



Acute coronary syndrome and Khat consumption in Yemeni women admitted to Coronary Care and Intensive Care in major hospital in Yemen

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ABSTRACT

Background: There is a significant percent of normal coronaries in patients with a history of documented myocardial infarction among Yemeni patients who have undergone diagnostic coronary angiogram, and they theoretically attributed that to the effect of Khat as a vasoconstrictor to the coronary artery. Also, unadjusted comparisons of mortality and major morbidity after acute myocardial infarction have generally indicated that women have a poorer outcome than men.

Methods: Data was collected prospectively from 15 hospitals in 8 governorates with acute coronary syndrome registry in the Gulf countries. All female patients who were admitted in any monitored bed in Coronary Care Units (CCU) or Intensive Care Units (ICU) with a provisional diagnosis of acute coronary syndrome (ACS) were included in the study. The presentations with khat chewing were compared with all other known and documented risk factor outcomes among women using multiple logistic regressions.

Results : There were 50.5% regular khat chewers of female patients at presentations to the general emergency department with an attack of acute coronary syndrome; 14.4% of all female patients have no other risk factors except khat. These patients were relatively younger and had a lower body mass index (BMI) when compared with the incidence of acute events in other populations. They had no significantly worse outcome during hospitalization in comparison to the males of the same age group.

Conclusions : It seems likely that there is at most only an intermediate association between Khat and the development of acute coronary syndrome in females, with less mortality and morbidity after suspected acute myocardial infarction. However, a larger study is needed, with more complete adjustment for coexisting risk factors, to determine whether the female has a worse outcome, which increases with khat.

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1. INTRODUCTION

Coronary artery disease (CAD) is the main leading cause of death [1] and a reduction in a person's ability to perform his daily activity—disability-adjusted life years (DALYs), as it creates enormous disability for those who survive [2]. Cardiovascular disease is the leading cause of morbidity and mortality worldwide. This burden is increasing in developing countries, with low- and

middle-income nations [3]. Khat, also known as “qat” in Yemen, is a fresh plant where the leaves and stem tips are chewed for their euphoric properties. It is estimated that more than 50% of females and 90% of males chew khat daily [4]. The main constituent of khat leaf is cathinone, which has an indirect sympathomimetic action (amphetamine-like mode of action) [5] and has been linked to increased risk of hypertension, acute car-

diovascular events, and cardiovascular complications in patients with acute coronary syndrome [6]. The relative risk of myocardial infarction is 39-fold higher in khat users (confidence CI 1.9–13.1) than non-users, according to a case-control study conducted in Yemen [7]. Cathinone, the active substance in khat, stimulates the release of catecholamines, which in turn raises the heart rate and increases the blood pressure; it also increases the demand for oxygen in cardiac cells, constricts coronary circulation, and can trigger platelet activation and aggregation, which are induced by catecholamine [8]. These effects contribute to the risk of ACS. The increase in blood pressure may induce stress in khat chewers by the effect of cathinone [9], which can also disrupt coronary atherosclerotic plaque, increasing the likelihood of ACS development more and more [10]. It is reported also that most khat chewers are using to smoke different types of tobacco. This was reported from three similar studies that reported a higher prevalence of cigarette smoking among khat chewers, with one study even documenting a 60% prevalence. The concurrent use of tobacco products and khat may increase the risk of ACS, potentially acting synergistically [11, 12]. There was only limited data concerning the prevalence and the clinical aspects of CAD in Yemen. In other Gulf countries, especially in the Kingdom of Saudi Arabia, until recently [13]. Women are thought to be protected from cardiovascular disease, especially CAD, by endogenous estrogen [14]. Estrogen positively affects the lipid profile by decreasing low-density lipoproteins and increasing high-density lipoproteins [15]. Estrogen also leads to lower blood pressure by relaxing smooth muscle cells and is thought to help in the body's clearance of cellular free radicals that may promote cardiovascular disease [16]. The cardiac risk factors affect the cardiovascular system differently in women and men, like diabetes, smoking, obesity, and hypertension [17]. Women and men with ACS may present with unusual symptoms. There is no reported chest pain in a large review of patients with ACS, 37% of women and 27% of men [18]. Women more often reported dyspnea, upper back, neck, or jaw pain, and weakness. The pathophysiology of ACS also differs by gender. Plaque erosion is the most frequent cause of ACS in women; in men, it is plaque rupture [19]. The uncommon cause of ACS is spontaneous coronary artery dissection (SCAD), which occurs in women almost exclusively in more than 90% of cases where 25.7% of all patients presented with ST-segment-elevation MI, and 74.3% presented with non-ST-segment-elevation [20]. The spontaneous coronary dissection (SCD) result from atherosclerotic ACS is more common in women, mainly in younger age [21]. Although khat chewing was not studied as a cause of spontaneous coronary dissection, it has been reported in some case reports [22, 23]. These factors often delay the diagnosis of ACS. However, even after diagnosis, women are less likely than men to be referred for coronary angiography,

