

Underrepresentation of Women in Cardiovascular Trials in Arab Middle East Region

Hanan Albackr^{1*}, Abdulaziz Backer Albacker² and Deema H. AlGhufaili³

¹Department of Cardiac Sciences, King Saud University, Riyadh, Saudi Arabia

²Department of Internal Medicine, King Saud University, Riyadh, Saudi Arabia

³Department of Internal Medicine, KSAU-HS College of Medicine, Riyadh, Saudi Arabia

Abstract

Cardiovascular Disease (CVD) is the leading cause of death in women worldwide. The burden of CVD is rising among Arab Middle Eastern (ME) women. Information regarding the prevalence and incidence of CVD and its risk factors in women in Arab ME is scarce and may be lacking in some countries. One of the reasons is low participation of Arab women in cardiovascular trials and research. The underlying reasons for the under-representation of women in clinical trials are complex and exploration of additional causes, such as socioeconomic and psychological factors is crucial to help us to address the gap in scientific evidence on women with cardiovascular disease in the Arab region.

Keywords: Women • Underrepresented populations • Cardiovascular diseases • Cardiovascular Clinical trials • Middle East • Congestive Heart failure • Coronary artery disease • Stroke

Introduction

Cardiovascular Disease (CVD) remains the leading cause of mortality and morbidity among men and women worldwide; yet, women have been underrepresented in cardiovascular clinical trials. A systematic review by Jin, et al. found that out of 740 completed CV trials including a total of 863000 adults, only 38.2% of were women [1]. Looking at available US Food and Drug Administration reviews of trials from 2005 to 2015, Scott, et al. found large variations in women participation (range from 22% to 81%; mean per trial, 46%) [2]. In 118 heart failure trials with at least 400 participants, only 27% were women [3].

Our national studies showed low percentage of women recruited in cardiovascular trials. In HEARTS (The heart function Assessment Registry Trial in Saudi Arabia registry) which is a prospective study enrolled 2610 Acute Decompensated Heart Failure (ADHF) patients admitted to 18 hospitals in Saudi Arabia between 2009 and 2010 in Saudi Arabia and followed mortality rates until January 2013, it included only 34% women [4]. In a recent trial from Middle East (ME) this number did not change in which only 30% women recruited in PEACE MENA registry pilot (Program for the Evaluation and Management of the Cardiac Events registry for the Middle East and North Africa (MENA) Region), prospective multi-country study included patients hospitalized with Acute Myocardial Infarction (AMI) and/or Acute Heart Failure (AHF)) to evaluate the clinical characteristics, socioeconomic and educational levels, management, in-hospital outcomes, and mortality rate of 1000 recruited hospitalized patients during 6 months in 14 Arab countries in the MENA region [5].

This low representation of women in cardiovascular clinical trials is a concerning issue giving the high mortality of CVD in this population [6]. In spite of increased awareness of sex differences in cardiovascular diseases, there are challenges in recruiting women to participate in clinical trials. The burden of CVD is rising among Middle Eastern women [7]. Information regarding the prevalence and incidence of CVD and its risk factors in women in ME is scarce and may be lacking in some countries. One of the reasons could be low recruitment of women in Arab ME in cardiovascular trials.

To our knowledge there is very few reviews looked at the percentage of Arab Middle Eastern women recruited in all cardiovascular clinical trials including registries. So the aim of this review article is to look at the magnitude of women underrepresentation in different cardiovascular trials and recent cardiac registries done in the Arab region of ME with an attempt to understand some of the challenges and gaps for their underrepresentation in this part of the world.

Literature Review

The prevalence of CVD and mortality in Arab Middle Eastern women

The increase mortality rate from CVD the Arab world of ME is among the highest in the world [8]. The Arab World consists of 22 countries in the Middle East and North Africa: Algeria, Bahrain, the Comoros Islands, Djibouti, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Mauritania, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, the United Arab Emirates, and Yemen [9].

