CHALLENGES IN EARLY DIAGNOSIS OF HEART FAILURE IN SUB SAHARAN AFRICA – A REVIEW

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Abstract
Heart Failure, a rising public health concern has become more prevalent in the Sub Saharan Africa (SSA) in recent times. It is a major cause of high mortality and morbidity with frequent hospitalizations and high economic cost. Majority of heart failure cases in the SSA are due mainly to hypertensive disease, non–Ischemic causes (Cardiomyopathy), and rheumatic disease. However, the reverse is the case in high-income countries where heart disease is linked to ischemic causes. Generally, hypertension has been reported to be a major cause of heart failure across the globe. The most challenging aspect in the diagnosis of heart failure in SSA is the lack of basic tools and the necessary human resources. Also, the unavailability of support facilities and services, high cost of drugs, weak health care systems that are over burdened with infectious diseases and poor access to guideline–directed medical treatment. Overall, prevention of hypertension, community blood pressure screening, physical activities, healthy living and working environment as well as access to effective health care are necessary preventive measures of cardiovascular diseases in SSA. This review is an observational study of 20-yr duration to examine the challenges of early diagnoses of heart failure in SSA and how to overcome them.

Keywords: Heart failure; cardiovascular diseases; sub-Saharan Africa

Introduction

Heart failure is a major health and socio-economic burden in SSA due to its high prevalence, high impact on the young working class and high mortality rates. It affects about 26 million people worldwide (1) especially those in low-income sub-Saharan Africa (SSA). Heart failure is a frequent disease in the adult population in Africa. It is the endpoint of most cardiac disorders and a central theme in cardiology practice in sub-Saharan Africa. In most cases, heart failure is first diagnosed during an episode of hospital care (2). It is one of the most common reasons for emergency admission, with about 20% of cases being new-onset and 80% an acute exacerbation of chronic heart failure (3). The burden and challenges of managing patients and individuals with heart failure are enormous in sub-Saharan Africa. This is because diagnostic and management of this disease require specific heart investigations and treatments that are often inaccessible in the developing countries (4,5). Furthermore, the absence of preventive measures and lack of early diagnosis has drastically increased the rate of morbidity and mortality. The prevalence of ischemic heart disease as the leading cause of heart failure should therefore, drive implementation of relevant preventive strategies. The clinical symptoms of heart failure include dyspnea, fatigue, and clinical signs of congestion due to structural or functional cardiac abnormalities leading to frequent hospitalizations, poor quality of life, and shortened

life expectancy (6). Hypertension, a major cause of heart failure is often asymptomatic. Many hypertension patients are unaware of their condition and therefore remain untreated. Untreated or poorly controlled hypertension and left ventricular hypertrophy (LVH) have been reported to be risk factors for cardiovascular diseases (CVD) (7), a major cause of morbidity and mortality, and sudden death (8). Poverty also contributes a great deal to the rising burden of heart failure in SSA. Most people in the sub-Saharan Africa lack sufficient income to address basic needs such as quality health compared to other parts of the world (9). SSA has been reported as home to 14% of the 7.8 billion world's inhabitants but contributes to more than half of the global poor (9). Previous study revealed that while the rest of the world has observed a significant decline in extreme poverty, SSA has recorded a rise in abject poverty from 278 million in 1990 to 413 million in 2015 (10). Although hypertension and diabetes play a major role as causes of heart failure in women (11), previous reports have revealed that the incidence and prevalence of heart failure is lower in women than men at all ages. However, due to the steep increase in incidence with age, and the larger population of elderly women in the developed world, the total number of men and women living with heart failure is similar (12). According to Mehta and Cowie (13), heart failure with preserved systolic function ("diastolic" dysfunction) is more common in women, perhaps related to gender differences in the myocardial response to injury, and the lower prevalence of coronary artery disease in premenopausal women as compared with men. Furthermore, myocardial cell death, apoptosis, and cellular hypertrophy of the remaining cells are more pronounced in the male than in the female myocardium (14,15). Previous studies have reported incidence and treatment of heart failure; however, this review's aim is to investigate the challenges involved in early diagnosis of heart failure in Sub-Saharan Africa, thereby providing the way forward concerning early intervention to reduce the mortality rates.

Methods

Study Characteristics and Selection Criteria

Studies were identified through a systematic literature search of scholarly articles published from 1992 to 2017. A search was conducted using Google Scholar, Research gate and PubMed with search terms including heart failure, sub–Saharan Africa, mortality, morbidity, risk factors, diagnosis, occurrence and prevention. Research papers on clinical trials were excluded from consideration.

Result

History of Heart Failure in Sub-Saharan Africa

Heart failure has been a health challenge in sub-Saharan Africa for more than 60 years (16). Historically, sub-Saharan Africa has had the greatest prevalence of clinically detected rheumatic heart diseases (RHD), ranging from less than 1 to 14 per 1000 (17; 18; 19; 20). The major causes of heart failure cases in sub-Saharan Africa have been traced to non-ischemic causes. Seventy five percent of these are due to rheumatic heart disease, hypertensive heart disease, and cardiomyopathy (21). However, ischemic heart diseases still remain an uncommon cause of heart failure with no apparent increase in its contribution to the cases of heart failure over the past 60 years. This corroborates the fact that non-ischemic heart disease is a major priority to tackle heart failure cases in sub–Saharan Africa needing immediate clinical intervention (22). According to (23), cor pulmonale and pericarditis contribute about 20% of the incidence of heart failure. Cor pulmonale has been implicated in post-tuberculosis lung damage. In an earlier study, (24) reported that over 70% of cases of rheumatic heart diseases in people younger than 20 years of age is majorly due to pure mitral regurgitation. On the other hand, mitral stenosis and mixed valvular disease is common among the elderly in developing Countries like South Africa.
Previous studies reveal that 20 to 25 million people