percutaneous intervention, and fibrinolysis, which delays definitive treatment for many and places the myocardium at further risk. Women also receive less intensive medical therapy both during and after an ACS event [18]. The study was aimed at investigating the association of Khat as an independent risk for developing coronary vasospasm in women and to raise awareness of cardiovascular disease as a cause of morbidity and mortality in females.

2. METHODS

2.1. STUDY DESIGN AND PATIENT POPULATION

This study is a part of the Gulf Heart Association study done over the six Gulf countries, during which all cases with a final diagnosis of acute coronary syndrome admitted in any one of the hospitals involved in this study were collected with no exclusion criteria. This study is a prospective, multicentre survey of consecutive female patients hospitalized with the final diagnosis of ACS in all Yemen governorates during the period from 29th January to 30th May 2007. The study was ethically approved by the institutional ethical bodies in all participating governorates. Recruitment in the pilot phase started on May 8, 2006, for 30 days. Enrollment in the next phase of the registry started on January 29, 2007, and continued for 5 months. Of the 17 medical centers invited to participate in the registry, 15 hospitals in 8 governorates confirmed their participation and enrolled patients according to the survey inclusion criteria. Each participating hospital completed a questionnaire describing its medical center. Diagnosis of the different types of ACS and definitions of data variables were based on the American College of Cardiology (ACC) clinical data standards [24]. These definitions are based on clinical presentations, electrocardiogram (ECG) findings, and cardiac biomarkers. The biomarkers were measured locally at each hospital's laboratory using its own assays and reference ranges. Data collected in a questionnaire that contained 231 fields included patients' demographics, past medical history, provisional diagnosis on admission and final discharge diagnosis, clinical features at hospital presentation, ECG findings, laboratory investigations, early in-hospital (administered within 24 hours of admission) and discharge medications, use of cardiac procedures and interventions, in-hospital outcomes, and in-hospital mortality. Patients were enrolled in the study by collecting all inpatients admitted with acute coronary syndrome and/or chest pain not yet diagnosed and proved finally to be acute coronary syndrome in any intensive care unit. Data of the patients were gathered manually by a questionnaire from 8 governorates in Yemen, including 15 hospitals, and the data was revised prior to its entry into the computer system and analysis by the SPSS 26-2018



system.

3. RESULTS

Of the 1513 collected patients in this study, there were 218 (14.49%) female patients admitted with acute coronary syndrome. All of the female patients presented with acute coronary syndrome. There were significant tendencies for the women to present later after the onset of symptoms, to have higher heart rates, and to be more likely to have diabetes.

4. RISK FACTORS

:Among the 218 females with acute coronary syndrome, there were 26 (11.9%) current cigarette smokers, 32 patients (14.7%) shish smokers, 8 (3.7%) smokeless tobacco users, and 110 (50.5%) Khat chewers (Table 1). In terms of the duration of Khat chewing, 57 (51.6%) of the khat chewer patients chew Khat for 5-7 days per week, 33 (30%) patients chew kKhatfor 3-5 days per week, and 20 (18%) patients chew Khat for <3 days per week (Table 2). Moreover, of these 110 female patients who are khat chewers, 71 female patients are purely khat chewers with no other bad habits.

