Introduction:

Down’s syndrome or trisomy 21, the most common human chromosome disorder predisposes affected individuals to a myriad of multisystemic manifestations and mental sub normality with an incidence between 1:700 and 1:800 live births.\(^1,2\) Congenital heart disease (CHD) is reported to occur in 40% to 60% of patients with Down’s syndrome, with complete atroventricular septal defect being the most common.\(^3,4\) Other frequently occurring lesion includes ventricular septal defect (VSD), patent ductus arteriosus (PDA), atrial septal defect (ASD) and Tetralogy of Fallot (TOF) in decreasing order.\(^5\)

Children with Down’s syndrome who do not have CHD have much better out comes and early corrective surgery for those with CHD greatly improves life expectancy.\(^6\)

Previous studies that evaluated outcomes after congenital heart surgery for patients with Down’s syndrome showed conflicting results. Some reported increased mortality rates, length of hospital stay, and morbidities such as duration of ventilation and infection rates, where as other suggested similar or improved outcomes for patients with Down’s syndrome who underwent atrio-ventricular septa defect repair.\(^3,4,7,8\)

The purpose of these study was to describe perioperative outcome of patients with Down’s syndrome undergoing surgical correction.

Methods:

We conducted a retrospective study of Down’s syndrome with congenital heart disease that
underwent cardiac surgery from January 2013 to July 2019, at Pediatric Cardiac Surgery unit in NICVD. Data collection included demographic information, preoperative data, ECG, Echocardiogram, thyroid status and surgical procedures. Operative data included duration of cardiopulmonary bypass time, cross clamp time. Outcome data include hospital death, total postoperative length of hospital stay, postoperative complications such as infections, pulmonary complications, arrhythmia, atrioventricular block, pulmonary hypertensive crisis are noted.

Results: A total of 49 patients of Down’s syndrome with CHD underwent surgery. Age of the patient at the time of surgery was 5 months to 13 years. Male were 20 and female were 29 in numbers and weight of them was 4 kg to 29 kg. Patients characteristics were analyzed in Table I.

Table-I
Distribution of patients by age (n=49).

| Age            | Number of Patients |
|----------------|--------------------|
| 5 to 24 months| 20                 |
| 2 to 4 years  | 13                 |
| 4 to 6 years  | 7                  |
| 6 to 8 years  | 5                  |
| > 8 years     | 4                  |

The 5 most common CHD found in patients with Down’s syndrome are presented in Table II. VSD was the most common (48.97%) found in this study. Among them inlet type was most common.

Table-II
Distribution of CHD in children with Down’s syndrome (n=49).

| Type of CHD            | Number (%)n=49 |
|------------------------|---------------|
| VSD                    | 24 (48.97)    |
| Inlet                  | 12            |
| Perimembranous         | 08            |
| Doubly committed       | 04            |
| AVSD                   | 12 (24.48)    |
| Partial                | 02            |
| Transitional           | 03            |
| Complete               | 07            |
| PDA                    | 06 (12.24)    |
| Large PDA              | 05            |
| Moderate PDA           | 01            |
| TOF                    | 06 (12.24)    |
| ASD                    | 01 (2.04)     |

43 of 49 patients presented with left to right shunt. Out of 43 patients of L-R shunt, 31 patients presented with pulmonary hypertension. Among which, moderate pulmonary hypertension was the most common. Table III showing the distribution of pulmonary hypertension in patients.

Table-III
Distribution of pulmonary hypertension in patients (n=49).

| Type of CHD       | Mild | Moderate | Severe |
|-------------------|------|----------|--------|
| n= 31             | PAH  | PAH      | PAH    |
| VSD               | 02   | 11       | 04     |
| PDA               | 00   | 03       | 02     |
| AV Canal Defect   | 01   | 04       | 04     |
| Total             | 3 (9.67%) | 18 (58.06%) | 10 (32.25%) |

14 (28.57%) patients presented with hypothyroidism.

Complete AV canal defect and TOF repair required longer CPB and cross clamp time. Table IV showing the distribution of operative characteristics.

Table-IV
Distribution of operative characteristics (n=49).

| Procedure              | CPB Time (minutes) | Cross Clamp Time (minutes) |
|------------------------|--------------------|----------------------------|
| ASD closure            | 44                 | 21                         |
| VSD closure            | 58 (45-79)         | 24.83 (15-45)              |
| AV canal defect repair | 108 (60-165)       | 64 (35-100)                |
| TOF repair             | 91 (80-160)        | 65 (55-95)                 |

Regarding post-operative outcomes TOF repair patients required longer mechanical ventilation time and ICU stay than AV canal defect repair. VSD patients required comparatively short ventilation and hospital stay time. Table V showing the distribution of post-operative outcome.

