

# Cardiovascular diseases in Southern Tunisia: current trends and future projections

## Les maladies cardiovasculaires dans le Sud Tunisien : tendances actuelles et futures projections

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### RÉSUMÉ

**Introduction :** Les maladies cardiovasculaires (MCV) représentent une cause majeure de morbi-mortalité, induite par la transition épidémiologique dans le monde.

**But :** Notre objectif était de décrire le profil épidémiologique des MCV, d'évaluer leurs tendances chronologiques et d'estimer leurs futures projections.

**Méthodes :** Nous avons collecté rétrospectivement les données du registre régional de morbi-mortalité du CHU de Sfax, Tunisie, entre 2003 et 2016. Nous avons inclus les patients atteints de cardiopathie ischémique (CI), d'insuffisance cardiaque (IC) et de trouble du rythme et de conduction (TRC).

**Résultats :** Le taux moyen d'incidence hospitalière standardisé selon l'âge (TIHSA) était de 94,8, 20,6 et 14/100000 habitants/an pour les CI, l'IC et les TRC, respectivement. L'analyse des tendances chronologiques des MCV a montré une augmentation significative du TIHSA des CI, passant de 54,3/100000 habitants en 2003 à 123/100000 habitants en 2016, avec un changement annuel en pourcentage (CAP) de 3,59% (IC95%=[0,4%-6,7%];p<0,001). Une tendance à la hausse était observée pour l'IC, avec un TIHSA passant de 8,6/100000 habitants en 2003 à 22,6/100000 habitants en 2016, avec un CAP de 8,29% (IC95%=[4,1%-12%];p<0,001). Pour les TRC, aucun changement significatif du TIHSA n'était observé. Les projections ont montré que le TIHSA estimé serait respectivement de 131 et de 36,5/100000 habitants pour les CI et l'IC, tandis que le RCD baisserait à 19,6/100000 habitants en 2026.

**Conclusion :** L'augmentation des CI et de l'IC était à un rythme alarmant et pourrait se poursuivre dans les 10 prochaines années. L'instauration des mesures de prévention primordiale, primaire et secondaire serait urgente afin de réduire le fardeau massif des MCV.

### Mots-clés

Cardiopathie ischémique ; Incidence ; Insuffisance cardiaque ; Projection ; Tendances ; Troubles du rythme et de la conduction

### SUMMARY

**Background :** Cardiovascular diseases (CVD) are a major cause of morbidity and mortality, driven by the epidemiological transition world-wide.

**Aim :** We aimed to describe the epidemiological profile of CVD hospitalizations, to assess their chronological trends and to estimate their future projected trends.

**Methods :** We retrospectively collected data from the regional morbidity registry of the University Hospital of Sfax, Tunisia, between 2003 and 2016. We included patients with ischemic heart disease (IHD), heart failure (HF) and rhythm and conduction disorder (RCD).

**Results :** The mean age-standardized hospital incidence rate (ASHIR) was 94.8, 20.6 and 14/100000 inhabitants/year for IHD, HF and RCD, respectively. Trends analysis of CVD showed a significant increase in the ASHIR of IHD from 54.3/100000 inhabitants in 2003 to 123/100000 inhabitants in 2016, with an Annual Percentage Change (APC) of 3.59% (95%CI:0.4–6.7%;p<0.001). An upward trend was observed for HF, with ASHIR rising from 8.6/100000 inhabitants in 2003 to 22.6/100000 inhabitants in 2016, with an APC of 8.29% (95%CI:4.1–12%;p<0.001). For RCD, no significant change in ASHIR was found. Projections showed that the estimated ASHIR would attend 131 and 36.5/100000 inhabitants for IHD and HF, respectively, while RCD would decline to 19.6/100000 inhabitant in 2026.

**Conclusions :** IHD and HF were rising at an alarming rate and were expected to continue up to the next 10 years. Therefore, there is an urgent need to emphasize on primordial, primary, and secondary prevention in order to reduce the massive burden of CVD.

