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Topics in Heart Failure Management



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This textbook represents a short update on original aspects of heart failure. It covers topics of heart failure management such as prevention, drug monitoring after heart transplant, and the critical care approach. There are also chapters on less common facets of this syndrome such as prevalence and features in a specific African region and the complexity of telemedicine in heart failure. In summa...

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1. Introductory Chapter: Heart Failure - A Multifaceted Syndrome

149

*By Giuseppe Rescigno**Open access peer-reviewed*

2. Telemedicine for Chronic Heart Failure: An Update

141

*By Emmanuel Andrès, Samy Talha, Mohamed Hajjam and Amir Hajjam El Hassani**Open access peer-reviewed*

3. Prevention of Heart Failure

168

By Oleksii Korzh

Open access peer-reviewed

4. Critical Care of Acute Heart Failure

By Chih-Hsin Hsu and Wei-Ting Li

Open access peer-reviewed

5. Heart Failure in Sub-Saharan Africa

274

*By Okechukwu S. Ogah,
Adewole Adebisi and Karen
Sliwa*

Open access peer-reviewed

226

6. Therapeutic Drug Monitoring of Micophenolate Mofetil in Cardiac Transplant Patients by Limited Sampling Strategy: An Update

By Massimo Baraldo, Sandro Sponga and Ugolino Livi

Heart Failure in Sub-Saharan Africa

Okechukwu S. Ogah, Adewole Adebisi and
Karen Sliwa

Additional information is available at the end of the chapter

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Abstract

Sub-Saharan Africa (SSA) is currently experiencing multiple burden of disease as a result of demographic and epidemiologic transition. This is occasioned rapid urbanization, unhealthy diets rich in fats and salt, western lifestyle and sedentary living. Heart failure (HF) has become a global public health issue. It is associated with high morbidity and mortality, frequent hospitalization and high economic cost. In SSA, HF is a disease of young and middle-aged adults with the attendant high disability-adjusted life years. This is unlike to the clinical profile and pattern of HF in high-income countries of North America, Western Europe and Japan where HF is a disease of the elderly. In addition, while ischaemic heart disease is the commonest aetiological risk factor for HF in high income countries, HF in SSA is essentially non-ischaemic in origin. Hypertensive heart failure, dilated cardiomyopathy, rheumatic heart disease, pericardial diseases and HIV associated cardiomyopathy are the common risk factors. The chapter reviews the contemporary information on HF in SSA in terms of socio-demographic features, clinical characteristics, aetiological risk factors, management, prognosis and economic burden.

Keywords: heart failure, cardiac failure, cardiac dysfunction, sub-Saharan Africa, Africa

1. Introduction

Africa has multiple burden of disease. While the continent is still grappling with traditional communicable and infectious diseases, there is increasing burden of non-communicable diseases (NCDs) such as hypertension, diabetes mellitus, cancers, etc., in addition to HIV/AIDS, malnutrition, wars and conflicts. The rapid epidemiologic transition from communicable to non-communicable diseases can be attributed to rapid urbanization, unhealthy diets rich in fats and salt, western lifestyle and sedentary living.

The global burden of disease 2015 report ranked NCDs only second to HIV/AIDS as the commonest cause of morbidity and mortality in SSA. It is projected that in the near future, NCDs will become the bigger cause of mortality in the region.

Like in other parts of the world, heart failure (HF) is associated with high morbidity and mortality, frequent hospitalization and high economic cost. In sub-Saharan Africa, HF has been shown to affect young and middle-aged adults with the attendant high disability-adjusted life years. This is contrary to the pattern of HF in high-income countries of North America, Western Europe and Japan where HF is essentially a disease of the elderly. Furthermore, while ischaemic heart disease is the commonest aetiological risk factor for HF in high-income countries, HF in SSA is essentially non-ischaemic in origin. Hypertensive heart failure, dilated cardiomyopathy, rheumatic heart disease, pericardial diseases and HIV-associated cardiomyopathy are the common risk factors.

The aim of this chapter is to review contemporary information on HF in SSA in terms of socio-demographic features, clinical characteristics, aetiological risk factors, management, prognosis and economic burden. We shall conclude with gaps in knowledge and possible future directions.

2. Sub-Saharan Africa

SSA is the geographical term used to describe the region of the African continent that lies south of the Sahara Desert. It covers a land area of 24.3 million square meters. In 2007, the



Figure 1. Map of sub-Saharan Africa.

population of the region was estimated to 800 million with a growth rate of 2.3% per annum. The United Nation has projected a population of 1.5 billion by 2050 [1]. **Figure 1** shows the countries that comprise the region including the sub-regions of: (1) West Africa, (2) Central Africa or Middle Africa, (3) Eastern Africa, (4) Horn of Africa and (5) Southern Africa. [2] The population of SSA is very diverse both physically and culturally and they have differing ethnic background. For instance, the Negroes inhabit most of West Africa; the Tuaregs Nilo-Hamites occupy the east horn of the continent, while the Bantus inhabit the Central and Southern Africa. There are also the Hottentots in rural Namibia and the pygmies of the Congo Basin [2].

3. Historical perspective

Albert Ruskin Cooke [3] appears to be one of the earliest workers to have reported on the pattern of diseases in Africa. In 1901, he analysed 1500 in-patients, whom he met at a hospital in Uganda. He observed that 3% of all hospital admissions and 6% of all medical admissions were due to heart disease. He wrote 'Valvular diseases of the heart are common', 'Atheroma and aneurysms are very rare, although syphilitic endarteritis obliterans is probably common' and 'high tension pulses are not often met with' [4].

Fifty years later, Sharper and his colleagues analysed 1957 medical admission seen at the Mulago Hospital in Kampala and noted that cardiovascular disease was responsible for 8–10% of medical admissions. The main cardiac conditions reported were hypertensive heart disease, rheumatic heart disease, endomyocardial fibrosis and syphilitic heart disease [5, 6].

Similar work carried out in other countries in the 1960s and 1970s reported similar percentage that cardiovascular diseases are of all medical admissions. For example, 11.2% for Ibadan, Nigeria [7], 8.6% for Mombasa, Kenya [8], 8.8% for Dar es Salaam, Tanzania [9], 4.3% for Blantyre, Malawi [10] and 8.6% for Sekhukhuneland, South Africa [11].

Studies in the late 1970s, 1980s and in the 1990s also show the prominence of hypertensive heart disease, rheumatic heart disease and dilated cardiomyopathy as the main causes of heart disease in the region and decreasing incidence of syphilitic heart disease.

More recent studies have used echocardiography in the evaluation of heart diseases in the region. These have documented peculiar characteristics of heart diseases in sub-Saharan Africa [12–20].

4. Contemporary epidemiology of HF in SSA

4.1. Incidence and prevalence

There is lack of population-based incidence and prevalence studies in SSA. The reported hospital prevalence studies indicate that HF is responsible for 9.4–42.5% of all medical admissions and 25.6–30.0% of admissions into the cardiac units.

4.2. Socio-demographic characteristics

4.2.1. Age at presentation

HF in SSA is a disease of young and middle age. It is commoner between the third and fifth decade of life when the individuals are in the prime of their life. The mean age ranges from 36.5 to 61.5 years (**Figure 2A**) [15, 19–33]. In high-income countries, it is commoner in the seventh decade of life.

4.2.2. Gender distribution

There is varying gender distribution. It is commoner in men in countries where hypertensive heart disease is the commonest aetiology. Women are predominating where rheumatic heart disease and cardiomyopathies (peripartum cardiomyopathy) is common (**Figure 2B**) [15, 18–39].

