

**ASCERTAINMENT AND OUTCOMES OF ATRIOVENTRICULAR
SEPTAL DEFECTS IN PIETERSBURG HOSPITAL, LIMPOPO
PROVINCE, SOUTH AFRICA**

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DECLARATION

I, Giyani Patrick Shibambu declare that ASCERTAINMENT AND OUTCOMES OF ATRIOVENTRICULAR SEPTAL DEFECTS IN PIETERSBURG HOSPITAL, LIMPOPO PROVINCE, SOUTH AFRICA is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references and that this work has not been submitted before for any other degree at any other institution. I am submitting this research report for the fulfillment of the requirements for the Master of Medicine of Paediatrics and Child Health.

Full names

Signature

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ABSTRACT

Background: Congenital heart disease (CHD) is a significant contributor to Under 5 Mortality rate(U5MR) in Limpopo. Atrioventricular septal defect (AVSD) is the best ascertained lesion in Limpopo and is strongly associated with Down syndrome. Few children from Limpopo with CHD including AVSD access cardiac diagnostic and surgical services.

Objectives: The study aimed to enumerate, describe syndromes associated with AVSD and outcomes of children with AVSD at Pietersburg hospital.

Methods: This is a Retrospective study of all children (n=80) diagnosed with AVSD from 1 January 2010 to 31 December 2014 at Pietersburg hospital. Data were drawn from echocardiogram reports and patient records. District Health Information Software (DHIS) data was used to obtain the number of live births per district during the 5 years study period.

Results: Eight hundred and sixty six (n=866) patients had a first diagnosis of CHD confirmed on echocardiography and 80 (9.2%) of these had AVSD (an estimated 31.5% of expected cases of AVSD). Eighty four per cent (84%) of AVSD patients were associated with Down syndrome. 42/67 (63%) AVSD patients were referred for surgical assessment and of those 15/42 (36%) had surgery. The median interval between diagnosis and surgery was 13 months. Seventy five percent (n=50/67) of patients defaulted follow up.

Conclusion: The study confirmed that most children with AVSD had associated Down syndrome and that the majority of children with AVSD from Limpopo do not access surgery. There is under referral of children with Down syndrome for screening of CHD.

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DEFINITIONS OF CONCEPTS

Congenital heart disease: is the structural abnormality present at birth that involves the heart and/or great vessels.

Down syndrome: is a chromosomal condition caused by an extra copy of a chromosome 21, resulting in intellectual impairment and physical abnormalities.

Under-5 mortality rate: The probability (expressed as the rate per 1,000 live births) that children born alive will die before reaching the age of 5 years.

Atrioventricular septal defects: refers to heart defects in which there are holes between the chambers of the heart, and the valves that control the flow of the blood between these chambers may not be formed correctly.

Complete Atrioventricular septal defect: is the presence of defects in all structures formed by the endocardial cushion. Therefore, there are defects (holes) in the atrial and ventricular septa and the atrioventricular valve remains undivided.

Incomplete atrioventricular septal defect: is present when part of the ventricular septum formed by the endocardial cushions has filled in, either by the tissue from the atrioventricular valves or directly from the endocardial cushion tissue, and the tricuspid and mitral valves are divided into two distinct valves.

ABBREVIATIONS

ACE	Angiotensin converting enzyme
AVSD	Atrioventricular septal defect
CHARGE	Coloboma, heart anomalies, choanal atresia, retarded growth, genital anomalies and ear anomalies
CHD	Congenital heart disease
DS	Down syndrome
PVR	Pulmonary vascular resistance
U5MR	Under Five Mortality Rate
VSD	Ventricular septal defect
DHIS	District Health Information software

CHAPTER ONE

BACKGROUND AND RESEARCH PROBLEM

1.1. Introduction and background

Congenital Heart Disease (CHD) is as a group the most common type of birth defect with an incidence of 1 in 100 live births (Hoffmann, J., Kaplan, S. 2002). A proportion of these children will have minor CHD that will be asymptomatic or minimally symptomatic if left untreated. However, about half of these children will have heart defects that will be symptomatic and reduce longevity unless they are surgical corrected. As a result, CHD is a significant contributor to Under-5 mortality rate (U5MR) and may account for as many as 4 deaths per 1000 live births (Casanova et al, 2010). With access to a paediatric cardiology and heart surgery service this number can be reduced to less than 1 death per 1000 live births as was shown in Cuba (Casanova et al, 2010). It is estimated that around 1250 children under the age of 5 years died from CHD in South Africa in 2000 (Bradshaw, 2003).

A previous study conducted in Limpopo compared the number of cases of CHD disease seen at Pietersburg hospital Paediatric cardiology clinic with the number of cases expected by comparison with the global epidemiology of CHD (Sutton, 2014). All forms of CHD were under ascertained. In this study the outcomes of children diagnosed with CHD was not assessed but it is known anecdotally that a proportion of these children do not manage to access surgery for a variety of social and health systems reasons. This suggests that there is a need to develop additional services for children in Limpopo with CHD.

It was estimated that around 800 heart surgeries were performed on children in public sector hospitals in South Africa in 2006 (Hoosen). Extrapolating from the published data the expected number of public sector paediatric heart surgeries was estimated to be around 3750. This suggests that fewer than 1 in every 4 children needing heart surgery in the public sector is able to successfully access care. It is likely that access to care is geographically asymmetrical with children living in major centres being more

likely to access care than those from rural provinces like Limpopo. Atrioventricular defect is an interesting CHD for evaluation in Limpopo for several reasons.

