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Gender-Specific Prevalence of Ischemic Heart Disease among Emergency-Department Patients: Saudi Arabia

معدل انتشار داء القلب الإقفاري حسب الجنس بين مرضى قسم الطوارئ: السعودية

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ABSTRACT

Few epidemiological studies have discussed the gender-specific prevalence of ischemic heart disease (IHD). We aimed to investigate the gender-specific prevalence of IHD among Saudi patients visiting the emergency department and if it is affected by diabetes mellitus and/or hypertension. Three hundred patients were recruited from Prince Sultan Cardiac Center in Al Ahsa, KSA. Hypertension was identified as systolic pressure equal to or more than 140 mmHg and/or diastolic pressure equal to or more than 90 mmHg or by the patient currently being on antihypertensive medication, and coronary artery disease (CAD) was diagnosed by electrocardiogram, cardiac markers, cardiac exercise testing or coronary angiography. Hypertension was found in 80% of males and 72% of females. A significantly higher rate of diabetes was noted in females (62%) compared to males (48%) (p<0.012). Co-existing diabetes and hypertension was found in 70% of females as compared to 38% of males. The occurrence of IHD in males was significantly higher than that in females (p<0.001). However, the incidence of myocardial infarction was greater in females (52%) compared to males (38%) (p<0.035). Co-existing hypertension and diabetes may affect the gender prevalence of myocardial infarction among emergency department patients, with more infarctions being noted among females. This finding helps to guide the treatment strategy for both genders.

الملخص

ناقش عدد قليل من الدراسات الوبائية انتشار داء القلب الإقفاري حسب الجنس؛ لذلك فإنَّ كان هدفنا التحقق من معدل انتشار داء القلب الإقفاري حسب الجنس بين المرضى السعوديين الذين يتردّدون على قسم الطوارئ، ومعرفة ما إذا كان هذا المعدل يتأثر بالإصابة بداء السكري و / أو ارتفاع ضغط الدم. أُجْرِيَت الدراسة على 300 مريض من المرضى السعوديين المترددين على قسم الطوارئ بمركز الأمير سلطان للقلب بالأحساء بالمملكة العربية السعودية. وقد حُدِّد ارتفاع ضغط الدم بأنه ضغط انقباضي يساوي 140 مم زئبق أو أكثر، و / أو ضغط انبساطي يساوي 90 مم زئبق أو أكثر أو أن المريض حاليًا يتعاطى الأدوية الخافضة للضغط، وبعد تشخيص داء القلب الإقفاري عن طريق مخطط كهربية القلب أو علامات القلب أو اختبار تمارين القلب أو تصوير الأوعية التاجية، تبين أن 80٪ من الذكور و72٪ من الإناث مصابون بارتفاع ضغط الدم، ولوحظ وجود داء السكري بشكل ملحوظ أعلى عند الإناث (62٪) مقارنة بالذكور (48٪)، وأن 70 ٪ من الإناث مصابات بداء السكري وارتفاع ضغط الدم مقارنة بالذكور (38٪). وقد لوحظ أن معدل حدوث داء القلب الإقفاري في الذكور أعلى بكثير مقارنة بالإناث. ومع ذلك، كان معدل حدوث احتشاء عضلة القلب أكبر عند الإناث (52٪) مقارنة بالذكور (38٪)؛ لذا قد يؤثر ارتفاع ضغط الدم والسكري المترافقين على انتشار احتشاء عضلة القلب بين الجنسين لدى مرضى قسم الطوارئ مع ملاحظة المزيد من حالات الاحتشاء بين الإناث. ومن الممكن أن تساعد هذه النتائج في توجيه استراتيجية العلاج في كلا الجنسين.

