



Essential Hypertension

Alternative Names

EHT
Primary Hypertension

Record Category

Disease phenotype

WHO-ICD

Diseases of the circulatory system > Hypertensive diseases

Incidence per 100,000 Live Births

101- ~

OMIM Number

145500

Mode of Inheritance

Multifactorial

Gene Map Locus

17q21-q22, 17q, 17cen-q11.2, 1q23-q25, 1q23, 15q, 1q22-q25, 12p12.2-p12.1, 12p13, 7q36, 7q22.1, 5p13-q12, 4p16.3, 3q21-q25, 1p36.1, 2p25-p24, 20q13.11-q13.13, 1q42-q43, 20q11-q13

Description

Essential hypertension is blood pressure that is consistently higher than normal when no cause for the high blood pressure can be found. Essential (or primary) hypertension is a frequent pathology (10% to 40% of the population, depending on the age group) causing significant cardiovascular morbidity and mortality. About 90-95% of patients with high blood pressure have essential hypertension. Black adults have a higher incidence of hypertension than Caucasian adults and typically a more severe form of the disease.

Among the many complications related to essential hypertension, a large percentage of patients develop a left ventricular as a physiological adaptation to high blood pressure.

Unlike secondary hypertension, there is no known cause of essential hypertension. However, there are

several factors that can increase blood pressure, such as the amount of blood pumped by the heart, size and condition of the arteries, water and salt content of the body, condition of the kidneys, nervous system, hormone levels, and or blood vessel tone in the body. This later could be mediated by enhanced sympathetic activity or by increased circulating levels of angiotensin II. Other factors that lead to essential hypertension include stress, being overweight, smoking, alcohol use, a diet high in salt, heredity, gender, age and race.

Molecular Genetics

Essential hypertension is a multifactorial genetic disease resulting from complex interactions between multiple environmental and genetic factors. Many familial studies have shown the partially inherited aspect of the disorder. According to estimates, 20 to 40% of blood pressure variance have a genetic origin. Variations in a variety of genes have shown an association with hypertension in some studies, but these associations are often not reproducible in studies of other populations. Candidate genes include angiotensinogen, angiotensin receptor-1, adducin, adrenergic receptors, and the human guanine nucleotide-binding protein beta-3 subunit gene. The product of the later gene is involved as a modulator or transducer in various transmembrane signaling systems, by integrating signals between receptors and effector proteins.

As a key enzyme of the renin-angiotensin-aldosterone system, the renin gene (REN) is a good candidate quantitative trait locus that may be implicated in the molecular etiology of essential hypertension. Among mixed reports on the subject, a REN MboI restriction fragment length polymorphism has been shown to be significantly associated with a family history of hypertension in a Japanese population. To date, however, there is no genetic variant with strong enough effect to be used for predictive purposes.

Epidemiology in the Arab World

Bahrain



In order to assess the effect of fasting during the holy month of Ramadan among diabetics, Al-Nasir (1999) studied seven hypertensive patients and four patients with both hypertension and NIDDM before, during, and after Ramadan. All patients showed a significant reduction in their weight, 2-weeks (stage 1) and 4-weeks (stage 2) after the beginning of Ramadan (stage 0). However, this reduction was significant only in males. Fasting blood glucose was found to have significantly increased in stage 1 and reduced in stage 2. However, the pre- and post-fasting levels of FBG showed no statistically significant difference. Systolic and diastolic pressures decreased significantly in the period of study; more so the diastolic pressure. Al-Nasir (1999) was able to demonstrate that patients with hypertension could observe fasting without any adverse effects, although they needed to be monitored closely during the period of fasting.

Egypt

El-Tagi et al. (1982) described the incidence, pathogenesis and management of hypertension in 1600 pregnant women admitted to El-Hussein University Hospital, Cairo, in 1980. A total of 100 women had pregnancy related hypertension. Twenty five subjects (1.56%) had essential hypertension. Termination of pregnancy occurred only in 2 patients, one with severe pre-eclampsia and the other with severe essential hypertension. Caesarean section was done in 12 patients, 7 of them for hypertension and in the remaining 5 for other reasons. Management of hypertension at the hospital consisted of 3 approaches: 1) rest in bed and sedation such as pethidine, valium or Algafan; 2) a combination of sedatives and hypotensives such as Brinerdin, Serpasil and Aldomet; and 3) a combination of sedatives, hypotensives and diuretics.