### Key-words

Heart Failure; Incidence; Ischemic Heart Diseases; Projection; Rhythm and Conduction Disorder; Trends

## INTRODUCTION

Cardiovascular diseases (CVD) are a major cause of morbidity and mortality, generating a substantial burden of illness world-wide. Globally, CVD led to 17.5 million deaths in 2012, among which 75% occurred in the developing countries [1]. This rate was driven by epidemiological transition consisting of industrialization, urbanization and related lifestyle changes that affected firstly the developed countries and spread secondary to developing countries [2]. In the past 20–30 years, Tunisia has experienced a crucial demographic transition, reflecting a sustained and integrated economic, social and health development [3]. Previously, the country's full attention was paid in combating the communicable diseases such as tuberculosis and HIV infections. Currently, CVD have assumed epidemic proportions and have represented the leading causes of death accounting for almost 30% of all deaths [4]. In front of the rapidly growing burden of non-communicable diseases, notably CVD, health policies have been redirected meanwhile to cope with the actual epidemiological situation. The emerging CVD epidemic trends in our region have not been given enough attention. In turn, the epidemiological pattern of CVD and the shifts need to be characterized in order to prioritize public health interventions. In light of this, the present study aimed to provide an update on the epidemiological features of CVD hospitalizations, to assess their chronological trends over a 14-year period and to estimate their future projected trends in our region.

## METHODS

### Study design and settings

We conducted a retrospective study including all patients with CVD hospitalized at HCUH from January 1st, 2003 to December 31st, 2016. Only patients who were residents of Sfax Governorate were included. Hedi Chaker University Hospital (HCUH) is an 889-bed tertiary level teaching hospital in the region of Sfax, Tunisia, with 15 hospital departments. It includes an intensive care unit for CVD and outpatient services. All departments are supported by experienced specialists and provide quality services and treatment.

### Population study and data collection

We obtained data from the regional morbidity register of HCUH. Then we checked collected data at the Community

Health and Epidemiology Department (CHED) and entered them with "SPSS" software. This register was implemented in the department of (CHED) since 1990 and received information periodically from all departments of HCUH. We included only the newly diagnosed cases of CVD in our study. Readmitted patients were excluded in order to calculate the incidence rates. We used the tenth revision of International Classification of Diseases codes (ICD-10) to identify morbid conditions. According to this classification, Diseases of the Circulatory System are coded from I00 to I99. In the present study, we focused on Ischemic Heart Diseases (IHD) (from I20 to I25), Heart Failure (HF) (I50) as well as Rhythm and Conduction Disorders (RCD) (I44, I45, I47, I48, I49). During the study period, the definitions of the diseases were unified and the decision criteria of entering and leaving hospital were not changed.

The database variables included patients' socio-demographic characteristics, length of hospital stay and the main diagnostic. We collected also exhaustive information dealing with the discharge status (home return, transfer to other departments or others hospitals, and death). For each department, data were collected by a supervisor on a data collection form created specifically for that purpose; the doctors responsible then had to verify its integrity.

### Crude and age-standardized hospital incidence rates

Eligible patients were divided into 4 age categories: under 20 years, between 20 and 39 years, between 40 and 59 years and 60 years or above. The crude hospital incidence rate (CHIR) of CVD was calculated based on Tunisian National Institute of Statistics data and was expressed as the number per 100000 inhabitants [5]. The average population was calculated as follows: (Sfax population in 2004 + Sfax population in 2014)/2. The age-standardized hospital incidence rate (ASHIR) per 100000 inhabitants/year was calculated using the direct method, on the basis of WHO population standard (2000-2025) and age-specific crude rates [6].

### Statistical analysis

Statistical analysis was performed using SPSS.20 software. The results of quantitative variables were presented as means  $\pm$  Standard deviation (SD) or medians and interquartile range (IQR). Those of qualitative variables were presented as numbers and percentages. In order to analyze chronological trends in CVD hospital

incidence, the Joinpoint Regression Analysis program, version 4.5.1.0 was performed. Joinpoint fits a linear regression model to the data to detect periods with statistically distinct log-linear trends over time. This analysis identifies inflexion points ('joinpoints'), using a series of permutation tests, with Bonferroni adjustment for multiple comparisons. 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 use of a natural log-linear model enables the analysis of a constant percentage change in rate over time. The annual percent change (APC) within each segment was calculated with 95% confidence intervals (95% CI).

