

Access to Care and Therapy for Kawasaki Disease in the Arab Countries: A Kawasaki Disease Arab Initiative (Kawarabi) Multicenter Survey:

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Abstract

Kawasaki Disease (KD) is still the most common acquired heart disease in children below the age of five years; it has been well described in the developed world; however, data from the Arab world are limited to case reports or single-center case series. In an effort of optimizing KD research in the Arab world, a group of physicians and researchers established the KD Arab Initiative (Kawarabi) in 2021, and published the first survey, which showed disparities in the availability of intravenous immunoglobulin (IVIG); this had prompted Kawarabi to assess the access to care and therapy of KD patients in Arab countries. A 32 structured questions survey was conducted in thirteen Arab countries and addressed KD patients' access to healthcare in urban and rural settings. The survey results showed that access to care was uniform across large, mid-size cities and rural areas in 7/13 (54%) countries, while in 6/13 (46%) countries, it was in favor of large and mid-size cities over rural areas. The quality of medical services received by children with KD in large cities was rated as excellent in 6/13 or good in 7/13 countries compared to fair in 4/13 or poor in 4/13 countries in rural areas. Availability of IVIG was limited (23%) in mid-size cities and almost impossible (23%) in rural areas. The KD patients in mid-size cities and rural areas have limited access to standard healthcare in the Arab world. This survey laid the foundation for future Kawarabi endeavors to improve the care of children with KD.

Introduction

Kawasaki disease (KD) is an acute febrile illness of childhood resulting in medium-size vasculitis, affecting the coronary arteries primarily. It is the most common cause of acquired heart disease in children under five years of age in developed countries. When missed or not treated promptly, coronary artery aneurysms (CAAs) develop in up to 25% of KD patients leading to myocardial infarction or death [1].

KD's primary etiology is still unclear, yet it is well described in the developed world. The experience of the Arab world is limited to single-center case series and case reports [2, 3]. In an effort to optimize KD research in Arab nations and ethnicities, a group of physicians and researchers established the KD Arab Initiative (Kawarabi) in 2021 [4]. In its first survey, Kawarabi noted disparities in the availability of intravenous immunoglobulin (IVIG), the mainstay therapy for children with KD, and a decreased awareness of the disease among the general population. This report aimed to assess further the diagnostic and therapeutic resources available in Arab countries members of Kawarabi for the diagnosis, management, and follow-up of children with KD by means of an online based survey. Results from this survey are expected to highlight unmet needs and ultimately help develop strategies to meet those needs.

Methods

An online data collection survey with 32 structured questions using Forms office Microsoft® was designed by the author (ND). For face validity, it was edited and approved by the Kawarabi steering committee [5]. The survey questions addressed KD patients' access to healthcare in urban and rural settings, healthcare cost coverage, access to subspecialty care (rheumatologists and cardiologists), and

timely access to diagnostic testing and medications. The survey also addressed changes to healthcare delivery over the past decade.

Principal investigators (PIs) from thirteen Kawarabi member countries (Fig. 1) filled out the survey with assistance from local resources when needed. The countries represented were Algeria, Egypt, Iraq, Jordan, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Tunisia, and the United Arab Emirates. The Survey link was emailed to twenty-seven participating PI, and these included pediatric cardiologists and rheumatologists from different institutions in the thirteen countries; each country then identified one PI to submit an aggregate of the responses from that country. The survey was conducted from March 29 through May 15, 2022. PIs consented on their behalf, and on behalf of their assisting resources, to the survey using a Forms office Microsoft. The survey was not anonymous or blinded (Supplemental box 1). Regular email reminders were sent to PIs to ensure an adequate response rate before the deadline.

Data were collected, analyzed, and presented as mean for continuous variables and frequencies for dichotomous and categorical variables. The survey was piloted before the official launch.

Results

Eight countries (62%) had more than one institution represented. Access to care was uniform across large, mid-size cities and rural areas in 7/13 countries (54%) and heterogenous in 6/13 (46%) countries favoring large and mid-size cities over rural areas. In 10/13 countries, children accessed care across borders. The quality of medical services received by children with KD in large cities was rated as excellent in 6/13 (46%) countries or good in 7/13 (54%). In mid-size cities, medical services were rated as excellent or good in 9/13 (69%) and fair in 4/13 (31%) countries. In rural areas, medical services were rated predominantly as either fair 4/13 (31%) or poor 4/13 (31%) (Fig. 2). Over the last ten years, access to healthcare was viewed as good and improving in 6 countries (46%), very good in 3 (23%), fair and stable in 3 (23%), and fair but regressing in 1 country (8%).