A study by Woodhouse et al. (2003) to investigate the possibility of familial hypertension being due to mineralocorticoid hypersecretion included an Egyptian patient [See: Oman > Woodhouse et al., 2003].

Eritrea

Mufunda et al. (2006) conducted a cross-sectional baseline survey of the risk factors for hypertension in the Eritrean population. All the nine ethnic groups in Eritrea were included in the study. The total sample consisted of 2352 subjects belonging to 123 primary sampling units from the six regions of the country. The prevalence of hypertension was found to be 16% in the general population (males: 16.88%, females: 15.28%). This rate is higher than values reported from Western African countries. A positive correlation was seen between BMI and

hypertension. This association was however, significant only in women with normal BMI. In addition, the prevalence was higher in urban (16.5%) than in rural (14.5%) areas, and increased with age. Interestingly, only 20% of the hypertensive respondents were aware of their hypertensive state.

Kuwait

A review of data on hypertension in Kuwait by El-Reshaid et al. (1999) detected a prevalence rate of 26.3%, and mild to moderate hypertension in 86% of subjects studied. The proportion of hypertensives increased with age and obesity levels. The study also identified a very low level of awareness about the disease among affected patients. In 1997, hypertension was found to be responsible for 935 hospital admissions. Co-morbid conditions related to hypertension were responsible for several more admissions.

Saleh et al. (2000) studied a multistage, stratified random sample of 1312 Kuwaiti students (619 boys and 693 girls) aged 6-10 years to understand the prevalence of hypertension and the related risk factors in this population. The overall prevalence rate of hypertension in this group was calculated to be 5.1% (5.7% among boys, and 4.6% among girls). Multivariate analysis revealed that **obese children and those with a family history of hypertension as well as children of consanguineous parents were particularly predisposed to developing hypertension.**

A study to examine the correlates of compliance and non-compliance to hypertensives in Kuwait was undertaken by Al-Yahya et al. (2006). A total of 154 hypertensives attending a single clinic in the Hadiya region were followed for at least 3-months. Blood pressure measures were taken at intervals while patients were maintained on anti-hypertensive medications. Compliance rate was assessed based on questionnaires and taking a pill count. Follow-up was completed in 132 subjects; 84% of who had uncontrolled hypertension. Overall rate of compliance was found to be high at 89%. Among the controlled hypertensives, compliance was significantly greater than among the non-controlled patients. The non-compliant group also showed a significant increase in the following parameters: lack of knowledge of hypertension, increased number of drugs and daily frequency of medication, and negative family history of chronic diseases. Multiple logistic regression analysis revealed patient's knowledge of hypertension and daily dose frequency of medication to be independent predictors of non-compliance, while family history of chronic diseases was not.



Morocco

A study by Woodhouse et al. (2003) to investigate the possibility of familial hypertension being due to mineralocorticoid hypersecretion included a Moroccan patient [See: Oman > Woodhouse et al., 2003].

Oman

Muhammed (1992) reviewed hypertensive patients attending an Omani Hospital and found that 90% were of the age group 35 – 55 years, predominantly males, with the majority being asymptomatic. Nearly, 60% of the interviewed patients had morning occipital headache or non specific complaints, 50% had positive family history, 30% had end organ damage and on antihypertensive, and the majority had muscular weakness (probably caused by an iatrogenic effect). Three out of 100 patients had cushionoid features, two had absent femoral pulse, four had abdominal bruit due to renal artery stenosis, two had ectopic kidney, and 40% of the patients had some degree of hypertensive retinopathy. Ten elderly patients had isolated systolic hypertension on sustained release isosorbide nitrate (calcium channel blockers showed flushing, vasodilation and ankle edema). It was found that 30% of hypertensive patients attending the clinic were diabetic as well. Muhammed (1992) advised early control of blood pressure in diabetics to reduce morbidity and early death, as well as early detection and management of microalbuminuria to prevent or delay the onset of nephropathy. Muhammed (1992) suggested the use of ambulatory blood pressure monitoring to obtain day and night readings to assess the control of blood pressure.