To perform incidence projection up to 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 CVD in each year, with lower and upper credible intervals (LCrI, UCrI). Then we calculated the estimated crude and standardized incidence rates up to 2026 based on the Tunisian projected population of 2021 and the WHO population standard [6,7]. A p-value of <0.05 was considered statistically significant.

## RESULTS

### Patients' characteristics

During the 14-year study period, we recorded 145166 hospitalizations of any age, all diseases combined. All diseases of the circulatory system accounted for 18924 cases, including IHD, HF, RCD, Rheumatic heart diseases, Hypertension and other CVD. Of these, we included in the present study only IHD, HF, and RCD cases, which were the most frequent CVD, with 15760 cases (83.2% of all CVD, 10.85% of all hospitalizations). In our study, we found 9946 males (63.1%), with a sex ratio of 1.7. At enrollment, the mean age of patients with CVD was  $62 \pm 13.7$  years. There were 9528 cases (60.4%) aged 60 years and above (Table 1). Home return was the most common discharge status (95.5%). The median hospital length of stay was 6 days (IQR, 3–10 days). The main CVD subgroup was IHD with 11558 cases (73.3%).

**Table 1.** Patients' characteristics

Variables		
All cardiovascular diseases (N, %)		
Gender		
Male (N, %)	9946	63.1
Age (years)		
Mean, SD	62	13.7
Age categories (years) (N, %)		
<20 years	153	1
[20-40[	674	4.3
[40-60[	5405	34.3
≥60	9528	60.4
Length of hospital stay (days) (median, IQR)	6	[3-10]
Discharge status (N, %)		
Home return	15045	95.5
Transfer to another department	284	1.8
Deaths	237	1.5
Against medical advice	194	1.2
CVD subgroups (N, %)		
Ischemic Heart Diseases	11558	73.3
Rhythm and Conduction Disorders	2511	15.9
Heart Failure	1691	10.8

N: Number; SD: Standard Deviation; CVD: Cardiovascular Diseases.

### Cardiovascular diseases hospital incidence rates

The mean annual number of IHD, RCD and HF were respectively 825.57, 193.15 and 120.78 cases/year. The HCIR was 88.6, 20.7 and 13 for IHD, RCD and HF, respectively. The ASHIR was 94.8/100000 inhabitants/year for IHD and 20.6/100000 inhabitants/year for RCD. As to HF, the ASHIR was 14/100000 inhabitants/year (Table 2).

### Chronological trends of cardiovascular diseases incidence rates

On analysis of different CVD subgroups trends using Joinpoint regression, there was a significant increase in the ASHIR of IHD from 54.3/100000 inhabitants in 2003 to 123/100000 inhabitants in 2016, with an APC of 3.59% (95% CI: 0.4–6.7%;  $p < 0.001$ ) (Figure 1a). Likewise, HF had a growing trend, with an ASHIR rising from 8.6/100000 inhabitants in 2003 to 22.6/100000 inhabitants in 2016, with an APC of 8.29% (95%CI: 4.1–12.7;  $p < 0.001$ ) (Figure 1b). With regards to RCD, the ASHIR increased from 14.1/100000 inhabitants in 2003 to 25.7/100000

