

letters

Risk factors, clinical features and outcome of acute myocardial infarction in Sana'a, Yemen

To the Editor: According to the World Health Organization, developing countries contributed to 85% of cardiovascular disease (CVD) deaths.¹⁻³ A particular cause for concern is the relatively early age of CVD deaths compared with those in developed regions. Since there are few data on the incidence and clinical course of acute myocardial infarction (AMI) in the Middle East,⁴⁻¹² we retrospectively studied the demographic and clinical characteristics of patients, the prevalence of major risk factors and factors associated with morbidity and mortality during hospitalization in the intensive care unit (ICU) of the Al-Thawra University Hospital in Sana'a. All patients with confirmed AMI who were admitted and treated at the intensive care unit (ICU) during 36 consecutive months were enrolled in the study. The diagnosis of AMI was based on a history of typical chest pain or its equivalent, ECG changes plus an increase in peak serum creatine kinase (CK) activity from a minimum to twice the normal level. During the 3-year study period 386 patients with AMI were admitted to the ICU. Of all patients, 348 (90.2%) were men with a mean (\pm SD) age 54 ± 11 years (range, 27-82 years) and 38 (9.8%) were women with a mean age of 59 ± 11 years (range, 38-80 years). Almost all patients (97.9%) were Yemeni. The prevalence of risk factors was as follows: khat chewing (88%), smoking (81%), total serum cholesterol (29%), diabetes mellitus (25%) and hypertension (18%). When classified according to site, recurrence and severity of AMI, in 57.0% there was an anterior infarction, in 35.2% an inferior infarction,

in 7.0% an inferoseptal infarction, in 1.8% a lateral infarction and location was undetermined in 2.5%. Only 34 (8.8%) patients had a previous history of AMI; in 352 (91.2%) patients, it was the first AMI. In 341 (88.3%) it was a Q-wave infarction while a non Q-wave infarction was found in 35 (9.1%) and in 10 (2.6%) it was undetermined. The complications of AMI were heart failure in 94 cases (24.6%), primary ventricular fibrillation or tachycardia in 18 cases (4.7%), and second or third degree atrioventricular block in 17 (4.4%). The ICU mortality rate was 11.4% (44 patients) and the total in-hospital mortality was 14.2% (55 patients). Causes of death during hospitalization were cardiogenic shock (62%), sudden death (18%), resistant arrhythmia (13%), brain embolization (5%), and hypoxic brain damage after CPR (2%).

Compared with studies from the Arabian Gulf, the incidence of admission for AMI was similar, but differed from that in Western countries.¹⁻³ We found that the mean age of patients was approximately 5 to 10 years younger than in Europe and the USA, which could be due to ethnicity or genetic predisposition, but also to changes in lifestyle (especially in the last 40 years), which have become more stressful and sedentary,^{1,10} with excessive smoking and eating of very high-calorie and fatty food. In patients with AMI, there was a very high rate of smoking (81%), but diabetes mellitus (25%), hypertension (18%) and hyperlipoproteinemia (29%) were similar in incidence to that in Middle East and Western countries. The rate of smoking was similar to that in other developing countries and Europe (range of 49-81%),⁴⁻¹⁴ and includes the chewing of khat (*Catha edulis* Forsk), especially in men. The leaves of this plant contain cathine and cathinone, an amphetamine-like

substance with a strong sympathomimetic effect, which increases heart rate and blood pressure.^{15,16} This factor could be critical in some patients, especially in patients with CVD, as was found with other amphetamines.¹⁷ Inadequacies in the evaluation of CVD before the occurrence of AMI and preventive care in Yemen due to the lack of diagnostic or therapeutic facilities may also be a factor in the incidence of AMI admissions. Another significant influence in this area has been the lack of practical health education in Yemen. Many elderly patients do not seek medical care or wait for a long time and die before reaching a hospital. More frequent and atypical clinical signs and symptoms in inferior AMI could explain the high frequency of anterior AMI. The only explanation for the very low rate of non-Q wave AMI is less marked ECG changes and symptoms.

Our study was limited in being a retrospective analysis carried out in only one hospital in Sana'a. We hope our finding will serve as a baseline for other epidemiological studies in the field of coronary heart disease and studies related to the prevalence of cardiovascular risk factors, including khat. This should provide an impulse for initiating the primary prevention of cardiovascular diseases, especially coronary heart disease.