4.3. Clinical profile

4.3.1. Mode of presentation and diagnosis

Most patients present in advanced heart failure (NYHA class III and IV) [26, 40]. Diagnosis of HF in SSA is mostly based on clinical features, mostly by the Framingham criteria (in 28.6%)

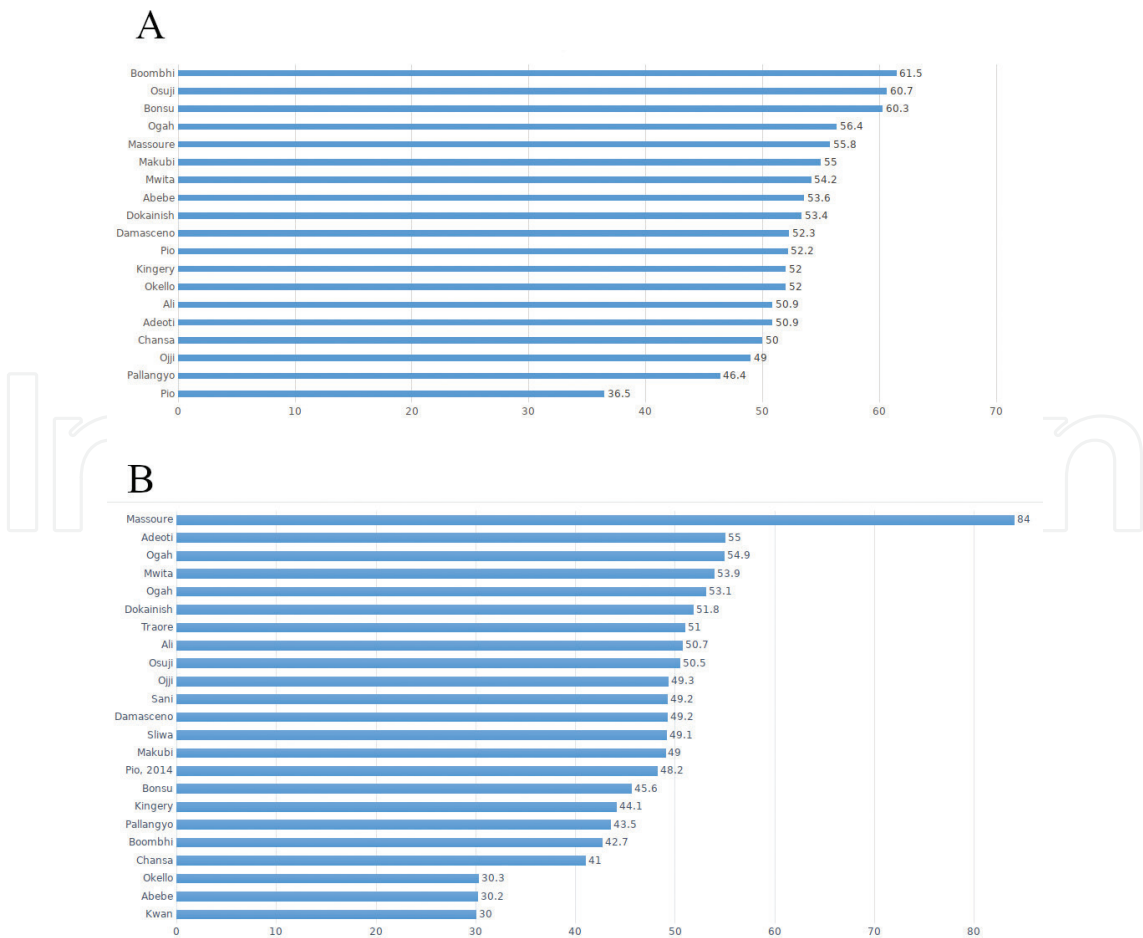


Figure 2. (A) Mean age of HF patients from various studies in SSA. (B) Proportion of men in various HF studies in SSA.

and European Society of Cardiology criteria (in 20%). Support facilities and services for diagnosis of HF in SSA are generally lacking in many parts of SSA [41]. Common diagnostic tools employed are chest radiography, 12-lead ECG and echocardiography. Biomarkers are less often used because of non-availability and high cost [39, 42].

4.3.2. Symptoms and signs

Common symptoms of HF in SSA include cough, dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea, pedal oedema and easy fatiguability. Rales, displaced apex beat, elevated jugular venous pressure and third heart sound are common signs. Others include peripheral oedema, tender hepatomegaly and systolic murmur [18].

Baseline rales and change to day 7 or discharge in general well-being are associated with death or readmission through 180 days. In addition, baseline orthopnoea, rales, oedema, oxygen saturation and changes to day 7 or discharge in respiratory rate or general well-being have been shown to be predictive of 6-months readmission or death [37].

4.3.3. Clinical class of heart failure

HF patients in SSA most often than not present in severe HF (NYHA class III and IV) [26, 27, 40].

In the INTER-CHF study, 35.5 and 20.9% of African HF patients were in NYHA classes III and IV, respectively.

4.3.4. Precipitating factors

Precipitants of HF in SSA are infections (especially chest and urinary tract infection), uncontrolled hypertension and arrhythmias especially atrial fibrillation. Other precipitants include anaemia, excessive physical activity and electrolyte imbalance (e.g. hyponatremia and hypokalemia) [17, 18, 43].

5. Aetiology HF in SSA

Hypertensive heart disease is the identified number one risk factor for HF in SSA. It is responsible for about 39.2% (95% CI: 32.6–45.9%). This is followed by dilated cardiomyopathy, 22.7% (95% CI: 16.8–29.1%) and rheumatic heart disease, 13.8% (95% CI: 9.9–18.0%). These three aetiological risk factors are responsible for over 75% of HF in the region. Ischaemic heart disease accounts for about 7.2% (95% CI: 4.1–11%). The general trend is that ischaemic heart disease is gradually rising in many parts of SSA. **Table 1** shows the aetiology of HF from recent publications from SSA.

5.1. Aetiological risk factor for HF in SSA

5.1.1. Hypertensive heart disease

Many years ago, Donnison [44] reported that hypertension was uncommon in Africa. This observation was later supported by the post-mortem studies by workers like Jex-Blake [45],

Author	Year	Country	Mode	Number	HHD (%)	DCM (%)	RHD (%)	IHD (%)	PPCM (%)	PDX	CHD(%)	CP (%)
Kingery [29]	2017	Tanzania	Prospective	145	42.8	19.3		6.2				7.6
Boombhi [21]	2017	Cameroon	Retrospective	148	30.16	28.57		6.35	3.18	3.96		8.73
Traore [35]	2017	Ivory Coast	Retrospective	257	22.9	55.57		11.23				
Ansa [209]	2016	Nigeria	Retrospective	144	48.6	35.4	1.4					
Abebe [25]	2016	Ethiopia	Retrospective	311	16.1	12.5		15.8				4.5
Dokainish [26]	2015	Multi-country	Prospective	1294	35	14.5	7.2	20				
Makubi [210]	2014	Tanzania	Prospective	427	45	28	12	9				
Ogah [18]	2014	Nigeria	Prospective	452	78.5	7.5	2.4	0.4		3.3		4.4
Pio [28]	2014	Togo	Prospective	297	43.1			19.2	11.8		2.7	2.7
Pio [32]	2014	Togo	Retrospective	376	42.8	5.8		2.7	15.4	1.1	2.7	2.1
Kwan [211]	2013	Rwanda	Retrospective	138	8	54	25	0				
Massoure [211]	2013	Djibouti	Prospective	45	18	7	13					
Ojji [212]	2013	Nigeria	Prospective	1515	60.6	12	8.6	0.4	5.3			
Damasceno [27]	2012	Multi-country	Prospective	1006	45.4	18.8	14.3	7.7	7.7	6.8		
Onwuchekwa [213]	2009	Nigeria	Retrospective	423	56.3	12.2	4.26	0.24			0.24	2.13
Stewart [17]	2008	South Africa	Prospective	884	33	35		9				
Ogah [34]	2008	Nigeria	Retrospective	1441	56.7	3	3.7	0.6		1.8		1.6
Familoni [214]	2007	Nigeria	Prospective	82	43.4	28	9.8	8.5				3.7
Owusu [215]	2007	Ghana	Prospective	167	42.5	17.4	21.6	3.6		4.2	2.4	2.4
Kingue [216]	2005	Cameroon	Retrospective	167	54.5	26.3	24.6	2.4				
Thiam [217]	2003	Senegal	Prospective	170	34			18.9				

HHD = hypertensive heart disease, DCM = dilated cardiomyopathy, RHD = rheumatic heart disease, IHD = ischaemic heart disease, PPCM = peripartum cardiomyopathy, CHD = congenital heart disease, PDX = pericardial disease, CP = cor pulmonale.

