World Journal of Cardiology

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DOI: 10.4330/wjc.v9.i3.277

World J Cardiol 2017 March 26; 9(3): 277-282
ISSN 1949-8462 (online)

ORIGINAL ARTICLE

Prospective Study

Children with transposition of the great arteries: Should they actually be born in Nigeria?

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Author contributions: Animasahun BA, Madise-Wobo AD, Gbelee HO and Omokhodion SI contributed equally to this work; Animasahun BA designed the research study; Animasahun BA, Madise-Wobo AD and Gbelee HO performed the research; Animasahun BA, Madise-Wobo AD, Gbelee HO and Omokhodion SI supplied the analytic tools; Animasahun BA and Madise-Wobo AD analyzed the data; Animasahun BA, Madise-Wobo AD, Gbelee HO and Omokhodion SI wrote the data; all the authors approved the final manuscript.

Institutional review board statement: The authors declare that no patient personal data appeared in this write-up. Echocardiography was done as part of the needed investigations in the care of the patients. No experiments were performed on the patients for this article.

Clinical trial registration statement: None of the subjects in this study were used for clinical trial.

Informed consent statement: Informed and written consent were obtained from the parent of the subjects before enrolment in the study.

Conflict-of-interest statement: No conflict of interest among the authors.

Data sharing statement: The data of the subjects in the study has not been shared with any individual or institution.

Manuscript source: Invited manuscript

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Received: August 24, 2016
Peer-review started: August 25, 2016
First decision: October 20, 2016
Revised: December 8, 2016
Accepted: January 2, 2017
Article in press: January 3, 2017
Published online: March 26, 2017

Abstract

AIM

To describe the clinical and echocardiographic features of Nigerian children with transposition of the great arteries and emphasize the need for collaboration with cardiac centres in the developed countries to be able to salvage the children.

METHODS

Prospective and cross sectional involving consecutive patients diagnosed with transposition of the great arteries using clinical evaluation and echocardiography at the Paediatric Department of Lagos State University

Teaching Hospital, Lagos Nigeria as part of a large study between January 2007 and December 2015.

RESULTS

There were 51 cases of transposition of the great arteries within the study period with a male to female ratio of 2:1 and a prevalence of 1.55 per 10000 among population of children who presented to centre during the study. Its proportion amongst children with congenital heart disease was 4.9%, while it was 15.4% among those with cyanotic congenital heart disease. The mean age ± SD of the subjects was 10.3 ± 21.8 mo. Up to 70% of the patients were less than 6 mo of age at initial presentation. The most common mode of presentation was cyanosis. The most common associated intracardiac anomaly was ventricular septal defect which occurred in 56% of the patients.

CONCLUSION

Transposition of the great arteries is as common in Nigeria as in the other parts of the world. The most common mode of presentation was cyanosis. There is an urgent need to establish paediatric cardiac centres in Nigeria if these children are to be salvaged.

Key words: Transposition; Cyanosis; Children; Salvage; Nigeria

Core tip: Transposition of the great arteries is as common in Nigeria as in the other parts of the world. The most common mode of presentation in our subjects was cyanosis. Palliative and definitive interventions are currently not available for them in Nigeria. A lot of lives are being wasted yearly because of unavailable and inaccessible surgical care.

Animasahun BA, Madise-Wobo AD, Gbelee HO, Omokhodion SI. Children with transposition of the great arteries: Should they actually be born in Nigeria? *World J Cardiol* 2017; 9(3): 277-282 Available from: URL: http://www.wjgnet.com/1949-8462/full/v9/i3/277.htm DOI: http://dx.doi.org/10.4330/wjc.v9.i3.277

INTRODUCTION

Transposition of the great arteries (TGA) affects children of all races as documented earlier[1,2] and African children are no exception[3,4]. Advance surgical techniques to manage children with congenital heart lesions is still in infancy stage in Nigeria[5,6]. That notwithstanding, cases of TGA are seen and managed within the available limitations. There are only very few reports on TGA in Africa especially from sub-Saharan Africa. At best TGA is only mentioned as part of other congenital heart disease or as case reports. There has been no report on cohorts of children with TGA in West Africa. This article will describe the pattern and presentation of children diagnosed with TGA and the management and outcome of such patients in a tertiary hospital in sub-Saharan Africa. This is to make data available on these group of subjects for reference purpose for future research in the region, create awareness on TGA among health professionals in the region and for advocacy on the urgent need to establish paediatric cardiac centres in Nigeria so that these children can be salvaged, especially the need for collaboration with established paediatric cardiac centres in the developed countries in order to improve the outcome of children born with TGA in the West Africa region through early diagnosis and prompt intervention.

