ORIGINAL ARTICLE

THIRTY-YEAR TREND OF NON-RHEUMATIC VALVULAR HEART DISEASE: A COMPARISON OF PAKISTAN WITH SOUTH ASIA AND GLOBAL SCENARIO

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Objectives: This study aimed to evaluate the burden and trends of non-rheumatic valvular heart disease (VHD) in Pakistan compared to the South Asian (SA) and Global figures based on estimates of the Global Burden of Disease (GBD) study for the years 1990 to 2019.

Methodology: Data for the estimated prevalence, deaths, and disability-adjusted life years (DALYs), along with age-standardized death rate (ASDR) due to non-rheumatic VHD in Pakistan, was extracted from the GBD study.

Results: The prevalence of non-rheumatic VHD in Pakistan increased by 14.1% from 1990 to 2019, from 6.4 to 7.3/100,000. The ASDR per 100,000 population has shown a 12.9% increase between the years 1990 and 2019 (from 1.32 to 1.49) with an IRR of 1.102 [1.002-1.1983]. However, global and SA's decreased slightly with an IRR of 0.997 [0.971-1.024] and 0.996 [0.959-1.034]. The estimated number of deaths has shown a 1.1% increase from 0.6 to 0.6/100,000 from 1990 to 2019. Similarly, the estimated number of DALYs has shown an increased (17%) from 14.1 in 1990 to 16.5/100,000 in 2019. Interestingly, Sindh, Baluchistan, and Azad Jammu & Kashmir also had seen the most significant increase in DALYs over 30 years, accounting for 30.3%, 23.7%, and 23.9% respectively.

Conclusion: Based on the analysis of GBD estimates, it can be concluded that, in Pakistan, the prevalence, deaths, and DALYs rate of non-rheumatic VHD per 100 thousand individuals increased substantially between 1990 and 2019. The age-standardized death rate also significantly increased over the past 30 years.

Keywords: Pakistan, non-rheumatic valvular heart disease, burden, GBD

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INTRODUCTION

The global spectrum of valvular heart disease (VHD) has changed from rheumatism to non-rheumatic (such as calcific or degenerative) etiology due to an increase in the use of penicillin-based prophylactic and preventive measured and improvement in quality of life and living standards.[1-3] The rheumatic VHD has been nearly eradicated from high-income counties,[1,4]. Still, it remained a significant contributor to morbidity and mortality in the LMCs (low-to-middle income countries), such as South Asian (SA) countries.[2,5] In addition to the rheumatic VHD, the prevalence of non-rheumatic VHD is also on the rise due to substantial economic growth, increasing urbanization, and the aging population in this population.[5,6] The healthcare systems are significantly affected by the burden of non-rheumatic VHD in isolation as well as through their association with adverse clinical conditions such as atrial fibrillation and adverse effects on fetal as well as mothers during pregnancy, such as placental abruption.[7,8]

The population in SA countries, mainly including "Pakistan, India, Bangladesh, Sri Lanka, Bhutan, and Nepal," is at an increased risk of cardiovascular diseases (CVD),[9-11] due to various economic, environmental, and genetic factors.[12,13] After India, Pakistan is the 2nd largest country in the region with a population figure approaching 208 million with over 12 million elderly (≥60 years) individuals.[14] The increasing burden of CVD, particularly non-rheumatic VHD, poses an economic and management burden for the already struggling economies of these countries. Reliable estimates of the disease burden are of extreme value to policymakers for effective decision-making and policymaking. However, unreliable estimates for Pakistan are either limited or unavailable due to improper healthcare structure. Hence, the Global

Burden of Diseases (GBD) study provides an opportunity to evaluate the burden of disease from the regional perspective of Pakistan and its administrative sub-territories (provinces). Therefore, this study aimed to evaluate the burden and trends of non-rheumatic VHD for Pakistan compared to the South Asian and Global figures based on estimates of the GBD study for the years 1990 to 2019.