KEYWORDS
الكلمات المفتاحية
Al Ahsa, cardiovascular risk, coronary artery disease, ischemic heart disease, systemic hypertension, type 2 diabetes mellitus
الأحساء، ارتفاع ضغط الدم، أمراض الشرايين التاجية، أمراض القلب والأوعية الدموية، داء السكري من النوع الثاني، داء القلب الإقفاري

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1. Introduction

The leading cause of death worldwide is still cardiovascular disease (Lopez, 1993). Two major risk factors for cardiovascular disease, including ischemic heart disease, cerebrovascular disease and peripheral vascular disease, are hypertension (HTN) and diabetes mellitus (DM) (Petrie et al., 2018). Mortality and morbidity of patients with diabetes originate from associated vascular complications (Kannel and McGee, 1979), hence the consideration of diabetes as a vascular disease. Hypertension is also considered an important cardiovascular risk factor. Hypertension has been shown to be the world's most significant risk for coronary artery disease (CAD), which is present in 80.3% of patients (Bhatt et al., 2006). According to the American Heart Association, 40% of deaths due to heart disease are associated with high arterial blood pressure (De Ferranti et al., 2014). The number of cases of hypertension, stroke and CAD are estimated to have doubled by the year 2050 (Fox et al., 2015).

Evidence from epidemiological studies suggest a close correlation between CAD and hypertension. Most trials to detect the effect of hypertension control on the risk of CAD reported a modest short-term decrease in blood pressure, which provides a 16% reduction in CAD events. These trials were largely performed in men with uncomplicated, mild to moderate hypertension. However, it is unlikely that ischemic heart disease would be preventable in most hypertensive patients by treating high blood pressure alone (McInnes, 1995).

Published results from a national study on CAD in Saudis Study (CADISS) in 2004 and 2007 revealed that the prevalence of CAD and hypertension in the general population of Saudi Arabia was around 5.5% and 26.1 %, respectively (Al-Nozha et al., 2004).

Type 2 diabetes and hypertension are each clearly associated with cardiovascular disease, including coronary artery disease. In many instances systemic hypertension and diabetes co-exist from the start or develop sequentially in the same patient. This co-existence arises from the fact that they have common pathogenic mechanisms, including obesity, stress and insulin resistance (Wilson et al., 2005). The frequency of hypertension in patients with diabetes is double that of those without diabetes (Petrie et al., 2018). Moreover, the risk

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of diabetes rises in those with hypertension as compared to the general population (Kim et al., 2015).

In patients with both DM and HTN, the chance of suffering from cardiovascular disease (CVD) is four times greater than in normotensive, non-diabetic control subjects (Stamler et al., 1993; Hu et al., 2007).

The Framingham cohort research revealed that hypertensive patients at the time of diagnosis with diabetes, in addition to cardiovascular incidents, had a greater risk of all-cause mortality than diabetic subjects without hypertension (Chen et al., 2011).

Despite the well-known effects of both type 2 diabetes and systemic hypertension on cardiovascular events, the interaction of these factors when they co-exist is not well characterised in studies. Furthermore, the effect of this co-existence of risk factors on the other characteristics of CVD risk specifications (e.g. gender-specific prevalence, severity or outcome) is not well studied. In this study we aimed to ascertain the consequences of co-existing hypertension and type 2 diabetes on ischemic heart disease in patients visiting the emergency room at the Prince Sultan Cardiac Center. We hypothesised that the presence of both hypertension and diabetes may affect the gender-specific prevalence of ischemic heart disease and, additionally, affect both the risk and outcome of coronary disease as compared to that expected with the presence of each condition alone.

2. Materials and Methods

2.1. Study Design:

This is an observational cross-sectional study based on a random collection of data from the electronic files of patients visiting the emergency department at the Prince Sultan Cardiac Center Hospital, Al-hasa, Kingdom of Saudi Arabia. A total of 300 Saudi adult patients (126 men and 174 women) were enrolled. Sample size was calculated using a target population of all hypertensive people in Hofuf and Almubaraz. According to figures from 2010, the total population of Hofuf and Almubaraz was estimated to be 660,800 (Salam, 2013) and, with a projected growth rate of 2.41%, the estimated population in 2018 was 788,202. Considering hypertension affects 15.2 % of the population (Al-Turki et al., 2008), the estimated hypertensive population in the cities of Hofuf and Al Mubarraz is 119,806. The sample size was 272, determined using Steven Thompson's formula for sample size (2012), with the margin of error (confidence interval) determined as 5.65%, the confidence level as 95% and the total population as 119,806.