MATERIALS AND METHODS

This was a review of prospectively collected data of all patients less than 13 years of age diagnosed with TGA using echocardiography at the Paediatric Department of Lagos State University Teaching Hospital Lagos Nigeria between January 2007 and December 2015.

The hospital is a tertiary institution in Southwestern Nigeria and receives referral from the region. Patients with suspected cardiac lesion are referred to the department for evaluation from within the state and sub-region. A paediatric cardiologist is in charge of the cardiology unit. Patients referred to the cardiology unit of the department are evaluated with chest radiograph, electrocardiography other ancillary investigations as required including echocardiography.

One echocardiography machine was used on all the subjects throughout the study period, a GE Vivid Q echocardiography machine reference number 14502 WP SN 2084. It has facility for two dimensional, M-mode and color flow Doppler imaging. The paediatric cardiologist performed the echocardiography on all the subjects.

Definitive diagnosis is based on echocardiography which demonstrates the characteristic bifurcation of the pulmonary artery arising posteriorly from the left ventricle in the parasternal long axis view and the aorta anterior and to the right of the pulmonary artery. Other associated cardiac anomalies such as the atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus, double outlet right ventricle (DORV), pulmonary stenosis (PS) and abnormal coronary arteries were documented for all the patients. A diagnosis of TGA was made based on the combination of clinical signs and symptoms, with or without a chest radiograph features described above with the characteristic echocardiographic features[7,8].

All the patients were followed up at the paediatric cardiology clinic. Surgical correction was required by all the subjects but this is not available in Nigeria and thus the patients were referred outside Nigeria for the correction. The patients who had surgical correction were referred back to the unit after the correction and they were followed up in the unit.

The data were imputed in a personal laptop and

Table 1 Yearly incidence and percentage of transposition of the great arteries amongst the congenital heart disease

Year	Total patients seen	Patients with CHD (*n*)	Patients with TGA (*n*)	Prevalence of TGA amongst CHD (%)	Prevalence of TGA per 10000 children
2007	47343	87	1	1.15	0.21
2008	49387	119	8	6.72	1.62
2009	49141	90	2	2.22	0.41
2010	36400	103	14	13.59	3.84
2011	37404	153	6	3.92	1.60
2012	28475	143	4	2.79	1.40
2013	32220	180	6	3.33	1.86
2014	32800	108	7	6.48	2.13
2015	13492	140	3	2.14	2.22
Total	326662	1123	51	4.54	1.56

TGA: Transposition of the great arteries; CHD: Congenital heart disease.

analysed using Statistical Package for Social Sciences version 20. The children's age, sex, indication for echocardiograph, echocardiographic findings and outcome and were documented. Tables and charts were used to depict those variables. Means of continuous variables were compared using the Student *t* test, and proportions using χ^2 test. Level of significance set at $P < 0.05$.

RESULTS

Prevalence of TGA

Prevalence rates were based on 51 cases of TGA diagnosed between January 2007 and December 2015. A total of 326662 children were seen at the department during the study period and 1693 had echocardiography done. Of the 1693 who had echocardiography done, 1123 had congenital heart diseases (772 and 351 for acyanotic and cyanotic congenital heart defects respectively).

Table 1 shows the yearly distribution, prevalence of TGA and proportion of subjects with TGA amongst the cases of congenital heart disease. The prevalence of TGA within the study period was 1.55 per 10000 populations of children who present to the hospital. The percentage of TGA amongst children with congenital heart disease was 4.5% and 14.5% amongst those with cyanotic congenital heart disease.

Clinical presentation

There were 51 cases of TGA within the study period. They comprised 34 males and 17 females with a male to female ratio of 2:1. The mean age of the children at initial presentation in month was 10.3 ± 21.8 with a median age of 4 mo and a bimodal age of 1 and 4 mo. The mean age of the males was 9.3 ± 24.3 while that of the females was 12.2 ± 16.8 ($P = 0.28$). The distribution of the age of the patients was the same across both sexes. The median age for the males and females was 3.5 and 5.5 mo respectively. The modal age for the males was 4 mo while that of the females was bimodal, 2 and 6 mo. Up to 70% of the patients were less than 6 mo of age at initial presentation. The youngest patient was 14 d old while the oldest patient was 11 years old. Table 2 depicts the age distribution of the children at diagnosis.