Firstly, this was the most successfully (by proportion of expected cases) ascertained of the CHDs in the study by Sutton. Secondly AVSD is often associated with Down syndrome and this association may explain in part why this lesion is better ascertained than others. Thirdly most children with AVSD will require heart surgery to prevent life threatening complications. Fourthly, as with many CHD, there is a restricted window of opportunity during which surgery should be performed.

Beyond this time period surgery will no longer be possible due to pathophysiological changes of the pulmonary vascular bed. A study of the ascertainment and outcomes of AVSD should provide insight into how successfully children with CHD in Limpopo access heart surgery. This will provide a model for all forms of CHD diagnosed in the Limpopo province. It may also provide insights into why children with other types of CHD are proportionally less often referred to the paediatric cardiac clinic at Pietersburg Hospital.

1.2. Research problem

CHD is a significant contributor to U5MR. It is known that far fewer children than expected access a diagnostic service and that access to surgery for Limpopo children, is only available in Gauteng. The CHD with the best ascertainment in Limpopo is atrioventricular septal defect (AVSD) and this CHD is strongly associated with Down syndrome (DS). A study of children with AVSD would provide further information about the diagnosis and referral of children with CHD and the extent to which they are able to access heart surgery. This information can be used to inform the planning of future services for CHD in Limpopo.

1.3 Aim and Objectives of the study

1.3.1 Study aims

To enumerate and describe children diagnosed with AVSD and associated syndromes in Pietersburg Hospital, Limpopo Province, South Africa.

1.3.2 Study objectives

- To enumerate the children diagnosed with AVSD at Pietersburg hospital from 01 January 2010 to 31 December 2014.
- To describe the syndromes associated with the diagnosis of AVSD at Pietersburg hospital.
- To establish whether there is overrepresentation of Down syndrome in children with AVSD in Pietersburg hospital.
- To describe the outcome of patients with AVSD.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Congenital heart defects (CHD) are present in nearly 1% of all newborns and continue to be a significant cause of death in infancy. Atrioventricular septal defect (AVSD) account for about 4 to 5 % of congenital heart disease (Gelb,2004) and are the most common cause of severe congenital heart disease seen at Pietersburg hospital between 2001-2010 (Sutton,2014).

2.2 Subtypes and clinical presentation of AVSD

AVSD represents a spectrum of cardiac malformations and includes 3 subtypes: incomplete, transitional and complete AVSD. The clinical presentation of AVSD is not uniform and depends on the size of the defect, the degree of the shunting, as well as the presence of other malformations. In general, untreated complete AVSD results in congestive heart failure within the first few months of life, while the symptoms of incomplete AVSD are subtle and may not manifest until later in life (Briggs et al, 2012).

2.3 Syndromes associated with AVSD

Cardiac malformations including septal defects often occur in the context of a syndrome and in association with other abnormalities. AVSD is often associated with Down syndrome, CHARGE (coloboma, heart anomalies, choanal atresia, retarded growth and development, genital anomalies and ear anomalies) syndrome, Ellis-Van Creuvelde, Kaufman-Mckusick, Pitcher-Schinzel, Smith-Lemlu-Opitz and 3P deletion syndrome among other conditions (Briggs et al, 2012).

The most common genetic syndrome, Down syndrome (Trisomy 21), is strongly associated with AVSD. Approximately one quarter of children with Down syndrome possess this malformation and roughly two thirds of complete AVSD occur in association with Trisomy 21. However, not all children with Down syndrome possess defects suggesting that its pathogenesis is multifactorial and may involve multiple genetic modifiers and/or environmental components (Briggs et al, 2012).

Trisomy for human chromosome 21 causes Down syndrome in approximately 1/800 live births. Individuals with Down syndrome show a wide range of defects in many organ systems. These include cardiac malformations, gastrointestinal anomalies, craniofacial and skeletal anomalies, and contrasting cancer phenotypes that lead to increased frequency of childhood leukaemia and reduced prevalence of many types of cancer in adults (Haydar et al, 2012).

Approximately 40% of children born with Down syndrome have congenital heart disease. Atrioventricular septal defects and ventricular septal defects are the most common lesions. Therefore, all babies born with Down syndrome should have an early echocardiogram to screen for congenital heart diseases (Seale et al, 2004). The study done in Ireland also recommended screen with early and regular pre-ductal and post-ductal pulse oximetry in addition to the early echocardiographic examination to document pulmonary hypertension and congenital heart disease (Martin et al,2018).

Neonates with Down syndrome often lack physiological signs that would raise suspicion of CHD. The fall in pulmonary vascular resistance (PVR) takes longer in children with Down syndrome or may not fall as pulmonary vascular disease may have already developed. With consistently high PVR, pulmonary blood flow will not increase and therefore the child is unlikely to present with breathlessness (Marder et al). Another study also indicated that even Major CHD may not be evident on initial examination and recommended screen before discharge from the hospital (Charleton).