**Table 2** Number of cases, crude and age-standardized hospital incidence rates of cardiovascular diseases subgroups

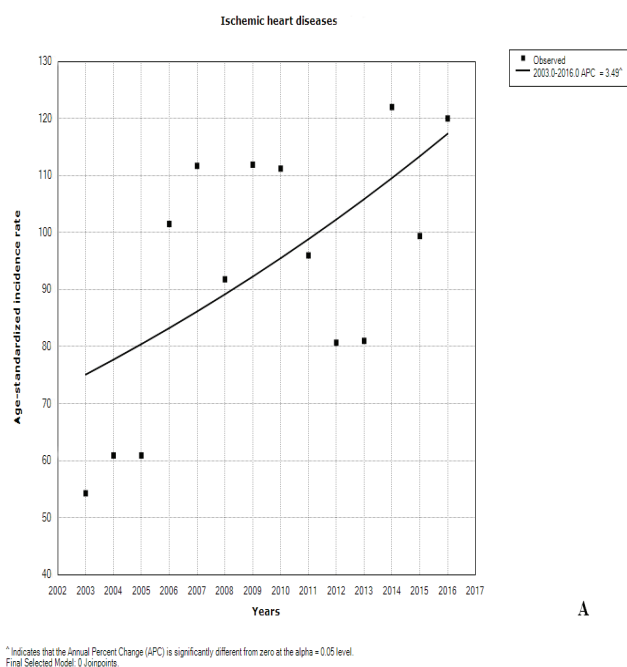
CVD Unit	Average population	N of cases N over 14 years (mean number/year)	HCIR (/100000 inhabitants/ year)	ASHIR (/100000 inhabitants/ year)
Ischemic Heart Diseases				
Total	931519	11558 (825.57)	88.6	
< 20 years	303618	8 (0.57)	0.18	
[20-40[ years	328553	341 (24.35)	7.4	94.8
[40-60[ years	213571	4397 (314.07)	147	
≥60 years	98567	6812 (486.57)	494	
Rhythm and conduction disorders				
Total	931519	2511 (193.15)	20.7	
<20 years	303618	88 (6.28)	2.1	
[20-40[ years	328553	250 (17.85)	5.2	20.6
[40-60[ years	213571	582 (41.57)	19.5	
≥60 years	98567	1591 (113.64)	115	
Heart Failure				
Total	931519	1691 (120.78)	13	
<20 years	303618	57 (4.07)	1.3	
[20-40[ years	328553	83 (5.93)	1.8	14
[40-60[ years	213571	426 (30.42)	14.2	
≥60 years	98567	1125 (80.35)	81.5	

N: Number; CVD: Cardiovascular diseases; HCIR: Hospital crude incidence rate, ASHIR: Hospital age-standardized incidence rate.

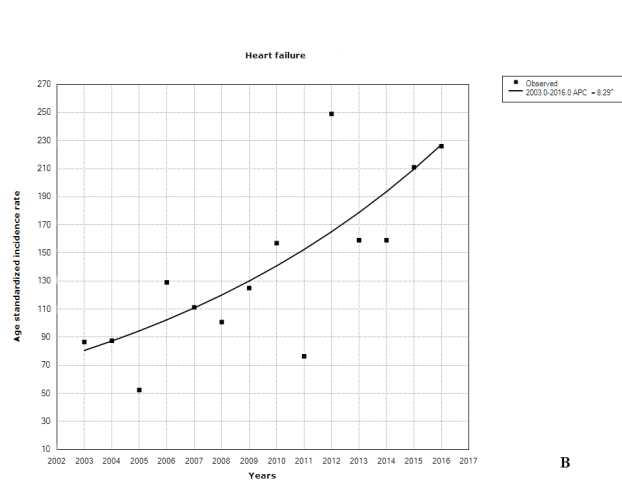
inhabitants in 2016, but with no significant change over time (APC=0.7; CI 95%: -2.6-4.2; p=0.6) (Figure 1c).

