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Research Article

Is Rheumatic Heart Disease Still Endemic in Tunisia? A Review of 14-year Period and Future Projections

Houda Ben Ayed[1*], Sourour Yaich[1], Mariem Ben Hmida[1], Maissa Ben Jemaa[1], Maroua Trigui[2], Jihene Jedidi[1], Raouf Karray[1], Habib Feki[2], Yosra Mejdoub[1], Mondher Kassis[1] & Jamel Damak[1]

[1]*Community Health and Epidemiology Department, Hedi Chaker University Hospital, University of Sfax, Tunisia*

[2]*Preventive Medicine and Hygiene Department, Hedi Chaker University Hospital, University of Sfax, Tunisia*

[*]**Correspondence to:** Dr. Houda Ben Ayed, Community Health and Epidemiology Department, Hedi Chaker University Hospital, University of Sfax, Tunisia.

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Abstract

Introduction

Rheumatic heart disease (RHD) ranks among the leading causes of non-communicable diseases in developing countries. Tunisia is recognized as an endemic area of RHD. Our study aimed to determine the epidemiological specificities of RHD and to assess its chronological trends over time.

Methods

We retrospectively collected data from the regional morbidity register of Hedi Chaker University Hospital, South of Tunisia between 2003 and 2016. Joinpoint regression analysis was performed to study the chronological trends of RHD over time (Annual Percentage Change (APC); p).

Results

Overall, 1063 patients were hospitalized for RHD. We noted 635 women with RHD (59.7%). There were 432 cases (40.6%) aged between 40 and 59 years. The case-fatality rate was 1.6%. The mean annual number of RHD new cases was 76 cases/year. The incidence rate of RHD was 7.95 cases/100000 person-year. Trends analysis showed a decreasing trend in overall RHD new cases from 2003 to 2016, but no significant change was noted (APC = -4.4%; 95%CI = [-10.4;2.1%]; p = 0.2). The same results were applied for males (APC = -5.4%; 95%CI = [-12.4; 2.2%]; p = 0.1) and females (APC = -3.8%; 95%CI = [-9.3; 2.2%]; p = 0.2). According to age-groups, we noted a significant decline in RHD new cases for patients aged under 25 years (APC = -15.95%; 95%CI = [-21.8; -9.6%]; p < 0.001). The number of new RHD cases predicted by the age–period–cohort model would attend 35 cases by 2026 ([Lower credible interval = 27, Upper credible interval = 46]).

Conclusions

Inspite of declining curves in the hospitalizations of RHD, it still remains a major public health problem for both sexes and in all age-groups. The decreasing trend was mainly observed among young patients, with a significant change over time.

Abbreviations

RHD: Rheumatic Heart Disease; APC: Annual Percentage Change; LcrI: Lower credible interval, UCrI: Upper credible interval; HCUH: Hedi Chaker University Hospital; HCIR: Hospital Crude Incidence Rate; 95% CI: 95% Confidence Interval; SD: Standard deviation; PY: Person-year.

Introduction

Rheumatic heart disease (RHD) ranks among the leading causes of non-communicable diseases in low-income and middle-income countries and causes up to 250000 premature deaths every year [1]. It results from a primary infection in the upper respiratory tract or from a re-infection or a relapse associated with an inappropriate inflammatory response to the group A beta hemolytic *Streptococci* [2]. According to the WHO, 12 million people worldwide are affected by rheumatic fever and rheumatic heart disease, among whom 79% live in the developing countries, particularly those in the African continent [3]. It continues to be a major public health challenge in limited resources countries, accounting for a great cardiovascular-related loss of disability-adjusted life-years worldwide [4]. RHD affects the most productive part of the population, which may lead to undermine national productivity. Its epidemiology parallels most indicators of poverty, notably poor hygiene, household crowding, poor living conditions, social inequality and limited access to healthcare. In high-income countries, the burden of RHD decreased markedly during the 20th century, attributable to socioeconomic development and advances in medical management [5].