This work was performed in compliance with the approval of the Committee for Ethics of the King Faisal University College of Medicine and the Helsinki Declaration and its amendments by the World Medical Association (WMA). After providing appropriate instructions on the study's goals and results, written forms of consent were collected from the patients. The study was carried out during the year 2018. Hypertension was prospectively identified when systolic blood pressure equalled or exceeded 140 mmHg and/or diastolic blood pressure equalled or exceeded 90 mmHg or when the patient was currently on antihypertensive medications. CAD was diagnosed by electrocardiogram, cardiac markers, cardiac exercise testing or a coronary angiography. Patients' data were collected from the electronic files.

HTN was diagnosed by a correct blood pressure (BP) measurement. The standard precautions before measurement of arterial blood pressure were followed. It is made after the measurement of BP on 3–5 different visits. Saudi guidelines for hypertension, published online in 2017, were used as a reference. They state that 80% of the arm should be encircled by the cuff bladder, and the cuff width should be 40% of the arm diameter. A sphygmomanometer was used in the initial diagnosis. Automated blood pressure machines were used only for follow-up visits. In the office or out-of-office (including home) setting, HTN can be diagnosed. None of the included patients were diagnosed using the ambulatory method.

Diabetes mellitus was diagnosed according to the American Diabetes Association guidelines included in 'Standards of medical care in diabetes 2018', which consider the patient diabetic when the level of fasting blood glucose (FPG) is equal to or more than 126 mg/dL (7.0 mmol/L), the 2-hour plasma glucose (PG) is equal to or more than 200 mg/dL (11.1 mmol/L) during the oral glucose tolerance test (OGTT) or if the glycated haemoglobin (HbA1C) is equal to or more than 6.5% (48 mmol/mol). The findings can be verified by repeated testing if unequivocal hyperglycaemia is absent (American Diabetes Association, 2018).

Data for the presence of ischemic heart disease were collected from the electronic files based on one or more of the ischemic findings in resting 12-lead electrocardiogram, blood cardiac markers, cardiac stress testing and invasive coronary angiography. Ischemia was diagnosed using the guide of abnormalities of the ST-segment (Code4) and T-wave (Code5) of the Minnesota Code (Sawai et al., 2017). Other ECG abnormalities (e.g. arrhythmia, left ventricular hypertrophy and left bundle branch block) were taken into consideration. Troponins of the heart, namely troponin I (TnI) and troponin T (TnT), and creatinine kinase MB were used to help diagnose myocardial injury and ischemia, according to the 2014 guidelines of the American Heart Association, depending mainly on cardiac troponin T. The cut-off values were at the 99th percentile reference limit (Amsterdam et al., 2014).

2.2. Inclusion Criteria:

Saudi adult male and female patients of 18 years of age or above with different presentations at the emergency room of the cardiac centre.

2.3. Exclusion Criteria:

Patients with secondary diabetes or secondary hypertension, or those who were taking medications that affect diabetes or hypertension control (e.g. steroids and immunosuppressive drugs) were excluded from the study, as these factors may confound the results. Patients with autoimmune and rheumatologic conditions as well as patients with end-stage renal or liver disease were excluded. Additionally, the study excluded pregnant patients and those with rheumatic or valvular heart diseases.

2.4. Data Collection:

The records of all patients enrolled in the study that included demographic data such as age, sex and educational/occupational status were revised. Details of hypertension history, duration and medication were obtained. The history of diabetes, including its duration, type, medications, complications and glycaemic control parameters, was assessed. CAD characteristics were evaluated, including age at CAD diagnosis, current protocols for management, complications, admission frequency and details of previous strokes or myocardial infarctions. Laboratory data on cardiac markers, lipid profile and diagnostic ECG, cardiac exercise testing and a coronary angiography were also evaluated. Detection of the primary end point was the cause of admission of select patients.

