Evaluating Health of Emerging Economies Through the Eyes of Heart Valve Disease in the Transcatheter Era

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ABSTRACT

China and India are the 2 fastest growing major world economies. However, they suffer from great differences in health policies, demographics, and rates of population growth. Whereas China has seen a steep decline in rheumatic heart disease (RHD) and a rise in life expectancy, India continues to suffer from a significant burden of RHD due to insufficient distribution of economic prosperity to health care, denser population, and ineffective application of World Health Organization RHD prevention guidelines. As China faces the burden of the world's largest geriatric population, focus has shifted to calcific aortic stenosis for which it prepares by expansions in the field of transcatheter aortic valve replacement. Conversely, India has a younger population and a lower average life expectancy. Therefore, focus in India has still not shifted to calcific aortic stenosis as a major cause of morbidity and mortality as RHD continues to constitute the bulk of valvular heart disease.

China and India, the world's 2 most populous countries, have traditionally lived through economic inferiority as compared with Western countries. Whereas an age-related degenerative valve disease, such as calcific aortic stenosis (AS), constitutes the majority of valvular heart disease in the developed world [1,2], rheumatic heart disease (RHD) continues to be the most common cause of valvular heart disease in the developing world [3,4]. This is largely due to the paucity of resources available to be invested in health care and disease prevention in these countries [5]. Over the past decade, the gross domestic product (GDP) annual growth rates in China and India averaged between 6% and 10% [6]. This rapid surge in economic development is expected to lead to improvements in health care in these countries [7]. As such, preventable diseases, such as RHD, will likely decline with subsequent increases in both life expectancy and age-related diseases such as degenerative calcific AS. AS carries a high mortality if left untreated. We have entered an era of transcatheter intervention where even the inoperable diseases in the aortic and mitral valves have been treated with reduced risk [8]. However, these predictions are based on the assumption that China and India will choose to prioritize improving health care for their citizens, which has often been deprioritized despite economic progress in other countries [9]. We here review the experiences of 2 of the world's fastest growing economies, China and India, through the eyes of valvular heart diseases and assess whether economic progress has indeed transformed the health care systems of these 2 countries.

RHEUMATIC HEART DISEASE

RHD is caused by group A streptococcus (streptococcus pyogenes), which continues to cause significant morbidity and mortality throughout the world, mostly affecting developing and underdeveloped countries [10,11]. Acute rheumatic fever usually affects children between 5 and 18 years of age and develops a few weeks after exposure to infection by streptococcus pyogenes [12]. The World Health Organization (WHO) Global Health Burden framework has been widely adopted since its publication in 1990, and it provides estimates of global disease burden for both noncommunicable and communicable diseases using disability-adjusted-life-years (DALY) [13,14]. RHD is among the diseases included in the Global Health Burden report. Overall mortality and DALY for all diseases have been steadily declining in the world (Figure 1). Correspondingly, China has experienced a steady decrease in mortality and DALY related to RHD in the last 25 years (Figure 1). Liu et al. [15] conducted a study between January 2009 and December 2013 in 19,428 adults with abnormal valve structures and concluded that although the prevalence of RHD steadily declined from 42.8% to 32.8% at the end of the study, the prevalence of degenerative heart disease increased from 8.8% to 14.5%. This reduction of RHD has been attributed to improving living conditions, better housing, and improving socioeconomic status, whereas the increased rate of degenerative valvular heart disease has been attributed to higher longevity.

Conversely, the burden of RHD in India has remained persistent (Figure 1). According to the Indian Council of Medical Research, the rates of RHD in India dropped from

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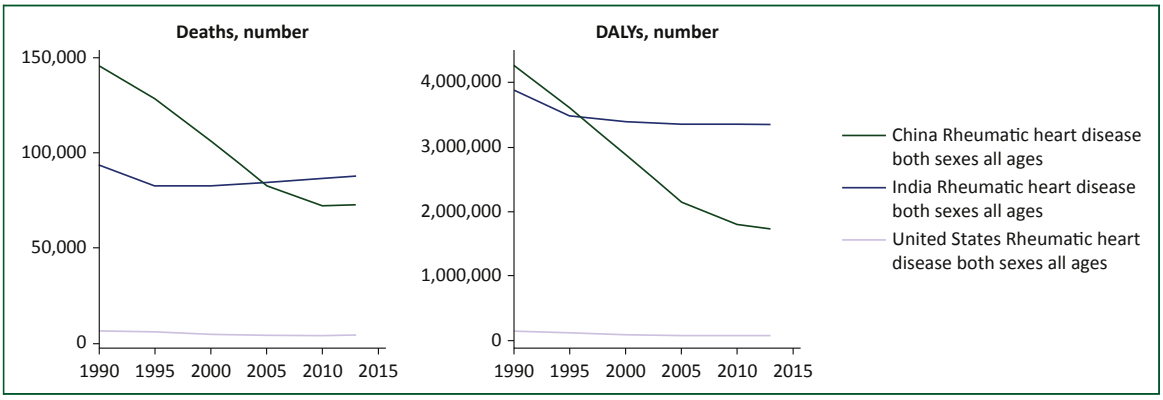

