Hyperhomocysteinemia, Lifestyle Factors and Cognitive Impairment in Healthy Older Subjects in Jordan

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Abstract: Hyperhomocysteinemia (HHcy) is a well recognized risk factor for cognitive impairment in the elderly. Homocysteine levels (Hcy) are influenced by a many factors such as age, gender and some lifestyle factors such as smoking, coffee and tea consumption. The aim of the present study is to explore the relationship among plasma Hcy, lifestyle factors including coffee and tea consumption, smoking and cognitive impairment risk. A cross-sectional sample of 83 healthy Jordanian elderly subjects of either sex of age >60 years were examined. All participants completed a questionnaire about lifestyle and health. Plasma Hcy levels were determined for all subjects. The cognitive function was assessed using Mini-Mental State Exam (MMSE). A significant positive associations were seen between the levels of Hcy and the intake of both tea (B = 1.15, p<0.05) and coffee (B = 2.3, p<0.05). Only age (B = -0.2, p<0.05) and tea intake (B = -0.1, p<0.05) were significantly negatively associated with MMSE scores. Only MMSE scores [0.77 (0.62-0.93); p = 0.00] and tea intake [1.7 (1.1-2.7); p = 0.01] were significantly associated with the risk of HHcy. Smoking and coffee consumption were insignificantly associated with the risk of HHcy. Homocysteine was positively associated with cognitive impairment [1.3 (1.1-1.6); p = 0.00]. Only tea intake was associated with the risk of cognitive impairment [1.8 (1.1-2.8); p = 0.00]. Finally, further studies are needed to elucidate the observed non-significant associations among Hcy levels, smoking, coffee intake and the associated cognitive impairment risk.

Key words: Cognitive function, homocysteine (Hcy), tobacco use, tea and coffee intake

INTRODUCTION
The number of elderly population aged 60 years and older is increasing rapidly in the world. It has been estimated that this population group constitutes about 10% of the world’s population in 1999 (Tucker and Buranapin, 2001). Moreover, based on information obtained from the Department of Statistics (2004) in Jordan, it has been reported that individuals aged 60 years and above constitute about 5.8 % for males and 6.4% for females. Cognitive impairment in the elderly has been a common problem worldwide (Tani et al., 2008). Previously, it has been shown that Hyperhomocysteinemia (HHcy) is a well recognized risk factor for many diseases including vascular disease (Rydeliewicz et al., 2002) and cognitive impairment in the elderly (Refsum et al., 2004). Recently, Elias et al. (2000) reported a significant inverse association between Hcy levels and cognitive function. It is believed that plasma Hcy levels are influenced by a number of factors. After vitamin concentrations, the factor more closely associated with HHcy is old age. In fact, Hcy levels are relatively stable through the first 4 decades of life and then rise sharply especially after the age of 70 (Lokk, 2003). Diaz-Arrastia (2000) reported that being male is associated with higher Hcy levels at all ages except in the very old ages. However, sex-dependent variations in Hcy levels may be attributed to the influence of sex hormones on Hcy metabolism. Coffee and tea consumption is a traditional custom in Jordan. Both beverages are considered an essential dietary constituent and are highly consumed by Jordanians. However, it has been reported that coffee consumption is positively associated with Hcy concentration (Nygard et al., 1997; Stolzenberg-Solomon et al., 1999). Conversely, many studies have shown that tea consumption (Rasmussen et al., 2000), estrogen replacement therapy (Diaz-Arrastia, 2000) and supplemental and dietary B vitamin intake (De Bree et al., 2002) are inversely associated with plasma Hcy levels. Based on information obtained from the report of the Ministry of Health (1991) in Jordan, the prevalence of smoking habit among adult male and female population was 46% and 10%, respectively. However, many studies have reported that smoking status (Nygard et al., 1997; Rasmussen et al., 2000) and physical activity (Rasmussen et al., 2000; Saw et al., 2001) are positively associated with Hcy levels. Recently, more Jordanians are adopting a sedentary lifestyle and consuming more foods that are rich in fat and carbohydrate. This is due to that fact that eating pattern and lifestyle behaviors have been changed in the last few decades. In addition, it is believed that cognitive impairment is irreversible (Diaz-Arrastia, 2000; Garcia and Zanibbi, 2004). Therefore, detection of elevated levels of Hcy and supplementation with B vitamins in
elderly population before cognitive decline is clinically apparent may be considered as an effective intervention. As in other Arab countries, information on the biochemical status of Hcy and other risk factors among Jordanians is not available. Therefore, results from the resent study will provide background information about H-Hcy and some lifestyle factors for other researchers. Overall, the aim of the present study is to explore the relationship among plasma Hcy, lifestyle factors including coffee and tea consumption, smoking and cognitive impairment risk.