The payment method for medical services was mainly via third-party payors (government and ministry of health) in nine (69%) and divided between private insurance and self-payors in four (31%) countries. In the last ten years, the method of payment distribution changed in 7/13 (54%) countries. Out of these seven countries, two (15%) moved towards a third-party payor, two (15%) switched to a more self-paid model, and three (23%) leaned into a private insurance model. (Table 1)

Table 1
Access to healthcare in general and based on payment methods

• Rate of patient access to healthcare in general in the country during the last two years				
Very good	Good and improving	Fair and stable	Fair but regressing	Poor
3	6	3	1	0
• Access to healthcare distribution for children across the country's geography				
Balanced	Unbalanced			
3	10			
• Access to healthcare distribution between the various communities of the country				
Even	Vary			
7	6			
• The mode of payment for healthcare for children in the country:				
Mostly third-party payor (government /ministry of health)	A mix between private insurance and Self payor	Private insurance	Self payor	
9	4	0	0	
• Payor distribution change over the past 10 years ago				
It has not changed much	It has moved closer to Government coverage	It has become out of pocket	has moved closer to private insurance	
6	2	2	3	

KD advocacy groups were established in 7/13 (54%) countries. In 5/13 (38%) countries, the advocacy groups were either in the development phase, or the PIs were unsure of the presence of advocacy initiatives. There was no advocacy group in 1/13 (8%) of countries. (Fig. 3)

Availability of IVIG was excellent in the majority of large cities (69%), fair (46%) to limited (23%) in the majority of mid-size cities, and limited (38%) to almost impossible (23%) in the majority of rural areas. Accessibility to IVIG improved in 10/13 (77%) and remained unchanged in 3/13 (23%) over the past decade (Table 2). Similarly, the availability of biological immunotherapy varied between large cities, mid-size cities, and rural areas. It was rated as excellent in large cities in seven (54%) countries, fair in three (23%), or limited in another three (23%) countries. In mid-size cities, the availability of biological immunotherapy was rated predominantly as fair (23%) to limited (31%) or almost impossible (31%). In remote cities or rural areas, the availability was rated as almost impossible in eight countries (62%). Availability of biological immunotherapy other than IVIG improved in the past decade in 12/13 (92%) countries and remained the same independent of cost in 1/13 (8%). These results were independent of cost.

Anticoagulants such as heparin, low molecular weight heparin (LMWH)/fractional heparin, and vitamin K antagonists were always accessible in twelve (92%) countries and limited in only one (8%) country. Availability of direct oral anticoagulants (non-vitamin K antagonists) was rated as excellent in six (46%) countries, limited in six (46%), and not available in one (8%). (Table 2) Access to anticoagulation improved in the last ten years in ten (77%) countries and remained unchanged in three (23%).

Table 2
Access to treatment, geographical concerns and ten years progress

• IVIG availability across the country			
	Large cities	Mid-size cities	Remote/rural areas
Excellent	9 (69%)	4 (31%)	1 (8%)
Fair	4 (31%)	6 (46%)	4 (31%)
Limited	0 (0%)	3 (23%)	5 (38%)
Almost impossible	0 (0%)	0 (0%)	3 (23%)
• Has access to IVIG improved in the country in general compared to 10 years ago?			
It has improved	It remains comparatively unchanged		It is worse now
10 (77%)	3 (23%)		0 (0%)
• Biologics immunotherapy availability (e.g., Infliximab, Etanercept, Anakinra)			
	Large cities	Mid-size cities	Remote / rural areas
Excellent	7 (54%)	2 (15%)	1 (8%)
Fair	3 (23%)	3 (23%)	2 (15%)
Limited	3 (23%)	4 (31%)	1 (8%)
Almost impossible	0 (0%)	4 (31%)	8 (62%)
• Change in the access to biologics immunotherapy (e.g., Infliximab, Etanercept, Anakinra) in the country over the past 10 years			
It has improved	It remains comparatively unchanged		It is worse now
12 (92%)	1 (8%)		0 (0%)
• Access to anticoagulants by category:			
	Always accessible	Limited access	Not available
Regular heparin	12 (92%)	1 (8%)	0 (0%)
LMW / F Heparin	12 (92%)	1 (8%)	0 (0%)
Anti-vitamin K	12 (92%)	1 (8%)	0 (0%)
NOAC	6 (46%)	6 (46%)	1 (8%)
• Anticoagulants availability across the country			
	Large cities	Mid-size cities	Remote / rural areas
Excellent	12 (92%)	7 (54%)	4 (31%)

