, the following additional information was collected: oral hygiene status (Good, Fair, Poor, Unknown) prior to treatment under GA, age at the time of GA, cost of treatment, and the type of treatment rendered. For children who underwent subsequent GA's for ECC, the initial visit was used to calculate age at GA, however the cumulative treatment required and cumulative cost was recorded. Cumulative scores of decayed, extracted, and filled primary teeth (dmft) were also calculated from the post-operative report after treatment was rendered. All data were collected by the principal investigator (FS). Imputation using substitution of mean age at time of surgery was used for those children with missing age information at the time of surgery.

Data were analyzed using standard descriptive (e.g. frequencies, means ± standard deviations (SD)) and bivariate statistics (chi square, t test) using NCSS and SPSS. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. A p value ≤ 0.05 was significant.

RESULTS:

There were 182,586 live births in Manitoba from 2008-2019 (Province of Manitoba Stats, 2019). A diagnosis of orofacial clefting was made in 441 of these children (Figure 1). Overall, 54% had a CL±P (17% CL; 37% CLP) and 46% had an isolated CP. The mean birth prevalence in Manitoba from 2008-2019 was 2.46 per 1000 live births for orofacial clefting. More specifically, it was 1.33 per 1000 live births for CL±P, 0.46 per 1000 per live births for isolated CP, and 0.41 per 1000 live births for isolated CL. When compared to existing published Canadian data for 2005-

2014, chi-squared analysis revealed a statistically significant difference in orofacial clefting for Manitoba (z-score 7.718 and p-value <0.001). Overall, the prevalence was almost 1.5 times greater than the Canadian national average.

The birth prevalence of CL±P was higher in males than females at 1.4:1 and almost equal for CP at 1.06:1. The mean birth prevalence for CL±P in Manitoba from 2008 – 2019 was 0.76 per 1000 live births for males and 0.55 per 100 live births for females. The prevalence of isolated CP was 1.04 per 100 live births in males and 0.98 per 1000 live births in females. The sex prevalence was not found to be statistically significant when compared to published Canadian data and appears to be on par with national trends.

Analysis of the first 3 digits of the postal code for participants revealed that 49% resided in urban Manitoba, 34% in rural Manitoba, 2% were from the Northwest Territories, and 5% were from northern Ontario. Postal code data were missing for 9% of participants.

Approximately 10% of patients with a confirmed orofacial cleft also presented with one or more additional medical comorbidity. Of the patients with an additional comorbidity, over 40% expressed a syndrome associated with their CLP; translating to approximately 4.5% of the total CLP population in Manitoba having an associated syndrome. Table 1 reports a list of associated medical conditions and syndromes expressed in the Manitoba CLP population.

The average age of a patient requring dental treatment under GA was 47.4 ± 19.2 months. A 2016 study reported that the overall rate of dental surgery to treat ECC was 12.1 per 1000 children 12 – 59 months of age in Canada (Schroth, 2016). Of the cohort described in this study,

approximately 1/4 of the patients required treatment under GA for ECC, of which we had the age on surgery date for 86 patients. A total of 63 of these patients were in the age range of 12 - 59 months (Figure 2). For those patients whose age at surgery data was missing, we imputed the number that would have been in the same age range at the time of their surgery, assuming a similar age distribution as the patients for which we did have an age on surgery date. Thus, we estimated a total of 84 children that required GA to treat ECC in the age range of 12 - 59 months. The groups were then broken down into (1) All CLP children requiring GA, (2) Otherwise healthy CLP children requiring GA, (3) CLP children with any additional medical comorbidity requiring GA, and (4) CLP children with associated syndrome requiring GA.

The proportion of CLP patients (in the 12-59 month age category who required GA to treat ECC) per 1000 with a 95% confidence interval can be found in Table 2. To test whether the rate of GA for ECC in the CLP population was different from the rate of GA for ECC in the general Canadian population, as well as to test whether the rates of GA for CLP patients who are otherwise healthy to the CLP population who have an associated syndrome, in Canada in the same age range, we used the proportion chi-squared test. A child with any form of CLP, including those who are syndromic or present with additional medical comorbidities between 12 – 59 months were 15 times more likely to require GA to treat their ECC than a healthy child (the test statistic on the z scale was 34.097, p-value of 0). A CLP patient who had an associated syndrome was 32 times more likely to require GA to treat ECC than their aged matched healthy counterparts, and 3.5 times more likely to require GA to treat ECC than a CLP patient who is otherwise healthy (The test statistic on the z scale was 3.547, p=0.00039).

Finally, The cost of the dental treatment under GA ranged from $687.10 to $4158.00 with an average of $2448.18 per child. The decayed, missing, and filled (dmft) primary teeth score was calculated from operative reports. The average dmft score of patients after their GA was reported to be 11.8±5.0 (extractions 4.4±2.1, stainless steel crowns 7.2±3.1, amalgam restorations 2.5±0.4, composite restorations 2.9±0.9, sealants 1.8±0.2) (Figure 3).

DISCUSSION

The goal of this study was to update the epidemiological data on CLP patients in Manitoba. Orofacial clefting has a significant impact on both the patient and the family. Patients with CLP utilize a higher prevalence of health care resources over their lives. In a publicly funded health care system as we have in Canada, the birth prevalence could influence both economic and resource planning for centers that attend to the needs of the CLP population (Matthews, 2015).

While the birth prevalence of CLP in Manitoba was relatively stable from 2008 – 2019, the trend has increased from 2 per 1000 live births in the period of 1948-1977 to 2.46 per 1000 live births currently. The reason for this increase was outside the scope of this study, but we postulate that due to advanced medical interventions, more children with orofacial clefting are surviving beyond the perinatal period. It is also possible that the increase could be attributed to a growing Indigenous population who make up approximately 18% of the population in Manitoba versus the Canadian provincial average of 4.9% (Statistics Canada, 2016), who are estimated to have up to 3 times higher rate or orofacial clefting than the non-Indigenous population (Vrouwe, 2013).