Table 1. Aetiology of heart failure in some studies conducted in SSA since the year 2000.

Vint [46] as well as clinical study by William [47] in 1941. However, by 1946, workers started reporting on the impact of hypertension on the cardiovascular health of the African. Davies [48] noted that hypertensive heart disease was the commonest cause of congestive heart failure in Kampala. Similar report was also noted in South Africa [49]. Within same period, many other authors from different parts of Africa also documented that the disease is common in the continent, occasionally with prevalence similar to data from Europe and America.

It is known that in isolated and primitive areas of the continent, the prevalence of hypertension is very low and in these populations, blood pressure remains within a narrow range throughout adult life [50]. Blood pressure rises modestly with age in rural dwellers and much more in those who live in the cities.

More recent data from the continent suggest that hypertension is a major cause of cardiac morbidity and mortality [51, 52]. High blood pressure is in fact regarded as the foundation of cardiovascular disease in Africa [53]. In a recent systematic review of hypertension survey in Africa, it was shown that hypertension increased from 54.6 million cases in 1990 to 130.2 million in 2010. The prevalence is projected to rise to 216.8 million cases by 2020, each with an age-adjusted prevalence of 19.1% (13.9, 25.5), 24.3% (23.3, 31.6) and 25.3% (24.3, 39.7), respectively [54].

In the Heart of Soweto study, among the 1196 persons with the diagnosis of secondary hypertension, 682 or 57% (mean age 60 ± 14 years) had hypertensive HF [16]. In the INTERHEART study, hypertension was reported as a strong contributor to the hazards of CVD in black Africans, with an odd ratio of 7.0 versus 2.3–3.9 in other ethnic groups ($p < 0.0002$) [55].

Hypertension in Africa is associated with body weight, lower intake of potassium and salt sensitivity [56]. The peak age group is 40–49 years. Men are affected more than women. The patterns of presentation of hypertensive HF vary. Some present with acute left ventricular failure and severely elevated blood pressure. A sub-group present with HF and normal blood pressure which tends to rise as the HF is being treated. And yet a third group present with HF and normotension all through. The last group is usually difficult to differentiate from dilated cardiomyopathy in the absence of other signs of long-standing hypertension [57].

The mortality attributable to high blood pressure in most West African Countries ranges between 3 and 7% and cardiovascular mortality is in the range of 20–45% [58]. Women may have added morbidity in Africa if the role of hypertension in pregnancy is factored in. Hypertension is largely asymptomatic until end-organ damage ensues and this is partly responsible for late diagnosis of the disease. Inadequate screening and sub-optimal health facility utilization are also implicated. Therefore, early diagnosis and appropriate therapy would lead to a significant reduction in the prevalence of hypertensive HF in Africa [59].

5.1.2. Rheumatic heart disease (RHD)

It is estimated that 12 million people live with the disease and it results in about 400,000 deaths each year. Two million people will require repeated hospital admission and over a million will need surgery to improve their quality of life. It is common in areas with poor housing condition and an indicator of their plight.

Like hypertension, this was initially thought to be uncommon in Africa [44]. But Cooke in 1901 reported that valvular diseases are common in the continent [3]. This was also supported by reports by other workers [60]. Post-mortem studies have been inconsistent. This may be due to the attitude of Africans towards autopsy.

SSA has a high prevalence of RHD which is in the range of 1–14/1000 children [61–63]. Echocardiography-based population studies report higher prevalence of 7.5–51.6/1000 children [64, 65]. School surveys have given a prevalence of 2.7/10³ in Kenya [66], 4.3/10³ in Ethiopia [67] and 6.9/10³ in South Africa [68] (among black children). Marijon et al. reported a prevalence of 30/10³ from an echocardiography-based school survey [69].

RHD accounts for 12–32% of cardiovascular admissions in SSA. Recent reports suggest that that 6.6–34% of CV-related hospital admissions or echocardiographic data in SSA are due to RHD and up to 2.3% of pregnant women have the disease [70–74].

There are peculiar features of rheumatic heart disease in Africa (similar to reports from other tropical environments). These are the young age at presentation, the severity of the lesions, as well as the high mortality associated with it. History of rheumatic fever can be obtained in only less than 50% of patients. Pure mitral incompetence and mixed mitral valve disease were the commonest valvular lesions that were demonstrated [75]. This is consistent with the findings of other workers in Africa [74, 76–78]. A rheumatic carditis has been shown to run a more fulminant course in sub-Saharan Africa (like in other tropical countries) compared to the developed countries [79–82]. In earlier studies, 33% of 124 mitral valvotomies were in patients under the age of 16 years in one report from Kenya.

The disease appears to be commoner in women. Events in women's life such as pregnancy frequently unmask the condition [83]. Morbidity and mortality is said to be high especially in women and young people [83, 84]. Mortality at 6 month is estimated as 17.8% [85]. In one report from Ethiopia, the annual mortality from RHD is as high as 12.5%, and 70% of such deaths were before the age of 26 years [67].

Sliwa et al. [86] reported on the characteristics of 344 adult rheumatic heart disease cases in the Heart of Soweto study. The disease was commoner in black women (68%). The most common valvular lesion (n = 204, 59%) was mitral regurgitation (MR), with 48 (14%) and 43 (13%) cases, respectively, having combination lesions of aortic plus MR and mixed mitral VHD. Impaired systolic function was demonstrated in 28/204 cases (14%) of predominant MR and in 23/126 cases (18%) with predominant aortic regurgitation. The finding from the study makes a case for the first episode of RHD to be made a notifiable condition in high-burden countries in order to ensure control of the disease through register-based secondary prophylaxis programmes.

In many countries in SSA, facilities for accurate diagnosis are unavailable. Treatment options such as valvotomy, valvuloplasty and prosthetic valve replacement are either unavailable or unaffordable to a vast majority of the population. Worse still secondary preventive measures are also either unavailable or unaffordable.

The lack of infrastructure, political, economic and social instability, malnutrition and poverty are all factors implicated in the high prevalence of rheumatic fever in Africa which is, otherwise, largely preventable [80]. This culminates in a great burden of rheumatic valvular heart disease and infective endocarditis.

5.2. The cardiomyopathies

Dilated cardiomyopathy (DCM), endomyocardial fibrosis (EMF) and peripartum cardiomyopathy (PPCM) are common and endemic in SSA. Other forms of cardiomyopathy are less common.

5.2.1. Dilated cardiomyopathy (DCM)

DCM is a major cause of HF in SSA. It has been plagued with diagnostic and therapeutic challenges due to lack of appropriate facilities, definitive diagnosis and interventions in resource-poor African centres. It typically presents with progressive HF and is associated with high mortality. In one study, the 4-year mortality was found to be 34%.

There are marked regional differences in the pathogenesis of dilated cardiomyopathy in Africa. The causative factors that have been implicated in several studies across Africa include infection [87, 88] and myocarditis [89, 90], 'burnt out' untreated hypertension [91], genetic factors, alcohol, nutritional deficiencies, autoimmune mechanisms, iron overload and pregnancy [92].