Recently, there has been an increasing interest in the burden of RHD, driven in part by the growing costs attributable to this disease and the utmost need to yield standards level in cardio-vascular health. Epidemiological surveillance is particularly interesting in endemic area, allowing health authorities to prioritize preventive and curative interventions accordingly. Tunisia is recognized as an endemic area of RHD. Otherwise, updated and reliable data of RHD incidence in South of Tunisia are weakly documented. Therefore, our study aimed to determine the epidemiological specificities of RHD and to assess its chronological trends over time.

Methods

Study Design and Settings

We retrospectively collected data from the regional morbidity register of Hedi Chaker University Hospital (HCUH), South of Tunisia, from January 1st, 2003 to December 31st, 2016. The register was implemented by the community health and epidemiology department since 1990 and received information periodically from all departments of HCUH. Patients were hospitalized essentially in cardiology department, which included intensive care unit and applied the highest cardiologic expertise and advanced diagnostic investigations to make definitive diagnoses and provide medical care.

Inclusion Criteria and Data Collection

We included all newly diagnosed patients with RHD, who were hospitalized at HCUH during the study period. Patients ultimately diagnosed RHD were encoded according to the International Classification of Diseases-10 (ICD-10) (I01, I05, I06, I07, I08, I09). Patients hospitalized for acute articular rheumatism without carditis or other complications coded in ICD-10 as I00. I02 were not included. We included only patients living in Sfax governorate.

During the study period, the definitions of RHD were unified. The database variables included patients' socio-demographic characteristics and hospitalization characteristics such as length of hospital stay, the discharge status (home return, transfer to other departments or others hospitals and death). The crude hospital incidence rate (CHIR) of RHD was calculated based on Tunisian National Institute of Statistics data and was expressed as the number per 100000 person-year (PY).

Chronological Trends and Projected Incidence Rates

In order to analyze trends in RHD hospitalizations, the Joinpoint Regression Analysis program, version 4.6.0.0 was performed. Joinpoint fits a linear regression model to the data to detect periods with statistically distinct log-linear trends over time. A significance level of 0.05 was used for the permutation test, which determines the minimum number of "joinpoints" necessary to fit the data. The annual percent change (APC) within each segment was calculated with 95% confidence interval (95% CI).

To perform RHD projection for 2026, an age-period cohort model was performed assuming a Poisson regression model for the counts of the cases. We estimated the mean number of new cases of RHD in each year, with lower and upper credible intervals (LCrI, UCrI).

Statistical Analysis

Statistical analysis was performed using SPSS.20 software. The Kolmogorov-Smirnov test was used to assess the distribution of quantitative variables. The results of quantitative variables were presented as means ± Standard deviation (SD) or medians and interquartile range (IQR). Those of qualitative variables were presented as numbers and percentages. We used Spearman test (Rho coefficient, p) to study the correlation between two quantitative variables. A p-value of <0.05 was considered statistically significant.

Results

Patients' Characteristics

During the 14-year study period, we registered 145166 hospitalizations of any age, all diseases combined, among whom 1063 patients hospitalized for RHD (0.73%). We noted 635 women with RHD (59.7%), with a sex ratio of 0.7. The mean age of patients with RHD was 46 ± 17.8 years. There were 432 cases (40.6%) aged between 40 and 59 years (Table 1). Cardiology department hosted 1057 patients with RHD (99.4%). Home return was the most common discharge status (991 cases; 93.3%). The median hospital length of stay was 7 days (IQR, 4-13 days). There were 18 deaths, accounting for a case-fatality rate of 1.6%. Rheumatic mitral valve was the dominant RHD localization (547 cases; 51.5%) (Table 2).

