

# Status of Congenital Heart Defects in Nigeria: The Role of Cardiac Surgery

Ikechukwu A. Nwafor\*, John C. Eze

National Cardiothoracic Center of Excellence, University of Nigeria Teaching Hospital, Ituku-Ozalla, Nigeria

Email: Igbochinanya2@yahoo.com, \*ikechukwu.nwafor@unn.edu.ng

**How to cite this paper:** Nwafor, I.A. and Eze, J.C. (2019) Status of Congenital Heart Defects in Nigeria: The Role of Cardiac Surgery. *World Journal of Cardiovascular Surgery*, 9, 63-72.

<https://doi.org/10.4236/wjcs.2019.97008>

**Received:** May 27, 2019

**Accepted:** July 3, 2019

**Published:** July 5, 2019

Copyright © 2019 by author(s) and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution-NonCommercial International License (CC BY-NC 4.0).

<http://creativecommons.org/licenses/by-nc/4.0/>



Open Access

## Abstract

**Background:** Unlike in developed countries, the delivery of cardiovascular services to children born with congenital heart defects in Nigeria is inadequate. There are problems at both pediatric and adult ages with high morbidity and mortality on account of inadequate surgical care. **Objective:** To determine the status of congenital defects and assess the impact of foreign cardiac missionary missions vis-à-vis the effects on the magnitude as well as on the educational program for the local cardiac team. **Materials and Method:** In the last 5.5 years, Foreign Cardiac Surgery missions were reinstated at National Cardiothoracic Center of Excellence, Enugu, Nigeria. The participants performed cardiac interventions on a variety of patients with CHD. We performed a retrospective review of this endeavor. Patients' demographics, number of patients, age ranges, types of CHD and clinical evaluation methodology were obtained from our hospital's record department. We also assessed types of cardiac interventions, outcome and challenges and the impacts of the foreign cardiac surgery missions. **Results:** During the study period, a total of 72 children with CHD were evaluated. They were 39 males and 33 females. The age ranged between 0 - 10 years in children and 41 - 50 years in the adult. We studied both simple and complex anomalies. A VSD was the commonest (n = 22, 27.16%). **Conclusion:** Foreign congenital cardiac surgery missions were not able to provide adequate services for the care of CHD that require cardiac surgery both in terms of reduction in magnitude as well as adequate educational program for the local cardiac team. Thus infants, in particular, suffer an early death. The need for governmental support to develop a comprehensive program to care for these patients is essential in Nigeria and other developing countries.

## Keywords

Status, Heart, Congenital, International, Mission

## 1. Introduction

Congenital Heart disease is a structural or a functional defect in the heart and or proximal blood vessels that are present at birth. The incidence is about 8 - 10 per 1000 live births across the globe [1]. Geographically, populations may vary from country to country but the incidence has remained constant worldwide [2]. Children born with CHD in developing countries do not have access to adequate care. There are no country based data for the incidence of CHD birth in Nigeria. However, preliminary data from the National Paediatric Cardiac Registry estimate that about 1296 children are born with CHD annually in Nigeria [3]. Moreover, in a survey by Chinawa JM *et al.*, 71 (0.22%) of children with CHD were detected out of 31,795 children evaluated in an outpatient clinic over a 5-year period in a tertiary hospital in southeastern Nigeria [4]. Since a large number of births in Nigeria take place at home, mostly unsupervised by a qualified doctor or midwife, the above hospital statistics are unlikely to be truly representative. More extensive multicenter studies have provided a consensus that the incidence of CHD in Nigeria is similar to the worldwide estimate of 8 in a thousand live births [5]. The distribution of the anomalies across the country is difficult to estimate. In the tribal inhabitants of parts of the country autopsy is a taboo. Thus determining the distribution of CHD in these areas is impossible.

In Nigeria and other African countries, resources for the management of CHD are overlooked. It is often overshadowed by communicable diseases like malaria, HIV and diarrhea. [6]. Therefore few children with CHD received cardiac interventions via medical tourism, which became popular in the country due to poorly funded and badly managed health sector. Few children whose parents had the financial wherewithal were referred to a neighboring country like Ghana and even to far away India. The country lost about eight hundred million dollars through medical tourism in 2013/2014 [7] [8].