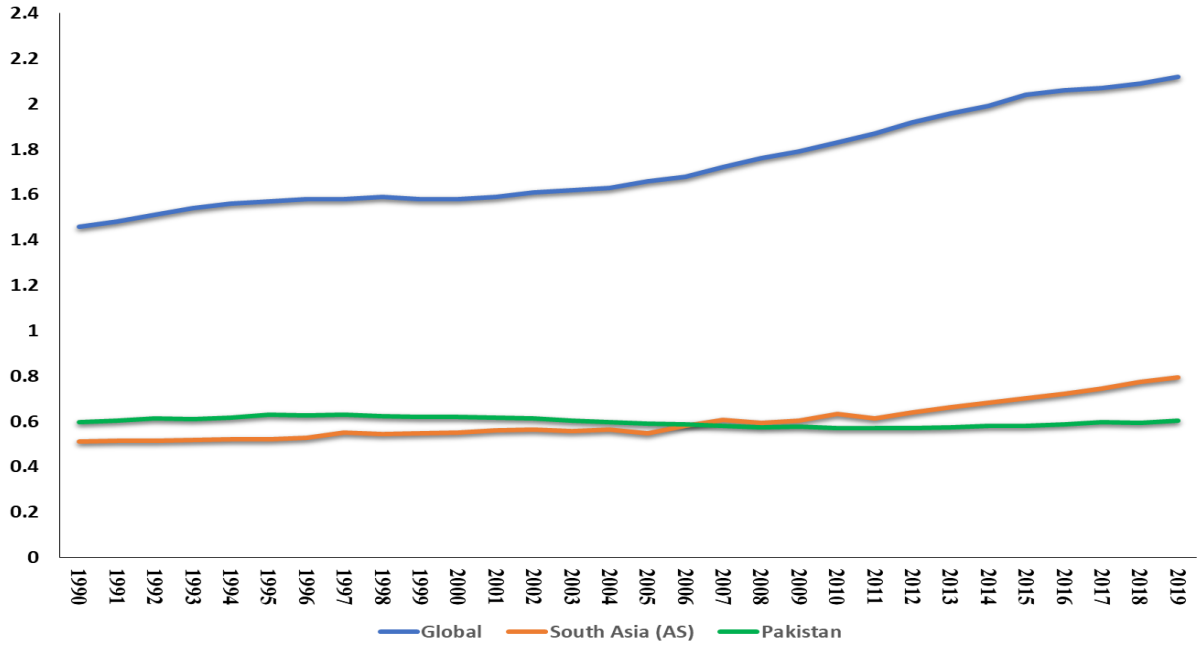
METHODOLOGY

We extracted Pakistan data for prevalence, death rates, DALYs, and the age-standardized death rate from 1990 to 2019 and further divided by gender, subcontinent including, Pakistan, South Asia, and Global region, and Non-rheumatic valvular heart disease including and its type, calcific aortic valve, degenerative mitral valve, and Other non-rheumatic valve diseases were extracted from the Global Burden of Diseases (GBD) study by the Institute of Health Metrics and Evaluation (IHME). Ethical clearance for this study was not required, as this study uses secondary data from the GBD, which is publicly available.

This ecological study consisted of analyzing data extracted from the Global Health Data Exchange query tool.[15] Data set consisted of 30 years (from 1990 to 2019) trend of prevalence, death, DALYs, and Age-standardized rate per 100,000 were analyzed with the help of Microsoft Excel 2013 and R-Studio version by 4.2.2. A complete methodological detail used by the Global Burden of Diseases (GBD) study for estimating statistics is reported elsewhere. Percentage change in prevalence and deaths over 30 years was calculated for 2019 against 1990 as benchmark insights from the GBD study are summarized in tables and figures. Percentage change (%Δ) in 30 years was calculated at an overall level. In addition, we evaluated the 30-year trend in Non-rheumatic Valvular Heart Disease age-standardized death rate for the Global SA region as a whole and at the country level using Poisson regression analysis. As an indicator of annual percentage change, the incidence rate ratio (IRR) and the confidence interval of 95 percent were reported.

RESULTS

Table 1 shows the estimated prevalence rate due to Non-rheumatic Valvular Heart Disease in Pakistan has shown a relative increase of 14.4% per 100 thousand population from 6.4 in 1990 and 7.3 cases in 2019. The highest prevalence percentage showed in the Islamabad capital city increase of 76.4%, 8.7 in 1990, and 15.3 cases in 2019, followed by 17.8% in Azad Jammu & Kashmir, 32.6% in Sindh, 15.2% in Punjab while it was Baluchistan and Gilgit Baltistan showed a decreased trend of prevalence cases. Both male and female gender showed a relative percentage increase, but relative males showed a higher percentage increase, accounting for 18% cases per 100 thousand population.