### Projected trends of cardiovascular diseases up to 2026

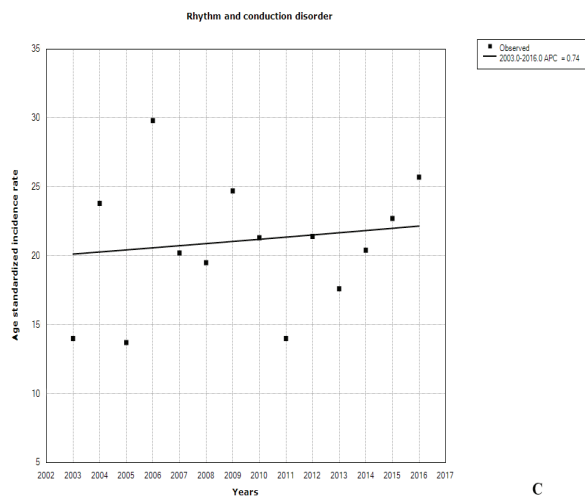
The number of new CVD cases predicted by the age-period-cohort model would attend 1377, 396 and 211 cases around 2026 for IHD, HF and RCD, respectively. The mean estimated number of new CVD cases for patients aged 60 years and above was 811 [LCrI=751, UCrI=876], 134 [LCrI=114, UCrI=158] and 264 [LCrI=217, UCrI=320] for CHD, RCD and HF, respectively. The estimated ASHIR and HCIR of IHD were 125 and 131/100000 inhabitants/year, respectively. Concerning HF, the estimated ASHIR would increase to 36.5/100000 inhabitants/year in 2026 (Table 3). As to RCD, the estimated ASHIR would decline from 25.7/100000 inhabitants in 2016 to 19.6/100000 inhabitants in 2026 (Table 3, Figure 2).



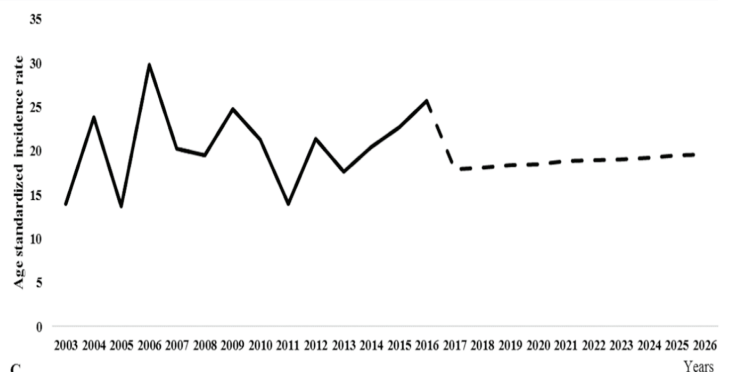
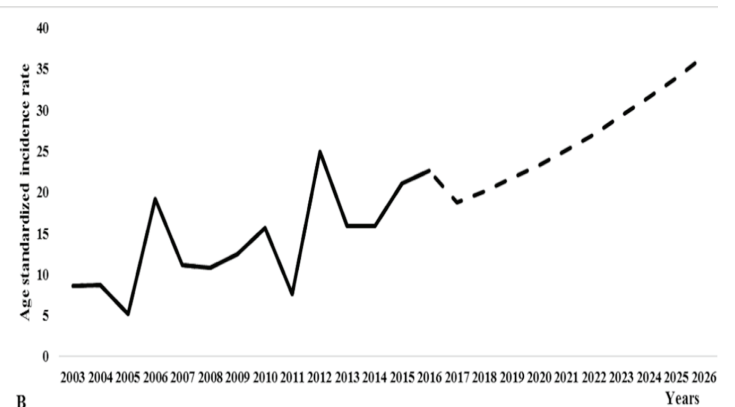
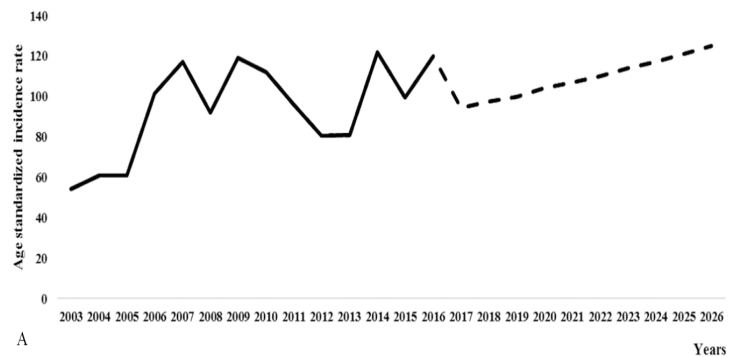
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\* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.  
Final Selected Model: 0 Joinspoints.