The first recorded foreign congenital cardiac surgery mission for children in Nigeria was in 2003 [9] [10]. Few children with CHD received interventions but the participants were not satisfied owing to poor handling of essential drugs by the local team. Consequently, a period of abeyance occurred. In February 2013, the cardiac missions resumed. The program included both children and adult patients. The missions were relatively regular and some cardiac interventions were carried out at NCTCE/UNTH, Ituku-Ozalla, which hitherto was abandoned due to bad military governance, brain drain, nepotism and interpersonal conflict [11]. The new cardiac missions started because some Nigerians in diaspora wanted to bridge a wide gap created by government's insensitivity to the yelling of many Nigerians with CHD. Their aim actually was to do humanitarian services especially to the indigent patients who cannot afford medical tourism to India, Ghana, Sudan, Egypt, South Africa, UK and USA. Their contributions were like a drop of salt in an ocean, because nongovernmental organizations formed by them concentrated more on Safari or Blitzter types of cardiac surgery missions without inculcating structured educational program for the local staff [12]. Thus after 5.5 years, the local staff who ought to have expanded the man-

agement of cardiovascular services to patients with CHD, failed because of the inadequate educational program for them. Out of many cardiac surgery missions that participated during the period under review, Cardiostart International headed by Dr. Barath Aubyn and ably assisted by Dr. Emily Fakaas provided the most effective and functional educational program that would have positively impacted on the locals but unfortunately, the team had only 2 missions to our center.

## 2. Materials and Method

In the last 5.5 years, from February 2013 to July 2017, Foreign Cardiac Surgery missions restarted in our center and have performed cardiac interventions on some patients with CHD. Patients' selection for interventions was done by the local cardiologists alongside the local surgeons. Inclusion criteria for intervention after assessment included those whose New York Heart Association criteria were from 1 to 2. Those in stages 3 and 4 were often optimized to convert them to stage 2. Exclusion criteria included advanced stage 4 and those in stages 3 and 4 who fail to convert to 2 after optimization.

We performed a retrospective review of those patients assessed during the period including those that were offered surgery and other cardiac interventions. Patient demographics, number of patients, age ranges and sex distribution were obtained from our hospital information technology department. Other data obtained were types of CHD, clinical evaluation methodology, types of cardiac interventions and outcome. The impacts of the missions were assessed by the number of patients treated and the ability of the local team to successfully treat such patients independently. The data were analyzed using Microsoft Excel and presented in percentages using tables and pie charts.

The limitation of the study is a failure to get the memoriam of understanding between the missions and the authorities of the hospital so as to determine whether the missions were purely safari type or for educational program.

## 3. Results

The ages ranged from 0 - 10 to 41 - 50 years (**Table 1**). The range of 0 - 10 was the highest (n = 54, 75.00%), followed by 11 - 20 (n = 12, 16.67%). Other ranges had equal frequency (n = 2, 2.78%). The age ranges above 18 years were regarded as untreated adult congenital heart defects.

**Table 2(a)** shows the common types of CHD. The most common was VSD (n = 22, 27.16%), followed by PDA (n = 20, 24.69%). There was another uncommon complex CHD as shown in **Table 2(b)**. Like other studies, the common CHD like ASD, VSD and PDA predominated in our study. Initially, complex congenital cardiac defects were thought to be nonexistent in Nigeria and indeed other African countries but with advanced technology coupled with expatriate expertise, some are being discovered and treatment offered to them with a relatively good outcome. At the beginning, the complex CHDs were left untreated until William Novick Cardiac Alliance joined the program. Virtually all the

complex CHD treated were done by them.

The symptoms and signs below (**Table 3**) were detected and used in making a provisional diagnosis of CHD. They are not specific. Confirmation was usually obtained from echocardiography. The use of neonatal pulse oximetry in conducting deliveries in hospital is currently not obtainable in Nigeria. To this extent, critical CHD are missed as deaths caused by them are attributed to witches and wizards and in many regions of Nigeria, autopsy in children is regarded as a taboo.