Despite a lower prevalence of CVD in women than men, the mortality rate are worse in women in which more women than men have died of CVD every year since 1984 [10,11]. Women have been historically considered more protected, and, therefore, their real CVD risk has been largely underestimated [12]. In addition, women are generally under-represented in most clinical trials especially in cardiology and pediatrics which had the greatest negative associations with female enrollment [13]. These factors result in less aggressive management strategies used in women than men as well as gender disparities in access to care for CVDs [14,15].

Historically, obtaining reliable mortality data in the ME has been a challenge, with the exception of a few countries, such as Israel and Turkey. Despite this challenge, the Global Burden of Disease study (GBD) reported that ischemic heart disease is the leading cause of death worldwide,

***Address for Correspondence:** Dr. Hanan Albackr, Department of Cardiac Sciences, King Saud University, Riyadh, Saudi Arabia; Tel: +966-1-4679353; E-mail: halbackr@gmail.com

Copyright: © 2022 Albackr H, et al. This is an open-access article distributed under the terms of the creative commons attribution license which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Received: 20-Oct-2022, Manuscript No. JCDD-22-77839; **Editor assigned:** 24-Oct-2022, Pre QC No. JCDD-22-77839(PQ); **Reviewed:** 07-Nov-2022, QC No. JCDD-22-77839; **Revised:** 15-Nov-2022, Manuscript No. JCDD-22-77839(R); **Published:** 22-Nov-2022, DOI: 10.37421/2329-9517.22.10.S1.001

followed by stroke [16].

A study from Oman analyzed all-cause mortality in the Middle East, concluded that while communicable diseases incidence has decreased as a cause of death over the 35 years, chronic conditions have emerged, specifically CVD and diabetes mellitus [17]. In 2001, a cohort study from Lebanon showed that while the mortality rate from Ischemic Heart Disease (IHD) higher in men compared to women, the mortality rate from stroke was 1.5 times higher in women than men [18]. In Syria, heart disease prevalence in 2004 was 4.8% (6.2% in men and 3.7% in women) and stroke prevalence was 1% in both genders. Mortality rates from heart diseases were higher in men compared to women while stroke mortality was higher in women [19].

CVD risk factors in women in Arab Middle East

Although Arab women in the ME share the same cardiac risk factors with women in other parts of the world but they were found to be younger at time of their cardiac event have and have more incidence of metabolic syndrome, DM, obesity and sedentary life style. This has been shown in multiple national studies from Arab ME region. The Gulf Registry of Acute Coronary Events (Gulf RACE) showed that the patients from gulf area young with mean age of were 56 years and 40% of them had diabetes. The percentage of women was 21% in this study [20]. The international case-control analysis of risk factors for a first myocardial infarction (INTERHEART-ME) conducted in eight ME countries and showed that the overall population attributable risk of the nine risk factors to Acute Myocardial Infarction (AMI) was higher in the ME (97.5%) than worldwide (90.4%) and both diabetes and hypertension had greater association with AMI in women than men [21].

The Prospective Urban Rural Epidemiology (PURE Saudi) study of 2047 participants recruited from 19 urban and 6 rural communities randomly selected from the Central province to assess associated demographic, behavioral, and CVD risk factors. 43.1% women found that Compared to women, men were more likely to be current smokers and have diabetes and a history of IHD. Women were more likely to be obese, self-report sadness, experience stress, and have low education [22]. In addition to the metabolic risk factors, unique behavioral factors and socioeconomic factors contribute to increase risk of cardiac diseases in women in Arab ME region. Furthermore, changes in Socioeconomic Status (SES) also may lead to changes to behavioral risk factors. In a recent international Prospective Urban Rural Epidemiological (PURE) analysis of study, recruited participants from the general population from 21 high-income, middle-income, and low-income countries including Arab ME countries and followed them up for approximately 10 years [23]. The study looked at metabolic, behavioral, and psychosocial risk factors for CVD. In their analysis, they have showed that most of the metabolic risk factors were similar in women and in men, on the other hand, behavioral risk factors, such as consumption of a diet was more strongly associated with cardiovascular disease in women than in men. The similarities in other cardiac risk factors in women and men emphasize the importance of similar preventive therapeutic measures of cardiovascular disease in both men and women.