2.4 Management of AVSD

Basic management must include nutrition and supplements for children to gain enough weight and thrive. The management of CHD in a child with DS is dependent upon the defect. Previously, it was debated whether CHD in children with DS should be managed operatively but evidence now suggests early correction of the defects has beneficial results in preventing the likelihood of later complications and that similar surgical success is achieved compared to the patient without DS. Initially, an AVSD or large VSD is managed medically in order to treat the heart failure, with surgical repair of the defect at 3 to 6 months. The delay allows for a fall in the PVR, an increase in

the weight of the child and time for the atrioventricular valve to become thicker and better able to accept the surgical suture. Such medical management includes added calorie supplementation, or even nasogastric tube feeding, use of diuretics and often

ACE inhibitors such as captopril to reduce the left-to-right shunt. Several studies have now demonstrated that there is no additional risk of surgical mortality or morbidity in DS patients for either partial or complete AVSD, and other groups have shown a reduced need for re-operation in the DS patient compared to the child with a normal karyotype. Early surgical management of AVSD is advantageous, with interventions having maximum success within 4 months of birth, however surgical correction of partial AVSD can take place later in the child's life, at 3 to 5 years (Flanders et al, 2010, Miller et al, 2010, Evans et al, 2014)

A study by Miller indicated that presence of Down syndrome was not a prognostic factor. The presence of Down syndrome does not seem to deteriorate long-term results when the defect is repaired during the first year of life. (Miller et al, 2010)

Most patients require inotropic and diuretic therapy in the first weeks to months of life to control symptoms of congestive heart failure and to improve feeding intake and weight gain. Often it is difficult to determine the primary cause of poor feeding in the setting of patients with Down syndrome who may be feeding poorly because of non-cardiac issues. When failure to thrive is evident despite optimal medical therapy, complete repair should be considered in the first month or two of life. Initial pulmonary artery banding followed later by complete repair in balanced AV canals is no longer a consideration even in small infants (Apfel et al, 1999).

Management of these defects requires surgical corrections, which may be complicated by the presence of other cardiac abnormalities including dysplastic atrioventricular valve leaflets, isometric atrial appendages, Tetralogy of Fallot or double outlet right ventricle (Briggs et al, 2012).

Surgical repair for partial or transitional AVSD is associated with low morbidity and mortality, short hospital stays and catch-up growth particularly in underweight children repaired between 3 and 18 months of age. (Minnich et al, 2010)

In patients with complete atrioventricular septal defect, primary repair is the treatment of choice and can be accomplished with good results. The reconstructed atrioventricular valve shows a good and long-lasting performance (Gunther et al, 1998).

2.5 Outcome of children with AVSD

Without surgery only 35% to 50% of infants with AVSD survive to 12 months of age (Al-hay et al, 2003, Miller et al, 2010). In recent years, there has been a major reduction in mortality in children with AVSD because of advances in surgical repair. The 10-year survival probability of infants with AVSD increased from 78% during 1975 to 1995 to 86% to 94% during 1992 to 2002. (Al-hay et al, 2003, Miller et al, 2010).

A study by Miller demonstrated that Infants with Down syndrome had a significant higher survival probability than infants without Down syndrome. The study also indicated that in infants with Down syndrome, surgical prognosis of those with Down syndrome was better compared with those without Down syndrome. The presence of Down syndrome does not seem to deteriorate long-term results when the defect is repaired during the first year of life. (Miller et al.)

Large study done in United State indicated that the children with Down syndrome who underwent repair of CHD were more likely to survive to discharge than children without Down syndrome. Children with normal chromosome undergoing AVSD repair were more likely to have a dysplastic atrioventricular valve and having dysplastic atrioventricular valve was a risk factor for re-operation. The study also demonstrated that a diagnosis of Down syndrome was associated with a decreased 30-day mortality after AVSD repair and lower incidence of re-operation to repair the left-sided atrioventricular valve. (Evans et al. 2014).

Another study by Landis also demonstrated that survival after cardiac surgery is generally favorable, in-hospital mortality risk decreased and re-operation rate was low in children with Down syndrome compared with children without Down syndrome (Landis et al, 2016).

2.6 In summary

It is easy to diagnose Down syndrome clinically. Children with Down syndrome should be referred for cardiac screening. A study of AVSD will be helpful to measure how many patients with AVSD have Down syndrome and the ascertainment of AVSD as a lesion with or without a syndrome. A study will also help in establishing how many patients with AVSD have access to health care services including surgery.

CHAPTER THREE

METHODOLOGY

3.1 Study design:

This was a retrospective descriptive study involving review of paediatric cardiology echocardiography records and patient records (January 1, 2010-December 31, 2014).

3.2 Study setting:

The study will be conducted at Pietersburg Hospital located in Polokwane City, Limpopo Province. Pietersburg hospital is the only public referral centre for all children with suspected or diagnosed with congenital heart diseases in the Limpopo Province. Most children born in Limpopo and thought to have congenital heart disease will be referred to Pietersburg Hospital.

3.3 Study Population and Sample:

The study population is the group of all children diagnosed with AVSD at the Paediatric Cardiac clinic in Pietersburg Hospital. Children are defined as individuals aged from birth up until, but excluding, the date of their 13th birthday. The study sample will be the group of children diagnosed with AVSD between January 2010 and 31 December 2014 inclusive. It is estimated that this will be a sample of around 70 children.

- **Inclusion criteria:** Inclusion criteria will be all children aged 0 to 13 years diagnosed with AVSD at Pietersburg Hospital from 01 January 2010 to 31 December 2014 as recorded on the echocardiography records kept at the paediatric cardiology clinic.
- **Exclusion criteria:** All patients more than 13 years old, all children diagnosed before 2010 and after 2014, and all children without AVSD.

3.4. Data collection

The data collection process will draw upon the paediatric cardiology echocardiography records and patient records of all children diagnosed with AVSD at Pietersburg hospital

from 01 January 2010 to 31 December 2014. District Health Information Software (DHIS) data will be used to obtain the number of live births per district during the study period.