**Table 1.** Age ranges of patients.

SNO	Age range(yrs)	Number	Percentage(%)
1	0 - 10	54	75.00
2	11 - 20	12	16.67
3	21 - 30	2	2.78
4	31 - 40	2	2.78
5	41 - 50	2	2.78
<b>Total</b>		<b>72</b>	<b>100</b>

**Table 2.** (a) Common types of CHD; (b) Other types of CHD.

(a)			
SNO	Types of Congenital Heart Defects	Number	Percentages(%)
1	Atrial Septal Defect(ASD)	14	17.28
2	Ventricula Septal Defects(VSD)	22	27.16
3	Tetraology of Fallot(TOF)	13	16.05
4	Patent Ductus Arteriosus(PDA)	20	24.69
5	Ventricular septal defect(VSD) + Atrial Septal defect(ASD)	3	3.70
6	Others	9	11.11
<b>Total</b>		<b>81</b>	<b>100</b>

(b)			
SNO	Other CHD	Number	Percentages(%)
1	Truncus Arteriosus(TA)	2	22.22
2	Cortriatrium	1	11.11
3	Complete Atrioventricular Canal Defect	1	11.11
4	Pulmonary Atresia with MAPCAS	1	11.11
5	Double Outlet Ventricle(DORV)	2	22.22
6	Ruptured sinus of Vasalva aneurysm	1	11.11
7	Congenital absent posterior and anterior leaflet of tricuspid valve	1	11.11
<b>Total</b>		<b>9</b>	<b>100</b>

**Table 3.** Symptoms and signs of CHD patients.

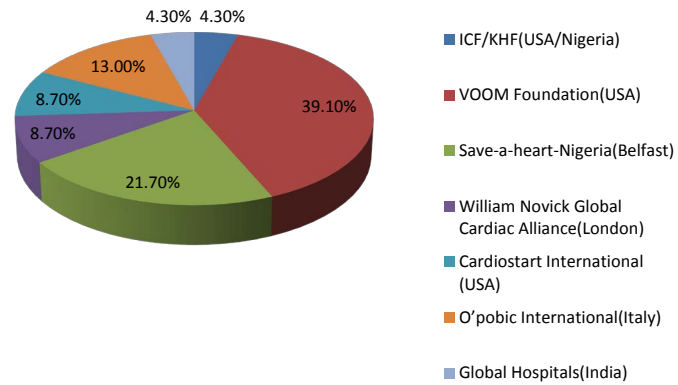
SNO	Pattern of presentations of patient with CHD	Number	Percentage(%)
1	Failure to thrive/delayed milestones	15	13.16%
2	Cyanosis +/- squatting	5	4.38
3	Dyspnoea on exertion – feeding, etc	17	14.91
4	Paroxysmal nocturnal dyspnoea	2	1.75
5	Orthopnoea	5	4.38
6	Cerebrovascular accident/TIA	3	2.63
7	Leg oedema	13	11.40
8	Clubbing of digits	14	12.28
9	Recurrent chest infections (fever, cough)	25	21.93
10	Palpitations	10	8.88
11	Chest pain	8	7.02
<b>Total</b>		<b>114</b>	<b>100</b>

**Table 4** shows the types of CHD, the types of surgical interventions and the outcome. The outcome in the simple CHD appeared excellent unlike the complex types whose outcome is slightly above the 50th percentile. The overall outcome is (n = 66, 81.5%), while in-hospital mortality was (n = 15, 8.5%). The outcome of hospital mortality is difficult to estimate as some of them were lost to follow up. Of the 254 patients with CHD evaluated, only 72 (28.3%) received surgical interventions.

**Figure 1** shows the frequency of visits by foreign cardiac teams to NCTCE, Ituku-Ozalla, Enugu, Nigeria. Apart from 2003, when ICF/KHF undertook pediatric cardiac surgery mission to NCTCE/UNTH, Enugu, Nigeria, none occurred until 2013. From then on five different cardiac teams visited the center during the study period. The frequency of their visits is as stated in the pie chart. VOOM Foundation started first and has undertaken more missions than others. This is closely followed by Save-a-heart Nigeria. Both missions are led by Nigerians in diaspora. The least frequency of missions was done by Cardiostart International and William Novick Global Cardiac Alliance respectively. Incidentally, the duo especially the cardio start had the best educational program for the local team, particularly for the surgeons. The philosophy of this particular team is that success or impact is determined by the number of successful operations the local team is able to undertake after their departure.

#### 4. Discussion

Few other medical disciplines have required for their development the degree of daring courage, tenacity, and drive that characterized the efforts of early pioneers in the field of congenital cardiac surgery. Only a century ago, Theodore Billroth publicly condemned the dream of cardiac surgical interventions by stating that “any surgeon who wishes to preserve the respect of his colleagues would never attempt to operate on the heart” [13].