Figures 1: A comparative trend of the death rate due to Non-rheumatic valvular heart disease in Pakistan, South Asia, and globally from 1990 to 2019

Table 1: Table 1: Total estimate prevalence of non-rheumatic heart disease and percentage of change in Pakistan by gender and province level (1990-2019)

Years	1990	1995	2000	2005	2010	2015	2019	30- years %Δ
Prevalence rate per 100,000 (cases)								
Pakistan	6.4 (7179.6)	7 (8814.7)	7.1 (10033.9)	7.1 (11509.8)	7.1 (12614.7)	7.1 (14628.7)	7.3 (16316)	14.40%
Gender								
Male	7.5 (4459.8)	8.1 (5315.2)	8.2 (6055)	8.4 (7051.2)	8.5 (7993.5)	8.5 (8932.8)	8.9 (10224)	18.00%
Female	5.1 (2719.8)	5.8 (3499.5)	5.8 (3978.9)	5.7 (4458.7)	5.7 (4621.2)	5.7 (5695.9)	5.6 (6092)	10.20%
Province level								
Baluchistan	5.5 (310.4)	6.2 (378.6)	6.1 (415)	5.8 (466.1)	4.9 (498.9)	4.9 (562.2)	4.7 (634.2)	-14.00%
Azad Jammu & Kashmir	6.9 (171)	7.5 (208.2)	7.7 (237.4)	7.7 (261.5)	8.1 (288.3)	8.1 (327.8)	8.1 (350.4)	17.80%
Gilgit-Baltistan	5.1 (40.2)	5.4 (50.7)	5.7 (63)	5.5 (73.8)	4.9 (81.1)	4.9 (95.7)	4.8 (107.2)	-4.90%
Islamabad Capital Territory	8.7 (46.6)	9.3 (63.5)	11.2 (97.7)	14.9 (168)	14.4 (224.9)	14.4 (264)	15.3 (329.9)	76.40%
Khyber Pakhtunkhwa	5.7 (994.8)	6.5 (1249.9)	6.5 (1406.9)	6.3 (1572.8)	5.9 (1704.3)	5.9 (2007)	5.6 (2119.1)	-3.10%
Punjab	6.9 (4202.6)	7.4 (5055.9)	7.4 (5670.7)	7.5 (6455.5)	7.5 (7014.6)	7.5 (7945.7)	7.9 (9012)	15.20%
Sindh	5.7 (1414)	6.5 (1807.8)	6.7 (2143.1)	6.9 (2512.1)	7.4 (2802.4)	7.4 (3426.4)	7.5 (3763.2)	32.60%

** Rate per 100,000 (Counts), Δ=relative change*

Table 2: Death of non-rheumatic heart disease and percentage of change in Pakistan by gender, province level and type of Non-Rheumatic VHD, and Age-standardized death rate for Pakistan, South Asia (AS), and Global from (1990-2019)

Years	1990	1995	2000	2005	2010	2015	2019	30-years %Δ
The death rate per 100,000 (cases)								
Pakistan	0.59 (674)	0.6 (793)	0.6 (881)	0.6 (954)	0.6 (1047)	0.6 (1195)	0.6 (1353)	1.1%
Gender								
Male	0.6 (350)	0.6 (406)	0.6 (447)	0.6 (477)	0.5 (514)	0.6 (584)	0.6 (659)	-3.1%
Female	0.6 (324)	0.6 (387)	0.6 (434)	0.6 (477)	0.6 (533)	0.6 (611)	0.6 (693)	5.4%
Province								
Baluchistan	0.5 (27)	0.5 (33)	0.5 (37)	0.5 (40)	0.4 (43)	0.4 (49)	0.4 (56)	-13.5%
Azad Jammu & Kashmir	0.7 (16)	0.7 (19)	0.7 (22)	0.7 (23)	0.7 (24)	0.7 (28)	0.7 (31)	10.0%
Gilgit-Baltistan	0.4 (3)	0.4 (4)	0.4 (5)	0.4 (6)	0.4 (7)	0.4 (8)	0.4 (9)	15.2%
Islamabad Capital Territory	0.5 (3)	0.5 (4)	0.5 (5)	0.5 (6)	0.5 (7)	0.4 (8)	0.4 (10)	-14.2%
Khyber Pakhtunkhwa	0.5 (80)	0.5 (97)	0.5 (114)	0.5 (131)	0.5 (148)	0.5 (169)	0.5 (194)	10.2%
Punjab	0.7 (425)	0.7 (491)	0.7 (530)	0.7 (564)	0.6 (612)	0.7 (694)	0.7 (778)	-1.8%
Sindh	0.5 (119)	0.5 (145)	0.5 (168)	0.5 (185)	0.5 (205)	0.5 (239)	0.6 (275)	15.1%
Cause								
Non-rheumatic valvular heart disease								