FIGURE 1. Trends of deaths and disability-adjusted-life-years (DALY) due to rheumatic heart disease in China, India, and United States in the last 25 years in the Global Burden of Disease study.

5.3 per 1000 in the early 1970s to 0.9 per 1000 in the last decade [16]. This was refuted by a study that showed significantly higher rates of RHD after echocardiographic evaluation that were not diagnosed with clinical evaluation [17]. In a large single-center study evaluating findings with first-time echocardiograms in 136,908 patients, RHD constituted the majority of valvular diseases with the most common valve involved being the mitral valve [18]. More than 20,382 cases of RHD were admitted by Sri Jayadeva Institute of Cardiovascular Science and Research in Bengaluru, India, between 1998 and 2010, constituting >10% of the hospital admissions [19].

It is important to evaluate why increased economic development in India has not led to a decline in RHD rates like those seen in China. Some may argue that India's economic development is more recent than China's. However, China saw a sharper decline in rates of RHD during their initial years of economic progress, whereas India is well into its second decade of economic development without any reduction in RHD rates. One contributing factor may be an inadequate allocation of GDP into health expenditure [20]. For example, India spent a mere 4% of GDP and only $157 per capita on health care in 2012, whereas countries that are part of the Organisation for Economic Co-operation and Development spent an average of 9.3% of their GDP and $3,484 per capita [21].

Another important factor is the higher demand for health care resources due to faster population growth rate in India. As demonstrated in Figure 2, population growth for China and India was parallel from 1950 through the late 1990s. However, at the turn of the twenty-first century, China's growth started to flatten, largely due to enforcement of the one child policy since 1980. Conversely, India's growth rate continues to steeply rise, placing a serious burden on the health care system [22]. Furthermore, India is expected to become the world's most populous country around 2030. However, even these statistics understate the seriousness of the situation. China occupies 9.597 million square kilometers and India occupies 3.287 million square kilometers. India's population density is 441 people per square kilometer which is almost 3 times China's population density of 146 people per square kilometer.

Lastly, one must consider the ramifications of ineffective application of WHO RHD prevention guidelines. Acute rheumatic fever is an autoimmune reaction to a group A streptococcus infection, which manifests as strep throat. This infection is highly contagious and tends to flourish in high-density areas with poor living conditions where people come in close contact with others. High-density populations are known to have higher transmission rates of infections [23,24]. It is paramount that group A streptococcus infections are properly diagnosed and treated with appropriate antibiotics to prevent rheumatic fever. However, the central government in India faced difficulties in providing antibiotics to rheumatic fever patients due to shortage of drugs in the market [16]. Coupled with the dense population, this contributes to a higher prevalence and rate of disease transmission.

CALCIFIC AS

Calcific AS is an age-related degenerative disease. It is very difficult to accurately assess the world's population being affected by this deadly disease. This is because a major portion of the world's population resides in China and India, and there is hardly any data from these countries regarding the prevalence of AS. Although studies have found significant difference in rates of calcific AS depending on race [25], the closest possible way is to use known data of AS from developed countries per geriatric population and use it to estimate the crude prevalence of AS in the developing countries. China already has the largest population of people >80 years of age. This age group is rapidly growing and causing serious concerns due to the weak social security system [26]. In fact, it is estimated that the population older than 80 years of age is the most rapidly growing age group in the Chinese population [27].