**Figure 1.** Frequency of visits by foreign cardiac teams to NCTCE, Ituku-Ozalla, Enugu, Nigeria.

**Table 4.** Types of Intracardiac Repair (ICR) or Extracardiac Repair (ECR) and outcome.

SNO	Types of CHD	Types of repair	Percentage (%) outcome
1	PDA	PDA ligation with prolene and Silk sutures	1 died, 1 taken (aneurismal) taken to Italy for repair, 95% outcome
2	ASD	Closure with a patch/direct suture closure	100% outcome
3	VSD	Patch closure of the defect	82% outcome
4	TOF	Closure of VSD with a patch + infundibulotomy/infundibulectomy	45% outcome
5	Truncus Arteriosus (TA)		50% outcome
6	Co-triatrium	Resection of the membrane	100% outcome
7	Partial AVCD	Repair of the defect with a patch/direct suture closure	100% outcome
8	ASD + VSD	Patch closure of both VSD and ASD	100% outcome
	Total AVCD		50% outcome
9	Ruptured sinus of Vasalva Aneurysm to RV	Suture closure of the defect	100% outcome
10	Congenital absence of posterior + Anterior leaflets of tricuspid valve	Creation of artificial leaflets using pericardium	100% outcome
11	Double Outlet Right ventricle(DORV)	1 received total correction, the other Modified Blalock-Taussig Shunt (MBTS)	50% outcome, one awaits definitive treatment.
12	Pulmonary atresia with MAPCAS	Unifocalisation	0% outcome

Over the last 6 decades, the specialty of pediatric cardiac surgery has evolved from a heroic effort with occasional success into a consolidated, sophisticated specialty with excellent outcome [12]. The large strides made in the developed

regions of the world in diagnostic accuracy and surgical catheter interventional management of complex CHD have not been replicated in Nigeria in particular and other African countries in general [14] [15].

In low economic countries like Nigeria, the status of CHD is far from desirable. The National Pediatric Care Registry revealed that about 1296 children are born with CHD in Nigeria annually [3], but this did not capture those born in rural areas without access to hospitals for appropriate diagnosis and documentation. Thus, an estimated figure of about 24,000 children is born with CHD in Nigeria annually. According to local studies, few of them are detected in the hospital setting and many of these children die due to lack of treatment [16] [17].

Subsequently, children born with CHD especially the critical ones died untreated and at times undiagnosed. Few of them, however, benefited from transfer to Ghana, Sudan, Egypt and India [18]. However, by 2013, another foreign cardiac surgery program started and this time it focused on both children and adults. Data from this mission revealed that in children and adults with CHD, the prevalence has been found to be dramatically higher than that observed in Sudan [19]. In our study, the age of the patients treated ranged from 0 - 50 years. See **Table 1**. In a similar study, Sadoh WE *et al.* found 81.7% of patients with CHD to be <2 to 10 years and 6.9% among those above 10 years [20]. In Cameroon, 13.1% of patients with suspected pathologies aged between 2 months and 41 years (mean  $10 \pm 9$  years) during a 4 year study period. [21]. A survey conducted in Mozambique provided the prevalence rate of CHD in the general population of public school children in Maputo. 5 out of 2170 with a prevalence of 2.3 in 1000, of which 80 were newly diagnosed [22].

In addition, data from Northern Nigeria (Northwest, Northeast, and North-central geopolitical zones), showed that 1312 patients aged between 9 days to 30 years had an abnormal echocardiogram, 122 (9.3%), demonstrating CHD [23]. In this study, almost all types of CHD were represented with VSD topping the list of simple or common CHD (27.16%) and is closely followed by PDA (24.69%). Among the uncommon or complex ones, truncus arteriosus was the most common (22.22%) while the rest appeared single (11.11%). See **Table 2(a)** & **Table 2(b)**. We confirm a similar study in Nigeria, the predominant lesions noted were VSD and among cyanotic lesions, TOF [24]. However, in our study and in others, critical congenital heart defects such as left-sided obstructive lesions were rare, suggesting the poor survival of affected children. This finding suggests the Likelihood that the data available underestimated the true prevalence of CHD in Nigeria [15]. The symptoms and signs of CHD as presented in **Table 3** were noted among the patients reviewed, but lack of pediatric pulse oximeter prevented detections of critical CHD after births with such neonates dying of undetermined cause and autopsy in some regions in Nigeria, particularly in pediatric age group is regarded a taboo.

