

Sex-related differences in characteristics, management and in-hospital outcome in sub-saharan patients with acute coronary syndrome

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Abstract

Background: Coronary heart disease remains the leading cause of morbidity and mortality in both men and women worldwide. Cardiovascular disease (CVD) is on the rise in sub-saharan countries that are currently undergoing rapid urbanization, industrialization, and lifestyle changes. Recently, knowledge regarding sex differences in CVD has evolved.

Although, data on the incidence of acute coronary syndrome (ACS) in sub-saharan are not rare, few focused closely on sex differences. The purpose of this study was to examine sex-related differences in characteristics, management and in-hospital outcome in sub-saharan with acute coronary syndrome.

Methods: This was a retrospective study conducted at the cardiology department of Principal Hospital of Dakar over a period of 60 months (January 1st 2010 to December 31st 2014), in Dakar, Senegal. Two hundred and seven medical records of patients admitted for ACS based on anginal pain at rest, suggestive electrocardiographic changes and elevated troponin I levels, were included. We studied data on age, risk factors, symptoms, the time delay before admission, the management given, the vital parameters as well as evolution during hospitalization. Medical records were then stratified into two categories (males and females) to study differences. The studied parameters were entered into an electronic questionnaire using Epi Info version 3.3.5 of the World Health Organization.

Results: Hospital prevalence of ACS was 6.09% with a sex ratio M/F of 1.62(159/98). there was an overall rates increase of admissions for ACS in both men and women. The mean age of patients was 67.5 ± 10.1 years with a range of 44 and 93 years. Females were older than males ($p=0.08$) with a greatest incidence of ACS in those aged 60 to 69 years. Women had a higher prevalence of risks, such as diabetes, hypertension, dyslipidemia, and obesity than men. In addition, there are sex differences in an order of importance related to risk factors for ACS. Hypertension, diabetes, and obesity are the most important risk factors in women, whereas current smoking, hypertension and diabetes are the important risk factors in men. Chest pain was present in 249 patients (97%). Typical anginal pain was more common in men than women (76.1% vs 52.1%), this difference was statistically significant ($p=0.000$). The average time delay before medical care was given was 29.09 ± 8.5 hours. This time delay was higher in women than men (53.9 ± 18 hours vs 26.4 ± 12.3 hours; $p=0.005$) Mean troponin I level found was 1.9 ± 2.8 ng/ml, Creatine phosphokinase and Creatine phosphokinase-MB measured 824 ± 909.7 UI/l and 141.3 ± 245.9 UI/l respectively. Troponin I level was higher in men than women. Mean total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein cholesterol and, triglyceride were 2.06 ± 0.25 g/l, 0.90 ± 0.2 g/l, 0.90 ± 0.20 g/l, and 1.44 ± 0.20 g/l respectively. LDL cholesterol was higher in women than in men. Electrocardiogram revealed an ACS with persistent ST-elevation in 143 patients (90 males vs 53 females) and non ST-elevation ACS in 114 patients (69 males vs 45 females). Concerning treatment, thrombolysis using streptokinase was performed in 33 patients, accounting for 12.8% of patients with ST-elevation. Thrombolysis was performed in 10.2% of females compared to 14.5% of males ($p=0.32$). Six deaths (6.1%) were recorded in women and 10 (6.3%) in men. Complications was dominated by pulmonary oedema.

Conclusion: Our study confirms that acute coronary syndrome is not a “man’s only” disease in sub-sahara.

Although in our study there was no difference in mortality, atypical presentation and low elevations in biomarker were responsible of long time delay before medical care in women.

Keywords: acute coronary syndrome, risk factor, women, sub-saharan

Background

Despite major advances in diagnosis and treatment, coronary heart disease (CHD) remains the leading cause of morbidity and mortality in both men and women worldwide [1]. Cardiovascular disease (CVD) is on the rise in sub-saharan countries that are currently undergoing rapid urbanization, industrialization, and lifestyle changes. Recently, knowledge regarding sex differences in CVD has evolved. During the past 3 decades, numerous and remarkably consistent studies have reported sex differences in the epidemiology, clinical manifestations, risk factors, diagnoses,

outcomes, and prevention of acute coronary syndrome (ACS) [2,3].