Table 2 Ages at echocardiography and sex distribution of the patients

Age (mo)	Male	Female	χ^2	*P*
0-6	25	11	2.0	0.36
6.1-12	4	2		
⩾ 12.1	5	4		
Total	34	17		

$\chi^2 = 2.0$, $P = 0.36$.

All the children were ill at presentation. Forty-seven children were cyanosed while 4 were acyanosed at presentation. The indications for echocardiography are depicted in Table 3. In most cases there were more than one reasons/indication for echocardiography. All the study subjects had d-TGA. Other associated intracardiac anomaly are as highlighted in Table 4. The most common associated intracardiac anomaly was ventricular septal defect which occurred in 56% of the patients and this co-existed alone or in combination with other intracardiac connections.

Treatment and outcome

The patients received anti-congestive agents and angiotensin converting enzyme inhibitors. Five patients had surgical intervention done outside the study centre. One patient had atrial switch and is doing well on follow up three years post surgery. The other four had arterial switch surgeries. One patient succumbed at the immediate post up period. Another died about two months' post surgery in a secondary centre. Another died about one-year post surgery secondary to a non-cardiac illness. The remaining patient is on followed up in the department eight-year post-surgery and is stable. The other patients who could not afford treatment succumbed while sourcing for funds to do surgery. More than 90% of the patients died at infancy, a few at about 14 mo of age. All the patients who had surgery were operated in India.

DISCUSSION

TGA is the most common cyanotic congenital heart lesion in the newborn[9]. The Center for Disease Control (CDC) estimated that each year, 1901 babies in the United States are born with TGA or an approximate of 5 in 10000 babies born yearly with it[10]. It is present in 5%-7% of all patients with congenital heart disease[11]. There is a male predominance with a male to female ratio of 1.5:1 to 3:2[12-14]. The mortality in untreated patients is up to 50% in the first month and 90% by the end of the first year[7]. Maron *et al*[1] in the United States over four decades ago, documented that there was no racial difference in the frequency of TGA.

Table 3 Indication for cardiac evaluation of the subjects

Indication	Frequency	% of all patients
Cyanosis	47	92
ACHD	4	7.8
Breathlessness	10	19.6
CCF	1	1.9
Stroke	1	1.9
Murmur	1	1.9
Failure to thrive	1	1.9
Suspected TGA	1	1.9
Dextro Cardia	1	1.9
Down syndrome	2	3.9

Some patients had more than one indication. ACHD: Acyanotic congenital heart disease; CCF: Congestive cardiac failure.

Table 4 Associated intracardiac connections in subjects

Cardiac anomaly	Frequency	% of all TGA
ASD	19	37.3
AVCD	3	5.9
DORV	10	19.6
HLH	1	1.9
PDA	15	29.4
PFO	2	3.9
PS	6	11.8
TAPVC	1	1.9
TOF	1	1.9
TR	3	5.9
VSD	27	52.9

Most patients had more than one intracardiac connections. TGA: Transposition of the great arteries; ASD: Atrial septal defect; AVCD: Atrioventricular canal defect; DORV: Double outlet right ventricle; HLH: Hypoplastic left heart; PDA: Patent ductus arteriosus; PFO: Patent foramen ovale; TAPVC: Total anomalous pulmonary venous connections; TOF: Tetralogy of fallot; TR: Tricuspid regurgitation; VSD: Ventricular septal defect.

However, a more recent study by Botto *et al*[2] in the same country documented a higher occurrence of TGA in whites compared to negroes. In 10% of cases of TGA association with noncardiac malformations have been documented[15].

The aetiology is largely unknown. Associated risk factors include gestational diabetes mellitus[16,17], maternal exposure to rodenticides and herbicides[18] and maternal use of antiepileptic[19]. Genetic mechanisms have been implicated and some genetic mutations have been implicated[20,21].