Hassan et al. (2001) conducted a study to determine the blood pressure reactivity of young offspring of first cousin hypertensive parents, in response to their first blood pressure measurement. Three readings (10 minutes apart) of systolic (SBP) and diastolic (DBP) blood pressures as well as the heart rate of 135 boys aged nine to ten years were measured using an automatic blood pressure recorder, and their BMI was calculated from their weights and heights. Questionnaires were then sent home to the parents, to obtain details of the parents' relation to each other, and their hypertensive/normotensive state. A total of 41 parents were found to be first degree cousins and were selected for the study. Of these, 35 (85.4%) had their blood pressure measured, and 19 were found to be normotensive. Of the 16 hypertensive parents, 13 were already on medications and three were newly diagnosed in this study. The mean systolic and diastolic blood pressure of the offspring of the two groups (hypertensive and normotensive parents) was calculated, the

difference between the first and third readings was taken as the reactivity index, and the third reading was taken as the baseline value. Statistical analysis was done with the independent sample t-test with 95% confidence interval used for comparison. The mean age of fathers (42 years) was higher than that of mothers (33 years) in both hypertensive and normotensive groups. The three SBP (117, 108, and 102mmHg, versus 111, 103 and 98 mmHg in control group) and DBP (75, 66 and 65mmHg, versus 64, 62 and 60 mmHg in control group) readings of the offspring of hypertensive parents as well as their SBP and DBP reactivity indexes (15 and 10, respectively) was significantly higher than that of the control group (10 and 4, respectively). No statistical significant difference was found between the heart rates and the BMI of both groups. Hassan et al. (2001) concluded that since the offspring of hypertensive first degree cousins reacted with exaggerated SBP and DBP responses than controls, research of the heredity of such response needed to be carried out. They also advised on educating the community on the consequences of consanguineous marriage as well as on the effects of environmental factors on the development of hypertension.

Al-Riyami and Afifi (2003) investigated by a community based survey, the accuracy of self reporting of hypertension among Omani subjects as compared with the diagnosis of the disease according to the pre-set criteria by using Cohen Kappa, as well as the influence of certain characteristics on this accuracy by using logistic regression. The study included 1968 households representing 16 governorates with 7011 subjects aged >20 years, with a response rate of 77.5-91.5% according to physical and laboratory measurement. Household health status questionnaire was used to collect data about hypertension from 6414 subjects and its prevalence was estimated by summing up those who self reported (6.1%) and those with a mean of two readings of 140mmHg systolic BP or 90 mmHg diastolic phase >5 BP, and was found to be 33.1%. The Kappa statistics of self reporting of hypertension was found to be higher among the female gender (0.33) and the middle age group (0.27) as compared to the male gender (0.17) and the younger age group (0.12). As regarding the variables, logistic regression showed that females, age >40 years, living in an urban area, obese subjects, and with impaired fasting glucose were more likely to report hypertension accurately than others. According to the results obtained from this survey, Al-Riyami and Afifi (2003) concluded that depending on self reporting of hypertension would give false prevalence rates and that clinical ascertainment in any population based epidemiological study should be included.



Woodhouse et al. (2003) conducted a study to investigate the possibility that familial hypertension was due to mineralocorticoid (MC) hypersecretion by using spironolactone, which selectively blocked the MC receptors, and would identify such patients. Over an 8-month period, out of 64 hypertensive patients with at least one or more affected parent or sibling, 45 patients (29 females and 16 males; mean age - 48 years; 28% being products of consanguineous marriages) had completed the therapeutic trial and had had hypertension for a range of one month to 33 years. Out of these, 22 were Omani patients. Routine serum potassium, calcium, creatinine and plasma rennin activity were determined, and renal ultrasound was performed in all patients before starting the treatment. Six patients, who were found hypokalemic, along with another eight normokalemic patients randomly selected (four were found to have raised aldosterone) were admitted for measurement of aldosterone and rennin, as well as CT scan of the adrenal gland. All patients received spironolactone 50-100 mg twice daily either alone to new patients or along with other antihypertensives which were gradually withdrawn every 2 weeks if the blood pressure was under good control, until the patient was on spironolactone alone. Out of 45 patients, 39 patients (10 with documented aldosterone hypersecretion, one with normal aldosterone level, and 28 of the 31 who received spironolactone alone and had achieved a 19% drop in blood pressure from baseline) had achieved control of their blood pressure by spironolactone. Most of the male patients developed gynecomastia and they were restarted on their previous medications or new antihypertensives. Four females had menstrual irregularities. Of the 14 patients admitted for determination of rennin and aldosterone, three were diagnosed with non-mineralocorticoid induced hypertension, four with presumptive diagnosis of familial hypertension (FHII), two with FHI, four with hyper-reninemic familial hypertension (HRFH), and one with Conn's tumor (removed with laparoscopy with normalization of aldosterone level and blood pressure). Woodhouse et al. (2003), therefore, detected that inherited forms of mineralocorticoid hypertension were common, as 84% of the patients under study responded to spironolactone, and recommended that all patients with familial hypertension should undergo therapeutic trial with an MC receptor blocking agent, before undertaking expensive endocrine investigations. Since identified responders came from three continents, they postulated that MC hypertension was a worldwide problem rather than a Middle Eastern one.