The current concept is that 30% of the disease has genetic basis. Familial DCM is caused by a mutation in more than 25 chromosome loci. The genes affected are those encoding contractile, cytoskeleton and calcium regulatory proteins.

In 1975, Owor and Rwomushana reported the first case of familial DCM in Africa [93]. They described twin brothers who were affected by the condition in Uganda. Subsequently, other workers have documented familial DCM in other parts of SSA especially from South Africa [94]. However, there are no systematic family studies of the condition in SSA. Some gene association studies have, however, been done especially in South Africa. Some of the findings include:

1. An association with HLADR1 and DRW10 antigens suggesting possible genetically determined immune factors may be responsible for the disease [95, 96].
2. An association with mutation in troponin T-gene (Arg141Trp) [97] and mitochondrial T16185c polymorphism.

On the other hand, there is no evidence of association with cardiac (ACTC1) and skeletal (ACTA1) alpha-actin gene, alpha-2c adrenoceptor (ADRB2c) gene, beta-1 adrenoceptor (ADRB1) gene and tumour necrosis factor-alpha (TNFA) gene.

Some data suggest the immune-modulating agent pentoxifylline may be beneficial in the management of DCM in the region. In one trial, patients on this agent had improvement in effort tolerance, left ventricular function and trend towards lower mortality than those on standard treatment for HF [98].

In a 14-year follow-up of DCM patients in South Africa, a mortality of 10% per year was recorded for both familial and idiopathic DCM. Heart transplantation was an independent predictor of survival, while NYHA III and IV and use of digoxin were associated with poor outcome.

5.2.2. Endomyocardial fibrosis (EMF)

This is a form of restrictive cardiomyopathy in which there is a deposition of fibrous tissue in the mural endocardium resulting in impaired diastolic function as well as valvular

dysfunction resulting from entrapment of papillary muscles of the atrioventricular valve. It occurs mainly in the tropical and subtropical areas of Africa. It was first described by William in 1938. It is also called Davies disease because of the seminal work done by Davies on this disorder in Uganda [99–101]. A comprehensive description of the clinical features has been documented by Hutt [102] as well as other workers [103, 104]. Recently, Mocumbi et al. have suggested diagnostic criteria for diagnosis [105].

EMF has been reported in at least 17 SSA countries: Congo, Cameroon, Egypt, Ethiopia, Gabon, Ghana, Kenya, Malawi, Mozambique, Nigeria, Senegal, South Africa, Sudan, Tanzania, Uganda, Zambia and Zimbabwe. It has also been reported in India and South America. It is rare in Northern and Southern Africa. Right-sided EMF appears to be commoner. The peak age incidence is 11–15 year in both sexes. In a population-based study in Mozambique, a prevalence of 8.9% was found.

EMF is a disease of childhood and early adolescence. It has also been reported in older adults and infants. A second peak of incidence has been shown during the reproductive age of women. The preponderance of one gender over the other is inconsistently reported. In a large database from Mozambique, it was reported to be more prevalent in males.

The pathophysiology postulated is as follows: endocardial thickening of the ventricles leads to cardiac constriction or restriction and atrioventricular valvular incompetence resulting in regurgitation. The right ventricular cavity is usually obliterated from below by the advancing fibrosis of layered mural thrombi. In severe and late cases, the papillary muscles are buried in a layer of fibrous tissue leading to functionless tricuspid valve and aneurysmal right atrium. When the left ventricle is involved, dense fibrous tissues are deposited at the apex, spreading around the cavity of the LV or may first appear around the papillary muscles of the posterior cusp of the mitral valve (leading to anchoring of the muscle and valvular regurgitation) [99, 104].

Chronic pericardial effusion commonly complicates right-sided EMF, while pleural effusion is commoner with left or biventricular disease [104]. The clinical features depend on the stage of the disease, the anatomical damage done on the affected valve as well as the resultant effect on heart function. An initial illness with fever, chills, night sweats, facial swelling and urticaria can occur and is reported in 30–50% of cases. This can be fatal within months but little is known about this phase of the disease [104].

In left-sided EMF, the ventricle is not enlarged and there is almost always mitral incompetence and a loud pulmonary component of the second heart sound and progressive pulmonary hypertension. There is usually an early third heart sound. When the right ventricle is involved, the classical picture is that of a young patient with ‘egg on stick’ or ‘orange on stick’ appearance (massive ascites and minimal pedal oedema; often with delayed puberty, some exophthalmos and central cyanosis) [104]. The arterial pulse is usually of small volume or feeble. Atrial fibrillation is common. Massive pericardial effusion or a rotated heart (because of massive right atrium) could give an impalpable heart. An abrupt third heart sound is common but murmur may be absent.

The pathogenic process is explained by eosinophil and its constituents. The suggested sequel is as follows [104]:

1. A trigger to eosinophilia (helminthic or other infections and liberation of eosinophilic major basic proteins and cationic proteins which are toxic to the cardiac cells as well as other cells in the body;
2. The damaged endocardium serves as a nidus for thrombus formation;
3. Thrombus formation builds up due to release of platelet-activating factors by the eosinophils;
4. Further mural thrombi are laid down at the original and adjacent sites leading to the formation of fibrotic mass.

Although this explanation appears plausible, it does not offer reason why the disease is rare in some parts of the tropics, the reported ethnic differences [106] and some familial cases of EMF [107].

Despite the fact that the aetiology of this condition has not been resolved by scientist since the first description, the volume of publication on it has dwindled in the last decade. The cause has remained a mystery despite several proposed aetiological factors [108]. Some of the factors that have been implicated in the past include: (1) infections/infestations, for example, cardiotropic viruses, mycoplasma pneumonia, malaria, schistosomiasis, (2) autoimmunity, (3) Hypereosinophilia, (4) genetics and (5) traditional medications.

Trend in the incidence and prevalence of EMF has not been well studied in SSA. Ellis et al. showed that the prevalence has not changed in Uganda [109]. On the other hand, in Nigeria, EMF was shown to have declined from 10% in the 1960/1970s to 0.02% from medical admissions and 0.04% for cardiac-related admissions in the first decade of twenty-first century. This may not be unconnected with improvement in health-care delivery as well as control of communicable diseases in that part of the country [110].

The prognosis of EMF is poor. The survival of patients after diagnosis is about 2 years [104].

5.2.3. *Peripartum cardiomyopathy (PPCM)*

This is defined as heart muscle disease in which left ventricular systolic dysfunction and symptoms of HF occur between the last month of pregnancy and the first 5 months postpartum. In many parts of Africa, the prevalence is about 1/1500 deliveries. However, the northern part of Nigeria appears to be the hot spot for the condition where it affects 1/100 women after delivery. Recent echocardiography-based study from this part of Nigeria confirms similar prevalence [111]. The epidemiology, pathophysiology and clinical features of this condition have been reviewed in detail elsewhere [112–115]. Most patients present within the first 4 months after delivery. Only about 10% present in the last month of pregnancy.

Symptoms and signs are similar to other forms of systolic dysfunction. In addition, they are prone to thromboembolic phenomenon [116].

Aetiological factors implicated include multiparity, advanced maternal age, multiple gestation, preeclampsia, gestational hypertension and black race. Several plausible aetiological mechanisms have been advanced. These include genetic predisposition, myocarditis, cardiotropic

viral infections, chimerism, apoptosis and inflammation. Others include abnormal haemodynamic response, immune complexes, cardiac nitric oxide synthase, immune dendritic cells, cardiac dystrophin, etc. [113, 117].

