Normal Range of Total Plasma Homocysteine Concentrations in Southern Iran

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Abstract

The distribution of total plasma homocysteine concentrations in relation to the sex and age is described, in a population of Shiraz, South West of Iran and compared to those reported in other populations. Two hundred and one healthy males and 201 healthy females aged >15 y were randomly selected. Total Plasma homocysteine concentrations were measured using high performance liquid chromatography. The mean plasma homocysteine level was significantly higher in men (geometric mean 7.3µmol/L) than in women (geometric mean 6.3µmol/L, p<0.001). The geometric mean levels for age ranges 15-25, 26-36, 37-47, 48-58, 59-69 and 70-80 years, were 5.9, 5.4, 5.2, 6.7, 7.3 and 7.6 µmol/L in women and 7.5, 8.7, 5.9, 5.9, 7.2 and 9.1 µmol/L in men respectively. The first data on homocysteine distribution in a representative sample from South West of Iran indicate that the ethnic differences have an important impact on homocysteine metabolism.

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Keywords • Homocysteine • age • sex • Iran

I t is now well documented that elevation of total circulating homocysteine concentrations in a fasting state is associated with an increased risk of cardiovascular disease[1]. Factors such as age, sex, racial and ethnic differences as well as geographical variations, genetic, dietary, and life style have all shown to be determinants of plasma homocysteine concentration.[5] Total plasma homocysteine levels are higher in men than in women and in older age.[2-3] Elevated fasting homocysteine concentration is associated with lower circulating level and intake of folate and vitamin B12.[4] Although the distribution of plasma concentration of homocysteine has been reported in certain populations of America and Europe, there is little or no available information describing homocysteine concentrations in the healthy Iranian adults. In the present study, total homocysteine concentrations were measured in the plasma of 402 healthy Iranians from Shiraz, South West of Iran. Four hundred and two persons (201 men and 201 women), aged between 15 to 80 and a mean of 67.3±8.5 years, were selected from all districts of Shiraz. Using the telephone directory with the first three digits representing the districts of the city, 700 individuals were called for interview sampling, of whom 174 did not show interest, and 124 did not meet the inclusion criteria. Thus, a total of 402 subjects were studied. At the time of enrolment, relevant data on the past medical

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Table 1: Distributions of Plasma Homocysteine (µmol/L) among Iranian adults aged 15 to 80 years

Group	N	Mean ± SD	Geometric Mean (95% CI)	Range	Percentile Levels of Plasma Homocystein						
					5	10	25	50	75	90	95
All	402	7.4 ± 3.2	6.8 (6.4-7.2)	1.3-19.4	2.5	3.7	5.5	6.9	8.8	11.9	13.6
Females	201	6.7 ± 2.70[1]	6.3 (5.9-6.7)	1.5-19.4	2.4	3.8	5.4	6.7	8.0	9.5	11.8
Males	201	8.0 ± 3.6	7.3 (6.6-7.6)	1.3-18.6	2.6	3.6	5.5	7.4	9.4	13.2	15.3

[1]Significantly different from male values (p < 0.001; Student's t- test).

history, current smoking habit, and alcohol consumption were obtained from all participants. Exclusion criteria for male and female participants included: cardiovascular or systemic illness, elevated blood creatinine levels, current use of vitamins or other supplements, heavy drinking or smoking habit and anticonvulsant therapy.

Fasting venous blood samples were drawn for estimation of total plasma homocysteine concentration. All subjects were of Iranian ancestry and were not first- or second-degree relatives. This study was approved by the local ethics committee and all participants gave written, informed consent.

Plasma homocysteine was analyzed by HPLC according to the method described by Gilfix et al, 1997[6] using reduction of plasma disulfides by tris-(2-carboxyethyl) phosphine, precipitation of proteins with trichloroacetic acid, derivatization with 7-fluoro-2,1,3-benzoxadiazole-4-sulfonate (SBD-F), and fluorescent detection. The inter-assay coefficient of variation for determination of homocysteine in plasma was less than 7.2%.

Distribution of plasma homocysteine was skewed to the right. Therefore, values were loga-

rithmically transformed and presented as geometric means and 95% confidence intervals. Geometric mean values were used for interactions between age and sex. Continuous variables were compared by Student's t test. A *P* value of <0.05 was considered statistically significant.

Mean, geometric mean, 95% confidence intervals, ranges and percentiles of plasma homocysteine level of all 402 samples of females and males are shown in Table 1. The mean plasma homocysteine level was significantly higher in men than in women (p<0.001).