*Age-standardized death rate (ASR) per 100,000, (95% C.I), Δ=relative change, * Rate per 100,000 (Counts), Δ=relative change*

Non-rheumatic calcific aortic valve disease	0.3 (379)	0.4 (442)	0.3 (494)	0.3 (541)	0.3 (599)	0.3 (691)	0.4 (791)	5.1%
Non-rheumatic degenerative mitral valve disease	0.2 (274)	0.3 (325)	0.3 (360)	0.2 (385)	0.2 (417)	0.2 (471)	0.2 (525)	-3.3%
Other non-rheumatic valve diseases	0 (21)	0 (25)	0 (27)	0 (29)	0 (30)	0 (33)	0 (36)	-12.7%
The age-standardized death rate per 100,000								
Global	2.48 [2.21 - 2.64]	2.57 [2.27 - 2.75]	2.45 [2.15 - 2.63]	2.41 [2.09 - 2.58]	2.41 [2.05 - 2.61]	2.41 [2.03 - 2.62]	2.25 [1.89 - 2.47]	-9.3%
South Asia	1.3 [0.88 - 1.66]	1.27 [0.89 - 1.57]	1.29 [0.92 - 1.59]	1.23 [0.92 - 1.46]	1.17 [0.92 - 1.38]	1.19 [1.38 - 0.96]	1.21 [0.98 - 1.44]	-6.7%
Pakistan	1.32 [0.87 - 1.73]	1.47 [0.95 - 1.91]	1.55 [1.01 - 2.01]	1.55 [1.02 - 1.98]	1.53 [1.02 - 1.95]	1.5 [1.02 - 1.93]	1.49 [1.05 - 1.96]	12.9%

Table 3: Disability-adjusted life years (DALYs) due to Non-Rheumatic valvular heart disease and percentage change rate by province, gender, and type of Non-Rheumatic VHD from (1990-2019)

	1990	**1995**	**2000**	**2005**	**2010**	**2015**	**2019**	**30-years %Δ**
DALYs rate per 100,000 (cases)								
Pakistan	14.1 (15915)	15.6 (19709)	16.1 (22871)	15.8 (25576)	15.6 (28465)	16 (32864)	16.5 (36973)	17.0%
Gender								
Male	14.1 (8353)	15.6 (10260)	16.2 (11961)	15.9 (13304)	15.5 (14649)	16 (16883)	16.5(18994)	17.1%
Female	14.1 (7562)	15.6 (9449)	16 (10910)	15.7(12272)	15.6(13816)	16 (15982)	16.5(17979)	16.9%
Province Level								
Baluchistan	12 (679)	13.9 (848)	14.7 (1006)	14.1 (1128)	13 (1243)	12.7 (1467)	12.6 (1692)	16.9%
Azad Jammu & Kashmir	14.8 (370)	16.5 (457)	17.4 (537)	17.2 (584)	16.9 (628)	17.5 (712)	18.4 (796)	23.7%
Gilgit-Baltistan	9.9 (78)	11.3 (106)	12.8 (142)	12.7 (170)	12.2 (196)	12.1 (234)	12.2 (272)	23.9%
Islamabad Capital Territory	12.6 (68)	13.7 (94)	14.2 (124)	13.6 (154)	12.4 (180)	12.2 (223)	12.2 (263)	-3.2%
Khyber Pakhtunkhwa	11.1 (1926)	12.6 (2426)	13.5 (2925)	13.8 (3431)	13.4 (3874)	13.2 (4477)	13.4 (5088)	20.2%
Punjab	16.1 (9865)	17.5 (11985)	17.6 (13548)	17.3(14927)	17.1 (16531)	17.8 (18971)	18.6 (21198)	15.4%
Sindh	11.8 (2929)	13.5 (3794)	14.4 (4588)	14.3(5182)	14.2 (5814)	14.7(6780)	15.4(7664)	30.3%
Cause								
Non-rheumatic calcific aortic valve disease	7.3 (8216)	8 (10066)	8.3 (11755)	8.3(13322)	8.2(14982)	8.5(17480)	8.9(19877)	21.8%
Non-rheumatic degenerative mitral valve disease	6.2 (7043)	7 (8815)	7.2 (10167)	6.9(11216)	6.8(12364)	6.9 (14130)	7 (15729)	12.5%
Other non-rheumatic valve diseases	0.6 (655)	0.7 (828)	0.7 (949)	0.6 (1038)	0.6 (1119)	0.6 (1253)	0.6 (1367)	5.1%