A novel molecular mechanism of PPCM has been documented. Such mechanisms include elevated pro-inflammatory markers such as sFas/Apo 1, interferon-gamma, interleukin-6 and C-reactive protein. These points to the pro-inflammatory mechanism in the initiation, progression and prognosis of the disease. A pathophysiological circuit that involves unbalanced oxidative stress which leads to enhanced cleavage of prolactin into pro-apoptotic and angiogenic 16-kDa sub-fragments has been described. This process results in endothelial damage and LV dysfunction. Presence of endothelial damage in PPCM is further supported by the presence of endothelial microparticles suggesting apoptosis with impaired microcirculation. Furthermore, the angiogenic imbalance in this condition may also be contributed by soluble fms-like tyrosine kinase [118].

About 23–54% of PPCM patients have normalization of LV function at 6 months. Poor outcome is associated with increased LV systolic dimension, lower body mass index and low serum cholesterol at the time of presentation. On the other hand, older age and smaller LV end-systolic diameter is associated with higher chances of recovery of LV function [118].

The mortality associated with PPCM is 15% at 6 months, 28% at 2 years and 42% in over 25 years of follow-up. Predictors of mortality include NYHA functional class at presentation, cardiothoracic ratio, electrocardiographic QRS duration and higher diastolic pressure [119, 120]. A proof-of-concept pilot study has provided some evidence of the benefit of bromocriptine in PPCM patients [121].

5.2.4. *Other cardiomyopathies*

5.2.4.1. *Hypertrophic cardiomyopathy*

Earlier reports of this condition were mainly anecdotal and it was generally thought to be uncommon in Africa. The earliest report appears to be that of Lewis et al. in 1973 [122]. Thereafter, other reports followed [123–127]. In 1240 consecutive echocardiography in Ethiopia, the prevalence of HCM was 4.3% (54 subjects) and accounted for 34.4% of cardiomyopathies [128]. In a similar study in Tanzania, it accounted for 0.2% of 6680 echocardiograms [129]. HCM is the third commonest cardiomyopathy in Ghana [13].

The genetic studies done on this condition have emanated only from South Africa where facilities are available [130–139]. The disease-causing genetic mutation or loci has been documented. These include beta-myosin heavy chain (MYH7) gene, myosin binding protein c (MYBPC3) gene and troponin T (TNNT2) gene. Carriers of T (TNNT2) R92W mutation develop cardiac hypertrophy after the age of 35 years. They also have abnormal response to exercise which may explain the high mortality associated with this mutation [140].

The physiological effects of genetic mutations that cause HCM have also been studied in the continent. TNNT R92W mutation is associated with a relative increase in LV systolic

functional parameters. Reduced diastolic function has been demonstrated in MYH7 A797T mutation, while MYH7 R403W mutation is associated with reduction in both systolic and diastolic functions [141, 142].

Furthermore, angiotensin II type 2 receptor (AGTR2) gene and angiotensin converting enzyme 2 (ACE2) gene have been identified as genetic risk factors (i.e. genetic polymorphism with evidence of association with HCM) [130, 143].

5.2.4.2. Arrhythmogenic right ventricular cardiomyopathy (ARVC)

The first report of ARVC from the region was in the year 2000 [144]. Kindred that are linked to ARVC type 6 locus have been documented [145]. The first multicentre registry of ARVC was reported from South Africa [146]. Data from the registry show that the disease occurs in all racial and ethnic groups in the country. Symptoms start from the third decade of life and the most common symptoms are palpitation, dizziness, syncope and chest pain. Symptoms are more pronounced in males. The reported male to female ratio is 2:1. About 28% were professional endurance athletes at some point in their lives. About 30% of the participants have family members who are also affected and 25% had plakophilin-2 gene defect [146, 147].

Interestingly, the rare 'allele-dose-defect' was demonstrated in one of the subjects, while haplotype analysis also demonstrated the uncommon 'founder effect' in many of the subjects [146, 147].

The annual mortality is 2.8% and 5-year cumulative mortality is 10% [146, 147].

5.2.4.3. Isolated left ventricular non-compaction (ILVNC)

Ker et al. [148] reported the first case of ILVNC in SSA in 2006. Since then, there have been reports from Djibouti [149], South Africa [150, 151] Sudan [152] and Nigeria [153]. The disorder is a common cause of HF, disorders of cardiac rhythm and cardioembolism and is as a result of failure of the myocardium to compact in utero.

In a series comprising of 54-ILVNC patients, Peters et al. [150] in Johannesburg showed that the prevalence is 6.9% and the mean age of presentation is 45.4 ± 13.1 years. It occurs commonly in males (55.6%) and majority (63.0%) present in NYHA class II. HF with systolic dysfunction is the common mode of presentation (98.1%). The identified sites of non-compaction include apical (100%), mid-inferior (74.1%) and mid-lateral walls (64.8%). The disorder has also been documented to be associated with pulmonary hypertension (83.3%), right ventricular (RV) dilation (74.1%) and impaired RV function (59.3%).

5.2.4.4. HIV-associated cardiomyopathy

This is another cause of HF in Africa. Globally, the prevalence was 2–40% in the pre-highly active anti-retroviral treatment (Pre-HAART) era [154, 155]. However, with the introduction of HAART, the prevalence has fallen in many parts of the world. But in some parts of SSA, due to poverty, ignorance, weak health system, malnutrition and low utility of HAART, the

high of HIV-associated cardiomyopathy is prevalent. The effectiveness of HAART is also supported by data from Uganda that showed low prevalence of this condition in children on this treatment [156].

The true prevalence of HIV-associated cardiomyopathy is unknown in the sub-region. Prevalence from reported literature ranges from 5% in Nigeria to 57% in Burkina Faso [157–159]. It is the commonest cardiac diagnosis in HIV-infected people in the Heart of Soweto study and more common in those with high viral load and lower CD4 count [160].

6. Pericardial diseases

Pericarditis and pericardial effusion are common in SSA and are frequently a cause of HF in the region. In some areas, over 15% of cardiovascular admission may be due to primary pericardial diseases. Tuberculosis is the leading cause of pericardial disease in Africa and this is often complicated by constrictive pericarditis. The burden of pericardial disease in SSA has escalated due to the impact of HIV/AIDS.

Next to tuberculosis is purulent pericarditis secondary to streptococcal or staphylococcal infection. Viruses may be responsible for most cases of benign pericarditis without demonstrable aetiology. Other causes include parasitic infections such as trypanosomiasis and malaria.

7. Congenital heart disease

Few publications have looked at cardiovascular disease in young Africans despite the fact that two-thirds of the population of SSA are made up of children and young adults. Congenital heart diseases constitute about 0.3% of heart diseases seen in northern Nigeria [161] to 12% in the series documented by Bertrand in Ivory Coast [162]. The high value in the later may be because the centre at a time served a large referral centre for cardiac surgery in West Africa.

A prevalence of 13.1% was documented in Cameroon (mean age: 10 ± 9 years, range: 2 months–41 years) [163]. About 35% of children with HF in Uganda have congenital heart disease [109].

To the best of our knowledge, the only population-based data on congenital heart disease is from Mozambique where the prevalence was reported as 2.3/1000 children [164].

The pattern of cardiac lesions appears not to be different from reports from other parts of the world in terms of the most frequent lesions. In the decreasing order of frequency, ventricular septal defect, atrial septal defect, Fallot's tetralogy and patent ductus arteriosus are the common congenital heart diseases that may lead to cardiac failure in Africa [164–179]. Recognition of cyanosis in the dark skin may pose a challenge coupled with the fact that anaemia is common in SSA population.

Lack of trained man power, scarcity of diagnostic tools as well as poverty mitigates the care of patients with congenital heart disease in the region.