A general consensus in CLP literature is that males are more frequently affected with CL±P (2:1) with an inverse seen in isolated CP (0.5:1) (Worley, 2018). Previous research by Matthews et al. indicated that there was an increase female prevalence for CP in Manitoba, however our study did not find this. While the rates of CL±P in our study were higher (1.4:1) in males, the ratio of isolated CP was almost 1:1.

In Canada, there has been a reportedly stable incidence of orofacial clefting within the last few decades, despite efforts to reduce known risk factors such as increasing perinatal folate intake, encouraging peripartum smoking cessation and earlier and more accurate prenatal screening. It is unclear if other factors such as sociodemographic (rural vs urban households or socioeconomic status), maternal health history or prenatal care are greater influencers than previously suggested (Malic, 2020). In this study, we did find that 49% of our population were from an urban community and 41% were from rural communities in Manitoba, Northwest Territories, and Northern Ontario. Data was missing for 9% of our population. Currently there is no evidence for the magnitude of the contribution of urban vs rural demographics and whether this is correlated or coincidental in Manitoba was undetermined.

Approximately 1 in 25 infants are born with a congenital anomaly in Canada (Navaneelan, 2016). Our study found that 4.5% of the CLP population in Manitoba had an associated syndrome. Most pregnancies and births affected by congenital anomalies do not result in death of the fetus or infant. In developed countries such as Canada, individuals with congenital anomalies are surviving to a much older age than in previous decades, or in developing

countries. (Navaneelan, 2016). A previous study by Malic et al. demonstrated that the mortality rate for children with orofacial clefting is higher during first 2 years of life, particularly in children who present with a congenital or chromosomal anomalies within the first 30 days of life. However, after that initial increase, the death rate of children with orofacial clefting is similar to non-orofacial clefting children (Malic, 2020). While the proportion of infant deaths associated with a congenital anomaly has decreased since the early 1990's, in 2012 congenital anomalies were a leading cause of infant death in Canada at a rate of 1.1 deaths per 1000 births (Navaneelan, 2016).

Children with ECC often require oral rehabilitation under GA, which is the most frequent hospital day surgery procedure for preschool children in Canada (Schroth, 2016). The average age of CLP patients requiring treatment of their ECC under GA was 47.4±19.2 months with a dmft score of 11.86±5.04. When compared to a study by Grant et al. in 2019 where healthy children who lived within 2 hours drive of Winnipeg, MB who had their ECC treated under GA at a surgical centre had an average age of 47.7±14.2 and a dmft score of 10.3±3.4. The dmft scores of CLP vs non-CLP patients who were treated under GA for S-ECC not found to be statistically significant. This was unexpected, but some of the limitations of dmft scores include a significant amount of inter-observer bias and variability, and gives equal weight to missing, untreated decay or well restored teeth (Lo, 2020). In addition, due to the aggressive nature of ECC and a desire to avoid requiring retreatment for dental caries under GA, therapeutic intervention under GA should be definitive. This often dictates a more aggressive treatment approach and the judicious use of stainless steel crowns (SSC's) (AAPD Reference Manual, 2019). It appears

that once a decision has been made to treat a child under GA for ECC, the level of treatment rendered is similar between CLP and non-CLP children.

The cost of treating ECC/S-ECC in a hospital setting are significant, with an average hospital associated cost of $1564 (Schroth, 2016) and an average dental treatment associated cost of $2448.18. This of course excludes the travel cost and other costs borne by the family. In Manitoba, both the hospital associated and dental caries associated costs are borne by the provincial health care system. Given that the hospital costs alone for dental day surgery to treat ECC exceed 21 million annually, more appropriate and sustained funding should be dedicated towards establishing effective preventive strategies for ECC (Schroth, 2016).

Limitations of this study would be the nature of retrospective study design including incomplete data collection and limited variables to consider for inclusion in the study. A challenge in the research of CLP epidemiology is how stillbirth, neonatal death and terminations should be counted, whether children with associated congenital anomalies should be considered separately, how to categorize clefts, and how to account for variations in prenatal diagnosis and pregnancy termination (Matthews, 2015). The frequency of repeat dental surgery for treatment in ECC were not considered, nor were children who underwent treatment for ECC under GA in combination with other procedures. In Manitoba, dental data collection for patients born with CLP is not collected in a systematic manner. Secondly, accuracy of initial diagnosis and consistency in reporting were lacking. Finally, there was also an inability to collect data on ethnic and cultural classifications, use of prenatal care, parental involvement in dental care, miscarriages or therapeutic abortions with orofacial clefts.

From this study, further research could focus on looking at why the prevalence is higher in Manitoba when compared to the rest of Canada (Vrouwe, 2013). If a racial, environmental or genetic difference can be identified, further etiological studies can be conducted. This could also guide studies directed at intervention and prevention of orofacial clefting.

CONCLUSION:

While the birth prevalence of CLP in Manitoba was relatively stable from 2008-2019, it has increased from 2 per 1000 live births in the period of 1948-1977 to 2.46 per 1000 live births. The rates of GA for treatment of ECC are significantly higher in the CLP population than the general population, however the dmft scores were comparable. When taking into consideration patients who have an associated medical comorbidity or an associated syndrome, the rates of GA increase 34 fold.

In the absence of information on which to base primary preventive strategies, CLP continue to pose a major challenge to the affected individuals, their families and society. This study provides an update in the epidemiology of CLP in Manitoba. It also provides new data regarding the caries burden experienced by these children. Further research should also focus on developing a system to ensure higher quality data collection.

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