The Effect of Potentially Modifiable Risk Factors Associated with Myocardial Infarction in 52 Countries (INTERHEART) study was assessed in a large case-control study that screened all patients admitted for a first MI at 262 participating centers in 52 countries. INTERHEART identified 9 easily measured risk factors (smoking, lipids, hypertension, DM, obesity, diet, physical activity, alcohol consumption, and psychosocial factors) [24]. Similar to PURE, INTERHEART showed that the magnitude of the cardiac risk factors for men and women were similar, but the impact of modifying the risks was greater in women. Thus, large studies have demonstrated that lifestyle intervention for primary prevention can decrease the incidence of Atherosclerotic Cardiovascular Disease (ASCVD) as well as the associated mortality rates in both women and men.

The impact of obesity on development of Coronary Artery Disease (CAD) is more in women compared to men. In Framingham Heart study, obesity increased the risk of CAD in women by 64% and in men by 45%. Moreover, the prevalence of inactivity and sedentary behaviors is higher

among women than men. In addition to the traditional cardiac risk factors for ASCVD, Women have unique risk factors that put them at higher risk for ASCVD at young age compared to men like preeclampsia, gestational diabetes, preterm labor, autoimmune diseases and depression [25].

Women's Participation in cardiovascular clinical trials in Middle East compared to the rest of the world

From 2013-2016, about 60 million women in USA were affected by different CVDs mainly Ischemic Heart Disease (IHD) and stroke, out of those women only about 50% recognize that CVDs are the major cause of death among them [26,27]. Arab countries of the Middle East have a high prevalence of CVDs with higher mortality rates, in comparison with well-developed countries [28]. In this 2019 update of global burden of CVD and risk factors showed that the excess CVD deaths in women due to IHD begins at ages 80 to 84 years. Among women, the age-standardized rates for Disability-Adjusted Life Years (DALYs) were highest lower income countries namely Central Asia, North Africa and the Middle East, and Eastern Europe; and it was lowest in High-Income countries like Asia Pacific, Australasia, and Western Europe. Meanwhile Age-adjusted mortality due to stroke was greater in men compared to women, but prevalence was greater in women.

In a systematic review of the participation of Arab women in randomized clinical trials for cardiovascular diseases [29]. AL Sharie Sarah and her colleagues showed that, out of the 9071 patients enrolled in the 71 included RCTs, 38.02% were women. This percentage remarkably improved over the years. Women's recruitment in ME CVD randomized clinical trials has increased over the years from 29.73% from 1990 to 2009, to 40.1% in the 10-year period from 2010 to 2020. The most common indications for Women's enrolment in the trials were Valvular Heart Diseases (VHDs) and hypertension (61% and 50%, respectively) and the least common indication of women's enrollment was in coronary artery disease trials (20%). In Arab population, women were fairly represented in trial of heart failure [30]. The high prevalence of heart failure with preserved ejection fraction in women is an important reason for this fair presentation of women in heart failure trials.

Furthermore, they have showed in their review a large variation among different Middle east north Africa countries in the percentage of women enrolled in RCT CVD clinical trials in which Sudan, Egypt and Saudi Arabia have the highest percentage of women participation in RCT (80%, 40% and 38%, respectively) while the lowest participation rate of women was from Qatar and Kuwait (9% and 10%) [29]. One important reason for this variation is the number of RCT conducted in each country raising doubt in their real women representation rates. It was found that factors associated with enrolment of women in RCTs are, age, clinical indication, year of study publication, intervention, prevention type and location of trials. It was found that Egypt has the highest number of CVD clinical trials thus the presentation of women there may be more accurate than other countries.

Studies of heart failure showed that women account for higher prevalence rates of Heart Failure (HF) than men [25,31-33]. The most common phenotype of HF in women is heart failure with preserved ejection fraction, was classified before as diastolic heart failure with higher prevalence of hypertension and atrial fibrillation in women compared to men [25]. Arab heart failure RCTs showed 43% women participation percentage which is fairly representative of women among the disease population. Jin et al in their review demonstrated that women were underrepresented in clinical trials for CAD, hypertension, HF, stroke and arrhythmia randomized clinical trials.