The data collection sheet will be designed looking at the following information:

1. Patients allocated number
2. Date of birth
3. Gender
4. Date of data collection
5. Date of diagnosis
6. Diagnosis (Complete or incomplete AVSD)
7. Additional cardiac abnormalities
8. Associated syndrome
9. Surgical assessment and nature of operation if done
10. Outcome (attending follows up, on cardiac medications, lost follow up, died)
11. Referring hospital

3.5. Data analysis

The data will be entered anonymously into a database programme. Descriptive statistical data will be generated for all relevant variables as described in the objectives above. Proportions will be used to depict frequencies of categorical data with exact confidence intervals for the proportions. Continuous data will be tested for normality after which the mean and standard deviation or median and interquartile range, as appropriate, will be used to summarise the data.

The Chi-squared test or Fisher exact test will be used to assess the association between syndromes and categorical variables. Continuous data will be tested for normality and the appropriate statistical test (Student t test or Mann-Whitney test) used to compare for significance of association between groups. A significance level of $P < 0.05$ will be used for all analysis.

3.6. Significance of the study

The study will provide evidence of the level of ascertainment of cases relative to the epidemiologically expected burden of disease and will provide an indication of access

to care for this group of patients. This will include access to diagnosis and to further treatment. This information will be of value in planning health services for this group of patients.

3.7. Ethical considerations

There are no potential harms associated with this study as it does not interfere with the patients' treatment. The data collected will not include patient identifiers. The information gathered will be treated confidentially and no patient's names will be recorded, they will each be assigned a number based on chronological order. The permission to perform the study will be obtained from Turfloop Research Ethics Committee and the Pietersburg Hospital Clinical Director as hospital patient records will be used. Informed consent will not be obtained.

PRESENTATION AND INTERPRETATION OF FINDINGS

4.1 Introduction

In the previous chapter, the methodology used for the study is outlined. In this chapter, the results of the study are presented and interpreted.

4.2 Prevalence of AVSD

During the period of the study, a total of 866 children had a first diagnosis of congenital heart disease confirmed by echocardiography. Of these 80 (9.2%) had AVSD as the major heart lesion. Table 1 shows the detailed information of the AVSD rates per year.

Table 1: Annual AVSD rates

	Total number of patients with echocardiographic first diagnosis	Patients with AVSD	Rate for AVSD %
2010	182	12	6.6
2011	181	10	5.5
2012	157	14	8.9
2013	165	20	12.1
2014	181	24	13.3
2010-2014	866	80	9.2

Table 2: Expected AVSD cases per district

	Live births 2010-2014	Expected AVSD cases per million (Hoffman)	AVSDs Cases	% of expected AVSD cases
Capricorn	141 388	56	18	32%
Mopani	134 743	53	18	34%
Vhembe	162 606	64	17	27%
Sekhukhune	128 588	51	14	27%
Waterberg	74 361	30	13	43%
LIMPOPO	641 686	254 cases	80 cases	31.5%

4.3 Demographic profile of the children

Figure 1 shows the age at diagnosis of the children. Most (61%) of the participants were in the age group 0-6 months followed by those age 7-11 months. Sixty percent of patients were females (Figure 2).