Early postoperative pulmonary complications were more common. One patient required tube thoracostomy for pleural effusion. One TOF patient needed mediastinal re-exploration due to mediastinal hematoma. One patient of complete AV canal defect required permanent pace maker implantation. Other complications include arrhythmia in 2 patients, low output syndrome in 3 patients and renal failure in 1 patient. Table VI showing distribution of postoperative complications.
Table-V

Distribution of postoperative complications (n=49).

| Post-operative morbidity     | Number (%) |
|------------------------------|------------|
| Pulmonary infection          | 10 (20.40) |
| Wound infection              | 03 (6.12)  |
| Pleural effusion             | 01 (2.04)  |
| Low cardiac output syndrome  | 03 (6.12)  |
| Renal failure                | 01 (2.04)  |
| Arrhythmia                   | 02 (4.08)  |
| Heart block                  | 01 (2.04)  |
| Mediastinal haematoma        | 01 (2.04)  |

In-hospital mortality occurred in 6 (12.24%) patients. Among these 3 VSD patients were due to intractable pulmonary hypertensive crisis, septicemia and hyperpyrexia with convulsion.

Discussion:
The earliest representation of Down’s syndrome dates back to 1505. It was later described by Sequis 1846 and John Langdo Down in 1866. The association of congenital heart disease and Down’s syndrome was recognized by Garrod in 1894. Patients with Down’s syndrome tended to have reduced life expectancy in the context of multiple congenital anomalies involving the cardiovascular, pulmonary, gastrointestinal, hematological, endocrine, neurologic and immunologic systems. The advancement in medical and surgical care and de-institutionalization improved the survival of patients with Down’s syndrome. Congenital heart disease affecting almost half the patients with Down’s syndrome. The purpose of our study to share experiences of surgical outcome of Down’s syndrome with congenital heart disease who underwent for corrective cardiac surgery.

The types of heart defect with Down’s syndrome may vary according to geographic region. In this study the most common type was VSD (48.97%) which is similar to China population (40%) but different from United States and France where atrioventricular septal defect was more frequent.

59.18% population of this study was female which is similar in Brazilian study. In evaluation of patient characteristics, we found that children with Down’s syndrome were younger at the time of surgery for all procedures evaluated except the AV canal defect and TOF.

Pulmonary arterial hypertension (PAH) was recorded in 63.26% of the children with Down’s syndrome. Shrestha reported 52.5% having PAH and Mourato recorded 37.5% developing PAH. It has been reported that patient with Down’s syndrome develop pulmonary hypertension early when they have left to right shunt lesions. Individuals with Down’s syndrome may have pulmonary hypertension for various reasons such as chronic airway obstruction, abnormal growth of alveoli, and thinner pulmonary arteriol.

In this study, nearly half of patients underwent VSD closure done by traditional manner. CPB and cross clamp time was as like of usually VSD closure without Down’s syndrome but take a little longer time in complete A-V canal defect and TOF repair. Where all patients need transannular patch.

Patient with Down’s syndrome undergone, TOF repair and A-V canal defect had significantly longer ventilation time and length of hospital stay compare with patient without Down’s syndrome.

Postoperative pulmonary infection was the most common complication affecting 20.40%, other reported 28%. Malecand and his colleagues reported higher rates of post-operative complications including respiratory infections and sepsis, which led to prolonged ventilation and...
longer length of ICU stay.\textsuperscript{25} Chronic upper airway obstruction increased secretion and gastroesophageal reflux leading to chronic aspiration and concomitant immunodeficiency may play a role.\textsuperscript{26} A patient of complete AV canal defect repair had post-operative complete heart block requiring permanent pacemaker placement. Anomalies in the conductive system in patients with AV canal defect have been reported.\textsuperscript{27}

In this study, there were 6 (12.24\%) in-hospital deaths. Causes of death includes aspiration pneumonia, intractable pulmonary hypertensive crisis, high pyrexia with convulsion in VSD patients, arrhythmia in AV canal defect and low output syndrome with multi organ failure in TOF patients. FA Bacieuicz Jr and his colleagues reported mortality 16.40\% and TOF was the highest.\textsuperscript{28} There was trend towards increase mortality for patients with Down’s syndrome undergoing TOF repair and decreased mortality rate for patients with Down’s syndrome undergoing AV canal defect repair.\textsuperscript{23}

Conclusion:
Congenital heart disease is the most frequent association with Down’s syndrome and remains a major cause of morbidity and mortality. Surgery plays a major role for better outcome with acceptable morbidity and mortality.

Conflict of Interest - None.