Multiple registries done in the Arab world revealed a low percentage of women representation in those registries ranging from 22% to 38% depending on the type of the cardiovascular disease of the trial. A sub study of HEARTS (The Heart function Assessment Registry Trial in Saudi Arabia) looked at sex-specific differences in clinical features and outcomes of patients with Acute Heart Failure (AHF), a prospective registry, enrolled 2609 patients with AHF between 2009 and 2010, 34.2% were women [34]. Women were older and more likely to have risk factors for atherosclerosis, history of chronic Heart Failure (HF), rheumatic heart and valve disease.

In terms of management and outcomes, a higher use of angiotensin converting enzyme inhibitors, beta blockers, and aldosterone inhibitors was observed in men. A higher atrial fibrillation in women however, no differences were observed in hospital outcomes and the overall survival did not differ between men and women. Gender inequality in the clinical outcomes of equally treated acute coronary syndrome patients in Saudi Arabia (SPACE Registry) showed that of 5061 patients, 1142 (23%) were women [35]. Women were more frequently diagnosed with Non St-Segment Elevation Myocardial Infarction (NSTEMI (43%)) than unstable angina (UA (29%)) or St-Segment Elevation Myocardial Infarction (STEMI (29%)). Also showed in-hospital mortality was significantly worse for women and, by ACS type, was significantly greater in women for STEMI and NSTEMI. However, after age adjustment there was no difference in mortality between men and women in patients with NSTEMI. Another study from Saudi Arabia looked at Clinical characteristics, management and outcomes of patients with chronic heart failure, included chronic HF patients referred to four heart function clinics between September 2009 and December 2011, showed also that the percentage of women recruited was 30% [36].

Studies done in the Gulf region revealed similar results to international figures, in which it was found that women presentation in Ischemic heart disease trials is far less than their presentation in heart failure cardiovascular trials. In Gulf RACE-2 (Baseline characteristics, management practices, and long-term outcomes of Middle Eastern patients in the Second Gulf Registry of Acute Coronary Events) which is 9-month prospective, multicenter study conducted in 65 hospitals from 6 countries and included 30 day and 1-year mortality follow-up, only 21 % of the cohort were women [37]. On the other hand the presentation of women in Gulf CARE heart failure registry in the gulf area (Clinical characteristics, management, and outcomes of acute heart failure patients: observations from the Gulf acute heart failure registry)

was much higher than Gulf RCA-E 2, (37%) [38]. This finding was confirmed in a recent registry from MENA region (Middle East and North Africa) called Acute myocardial infarction and acute heart failure in the Middle East and North Africa: Study design and pilot phase study results from the (PEACE MENA registry) which showed again that women recruitment in MI part of the study was 18 % while it was 33% in the AHF part of the registry.

Another study from Egypt, Gender differences in Egyptian patients hospitalized with heart failure: Insights from the European Society of Cardiology Heart Failure Long-Term Registry, 1634 patients hospitalized with AHF were enrolled by 20 hospitals all over Egypt over three years [39]. Of these patients, 522 (32%) were female. Also showed there was no significant difference in in-hospital (5.7% vs. 4.6%, P=0.39) and 1 year mortality (27.9% vs. 25.9%, P=0.48). A similar percentage of women presentation (35%) was found in a fairly recent registry in Egypt, the Preliminary results of the acute Heart Failure registry in the DELTA region of Egypt (DELTA-HF) [40].

Diastolic Heart Failure (DHF) was more common in women compared to Systolic Heart Failure (SHF). This was shown in a study looked at The frequency of systolic versus diastolic heart failure in an Egyptian cohort (Egyptian chronic), revealed 54% of women had DHF, 24 % pf women had SHF [41].