El-Badawy et al. (2005) carried out a study on 100 randomly selected Omani hypertensive patients (43 males and 57 females) with a mean age of 51.47 years (36% were 50 – 60 years old) over a period of nine months, to determine their health habits and risk factors. Data were collected by a questionnaire which included their socio-demographic information, health history, and detailed lifestyle history. Their blood pressure was measured by manual mercury sphygmomanometer and their BMI was calculated from their weights and heights. Patients were divided into two groups according to the control of their blood pressure (uncontrolled if blood pressure was >140/90 mmHg). Data were analyzed by chi square, t-test, or analysis of variance for comparison between groups, and Person correlation was used to measure the association between dietary lifestyle, BMI and hypertension, while multiple linear regression was used to measure the strength of relationship between risk factors and hypertension. It was found that 73% had uncontrolled hypertension, 88% had hypertension related complications, and 63% had a positive family history of hypertension. 87% were compliant with the antihypertensive drugs, with 46.1% of the non compliant group stated that they felt that their blood pressure was normal. When studying the risk factors in this cohort, poorly controlled hypertension was found among those who were unemployed, had salty and fatty dietary intake, drank more coffee than those with controlled hypertension, and had less exercise and high BMI. The most common risk factors were found to be stress, drinking more coffee, and increased salt intake, while the least common factor was smoking. The main source of stress was found to be the disease itself in 38%, while in 34% it was social (large family size with low income).

Qatar

Bener et al. (2004a, 2004b) studied the prevalence of hypertension and its associated risk factors in the Qatari population through a cross-sectional study conducted between January and July 2003. A total of 1,500 Qatari subjects, selected by a multi-stage stratified cluster sampling method, were interviewed by means of a questionnaire. Of these, 80.5% (1,208 subjects; 42.1% males, and 57.9% females) responded to the questionnaire. The subjects then underwent standardized interviews and blood pressure measurements. The study revealed a high prevalence of hypertension among the subjects (32.1%; 508 subjects). Males showed a statistically insignificant higher prevalence (31.1%) as compared to the females (30.2%). Mean age was higher among the hypertensive (50.5 years) as compared to the normotensive group (39.6 years). In this study group, obesity was found to be a significant risk factor associated with hypertension.



Bener et al. (2004a, 2004b) guessed that this could be due to the peculiar dietary and behavioral habits of the Qataris and a low level of awareness. Other risk factors significantly associated with hypertension were found to be low-educational level, advanced age, and predominantly sedentary life. Interestingly, current smoking habit was less frequent among hypertensive subjects, possibly an effect of education and anti-smoking campaigns. Almost all hypertensives were found to be diabetic. Other diseases seen in the hypertensives included heart disease and hormonal disorders. The hypertensive subjects were also found to include animal fat/butter and coffee in their diet as opposed to the normotensives, who relied on vegetable oils.

Sudan

A study by Woodhouse et al. (2003) to investigate the possibility of familial hypertension being due to mineralocorticoid hypersecretion included nine Sudanese patients [See: Oman > Woodhouse et al., 2003].

United Arab Emirates

In 1997, the National Epidemiological Study of Hypertension in the United Arab Emirates (NESH-UAE) project was initiated to understand the extent of prevalence of hypertension in the country. In 1998, El-Shahat et al. (1999) presented a prospective study comprising 3,150 individuals from the Emirate of Sharjah. Overall, the prevalence of hypertension in the screened sample was 36.6%. Most of the study subjects were aged from 30-50 years and hypertension occurred more in females than in males. This preliminary study is an important indication that hypertension is highly prevalent in the United Arab Emirates and stresses the importance to initiate a nation-wide effort to prevent and control high blood pressure in the population (El-Shahat et al., 1999).