Table 1: *Number, percentage and incidence/mortality rates of rheumatic heart disease hospitalizations by gender and age groups*

Variables	N (%)	Average population	Mean number/year	HCIR (/100000 PY)	Mortality	
					Deaths	HCMR (/100000 PY)
Total	1063 (100)	955421	76	7.95	18	0.13
Gender						
Males	428 (40.3)	457485	30.6	6.68	4	0.06
Females	635 (59.7)	497936	45.3	9.1	14	0.14
Age groups (years)						
<25	141 (13.3)	230735	10	4.33	1	0.03
25-39	237 (22.3)	387424	17	4.39	4	0.073
40-59	432 (40.6)	228633	31	13.56	5	0.15
≥60	253 (23.8)	108536	18	16.5	8	0.53

N: Number; %: Percentage among all rheumatic heart disease hospitalizations; HCIR: Hospital crude incidence rate, HCMR: Hospital crude mortality rate; PY: person-year.

Table 2: *Characteristics of rheumatic heart disease hospitalizations*

Variables	Number	Percentage
All localizations	1063	100
I05: Rheumatic mitral valve	547	51.5
I06: Rheumatic diseases of the aortic valve	262	24.6
I07: Rheumatic tricuspid valve	65	6.1
I08: Diseases of several valves	173	16.6
I09: Other rheumatic heart disease	13	1.2
Discharge status		
Home return	991	93.3
Transfer to another department	54	5.1
Death	18	1.6
Departments		
Cardiology	1057	99.4
Pediatrics	3	0.28
Other departments	3	0.28

Incidence and Mortality Rates of RHD

The mean annual number of RHD new cases was 76 cases/year during the study period. Overall, the HCIR was 7.95 cases/100 000 PY. It was higher among females (9.1 cases/100 000 PY). According to age groups, the highest HCIR was observed among patients aged 60 years and above (16.5 cases/100 000 PY). The hospital crude mortality rate was 0.13/100 000 inhabitants/year. It was 0.14/100 000 inhabitants/year for females and 0.06/100 000 inhabitants/ year for males (Table 1). A significant and low increase of RHD patients' mean age was notified from 2003 to 2016 (Rho = 0.2; $p < 0.001$).

Chronological Trends and Projection of RHD New Cases up to 2026

Joinpoint regression analysis showed a decreasing trend in overall RHD new cases from 2003 to 2016, but no significant change was noted (APC = -4.4%; 95%CI [-10.4; 2.1%]; $p = 0.2$). The same results were applied for males (APC = -5.4%; 95%CI [-12.4; 2.2%]; $p = 0.1$) and females (APC = -3.8%; 95%CI [-9.3; 2.2%]; $p = 0.2$) (Figure 1). As for age-specific curves, trends analysis of RHD new cases showed a significant decline from 2003 to 2016 for patients aged under 25 years (APC = -15.95%; 95%CI [-21.8; -9.6%]; $p < 0.001$). For patients aged between 25 and 39 years (APC = -6.8%; 95%CI [-13.7; 0.7%]; $p = 0.1$) and those aged between 40 and 59 years (APC = -2.69%; 95%CI [-9.5; 4.7%]; $p = 0.4$), we noted a declining trend, but without significant change over time, while for those aged 60 years and above, trends curve remain stable from 2003 to 2016, with an APC of 0.64% (95%CI [-6.3; 8.1%]; $p = 0.9$) (Figure 2).