In this study, all the patients received traditional open surgical intervention

despite the availability of Cardiac catheterization equipment. This is because at the initial stage of the missions UPS was not available to run the machine and also of the fact that many of the visiting teams did not come with personnel (s) with requisite skills in interventional technique. In similar work done in Croatia, Novick WM *et al.* stated that International Children Heart Foundation (ICHF) interventional cardiologist was involved in training the local cardiologists during the 10-year International pediatric Cardiac Assistance in Croatia [25].

The challenges of managing CHD by foreign cardiac surgery missions can be divided into four types, Viz: 1) late presentation of patients, 2) Many patients to attend to in a limited period of time, 3) Inaccurate diagnosis of cases prior to their visits due to the limited knowledge of the local team as well as nonavailability of the requisite equipment and 4) Poor postoperative management especially in cases with eventful and prolonged postoperative course, again due to absent requisite skills from the local team to deal with them upon the departure of the visiting teams [26] [27].

## 5. Conclusion

The status of CHD in Nigeria calls for urgent attention from government including public-spirited individuals, nongovernmental organizations and International Agencies. A properly structured pediatric cardiac program will bring the problems of CHD patients in Nigeria to a manageable size. While the International cardiac Surgery missions are providing some relief, their efforts are definitely not enough. They should, in addition, do more on educational program of the local team, who will in turn expand and take care of a greater number of patients.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

- [1] Fyler, D.C., Buckley, L.P., Hullebrand, W.E. and Cohn, H.E. (1980) Report of the New England Regional Infant Cardiac Program. *Pediatrics*, **65**, 375-461.
- [2] Abdulla, R. (1997) What Is the Prevalence of Congenital Heart Defect? *Pediatric Cardiology*, **18**, 268. <https://doi.org/10.1007/s002469900172>
- [3] Ekure, E.N., Bode-Thomas, F., Sadoh, W.E., Orogade, A.A., Otaigbe, B.E., Ujunwa, F., *et al.* (2017) Congenital Heart Disease in Children; Preliminary Data from the National Paediatric Cardiac Registry. *World Journal for Pediatric and Congenital Heart Surgery*, **8**, 699-706. <https://doi.org/10.1177/2150135117725457>
- [4] Chinawa, J.M., Eze, J.C., Obi, I., Arodiwe, F., Ujunwa, F., Daberechi, D.K. and Obu, H.A. (2013) Synopsis of Congenital Heart Defects among Children Attending University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu. *BMC Research Notes*, **6**, 475. <https://doi.org/10.1186/1756-0500-6-475>
- [5] Ejim, E.C., Ike, S.O., Anisuba, B.C., Onwubere, B.J. and Ikeh, V.O. (2009) Ventricular Septal Defect at University of Nigeria Teaching Hospital, Enugu: A Review of