2.5. Management of Data and Analysis of Statistics:

Data have been analysed using version 20.0 of SPSS (SPSS Inc. Chicago, IL). Numerical data were tested for distribution normality.

Proportions, ratio and frequency of expression were used for categorical data, and Chi square and t-test were used for comparison. Using mean and standard deviation, continuous data was conveyed. Differences of p<0.05 were considered significant.

3. Results

Out of the 300 participants in our study, 126 were male (42%) and 174 (58%) were female. The age differences between male (61.8±13.9 years) and female (57.6±19.4 years) subjects were not statistically significant. Among the 126 male subjects, 101 (80%) had hypertension and 60 (48 %) had diabetes, and 64 (51%) displayed evidence of the presence of ischemic heart disease. In the female subjects, 126 (72%) had hypertension and 108 (62 %) had diabetes, and 42 (24 %) showed symptoms of ischemic heart disease. A higher proportion of male subjects, 96 (76%), were hospitalised as compared to 78 female subjects (45%) (Table 1).

Table 1: Clinical characteristics of the studied population

	Number	Age	HTN	DM	IHD
Male	126	61.8±13.9	101 (126) (80%)	60 (126) (48%)	64 (126) (51%)*
Female	174	57.6±19.4	126 (174) (72%)	108 (174) (62%)*	42 (174) (24%)
Male (H)	96 (126) (76%)*	64.4±14.7	71 (96) (74%)	54 (96) (57%)	64 (96) (67%)*
Female (H)	78 (174) (45%)	65.8±15.4	72 (78) (92%)*	59 (78) (75%)*	41 (78) (52%)
Male (NH)	30 (126) (24%)	59.8±10.4	30 (30) (100%)*	6 (30) (20%)	0 (30)
Female (NH)	96 (174) (55%)	62.3±7.4	54 (96) (56%)	48 (96) (50%)*	0 (96)

Note. HTN [hypertension], DM [diabetes mellitus] and IHD [ischemic heart disease]. H [admitted to hospital] and NH [not admitted to hospital].

No statistically significant difference was found between male and female groups in regard to clinically established hypertension (p=0.08). However, significant difference was found between the prevalence of diabetes in male and female groups, with more instances of diabetes mellitus being found in females (p<0.012). The occurrence of ischemic heart disease was significantly greater in males than in females (p<0.001).

A significantly higher prevalence of admission was noted in males (75%) as compared to females (44%) (p<0.001). Furthermore, females had a lower incidence of ischemic heart disease but a higher prevalence of myocardial infraction (52%) in comparison to the male subjects (38%); this difference is statistically significant (p<0.035). Stroke (12.6%) was reported in male subjects only (Table 2).

Table 2: Clinical data of male and female subjects admitted to hospital

	N	Age	HTN	DM	IHD	MI	Stroke
Male (H)	96 (126) (75%)	62.4±14.7	71 (96) (74%)	54 (96) (57%)	64 (95) (67%)	36 (96) (38%)	12 (96) (12.6%)
Female (H)	78 (174) (44%)	65.8±15.4	72 (78) (92%)	59 (78) (75%)	41 (78) (52%)	41 (78) (52%)	0 (78)
P- value	0.001	0.178	0.003	0.004	0.001	0.031	0.001

Note. HTN [hypertension], DM [diabetes mellitus], IHD [ischemic heart disease] and MI [myocardial infraction]. H [admitted to hospital]. N [number], significant at P-value <0.05.