Figure 1: Age at diagnosis of children with AVSD

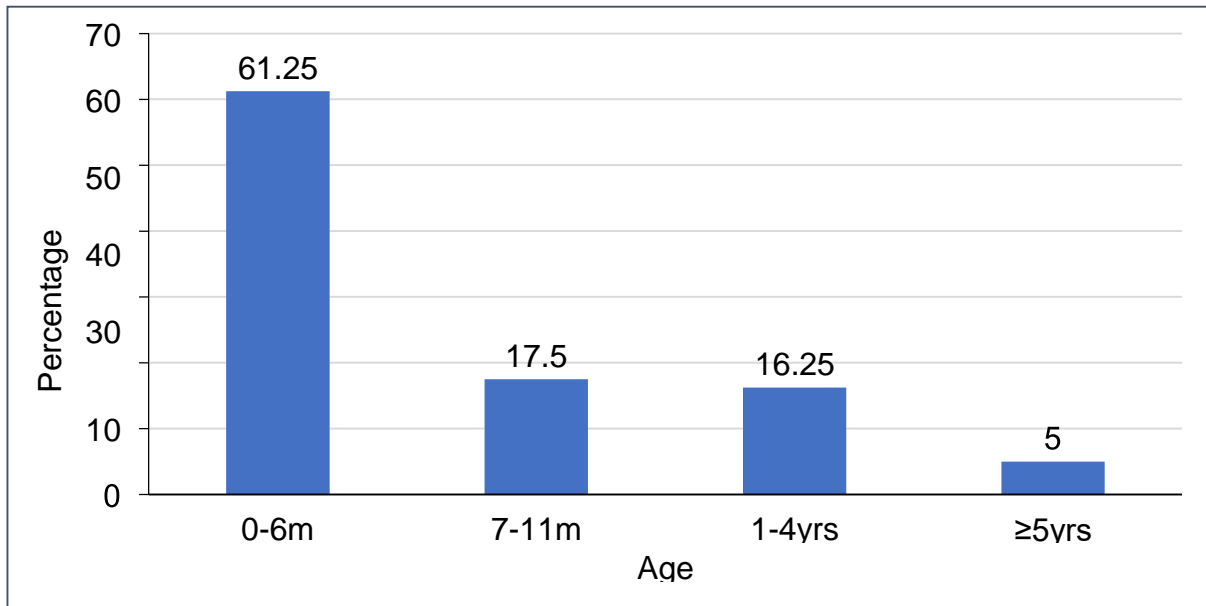


Figure 2: Gender distribution of children with AVSD

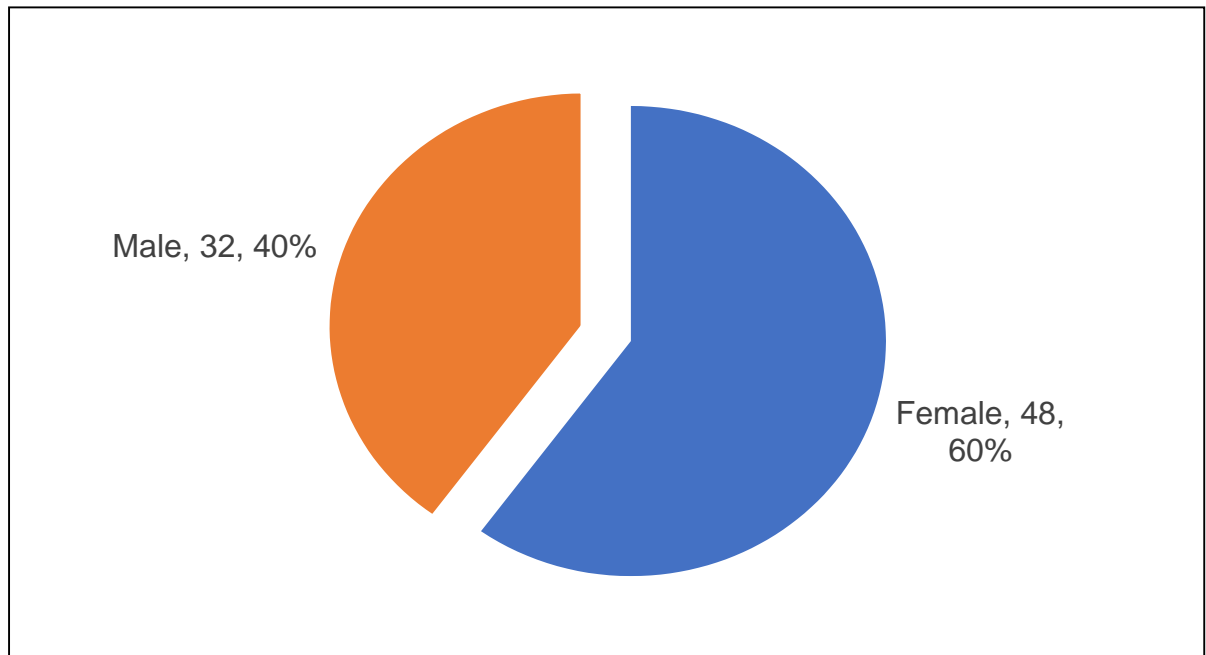


Table 3: Referral Facilities

Referral Facility	Number	Percentages
Capricorn	18	22.5
Mopani	18	22.5
Sekhukhune	14	17.5
Vhembe	17	21.25
Waterberg	13	16.25
Total	80	100

Figure 3: Map of Referral Districts

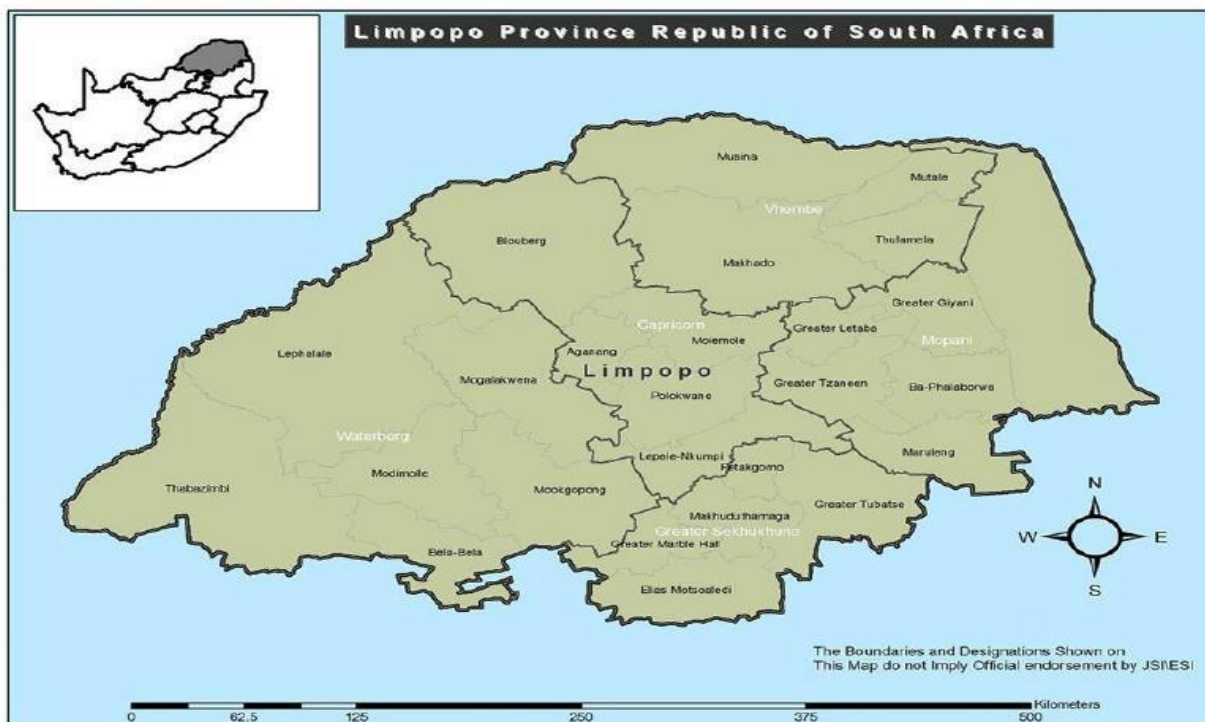


Figure 3 shows map of Limpopo Province districts. All districts refer patients with heart disease or suspected to have heart disease to Pietersburg hospital for assessment and diagnosis. Patients who are diagnosed with CHD are then referred to Steve Biko Academic Hospital for surgical assessment. The distance from Pietersburg hospital to Steve Biko Academic Hospital is 270 kilometers.