Association of essential hypertension with the human angiotensin-converting enzyme gene: In 1997, Frossard et al. (1997a) studied an insertion/deletion dimorphism in the human angiotensin-converting enzyme (ACE) gene amongst United Arab Emirates (UAE) nationals from the Abu Dhabi Emirate. There was a lack of association between the I/D allele marker system and clinical diagnosis of essential hypertension, suggesting that variations of the angiotensin-converting enzyme gene do not play a major role in the determination of elevated blood pressure in this Arab population. This agrees with results reported on other ethnic groups. In 1998, Frossard et al. (1998c) carried out a retrospective case-control study of the angiotensin-converting enzyme insertion/deletion dimorphism in relation to circulating angiotensin-converting enzyme activity,

as well as to hypertension, ischemic heart disease, myocardial infarction, and left ventricular hypertrophy in a sample population of 285 United Arab Emirates nationals. The analyzed group comprised controls and patients with clinical diagnoses of hypertension, ischemic heart disease, myocardial infarction, and left ventricular hypertrophy. Frossard et al. (1998c) found out that the D allele was associated with increased circulating angiotensin-converting enzyme activity, and the angiotensin-converting enzyme insertion/deletion marker accounted for 28% of the variance of the phenomenon determining angiotensin-converting enzyme levels. However, Frossard et al. (1998c) did not find an association between angiotensin-converting enzyme insertion/deletion and clinical diagnoses of hypertension, ischemic heart disease, myocardial infarction, and left ventricular hypertrophy. Frossard et al. (1998c) concluded that the angiotensin-converting enzyme insertion/deletion dimorphism does not constitute a predictive marker for cardiovascular diseases in the population of the United Arab Emirates. In 2003, Saeed Mahmood and colleagues assessed the value of genotyping the ACE G2350A dimorphism in a retrospective case-control study for a putative association with essential hypertension in the UAE population. Polymerase chain reaction and restriction endonuclease analyses were used to investigate a sample population of 254 Emirati from Abu Dhabi, comprising 136 normotensive controls, and 118 patients with clinical diagnoses of essential hypertension. Detailed analysis revealed that the ACE G/G 2350 genotype was positively associated with essential hypertension. According to the literature, this was the first association study of the ACE G2350A dimorphism with essential hypertension. Saeed Mahmood et al. (2003) concluded that this positive result might indicate that ACE could be a quantitative trait locus for essential hypertension as originally thought.

Association of essential hypertension with the human atrial natriuretic factor gene: Frossard et al. (1997b) also studied an insertion/deletion (I/D) dimorphism located in the second intron of the human atrial natriuretic factor (ANF) gene among 232 UAE nationals (112 normotensives and 120 hypertensives) from the Abu Dhabi Emirate, with a view to evaluating the value of this marker in relation to hypertension. Results reveal that genotype frequencies of this I/D marker occur in Hardy-Weinberg proportions (respective genotype frequencies in the overall sample population are: II, 51%; ID, 42%; DD, 7%). No association, however, was evidenced between this dimorphic site and clinical diagnosis of essential hypertension. This suggests that: 1) this I/D dimorphism is not a useful



marker to study the relationship between the ANF gene and hypertension in the UAE; and 2) variations of the ANF gene that may be in linkage disequilibrium with this marker do not play a major role in the determination of hypertension in this Arab population. Obineche et al. (2002) carried out a case-controlled study on a group of 151 UAE nationals (62 normotensives with and without left ventricular hypertrophy and 89 hypertensives, also with and without left ventricular hypertrophy) with a view to evaluate the value of an insertion/deletion (I/D) dimorphism located in the second intron of the human atrial natriuretic factor gene in relation to left ventricular hypertrophy. Obineche and colleagues found a significant difference in the distribution of the I and D alleles between the two groups. The significant association of the D allele with left ventricular hypertrophy could implicate the involvement of variants of the ANF gene in the determination of left ventricular hypertrophy.

Association of essential hypertension with the human renin gene: Frossard et al. (1998a) described a polymerase chain reaction-based assay for the detection of the REN MboI dimorphic site located in the ninth intron of the gene. MboI genotype distributions were investigated in 331 hypertensive and 279 normotensive subjects from the United Arab Emirates (UAE), a genetically homogeneous ethnic population with no history of smoking or alcohol consumption. A statistically significant association was found between alleles on which the MboI site is present and clinical diagnosis of essential hypertension, indicating that 1) the presence of the MboI site is a marker for susceptibility to hypertension in the UAE (the associated odds ratio is 3.16); and 2) variations of the REN (or of a nearby) gene that may be in linkage disequilibrium with this marker play a role in the development of essential hypertension in the UAE. Later on, Frossard et al. (1999b) found a statistically significant association between alleles on which the BglI site was present and the clinical diagnosis of essential hypertension in the UAE population, and to a lesser extent, in a U.S. Caucasian group that was studied for hypercholesterolemia. Frossard and colleagues (1999b) also postulated that such a genetic influence, which seems to show a recessive mode of inheritance, could also be implicated in raising both systolic and diastolic blood pressures.