in low- and middle-income countries have some form of pulmonary vascular disease, representing >97% of the global burden (25). Amongst these, cardiovascular diseases predominantly affect people of working age (30–64 years). In Africa, rheumatic heart disease RHD has demonstrated a particular prevalence in the younger African population (26). More often, the poorer and disadvantaged people suffer the largest burden of cardiovascular diseases (27). Previous studies confirmed an inverse relation between birth weight and cardio vascular diseases in later life (28). Meanwhile, only a small and insignificant portion of the population in Sub-Saharan Africa can afford the cost of diagnosis, medical treatment and/or surgical correction of congenital heart diseases (29). About 27% of 844 *de novo* cases in South Africa have been linked to right heart failure (30). The history of heart diseases in adults Sub-Saharan Africa has also been traced to environmental factors and particularly poor maternal nutrition during pregnancy (31).

Previous studies reveal that urbanization and economic development have also contributed immensely to the emergence of marked reduction of physical activity and a nutritional transition characterized by a shift to a higher caloric content diet (32). These transitions result in enormous public health challenges, and failure to address the problem may impose significant burden for the health sector and the economy of sub-Saharan African countries (33).

Causes of Heart Failure

Valvular heart disease in SSA is almost always due to sequelae of an infectious disease rather than degenerative changes (24). Recurrent pharyngeal infections with group A beta- hemolytic streptococci and subsequent acute rheumatic carditis predispose to the development of rheumatic heart disease - a chronic progressive condition with no known medical therapy. Valvular thickening eventually impairs function with subsequent valvular regurgitation. With time, valvular stenosis start to predominate with more restriction in leaflet mobility and development of a transvalvular pressure gradient. In a similar study, (34) reported that the causes of hypertensive heart disease in SSA seem to be similar to the rest of the world. Several genes have been linked to the development of cardiomyocyte hypertrophy in patients with essential hypertension which affect intracellular signaling, degradation of normal extracellular collagens and contractile dysfunction among other functions. All these eventually lead to left ventricular hypertrophy and heart failure. The essential causes of heart failure in SSA include hypertensive heart disease, HIV associated cardiomyopathy, peripartum cardiomyopathy, myocarditis, infiltrative disease (i.e., iron overload), alcohol induced and familial/genetic forms (35). Some other causes of heart failure that contribute to morbidity in SSA are hemoglobinopathies, chronic obstructive pulmonary disease, interstitial lung disease, high altitude and chronic thromboembolic disease (36). A major compounding factor of heart failure in Sub-Saharan Africa is the lack of early diagnosis of simple lesions that can result in timely referral before onset of permanent damage. This is as result of limited resources in Sub-Saharan Africa. Quite a number of congenital cardiac lesions are not diagnosed prior to birth, due to severely limited antenatal screening for congenital heart disease. Poverty is also a reason behind the rising burden of heart failure in sub–Saharan Africa (37). Poverty is a major reason for poor access to healthcare services that can prevent and control incidence of heart failure. This ultimately contributes to an unhealthy lifestyle among the poor who are helpless (38). With poverty encompassing low income and consumption, poor education, health, nutrition, and other human development parameters, its effect on cardiovascular diseases is complex (39). Thiamine deficiency has been reported as a less common cause of heart failure in the past. However, it has been linked to a number of cases of heart failure in SSA. In recent times, it has accounted for up to 32% of cases of heart failure in a South African center (40). Thiamine performs a

critical role in the metabolism of carbohydrate (41). It is not produced endogenously and is usually stored in the body in small amounts. Adequate intake or supplementation of thymine is therefore very necessary to avoid deficiency (42). The heart failure as a result of thiamine deficiency (so called wet beri-beri) is a chronic disease characterized by a peripherally vasodilated state that leads to fluid retention through activation of the renin-angiotensin-aldosterone system. The consequent clinical effect is heart failure.