In a recent review looked at Comparison between heart failure registries in Middle East Arab countries and data from the USA and Europe in patients with acute and chronic heart failure (Table 1) [42-44]. The purpose of this review is to summarize the current status regarding the epidemiology and management of heart failure in Middle East Arab countries. The percentage of women recruitment in this review ranges anywhere from 29.9%-35.9%

Table 1. HEARTS, heart failure assessment registry trials in different countries.

Registry	HEARTS (Acute) [34]	HEARTS (Chronic) [36]	Gulf CARE [38]	Egyptian (Acute) [40]	Egyptian (Chronic) [39]	ADHERE [43]	ESC HF Long-Term Registry [44]
Region	Saudi Arabia	Saudi Arabia	7 GULF countries	Egypt	Egypt	USA	Europe
Number of patients	2610	685	5005	1475	670	105388	5039
Age, Mean (years)	61.4	55.66	59	61	57	75	71
Female, %	34.2	29.9	37	30.4	35.8	51	37.3
DM, %	64	52.7	50	45.4	31.8	44	38.9
HTN, %	71	66	61	43.5	40.8	73	62
COPD, %	19	19.5	N/A	14.8	13.3	31	15.2
AF, %	15.7	11.8	12	24.3	24.8	31	43.7
CKD/dialysis, %	29.6	22	15	17.6	13.4	29/5	-
Median EF	N/A	N/A	35	36	40	34	38
HFpEF, %	27.1 (LVEF 0.40, %)	13.3 (LVEF 0.40, %)	31 (LVEF, >40%)	22.0 (LVEF >45%)	25.6 (LVEF >45%)	46 (LVEF 0.40, %)	32.8 (LVEF >45%)
Ischemic aetiology, %	55.7	38.8	53	68.1	41	65	54
Beta-blocker, at admission, %	79	91.6	44	65.8	67	59	71.8
ACE inhibitor/ARB, admission, %	68.3	81.6	56	85.8	89.8	69	77
Aldosterone antagonists, admission, %	29	43.6	17	68.2	86.4	NA	55.3

Abbreviations: Acute Decompensated Heart Failure National Registry (ADHERE); European Society of Cardiology (ESC); Heart Failure (HF); Diabetes Mellitus (DM); Hypertension (HTN); Chronic Obstructive Pulmonary Disease (COPD); Atrial Fibrillation (AF); Chronic Kidney Disease (CKD); Heart Failure with Preserved Ejection Fraction (HFpEF); Angiotensin Converting Enzyme (ACE); Angiotensin Receptors Blocker (ARB); Not Available (NA).

which is lower than western registries like ADHERE and ESC HF long term registry in which the percentage was from 37.7%-50%.

The reasons for this discrepancy should be studied more thoroughly in the Arab Middle east countries. Some of these causes are Lack of patient awareness of available CV studies among women. Also women in child bearing age may not able to participate in randomized controlled trials for treatment and intervention. Other social factors like caregiving responsibilities, lack of transportation, and long work hours. Other factors related to clinical care, governmental, funding and research investigational causes may play a role in this underrepresentation of women in cardiovascular clinical trials and need to be looked at more carefully to address the gap in women recruitment in such trials.

Discussion and Conclusion

The reasons for this discrepancy should be studied more thoroughly in the Arab Middle east countries. Some of these causes are Lack of patient awareness of available CV studies among women. Also women in child bearing age may not able to participate in randomized controlled trials for treatment and intervention. Other social factors like caregiving responsibilities, lack of transportation, and long work hours. Other factors related to clinical care, governmental, funding and research investigational causes may play a role in this underrepresentation of women in cardiovascular clinical trials and need to be looked at more carefully to address the gap in women recruitment in such trials. Women in Arab world of ME are at high risk of mortality related to CVD. They have low awareness of this risk. In spite of this, Arab women recruitment in the CVS clinical trials and registries is low. The reasons for this are multifactorial and need to be addressed at many levels to improve the outcomes of CVD in Arab women.

Conflict of Interest

The author has no conflicts of interest to declare.

Acknowledgement

This project is supported by college of medicine research center, deanship of scientific research, King Saud University. King Saud university medical city.