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**Figure 1 :** Chronological trends for age-standardized hospital incidence rates (per 100 000 inhabitants/year) for ischemic heart diseases (1A), heart failure (1B) and rhythm and conduction disorders (1C), 2003-2016

**Figure 2 :** Age-standardized hospital incidence rates (per 100 000 inhabitants/year) for the observed (2003-2016) and predicted periods (2017-2026) of ischemic heart diseases (2A), heart failure (2B) and rhythm and conduction disorders (2C)

**Table 3.** Ischemic heart diseases, rhythm and conduction disorders and heart failure incidence projections in 2026 stratified by age with lower and upper credible intervals, estimated crude and age-standardized incidence rates

Age categories (years)	Ischemic Heart Diseases			Rhythm and Conduction Disorders			Heart Failure		
	Mean	LCrI	UCrI	Mean	LCrI	UCrI	Mean	LCrI	UCrI
<20	1	0	2	7	6	10	13	10	18
[20-40[	41	36	46	21	17	26	19	15	26
[40-60[	524	484	566	49	41	59	100	81	123
≥60	811	751	876	134	114	158	264	217	320
Total	1377	1271	1490	211	178	253	396	323	487
HCIR*		131			20.1			37.8	
ASHIR*		125			19.6			36.5	

\*: per 100000 inhabitants; LCrI: Lower credible Interval; UCrI: Upper credible Interval; HCIR: Hospital Crude Incidence Rate; ASHIR: Hospital age-standardized Incidence Rate



## DISCUSSION

Nowadays, there is a global epidemiological transition in the developing countries through the changing disease pattern from infectious diseases to non-communicable diseases. This study revealed an era in the history and the epidemiological pattern of three cardiovascular disease conditions in a Tunisian university referral hospital.

Although, 50% of incident IHD are clinically silent, the latter represented a common cause of hospitalization [8]. Previous studies showed that IHD were the most commonly reported disease among the CVD admissions [9]. This was enlightened in our study, with 73.3% of all CVD. According to the Global Burden of Diseases, IHD were the leading cause of CVD health lost globally, as well as in each world region [10]. An Indian systematic review reported that in India and in other developing countries, premature occurrence of IHD is a concern, with an average prevalence of hospitalizations of 6% [11]. Likewise, disease burden of IHD in Korea accounted for a large share of burden of CVD, which was associated with the rapid aging in the Korean population [12]. Similarly, the leading cardiac disease etiologies in a study performed in Bangladesh were IHD and HF [13], as opposed to Ethiopia, where hypertension and rheumatic heart diseases were the leading CVD [14,15]. This might be due to the fact that hypertension patients were mostly treated in ambulatory firstly, and to the early treatment of respiratory tract infections and the early detection of rheumatic fever secondary. Furthermore, the lack of policies of control primordial CVD risk factors such as smoking and unhealthy diet as well as poor-quality preventive management may justify in part this high prevalence of IHD.

Knowledge of trends in the incidence of CVD in a community setting is of a paramount importance to better understanding contemporary patterns of the CVD morbidity profile and subsequently to target preventive interventions accordingly. Our study pointed out a rise in the age-standardized incidence rates among CVD patients during the last decade. Although the event trends observed in our University Hospital may not be representative of the entire Tunisian population, the increase in IHD and HF incidence rates were statistically significant. This rise could engender a rapidly growing burden in our country, since IHD accounted for 77% of CVD deaths, and mortality rates had significantly increased between 1997 and 2009 [16]. A previous review analyzing the growing epidemic of coronary heart disease reported that IHD