Association of essential hypertension with the human angiotensinogen gene: In 1998, Frossard et al. (1998b) assessed the value of genotyping the human angiotensinogen gene in a genetically homogeneous population. They carried out a retrospective, case control study of variants M235T and T174M for putative correlations with

cardiovascular diseases among UAE. A sample population of 229 Emirati (119 males and 110 females) was investigated. This comprised groups of controls and patients with clinical diagnoses of essential hypertension, left ventricular hypertrophy, ischaemic heart disease and myocardial infarction. M235T and T174M alleles were determined via assays based on the polymerase chain reaction. T174M showed no correlation with any of the four clinical entities included in this study. T235 alleles, however, occurred more frequently in the essential hypertension group and less frequently in the group of myocardial infarction survivors. Frossard and colleagues (1998b) found that T235 allele frequencies decreased with age, indicating that in the Emirati population, T235 alleles are associated with a reduced life span and that this effect could occur through independent mechanisms underlying genetic susceptibilities to both essential hypertension and myocardial infarction.

Association of essential hypertension with the human apolipoprotein B gene: Frossard and Lestringant (1999) used a polymerase chain reaction-based assay to investigate the allele and genotype frequency distributions of the alleles of a hypervariable region located in the 3' of the human apolipoprotein B (apoB) gene. The analysis of DNA samples of 367 unrelated UAE nationals (201 males and 166 females) revealed the presence of 18 different alleles, ranging from 21 to 55 repeats, making up 51 genotypes occurring in Hardy-Weinberg proportions with a heterozygosity index of 80.9%. This observation leads to the conclusion that this marker is very informative in the Emirati population and may be very useful for UAE-specific DNA fingerprinting as well as to assess the role of the apoB gene in cardiovascular diseases. Frossard et al. (1999a) investigated the associations between genetic variations of the apoB gene and clinical diagnosis of essential hypertension. They compared the distribution of the alleles of a highly polymorphic variable number of tandem repeats localized 3' to the human apoB gene, the apoB 3' hypervariable region (HVR), in a group of normotensive and a group of hypertensive individuals. DNA samples from 437 unrelated UAE nationals (215 normotensives and 222 hypertensives) were collected. The apoB 3' HVR allele and genotype status were determined using a polymerase chain reaction-based assay. In the UAE population, Frossard and colleagues (1999a) found 18 alleles underlying a total of 51 genotypes. The distribution of these alleles is significantly different between normotensive and hypertensive UAE nationals. The main peak of the distributions occurred at 35 repeats among hypertensives (with a relative frequency of 25.7% versus 19.6% in normotensives) and at 37 repeats among



normotensives (28.8% versus 20.3% in hypertensives). Alleles with 21, 23, 25, 49, and 55 repeats are found in hypertensives only (with a combined relative frequency of 7.6%). Frossard et al. (1999a) concluded that variations of the apoB gene, or of a nearby gene, that may be in linkage disequilibrium with these alleles play a role in the development of essential hypertension in UAE nationals.

Association of essential hypertension with the human guanine nucleotide-binding protein beta-3 subunit gene: Obineche et al. (2001) investigated the relationship of left ventricular hypertrophy with five candidate genes in a genetically homogenous population group of 213 UAE nationals (98 subjects with left ventricular hypertrophy and 115 age- and sex-matched controls). The study focused on the distributions of genotypes of intragenic markers in the human guanine nucleotide-binding protein beta-3 subunit gene variant; methylene tetrahydrofolate reductase gene; angiotensin converting enzyme gene; and paraoxonase 1 and 2 genes. Of the five candidate gene markers studied, no significant differences in the genotype distribution of the methylene tetrahydrofolate reductase gene; angiotensin converting enzyme gene; or paraoxonase 1 and 2 gene markers were found between the left ventricular hypertrophy and control groups. However, data on the homogenous cohort of Emirati lead Obineche and colleagues to suggest a possible association between the C825T marker of the human guanine nucleotide-binding protein beta-3 subunit gene and left ventricular hypertrophy ($p=0.0445$).