• IVIG availability across the country			
Fair	1 (8%)	4 (31%)	2 (15%)
Limited	0 (0%)	2 (15%)	4 (31%)
Almost impossible	0 (0%)	0 (0%)	3 (23%)
• Change in the access to anticoagulants in the country over the past 10 years			
It has improved	It remains comparatively unchanged		It is worse now
10 (77%)	3 (23%)		0 (0%)
IVIG: Intravenous immunoglobulin, LMW: low molecular weight, F: fractionated, NOAC: New oral anticoagulants			

On a scale from 1 to 5 (5 being excellent), outpatient pediatric echocardiography and pediatric cardiology access in major cities were rated at an average of 4.2 and 4.3, respectively. On a similar scale, access to a pediatric rheumatology consultation was rated at an average of 4.2 in major cities and at an average of 2.6 in remote cities and towns (Fig. 4). Outpatient echocardiograms performed on follow-up were predominantly interpreted by a pediatric cardiologist in large cities 12/13 (92%). Instead, in remote cities, many of those studies were interpreted by either an adult cardiologist 4/13 (31%), a non-cardiologist 2/13 (15%), or an ultrasonographer 1/13 (8%). On a scale from 1 to 5 (5 being excellent), diagnostics for inducible ischemia and coronary artery imaging was rated in large cities as follows: exercise stress testing 3.54, pharmacological stress testing 2.62, non-invasive myocardial perfusion and coronary circulation imaging 3.46 and invasive coronary angiography 3.62.

Discussion

The Kawasaki Disease Arab Initiative (Kawarabi) was established to identify the impact of KD on cardiovascular health in the Arab world and address the challenges faced by physicians caring for children with KD in that region [4]. This survey shows significant heterogeneity in the care for children with KD between large, industrialized cities and rural areas. The majority of respondents rated access and quality of care as excellent in large cities yet fair or poor in remote areas. These results apply to standard therapy, biologics, and anticoagulants, as well as to the availability of diagnostic technology and subspecialty expertise. The quality of care, in general, was perceived by the respondents to have improved over the past decade, yet there was also a trend towards a self-pay or private insurance payment model. Standard therapy for KD consists of IVIG 2g/kg given within the first ten days of treatment [6]. IVIG is an expensive human blood product and, thus, might not be available for a large section of Arab children, especially if health insurance is not available. Using the World bank income status from the same year, a 2018 survey of patients with an autoimmune disorder in over 60 countries showed that in developing countries, close to 70% of respondents from low-income countries do not access care because of unaffordable drug prices compared to close to 30% of those living in high-income countries [7]. In other developing countries such as India, only two of the marketed formulations of IVIG

are approved for use by the United States Food and Drug Administration (FDA)/European Medicines Agency (EMA). Yet they are also the most expensive [8]. Other available preparations that are manufactured locally are cheaper yet may be subject to less stringent quality and safety regulations [9].

The study also showed that only 54% of Arab countries that participated in the survey had established KD advocacy groups. These results are in line with a prior survey from Kawarabi that showed a decreased level of awareness of KD in the general population in the Arab world [4]. In areas where awareness about KD is still not optimal, the treating pediatrician may not be aware of the clinical features of KD. This often results in a wrong, delayed, or missed diagnosis. Studies from other resource-limited countries, such as Brazil, showed that only 46% of children with KD were referred and treated promptly within the first ten days of onset of symptoms, and only 21% of them were referred with the correct diagnosis [10]. Among that cohort CAAs developed in 18.5%. This is comparable to the rates of coronary artery aneurysms in untreated children with KD and supports the data from industrialized countries that the delay in diagnosis leads to an increase in the rate of CAAs.

According to our survey, access to subspecialty services and to echocardiography imaging was suboptimal in remote cities as opposed to optimal in major cities. For instance, echocardiography studies in remote cities are interpreted by an adult cardiologist or a non-cardiologist in 45–50%. To another extent, access to diagnostics imaging for inducible ischemia and coronary artery imaging was suboptimal in major cities on average for exercise stress testing 3.54/5, pharmacological stress testing 2.62/5, non-invasive myocardial perfusion and coronary circulation imaging 3.46/5, and for invasive coronary angiography 3.62/5.