Current knowledge about the prevention of CHD and CVD is mainly derived from studies in European populations. However, the extent to which these findings apply worldwide is unknown.

Although, data on the incidence of ACS in sub-saharan are not rare [4-7], few focused closely on sex differences.

The purpose of this study was to examine sex-related differences in characteristics, management, and in-hospital outcome in sub-saharan with ACS.

Methods

This was a retrospective study conducted at the cardiology department of Principal Hospital of Dakar over a period of 60 months (January 1st 2010 to December 31st 2014), in Dakar, Senegal.

After approval by the ethics committee of the Ministry of Health and Social Welfare, Senegal, medical records of patients over a five-year period admitted for ACS on the basis of anginal pain at rest, suggestive electrocardiographic changes and elevated troponin I levels, were included. Patients with stable angina, and those with semi-recent or sequel of coronary syndrome were excluded from the study.

Medical records of 257 patients were evaluated.

We studied data on age, past history including history of diabetes, hypertension, smoking, alcoholism, sedentarism (less than 30 minutes or more of moderate intensity physical activity on most days of the week), obesity, family history of CHD at a young age (before 55 years in men and 65 years in women), use of estrogen-progestin contraceptives, stable angina, and stress.

We sought the presence of chest pain, dyspnea, and gastrointestinal symptoms. We also noted the time delay before admission, the management given, and the vital parameters (blood pressure, heart rate, respiratory rate, temperature, and body mass index).

All patients had a complete physical examination and a laboratory assessment. Troponin I assay was done using Architect STAT chemiluminescent microparticle immunoassay (Abbot). The other tests included blood glucose level on admission, total cholesterol and its fractions, and triglycerides. On the electrocardiogram, we looked for subepicardial or subendocardial lesion, subepicardial or subendocardial ischemia, abnormal Q waves, and rhythm and conduction abnormalities. We have also looked for signs of venous stasis on the chest X-ray and evaluated using doppler echocardiography (which was performed during the first 24 hours of admission), the left ventricle wall motion, left ventricular ejection fraction using Simpson's biplanar method, and the presence of intracavitary thrombus. Treatment modalities were evaluated as well as evolution during hospitalization. Medical records were then stratified into two categories (males and females) to study differences.

The studied parameters were entered into an electronic questionnaire using Epi Info version 3.3.5 of the

World Health Organization. Data analysis was performed using SPSS 15.0 (Statistical Package for Social Sciences). Quantitative data were expressed as mean plus or minus standard deviation and data analyses were performed using chi-square (and Fischer's exact) test.

Results

Hospital prevalence of ACS was 6.09% with a sex ratio M/F of 1.62(159/98), there was an overall rates increase of admissions for ACS in both men and women (Figure 1).

The mean age of patients was 67.5 ± 10.1 years with a range of 44 and 93 years. Females were older than males (68.8 ± 9.5 vs 66.8 ± 10.3 ; $p=0.08$) with a greatest incidence of ACS in those aged 60 to 69 years. (Figure 2).

The risk factors in our patients were dominated by hypertension in women (63.3%) and active smoking in men (69.8%). Half of patients had more than one risk factor.