References:
1. Descartes M, Carroll AJ. Cytogenetics. In: Kleigman RM, Berhman RE, Jenson HB, Stanton BF. Editors. Nelson Textbook of Pediatrics. 18th Edn. Philadelphia: Saunders 2007: 507-508.
2. Weijerman ME, Van Furth AM, Vonk Noordegraaf A, et al. Prevalence, neonatal characteristics, and first-year mortality of Down’s syndrome: a national study. J Pediatr 2005; 152: 15-19.
3. Anaclerio S, Di Ciommo V, Michielon G, et al. Conotruncal heart defects: impact of genetic syndromes on immediate operative mortality. Ital Heart J 2004;5(8):624–628.
4. Formigari R, Di Donato RM, Gargiulo G, et al. Better surgical prognosis for patients with complete atrioventricular septal defect and Down’s syndrome. Ann Thorac Surg 2004; 78(2): 666–672.
5. Cleves MA, Hobbs CA, Cleves PA, et al. Congenital defects among live born infants with Down syndrome. Birth Defects Res A Clin Mol Teratol 2007; 78: 657-663.
6. Kazemi M, Salehi M, Kheirollahi M. Down syndrome: Current status, challenges and future perspectives. Int J Mol Cell Med 2016; 5: 125-133.
7. Lange R, Guenther T, Busch R, Hess J, Schreiber C. The presence of Down syndrome is not a risk factor in complete atrioventricular septal defect repair. J Thorac Cardiovasc Surg 2007; 134(2): 304–310.
8. Safûrio C, Marino B, Formigari R. Better surgical prognosis for patients with Down syndrome. J Thorac Cardiovasc Surg 2008; 135(1): 230.
9. Tolked M, Weidemann HR. Clinical aspects of Down’s syndrome from infancy to adult life. Hum Genet 1981; 2: 3-31.
10. Perloff JK. Clinical Recognition of Congenital Heart Disease, 5th edn. Philadelphia, Pa: Saunders; 2003.
11. Baint PA, Sandovick AD. Life expectancy in Down Syndrome adults. Lancet 1988; 2: 1354-1356.
12. Center for Disease Control and Prevention (CDC). Improved national prevalence estimates for 18 selected major birth defects—United States, 1999–2001. MMWR Mortal Mortal Wkly Rep 2006; 54: 1301–1305.
13. Bittles AH, Bower C, Hussain R, Glasson EJ. The four ages of Down syndrome. Eur J Public Health 2006; 17: 221–225.
14. Yang Q, Rasmussen SA, Friedman JM. Mortality associated with Down’s syndrome in the USA from 1983–1997: a population-based study. Lancet 2002; 359: 1019–1025.
15. Lo NS, Leung PM, Lauke, Yeug CY. Congenital Cardiovascular Malformations in Chinese Children with Down’s Syndrome. Chin Med J (Engl) 1989; 102(5): 382-386.
16. Freeman SB, Taft LF, Dookey KJ, et al. Population based study of congenital heart disease in Down syndrome. Am J Med Genet 1998; 80: 213-217.
17. Kallen B, Mastinoivo P, Robert E. Major Congenital Malformations in Down’s Syndrome. Am J Med Genet 1996; 65(2): 160-166.
18. Bermudez BE, Medeinos SL, Bermudez MB, Novadzki IM, Magdalena NI. Down syndrome: Prevalence and distribution of congenital heart disease in Brazil. Sao Paulo Med J 2015; 133(6): 521-524.
19. Shrestha M, Shakya U. Down syndrome and congenital heart disease: Single center prospective study. NJMS 2013; 2: 96-101.
20. Mourato FA, Villachan LRR, Mattos SDS. Prevalence and profile of congenital heart disease and pulmonary hypertension in Down syndrome in a pediatric cardiology service. Rev Paul Peditr 2014; 32: 159-163.
21. Chi TPL, Krovetz J. The pulmonary vascular bed in children with Down syndrome. J Pediatr 1975; 86: 533-538.
22. Banjar HH. Down syndrome and pulmonary arterial hypertension. *PVRI Review* 2009; 42: 213-216.

23. Fudge JC, Li S, Jaggers J, Brien SM, Peterson ED, Jacobs JP, Welke KF, Jacobs ML, Li JS and Sara K. Congenital heart surgery outcomes in Down Syndrome: Analysis of a National Clinical Database. *Pediatrics* 2010; 126: 315.

24. Parvathy U, Balakrishnan KR, Ranjith MS, Saldanha R, Sai S, Vakamudl M. Surgical experience with congenital heart disease in Down's syndrome. *Indian Heart J* 2000; 52: 438–441.

25. Malec E, Mroczek T, Pajak J, Januszewska K, Zdebska E. Results of surgical treatment of congenital heart defects in children with Down’s syndrome. *Pediatr Cardiol* 1999; 20: 351–354.

26. Kusters MA, Verstegen RH, Gemen EF, de Vries E. Intrinsic defect of the immune system in children with Down syndrome: a review. *Clin Exp Immunol* 2009; 156(2): 189–193.

27. Blom NA, Ottenkamp J, Deruiter MC, Wenink AC, Gittenberger-de Groot AC. Development of the cardiac conduction system in atrioventricular septal defect in human trisomy 21. *Pediatr Res* 2005; 58(3): 516–520

28. Baciewicz FA Jr, Melvin WS, Basilius D, Davis JT. Congenital heart disease in Down’s syndrome patients: a decade of surgical experience. *Thorac Cardiovasc Surg* 1989; 37: 369–371.