Cardiac disease, both congenital and acquired, contributes significantly to morbidity and mortality in children. Congenital heart disease is the most common birth defect and the leading cause of death in the first year of life [1]. The prevalence of congenital heart disease (CHD) has been remarkably constant throughout the world and over the years. Not only is the incidence of CHD relatively predictable, but the relative frequency of the various congenital heart defects varies little [1].

Worldwide, heart disease in children continues to be a major public health problem. This is largely because of rheumatic heart disease [2-3]. Rheumatic fever is more common in developing countries where poverty exists and is rarely present in developed countries. In developing countries, rheumatic fever is more common in developing countries where poverty exists and is rarely present in developed countries. In developing
countries, CHD accounts for almost all heart diseases in children averaging about 10/1000 live births, or 1% of children born each year, which constitute the patient material for pediatric cardiology. A number of factors influence the reported incidence of CHD, including consanguinity, ethnic background, and environmental factors [4-5].

This article addresses the status of pediatric cardiology at the Children’s Heart Center in the American University of Beirut Medical Center (AUBMC) in Lebanon. It describes the epidemiology of CHD at a tertiary center in a developing country, and addresses the available clinical resources as well as the research and educational services.

DEMOGRAPHIC DATA

Lebanon, a developing country with an estimated population of 4 million and an estimated birth rate of 65,000-70,000 live births per year [1-3], has witnessed major developments in the field of pediatric cardiology over the past ten years. At the present time, pediatric cardiac surgeries are performed in five cardiac centers in the country; eight pediatric cardiologists and five surgeons are currently practicing in Lebanon [3].

EPIDEMIOLOGY

The Children’s Heart Center (CHC) at AUBMC provides a complete range of diagnostic, therapeutic, interventional, surgical and follow-up services for children with congenital heart disease. In addition to our center, there are other centers in Lebanon that are involved in delivering care to children with congenital heart disease (CHD) with excellent services.

In a study that was conducted at our center and included 1000 pediatric patients enrolled at the Children’s Cardiac Registry Center (CCRC) between March 1, 1997 and July 30, 2000 [1-2], we noted that 917 (91.7%) had CHD and the rest had acquired AHD (acquired heart disease). Ventricular septal defect was the most common cardiac malformation with a relative frequency of 25.3%, followed by pulmonary stenosis (14.6%), aortic anomalies (8%), ASD (8%) and tetralogy of Fallot (7.8%). Complex cardiac lesions like HLHS, TGA and AVC had lower frequencies at 0.4%, 3.7% and 3.5% respectively (Figure 1). The most common AHD was rheumatic heart disease. The prevalence of many of the cardiac malformations in the CCRC was similar to that reported in the literature. However, some of the complex cardiac lesions were less common; this may have been due to referral bias, or early death of the newborn with complex CHD without recognition of the cardiac malformation. However, due to increased awareness and resources relating to the field of pediatric cardiology over the past few years, the relative frequency of complex CHD recently seen at our center is approaching that in developing countries.

CONSANGUINITY AND CHD

The etiology of CHD is unknown in about 80% of the cases. The causation of different types of congenital heart malformations is suspected to follow a multifactorial pattern of inheritance. The association between different types of congenital heart disease and consanguinity among 759 Lebanese patients were evaluated at the Children’s Cardiac Registry Center (CCRC) at our center [4]. The proportion of first-cousin mating among cardiac subjects was compared to that of the National Collaborative Perinatal Neonatal Network (NCPNN), a voluntary collaborative network of professionals from different health care institutions in Lebanon which have formed an integrated perinatal neonatal database covering deliveries at major hospitals throughout Lebanon. In general, the incidence of overall parental consanguinity and of first-cousin mating among CCRC subjects (34.7% and 20.2% respectively) was much higher than those of the NCPNN subjects (12.8% and 6.5% respectively), the difference being statistically significant ($p < 0.0001$). An increased incidence of parental consanguinity was also observed in each of the following categories: defects of outflow and inflow and of the atrioventricular junction, severe obstructions from hypoplasias and atresias, simple defects of septation and patent arterial duct ($p < 0.017$). The above study emphasizes the role played by homozygous recessive genes in the causation of different types of congenital heart malformations, known to follow a multifactorial pattern of inheritance.

Another study [5] was also conducted to assess the independent effect of consanguinity on the prevalence of congenital heart defects (CHDs), including general and specific types prevalent in newborns admitted to nine hospitals located in Beirut and members of the NCPNN. Cases were 173 newborns admitted to the Neonatal Intensive Care Units (NICU) of participating hospitals during a 3-year period from January 1, 2000 to December 31, 2002 and diagnosed during their hospital stay as having CHD.
Controls consisted of a random sample of 865 newborns without a CHD admitted to the NICU during the same period. After controlling for confounders, first cousin consanguinity remained significantly associated with an increased risk of CHD; infants born to first cousin marriages had a 1.8 times higher risk of having a CHD diagnosed at birth compared to those born to unrelated parents. The results of this study suggest a familial factor in the multifactorial etiology of CHDs. It is worth noting that other studies that were conducted in our country revealed similar findings to ours [6-7].