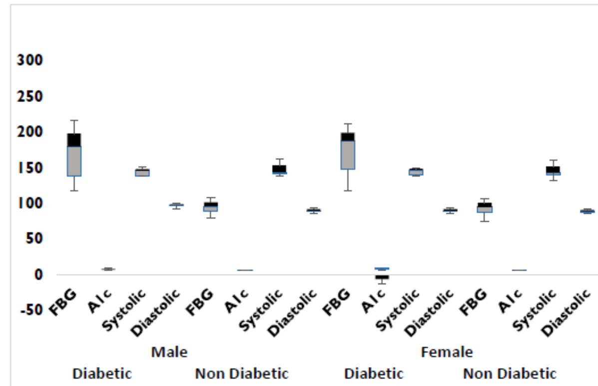
The prevalence of myocardial infractions was higher in females with diabetes (71%) than in males with diabetes (22%), and there was a statistically significant difference (p<0.0001). This observation suggests that, for females, diabetes may be an important factor contributing to the occurrence of myocardial infraction (Table 3). A higher percentage of female subjects (70%) had both DM and HTN as compared to male subjects (38%), as shown in Table 4.

Table 3: The clinical data of male and female subjects with diabetes mellitus who were admitted and not admitted to hospital

	N	Age	DM	HTN	IHD	MI
Male (H) (with DM)	54 (96) (56%)	69.2±12.3	54 (54) 100%	36 (54) 66%	35 (54) 65%	12 (54) 22%
Female (H) (with DM)	60 (78) (76%)	62.8±13.8	60 (60) (100%)	54 (60) (90%)	41 (60) (69%)	42 (60) (71%)
P-value	0.78	0.178	0.78	0.002	0.83	0.0001
Male (NH) (with DM)	6 (30) (20%)	59.8±10.4	6 (6) (100%)	6 (6) (100%)	0 (6)	0 (6)
Female (NH) (with DM)	48 (96) (50%)	62.3±7.4	48 (48) (100%)	42 (48) (88%)	0 (48)	0 (48)
P-value	0.3	0.7	0.78	0.358	0.7	0.8

Furthermore, patient data on fasting blood glucose and Hb1AC were analysed to investigate whether hypertension is modified in the presence of diabetes. It appears that the presence of diabetes has no significant effect on the presentation of hypertension in male or female subjects (p= 0.54), as shown in Figure 1.

Figure 1. Presentation of blood pressure levels, fasting blood sugar (FBS) and glycated haemoglobin (HbA1c) in male and female diabetic and non-diabetic subjects. In diabetic and non-diabetic subjects, systolic and diastolic pressures in men and women are not significantly different. (p<0.45 and p<0.58)



4. Discussion

The current cross-sectional observational study performed on a random sample of emergency-room visitors at Prince Sultan Cardiac Center attempted to evaluate the prevalence of hypertension, type 2 DM and their co-existence, as well as their effects on the gender-specific prevalence of ischemic events among the studied group. The study revealed that the presence of co-existing diabetes mellitus and hypertension in females favours the prevalence of myocardial infarction (MI); however, the total number of ischemic events remained significantly higher in males.

No statistically significant difference was found in age and body mass index between the male and female groups; hence, these will not confound the results. The prevalence of HTN and DM in both males and females is high among visitors to the emergency room in comparison to average population. The statistically significant difference appeared only with the prevalence of diabetes, which was higher in the female group.

Hypertension and diabetes mellitus are common co-existing disorders, and hypertension is twice as common in diabetic patients as in non-diabetics. Patients with hypertension also display insulin resistance and are at greater risk of diabetes than people with normal blood pressure. Both diabetes and hypertension are important risk factors for the morbidity and mortality of cardiovascular disease. For diabetics, the risk of CVD is increased by two to three times.

Hypertension and diabetes are both independent risk factors for heart disease. Masoudkabir et al. (2015) studied 10,502 consecutive patients who underwent coronary angiography, regarding cardiovascular risk factors and their synergistic effects on the severity of CAD, and found that hypertension has a synergistic impact on DM and the severity of CAD in males. Interestingly, they did not find an interaction between hypertension and smoking, dyslipidaemia or a family history of CAD.

Multiple studies have checked the effects of clustering cardiovascular risk factors on CVD incidence and outcome. The results of the Multiple Risk Factors Interventional Trial demonstrated the additional impact of diabetes along with other risk factors for cardiovascular disease in a cohort of 5,163 men taking diabetes medications and 342,815 who were not taking any drugs for diabetes. They found that the absolute risk of death due to CVD increased steeply in diabetic men compared to non-diabetic men. The absolute risk was thus increasingly higher in diabetic men, rather than in non-diabetic (Masoudkabir et al., 2015).