8. Coronary artery disease

It is generally believed that coronary artery disease is uncommon in SSA. However, recent reports emanating from the region suggest that the disease is emerging, and when it occurs, the clinical as well as the pathological features are similar to that seen in Caucasians [180]. In early reports, Edington [181] in 1954 noted only 3 cases in about 3500 consecutive autopsies in present-day Ghana. Sharper and Williams [5] documented nine cases seen in Uganda over a 3-year period (1955–1957). Falase et al. [182] reported 26 cases over a period spanning 1961–1970 and calculated a prevalence rate of 1:20,500 for Ibadan, Nigeria. In another study by the same author, the prevalence has increased to 1:10,000. Okuwobi [183] saw seven cases over a period of 3 years. Bertrand [184] reported 75 cases over a 6-year period and this accounted for 0.83% of total cardiac-related admission.

Recent reports still report low prevalence of this condition but the trend is that it is on the increase. In a study of HF in elderly subjects (60 years and above), Ikama and his colleagues reported a prevalence of 25.6% in this age group [185].

Studies done in South Africa between 1992 and 2008 show remarkable increase in the prevalence of the disease. In 1994, the prevalence was 0.2% [186] but the recent report from the Heart of Soweto study shows a prevalence of about 10%. This is remarkable evidence of gradual shift in disease pattern (epidemiologic transition) in this population. The prevalence reported in earlier studies ranged from 0.4 to 1.0% [187–189].

9. Pulmonary heart disease (cor pulmonale) and pulmonary hypertension

This is also emerging as a common cause of heart disease in SSA. In the Heart of Soweto study, right HF or cor pulmonale was documented in 27% of individuals admitted for HF. The prevalence in other regions is as follows: 0.8–9.5% in West Africa and 0.3–7.7% in Eastern Africa.

At least six reports have looked at the aetiology of pulmonary heart disease in SSA [190–195]. The common aetiological factors described include left heart disease, chronic obstructive pulmonary disease, bronchiectasis, tuberculosis, bronchial asthma, pulmonary fibrosis of unknown origin, pulmonary embolism (acute cor pulmonale), HIV/AIDs and thromboembolic obliterative pulmonary hypertension.

Tuberculosis and chronic obstructive pulmonary disease is the major culprit. The situation is worsened by the emergence of HIV/AIDS. Globally, there has been an increase in the incidence of tuberculosis by 2.2 million from 1997 to 2005 and 95% of this is occurring in developing countries. In a recent autopsy report from South Africa, it was reported that 31% of cases had pulmonary hypertension as cause or part of their cardiac lesion.

HIV-associated pulmonary hypertension is being increasingly reported in SSA [196]. Hakim et al. [197] and Niakara et al. [158] recently reported a prevalence of 5%. Other causes of

pulmonary hypertension in SSA include sickle cell anaemia [198], connective tissue disease, congenital heart disease [199], valvular heart disease [74], schistosomiasis [200, 201], laryngeal papillomatosis [202], sarcoma [203], herbal remedies [204], hypertensive disorders of pregnancy [205], vaso-occlusive disorders [206] and primary pulmonary hypertension [207].

10. Gender differences

In the THESUS HF registry, men were significantly older and presented in poorer NYHA functional class. Men are also more likely to be current or previous smokers and have higher blood pressure. Renal dysfunction, poorer left ventricular ejection fraction and higher trans-mitral E/A ratio are also more frequent in men. Atrial fibrillation, anaemia and valvular heart disease are significantly more common in women [216].

11. Regional differences

Hypertensive HF as aetiological risk factor for HF is less reported in countries in the horn of Africa, for example, Ethiopia, Eritrea and Djibouti contrary to reports from west and central Africa [18]. Ischaemic heart disease is now the commonest cause of HF in Sudan (an example of country undergoing rapid epidemiologic transition; see **Figure 3**) This explains the difference in the picture presented by the THESUS HF survey [27] and the African data in the INTER-CHF study [26, 40]. Data from Nigeria and Sudan predominated in the two studies, respectively. Cardiomyopathy appears to be commoner in southern and eastern (except Tanzania) parts of the continent. HIV-associated cardiomyopathy has been commonly reported from the southern region of the continent (**Figure 4A–D**).

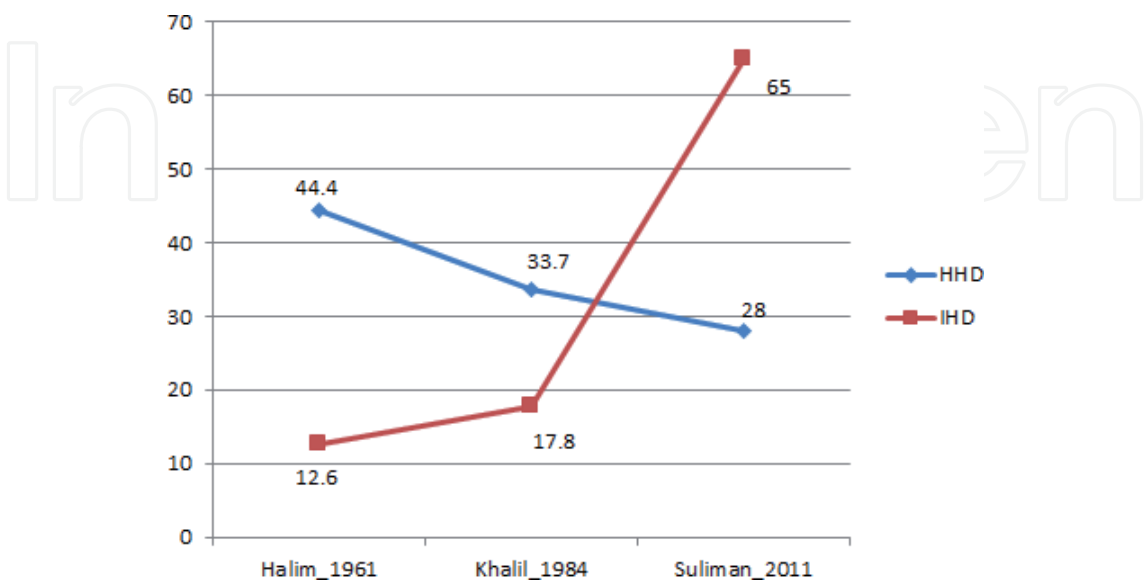


Figure 3. Sudan epidemiologic transition.