The prevalence of TGA in this study was 1.55 per 10000 populations of children who presented to the hospital. This result is less than the CDC report of 5 in 10000 live births in the United States[12]. However the CDC report is a study on the proportions of live birth which is a different denominator compared to the present study. We have also documented the yearly prevalence of TGA. It was highest in 2010, 3.84 per 10000 children and lowest in 2007, 0.21 per 10000 children per year. Reasons why it may have been low in the first year is because the echocardiography machine was just made available and there was little awareness of its availability for evaluation of children with structural heart disease within the region. Thus there were little referral for cardiac evaluation at that time. The prevalence rate documented in this study may be a far cry from the actual prevalence rate because a lot of cases may have been missed in the neonatal period and early infancy for a number reasons. Firstly, prenatal cardiac evaluations are rarely done in Nigeria thus a sizeable number may have been missed at birth. Secondly, the clinical presentation of TGA is non-specific and thus a number of cases may have been ill and in the absence of proper evaluation with a high index of suspicion of a congenital heart disease some babies may have be managed for other morbidities and died without a cardiac evaluation. Thirdly, because of cultural practices prevalent in the region, infants who died before a proper evaluation was done may not have autopsy done to confirm a suspicion of a congenital heart disease and TGA to be specific[22].

TGA was documented in 4.5% of all congenital heart disease within the study period. Two decades ago, Jaiyesimi *et al*[23] in UCH Ibadan documented a prevalence rate of 4.8% in cardiac lesions which is similar to findings in the present study. International rate of TGA amongst all congenital heart lesion is 5%-7%[14] and this is also similar to the value documented in the present study. We also documented a male predominance in TGA with a male to female ratio of 2:1. This is consistent with international ratio of 1.5:1-3.2:1[12-14].

The mean age of the children with TGA was 9.3 ± 24.3. The mean age was not different in both sex. The youngest child was 2 wk and the oldest was 11 years old. Although 70% of the patients were ≤ 6 mo old there were three patients who were three, six and eleven years old and those values significantly affected the mean age and resulted in a large standard deviation. In an earlier study by Adegboye *et al*[4] in Ibadan, southwestern Nigeria, the mean age of the children with TGA who underwent palliative surgery was 6.8 ± 2.4. The mean age recorded in Ibadan was not significantly different from that documented in this study although the subjects were fewer in the later study. In contrast, in advanced countries, diagnosis of TGA is made in neonatal period.

Patients with TGA present with central cyanosis from the first month of life with varying clinical manifestation based on the degree of mixing between the two circulations[17]. Patients with a large ventricular septal defect and or a patent ductus arteriosus (PDA) may present early with congestive cardiac failure. Long term complications are secondary to cyanosis. A definitive diagnosis of TGA is made with an echocardiogram[8].

The most common mode of presentation in our subjects was cyanosis and some patients presented with more than one presentation. This is not an unusual finding as the signs and symptoms of TGA varies depending on the associated intracardiac lesion[8].

Cyanosis may go unnoticed in some patients with large ventricular septal defects without right outflow. Similarly, 8% of our study subjects were not cyanosed at presentation and one had congestive cardiac failure.

Complications from cyanosis and polycythemia may occur especially in untreated cases. One of the subjects was a 3.25-year-old male who had been cyanosed from infancy, he presented to the hospital for the first time with cerebrovascular accident and cardiac evaluation revealed a TGA.

D-TGA is the common form of TGA worldwide and all our study subjects had d-TGA. Simple TGA is not compatible with extra-uterine life except there are intracardiac connections for admixture of blood[24,25]. All our subjects had intracardiac connections and not surprisingly the most common was a VSD which occurred either alone or in combination with other intracardiac lesions. ASD was the second most common closely followed by a PDA in 37.3% and 29.4% respectively. Left ventricular outflow obstruction may occur in one eight to a third of patients with TGA. We report in this study 12.5% of cases of pulmonary stenosis and all but one of those subjects had an associated VSD while the other patient had an atrioventricular canal defect. Other complex lesions documented in this study are TOF, hypoplastic left heart, TAPVC, DORV and tricuspid atresia.

TGA is known to be associated with other congenital disorder in 10% of cases[6]. Sporadic association of TGA with trisomy 8, 18, VACTERL and CHARGE syndrome have been documented[26,27]. Two (3.9%) of our subjects had Down syndrome and the others had no dysmorphologies.