** Rate per 100,000 (Counts), Δ=relative change*

Table 2 shows the death and age-standardized death rate from Non-rheumatic Valvular Heart Disease caused by Pakistan national, gender, and type of Non-Rheumatic VHD from 1990 to 2019. The ASR per 100,000 population has shown a 12.9% increase with an IRR of 1.102 [1.002-1.1983]. However, global and SA's showed declining percentage changes -9.3% and -6.7%, with IRR decreased slightly with an IRR of 0.997 [0.971 – 1.024] and 0.996 [0.959 -1.034].

There has been a considerable increase in Pakistan's death rates from non-Rheumatic heart disease (1.1%), from 0.59 in 1990 to 0.6 per 100 000 in 2019. Females had seen an increasing trend, and males showed declined percentage change in the death reduction, accounting for 5.4%% and -3.1%, respectively. Baluchistan, Azad Jammu & Kashmir Islamabad Capital Territory, and Sindh showed an inclined percentage change in the death rate, except Islamabad Capital Territory and Punjab province. The death rate due to degenerative and other non-rheumatic valve diseases has reduced over 30 years with a percentage reduction of -3.3 and -12.7%, respectively. In contrast, deaths by Non-rheumatic calcific aortic valve disease had an upward percentage change trend (5.1%), respectively.

The overall DALYs from Non-rheumatic Valvular Heart Disease in Pakistan have increased (17%) from 14.1 (15914.6) in 1990 to 16.5 (36973.5) in 2019. DALYS in males and females has equally increased, accounting for 17.10% and 16.9%. Sindh, Baluchistan, and Azad Jammu & Kashmir also had seen the most significant increase in DALYs over 30 years, accounting for 30.3%, 23.7%, and 23.9%. The highest percentage change increase in Non-rheumatic calcific aortic valve disease has seen 21.8%, an upward increase from 7.3 per 100,000 in 1990 to 8.9 per 100,000 in 2019 (Table 3).

The global death rate also showed a significant upward trend, from 1.46 per 10,000 per population in 1990 to 2.12 in 2019. Similarly, the death rate has increased in Pakistan as compared to South Asia, whereas, globally, the highest number of death was noted at 15,525,346 in 1990 and 32,598,376 in 2019, respectively (Figure 1).