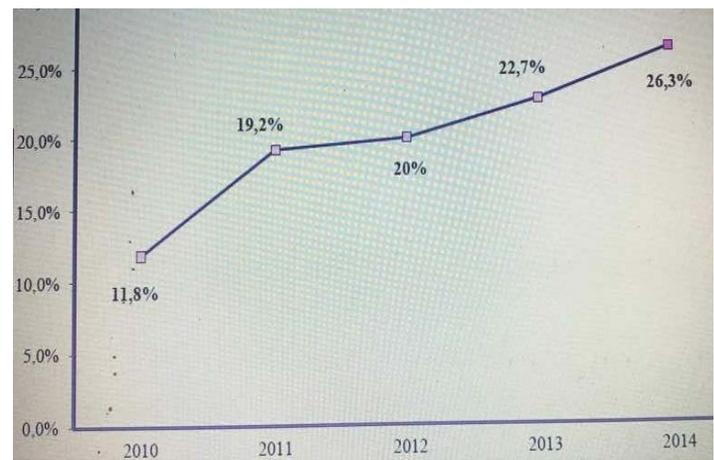


Figure 1. Trends of hospitalizations for ACS, 2010-2014.

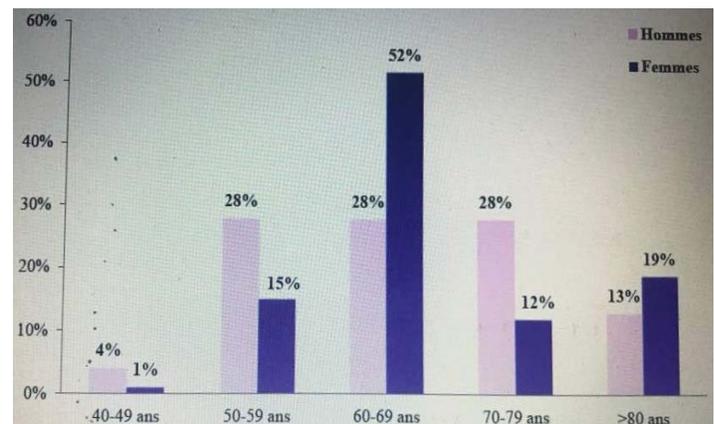


Figure 2. Acute coronary syndromes by age groups and sex

	All	Women	Men	p-value
Age (years)	67.5 ± 10.1	68.8 ± 9.5	66.8 ± 10.3	0.08
Risk factors (%)				
Hypertension		63.3	50.9	0.053
Diabetes		54.1	40.9	0.03
Dyslipidemia		26.5	20.7	0.284
Obesity		33.7	13.8	0
Tabacco smoking		6.1	69.8	0
Heredity		10.2	12.6	0.76
Heart rate (bpm)	90.14 ± 8.72	91.02 ± 9.6	89.5 ± 8	0.04
SBP (mmHg)	128.8 ± 20.7	132.04 ± 24.3	126.8 ± 17.9	0.05
DBP (mmHg)	81.6 ± 10.5	83.4 ± 11.5	80.5 ± 9.7	0.02
BMI (Kg/m ²)	25.6 ± 4.8	26.1 ± 3.4	24.9 ± 1.6	0.0001
Killip Class				
I	N=178 %= 69.3	N= 60 %=61.2	N= 118 %=69.3	0.52
II and III	N=79 %= 30.7	N= 38 %=38.8	N= 41 %=25.7	0.52
LDL CHOL (g/l)	0.90 ± 0.2	0.91 ± 0.2	0.89 ± 0.2	0.48
Troponine (ng/ml)	1.9 ± 2.8	1.68 ± 2.3	2.04 ± 3.07	0.55
STEMI	N=143 %=55.6	N=53 %=54.1	N=90 %=56.7	

Abbreviations: SBP=systolic blood pressure; DBP=diastolic blood pressure; BMI=body mass index; LDL CHOL=low-density lipoprotein cholesterol; STEMI=ST-elevation myocardial infarction

Table 1. Baseline characteristics and risk factors in the population study.

Complications	Women (%)	Men (%)
Congestive Heart Failure	5.1	2.5
Pulmonary Oedema	21.42	17.6
Cardiac Arrhythmias		
<i>Atrial Flutter</i>	1.02	1.9
<i>Ventricular Fibrillation</i>	1.02	0
Cardiac conduction Troubles		
<i>2nd degre AV block</i>	2.04	0
<i>Complete AV block</i>	2.04	1.26

Table 2. Complications encountered

Table 1 demonstrated the comparison of baseline characteristics and risk factors between men and women

Chest pain was present in 249 patients (97%). In 67.1% of cases, it was typical anginal pain.