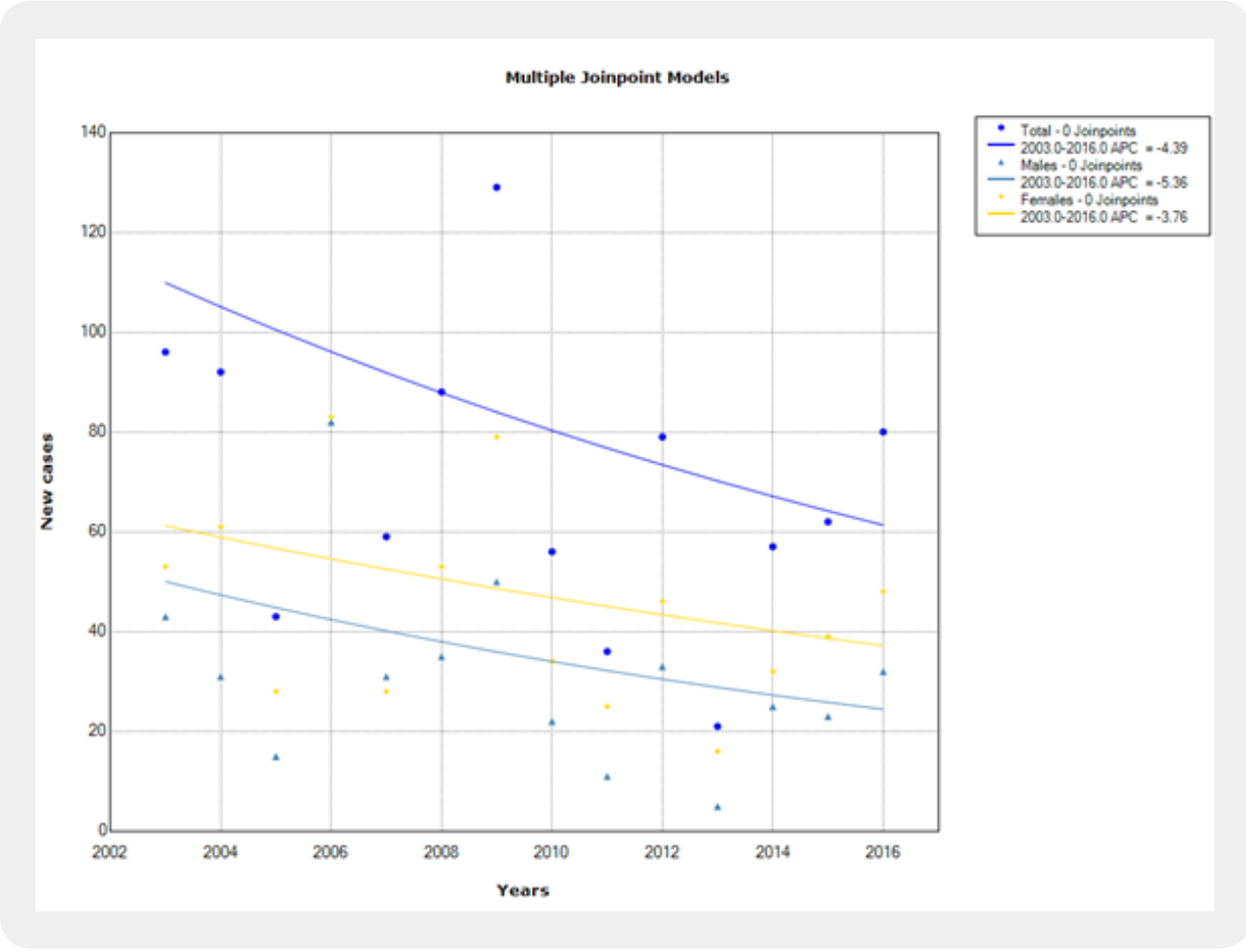

Figure 1: *Global and sex-specific chronological trends of rheumatic heart disease hospitalizations in Southern Tunisia during the period 2003-2016*