would increase by 160% in the region of Middle East and North Africa [17]. Similarly, the incidence of IHD in China increased by 1-2.7% annually [18]. This result was also exhibited in a Brazilian survey where the number of IHD hospitalizations grew up substantially (doubled) between 2008 and 2015 [19]. In fact, the increase in life expectancy has been accompanied by a large rural to urban migration pattern, rapid urban modernization, aging of the population, major dietary changes and increasing tobacco use. These interlinked forces explain much of the rise in IHD rates [17]. On the other hand, the incidence of IHD has decreased over time in developed countries, from 133 to 114/10000 persons per year of follow-up between 1982 and 1992 in the USA [20]. Similar findings were also found in Europe with a substantial decline of myocardial infarction incidence rate [21]. The trends in the incidence of IHD constitute a powerful gauge of the effectiveness of prevention and clinical interventions. It is worthy to note the varying incidence rates and secular trends in IHD reflect the different levels of risk factors and the availability of resources devoted to CVD care, and the stage of epidemiologic transition of each country or region in the two last decades.

Heart failure patients are frequently hospitalized, resulting in an important socio-economic burden both in developed countries and in countries in transition. As a consequence of population ageing, HF admissions are potentially increasing [22,23]. A recent study conducted in the UK reported that the estimated absolute number of individuals with newly diagnosed HF increased by 12% between 2002 and 2014, largely due to an increase in population size and age [24]. These findings agree with our study suggesting a significant rise in the incidence of HF, with an APC of 8.29%. There are many potential reasons for these findings, including mainly the significant rise in IHD, which was commonly complicated by HF. Moreover, CVD patients were habitually aged above 60 years and had frequent co-morbidities, which was therefore not surprisingly associated with further increased risk of HF occurrence. As a result, interventions to reduce HF hospitalizations should include consideration for treatment of comorbid conditions. Nevertheless, previous European large population surveys showed a significant decrease in the age-standardized rates of first HF admissions in Scotland and Slovenia over time [25,26]. This was similar to a nationally representative sample of hospitalizations in the USA, where HF age-standardized hospitalizations declined steadily over 2001-2009 [27].

The frequency of cardiac arrhythmias, particularly atrial fibrillation and ventricular tachyarrhythmia, is projected to increase as the population ages, greatly impacting health care resource utilization [28]. Tefera YG reported that rhythm disorder was a leading cause of hospitalizations, accounting for 11.3% of all CVD [14]. In our study, RCD disorders represented 15.9% of the population survey and remain relatively stable over time. An essential point must be surmised: RCD englobe a myriad heterogeneity of diagnoses varying according to sociodemographic characteristics and clinical presentations. These disorders may either be asymptomatic, or cause hemodynamic changes requiring specific care, notably in older adults who are particularly predisposed to these conditions due to the age-related changes in cardiac conduction system. A deeper investigation in incidence and secular trends of each RCD category by age group is therefore a starting point for determining the real burden of this disease. Projected trends of CVD showed a predicted increase either for HF or IHD. Similar to our findings, projected annual cardiovascular events including CHD would increase by >50% in China between 2010 and 2030 based on prior trends [29]. Likewise, previous studies reported that projections indicate that the prevalence of CVD in the United States may escalate by 10% between 2010 and 2030 [30]. The estimated increase stems in part from the aging of the population in our country and is also fueled by the concomitant trends for increasing risk factors such as obesity rates, hypertension rates and diabetes mellitus [16]. Moreover, the estimated burden of CVD in the developing countries is largely a result of a relative lack of access to the preventive and curative interventions.

## CONCLUSIONS

This study highlighted the massive burden of CVD in our region in the last decade and expanded upon previous works dealing with epidemiological description of the Tunisian hospital morbidity profile. IHD and HF were rising at an alarming rate and were expected to continue up to the next 10 years. Therefore, there is an urgent need to emphasize on primordial, primary, and secondary prevention strategies in order to promote a successful public health policy and to achieve Millennium Development Goals. Thus, rigorous and continuous efforts from clinicians, public health experts and health authorities are highly recommended.

## Compliance with Ethical Standards

### Disclosure of potential conflicts of interest

The authors reported no conflict of interest

### Research involving Human Participants and/or

Animals: Non-applicable

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