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Remission in Cushing disease with cabergoline

To The Editor: Transsphenoidal surgery (TSS) is the first-line treatment of Cushing disease (CD) with remission rates between 60% and 80% (<15% for macroadenomas) with a relapse rate of up to 20%.¹ Pituitary radiotherapy (RT) and total bilateral adrenalectomy (BA) are second line treatments in patients not cured by surgery. Patients undergoing BA need lifelong treatment with glucocorticoids and mineralocorticoids with a risk of Nelson syndrome, while RT is associated with risk of hypopituitarism. Medical treatment usually consists of use of adrenal-blocking drugs and neuromodulatory drugs acting at the pituitary level.^{2,3}

We describe a 12-year-boy with persistent CD after TSS and RT, in whom short-term cabergoline treatment was effective in inducing a remission. The patient presented in October 2005 with history of progressive weight gain and short stature for the past 3 years. Persistent uncontrolled hypertension had been documented for 2 years previously. He had classical clinical features of CD, including obesity (BMI 34 kg/m²), moon facies, facial plethora vellous hypertrichosis, acanthosis nigricans (axilla, neck and knuckle) and pink striae. He was prepubertal. Investigations were suggestive of adrenocorticotrophin (ACTH)-dependent CD: a basal cortisol (BC) of 35 µg/dL, a basal ACTH of 25.4 pg/mL and a low-dose dexamethasone suppression (LDDS) cortisol of 21.8 µg/dL; MRI of the abdomen showed an adrenal hyperplasia and an MRI of the pituitary was normal. Corticotrophin releasing hormone stimulated IPSS (inferior petrosal sinus sampling) showed a central to peripheral ratio of 46 and lateralization to the right side with a ratio of

1.5. The patient underwent TSS in January 2006. Histopathology confirmed pituitary adenoma (immunohistochemistry by ACTH stain was positive). Postoperatively, he continued to have evidence of persistent CD. One year post-surgery he was still uncured (BC of 22.2 µg/dL, basal ACTH of 59.6 pg/ml and post-LDDS cortisol of 20.9 µg/dL). He received conventional fractionated RT, with a total dose of 45Gy over 38 days beginning in March 2007. In May 2007 he was started on cabergoline 1 mg/week for 1 month which was progressively increased to 3 mg/week. At the end of 3 months, marked clinical and biochemical remission was achieved (decrease in pigmentation of skin and hair growth, weight loss of 7 kilograms, BC of 3.26 µg/dL and basal ACTH of 38.5 pg/mL). The patient omitted cabergoline for 2 months following which he had recurrence of CD (BC of 19.3 µg/dL, basal ACTH of 45.12 pg/mL and LDDS of 5.3 mcg/dL). The patient was restarted on cabergoline and is due for follow-up. Neuromodulatory drugs (sodium valproate, cyproheptadine, rosiglitazone^{4,5} and dopamine agonists with pharmacological action at the level of the hypothalamus and pituitary) have been tried in patients with uncured CD.^{6,7} Dopamine agonists have been tried in CD because of their established efficacy in prolactinomas. Dopamine receptors are expressed in normal adrenals, adrenal tumors (adenomas and carcinomas),⁷ 80% of corticotroph pituitary tumors and ectopic corticotroph tumors. There are various case reports of remission of CD with dopamine agonists with tumor shrinkage in some cases.^{2,3} Cabergoline is likely to be superior in efficacy as compared with bromocriptine.⁸ Our patient improved with short-term treatment with cabergoline. This is the first documented case report from

India with cabergoline showing a response in uncured CD. Although our patient received RT, the time interval between RT and clinical and biochemical remission was very short suggesting that this remission was unlikely due to RT. A mean interval of 11.2 months has been reported in children and adolescents with uncured CD before any benefit from RT was observed.⁹ Since our patient had an initial remission and recurrence on discontinuing the drug, this suggests that the observed benefit is likely due to cabergoline. Thus cabergoline could be a useful option for inducing remission in uncured CD patients who have undergone TSS and radiotherapy.