The overall geometric mean levels in both males and females for ages 15 to 25, 26 to 36, 37 to 47, 48 to 58, 59 to 69 and 70 to 80 years were 6.7, 7.1, 5.6, 6.3, 7.3, and 8.4 µmol/L, respectively. Mean, geometric mean, 95% confidence intervals and ranges of plasma homocysteine level for ages 15 to 25, 26 to 36, 37 to 47, 48 to 58, 59 to 69 and 70 to 80 are shown in Table 2. The plasma homocysteine levels were significantly higher in males than in females in the age groups 26-36 (p<0.001), 48-58 (p<0.05) and 70-80 (p<0.001). In female, the oldest age group had significantly higher homocys-

Table 2: Distributions of Plasma Homocysteine (µmol/L) among Iranian adults

Age group (Y)	Sex	N	Mean ± SD	Geometric Mean[1] (95% CI)	Range
15-25	Female	15	6.7± 3.9	5.9 (5.8-6.5)	2.5-19.4
	Male	19	8.0± 3.5[2*]	7.5 (6.7-9.7)	4.0-17.5
26-36	Female	32	6.0± 2.5[1***,2**]	5.4 (3.9-6.5)	1.6-10.9
	Male	24	9.2± 3.9	8.7 (5.7-9.4)	2.6-17.1
37-47	Female	39	5.8± 2.6[2***]	5.2 (3.7-6.6)	1.5-13.6
	Male	29	7.0± 3.7[2**]	5.9 (3.9-7.6)	1.4-15.3
48-58	Female	39	7.1± 2.9[1*]	6.7 (5.4-8.9)	2.4-17.7
	Male	50	6.7 ± 2.9[2***]	5.9 (5.8-7.9)	1.4-14.4
59-69	Female	44	7.3± 2.7	7.3 (5.5-7.7)	4.4-15.4
	Male	55	8.1±3.9	7.2(4.0-7.5)	1.7-18.5
70-80	Female	32	7.1 ±1.3[1***]	7.6(7.2-8.8)	6.10-10.8
	Male	24	9.1±3.4	9.1 (7.6-11.4)	4.3-16.57

[1]Significantly different from male values
[2]Significantly different from age group 70-80
(*p < 0.05, **p< 0.01, ***p<0.001; Student's t-test)

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teine levels as compared to 26-36 (p<0.01) and 37-47 (p<0.001) age groups. In males, the oldest age group showed significantly higher homocysteine levels compared to 15-25 (p<0.05), 37-47 (p<0.01) and 48-58 (<0.001) age groups.

Our results show that the total homocysteine concentration increased across the age groups and was higher in males than in females. The age and sex differences in total plasma homocysteine levels observed in this study were consistent with observations from previous studies on large and small samples of adult men and women in some reported populations.[7-8] In our study, the total homocysteine concentration in older men and women were 7.1 and 9.3 μmol/L, respectively, showing a 17% increase in men (aged 15-25) and a 22% increase in women (aged 70-80). These results are consistent with the data in a larger population of Hordaland (Norway) homocysteine study that suggest an increasing of homocysteine level with age in women compared to men.[3] The reason for higher homocysteine concentrations at the older age is not well understood although changes in renal function and impaired renal metabolism of homocysteine are certainly involved[9]. Higher homocysteine concentrations in males may be explained by differences in body size, estrogen and vitamin status.[2]

Differing mean plasma homocysteine values for healthy people from various countries have been reported and range from 6 μmol/L in Japan to 13 μmol/L in South Africa.[5] Alfthan et al, 1997[5] reported the mean plasma homocysteine concentrations in 13 different countries which ranged from 7.1 in Germany to 10.7 in Finland. They reported that the mortality rate from cardiovascular disease was highest in Finland and Northern Ireland where homocysteine levels are higher compared to Spain, France and Japan where the relevant mortality rate is lower. The reason for inter-country variations of plasma homocysteine is not clear but Alfthan et al, 1997[5], argued that these differences are real and not due to non-compatible sampling and assay procedures. The lower homocysteine levels reported in France, Spain and Japan[5] are comparable with the homocysteine levels obtained in our study. Geographical variation in fruit and vegetable intakes and particularly in dietary folate, might explain these inter-country differences. It has been suggested that a high dietary intake of folate can make a substantial contribution to the reduction in total plasma homocysteine concentrations in the general population. This is because each 3μmol/L decrease in total homocysteine may be associated with a reduction in risk of ischemic heart disease by 16%, deep vein thrombosis by 25% and stroke by 24%.[1] In addition, there is a marked positive correlation between coffee consumption and total homocysteine level. Tea consumption, in contrast, is associated with lower total homocysteine levels[10]. In a typical daily Iranian diet the consumption of fresh fruits, vegetables, fresh herbs, tea, bread and rice is comparatively higher than a typical diet in Western Europe and the US. This might explain the lower homocysteine levels observed in our population as compared to other populations. This study underlines, in a population-based setting, the importance of the known determinants of fasting total homocysteine and emphasizes the significance of age, sex in the biology of homocysteine. Furthermore, the results from this study underscores lower plasma homocysteine concentration in our population compared to Europeans and Americans. Case control studies are underway to investigate the impact of plasma homocysteine level on cardiovascular disease in our population.

Acknowledgment

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