4.4 Characteristics of AVSD lesions and their associations

Ninety-five percent (76/80) of children had complete AVSD and only five percent (4/80) had incomplete AVSD as shown in table 4.

Table 4: AVSD Status

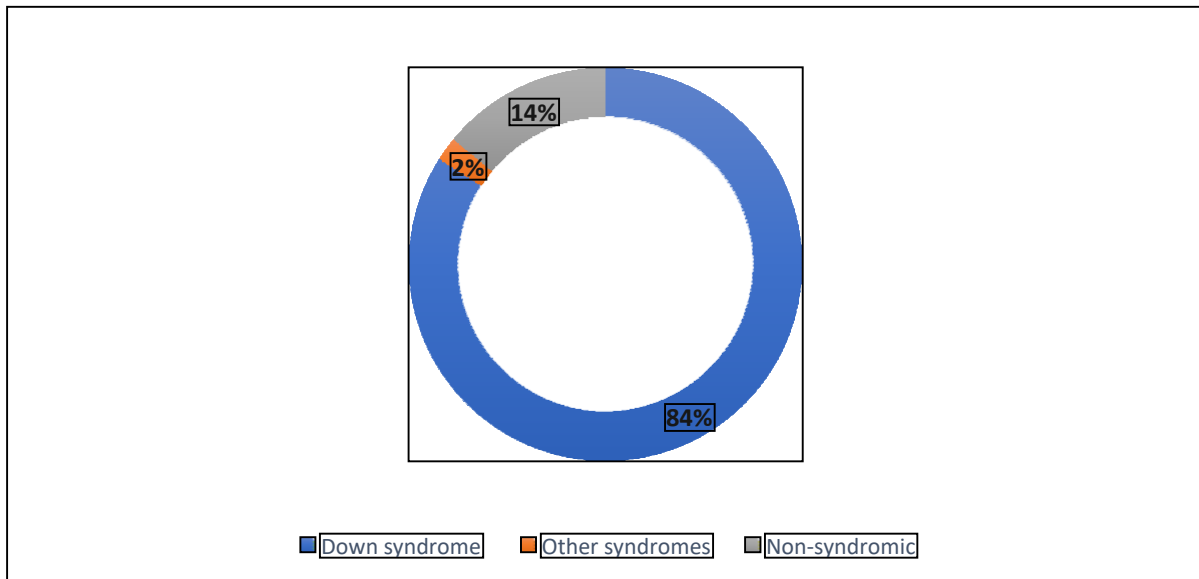
AVSD type	Number	%
Complete	76	95
Incomplete	4	5
TOTAL	80	100

Thirty-nine per cent (31/80) of the children had additional cardiac abnormalities (See Table 5).

Table 5: Associated cardiac abnormalities

Additional cardiac abnormality	Number	%
PDA	17	55
PDA & PS	1	3
PDA & PA	2	6
PS	8	26
PA	1	3
HYPOPLASTIC AORTA	1	3
TRUNCUS ARTERIOSUS	1	3
TOTAL	31	100

Figure 4: Associated syndromes



The majority (86%) of the children had an associated syndrome, of which Down syndrome 97% (67/69) was the most prevalent (figure 4). Of the patients with associated syndrome (n=69), only 3 had chromosomal studies and all 3 confirmed trisomy 21.

4.5 Outcomes

Sixteen percent (13/80) patients records files were missing and therefore excluded from the outcome analysis. Of the remaining patients (n=67), 42/67 were referred for surgical assessment at Steve Biko Academic hospital (Table 6). The nature of surgery is shown in Table 7. Eighty one percent (34/42) of patients referred for surgical assessment had Down syndrome and eighty seven percent (13/15) of those who were operated had Down syndrome.

Table 6: Patients referred for surgical assessment

	Number	%
Documented surgery	15	36
Documented inoperable	8	19
No evidence of assessment at surgical centre (lost to follow up prior to assessment)	19	45
TOTAL	42	100

Table 7: Nature of surgery

	Number	%
AVSD REPAIR	11	73
AVSD REPAIR & PDA LIGATION	2	13
TET CANAL REPAIR	1	7
PDA LIGATION	1	7
TOTAL	15	100

None of the patients had documented surgery in the first year of life. See attached table of Age at surgery. Table 8

Table 8: Age at surgery

	Number	%
Birth to 12 months	0	0
13 months to 60 months	10	67
Older than 5 years	2	13
Missing data on the age of surgery	3	20
Total	15	100

Table 9: Outcome of patients with AVSD

	Not operated patients	Operated patients	Total
On cardiac medicines	7	3	10
Not on cardiac medicines	1	5	6
Died	1	0	1
Lost to follow up	43	7	50
Total	52	15	67

Of the 67 patients included in the outcome analysis, 6 patients were not on cardiac medicines, 5 of these had had surgery and were clinically well. A further 10 patients were on cardiac medicines (usually diuretics) and 3 of these had had heart surgery. 1 patient was known to have died. Table 9

The remaining 50 were lost to follow up including 7 patients who had had heart surgery. See table 10

Table 10: Lost to follow-up per District

	Total	Follow up	Defaults	Missing files
Capricorn	18	6	6	6
Mopani	18	3	12	3
Vhembe	17	4	13	0
Sekhukhune	14	2	11	1
Waterberg	13	2	8	3
Total	80	17	50	13

Seventy five percent 50/67 of the patients were lost to follow at the time of the study. Of these patients, the majority were from Vhembe district followed by Mopani and Waterburg districts. Table 10. Patients who did not attend follow up for more than 12 months are considered to be lost to follow up. The follow up rate for patients from the local Capricorn district was significantly better than that for the other districts ($p < 0.05$).