Funding

None

References

- Jin, Xurui, Chanchal Chandramouli, Allocco Brooke and Gong Enying, et al. "Women's Participation in Cardiovascular Clinical Trials from 2010 to 2017." *Circulation* 141(2020): 540-548.
- Scott, Pamela E, Ellis F Unger, Marjorie R Jenkins and Mary Ross Southworth, et al. "Participation of Women in Clinical Trials Supporting FDA Approval of Cardiovascular Drugs." *J Am Coll Cardiol* 71(2018): 1960-1969.
- Tahhan, Ayman Samman, Muthiah Vaduganathan, Stephen J Greene and Gregg C Fonarow, et al. "Enrollment of Older Patients, Women, and Racial and Ethnic Minorities in Contemporary Heart Failure Clinical Trials: A Systematic Review." *JAMA Cardiol* 3(2018): 1011-1019.
- AlHabib, Khalid F, Abdelfatah A Elasar, Hussam Alfaleh, and Tarek Kashour, et al. "Clinical Features, Management, and Short- and Long-Term Outcomes of Patients with Acute Decompensated Heart Failure: Phase I Results of The Hearts Database." *Eur J Heart Fail* 16(2014): 461-469.
- Alhabib, Khalid F, Habib Gamra, Wael Almahmeed, and Ayman Hammoudeh, et al. "Acute Myocardial Infarction and Acute Heart Failure in the Middle East and North Africa: Study Design and Pilot Phase Study Results from the PEACE MENA Registry." *PLoS One* 15(2020): e0236292.
- Meek, Caroline. "Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs." *Fed Regist* 58(1993): 39406-39416.
- Shara, Nawar M. "Cardiovascular Disease in Middle Eastern Women." *Nutr Metab Cardiovasc Dis* 20(2010): 412-418.
- Ramahi, Tarik M. "Cardiovascular Disease in the Asia Middle East Region: Global Trends and Local Implications." *Asia Pac J Public Health* 22(2010): 83s-89s.
- Kamrava, Mehran. "The Modern Middle East." (1st edn). California: University of California Press, USA.(2005).
- Mendirichaga, Rodrigo and Alice K Jacobs. "Sex Differences in Ischemic Heart Disease-the Paradox Persists." *JAMA Cardiol* 5(2020): 754-756.
- Hayes, Sharonne N. "Preventing Cardiovascular Disease in Women." *Am Fam Physician* 74(2006): 1331-1340.
- Connelly, Paul J, Zahra Azizi, Pouria Alipour, and Christian Delles, et al. "The Importance of Gender to Understand Sex Differences in Cardiovascular Disease." *Can J Cardiol* 37(2021): 699-710.
- Steinberg, Jecca R, Brandon E Turner, Brannon T Weeks, and Christopher J Magnani, et al. "Analysis of Female Enrollment and Participant Sex by Burden of Disease in US Clinical Trials Between 2000 and 2020." *JAMA Netw Open* 4(2021): e2113749.
- Calabrò, Paolo, Giampaolo Niccoli, Felice Gragnano and Erik Lerkevang Grove, et al. "Are We Ready for A Gender-Specific Approach in Interventional Cardiology?" *Int J Cardiol* 286(2019): 226-233.
- Shen, Xian, Stefan DiMario and Kiran Philip. "Gender Disparities in Health Resource Utilization in Patients with Atherosclerotic Cardiovascular Disease: A Retrospective Cross-Sectional Study." *Adv Ther* 36(2019): 3424-3434.
- Murray, Christopher JL and Alan D Lopez. "Mortality by Cause for Eight Regions of the World: Global Burden of Disease Study." *Lancet* 349(1997): 1269-1276.
- Ganguly, Shyam S, Mohammed A Al-Shafae, JA Al-Lawati, and Dutta PK, et al. "Epidemiological Transition of Some Diseases in Oman: A Situational Analysis." *East Mediterr Health J* 15(2009): 209-218.
- Sibai, A Mehio, Fletcher A, Hills M and Campbell O. "Non-Communicable Disease Mortality Rates Using the Verbal Autopsy in A Cohort Of Middle Aged and Older Populations In Beirut During Wartime, 1983-93." *J Epidemiol Community Health* 55(2001): 271-276.
- Wasim, Maziak, Samer Rastam, Fawaz Mzayek and Kenneth D Ward, et al. "Cardiovascular Health Among Adults in Syria: A Model from Developing Countries." *Ann Epidemiol* 17(2007):713-20.
- Zubaid, Mohammad, Wafa A Rashed, Wael Almahmeed and Jawad Al-Lawati, et al. "Management and Outcomes of Middle Eastern Patients Admitted with Acute Coronary Syndromes in the Gulf Registry of Acute Coronary Events (Gulf RACE)." *Acta Cardiol* 64(2009): 439-446.
- Gehani, Abdurrazzak A, Ali T Al-Hinai, Mohammad Zubaid and Wael Almahmeed, et al. "Association of Risk Factors with Acute Myocardial Infarction in Middle Eastern Countries: The INTERHEART Middle East Study." *Eur J Prev Cardiol* 21(2014): 400-410.
- Alhabib, Khalid F, Mohammed A Batais, Turky H Almigbal and Mostafa Q Alshamiri, et al. "Demographic, Behavioral, and Cardiovascular Disease Risk Factors in The Saudi Population: Results from The Prospective Urban Rural Epidemiology Study (PURE-Saudi)." *BMC Public Health* 20(2020):1213.
- Walli-Attai, Marjan, Annika Rosengren, Sumathy Rangarajan and Yolandi Breet, et al. "Metabolic, Behavioural, and Psychosocial Risk Factors and Cardiovascular Disease in Women Compared with Men in 21 High-Income, Middle-Income, and Low-Income Countries: An Analysis of the PURE Study." *The Lancet* 400(2022): 811-821.