ADULTS WITH CHD

Adults with CHD are an emerging population. A retrospective study was conducted at our center to assess the patterns of congenital heart disease in un-operated adults over the past 20 years [8]. It included 206 adult patients with CHD who were admitted to our hospital and didn’t have any previous cardiac surgeries. The age on hospitalization ranged from 18 to 71 years (32.8 ± 13.3). Atrial septal defect was the most common cardiac malformation with a relative frequency of 53.4% followed by ventricular septal defects (11.2%), tetralogy of Fallot (10.7%), aortic anomalies (7.3%), pulmonary stenosis (6.3%), Ebstein anomaly (3.9%) and coarctation of aorta (1.9%). Twenty-seven patients (13.1%) had cyanotic CHD. 113/179 patients (63.1%) underwent surgical intervention in the acyanotic group with an operative mortality rate of 2.7%. Total surgical mortality was 4/130 (3.1%).

ACQUIRED HEART DISEASE

Rheumatic fever is still a concern in Lebanon, although a significant decrease in the frequency of rheumatic fever has been noted over the past few years [9-12]. A novel modality for treatment of rheumatic fever has been reported from our center [13]; the national experience with bacterial endocarditis in the pediatric population in Lebanon has been mostly similar to that reported from developing countries and somewhat different from that in developed countries, although this pattern appears to be changing over the past few years. Bacterial endocarditis in Lebanon used to be common among patients with rheumatic heart diseases [14]. Aggressive bacterial endocarditis prophylaxis for patients with rheumatic heart disease should be emphasized.

Myocarditis is also a common cause for acquired heart disease in the pediatric population in Lebanon. However, no apparent endemics or epidemics of myocarditis have been noted in the past ten years.

Furthermore, awareness among the pediatricians about Kawasaki disease is improving and hence early initiation of appropriate therapy have led to decrease in the incidence of cases of Kawasaki disease with coronary artery involvement in Lebanon.
SURGICAL PROCEDURES

In Lebanon more than 650 babies are born with heart disease every year. About 425 of these children will need some form of treatment, either utilizing surgical intervention or the use of newly available nonsurgical procedures such as catheter-based therapy, coils, stents and implantable devices [1-3].

About 300 open and closed pediatric cardiac surgeries are performed per year in Lebanon (about 75 cases/million people). All types of cardiac surgeries are being performed in the country, except for pediatric cardiac transplantation and the majority of Norwood procedure for the hypoplastic left heart syndrome (HLHS), which is rarely being utilized in Lebanon. The surgical results at some of the medical centers in Lebanon are comparable to those being performed at major centers in the United States and Europe. The in-hospital surgical mortality rate for pediatric cardiac surgeries that were performed during 2008 at our center was 2.6%, an outcome that reflects the good level of care to the children with CHD in AUBMC and Lebanon. Although the overall mortality percentage can be confusing when drawing conclusions on outcome, especially in the specialty of pediatric cardiology since surgeries can be done on patients with CHD who have various complexities of CHD lesions, our case mix at AUBMC revealed that 38% of the cases that underwent cardiac surgery were in risk adjustment for congenital heart surgery (RACHS-1) Category 3 and above. The overall mortality rate for pediatric cardiac surgery in the United States in 2005 was 4.6% as reported by Welke et al. [15]. The aim of a medical activity is not size but quality. For the planner, size is one of the ways of trying to ensure quality. Smaller pediatric units are also acceptable, provided their results meet the standards of care in larger, specialized units. The absolute proviso, however, must be that the unit adheres to the same quality assurance systems as the larger units and that adequate measures are taken to provide good service around the clock and around the year.

INTERVENTIONAL CARDIAC CATHETERIZATION

Catheter interventional procedures in Lebanon have significantly increased over the past few years, following the decision of the Ministry of Health to cover a major part of the cost of the catheter therapeutic procedures [1]. More than 150 interventional cardiac catheterization procedures are being performed each year in Lebanon. Coil embolization of patent ductus arteriosus (PDA) was introduced to the country in the mid-1990’s (Figure 2). The Amplatzer occluder device for PDA (Figure 3) and atrial septal defect (ASD) followed few years later [16-20]. In 2004, Amplatzer device closure of VSD was performed for the first time at our center and in Lebanon. Nearly all types of interventional catheterization procedures are currently being performed at the AUBMC, including valvuloplasties, angioplasty of coarctation of the aorta and pulmonary arteries, Amplatzer device closure of ASD, PDA and VSD, coil embolization of PDA and collaterals and stent implantation; this is similar to what is available in the advanced centers in the world.