MATERIALS AND METHODS
A cross-sectional design is used to investigate the association among homocysteine, lifestyle factors including coffee and tea consumption, smoking and cognitive impairment in healthy elderly subjects. Sixty three healthy elderly subjects of either sex of age 60 years and above were examined. All subjects were recruited from a Hospitality House in Amman, Jordan. Only subjects who are apparently healthy and free of neurological disease were considered eligible to participate in this study. Furthermore, subjects with a history of chronic diseases such as: renal dysfunction, proliferating disease, rheumatoid arthritis, endocrine disorders, intestinal disease and/or subjects on medications that are known to interfere with Hcy metabolism were excluded from the study. All participants completed a questionnaire about lifestyle and health. The data were collected, stored, retrieved and reported in aggregate and confidential manner. The questionnaire provided information on demographic data including age, sex and health status. Subjects were asked to respond to some questions about their lifestyle such as type of work, smoking, coffee and tea intake, alcohol use, vitamin supplement use and physical activity. A pretest for the instrument was performed on 15 subjects. Overall, signed informed consent was obtained from all subjects who were eligible to participate in the study.

Biochemical analysis: Blood samples for analysis of plasma Hcy were obtained from all subjects after an overnight fast. All blood samples were drawn in EDTA tubes for the determination of plasma homocysteine levels. Plasma was obtained by centrifuging whole blood for 15 min at 4°C within 1.5 hr after collection. Then the plasma was stored at -20°C for one month until Hcy samples were analyzed. Total plasma homocysteine was measured using a Fluorescence Polarization Immunoassay (FPIA), Abbott system (Ganj and Kafai, 2005).

Cognitive performance: The cognitive function was assessed by using the Arabic version of a 30 points Mini-Mental State Exam (MMSE) (Folstein and Folstein, 1975; Huijbregts et al., 1998). The MMSE test was performed under the supervision of an experienced neurologist as instructed by Folstein and Folstein (1975). Cognitive impairment was considered present at score of 23 and below in the MMSE test (Huijbregts et al., 1998; Tucker et al., 2005). All subjects were divided into 2 groups: group 1 (Cognitively Impaired) includes those subjects who scored 23 and below in the MMSE and group 2 (Cognitively Normal) includes those who scored above 23 point in the MMSE.

Hyperhomocysteinemia and other life style factors: Due to the variability in the reference ranges for H-Hcy as well as the absence of such references among Arabs, two criteria was used to determine H-Hcy and. First, using The National Health and Nutrition Examination Survey, 1988-1994, 1999-2000 and 2001-2002 reference ranges, H-Hcy was defined as levels of plasma Hcy above 13 μmol/L (Ganj and Kafai, 2005). Second, HHcy was defined as levels above the 75th percentile of plasma Hcy distribution of the cognitively normal subjects. Smoking habit was defined as 1) nonsmokers, 2) current smoker and 3) former smoker. Current smokers were asked to report their average number of cigarettes smoked per day. To examine the effect of the type of coffee on tHcy levels, coffee was categorized into 4 categories: 1) Arabic coffee (boiled), 2) filtered, 3) instant, 4) decaffeinated (Nygard et al., 1997). Similarly, the specific effect of each type of alcohol consumed was examined. Thus the alcohol beverages were categorized as 1) wine, 2) beer and 3) spirits. Average alcohol intake was determined by asking the participants to report the number of drinks of each type consumed per month. Finally, physical activity was categorized into 4 groups and subjects were asked to select the best-fit activity during the previous year. These categories include: 1) sedentary, 2) moderately active (walking or cycling for ≥ 4h/wk), 3) active exercise (gardenning, exercise for ≥ 4h/wk), 4) heavy training for several times a week (Nygard et al., 1997; El-Khair et al., 1999). In our sample population, all of the subjects were sedentary and non-alcohol drinkers. Hence, the influence of alcohol consumption and the level of physical activity on Hcy levels and cognitive performance could not be explored in the present study.