KD management by non-experienced physicians might impact outcomes due to non-adherence to the current standard of care. The study showed that on a scale from 1 to 5 (5 being excellent), access to a pediatric rheumatology consultation rated at an average of 2.6 in remote cities compared to 4.2 in large cities. In addition, echocardiography was performed in more than half (54%) of KD cases by physicians or technicians other than pediatric cardiologists in remote cities compared to 92% of the echocardiography studies done by pediatric cardiologists in large cities. Lowry et al. conducted a pediatric hospitalists' survey (104 respondents) across the USA, which showed that hospitalized KD children were rarely managed by a dedicated KD team. Remarkably, respondents were not particularly compliant with the AHA surveillance statement for a scheduled second and third echocardiogram since only half and less than one-third, respectively, followed the recommendations. Of particular interest, 81% acknowledge the absence of a local clinical pathway or a formal process for outpatient echocardiogram follow-up scheduling. This prompted the authors to implement institutional changes to increase consistency and adherence to formal recommendations with respect to acute care and follow-up of KD patients [11].

Expensive therapy, compounded by decreased availability of diagnostic technology and expertise in the diagnosis of coronary artery lesions as well as decreased awareness, might lead to a rising number of KD patients with CAAs in Arab countries and may overburden healthcare resources in the region. This may eventually translate into a higher incidence of coronary artery sequelae in young adults who are at the

peak of their economic productivity. A study from Cairo University showed that ~ 8% of adults aged 40 or younger presenting with acute myocardial infarction had coronary artery lesions consistent with a prior history of KD [12].

Conclusions

Overall, the healthcare in general for KD in the Arab nation has improved over the past ten years. Nevertheless, a third of it is substandard. The KD patients in mid-size cities and remote/rural areas have limited access to standard therapy, diagnostic technology, and subspecialty care. KD patients, families, and caregivers' engagement in patient advocacy groups/ organizations is crucially needed. The results of this survey lay the foundation for future Kawarabi endeavors in the Arab world to improve the care of children with KD.