BASIC RESEARCH

Animal model of chronic hypoxia

Basic research in the field of pediatric cardiology is emerging in Lebanon. Funded research is increasing, though still limited. An animal model of neonatal chronic hypoxia is being utilized at our center to study the effect of chronic hypoxia on the brain, heart and endocrine system [21-28]. A multidisciplinary team at the Core Facility Laboratory at the AUB is active in conducting several funded research projects addressing the mechanisms and triggers of cardiac growth in the chronically hypoxic rat heart and the role of angiogenesis and sphingolipid pathway.

Molecular basis of CHD

A specialized center to study the molecular basis of CHD was established at the AUBMC. This center was entitled the CHD Genetic Program (CHDGP). Major discoveries relating to the molecular basis of CHD in the Lebanese population were reported. These findings were novel and established groundbreaking research which was reported worldwide.

A novel mutation in the GATA4 gene in patients with tetralogy of Fallot was reported at our center. Data
revealed a mutation in the gene encoding GATA4, a locus on human chromosome 8p, one of the earliest markers of heart development. This mutation was found in two patients with tetralogy of Fallot (TOF) out of the 26 screened (Figure 4), and in none of the 94 other patients with different phenotypes, nor in the 223 healthy individuals [29-30]. In another study, we speculated that NFATC1 gene is a VSD susceptibility gene [31]. Also, we described a Lebanese family with Alagille syndrome and a novel frameshift mutation in the JAG1 gene [32].

Moreover, we reported two Lebanese families with dilated cardiomyopathy secondary to carnitine deficiency. These families were harboring the same mutation in the OCTN2 gene encoding the transporter for carnitine [33]. This was the first case of primary systemic carnitine deficiency caused by mutations in the SLC22A5 gene, which encodes the Na+–dependent organic cation transporter which is reported in Lebanon. Our colleagues in Lebanon are also involved in studying the molecular basis of CHD [34-35].

The advantage for our program for screening for genetic causes of congenital heart disease in Lebanon is the availability of several pedigrees of families with more than two patients with a given phenotype and sometimes families have more than three patients with different phenotypes. This will help us conduct whole genome linkage analysis to find out gene(s) responsible of congenital heart disease. The CHD Genetic Program at the AUBMC was recently awarded the prestigious Harvard-Dubai Medical Research Grant.

THE CHARITABLE ORGANIZATIONS/SUPPORT GROUPS

The field of pediatric cardiology in Lebanon has been expanding due to various factors. On a national level, the need still exists to pool the resources in order to develop few specialized centers to offer the advanced care and expertise required to treat complex cases.

The Brave Heart Fund (BHF), based at the Children’s Heart Center at AUBMC, has contributed by providing financial assistance to needy families that would have otherwise had little or no financial means to treat their children. The BHF coordinates with the Ministry of Health of Lebanon, which also provides a significant part of the cost of treatment of children with CHD.

The Brave Heart Fund provides financial, emotional, and educational support to families who have children with heart diseases. Its mission states “no child should die of a heart disease because of lack of funds.” The Brave Heart Fund is a grassroots initiative supported by community for the benefit of the community. As of October 2010, the Brave Heart Fund has raised in excess of $ 5,000,000 – money that has been used to treat more than 1000 children since its conception seven years ago.
Similar programs have been established at other centers in the country.
In 2010, more than seventy-five percent of the children with congenital heart disease who were treated at AUB-MC were partially or totally supported by the Brave Heart Fund.

EDUCATIONAL/FELLOWSHIP TRAINING
IN PEDIATRIC CARDIOLOGY

The AUBMC started its fellowship training program in Pediatric Cardiology a few years ago and it is the only program in Lebanon. This important educational training program will open the door for physicians from Lebanon and the region to have appropriate training in Pediatric Cardiology and helps to provide supply for specialists in Pediatric Cardiology where the demand is needed.

In addition, educational and awareness programs to educate the public about congenital heart disease are ongoing events at our center with national and international programs being utilized.

CONCLUSIONS/RECOMMENDATIONS

Appropriate identification of cardiac disease, its epidemiology, prevalence, and outcome is of utmost importance in guiding adequate care. The estimated cost of therapy for children with heart disease in Lebanon is about 4.0 million US dollars per year [1-3]. Financial support to research and clinical services in pediatric cardiology should increase. Furthermore, facilities providing tertiary care should be centralized in order to improve level and quality of care. In addition, resources should be directed to establish a specialized center to deal with adults with CHD, since the number of adults with CHD will exceed the number of children with CHD in the next few years. Support groups should develop and the educational materials and websites which have been previously developed should be properly advertised.

REFERENCES

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