Statistical analysis: The statistical analyses were performed using the SPSS Graduate Pack 10.0 for Windows (1998). The group differences in cognitive impairment risk factors were examined using ANOVA for continuous variables and chi square test for categorical variables. Data was presented as means ± SEM and frequency distribution. To examine the association among homocysteine, cognitive function (dependent variables) and other lifestyle factors (independent), linear regression models were performed. Logistic regression analyses were performed to examine the
association between homocysteine and other determinants in relation to cognitive impairment risk. To examine the association among homocysteine, cognitive function and selected lifestyle factors, two models were used. All subjects were stratified into groups according to their Hcy level (Model I) and cognitive function (Model II) and coded as dummy variables. In these models, the binary variable was entered as the dependent variable and all other conventional risk factors were entered as the independent variables in the form of either continuous or dummy variables. The Relative Risk (RR) was reported as odds ratios with 95% Confidence interval (CI). All two-tailed p values of <0.05 were considered significant.

RESULTS

General characteristics of the sample population:

Demographic characteristics of the subjects are presented in Table 1. The total number of subjects was 63 in which 63.5% of participants were males and 35.5% were females. The mean age for the full cohort was 70.5±8.7 years. The age of the majority of the subjects was ranged from 60-69 years in which 75% of them were males. Approximately 49% of the participants were smokers. Smoking status differed significantly by gender in which 87% of the smokers were males (p<0.05). Similarly, the use of tobacco was significantly higher in males as compared to females (p<0.05). Coffee consumption was similar in males and females with an average of approximately 2 cups per day. All participants consumed more tea than coffee with an average of 3 cups per day. The average tea intake was significantly higher in males than that in females (p<0.05). Finally, both mean Hcy level and MMSE scores were 16.7±5.4 and 21.8±4.74 in all participants, respectively and were similar in both males and females. Among males, mean plasma Hcy was significantly higher in those who were cognitively impaired as compared to normal (p = 0.05). Similarly, cognitively impaired females had significantly higher mean plasma Hcy as compared to normal females (p = 0.003). Similarly, males with HHC had significantly lower MMS scores as compared to those without HHC (p = 0.004). Among females, mean MMS scores were significantly lower in those with HHcy as compared to those without HHcy (p = 0.009) (Fig. 1 and 2).

The associated differences in mean Hcy levels and MMS scores by selected lifestyle factors in the full cohort are presented in Table 2. Among the lifestyle factors, only coffee intake was significantly associated with Hcy levels (p<0.05). Coffee drinkers had significantly higher Hcy levels as compared to non-coffee drinkers (19.4±5.7 and 14.5±4.0, respectively; p<0.05). Mean Hcy levels did not differ significantly by tea intake and smoking status in the full cohort. On the other hand, only tea intake was significantly related to MMS scores in all subjects (p<0.05). Tea drinkers had significantly lower scores in the MMS than those who were non-tea drinkers (21.4±4.6 and 24.7±4.4, respectively; p<0.05). However, MMSE scores were non-significantly lower among coffee drinkers as compared to those who were non-coffee drinkers (20.6±4.9 and 22.8±4.3, respectively; p<0.06). Differences in mean Hcy levels and MMS scores by selected lifestyle factors in males and females are shown in Table 3. Both male and female coffee drinkers had significantly higher Hcy levels as compared to non-coffee drinkers (18.6±6.0 and 21.1±5.2, respectively; p<0.05). Among smokers and tea drinkers, mean Hcy levels did not differ between males and females as compared to those who were non-smokers and non-tea drinkers. Among females, coffee drinkers had significantly higher MMSE scores as compared to non-coffee drinkers (18.3±3.6 and 23.1±5.0, respectively; p<0.05). Conversely, male tea drinkers had significantly higher MMSE scores as compared to those who were non-tea drinkers (21.8±4.3 and 27.3±4.6, respectively; p<0.05).