24. Yusuf, Salim, Steven Hawken, Stephanie Ounpuu and Tony Dans, et al. "Effect of Potentially Modifiable Risk Factors Associated With Myocardial Infarction In 52 Countries (The INTERHEART Study): Case-Control Study." *Lancet* 364(2004): 937-952.
25. Garcia, Mariana, Sharon L Mulvagh, C Noel Bairey Merz and Julie E Buring, et al. "Cardiovascular Disease in Women: Clinical Perspectives." *Circ Res* 118(2016): 1273-1293.
26. Benjamin, Emelia J, Paul Muntner, Alvaro Alonso and Marcio S Bittencourt, et al. "Heart Disease and Stroke Statistics-2019 Update: A Report from the American Heart Association." *Circulation* 139(2019): e56-e528.
27. Mosca, Lori, Gmerice Hammond, Heidi Mochari-Greenberger and Amytis Towfighi, et al. "Fifteen-Year Trends in Awareness of Heart Disease in Women: Results of a 2012 American Heart Association National Survey." *Circulation* 127(2013): 1254-1263.
28. Roth, Gregory A, George A Mensah, Catherine O Johnson and Giovanni Addolorato, et al. "Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study." *J Am Coll Cardiol* 76(2020): 2982-3021.
29. Sharie, Sarah Al, Mohammad Araydah, Sayer Al-Azzam and Reema Karasneh, et al. "The Participation of Arab Women in Randomised Clinical Trials for Cardiovascular Diseases." *Int J Clin Pract* 75(2021): 14612-1413.
30. Agarwal, Ajit, Venugopalan P and de Bono D. "Prevalence and Aetiology of Heart Failure in an Arab Population." *Eur J Heart Fail* 3(2001): 301-305.
31. Beale, Anna L, Philippe Meyer, Thomas H Marwick and Carolyn S P Lam, et al. "Sex Differences in Cardiovascular Pathophysiology: Why Women Are Overrepresented in Heart Failure With Preserved Ejection Fraction." *Circulation* 138(2018): 198-205.
32. Raparelli, Valeria, Muhammad Ahmer Wali and Louise Pilote. "Personalized Medicine: Women in Heart Failure Clinical Trials, a Must." *JACC Heart Fail* 7(2019): 732-3.
33. Sciomer, Susanna, Federica Moscucci, Elisabetta Salvioni and Giovanni Marchese, et al. "Role of Gender, Age and BMI in Prognosis of Heart Failure." *Eur J Prev Cardiol* 27(2020): 46-51.
34. AlFaleh, Hussam F, Lukman Thalib, Tarek Kashour and Ahmad Hersi, et al. "Sex Differences in Patients With Acute Decompensated Heart Failure: Insights From the Heart Function Assessment Registry Trial in Saudi Arabia." *Angiology* 67(2016): 647-56.
35. Hersi, Ahmad, Khalid Al-Habib, Husam Al-Faleh and Khalid Al-Nemer, et al. "Gender Inequality in the Clinical Outcomes of Equally Treated Acute Coronary Syndrome Patients in Saudi Arabia." *Ann Saudi Med* 33(2013): 339-346.