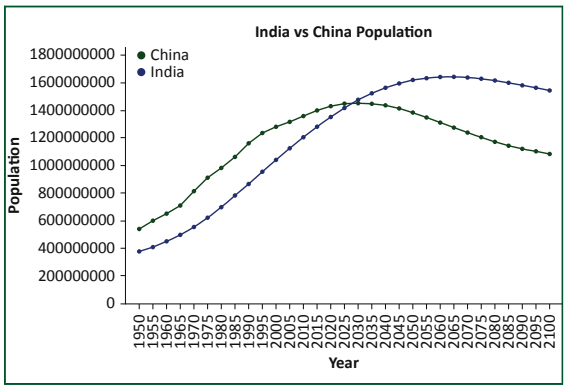

FIGURE 2. Expected future population trend comparing China and India showing India overtaking China as the world's largest population around 2030.

Pan et al. [28] found high rates of aortic valve calcifications in Chinese population >65 years of age.

Conversely, India has a younger population and a lower average life expectancy. According to the 2014 World Bank Statistic, the average life expectancy of an Indian is 68 years as compared to 76 years for a Chinese [29]. Therefore, focus in India has still not shifted to calcific AS as a major cause of morbidity and mortality as RHD continues to constitute the bulk of valvular heart disease.

IMPLICATIONS IN THE TRANSCATHETER ERA

The treatment of calcific AS was revolutionized in 2002 with the advent of the first transcatheter aortic valve replacement (TAVR) [30]. It is a minimally invasive way to treat severe symptomatic calcific AS, a disease that carries a mortality of 50% at 1 year without valve replacement [31]. Before the advances of technology for TAVR, many elderly patients with severe AS were denied surgery [32]. Following the success of the PARTNER (Placement of Aortic Transcatheter Valves) trial, the American College of Cardiology/American Heart Association recommended TAVR as a class I indication for patients with prohibitive surgical risk and as an acceptable alternative to surgery for patients with high surgical risk [33,34]. The U.S. Food and Drug Administration recently approved TAVR in intermediate surgical risk patients, as well. Transcatheter mitral valve repair, also known has MitraClip (Abbott, Chicago, IL, USA), is a percutaneous device used to treat severe degenerative mitral regurgitations and has been approved for use in patients with inoperable risk of surgery [35]. Therefore, the most complicated patients with degenerative AS and mitral regurgitation can now be treated percutaneously with reduced procedural risk. The popularity of these minimally invasive techniques to treat the most complicated valve diseases has mostly remained confined to the developed world. Developing countries continue to be plagued by RHD, which continues to constitute the bulk of the burden of valvular heart disease.

It is important to evaluate whether TAVR and MitraClip have begun to make an impact on valvular heart disease in China and India. China has the world's largest geriatric population. TAVR has already gained popularity in China with the results of the first Chinese clinical trial on TAVR reported [36]. Since the first TAVR procedure in China in 2010, >400 procedures have been performed in China. Goldman Sachs has realized the huge potential for TAVR in China and has invested $37 million in Venus Medtech (Irvine, CA, USA), the company that makes the Venus-A-valve. This is the only TAVR valve approved by Chinese Food and Drug Administration. Valve prosthesis manufacturing companies realize the potential for expansion due to the size of the Chinese geriatric population. The marketing analytics firm has predicted a compound annual growth rate for TAVR at 19.7% between 2013 and 2020, from 881 million to more than 3 billion largely due to involvement of emerging economies.

According to a U.N. report, India's population of people over 80 years old is >10 million [37]. About 5% to 6% (70 million people) of the Indian population is estimated to be >65 years of age according to recent Indian demographic data [38]. Applying Western prevalence data for AS to the Indian population, about 300,000 people would be eligible for TAVR [39]. The first TAVR in India was done in 2012 [40]. Since then, data continue to trickle in, in the form of isolated experiences as India continues to lack an official approval from its regulatory body for TAVR [41]. With persistently higher rates of RHD and the high prices associated with implementing TAVR, India's focus is likely to continue to address RHD for now. As its population continues to age, it will eventually have to rise to the needs of its aging people, and transcatheter technologies are likely to play key roles in doing that.

SUMMARY

Although the rates of RHD have declined, China faces high rates of calcific AS due to its aging population. Although it is preparing to expand into the field of TAVR, strengthening the weak social security system will be crucial for the Chinese population to redeem the benefits of this innovation. On the other hand, the burden of preventable RHD in India has persisted due to insufficient distribution of economic prosperity to health care, faster population growth, and ineffective application of WHO RHD prevention guidelines. Therefore, it is crucial for India to prioritize health care at this stage of its economic advancement. This requires a 2-pronged approach that involves increasing health care spending both on preventable diseases and promoting new technologies such as TAVR and MitraClip to tackle degenerative diseases.

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