![Table 1: General characteristics of the sample population](image)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Full Cohort n = 63</th>
<th>Male n = 40</th>
<th>Females n = 23</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)¹</td>
<td>70.5±8.7</td>
<td>69.3±8.9</td>
<td>72.5±8.2</td>
<td>NS</td>
</tr>
<tr>
<td>Age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69 yr</td>
<td>28 (44.4)</td>
<td>21 (75.0)</td>
<td>7 (25.0)</td>
<td>NS</td>
</tr>
<tr>
<td>70-79 yr</td>
<td>24 (38.1)</td>
<td>13 (54.2)</td>
<td>11 (45.8)</td>
<td></td>
</tr>
<tr>
<td>&gt;80 yr</td>
<td>11 (17.5)</td>
<td>6 (54.5)</td>
<td>5 (45.5)</td>
<td></td>
</tr>
<tr>
<td>Smoking n (%)</td>
<td></td>
<td></td>
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<td>0.000</td>
</tr>
<tr>
<td>Smokers</td>
<td>31 (49.2)</td>
<td>27 (67.1)</td>
<td>4 (12.9)</td>
<td></td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>3 (4.8)</td>
<td>2 (6.7)</td>
<td>1 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Non-smokers</td>
<td>29 (46)</td>
<td>11 (37.9)</td>
<td>18 (62.1)</td>
<td></td>
</tr>
<tr>
<td>Number of cigarettes¹</td>
<td>7.9±11.2</td>
<td>12.1±12.3</td>
<td>0.95±1.7</td>
<td>0.000</td>
</tr>
<tr>
<td>Tea intake (Cups/day)¹</td>
<td>3.2±1.7</td>
<td>3.6±1.5</td>
<td>2.1±1.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Coffee intake (Cups/day)¹</td>
<td>1.56±0.50</td>
<td>0.73±0.9</td>
<td>0.79±1.04</td>
<td>NS</td>
</tr>
<tr>
<td>Supplement users</td>
<td>19 (30.2)</td>
<td>8 (20)</td>
<td>11 (47.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Homocysteine levels (mmol/L)²</td>
<td>16.7±5.4</td>
<td>16.5±5.2</td>
<td>17.1±5.9</td>
<td>NS</td>
</tr>
<tr>
<td>Mini-mental state scores</td>
<td>21.8±4.74</td>
<td>22.25±4.5</td>
<td>21.26±5.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

¹Mean±SD
Predicted change in Hcy levels and MMSE scores per a unit change in the independent variables (regression coefficients) is presented in Table 3. When all predictors were entered into the model where Hcy level was the dependent variable, significant positive coefficients were seen for tea intake ($B = 1.15$, $p < 0.05$) and coffee intake ($B = 2.3$, $p < 0.05$) in the full cohort. Finally, age, gender and the use of tobacco did not predict Hcy levels in the full cohort. In contrast, when all predictors were entered into the model where MMSE scores were the dependent variable, only age ($B = -0.2$, $p < 0.05$) and tea intake ($B = -0.1$, $p < 0.05$) were significantly negatively associated with MMS scores. In this model, only a trend was observed between MMSE scores and coffee intake as shown in Table 3. Interestingly, in a separate model that examined the previous association in each gender, a significant positive association was found between MMSE scores and coffee intake among females ($B = 2.3$, $p = 0.01$) (Data not shown). Figure 3 shows predicted Hcy levels for coffee consumption from a separate model using the actual number of cups of coffee consumed per day with all other predictors held constant, however, 17% of the variations of Hcy levels can be attributed to the number of cups of coffee consumed per day. Moreover, the association between MMSE scores and tea intake was also examined in a separate model using the actual number of cups of tea consumed per day. Tea intake was negatively associated with MMSE scores in a dose response fashion in the full cohort ($B = 0.99$, $p = 0.00$) as illustrated in Fig. 4.

Results from Model 1 that examined the association among Hhcy risk, cognitive function and selected

Table 3: Homocysteine, cognitive function and Lifestyle factors by gender

<table>
<thead>
<tr>
<th>Indicators</th>
<th>MMSE*</th>
<th>Homocysteine (mmol/l)*</th>
<th>Males</th>
<th>Females</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee intake</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>21.7±5.2</td>
<td>18.3±3.8</td>
<td>18.0±6.0</td>
<td>21.1±5.2</td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>22.7±3.9</td>
<td>23.1±5.0</td>
<td>14.5±3.5</td>
<td>14.5±4.9</td>
<td></td>
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<tr>
<td>Tea intake</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Yes</td>
<td>21.8±4.3</td>
<td>20.4±5.2</td>
<td>16.7±5.3</td>
<td>17.9±6.0</td>
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<tr>
<td>No</td>
<td>27.3±4.8</td>
<td>23±5.4</td>
<td>12.7±1.0</td>
<td>14.0±5.1</td>
<td></td>
<td></td>
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<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>22.1±4.5</td>
<td>22.2±4.0</td>
<td>17±5.8</td>
<td>16.4±4.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>22.3±5.2</td>
<td>20.9±5.4</td>
<td>15.5±3.7</td>
<td>17.4±5.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Values with different letters in columns are significantly different from each other ($p < 0.05$).
The association between cognitive impairment risk and other predictors are shown in Table 5 (Model II). In the presence of all predictors, the RR for Hcy was positively significantly associated with cognitive impairment \( [1.3 (1.1-1.6); p = 0.00] \). In this Model, only tea intake was significantly associated with the risk of cognitive impairment after the adjustment of Hcy levels \([RR for tea intake: 1.8 (1.1-2.8); p = 0.00] \).