In this study, we did not consider cardiovascular death as an endpoint. Our endpoint was the prevalence of ischemic events. The measurable tool for this evaluation was the percentage of admissions and the diagnoses of ischemic events.

In the current study, in spite of having a significantly lower percentage of admission and total prevalence of ischemic events, females display a significantly higher prevalence of diabetes and a statistically significant percentage of diagnoses of myocardial infarction. Studies have shown that diabetes mellitus substantially reduces the well-known protective impact of being female on cardiovascular risk and can even reverse it (Booth et al., 2006; Kappert et al., 2012; Anand et al., 2008).

Data from meta-analyses that examine the relative risk of catastrophic diabetes-related coronary heart disease in both women and men indicate an elevated risk in women (Huxley et al., 2011).

The common view that the female 'advantage' in CAD incidence is caused only by the difference in sex hormones, the availability of oestrogen in particular, is not valid. Several other factors may play a role, including sexual dimorphism and sexual inequality in the management and treatment of cardiovascular risk factors, as well as genetic factors and sex chromosome genes in people with diabetes. The explanation of this effect on the gender-specific prevalence or outcome of CVD is not well explained. It has been postulated that among diabetic women there may be an increased constellation of multiple other cardiovascular risk factors or a decrease in risk-factor control (Madonna et al., 2019).

The results of this study could be further explained by the known lack of exercise and outdoor activities among Saudi females as compared to males (Al-Hazzaa, 2018), which may explain the increased prevalence of diabetes and/or MI. Another factor is that, in this study, the subject ages were 57.6±19.4 years and, during this time, the suggested protective effect of gender hormones may be lost or attenuated. These findings may raise suspicions regarding the precision of gender difference in cardiovascular disease in older age groups.

The risk prediction models (RPMs) currently available for CVDs, diabetes mellitus and hypertension were compared in a systematic analysis regarding their efficacy in properly identifying patients at risk of developing these diseases. This revealed that clear evidence is present only for the prediction of CVD; the Framingham score, by itself or in association with the Ankle-Brachial Index, and QRISK score can be considered as the gold standard. Further efforts must not be focused on the production of new scores but should, instead, focus on the external validation of existing scores, particularly in groups at high risk (Lucaroni et al., 2019). Results of this study and similar studies should add to the validation and/or modification of the RPMs that are currently available. The strength of this study comes from the fact that, to our knowledge, it is the first study to address gender-specific differences in CVD among the Saudi population. The limitation of this study is that it does not take into account some female-only factors that may confound the prevalence of CVD (e.g. exercise profile or intake of oral contraceptives). Additionally, we did not consider albuminuria, as it was not available for all patients. The sample size should be higher to increase the level of confidence. We recommend strict management of both diabetes and hypertension among females and further screening in symptomatic patients to detect early diabetes and early hypertension. Furthermore, the importance of lifestyle modification among Saudi women should be intensified. Additional studies are required to evaluate gender-specific CVD risk and outcome with different risk factor clustering. Furthermore, additional studies to determine the relative effects of control of these conditions on improving CVD outcome would be beneficial.

The limitations of this study are the relatively small sample size and single-centre experience, so further large-scale, and multi-centre studies are highly recommended.

5. Conclusion

Co-existing diabetes and hypertension may have synergistic effects on ischemic heart disease events and the rate of admission for emergency-room patients. The presence of type 2 DM in women may modify or even reverse the gender-specific prevalence of myocardial infarction, but it has no effect on the total number of ischemic events. In this group, this could be explained by the association of DM with multiple CVD risk factors and the targeted management of these risks. Strict diabetes control, diabetes mellitus screening and implementation of a cardiovascular risk management plan should be intensified among Saudi women as well as men. The validation and/or modification of currently available cardiovascular disease RPMs is justifiable.

Biography

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