Association of essential hypertension with other genes: Frossard et al. (2002) evaluated the putative involvement of cytokine gene variants in human essential hypertension. They carried out case-control study on 174 unrelated UAE nationals (81 hypertensives and 93 normotensives) from the Abu Dhabi Emirate. Five candidate genes were targeted: loci-transforming growth factor beta1 (TGF-beta1), interferon gamma (IFN-gamma), epidermal growth factor (EGF), interleukin-1 beta (IL-1beta) and tumour-necrosis factor (TNF-alpha). The distribution of genotypes and alleles of the six following dimorphic variants were assessed: TGF-beta1(*)10(T>C) and TGF-beta1(*)25(G>C), located at codons 10 and 25, respectively, of TGF-beta1; T874A in intron 1 of IFN-gamma; G61A in exon 1 of EGF; TaqI dimorphism at +3962 (exon 5) of IL-1beta; and -308A>G in the promoter of TNF-alpha. These six bi-allelic markers were visualised by methods based on the techniques of amplification refractory mutation system-polymerase chain reaction (for TGF-beta1, IFN-gamma, EGF and TNF-alpha) and by polymerase

chain reaction-TaqI restriction endonuclease analysis in the case of IL-1beta. In each of the two groups (normotensives and hypertensives), genotype frequencies of all six markers occurred in Hardy-Weinberg proportions. There were, however, no statistical differences in the allele and genotype frequencies of any of the six markers between the two groups of subjects. There was also no difference in distribution and frequencies of haplotypes constructed with combinations of TGF-beta1(*)10(T>C) and TGF-beta1(*)25(G>C) sites. However, although they do not reach statistical significance (which may be due to the relatively restricted number of subjects included in this study), the distribution differences (in normotensives and hypertensives) observed in the cases of EGF and TNF-alpha reflect trends that could be expected from a mechanistic explanation of the pathways that underlie the patho-physiology of hypertension.

References

- Al-Nasir FAL. Effect of Ramadan fasting on hypertension and diabetes. *Qatar Med J.* 1999; 8(2):53-7.
- Al-Riyami AA, Afifi MM. Accuracy of self-reporting of diabetes mellitus and hypertension and its determinants among Omani adults. *Saudi Med J.* 2003; 24(9):1025-6. PMID: 12973495.
- Al-Yahya AA, Al-Mehza, Al-Ghareeb H. Comparison of compliance versus non-compliance to anti-hypertensive agents in primary health care-An area based study. *Kuwait Med J.* 2006; 38(1):28-32. [FT]
- Bener A, Al-Suwaidi J, Al-Jaber K, Al-Marri S, Dagash MH, Elbagi IE. The prevalence of hypertension and its associated risk factors in a newly developed country. *Saudi Med J.* 2004a; 25(7):918-22. PMID: 15235700
- Bener A, Al-Suwaidi J, Al-Jaber K, Al-Marri S, Elbagi IE. Epidemiology of hypertension and its associated risk factors in the Qatari population. *J Hum Hypertens.* 2004b; 18(7):529-30. PMID: 14973519
- El-Badawy AM, Al-Kharusi HM, Al-Ghanemy SA. Health habits and risk factors among Omanis with hypertension. *Saudi Med J.* 2005; 26(4):623-9. PMID: 15900373
- El-Reshaid K, Al-Owaish R, Diab A. Hypertension in Kuwait: the past, present and future. *Saudi J Kidney Dis Transpl.* 1999;10(3):357-64. PMID: 18212446
- El-Shahat YIM, Bakir SZ, Hashim T, BoHaliga A, Al-Hossani H, Jaffar A-R. Hypertension in UAE citizens – preliminary results of a prospective study. *Saudi J Kidney Dis Transplant.* 1999; 10(3):376-81.