The median age at diagnosis of children who had surgery was 6 months (range 1 to 68 months).

The median age at diagnosis of those children who were declared inoperable was 10 months (range 1 to 128 months).

Median interval age between diagnosis and surgery was 13 months with the earliest AVSD repair performed at 8 months and latest at 40 months after diagnosis.

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Introduction

In the previous chapter, the results of the study were presented and interpreted. In this chapter, the findings of the study are discussed.

5.2 Ascertainment of AVSD

This study uses 2 parallel mathematical models to estimate the ascertainment of AVSD in children in the Limpopo Province over a 5-year period. The first method is based on the incidence of AVSD in the global population as reported by Hoffman. The second is based on the incidence of trisomy 21 in the general population and the measured association of AVSD with trisomy 21. There was significant and correlating under-ascertainment of AVSD lesions in children based on the 2 methods.

The study enrolled a cohort of all patients diagnosed with AVSD over a 5-year period. During the same 5-year period; 641 686 children were born in Limpopo Province. Not all of study subjects may have been born into this cohort of 641 686 children either because of being born outside the Limpopo Province or because of late diagnosis in a child born prior to the 5-year period. It is also possible that some children born during the 5-year period of the study may have migrated to another province and been diagnosed with heart disease there.

Accepting these possibilities, it still seems reasonable to use 80 as a numerator and 641 686 as a denominator as an approximation of the incidence of AVSD in the Limpopo Province as measured by the number of new cases diagnosed at the cardiology each year. This gives a rate of 125 cases per 1 million live births. This is one third of the approximately 400 per 1 million live births figure for the global incidence of AVSD proposed by Hoffman.

Based on an expected incidence of Down syndrome of 1 in 800 (Haydar et al, 2012) it is estimated that there should have been about 800 children born with Down

syndrome during the 5-year period (125 per 100 000).

Of these about 25% would be expected to have an AVSD (Briggs et al, 2012). This yields an estimated 200 expected cases of AVSD in children with Down syndrome. Again the 67 identified cases of Down syndrome represent about 1/3 of the expected number.

Both estimates suggest that AVSD is significantly under-recognized and under-referred in children in the Limpopo Province. Under-diagnosis of CHD among children in the Limpopo Province has been demonstrated previously (Sutton).

In the instance of AVSD the association with Down syndrome allows for possible earlier recognition than identification through clinical features of a left to right shunt lesion or a murmur. It is notable that there were fewer than expected non-syndromic children in this cohort suggesting that congenital heart disease diagnosed by symptoms and signs of the heart disease alone is likely to be more poorly ascertained.

It is an additional concern that many of these children, nearly 40%, are diagnosed after 6 months of age. This delay points to a pattern of late recognition and referral of this form of congenital heart disease for whatever reason. The delay could be related to the family, the local clinic, the local hospital or all three. The waiting time for assessment at the paediatric cardiology clinic at Pietersburg hospital is seldom more than 2 weeks and usually less than a week. Bookings via a cell phone number are facilitated as much as possible.

5.3 Outcomes

Only 42/67 AVSD patients had documented referral to the surgical centre.

Of these patients, only 15 had documented operations and all were operated late - after 12 months of age. Using the 1 in 3 cases diagnosed figure from the previous discussion fewer than 8% of patients born with an AVSD in the Limpopo Province receive surgery ($15/67 \times 1/3 = 15/201$).

The reasons for this very low access to heart surgery seem to be 3-fold:

1. Failure to recognize and refer children born with AVSD. This conclusion is based on the epidemiological assumptions made above.
2. Late diagnosis and referral of patients to the cardiac centre. All patients were operated after 1 year of age and 8 were deemed inoperable (possibly due to irreversibly increased pulmonary vascular resistance).
3. Loss to follow up following diagnosis. Because this is a retrospective study there may be missing data, but this measured loss to follow up is also of great concern. It may reflect that the idea of heart surgery did not rest well with the caregiver or it may reflect challenges with attending follow up visits. A referral visit to the surgical centre in Gauteng is a 3-day enterprise involving travelling from home to the local hospital then on to Pietersburg Hospital and finally the surgical centre and then back again. This may be too great a socioeconomic cost for the caregivers. In this regard it is notable that patients living outside the local Capricorn District in Limpopo had a much higher rate of default than those from within the Capricorn District. This points to a possible effect of geographical distance from point of care on the attendance pattern of the patients and their caregivers.

5.4 Conclusion

By applying known global epidemiology to census data for an area serviced primarily by a single paediatric cardiology diagnostic centre it was possible to estimate the effectiveness of care for children with AVSD born in the Limpopo Province.