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Predictors of obstructive sleep apnea: special considerations for females

To the Editor: I read with interest the article by Ibrahim et al exploring the predictors of obstructive sleep apnea (OSA) in snorers.¹ The authors reported no age difference between females with and without OSA. For females, including age without considering the menopausal status can be misleading. In females, the menopausal status is one of the most important risk factors and predictors of OSA and its assessment is an essential part of any study looking into OSA in females. Young et al assessed the association between the menopausal status and sleep-disordered breathing (SDB) in women.² After adjusting for potential confounders like age, body mass index and smoking, the authors calculated the odds ratio (95% CI) for an apnea/hypopnea index (AHI) of more than five per hour of sleep to be 1.2 (0.7-2.02) in perimenopausal and 2.6 (1.4-4.8) in postmenopausal women.² After menopause, the prevalence of OSA in women approaches that in men and reaches its peak in the fifth and sixth decades.^{2,3} In general, the prevalence of OSA peaks at around 55 years in men and at around 65 years in women.⁴ This can be related to postmenopausal status as the risk of SDB was shown to be at least 2.5 times higher in post- than in premenopausal women,² and it approximates that of men at the time of menopause.⁵ Female hormones (especially progesterone) may play a role in increasing upper airway muscle activity during wakefulness and non-rapid eye movement sleep.⁶ Furthermore, there are important gender differences in central ventilatory control. Women have a lower apnea threshold, compared to men and they are less likely to exhibit apneas during non-rapid eye

movement sleep despite inspiratory flow limitation.^{7,8} It is possible that the above protective mechanisms disappear after menopause. Another point to remember when evaluating females for SDB is the fact that a good proportion of females with OSA present with insomnia rather than excessive daytime sleepiness. Sheperdycky et al in a study of 260 patients found that 1 in 5 women with OSA had a presenting complaint of insomnia compared to 1 in 20 in men.⁹ We found similar findings in Saudi females with OSA (under review).

We agree with the listed predictors of OSA in Ibrahim's study. However, it is important for clinicians to realize that SDB in females is slightly different from that in males. Menopausal status is an important risk factor for OSA. Additionally, it is important to recognize that insomnia could be the presenting symptom of OSA in females. Focusing on daytime sleepiness in this group of patients may result in under-recognition of this serious disorder.

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Reply

The letter to the editor considering the predictors of obstructive sleep apnea (OSA) emphasized the effect of menopause as an important predictor of OSA in females. The effect of menopause on the quality of sleep and the presence of obstructive sleep apnea were well discussed in this letter to the editor. But it is interesting to note the disconnection between the subjective reports of poor sleep in menopause and the objective data obtained during sleep studies.¹ The mean age was not different in our study between females with and without OSA (50.3±10.7 years versus 51.8±8.2 years; $P=.609$). It is of interest to note here that referral bias suggested by Lynne Lamberg¹ may play a factor in the differences noted in OSA between males and females in epidemiological studies, and in addition, the small study sample of females would explain the lack of significance of age differences in females with or without obstructive sleep apnea in our study. This difference may only be shown in population-based studies rather than in a referral based like our study.

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RE: Call to establish a national lower limit of viability

To the Editor: I read with interest your article, on establishing a national lower limit of viability.¹ Two important problems are evident: 1) the lower limit of gestational age and the birthweight of the neonate should be assigned. This will determine whether to resuscitate and admit the neonate in the neonatal intensive care unit (NICU) or not. There is a need to have a uniform national guideline for such neonates. At present different centers have different criteria for admitting such extreme low birthweight neonates (ELBW) to the NICU. Outcome as regards to mortality and morbidity of these neonates is high as compared to term neonates as is evident from recent studies. Khan et al² observed that in infants <33 weeks gestational age who were serially assessed, of the 159 enrolled children, 65% survived, 16% died and 19% were lost to follow-up. Those who survived were followed up for neurodevelopment by physicians and developmental psychologists. At a mean age of 31 months, the developmental status of 85 children followed-up for 12 months was normal in 32%, while 45% had mild and 23% had serious neurodevelopmental impairments.²

Unlimited population growth is a result of increased birth rate, including preterm neonates. Most of the preterm neonates get admitted to the NICU. Prematurity is a major factor for neonatal mortality.³ In Ministry of Health hospitals there is shortage of NICU beds. Shortage

of beds and over admission of neonates results in overcrowding. This is one of the major contributing factors for neonatal sepsis. Preterm neonates are prone to infection in view of their immunological status. The other side of the coin is the acute shortage of trained medical staff (doctors and nurses). The ELBW neonate needs a highly skilled and qualified staff for better outcome. The Ministry of Health is doing its best by opening new hospitals with NICU units and upgrading the existing NICU.