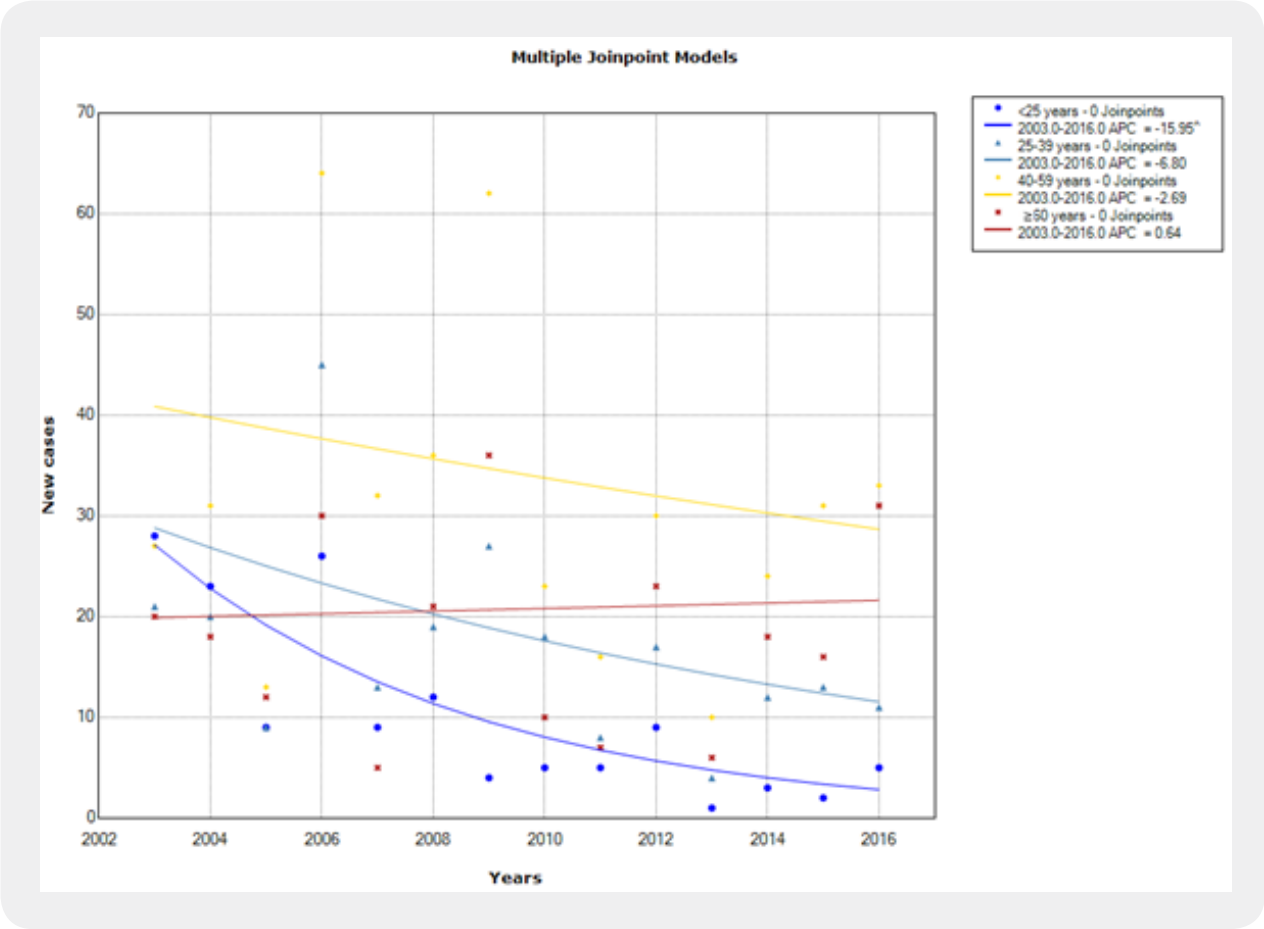

Figure 2: *Chronological trends of rheumatic heart disease hospitalizations by age-group in Southern Tunisia during the period 2003-2016*

The number of new RHD cases predicted by the age–period–cohort model would attend 35 cases by 2026 ([LCrI = 27, UCrI = 46]). According to age groups, the mean estimated number of new RHD cases would attend 5 cases up to 2026 ([LCrI = 3, UCrI = 6) for patients aged under 25 years, 8 cases([LCrI = 6, UCrI = 11]) for those aged between 25 and 39 years, 14 new cases ([LCrI = 11, UCrI = 19]) for those aged between 40 and 59 years and 8 new cases ([LCrI = 6, UCrI = 11]) for those aged 60 years and above (Figure 3).