Epidemiology and prevalence

Hypertensive heart disease in SSA consistently ranks in the top three causes of heart failure from the 1950s till date (24). Previous studies have shown that progression to systolic failure and ventricular dilatation is less common than the development of high end-diastolic pressure and diastolic dysfunction in 60-80% of people having heart failure diagnosis (29, 43-45). In SSA, other forms of high-output heart diseases have been reported. They include those that are due to thiamine deficiency and arrhythmogenic right ventricular cardiomyopathy (ARVC). In Uganda, up to 20% of patients referred for echocardiography are found to have the disease. It is equally prevalent amongst boys and girls of ages 10 to 30 in Uganda. However, it is more prevalent in adult women than men (46). The occurrence of EMF is not necessarily a result of ethnicity as reported by (24). This is because it occurs not only amongst immigrants from neighboring countries such as Rwanda and Burundi (47) but also in non-natives who have lived in endemic locations (48). In South Africa, the major type of heart failure has been discovered to be Right heart failure. Also, in countries where schistosomiasis is endemic, such as Zimbabwe and Ethiopia, pulmonary hypertension and right heart failure have been commonly encountered. Previous studies reported that HIV-related pulmonary hypertension was more prevalent amongst women in Soweto. It was found in 8% of *de novo* cases of heart failure. However, the prevalence rates in Burkina Faso and Zimbabwe are 0.6% and 6%, respectively (49, 50). Amongst patients that presented with pulmonary embolism, chronic thromboembolic pulmonary hypertension or symptomatic heart failure developed in 30 (23%) patients out of 128 patients tested in Kenya (51). Amongst the genetic cardiovascular diseases, hypertrophic cardiomyopathy (HCM) has been reported to be the most common (52), and over 150 distinct mutations in at least nine different genes are involved (53). Left ventricular hypertrophy of various morphologies, accompanied with a wide array of clinical manifestations and hemodynamic abnormalities typically characterize hypertrophic cardiomyopathy. However, patients may develop mitral regurgitation or diastolic dysfunction, myocardial ischemia, left ventricular outflow obstruction, based on the degree and specific site of cardiac hypertrophy (54). However, the risk relationship between extent of left ventricular hypertrophy and the risk for sudden cardiac death is linear and more serious for younger age groups (54, 55). In the same vein, dilated cardiomyopathy is very common in SSA and has been linked to HIV cardiomyopathy, peripartum cardiomyopathy, myocarditis, infiltrative disease (i.e., iron overload), alcohol induced and familial/genetic forms (35). In a study of prevalence of hypertension treatment among people with hypertension across Africa, (56) reported that hypertension prevalence was positively correlated with the proportion of participants who were overweight or obese but not with the proportion of participants who had a post-primary or higher level of education. The study reported the increase in the prevalence of hypertension with age while it was broadly comparable between rural and urban areas, or between females and males. Pulmonary hypertension narrows the pulmonary vasculature causing right heart failure which is a common clinical syndrome in SSA and other low- and middle-income countries (LMICs) (57). In South Africa, a study identified pulmonary hypertension as one of the most common causes of death accounting for 31% of total cardiovascular deaths

(58). In the same vein, a Nigerian case-control study showed that among patients with sickle cell disease, there was a prevalence of 22.9% in patients with hemoglobin SS as compared to 2.3% in patients with hemoglobin AA (59). Another echocardiography study detected pulmonary hypertension in 23.9% of adults with sickle cell disease (60), with reported higher mortality in these group of patients (61).

Diagnostic Methods

Sub-Saharan Africa is typically associated with poverty. Till date, it is estimated that sub-Saharan Africa is the poorest continent in the world (27). As a result, effective cardiovascular therapy is difficult to sustain financially (62).

Generally, in SSA, left ventricular hypertrophy is detected using both the electrocardiogram and the echocardiogram (24). The former provides information on voltage and cardiac rhythm while the echocardiogram will also provide determination of wall thickness, atrial size, left and right ventricular function and hemodynamics (24). The sensitivity and specificity of the electrocardiogram for left ventricular hypertrophy are approximately 7-74% and 41-98%, respectively, and no single criteria has the highest sensitivity, specificity, accuracy or correlation with cardiac magnetic resonance estimated left ventricular mass index (63). The most commonly used method to identify, quantify and monitor the progression of left ventricular hypertrophy is the Echocardiography. This is because of its portability, reproducibility and correlation with left ventricular mass at necropsy (64). According to Seedat (27), economics with regard to the cost: benefit ratio and social considerations continue to influence the low rate of detection, treatment and control of hypertension in the black population of Africa. In a study in Cameroon, patients with one or a combination of the following pathological features: past history of recurrent heart diseases, precordial murmurs, clinical indications of suspicious cardiopathy and/or cardiomegaly on chest X-ray examination (cardiothoracic index > 0.55) underwent further screening tests for detection of congenital heart diseases. Subsequently, a comprehensive transthoracic Doppler echocardiogram using an Acuson 4–7 MHz was performed. The patients diagnosed with congenital heart diseases were subjected to sanitary evacuation to a collaborative centre outside Africa where corrections of pathology were performed (45). Interestingly, previous studies reveal that hypertension, which is the largest contributor to global burden of heart failure is largely undiagnosed, untreated, or inadequately treated in SSA, creating high risk for morbidity and mortality from potentially preventable heart diseases (65). This has been generally found to be a major challenge. Therefore, to tackle cardiovascular diseases in the SSA, the most adequate and cost-effective approach will be to curb the rising burden of hypertension in this region. This will require efforts to create hypertension awareness in the various communities, encourage early detection of hypertension and improve access to affordable healthcare facilities (57). In some countries in SSA where resources are limited, a chest X-ray (CXR) may often be the only imaging modality available to the clinician. Echocardiography remains the most sensitive tool for the diagnosis of pericardial effusion by showing an echo-free space around the heart (66). Other diagnostic options in patients with interstitial lung disease include Transbronchial biopsy, bronchoalveolar lavage and open lung biopsy (27). Patients with cryptogenic pulmonary hypertension should undergo testing to detect pulmonary arterial emboli or other causes of obstruction with perfusion radionuclide testing or computed tomography scanning depending on availability.