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Figures

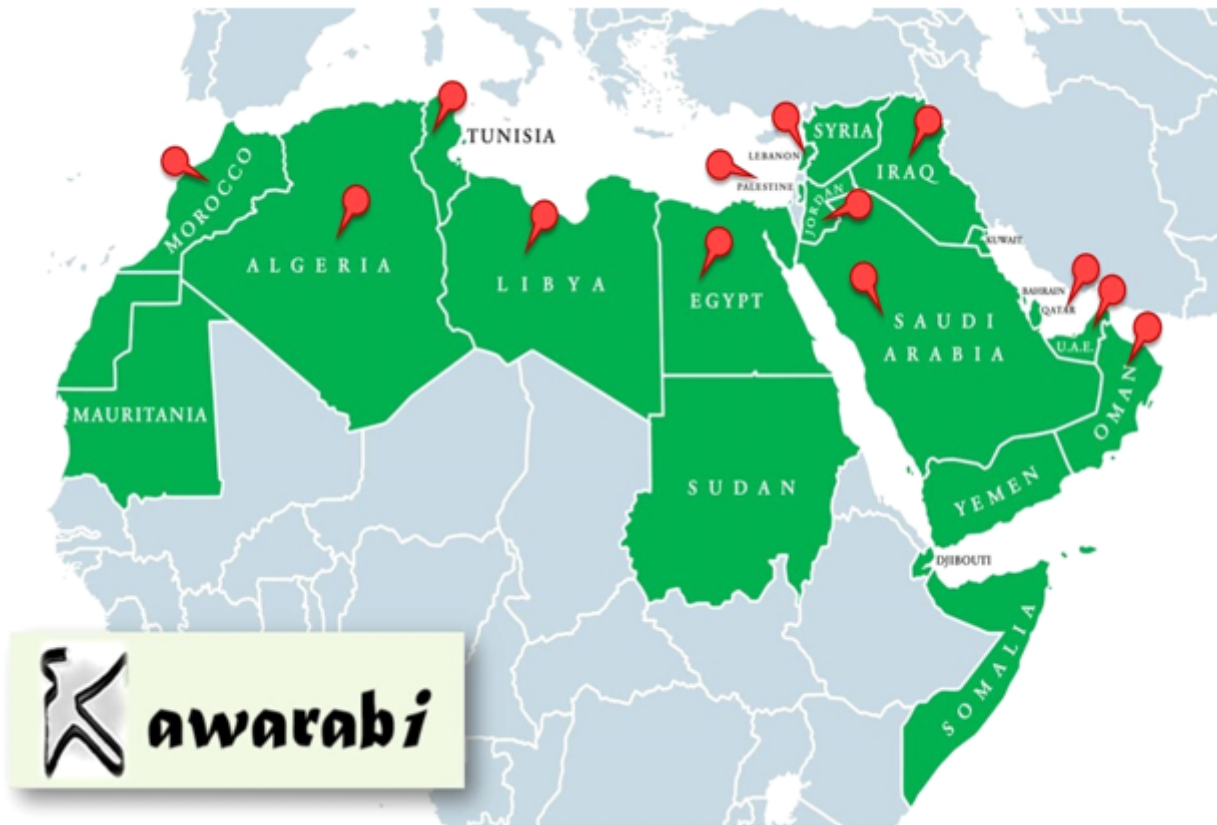


Figure 1

Participating Arab Countries corresponding to survey results. The 13 participating countries are labeled by a red pin.