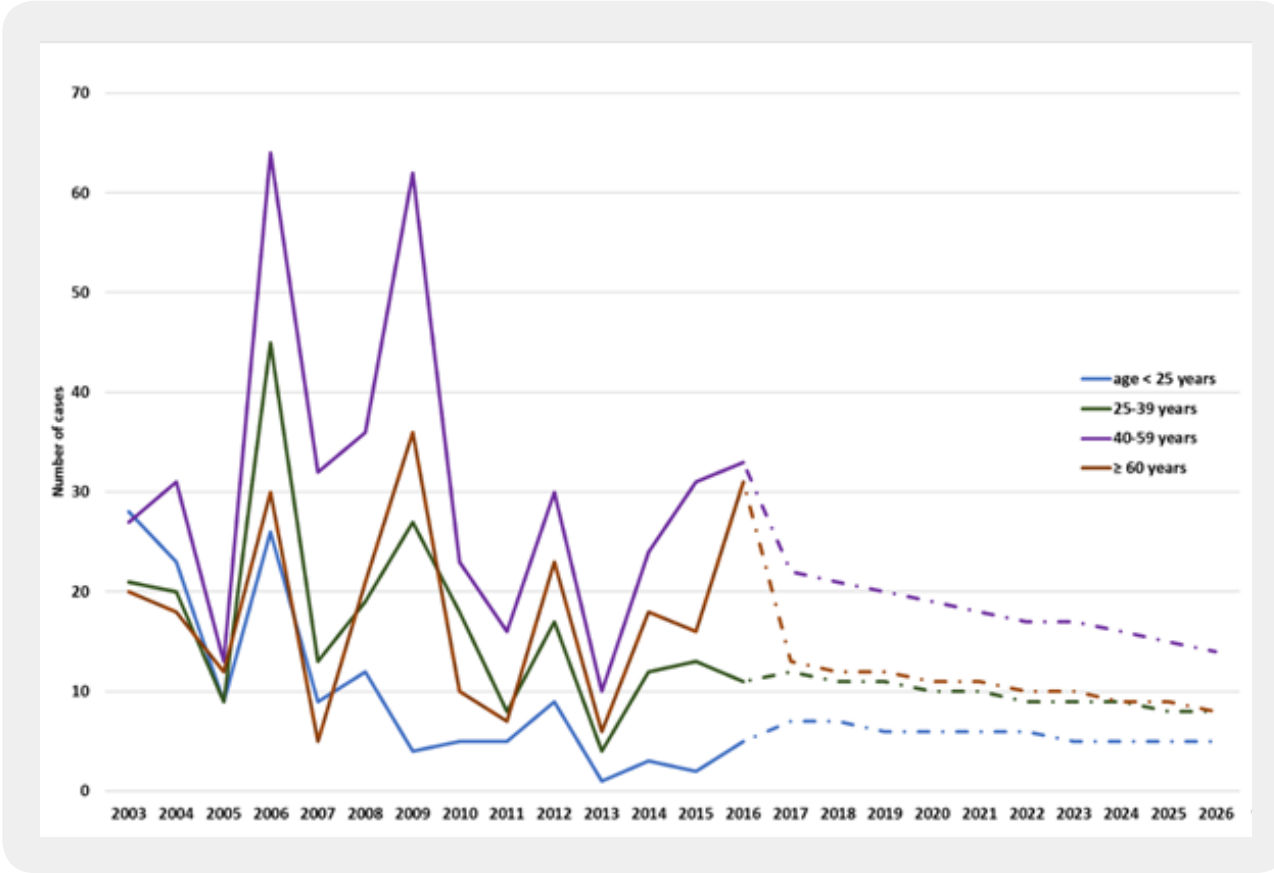

Figure 3: *Annual number new cases for the observed (2003-2016) and the predicted periods (2016-2026) of rheumatic heart disease hospitalizations in Southern Tunisia by age-group*

Discussion

Rheumatic heart disease is one of the most common and preventable acquired heart diseases. In high-income countries, the burden of RHD decreased markedly during the 20th century, attributable to improved living conditions associated with socioeconomic development and advances in medical management [6]. In the developing countries, militating against RHD remains a daily challenge, due to a poor awareness of physicians as well as patients of the importance of penicillin usage for acute rheumatic fever. The estimated number of RHD in 2015 was 33194900 cases that occurred in countries with an endemic pattern of disease, while only 221600 cases were in countries with a non-endemic pattern [5].The highest prevalence rates were in Western Pacific Region Oceania, followed by central sub-Saharan Africa and South Asia [5,6]. In 2015, the countries with the largest estimated numbers of cases of RHD were India (13.17 million cases), China (7.07 million), Pakistan (2.25 million), Indonesia (1.18 million) and the Democratic Republic of the Congo (805000), together accounting for 73% of global cases [5]. At a local level, a previous survey conducted on a hospital-based population in Central-east of Tunisia during the same period reported a total number of 1063 hospitalizations for RHD, with an incidence of 10.97/100 000 PY [7], which was similar to our findings.