Solutions

In view of the high prevalence of hypertension, as well as a low prevalence of hypertension awareness, treatment, and control in SSA, there is need for concerted efforts to avert the high health and economic burden that the disease entails. Some

important factors for a successful strategy against cardiovascular diseases in SSA include early detection, the availability of dedicated physicians, well-trained nurses with proper supervision by physicians, simplified protocols and basic echocardiography. These are approaches to integrated, decentralized care (67). A major solution will be to put an end to the current outflow of medical personnels from Africa as suggested in an article by Muula (68). Another perspective is the effective use of medications for controlling of hypertension in the SSA populations and of their appropriateness for these populations. Low-income countries can organize sustainable programs through primary healthcare systems and their integration in various infrastructures to tackle hypertension (46; 69). In addition to early detection of hypertension and necessary control strategies, behavioral risk factors such as reduced salt intake and increased physical activity should be encouraged. According to Zühlke et al. (70), the percutaneous approach is now the standard approach for definitive correction of defects such as patent ductus arteriosus and valvular pulmonary stenosis, the lack of cardiac catheterization laboratories has precluded this being introduced into routine clinical practice in many African countries. Furthermore, multisectoral and multidisciplinary platforms have given rise to new cardiac centers acting as continental centers of excellence, comprehensive integrated service frameworks and landmark research focusing on the African context (70). As the technology of echocardiography advances and devices become more portable, it becomes easier to diagnose and understand heart failure during its earliest manifestations (e.g., myocardial strain imaging) (71).

Treatment

Heart failure disease is both preventable and treatable. Therefore, early diagnosis and treatment of heart failure can lead to dramatic decreases in the morbidity and mortality (72). Diagnostic and curative services are being offered in Kenya in the capital cities of Nairobi and Mombasa, while rural communities are being accessed using different models of outreach (73). (74) reported the specific focus of outreach clinics in an integrated clinic in Nairobi. The most common diagnosis of congenital heart disease is those resulting from early detection and timely referral. Pulse oximetry screening for critical congenital heart disease is now recommended and adopted in many parts of the developed world (75). However, Sub-Saharan Africa needs to key in into this technology to be able to manage and treat congenital heart disease in a timely manner. Currently, several new paediatric cardiac centers are being funded by non-governmental organisations to run on a permanent basis in African countries. An example is the Salam Centre for cardiac surgery in Sudan. This centre is managed by an Italian humanitarian organization and it is the only center in North East of Africa offering a free-of-charge service for comprehensive cardiac services (76). More of such centers are needed to reduce the burden of heart failure in Sub-Saharan Africa. In the same vein, the Walter Sisulu Paediatric Centre for Africa in South Africa provides a continental referral centre to train surgeons who subsequently develop programmes in their own countries (77). Similarly, the establishment of the Ghanian National Cardiothoracic Centre in 1989 which has been accredited by the West African College of Surgeons, as a centre of excellence for the training of cardiothoracic surgeons has been of great impact. The Centre provides the much needed resource for West Africa, which happens to be one of the poorest regions in the world (78). The Pan African Society of Cardiology is a platform which allows for development of these critical partnerships to serve all the children of Africa: thus far, it has helped to establish links between African universities and institutions impacting on training, teaching and outreach (79). To date, penicillin, a low-cost drug, is the cornerstone to the treatment of rheumatic heart disease since it prevents the advent of acute rheumatic fever attacks following exposure to Group A streptococci (GAS) infections

(71). The interesting news is that many major cardiovascular drugs are no longer prohibitively expensive (80). According to Seedat (27), the role of biomarkers in diagnosing hypertensive heart failure is still being defined and does not yet impact treatment decisions.

Table 1: Prevalence of heart disease in some sub-Saharan-African countries from 1983-2020

S/N	Country	Gender Predominance	Risk factors	Forms of heart failure	Symptoms	Reference
1	Nigeria	Male	Hypertension (80.4%) Diabetes (34.8%) Dyslipidaemia (43.5%) Cigarette smoking (21.7%) Obesity (26.1)	Ischemic heart disease	Angina and ischemic cardiomyopathy	(81)
2	Togo	Female	Dyslipidaemia (76.9%) Hypertension (75.3%) left ventricular hypertrophy (72.8%), abdominal obesity (71.1%), hyperuricemia (50.5%), hyperglycemia (41.9%)	Ischemic heart disease	Stable angina, silent ischemia, myocardial infarction and unstable angina	(82)

Kenya	Adults	Hypertension, Diabetes Mellitus, obesity, dyslipidemia, smoking. Some anatomic risk factors; abnormal branching pattern, wide bifurcation angles, short arterial stems.	Myocardial Infarction	Atherosclerotic plaques, Occlusive intimal hyperplasia, Severe intimal hyperplasia	(83)
South Africa	young males	*βMHC* Ala797Thr mutation (25%) *cTnT* Arg92Trp (15%) *βMHC* Arg403Trp(5%)	Hypertrophic cardiomyopathy (HCM)	Left ventricular outflow obstruction, myocardial ischemia, mitral regurgitation or diastolic dysfunction	(84)
Soweto	Younger men	Increased immunosuppression HIV viraemia.	HIV-associated cardiomyopathy	Asymptomatic left ventricular dysfunction Cardiomyopathy (38%), Pericardial disease (13%) and Pulmonary arterial hypertension (8%).	(85)
Burkina-Faso	Younger age groups	Hypertension	Acute Heart Failure	Kidney dysfunction. hypertensive heart disease Smoking Rheumatic feve	(86)