Typical anginal pain was more common in men than women 76.1% vs 52.1%. this difference was statistically significant ($p=0.000$). Vomiting was present in 14.8% of cases and was more common in women than men (7.5% vs 1%; $p=0.020$; $OR=7.9$).

The average time delay before medical care was given was 29.09 ± 8.5 hours. This time delay was higher in women than men (53.9 ± 18 hours vs 26.4 ± 12.3 hours; $p=0.005$) (Figure 3).

On admission, average systolic blood pressure (SBP) was 128.8 ± 20.7 mmHg and diastolic blood pressure (DBP) 81.6 ± 10.5 mmHg.

SBP and DBP were higher in women than men and the difference was statistically significant ($p=0.005$ and 0.02 respectively)

Average body mass index (BMI) was 25.6 ± 4.8 kg/m². BMI was found to be higher in women than men (26.1 ± 3.4 kg/m² vs 24.9 ± 1.6 kg/m²; $p=0.0001$)

An abdominal obesity was found in 77.6% of women versus 25.8% in men ($p=0.0001$ $OR=9.94$) according to the criteria of the International Diabetes Federation (IDF) and in 52% of women versus 6.9% of men ($p=0.000$; $OR=14.6$) according to the criteria of the National Cholesterol Education Program (NCEP).

Systemic examination was strictly normal in 178 patients (69.3%). 38 women and 41 men however showed signs of left ventricular failure (Killip II and III).

Mean troponin I level found was 1.9 ± 2.8 ng/ml, CPK and CPKmb were 824 ± 909.7 UI/l and 141.3 ± 245.9 UI/l respectively.

Troponin I level was higher in men than women (2.04 ± 3.07 ng/ml vs 1.68 ± 2.3 ng/ml; $p=0.55$) and so were CPK and CPK-MB ($p=0.04$ and $p=0.33$ respectively).

Average blood glucose level was 1.15 ± 0.5 g/l (1.14 ± 0.53 g/l in men versus 1.15 ± 0.49 g/l in women). Mean total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride was 2.06 ± 0.25 g/l, 0.90 ± 0.2 g/l, 0.90 ± 0.20 g/l, and 1.44 ± 0.20 g/l respectively. LDL cholesterol was higher in women than in men (0.91 ± 0.2 g/l vs 0.89 ± 0.2 g/l; $p=0.48$).

Electrocardiogram revealed an ACS with persistent ST-elevation in 143 patients (90 males vs 53 females) and non ST-elevation ACS in 114 patients (69 males vs 45 females).

Topographically, the anterior and inferior territories were the most represented and found respectively in 68.4% and 31.6% in women and 74.2% and 25.8% in men.

Doppler echocardiography revealed impaired segmental kinetics in more than half of patients. The mean ventricular ejection

fraction was 43.6 ± 9.3 percent. there was no difference between males and females ($p=0.83$). Left ventricle enlargement was found to be more common in women (44.9%) than men (32.7%). This difference was statistically significant ($p=0.04$).

Concerning treatment, thrombolysis using streptokinase was performed in 33 patients, accounting for 12.8% of patients with ST-elevation.

Thrombolysis was performed in 10.2% of females versus 14.5% of males ($p=0.32$).

Low molecular weight heparin was used in 98% of women versus 91.8% of men, aspirin in 100% of patients, clopidogrel in 100% of patients, beta blockers in 65.3% of women versus 61.2% of men (65.3%), angiotensin converting enzyme inhibitors, statins, and analgesics in all patients.

The evolution during hospitalization after a mean hospital stay of 9.08 ± 3.4 days (9.5 ± 3.7 days for women versus 8.8 ± 3.2 days for men) was favorable in 182 patients (70.8%). Six deaths (6.1%) were recorded in women and 10 (6.3%) in men. Complications (Table 2) were dominated by pulmonary oedema.