36. Alhabeeba, Waleed, AbdelfatahElasfar, HananAlBackr and FayezeAlShaer, et al. "Clinical Characteristics, Management and Outcomes of Patients with Chronic Heart Failure: Results from the Heart Function Assessment Registry Trial in Saudi Arabia (HEARTS-Chronic)." *Int J Cardiol* 235(2017): 94-99.
37. AlHabib, Khalid F, Kadhim Sulaiman, Ahmed Al-Motarreb and Wael Almahmeed, et al. "Baseline Characteristics, Management Practices, and Long-Term Outcomes of Middle Eastern Patients in the Second Gulf Registry of Acute Coronary Events (Gulf RACE-2)." *Ann Saudi Med* 32(2012): 9-18.
38. Sulaiman, Kadhim, Prashanth Panduranga, Ibrahim Al-Zakwani and Alawi A Alsheikh-Ali, et al. "Clinical Characteristics, Management, and Outcomes of Acute Heart Failure Patients: Observations from the Gulf Acute Heart Failure Registry (Gulf CARE)." *Eur J Heart Fail* 17(2015): 374-384.
39. Hassanein, Mahmoud, Magdy Abdelhamid, Bassem Ibrahim and Mohamed Sobhy, et al. "Gender Differences in Egyptian Patients Hospitalized With Heart Failure: Insights from the European Society of Cardiology Heart Failure Long-Term Registry." *ESC Heart Fail* 5(2018):1159-1564.
40. Elasfar, Abdelfatah, Sherif Shaheen, Wafaa El-Sherbeny and Hatem Elsokkary, et al. "Preliminary Results of the Acute Heart Failure Registry in the DELTA Region of Egypt (DELTA-HF): A Database and a Quality Initiative Project." *Egypt Heart J* 71(2019): 27-28.
41. Ibrahim, Bassem S. "The Frequency of Systolic Versus Diastolic Heart Failure in an Egyptian Cohort." *Eur J Heart Fail* 5(2003): 41-45.
42. Elasfar, Abdelfatah A, Waleed Alhabeeb and Salma Elasfar. "Heart Failure in the Middle East Arab Countries: Current and Future Perspectives." *J Saudi Heart Assoc* 32(2020): 236-241.
43. Adams, Kirkwood F, Gregg C Fonarow, Charles L Emerman and Thierry H LeJemtel, et al. "Characteristics and Outcomes of Patients Hospitalized for Heart Failure in the United States: Rationale, Design, and Preliminary Observations from the First 100,000 Cases in the Acute Decompensated Heart Failure National Registry (Adhere)." *Am Heart J* 149(2005): 209-216.
44. Crespo-Leiro, Maria G, Stefan D Anker, Aldo P Maggioni and Andrew J Coats, et al. "European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT): 1-Year Follow-Up Outcomes and Differences across Regions." *Eur J Heart Fail* 18(2016): 613-625.

How to cite this article: Albackr, Hanan, Abdulaziz Backer Albacker and Deema H AlGhufaili. "Underrepresentation of Women in Cardiovascular Trials in Arab Middle East Region." *J Cardiovasc Dis Diagn* 10 (2022):001.