The results of this study suggest that most children with AVSD in the Limpopo Province do not access diagnostic evaluation. In addition, it seems likely that most children born in the Province with Down syndrome are not referred for screening for congenital heart diseases. It seems reasonable to infer that similar under-referral applies to all children born with congenital heart disease. This is supported by other data (Sutton).

The argument that there is under-referral is also supported by the finding that more

than a third of the children were referred after 6 months of age. These children are susceptible to the development of pulmonary vascular obstructive disease and delays in diagnosis put them at risk of being ineligible for surgery and of irreversible morbidity.

The study also showed that the rate of achieving successful surgical repair is very low. The cause of this was not investigated but all patients were operated after 12 months of age. This suggests the presence of bottlenecks in the service between diagnosis and surgery and could relate to delays in up-referral, under-capacitated paediatric cardiology and paediatric heart surgery services or challenges with logistical issues such as transport.

A considerable number of patients were lost to follow up, again the reasons for this were not explored further. However, there was an association between proximity to the service at Polokwane and successful follow up. This raises the possibility that geographic barriers add to other challenges faced by the caregivers of these children.

5.5 Limitations

This study is limited by its relatively small sample size and single-centre retrospective nature. There was missing information on patients' records and some patients' hospital files were missing. There is, however, no reason to suspect that the missing files would have systematically biased the findings in an adverse fashion.

5.6 Recommendations

Early referral and surgical intervention should be the goal in patients with AVSD to prevent complications like Eisenmenger and failure to thrive. All children born with Down syndrome should be referred for an early echocardiogram to screen for congenital heart disease.

Key clinical features of congenital heart disease with left to right shunts should be flagged for inclusion in educational opportunities with doctors and nurses working in

clinics and district hospitals in Limpopo. In addition, there is a need to raise awareness of all forms of congenital heart disease, its early symptoms and signs and the available referral services.

In order to facilitate better care for all children with CHD in Limpopo the development of a more extensive paediatric cardiology service with an associated paediatric cardiac surgical service is strongly recommended. This will help to eliminate barriers to access created by geographical distance between the child and the service. The population and birth rate in the province easily justify the need for such a service.

Caregivers of children with T21 and AVSD possibly need more support to ensure that they do not fail to follow up for social or logistical reasons. There is a serious need for a support group of caregivers of children with Down syndrome and AVSD. Further surveillance of new cases and the outcomes is merited to provide ongoing guidance to managers and health service planners.

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Annexure 1: Data collection sheet

Ascertainment and outcomes of Atrioventricular septal defects in Limpopo Province, South Africa

1. Allocation Number:

IDENTIFICATION:

2. DATE OF BIRTH: 3. GENDER:

4. DATE OF DATA COLLECTION:

5. DATE OF DIAGNOSIS:

6. AVSD: 1. COMPLETE:
2. INCOMPLETE / PARTIAL:

7. ADDITIONAL CARDIAC ABNORMALITIES

IF YES TO 7: -
1. _____
2. _____
3. _____

8. ASSOCIATED SYNDROME:

9. CHROMOSOMAL STUDIES DONE:

IF YES TO 8 OR 9:

RESULTS:

10. REFERRED FOR SURGICAL ASSESSMENT: YES NO

11. OPERATION DONE: - YES NO

IF YES TO 11:

▪ NATURE OF OPERATION: -

▪ DATE OF OPERATION:

12. DATE OF LAST VISIT:

13. OUTCOME:

▪ ATTENDING FOLLOW UP YES NO

IF YES: -

➤ ON CARDIAC MEDICATIONS:

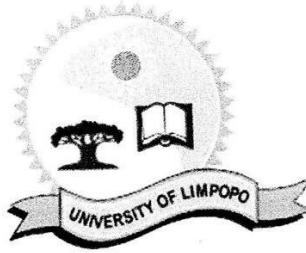
➤ NOT ON CARDIAC MEDICATIONS:

▪ LOST TO FOLLOW UP: YES NO

▪ DIED: YES NO NOT KNOWN

14. Referring Hospital:

Annexure 2



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Department of Research Administration and Development
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**TURFLOOP RESEARCH ETHICS
COMMITTEE CLEARANCE CERTIFICATE**

MEETING: 05 July 2016

PROJECT NUMBER: TREC/85/2016: PG

PROJECT:

Title: Ascertainment and outcomes of atrioventricular septal defects in Pietersburg Hospital, Limpopo Province, South Africa

Researcher: Mr GP Shibambu

Supervisor: Dr C Sutton

Co-Supervisor: N/A

School: Medicine

Degree: Masters in Paediatrics and Child Health


PROF. TAB MASHEGO
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: REC-0310111-031

Note:

- i) Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee.
- ii) The budget for the research will be considered separately from the protocol.
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.

Annexure 3



LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

Enquiries: Latif Shamila (015 293 6650)

Ref:4/2/2

Shibambu GP
University of Limpopo
Private Bag X1106
Sovenga
0727


Greetings,

RE: Ascertainment and outcomes of atrioventricular septal defects in Pietersburg Hospital, Limpopo Province, South Africa

The above matter refers.

1. Permission to conduct the above mentioned study is hereby granted.
2. Kindly be informed that:-
 - Research must be loaded on the NHRD site (<http://nhrd.hst.org.za>) by the researcher.
 - Further arrangement should be made with the targeted institutions, after consultation with the District Executive Manager.
 - In the course of your study there should be no action that disrupts the services.
 - After completion of the study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
 - The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
 - The above approval is valid for a 3 year period.
 - If the proposal has been amended, a new approval should be sought from the Department of Health.
 - Kindly note, that the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated.


Head of Department


Date