7	Côte d'Ivoire	No significant differences regarding to gender	High blood pressure, smoking, type 2 diabetes and hypercholesterolemia	Ischemic heart disease, hypertensive heart disease and rheumatic valvulopathy	Sinus rhythm, atrial fibrillation	(87)
8	Zimbabwe		smoking, obesity, diabetes, atherogenic lipid levels, cytokines C reactive protein (CRP) and myeloperoxidase (MPO)	Coronary heart disease	Asymptomatic left ventricular dysfunction	(88)
9	Cameroon	2months -41 years		Congenital heart disease		(45)
10	Uganda	Adult women	Eosinophilia, ethnicity, diet, poverty, young age, female sex and infection.	Endomyocardial fibrosis a	right, left or biventricular failure and atrioventricular valve regurgitation	(89)

Conclusion

This Review was carried out by the critical study of some papers published by Research Gate, Google Scholar, and PubMed. They all have things in common that point to the fact that heart failure is a disease of rising public health concern, that has high morbidity and mortality rates. The fact remains that heart failure syndrome remains a major public health issue in many countries in SSA. Systolic heart failure seems to dominate. Meanwhile, ischemic heart disease is more predominant in high income countries. The main causes in most countries in SSA are hypertension, valvular heart disease and non-ischemic cardiomyopathies being the most commonly reported forms. Over the last few decades, this trend has generally been consistent. In recent studies however, larger contemporary studies highlight the emergence of right-sided heart failure and ischemic heart disease and the waning importance of infectious causes. While atherosclerotic heart disease is still a relatively rare cause of heart failure, specific investigation for atherosclerotic heart disease using contemporary

means has only been performed in few studies studies. Several studies and researches have gone into the process of finding out the prevalence of heart failure in Sub Saharan Africa; however, just little is said about the challenges of diagnosing heart failure in good enough time and then overcoming those challenges. This Paper therefore, highlighted the challenges of early diagnosis of heart failure and ways to overcome those challenges.

REFERENCES

1. Andrew PA, Gregg CF, Javed B, Ovidiu C, Stephen JG, Muthiah V. et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. J Am Coll Cardiol. 2014; 63(12):1123-1133.
2. Johansson, S., Wallander, M. A., Ruigomez, A. Rodriguez, L. A. G. Incidence of newly diagnosed heart failure in UK general practice. Eur J. Heart Failure 2001; 3, 225-231.
3. Cleland, JG., McDonagh,T., Rigby, AS., Yassin,A., Whittaker,T., Dargie;, H.J. National Heart Failure Audit Team for England and Wales 2008-2009. Heart. 2011;97(11):876-886.
4. Abetel, G., Gruner, C. and Follath, F. One-Year Mortality among Unselected Outpatients with Heart Failure. Eur Heart J. 2002; 23:1861-1866.
5. Mosterd, A. and Hoes, A.W. Clinical Epidemiology of Heart Failure. Heart 2007; 93: 1137-1146.
6. Adebayo SO, Olunuga TO, Durodola A, Ogah OS Heart failure: Definition, classification and pathophysiology. A mini-review. *Nig J Cardiol*. 2017; 14: 9-1
7. Kannel WB, Levy D, Cupples LA. Left ventricular hypertrophy and risk of cardiac failure: insights from the Framingham study. J. Cardiovasc. Pharmacol.1987; 10(Suppl. 6): S135–S140.
8. Liao Y, Cooper RS, McGee DL, Mensah GA, Gtali JK. The relative effects of left ventricular dysfunction on survival among black adults. J Am Med Assoc. 1995; 273: 1592–1597
9. World Bank. Year in Review in 14 Charts 2018. [April 12, 2021]; Available from: https://www.worldbank.org/en/news/feature/2018/12/21/ year-in-review-2018-in-14-charts.
10. World Bank. Poverty and shared prosperity 2020: Reversals of fortune. The World Bank, 2020. [April 12, 2021]; Available from: https://www.ffms.pt/sites/default/files/2022-07/9781464816024.pdf
11. Regitz-Zagrosek, V., Lehmkuhl, E., Lehmkuhl, H. B., Hetzer, R. "Gender Aspects in Heart Failure," Archives Des Maladies du Coeur Et Des Vaisseaux, 2004; 97(9):1-10.
12. Blum, K. Gottlieb, SS. The Effect of a Randomized Trial of Home Telemonitoring on Medical Costs, 30-Day Readmissions, Mortality, and Health-Related Quality of Life in a Cohort of Community-Dwelling Heart Failure Patients. J Cardiac Failure 2014; 20(7)513-521
13. Mehta. PA.,Cowie, MR. "Gender and Heart Failure: A Population Perspective. Heart. 2006; 92(3)14-18.
14. Carroll, JD., Carroll, EP.,Feldman, T., Ward, DM., Lang, RM., McGaughey, et al. "Sex Associated Differences in Left Ventricular Function in Aortic Stenosis of the Elderly. Circulation 1992; 86(4): 1099-1107.
15. Guerra, S., Leri, A., Wang, X., Finato, N., Di Loreto, C., Beltrami, C. A et al. Myocyte death in the failing human heart is gender dependent," Circulation Res. 1999; 85(9): 856-866.
16. Damasceno A, Mayosi BM, Sani M, Ogah,OS., Mondo,C.,Ojji,D., et al. The

Causes, Treatment, and Outcome of Acute Heart Failure in 1006 Africans from 9 Countries: Results of the Sub-Saharan Africa Survey of Heart Failure. Arch Intern Med. 2012; (18):1386-1394.