- Echocardiographic Records. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **103**, 159-161. <https://doi.org/10.1016/j.trstmh.2008.06.016>
- [6] Hewitson, J. and Ziller, P. (2010) Children Heart Disease in Sub-Saharan Africa: Changing the Burden of Disease. *SA Heart*, **7**, 8-29. <https://doi.org/10.24170/7-1-1964>
- [7] Epundu, U.U., Adinma, A.O., Ogbonna, B.O. and Epundu, O.C. (2017) Medical Tourism Public Health and Economic Development in Nigeria: Issues and Prospects. *Asian Journal of Medicine and Health*, **7**, 1-10.
- [8] Omisore, E.O. and Agbabiaka, H.I. (2016) Factors Influencing Patronage of Medical Tourism in Metropolitan Lagos, Nigeria. *International Journal of Scientific & Technology Research*, **5**, 31-40.
- [9] The Kanu Heart Foundation. <http://www.kanuheartfoundation.ng.com>
- [10] Enugu, O.I. and Kanu Heart Foundation (2003) The Nigerian Tribune.
- [11] Orjiako, A.B. (1996) Interprofessional Conflict Resolution in the Health Sector. *Nigerian Journal of Medicine*, **5**, 28-31.
- [12] Nina, V.J.S., Farkas, E.A., Nina, R.V.A.H. and Aubyn, M. (2017) Humanitarian Missions: A Call for Action and Impact from Cardiovascular Surgeons. *Brazilian Journal of Cardiovascular Surgery*, **32**, 3-5. <https://doi.org/10.21470/1678-9741-2017-0197>
- [13] Nwafor, I.A., Eze, J.C., Anyanwu, C.H., Ezemba, N., Onyia, U.O.C., Enwerem, N.J., et al. (2017) The Scope of Cardiac Surgery at a National Cardiothoracic Center of Excellence (NCTCE) in Nigeria: A 3-Year Review. *Journal of Vascular Medicine and Surgery*, **5**, 308.
- [14] Mocumbi, A.O., Lameira, E., Yaksh, A., et al. (2011) Challenges on the Management of Congenital Heart Disease in Developing Countries. *International Journal of Cardiology*, **148**, 285-288. <https://doi.org/10.1016/j.ijcard.2009.11.006>
- [15] Mocumbi, A.O. (2012) The Challenges of Cardiac Surgery for African Children. *Cardiovascular Journal of Africa*, **23**, 165-167. <https://doi.org/10.5830/CVJA-2012-013>
- [16] Lakhota, S., Mathur, S.K., Das, N.N., Gupta, R.K. and Maiti, D. (2016) Surgical Outcome of Congenital Heart Disease Cases: A single Unit Analysis in an Upcoming Centre in Eastern Uttar Pradesh, India. *International Journal of Contemporary Medical Research*, **3**, 1842-1844.
- [17] Nwafor, I.A., et al. (2016) Management of Complex Congenital Heart at the National Cardiothoracic Center of Excellence, University of Nigeria Teaching Hospital, Enugu: The Role of Foreign Cardiac Mission in 3.5 Years. *Cardiology in the Young*, **27**, 1174-1179. <https://doi.org/10.1017/S1047951116002766>
- [18] Makinde, A.O. (2016) Physicians as Medical Tourism Facilitators in Nigeria: Ethical Issues. *Croatian Medical Journal*, **57**, 601-604. <https://doi.org/10.3325/cmj.2016.57.601>
- [19] Sufala, K.M. and Karani, Z. (2007) Diagnosis Management and Outcome of Heart Diseases in Sudanese Patients. *East African Medical Journal*, **84**, 434-440. <https://doi.org/10.4314/eamj.v84i9.9553>
- [20] Sadoh, W.E., Uzodimma, C.C. and Daniels, D. (2013) Congenital Heart Defects in Nigeria: A Multicenter Echocardiographic Study. *World Journal for Pediatric and Congenital Heart Surgery*, **4**, 172-176. <https://doi.org/10.1177/2150135112474026>
- [21] TaantchouTchoumi, J.C., Ambassa, J.C., Kingue, S., et al. (2011) Occurrence, Aetiology and Challenges in the Management of Congestive Heart Failure in

- Sub-Saharan Africa. Experience of the Cardiac Center in Shisong, Cameroun. *Pan African Medical Journal*, **8**, 11. <https://doi.org/10.4314/pamj.v8i1.71059>
- [22] Marijon, E., Tivane, A., Voicu, S., *et al.* (2006) Prevalence of Congenital Heart Disease in Schoolchildren of Sub-Saharan Africa, Mozambique. *International Journal of Cardiology*, **113**, 440-441. <https://doi.org/10.1016/j.ijcard.2006.06.049>
- [23] Sani, M.U., Mukhtar-Yola, M. and Karaye, K.M. (2007) Spectrum of Congenital Heart Disease in a Tropical Environment: An Echocardiography Study. *Journal of the National Medical Association*, **99**, 665-669.
- [24] Nwafor, I.A. and Eze, J.C. (2019) Surgical Management of CHD in the adult population: the role of humanitarian cardiac surgery missions in Nigeria. *Cardiology in the Young*, **29**, 11-15.
- [25] Novick, W.M., Aric Divancan, V. and Disesa, T.G. (2004) International Pediatric Cardiac Assistance in Croatia: Results of the 10-Year Program. *Croatian Medical Journal*, **45**, 389-395. [https://doi.org/10.1016/S0197-0186\(03\)00301-2](https://doi.org/10.1016/S0197-0186(03)00301-2)
- [26] Nguyen, N., Leon-Wyss, J., Iyer, K.S. and Pezella, A.T. (2015) Paediatric Cardiac Surgery in Low-Income and Middle-Income Countries: A Continuing Challenge.
- [27] Corno, A.F. (2016) Paediatric and Congenital Cardiac Surgery in Emerging Economies: Surgical “Safari” versus Educational Programmes. *Interactive CardioVascular and Thoracic Surgery*, **23**, 163-167. <https://doi.org/10.1093/icvts/ivw069>