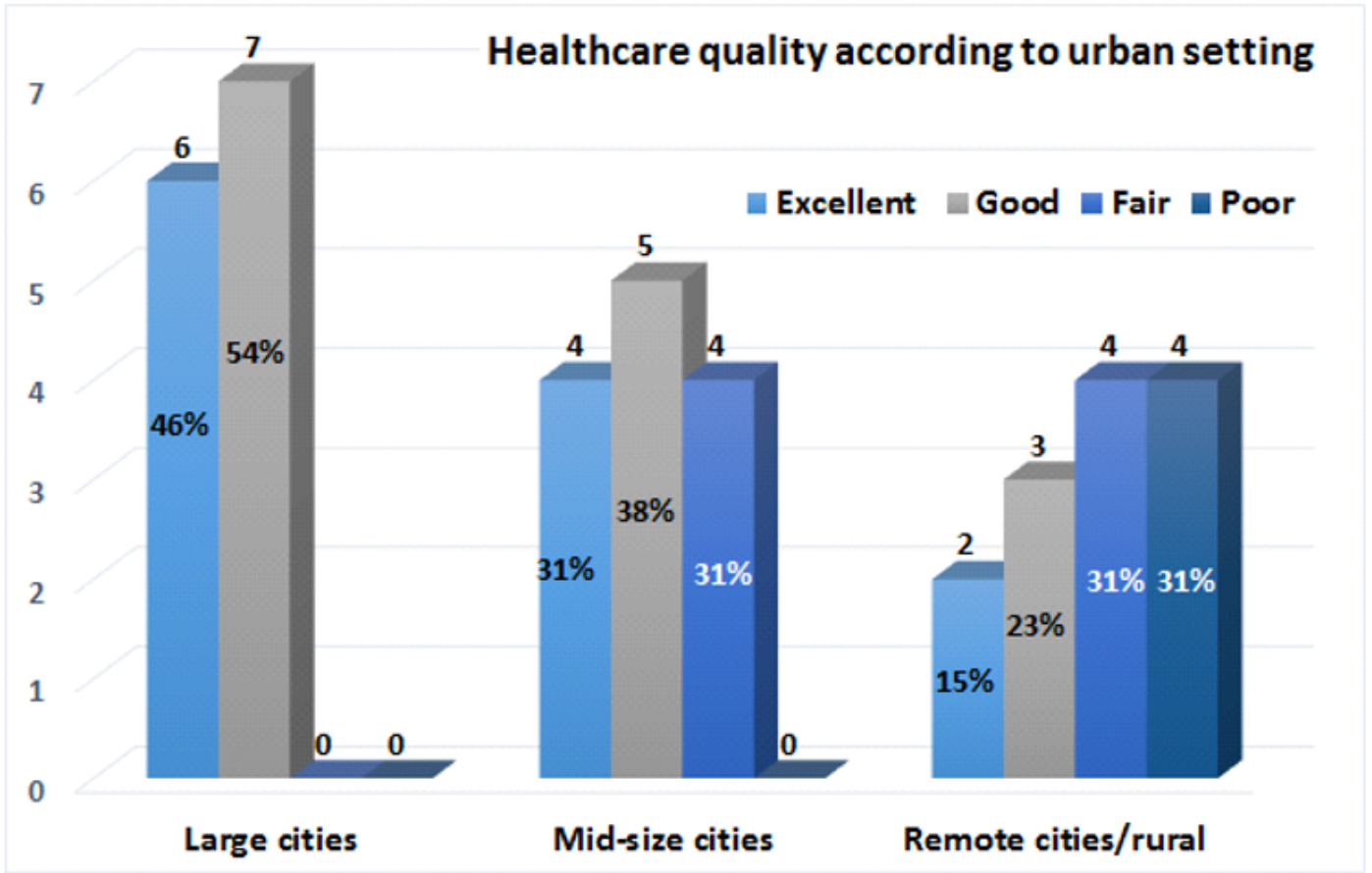


Figure 2

Healthcare quality of care for KD children in large, mid-size and remote cities

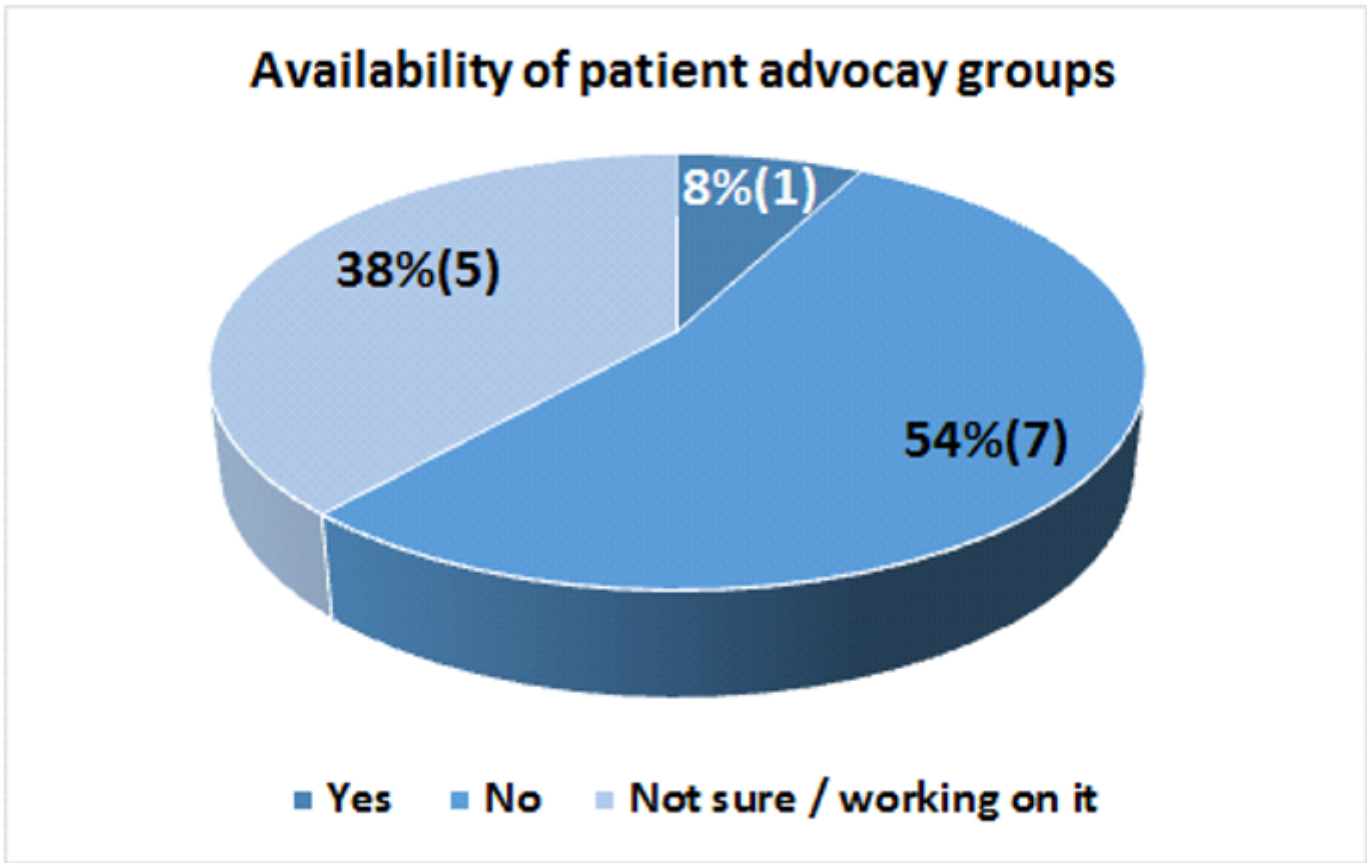


Figure 3