Table 1. The prevalence of social habits among women suffering from acute coronary syndrome in selected hospitals in Yemen

Habits	N	%
Khat	110	50.5
Cigarette smokers	26	11.9
Shish smokers	32	14.7
Smokeless tobacco users	8	3.7
No habits	42	19.2

Table 2. The duration of Khat chewing per day among women suffering from acute coronary syndrome in selected hospitals in Yemen

Days	<3 hours	3-6 hours	>6 hours
< 3 days	7	7	6
3-5 days	13	14	6
5-7 days	9	38	10

Of all the female patients enrolled, 85 (39%) were known to have diabetes mellitus (DM) at the time of presentations, 105 (48%) with hypertension, 36 (16.5%) with hyperlipidaemia, and 31 (14.2%) with a positive family history of cardiovascular insult (Figure 2), so some of them have combined risk factors. Khat chewing alone without any other risk factors was identified in 42 (18.8%) patients, and its relationship with other risk factors is depicted in Table 3. Of the patients who were khat chewers, 65 (29.8%) were known hypertensive at the time of presentation, and 8 patients who were not known to

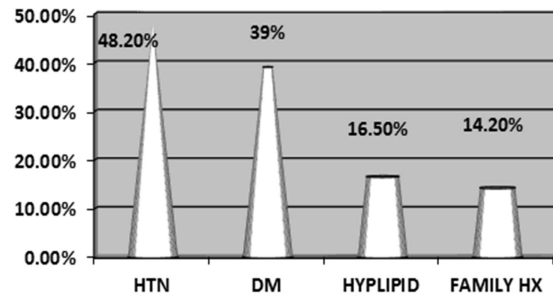


Figure 1. Combined risk factors for acute coronary syndrome in female patients

have hypertension were found to have elevated blood pressure records at the time of admission.

Table 3. The prevalence of ACS risk factors combined with kat consumption among women suffering from acute coronary syndrome in selected hospitals in Yemen

Risk factors	N	%
Khat and hypertension	65	29.8
Khat and DM	57	26.1
Khat and hyperlipidemia	27	12.4
Khat and positive family history	14	6.4
Khat and smoking	35	16.1
Khat only	42	18.8

5. HISTORY OF IHD AND ITS RELATED VASCULAR DISORDER

: history of clear angina was present in 63 (18.9%) patients and history of documented acute coronary syndrome in 38 (17.4%) patients: 18 patients of them undergone PCI and 10 patients had CABG. In addition, 75 (34.4%) patients were already on aspirin therapy, 19 (8.7%) patients had a history of stroke at the time of presentation, and peripheral vascular disease was present in 12 (5.5%) patients (Table 4). Of these, 38 women were considered to have a clear indication for fibrinolytic therapy.

Table 4. The vascular problems prevalence among women suffering from acute coronary syndrome in selected hospitals in Yemen

Variables	Angina	MI	Stroke	PVD	Aspirin use
N (%)	63(18.9)	38(17.4)	19(8.7)	12(5.5)	75(34.4)

The presenting symptoms of the patients before admission were different; most of them presented with typical ischemic chest pain in 168 (77.15) patients, 25 (11.5%) patients presented with dyspnea, 15 (6.9%) patients presented with atypical chest pain, 8 (3.7%) patients with loss of consciousness, and 2 (1%) patients with palpitations (Table 5).

Table 5. The vascular problems prevalence among women suffering from acute coronary syndrome in selected hospitals in Yemen

	N	%
Ischemic chest pain	168	77.1
Dyspnea	25	11.5
Atypical chest pain	15	6.9
Loss of consciousness	8	3.7
Palpitation	2	1

6. MAJOR CLINICAL EVENTS DURING HOSPITALIZATION

: In the unadjusted comparisons of the major clinical events that were recorded during hospitalization, which include recurrent ischemia, congestive heart failure, need for ventilations, re-infarctions, need for IABP, need for inotrope, cardiogenic shock, pericarditis, acute MR, VSD, or LV rupture, ventricular tachycardia or ventricular fibrillation, supraventricular tachycardia, need for pacemaker, major bleeding, and stroke are shown in Table 6.