17. Marijon E, Ou P, Celermajer DS. Prevalence of rheumatic heart disease detected by echocardiographic screening. N Engl J Med. 2007; 357:470–476.
18. Kimbally-Kaky G, Gombet T, Voumbo Y, Ikama-Méo S, Elenga-Mbola B, Mbika-Cardorelle A. et al. Rheumatic heart disease in schoolchildren in Brazzaville. Med Trop (Mars). 2008; 68:603–605.
19. Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. Lancet. 2012; 379(9819):953-964.
20. Beaton A, Okello E, Lwabi P, Mondo C, McCarter R, Sable C. Echocardiography screening for rheumatic heart disease in Ugandan schoolchildren. Circulation. 2012;125(25):3127-3132.
21. Damasceno, A., Cotter, G., Dzudie, A., Sliwa, K., Mayosi, B.M. Heart Failure in Sub-Saharan Africa: Time for Action. Journal of the American College of Cardiology. 2007;50(17):1688-1693
22. Commerford P, Mayosi B. An appropriate research agenda for heart disease in Africa. Lancet. 2006; 367:1884 –1886
23. Mayosi BM, Burgess LJ, Doubell AF. Tuberculous pericarditis. Circulation. 2005; 112:3608 –3716.
24. Bloomfield, GS., Barasa, FA., Doll, JA., Velazquez, EJ. Heart Failure in Sub-Saharan Africa. Curr Cardiol. Rev. 2013; 9:157-173
25. Butrous G, Ghofrani HA, Grimminger F. Pulmonary vascular disease in the developing world. Circulation. 2008; 118(17): 1758-1766.
26. Essop MR, Nkomo VT. Rheumatic and nonrheumatic valvular heart disease: epidemiology, management, and prevention in Africa. Circulation. 2005; 112:3584–3591
27. Seedat, YK. Impact of poverty on hypertension and cardiovascular disease in sub-Saharan. Card. J. Afr. 2007;18(5):316-320
28. McMillen IC, Robinson JS. Developmental origins of the metabolic syndrome: prediction, plasticity, and programming. Physiol Rev. 2005; 85:571– 633
29. Tantchou Tchoumi JC, Ambassa JC, Kingue S., Giamberti A, Cirri S, Frigiola A, et al. Occurrence, aetiology and challenges in the management of congestive heart failure in sub-Saharan Africa: experience of the Cardiac Centre in Shisong, Cameroon. Pan Afr Med J. 2011; 8:11.
30. Stewart S, Wilkinson D, Hansen C., Vaghela V, Mvungi R, McMurray J et al. Predominance of heart failure in the Heart of Soweto Study cohort: emerging challenges for urban African communities. Circulation. 2008;118(23): 2360-2367.
31. Opie-Martin, S., Lacoangeli, A., Topp, S. D., Abel. O., Mayl, K., Mehta, P. R. et al. The *SOD1*-mediated ALS phenotype shows a decoupling between age of symptom onset and disease duration. Nat. Comm. 2022; 13 (6901): 1-9
32. Popkin BM.,Du, S. Dynamics of the nutrition transition toward the animal foods sector in China and its implications: a worried perspective. *J Nutr.* 2003; 133:3898S–3906S.
33. Belue, R., Okoror, T. A., Iwelunmor, J., Taylor , K. D., Degboe, A. N., Agyemang,C., et al. An overview of cardiovascular risk factor burden in sub-Saharan African countries: a socio-cultural perspective. Globalization and Health. 2009; 5(10):1-12
34. Frohlich ED. State of the Art lecture. Risk mechanisms in hypertensive heart disease. State of the Art lecture. Risk mechanisms in hypertensive heart disease.