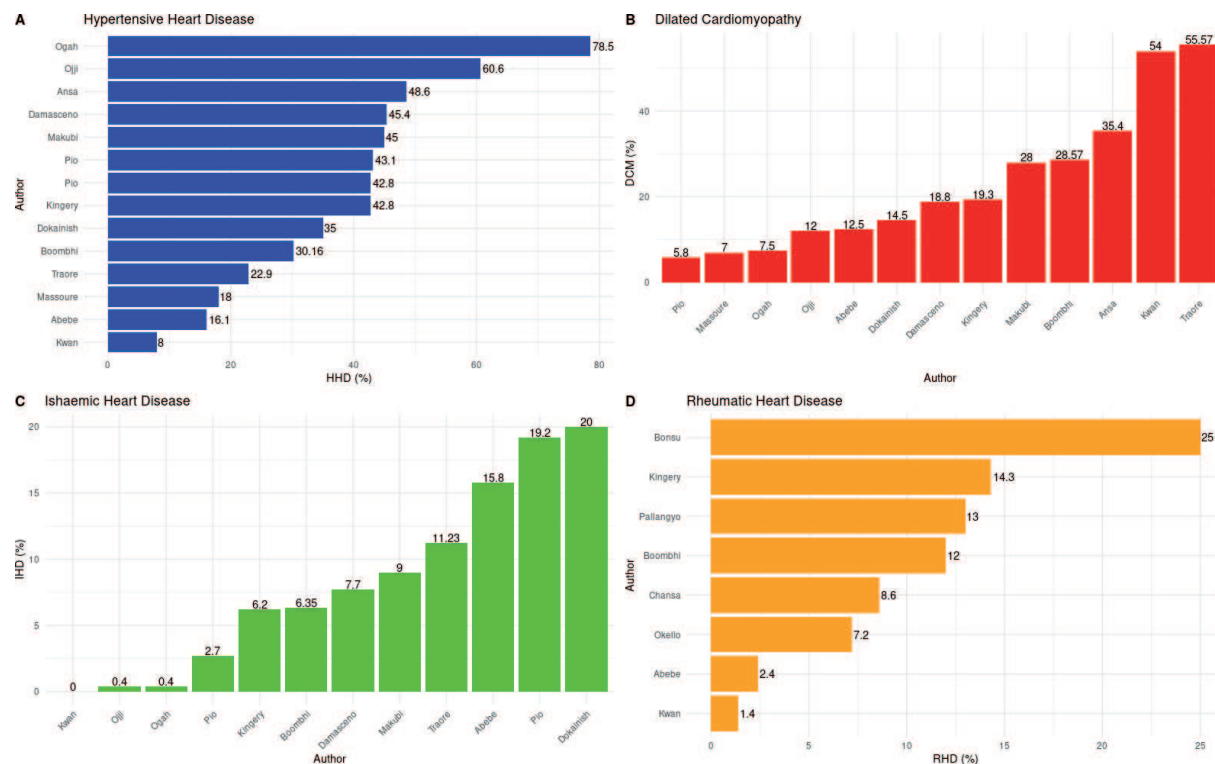


Figure 4. Spectrum of aetiology of HF in various studies in SSA.

12. Laboratory findings

12.1. 12-Lead ECG

ECG abnormalities are common in patients with HF in SSA [217, 218]. The common major ECG abnormalities are left ventricular hypertrophy, inverted T-wave, atrial fibrillation, Q waves compatible with myocardial infarction, premature ventricular and supraventricular beats and bundle branch blocks. Common minor abnormalities are axis deviation, ST-T changes, ST elevation, isolated pathological Q-wave and right ventricular hypertrophy [218].

In the THESUS HF study, a higher ventricular was associated with higher 180-day readmission or mortality. QRS duration and corrected QT interval were not associated with either composite of death or readmission through 60 days or death through 180 days [218].

12.2. Echocardiography

About 70% of HF patients in SSA have LV ejection fraction lower than 40% [17–19, 27]. This is associated with male gender, presence of pedal oedema, higher heart rate, lower blood pressure and renal dysfunction. Left atrial size among other clinical variables predicts rehospitalisation or death within 60 days. Left ventricular posterior wall added to clinical variables predicts 180-day mortality rates [219]. The recently described mid-range ejection fraction has not been fully described in Africa. In a recent retrospective report from Ghana, the distribution of HFrEF, HFmrEF and HFpEF are 23.2, 17.8 and 59%, respectively [220].

13. In-hospital care

13.1. Drug treatment

Loop diuretics are the commonest medication used for the treatment of HF in SSA (81.6, 95% CI: 72.7–89.1%) This is followed by angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (75%, 95% CI: 64.4–85.1%), aldosterone antagonists (51.5%, 95% CI: 32.4–70%), beta-blockers (31.4%, 95% CI: 22.6–40.9%) and digoxin (31.5%, 95% CI: 19.4–45%) [221, 222].

The use of nitrates is low (7.9%). Parenteral inotropes (dopamine and dobutamine) are uncommonly used (5.0 and 5.1%, respectively). Mechanical ventilation is rarely used (0.6%) [27].

13.2. Procedural investigations

Unlike in developed countries, the use of procedural investigations is not well documented in SSA. This is most likely due to limited access to these procedures, high cost as well as limited reports from various centres in the region.

14. Co-morbidities

14.1. Renal dysfunction

About 7.7–48% of HF patients in SSA have renal dysfunction. Worsening renal function occurs in about 10% of cases. This is commoner in West Africa. It is also associated with overweight/obesity and presence of basal crackles at admission. Presence of renal dysfunction is also independently associated with higher readmission rate over 60 days and all-cause mortality over 180 days [36].

14.2. Atrial fibrillation

In the THESUS HF survey, atrial fibrillation (AF) was documented in about 20%. Individuals with AF are older than the general HF population; they are more likely to be females and they have significantly higher heart rate but lower blood pressure. Presence of AF is not associated with poorer outcome; however, valvular AF is associated with all-cause readmission and mortality [223]. AF is associated with poorer outcome in Tanzania [19].

14.3. Anaemia

Rates of anaemia range from 8% in Abuja Nigeria to 64.3% in Uganda. Higher rates have been recorded in other East African countries and northern Nigeria [224, 225]. Iron deficiency anaemia occurs in about 57% of HF patients in Tanzania. This has been shown to be associated with poor prognosis. **Table 2** shows the prevalence of anaemia in some SSA countries.

Authors	Country	Year	Number	% Anaemia	Definition
Makubi [19]	Tanzania	2014	427	57	<10 g/dl
Ogah [18]	Nigeria (South)	2014	452	8.8	<10 g/dl
Damasceno [27]	Multi-country	2012	1006	15.2	<10 g/dl
Stewart [17]	South Africa	2008	699	10.0	Male, <11 g/dl, female <10 g/dl
Karaye [226]	Nigeria (North)	2008	100	45%	NA
Kuule [227]	Uganda	2009	157	64.3	Male, ≤ 12.9 g/dl, female, ≤ 11.9 g/dl
Inglis [233]	South Africa	2007	163	13.5	WHO
Dzudie [234]	Cameroon	2008	140	15.7	NA

NA = not available.

Table 2. Prevalence of anaemia in some HF studies in SSA.

14.4. Psychological dysfunction and depression

Psychological distress is common in SSA patients with HF. More than one-third (39%) have both depression and anxiety while about 16 and 13% have depression and anxiety respectively. Furthermore, two-thirds of in-patients and one-third of out-patients have depression [226, 227]. Psychological distress and depression is more common in young HF patients because of challenges of coping and adjusting with the condition [228].

14.5. Heart failure knowledge and compliance to treatment

HF patients in Africa have poor knowledge of their illness, the medications and side effects. The compliance to medications is also poor especially with diuretics because of the side effects. Ability to recall medications is also poor [229, 230].

15. Outcomes

15.1. Length of hospital stay

The median length of hospital stay ranges from 7 days in the THESUS HF survey, 11 days in Abeokuta, Nigeria and 13 days in a rural health facility in the Cameroun.

15.2. Readmission rate

Readmission after an initial or index case of HF is common, and CV reasons (worsening HF) are responsible in most of the cases. The rate of readmission or death at 60 days is about 15.4%.

15.3. Mortality

15.3.1. In-hospital mortality

The reported in-hospital mortality is in the range of 3.8–25.2% (see **Figure 5**) [18, 20, 24, 27, 29, 30, 233].