Treatment of patients with TGA is both medical and surgical. Initial palliative care is instituted to achieve optimal intercirculatory mixing and optimize the clinical condition[7,18]. Mechanical ventilation and oxygen may be needed for unstable infants, correction of metabolic acidosis and administration of prostaglandin E_1 to maintain arterial duct patency[7]. Balloon atrial septostomy may be done to maintain admixture of blood at atrial level. Surgery provides the definitive treatment. It may be offered within the first month of life depending on the clinical setting. The arterial switch procedure can be done. Others include the Rastelli operation and Nikaidoh's procedure[8].

In the current study, all our patients required definitive surgical corrections which is currently not available in Nigeria. Only three (5.9%) could afford to do corrective surgery outside Nigeria. Three patients presented within the first two weeks of life and all three had a PDA with either a VSD or an ASD. They required palliative surgery but could not afford one. Almost 90% of the patients could not access the much needed surgical care and succumbed before help could be provided. This was not surprising because the case fatality rate for TGA is as high as 50% by the end of the first month and 90% at one year for untreated cases. These are largely preventable deaths if diagnosis can be made on time and appropriate treatment instituted timely.

In conclusion, transposition of the great arteries is as common Nigeria as in the other parts of the world. The most common mode of presentation in our subjects was cyanosis. Palliative and definitive interventions are currently not available for them in Nigeria. A lot of lives are being wasted yearly because of unavailable and inaccessible surgical care. There is an urgent need to establish paediatric cardiac centres in Nigeria so that these children can be salvaged. Collaboration is needed from established paediatric cardiac centres from developing and developed world if this is to be achieved.

ACKNOWLEDGMENTS

The patients, parents and caregivers involved in this study are acknowledged including all the health professionals involved in their care.

COMMENTS

Background

Transposition of the great arteries (TGA) affects children of all races as documented earlier including African children. Prompt and advance surgical intervention needed to salvage these children is currently not available in Nigeria.

Research frontiers

Arterial switch is one of the surgical option for correction of TGA is preferable done during the neonatal period.

Innovations and breakthroughs

This article described pattern and presentation of children diagnosed with TGA and the management and outcome of such patients in a tertiary hospital in sub-Saharan Africa. Data on these group of subjects has been provided by this study for reference purpose.

Applications

The data provided in this study is useful for, future research in the region on the subject, awareness creation on TGA among health professionals in the region, for advocacy on the urgent need to establish paediatric cardiac centres in Nigeria if these children can be salvaged, especially the need for collaboration with established paediatric cardiac centres in the developed countries in order to improve the outcome of children born with TGA in the West Africa region through early diagnosis and prompt intervention.

Terminology

TGA is a congenital heart anomaly that occurs when the two main arteries of the heart, aorta and pulmonary arteries, are switched in position so that the aorta arises from the right ventricle and the pulmonary artery from the left ventricle. Other names or synonyms used to describe TGA are: Physiologically uncorrected transposition, complete transposition and atrioventricular concordance with ventriculoarterial discordance. TGA is classified based on the spatial relationship between the great arteries to each other and or the infundibular morphology. dextro-TGA (D-TGA) is when the aorta is anterior and to the right of the pulmonary artery and it is the most common form. levo-TGA (L-TGA) describes the aorta that is anterior and to the left of the pulmonary artery. Furthermore, irrespective of either the L- or D-TGA, the patients may still have a subaortic infundibulum, absence of a subpulmonary infundibulum and a fibrous continuity between the mitral and pulmonary valves. Aside the above classifications, different presentations and exceptions have been described. However, the unifying hallmark is the ventriculoarterial discordance. In TGA, the pulmonary and systemic circulations run in parallel rather than in series. Oxygenated blood flows through a closed circuit that involves the lungs and left

cardiac chambers, while deoxygenated blood also flows in a closed circuit that starts from the systemic circulation and ends in the right heart chambers. This parallel circulation is incompatible with prolonged survival, so there is usually admixture of blood through the atrial or ventricular septum and or a patent ductus arteriosus.

Peer-review

The paper is well-written and provides an appropriate view about the current situation and future interventions.

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P- Reviewer: Chello M, den Uil CA, Watanabe T
S- Editor: Gong XM **L- Editor**: A **E- Editor**: Wu HL

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