Hypertension. 1999; 34(4 Pt 2): 782-789.
35. Ntusi NBA, Mayosi BM. Epidemiology of heart failure in sub-Saharan Africa. Expert Rev Cardiovasc Ther. 2009; 7(2): 169-180.
36. Bloomfield GS, Lagat DK, Akwanalo OC., Jane Carter , E., Lugogo , N., Vedanthan ,R., et al. Conditions that predispose to pulmonary hypertension and right heart failure in persons exposed to household air pollution in LMIC. Global Heart. 2012; 7(3)
37. Bigna, J.J. and J.J. Noubiap, The rising burden of non-communicable diseases in sub-Saharan Africa. The Lancet Global Health, 2019; 7(10):1295-1296.
38. Mensah, G.A., , Roth GA, Sampson UK, Moran AE, Feigin VL, Forouzanfar MH, et al. Mortality and Causes of Death Collaborators. Mortality from cardiovascular diseases in sub-Saharan Africa, 1990-2013: a systematic analysis of data from the Global Burden of Disease Study 2013. Card J. Afr. 2015. 26(2 H3Africa Suppl): S6.
39. World Bank. World development report 2000/2001: Attacking poverty. 2000. http://documents1.worldbank.org/curated/en/230351468332946759/pdf/226840WDR00PUB0ng0poverty0200002001.pdf.
40. Tobias SL, van der Westhuyzen J, Davis RE, Icke GC, Atkinson PM. Alcohol intakes and deficiencies in thiamine and vitamin B6 in black patients with cardiac failure. S Afr Med J 1989; 76(7): 299-302.
41. Voskoboyev AI, Ostrovsky YM. Thiamin pyrophosphokinase: structure, properties, and role in thiamin metabolism. Ann N Y Acad Sci 1982; 378: 161-176.
42. Sole MJ, Jeejeebhoy KN. Conditioned nutritional requirements: therapeutic relevance to heart failure. Herz. 2002; 27(2): 174-178
43. Drazner MH. The progression of hypertensive heart disease. Circulation. 2011; 123(3): 327-334.
44. Stewart S, Wilkinson D, Hansen C., Vaghela V, Mvungi R, McMurray J, et al. Predominance of heart failure in the Heart of Soweto Study cohort: emerging challenges for urban African communities. Circulation. 2008; 118(23): 2360-2367.
45. Ibrahim MM, Damasceno A. Hypertension in developing countries. Lancet. 2012; 380:611–619.
46. Davies J, Spry CJ, Vijayaraghavan G, De Souza JA. A comparison of the clinical and cardiological features of endomyocardial disease in temperate and tropical regions. Postgrad Med J. 1983; 59(689): 179-185.
47. Connor DH, Somers K, Hutt MS, Manion WC, D'Arbela PG. Endomyocardial fibrosis in Uganda (Davies' disease). 1. An epidemiologic, clinical, and pathologic study. Am Heart J. 1967; 74(5): 687-709.
48. Beck W, Schrire V. Endomyocardial fibrosis in Caucasians previously resident in tropical Africa. Br Heart J. 1972; 34(9):915-918.
49. Hakim JG, Matenga JA, Siziya S. Myocardial dysfunction in human immunodeficiency virus infection: an echocardiographic study of 157 patients in hospital in Zimbabwe. Heart. 1996; 76(2): 161-165
50. Niakara A, Drabo YJ, Kambire Y, Nebie LV, Kabore NJ, Simon F. Cardiovascular diseases and HIV infection: study of 79 cases at the National Hospital of Ouagadougou (Burkina Faso). Bull Soc Pathol Exot. 2002; 95(1): 23-26.
51. Ogeng'o JA, Obimbo MM, Olabu BO, Gatonga PM, Ong'era D. Pulmonary thromboembolism in an East African tertiary referral hospital. J Thromb Thrombolysis. 2011; 32(3): 386-391.
52. Maron BJ, Seidman JG, Seidman CE. Proposal for contemporary screening strategies in families with hypertrophic cardiomyopathy. J Am Coll Cardiol. 2004;

44(11): 2125-2132.
53. Moolman-Smook JC, Mayosi BM, Brink PA, Corfield VA. (Molecular genetics of cardiomyopathy: changing times, shifting paradigms. Cardiovasc J S Afr. 2003; 14(3): 145-155
54. Olivotto I, Gistri R, Petrone P, Pedemonte E, Vargiu D, Cecchi F. Maximum left ventricular thickness and risk of sudden death in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 2003; 41(2): 315-321
55. Sorajja P, Nishimura RA, Ommen SR, Ackerman MJ, Tajik AJ, Gersh BJ. Use of echocardiography in patients with hypertrophic cardiomyopathy: clinical implications of massive hypertrophy. J Am Soc Echocardiogr. 2006; 19(6): 788-795.
56. Ataklte, F., Erqou, S., Kaptoge, S., Taye, B., Echouffo-Tcheugui, JB., Kengne, AP. Burden of undiagnosed hypertension in Sub-Saharan Africa, Hypertension 2015;65:291-298.
57. Dzudie, A., Twagirumukiza, M., Cornick, R., Abdou Ba, S., Damasceno, A., Ba, SA et al. Roadmap to achieve 25% hypertension control in Africa by 2025. 2017; 28(4): 262-273
58. Steenekamp JH, Simson IW, Theron W. Cardiovascular causes of death at Tshepong Hospital in 1 year, 1989- 1990. A necropsy study. S Afr Med J. 1992; 81:142-6.
59. Sokunbi OJ, Ekure EN, Temiye EO, Anyanwu R, Okoromah CA. Pulmonary hypertension among 5 to 18 year old children with sickle cell anaemia in Nigeria. PLoS One. 2017;12(9):e0184287.
60. Amadi VN, Balogun MO, Akinola NO., Adebayo RA, Akintomide AO. Pulmonary hypertension in Nigerian adults with sickle cell anemia. Vasc Health Risk Manag. 2017; 13:153-160.
61. Aliyu ZY, Kato GJ, Taylor IV J, Babadoko A, Mamman AI, Gordeuk VR, et al. Sickle cell disease and pulmonary hypertension in Africa: a global perspective and review of epidemiology, pathophysiology, and management. American journal of hematology. 2008; 83(1):63-70.
62. Opie, LH., Mayosi, BM., Cardiovascular Disease in Sub-Saharan Africa. Circulation 2005; 112:3536-3540
63. Gasperin CA, Germiniani H, Facin CR, Souza AM, Cunha CL. An analysis of electrocardiographic criteria for determining left ventricular hypertrophy. Arq Bras Cardiol. 2002; 78(1): 59-82
64. Devereux RB, Alonso DR, Lutas EM., Gottlieb GJ, Campo E, Sachs I, et al.. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986; 57(6): 450-458.
65. Addo J, Smeeth L, Leon DA. Hypertension in sub-Saharan Africa: a systematic review. Hypertension. 2007; 50:1012–1018.
66. Sagristà-Sauleda J, Mercé AS, Soler-Soler J. Diagnosis and management of pericardial effusion. World J Cardiol. 2011; 3(5): 135- 143
67. Kwan GF, Bukhman AK, Miller AC, Ngoga G, Mucumbitsi J, Bavuma C, et al A simplified echocardiographic strategy for heart failure diagnosis and management within an integrated noncommunicable disease clinic at district hospital level for sub-Saharan Africa. JACC: Heart Failure. 2013;1(3):230-6.
68. Muula AS. Is there any solution to the" brain drain" of health professionals and knowledge from Africa?. Croatian medical journal. 2005;46(1).
69. Janssens B, Van Damme W, Raleigh B, Gupta J, Khem S, Soy Ty K, et al. Offering integrated care for HIV/AIDS, diabetes and hypertension within chronic disease clinics in Cambodia. Bull World Health Organ. 2007; 85:880–885.
70. Zühlke, L., Mirabel, M. and Marijon, E.