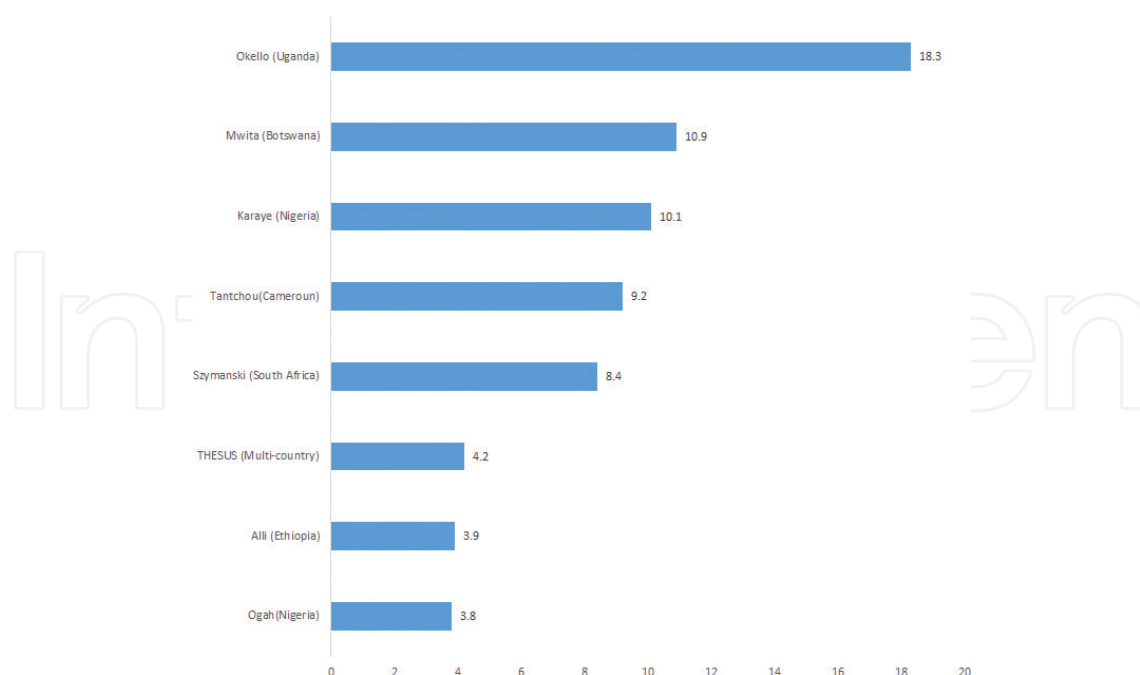


Figure 5. Intra-hospital mortality from various HF studies in SSA.

15.3.2. Short- and medium-term mortality

Thirty-day mortality rate ranges from 14.7 to 35% [221, 234]. The reported 60- and 180-days readmission or mortality is 15–57.8 and 21.9–57.9%, respectively. Common predictors of readmission or mortality include presence of malignancy, severe lung disease, admission for blood pressure, heart rate, signs of congestion, renal function and ejection fraction. Others include anaemia, history of smoking and HIV co-infection [221, 234].

15.3.3. Long-term mortality

A 3-year mortality rate of 67.1% was reported in patients with advanced heart failure from one centre in Nigeria [212]. In a recent retrospective report from Ghana, the 1-, 2- and 5-year survival rates were reported as 90.3, 64.7 and 38.4%, respectively. Those with HFpEF are older, are more often women and often have non-ischaemic etiology for the HF. They also have higher rates of CKD and atrial fibrillation but lower rates of DCM. On the other hand, those with HFrEF are more symptomatic and are more likely to receive disease-modifying medications [220]. Among individuals with HFpEF, anaemia, DCM, diabetes mellitus, presence of cerebrovascular event, use of statin and aldosterone antagonist independently predicted mortality. On the other hand, severe HF symptoms, history of smoking and use of beta-blockers were independent predictors of death in HFmrEF patients. Age is a predictor of mortality in all the three HF groups. HFpEF has a better long-term prognosis [220].

15.4. Quality of life (QoL) and spiritual well-being

Poor quality of life has been demonstrated in over 25% of HF patients in Nigeria. Age and educational attainment are major determinants of QoL [235]. In Kenya, spiritual distress is common and more often in younger patients [236].

15.5. Economic cost

In developing countries, about 15.1 billion US dollars was spent on the care of HF in the year 2012 [237]. The cost of HF in Nigeria in the year 2009 was estimated at 508,595 USD, translating to 2128 USD per patient per year. In-patient and out-patient care cost constituted 46 and 54% of total care cost, respectively. The relatively higher cost of out-patient care cost was attributed to the cost of transportation for monthly follow-up visits. Payment for the care of HF is out-of-pocket in most parts of SSA.

16. Comparison with other parts of the world

Compared to other regions of the world, HF patients in SSA are younger. The mean age in the THESUS HF survey [27] was 52 years compared to 69.9 years in the EURO HF survey, 72.4 years in the ADHERE study (in USA, 71 years in Japan and 60 years in Indonesia; Table 3) [27].

They are more likely to have rheumatic heart disease as the aetiology, while ischemic heart disease is less likely. They are also relatively less likely to have diabetes mellitus, atrial fibrillation and chronic obstructive airway disease as co-morbidity. The prevalence of chronic kidney disease and anaemia is lower in SSA HF patients. The mean left ventricular EF and median length of hospital stay appear to be similar to other parts of the world [27]. In the INTER-CHF study, the age-adjusted mortality is worse in SSA compared to other low- and middle-income regions [27].

17. Gaps and future directions

There is generally no population-based incidence or prevalence data on HF in SSA. The community or population-based data on the burden of systolic or diastolic dysfunction using echocardiography is unknown. In addition, apart from high blood pressure, the community burden of other aetiological risk factors for HF such as EMF, rheumatic heart disease and right HF is largely scanty.

The molecular pathobiology of HF in SSA is largely unexplored. The secular trend in HF in SSA is also unknown. This has been well studied in high-income countries of Europe and North America. There is also need for research into best strategies for treatment and prevention of common causes of HF in the region. More cohort studies and longer follow-up of HF patients are needed in SSA to fully describe the natural history of HF. An in-depth cost analysis or economic analysis as well as data on quality of care is also scanty and needs exploring. Clinical trials on HF are generally lacking.

Finally, in-depth scientific approaches to better understand the epidemiology, pathobiology, socio-cultural factors, treatment patterns as well as outcome of HF and diseases leading to HF should be the focus of future research. As suggested by Fonn, 'research conceptualized, conducted, analysed and published by Africans is crucial for Africa to meet the health needs of her people' [238].

Study	No	% Women	Mean age	Smoking	Hypertension	Diabetes	Anaemia	CKD	NYHA (III & IV)	Mean EF	HHF	DCM	VHDX	RHF	IHD	LOS	M
THESUS_ HF ^s [27]	1006	50.7	52	9.8	55.5	11.1	15.2	7.7	34.6	39.5	45.4	18.8	14.3	NR	7.7	7	4.2
EuroHeart failure [243]	3580	38.7	69.9	NR	62.5	32.8	14.7	16.8	NR	38	11.4	19.3		3.2	53.6	9	6.7
ADHERE, USA	105,388	52	72.4	NR	73	44	NR	30	76	34.4						4.3	4
OPTIMIZE, USA	48,612	52	73	NR	NR	NR	NR	NR	NR	39							3.8
ADHERE, Indonesia	1687	64.5	60	74	54.8	31.2	NR	NR	NR	37.9	54.8	NR	NR	NR	23.3	7.1	6.7
JCARE- CARD, Japan	2675	40.3	71	37.7	52.9	29.9	20.8	11.7	87.5	42.2	24.6	21.9	15.7	NR	32	NR	NR

EF = ejection fraction, NYHA = New York Heart Association, CKD = chronic kidney disease, HHF = hypertensive heart failure, DCM = dilated cardiomyopathy, VHDX = valvular heart disease, RHF = right heart failure, IHD = ischaemic heart disease, LOS = length of stay in hospital, M = intra-hospital mortality.

Table 3. Comparison of present study with other HF studies in SSA and other parts of the world.

18. Conclusions

African HF patients are the youngest compared to most regions of the world. They are most likely to be illiterate and often lack medication or health insurance. They are most likely to be in the worst NYHA functional class and less likely to be on any beta-blocker.

Hypertensive heart disease is the commonest aetiological risk factor. Other risk factors include dilated cardiomyopathy, rheumatic heart disease and ischaemic heart disease. HF-related mortality is also high in SSA.

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