- El-Tagi A, Nassar A, El Agizi H. Al-Azar experience in pregnancy associated hypertension. *Popul Sci.* 1982; (3):43-52. PMID: 12266217
- Frossard PM, Bokhari AM, Elshahat YL, Lestringant GG, Hill SH, Abdulle AM, Obineche EN. Angiotensin-converting enzyme insertion or deletion dimorphism in predisposition to cardiovascular diseases amongst United Arab Emirates nationals. *Saudi Med J.* 1998c; 6:713-9.
- Frossard PM, Gupta A, Pravica V, Perrey C, Hutchinson IV, Lukic ML. A study of five human cytokine genes in human essential hypertension. *Mol Immunol.* 2002; 38(12-13):969-76. PMID: 12009575
- Frossard PM, Hill SH, Elshahat YI, Obineche EN, Bokhari AM, Lestringant GG, John A, Abdulle AM. Associations of angiotensinogen gene mutations with hypertension and myocardial infarction in a gulf population. *Clin Genet.* 1998b; 54(4):285-93. PMID: 9831339
- Frossard PM, Lestringant GG, Elshahat YI, John A, Obineche EN. An MboI two-allele polymorphism may implicate the human renin gene in primary hypertension. *Hypertens Res.* 1998a; 21(3):221-5. PMID: 9786608
- Frossard PM, Lestringant GG, Malloy MJ, Kane JP. Human renin gene BglII dimorphism associated with hypertension in two independent populations. *Clin Genet.* 1999b; 56(6):428-33. PMID: 10665661
- Frossard PM, Lestringant GG. Analysis of the apolipoprotein B gene 3' hypervariable region among nationals of the Abu Dhabi Emirate and comparisons with other populations. *Ann Saudi Med.* 1999; (6):490-4.
- Frossard PM, Obineche EN, Elshahat YI, Lestringant GG. Deletion polymorphism in the angiotensin-converting enzyme gene is not associated with hypertension in a Gulf Arab population. *Clin Genet.* 1997a; 51(3):211-3. PMID: 9137889
- Frossard PM, Obineche EN, Lestringant GG, Elshahat YI. Association study between the ANF gene and hypertension in a Gulf Arab population. *Am J Hypertens.* 1997b; 10(11):1308-10. PMID: 9397252
- Frossard PM, Obineche EN, Lestringant GG. Association of an apolipoprotein B gene marker with essential hypertension. *Hypertension.* 1999a; 33(4):1052-6. PMID: 10205247
- Hassan MO, Al Kharusi W, Ziada A. Blood pressure and its reactivity in the offspring of first cousin hypertensive and first cousin normotensive parents: a preliminary report. *J Hum Hypertens.* 2001; 15(12):869-72. PMID: 11773990
- Mufunda J, Mebrahtu G, Usman A, Nyarango P, Kosia A, Ghebrat Y, Ogbamariam A, Masjuan M, Gebremichael A. The prevalence of hypertension and its relationship with obesity: results from a national blood pressure survey in Eritrea. *J Hum Hypertens.* 2006; 20(1):59-65. PMID: 16151443
- Muhammed B. Review of patients with hypertension in Royal Hospital. *Oman Med J.* 1992; 9(2):45.
- Obineche EN, Frossard PM, Bokhari AM. An association study of five genetic loci and left ventricular hypertrophy amongst Gulf Arabs. *Hypertens Res.* 2001; 24(6):635-9. PMID: 11768721
- Obineche EN, Frossard PM, Bokhari AM. Association between an ANF gene I/D dimorphism and left ventricular hypertrophy in a Gulf Arab Population. *Ann Saudi Med.* 2002; (1-2):22-5.
- Saeed Mahmood M, Saboohi K, Osman Ali S, Bokhari AM, Frossard PM. Association of the angiotensin-converting enzyme (ACE) gene G2350A dimorphism with essential hypertension. *J Hum Hypertens.* 2003; 17(10):719-23. PMID: 14504631
- Saleh EA, Mahfouz AA, Tayel KY, Naguib MK, Bin-al-Shaikh NM. Hypertension and its determinants among primary-school children in Kuwait: an epidemiological study. *East Mediterr Health J.* 2000; 6(2-3):333-7. PMID: 11556020
- Woodhouse NJ, Elshafie OT, Mehar A, Johnston WJ, Al-Kaabi JM. Spironolactone responsive familial hypertension. A potentially high prevalence of mineralocorticoid disease in Oman. *Saudi Med J.* 2003; 24(2):229-31. PMID: 12682699

Related CTGA Records

Angiotensin I
 Angiotensin I-Converting Enzyme
 Apolipoprotein B
 Cortisol 11-Beta-Ketoreductase Deficiency
 Guanine Nucleotide-Binding Protein, Beta-3
 Natriuretic Peptide Precursor A
 Renin

External Links

<http://www.cvphysiology.com/Blood%20Pressure/BP024.htm>
<http://www.hmc.psu.edu/healthinfo/e/essentialhypertension.htm>
<http://www.nlm.nih.gov/medlineplus/ency/article/00153.htm>
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=421

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