The retirement age limit of neonatologists has been raised to 65 years and in the private medical sector it is more than 65 years, a step in the right direction. Most of the NICUs are lacking neonatal surgical facilities, and under these circumstances the surgical neonates have to be transported to higher centers where the surgical facilities are available for surgical intervention. Transport of the sick neonate requires a special qualified trained team and a vehicle with modern equipment for surface and air transport from one hospital to the other. There is a need to update and expand the present neonatal transport system. I agree with the author that there are limited reports on neonatal admission, neonatal, perinatal mortality, and long-term outcome of neonates who get admitted to NICUs in this country. Arafa and Al Shehri from the Southern region (Abha) of Saudi Arabia have reported a high neonatal mortality rate.⁴ In another study from Madina Al Munawara, the neonatal mortality rate was 6% as reported by Nabi and Karim.⁵ There is a need to publish sufficient data on neonates who get admitted in the hospital and their outcome. This will give us an idea about the magnitude of the problem and will help to frame the national neonatal policy.

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Reply

Decisions about whether to resuscitate a newborn baby, and admit him or her to neonatal intensive care; and whether to continue intensive care or replace active treatment with palliative care, are complex, emotionally demanding and may have lifelong consequences.¹

Your first point regarding assigning both a lower limit of gestational age and the birthweight of the neonate is ideal but it is not free of confusion. We all agree that gestational age, if accurate, reflects the degree of immaturity which is the main factor in making decision to resuscitate or not. However, caregivers need to be extremely careful before taking such decisions for a specific gestational age unless it has been carefully defined. In contrast, for the birthweight, although it is accurate, there is an overlap in weight between different gestational ages of pre-viable and viable infants.² Combining both birthweight and gestational age are used for short and long-term outcome but a decision to resuscitate or not commonly takes place within a

short time prior to delivery or at the delivery room.

The reports from Saudi Arabia and other developing countries did not delineate the magnitude of the problem, because they included infants with a wide range of gestational ages resulting in less attention to the specific outcome of infants born at the cusp of viability. Moreover, although there is a consensus amongst perinatal care providers that the full gamut of intensive care should be provided at 26-weeks gestation and beyond, opinions and attitudes differ among different countries, centers and individuals with regard to the grey zone between 22 and 25 weeks of gestation.³ Additionally, the recent results of the European program MOSAIC (Models for Organizing Access to Intensive Care for Very Preterm Babies in Europe) evidently showed variations between the European countries.⁴ MOSAIC is a prospective cohort study of all preterm infants delivered between 22 and 31 weeks of gestation in 10 regions of nine European countries covering 494463 total live births in 2003. The study showed important differences in the approaches to the organization of perinatal care and a wide variation in neonatal survival. More interestingly, they documented the variation in Europe from extreme approaches, such as Poland, where despite financial and organizational difficulties, the treatment of all infants at the limit of viability is undertaken, to the Netherlands, where active intensive care treatment of newborns born before the 25th week of gestation is not routinely offered. A consensus conference in Australia⁵ concluded that 'between 23 weeks and zero days and 25 weeks and 6 days of gestation, it was reasonable to offer the option of noninitiation of resuscitation and intensive care.

In the presence of these varia-

tions in treating infants at the limit of viability, I believe that having guidelines is necessary for parents and professionals to make decisions for resuscitating and instituting intensive care for extremely premature and seriously ill babies. These guidelines should be drafted by a group of expert professionals and should be approved by Islamic Scholars to declare their implementation.

It will be very helpful if a Saudi neonatal network is developed to connect all hospitals in Saudi Arabia. The network will maintain a standardized NICU database and provide a unique opportunity for researchers to participate in collaborative projects on a national and international scale. This will give an opportunity to health care professionals, health services researchers and health administrators to participate actively in clinical, epidemiologic, outcomes, health services, health policy and informatics research aimed at improving efficacy and efficiency of neonatal care.

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