According to WHO, the RHD-related mortality varies widely, from1.8/10^5inhabitants in the region of the Americas to 7.6/10^5 inhabitants in the region of South-East Asia, which was lower than our rates [8], whereas other studies showed similar case-fatality rates to our study, ranging from 1 to 1.5% [1,7].

Another important finding in our study suggested the predominance of RHD among women. Various other studies also revealed higher rates among females [9,10]. It has been reported that female gender was associated with a higher risk of having borderline RHD, with an OR of 1.9 [11]. This might be the result of innate susceptibility or an increased exposure to group A *streptococcus* probably due to a greater involvement of women in child rearing.

During the study period, the diagnosis age of patients with RHD has significantly increased over time and the highest HCIR was observed among elderly (age ≥ 60 year). These results were in line with other Korean studies reporting higher prevalence rates of RHD among older age groups, resulting in high disease burden and increasing health-care costs [12,13]. These findings supported the hypothesis suggesting that RHD can occur at any age, even at an advanced age, which reflected the under-screening rate of RHD during childhood. Therefore, future designs of cardiovascular healthcare services in countries with a rapidly aging population should be urgently implemented. The lowest rate was observed among younger patients (age < 25 years). These results were not contrasting with previous researches reporting high prevalence of RHD among children and adolescents [14-16], but highlighted the long latency period between the pharyngeal infection with Group A β hemolytic *Streptococcus,* the acute rheumatic fever, followed by asymptomatic involvement of the heart valves fibrosis and the beginning of clinical signs in our population. Thus, we should emphasize on the value of school screening programs for detecting asymptomatic RHD as an effective alternative to morbidity registers that are based solely on clinical encounters.

The mitral valve was the most common localization of the RHD. The same findings have also been shown in previous studies [17-19]. An Indian survey reported that mitral valve disease accounted for 86% of cases, aortic valve involvement was seen in 7% of cases [18]. It has been reported that the tricuspid valve is rarely affected by rheumatic carditis, but functional tricuspid regurgitation may accompany mitral valve disease [17].

The number of cases in developed countries have reduced drastically [5]. However, the same did not apply to developing countries, like those in sub-Saharan Africa. In Nigeria, the prevalence of RHD has increased from 2.9 to 9.8% and from 17.4 to 57.7% for the structural and acquired heart diseases, respectively [19]. On the other hand, a significant decline was noted in a previous Tunisian study conducted from 2000 to 2013 [7], which was consistent with our study. This might be explicated by the implementation of acute articular rheumatism monitoring program in Tunisia since 1980, the delivery of penicillin for the treatment of sore throat, notably at an early age, and the health education of the parents concerning the therapeutic observance during the treatment of angina, which provided a strong explanation for the significant decrease of RHD among patients under 25 years. Furthermore, our country is undergoing an epidemiological transition during the last decades, characterized by the predominance of chronic diseases, mainly ischemic heart disease at the expense of infectious diseases.

Conclusion

Our study provided original findings about the substantial burden of RHD in Southern Tunisia. In spite of declining curves in the hospitalizations of RHD, it still remains a major public health problem for both sexes and in all age-groups. The decreasing trend was mainly observed among young patients, with a significant change over time. A reduction in social inequalities and unified global approach based on early screening of silent RHD at an early age represent the cornerstones of community-based prevention of RHD, particularly in low-resources countries.

Supplementary Files (if applicable)

Not applicable

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Conflicts of Interest

No conflicts of interest.

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