KD patient advocacy groups across participating countries

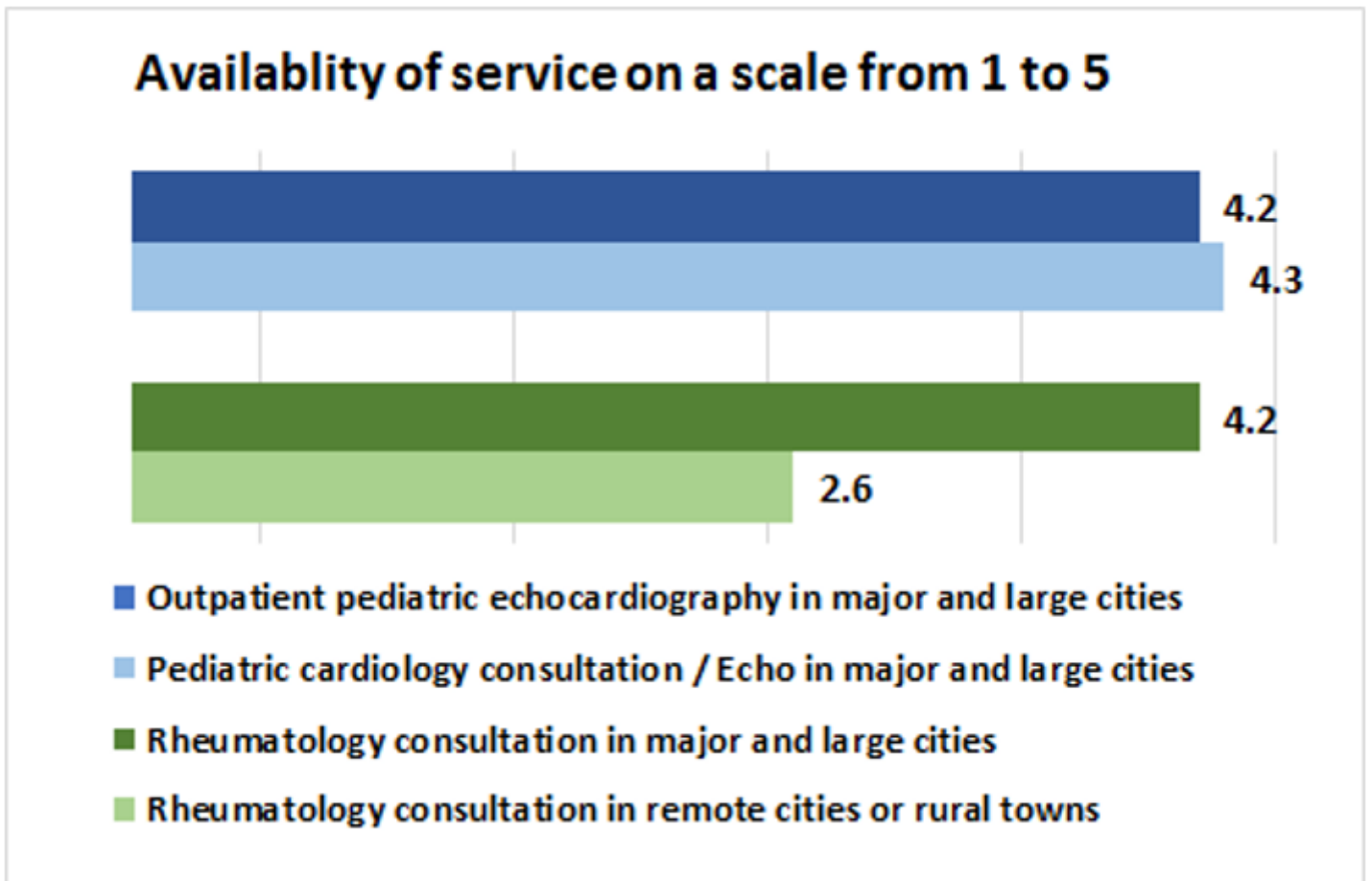


Figure 4

Accessibility to specialties in large and remote cities

Supplementary Files

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