Table 6. Major clinical events during hospitalization among women suffering from acute coronary syndrome in selected hospitals in Yemen

Clinical events	N	%
Recurrent ischemia	27	12.4
Re-infarction	3	1.4
Congestive heart failure	50	22.9
Ventilation	28	12.8
IABP	3	1.4
Inotrope	40	18.3
Shock	37	17
Pericardiaties	7	3.2
Acute MR	14	6.4
VSD or LV rupture	1	0.5
VT or VF	22	10.1
SVT	5	2.3
Pacing	8	3.7
Bleeding	2	0.9
Stroke	3	1.0

7. TREATMENT AND INVESTIGATIONS DURING HOSPITALIZATION

All the patients in this study received most of the investigations and treatment that is highly recommended, and its frequency is studied carefully in other parts of our study to receive some type of fibrinolytic therapy, and 17.9% of the women did receive fibrinolytic therapy. Similarly, all patients were assigned to receive aspirin, and some form of antiplatelet therapy (predominantly aspirin) was received in the hospital by 97.7% of the women. Half the patients were assigned to receive high-dose subcutaneous heparin, and 86.2% of the women received high-dose subcutaneous or intravenous heparin. Owing to the large numbers studied, these differences in management between women and men were statistically significant, but they were too small to be of much relevance to any

differences in outcome.

8. DISCUSSION

In Yemen, khat chewing is a major medical and social problem, as it leads to many medical conditions, especially in the cardiovascular system. It increases the heart rate and raises blood pressure and increases the risk of acute coronary syndrome by causing coronary artery spasms. Chewing Khat also increases the risk of stroke and cardiac death. Chewing khat has become an increasingly bad habit among women throughout Yemen and has become common not only among the elderly as it was before, but even very young women chew it daily and on every specific occasion, especially in major cities. It is also widespread in some villages, as it is believed that it gives them energy and strength to continue working. So far, no specific analytical study has been conducted on khat and its effect on the blood and why it causes high blood pressure, lowers blood sugar, or increases blood vessel spasms, although it is believed that all of these things are related to cathinone, a substance similar to amphetamine. This study examined cardiovascular risk factors among female patients diagnosed with acute coronary syndrome (ACS). It is the first study in the country to explore the association between gender, khat consumption, and the risk of ACS. Prevalent risk factors included smoking, hypertension, diabetes, hypercholesterolemia, body mass index, and family history of myocardial infarction, all of which were significantly associated with ACS [3, 4]. The study did not find a significant association between older age and ACS, which may be influenced by the age structure of the study population, as two-thirds of women were aged 50 years and less likely to be postmenopausal [25]. This study was limited to analyzing the association between khat and ACS among female patients admitted to the intensive care units of any government or private hospital that participated in this study. We found that 110 of our female patients who presented with ACS in the general emergency room were qat chewers and continued to chew qat up to one month before presentations. In this study, 42 studies were conducted on 42 patients who chewed khat only and had no other known risk factors at all. We could not accurately link the development of these events as acute coronary syndromes solely to khat chewing, although we found a strong association between qat chewing and hypertension in a large number of patients (65 patients, 8 of whom had hypertension during khat chewing during an attack). Most of our female patients were moderate khat chewers who chewed khat for 3-5 days a week with an average time of 3-6 hours each time, which raises a very important question: what is the time limit for khat to be eliminated from the body and whether its effect differs from female to male? We also found that the rate of complications among all



female patients admitted to intensive care units was less severe compared to males in the same study or to other female cohorts in other countries [22, 25].

9. CONCLUSIONS

It seems likely that there is an association between khat and the development of acute coronary syndrome in females, with reduced mortality and morbidity after suspected acute myocardial infarction. However, a larger study, with more complete adjustment for concomitant risk factors, is needed to determine whether females have a worse outcome with khat. Treatment of khat with other risk factors for primary and secondary prevention of adverse coronary events.

10. RECOMMENDATIONS

There is a need to increase awareness among female patients about the general and specific risks of khat chewing in relation to acute coronary syndrome and the benefits of early diagnosis of acute coronary syndrome. GPs in emergency departments should consider the potential for acute coronary syndrome among female patients even at a young age. Further analytical and comparative studies of khat on the cardiovascular and cerebral blood vessels are needed to understand its effect.

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