Congenital heart disease and rheumatic heart disease in Africa: recent advances and current priorities. Heart. 2013; 99:1554–1561.

71. Dandel M, Lehmkuhl H, Knosalla C, Suramelashvili N, Hetzer R. Strain and strain rate imaging by echocardiography - basic concepts and clinical applicability. Curr Cardiol Rev. 2009; 5(2): 133-48
72. Damasceno A, Mayosi BM, Sani M., Ogah, OS., Mondo, C., Ojji, D., et al. The Causes, Treatment, and Outcome of Acute Heart Failure in 1006 Africans From 9 Countries: Results of the Sub-Saharan Africa Survey of Heart Failure. Arch Intern Med. 2012; 172(18):1386-1394
73. Awori MN, Ogendo SW, Gitome SW., Ong'uti SK, Obonyo NG. Management pathway for congenital heart disease at Kenyatta National Hospital, Nairobi. East Afr Med J. 2007; 84:312–317.
74. Yuko-Jowi CA. African experiences of humanitarian cardiovascular medicine: a Kenyan perspective. Cardiovasc Diagn Ther. 2012; 2:231–239.
75. Thangaratinam S, Brown K, Zamora J., Khan KS, Ewer AK. Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis. Lancet. 2012; 379:2459–2464.
76. Geldenhuys A, Koshy JJ, Human PA., Mtwale JF, Brink JG, Zilla P. Rheumatic mitral repair versus replacement in a threshold country: the impact of commissural fusion. J Heart Valve Dis. 2012; 21:424–432.
77. Buchanan E. Walter Sisulu Paediatric Cardiac Centre opened by Nelson Mandela. S Afr Med J. 2004; 94:14
78. Edwin F, Tettey M, Aniteye E., Tamatey M, Sereboe L, Entsua-Mensah K, et al. The development of cardiac surgery in West Africa–the case of Ghana. Pan Afr Med J. 2011; 9:15.
79. Watkins DA, Omokhodion SI, Mayosi BM. The history of the Pan-African Society of Cardiology (PASCAR): the first 30 years, 1981–2011. Cardiovasc J Afr. 2011; 22:122–123.
80. Gluba A, Bielecka A, Mikhailidis DP., Wong ND, Franklin SS, Rysz J, et al. An update on biomarkers of heart failure in hypertensive patients. J Hypertens. 2012; 30(9):1681-1689.
81. Sani MU, Adamu B, Mijinyawa MS., Abdu A, Karaye KM, Maiyaki MB, et al. Ischaemic heart disease in Aminu Kano Teaching Hospital, Kano, Nigeria: a 5 year review. Niger J Med. 2006; 15(2): 128-131.
82. Damorou F, Yayehd K, Pessinaba S, Baragou R, Soussou B. Ischemic cardiomyopathy in Lome: epidemiologic aspects and risk factors (study of 461 cases). Mali Med. 2008; 23(3): 47-54.
83. Ogeng'o JA. Pattern of complications and anatomical risk factors for atherosclerosis among black Kenyans [Dissertation]. University of Nairobi; 2014 [cited April 12, 202]. Available from: http://erepository.uonbi.ac.ke/handle/11295/76753
84. Moolman-Smook JC, De Lange WJ, Bruwer EC, Brink PA, Corfield VA. The origins of hypertrophic cardiomyopathy-causing mutations in two South African subpopulations: a unique profile of both independent and founder events. Am J Hum Genet. 1999; 65(5): 1308-1320.
85. Khunnawat C, Mukerji S, Havlichek D, Touma R, Abela GS. Cardiovascular manifestations in human immunodeficiency virusinfected patients. Am J Cardiol. 2008; 102(5).
86. Mandi DG, Bamouni J, Yaméogo RA, Naïbé DT, Kaboré E, Kambiré Y, et al. Spectrum of heart failure in sub-Saharan Africa: data from a tertiary hospital-based registry in the eastern center of Burkina

Faso. Pan Afr. Med. J. 2020;36(1).
87. Koffi J, Coulibaly I, Gnaba A, Boka B, Koffi F, Tanoh M, et al. Pulse Pressure as a Risk Factor of Atrial Fibrillation in Black African Elderly Patients. World J. Cardiovas Dis. 2015; 5(10):303.
88. Zhou, D.T., Oktedalen , O., Chisango, T., Stray-Pedersen, B. HIV/AIDS and Coronary Heart Disease on a Collision Course? Review of Zimbabwe. Am J. Med. Res. 2016; 4(2): 26-32
89. Davies J, Spry CJ, Vijayaraghavan G, De Souza JA. A comparison of the clinical and cardiological features of endomyocardial disease in temperate and tropical regions. Postgrad Med J. 1983; 59(689): 179-185.