Discussion

Similar to many ACS trials and registries [8-11], more men than women were enrolled in this study. Atypical presentations and less predictive ischemic screening tests for women are the factors that most likely limit the enrollment of women in trials.

In our study, the prevalence of ACS in women was 2.32% with an incidence of 38.1% on all patients with CHD hospitalized during the same period. Data on the incidence of ACS in women are rare in Africa. However, Mboup [4], in a study realized in 2006 found an incidence of 5.7%.

In a French nationwide study from 2004 to 2014, Gabet [12] found an incidence of 32.2% ACS in women. This incidence was of 27% in the French registry on Acute ST-elevation Myocardial Infarction (FAST-MI)[13].

The increase in ACS hospitalizations in women observed in our study is in keeping with data from European and American literature [12-14] and could be related to a concomitant rise in the prevalence of cardiovascular risk factors secondary to an overall lifestyle changes.

However, reliable data on the evolution of risk factors are unfortunately lacking in Africa.

Our study showed that women were older than men. These findings were consistent with previous clinical trials and registries [8,15-18].

The onset of coronary artery disease (CAD) exhibits a delay of approximately 10 years' delay in women than in men [19]. An earlier study explained why women were older at presentation: it was attributed to the fact that aging is associated with progressive endothelial dysfunction, which appears to occur earlier in men than in women. In women, however, a steep decline of endothelial function

commences at menopause. This is consistent with a protective effect of estrogens on the arterial walls [20].

Although, the mean age on the occurrence of ACS in women is still high in France, analyses of mean annual trends by age group from 2004 to 2014 showed a significant increase in the rate of patients hospitalized for ACS in women aged between 45 and 64 years. The greatest increase was observed among those aged 45 to 54 years (+1.7% per year) [12].

This increase in young women is likely related to a concomitant rise in the prevalence of cardiovascular risk factors, particularly

smoking. In a 2014 French national survey estimating health characteristics in a representative sample of the French population, the prevalence of regular tobacco smoking increased considerably in women aged 45 to 74 years from 2005 to 2014 and doubled in the 55 to 64 years age group [21].

As emphasized in our work (6.1%), women were less likely to be smokers in Africa where there are strong levels of moral condemnation and social rejection of women smoking. Meanwhile tobacco smoking was the most prevalent risk factor in men (69.8%).

women had a higher prevalence of risk factors, such as diabetes, hypertension, dyslipidemia, and obesity than men.

In addition, there are sex differences in an order of importance related to risk factors for ACS. Hypertension, diabetes, and obesity are the most important risk factors in women, whereas current smoking, hypertension and diabetes are the important risk factors in men

Hypertension was found to be the main risk factor and is often found in the occurrence of coronary events in women [13;22-24]. This is reflected in our work where hypertension is found in 63.3% of cases.

Hypertension has long been established as a strong, independent, etiologically significant risk factor for cardiovascular disease. Obesity and diabetes are the next most important risk factors in men and women, but their relative effect varies in different regions of the world. In fact, the present study shows that the 3 most important risk factors in sub-saharan women are hypertension, diabetes, and obesity.

In the present study, obesity was found in 33.7% of cases.

One of the possible reasons is different dietary habits, especially in sub-saharan women with high-fat diet and sedentary lifestyle and on the other hand, obesity in black women and men has something to do with perceptions of beauty and attractiveness. There is a powerful anecdotal evidence that obesity signals wealth, beauty, influence, and power.

Clinically, the picture of acute coronary syndrome is dominated by pain in both men as well as in women [4,5,13].

However, atypical symptom is known more frequent in women than men [25] as the case in our study where atypical symptom was found in 47.9% of women versus 23.9% in men.

Regarding the type of ACS diagnoses at presentation, the proportion of patients with STEMI was higher than that with non STEMI and there was no difference between men and women. It seems that women are less likely to present with STEMI than men are. The results from other trials concurred with this finding [9,11,17].