DISCUSSION

The number of non-rheumatic VHD cases is increasing with every passing year, globally as well as in the South Asian region and Pakistan. Such an increase can be attributed to a trend toward an aging population and a general increase in life expectancy.[16] The socioeconomic growth and quality of healthcare infrastructure dramatically vary among the various administrative territories of the country.[17] Similarly, varying trends in the burden of non-rheumatic VHD have been witnessed for the different administrative territories of the country. In the analysis of the prevalence rate per 100,000, the highest growth rate of 76.4% between 1990 and 2019 (from 8.7 to 15.3 cases per 100,000) has been observed for the Islamabad capital territory, followed by the province of Sindh with a growth rate of 32.6%. Three administrative territories, namely Baluchistan (-14.0%), Gilgit-Baltistan (-4.9%), and Khyber Pakhtunkhwa (-3.1%), showed a negative trend. In comparison, four out of seven administrative territories showed positive growth resulting in an overall positive growth of 14.4% between the years 1990 and 2019 for the prevalence rate per 100 thousand individuals. Similarly, the death rate per 100 thousand also showed a positive growth of 1.11% over the past 30 years, with the highest positive growth for the Gilgit-Baltistan region (15.2%) followed by Sindh (15.1%), Khyber Pakhtunkhwa (10.2%), and Azad Jammu & Kashmir (10.0%). At the same time, there was a negative growth for the other three regions, namely Islamabad Capital Territory (-14.2%), Baluchistan (-13.5%), and the province of Punjab (-1.8%). The age-standardized death rate per 100,000 showed a positive growth of 12.9% between the years 1990 and 2019 (from 1.32 to 1.49).

The non-rheumatic VHD is an age-dependent degenerative or calcific process in which various risk factors and co-morbid conditions, such as hypertension, smoking, and diabetes mellitus, play an essential role in its development and progression.[18] These risk factors have shown an increasing trend in the Pakistani population in recent decades.[19] Such an increased risk factor can be attributed to this population's increasing burden of non-rheumatic VHD. In a population where non-rheumatic VHD is already a significant public health issue, the rising burden of non-rheumatic VHD is worrisome, considering its direct and indirect socioeconomic effects.[20]

Chen J et al.[6] conducted a comprehensive study of global trends of VHD for the years 1990 to 2017 based on GBD estimates. It has been reported that the estimated global incidence of non-rheumatic VHD has increased by 45.10% to 401.69 new cases (per 100,000) in the year 2017 from 276.84 new cases (per 100,000) in the year 1990 with an age-standardized incidence rate of 384.35 (/100,000) and 391.49 (/100,000) new cases for the year 1990 and 2017, respectively.[6] Additionally, the age-standardized incidence rate for non-rheumatic VHD was reported to

decrease only in nine countries and territories, while there was an increasing trend in 186 countries and territories. At the same time, a decreasing trend in age-standardized death rate has been witnessed during the exact duration of 1990 to 2017 in most (110) of the countries and territories and 85 countries and territories, including Pakistan, exhibit an increase in the age-standardized death rate due to non-rheumatic VHD.[6]

Many studies in the past focused on the non-rheumatic VHD burden in industrialized countries; rheumatic VHD is the general topic of discussion for underdeveloped or developing countries.[21] However, with the increasing rate of urbanization and aging population, non-rheumatic VHD too is gaining clinical importance in underdeveloped or developing countries.[6] An oversimplified traditional standpoint was a passive age-related degenerative phenomenon behind the development of non-rheumatic VHD. Still, in recent literature, various other pathophysiological processes have been found associated with the development of non-rheumatic VHD, which included sterile inflammation, endothelial injury/dysfunction, and/or lipid accumulation.[6,22,23] Surgery or percutaneous procedures are the only effective treatment strategies for most cases of non-rheumatic VHD in addition to palliative therapies. No effective pharmacological therapies are available to halt or slow the progression of non-rheumatic VHD.[18,24] Hence, it is essential to understand the underlying genetic, pathophysiological, and anatomic mechanisms behind the development of non-rheumatic VHD so the preventive and management option can be tailored to the task.[16]

In addition to the various other methodological limitations of the GBD estimation process described previously,[25] the lack of reliable national representative studies of the data for Pakistan to use for the computation of reliable national representative estimates is the main limitation in the first place.

CONCLUSION

Based on the analysis of GBD estimates, it can be concluded that in Pakistan, the prevalence, deaths, and DALYs rate of non-rheumatic VHD per 100 thousand individuals increased substantially between 1990 and 2019. The age-standardized death rate also significantly increased over the past 30 years. Hence, like other non-communicable diseases, the non-rheumatic VHD needs to be acknowledged as a significant health issue in LMCs, like Pakistan, and immediate policymaking is needed to handle the impending burden of non-rheumatic VHD.

AUTHORS' CONTRIBUTION

BA and WH: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. JH, AB, JH, ASM and AR: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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