Diagnosis and risk assessment of CAD in women has traditionally been more difficult than in men. The sensitivity and specificity of stress testing is lower in women [26,27].

Cardiac biomarkers play an important role in the risk stratification and choice of treatment strategies for patients with ACS.

Although not an entirely consistent finding, prior studies have shown that women were less likely to have biomarker evidence of myocyte necrosis, elevated CK-MB, or troponins but more likely to have elevations in newer markers used for risk stratification in ACS: hs-CRP and BNP [27].

In our study, mean troponin I level was found to be lower in women than men.

The older generation cardiac troponin assays had initially been

thought to be good gender-independent markers for diagnosis in acute coronary syndrome.

More recently, developments in assay technology have greatly enhanced sensitivity and, for the first time, have been able to quantify circulating troponin in the majority of individuals in a normal healthy reference population [28]. Measuring troponin using high-sensitivity assays has revealed important differences between men and women, with the 99th centile reference limits up to two-fold higher in men [28].

Atypical presentation and low elevations in biomarker could be responsible of long time delay before medical care in women.

Many studies have shown that women with ACS are less likely to undergo cardiac catheterization, as well as to receive timely reperfusion therapy [9,29,30].

The impact of thrombolytic therapy on mortality with a time-dependent effect has been reported by several studies [31-33]. It is now clear that thrombolysis can significantly reduce mortality of patients with ACS. In our work, no patients undergo cardiac catheterization and streptokinase being the only available thrombolytic in our hospitals, was used in 12.8% of patients admitted with an ST-elevation ACS. The reasons for the low use of thrombolytics in this study were due to many factors including low awareness level of the population about acute coronary syndrome, poor transport, and communication network to reach referral centers, lack of available electrocardiography in health centers which are located close to patients, delayed referral from health centers of suspected cases and inability to meet the high cost of thrombolytic treatment.

In our study, the low use of thrombolytics was similar in gender.

Mortality in our study was of 6.1% in women and 6.3% in men. This rate is bringing our numbers in the range of the European and American literature [14,16,34].

There are conflicting evidence and unconvincing explanations regarding the effect of sex on mortality following ACS. Generally, unadjusted comparisons of mortality after ACS have shown that women have worse outcomes than men do.

In the NCVAD-ACS registry [35], women with STEMI had higher unadjusted in-hospital mortalities than men did. However, after adjusting for differences in age and other covariates, the STEMI group's in-hospital mortality, OR was not significantly different between women and men (adjusted OR: 1.06, 95% CI: 0.67 to 1.70, p=0.769). In our study there was no difference in mortality between women and men in the same period.

In contrast, many studies on Western, Middle Eastern, and Asian patients found that women had a significantly higher rate of in-hospital mortality even after adjusting for age and other comorbidities [15,30,36]. Nevertheless, other researchers found that the sex difference in ACS mortality was dependent on the clinical presentation and severity of angiographically documented disease [18,37]. Some studies have suggested a link to the less aggressive hospital care of women, including the underuse of reperfusion, as an explanation for their increased mortality [18,37]. It is possible that other factors, including ethnicity, culture, psychosocial, educational, and socioeconomic statuses contribute to the sex differences in ACS mortality.

Conclusion

Our study confirms that acute coronary syndrome is not a "man's only" disease in sub-sahara.

The major concern is that there appeared to be continuing evidence of delayed medical care in women related probably to

atypical presentation and low levels of cardiac biomarkers.

The present study shows that the 3 most important risk factors in sub-saharan women are hypertension, diabetes and obesity.

Competing interest: The authors declare that they have no competing interests

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Rec: Jul 25, 2018; Acc: Aug 15, 2018; Pub: Aug 18, 2018

J Cardio Res. 2018;1(2):6
DOI: [gsl.jcr.2018.00006](https://doi.org/10.2196/gsl.jcr.2018.00006)

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