**DISCUSSION**

The relationship of Hcy concentrations in relation to cognitive impairment risk has been explored in several studies (Garcia and Zanibbi, 2004; Lei Feng et al., 2006). Recent studies indicate that certain lifestyle factors can influence Hcy levels and therefore, play an important role in the protection of cognitive function. Our findings demonstrate the associations among plasma Hcy levels, smoking, coffee and tea consumption as well as the relationship between these predictors and cognitive impairment risk in older Jordanian subjects. Information on nutrition and health status of the Jordanian older population is relatively scanty. Data from a previous work have illustrated for the first time that HHcy is highly prevalent and independently associated with coronary heart disease in Arab Jordanian sample (Mashal and Odeh, 2004). In the present study, mean Hcy levels were relatively high and above the established reference range of normal Hcy levels.

Besides genetics and nutritional deficiencies of B vitamins, Hcy levels can be influenced by other risk and environmental factors including age, gender, smoking, consumption of coffee, tea and alcohol and physical activity (Jacques et al., 2001). These interrelations were
illustrated in the present study. However, Hcy levels were not associated with age and gender. These findings are inconsistent with some previous reports that indicated a positive relationship between age and Hcy levels, which might be related to decreased levels of B vitamins in older subjects (Moustapha and Robinson, 1999). It has also been suggested that deterioration of kidney function (Schnee et al., 2000) and decreased activity of enzymes involved in Hcy metabolism may also account for the age-Hcy association (Moustapha and Robinson, 1999). Gender differences in Hcy levels may be related to hormonal factors and/or muscle mass (Nygard et al., 1997). In a case-control design that involved 100 patients known to have CHD of either sex and 110 healthy controls of age ≤ 60 y, Mashal and Odeh (2004) showed that Hcy levels were significantly positively associated with age in the full cohort and in cases but not controls and were higher in males than in females in both groups. The absence of sex-related differences in Hcy levels in the present study could be explained by the fact that the majority of the subjects were males and that both gender were of similar age. Further, these results are in line with the findings from many clinical trials that reported a minimum effect for gender on blood Hcy concentration in the later life (Bates et al., 1987; Diaz-Arrastia, 2000; Morris et al., 2000; Refsum et al., 2006).

Likewise, the weak effect of age on Hcy levels in elderly population were illustrated in many studies (Budge et al., 2002). Results from studies investigating the effects of the consumption of these beverages on health outcomes are contradicted. Recently, in a prospective cohort study that involved 13,988 Japanese participants aged ≥85 years, the association between tea and coffee consumption and incident functional disability including stroke, cognitive impairment and osteoporosis among elderly was examined. The authors reported a strong negative dose-response association between green tea consumption and incident functional disability in the elderly. In contrast, black tea and coffee consumption were not associated with incident functional disability (Tomata et al., 2012). Moreover, the association between tea and coffee consumption and cognitive impairment was examined Among 2501 community-living Chinese adults aged ≥55 y. Total tea intake was significantly associated with a lower prevalence of cognitive impairment, independent of other risk factors. The OR of cognitive impairment for high tea intake was 0.37 (95% CI: 0.14-0.98; p = 0.001). The authors concluded that the cognitive protective effect of tea may be related to the synergistic effect of several chemicals of its component including caffeine, polyphenols and phytochemicals. However, coffee consumption was not associated with cognitive function in the previous study (Tze-Pin Ng et al., 2008). In fact, data from human studies relating tea consumption to overall health are conflicting. These contradictions are due to the presence of certain confounders such as socioeconomic and lifestyle factors and lack of validated criteria to measure tea preparation and intake as well (Mckay and Blumberg, 2002).

Surprisingly, data from the present study showed that tea drinkers had significantly lower scores in MMSE as compared to nondrinkers (p<0.05). Similarly, males but not females had significantly lower scores in MMS as compared to those who were nondrinkers. This gender difference can be explained by the difference observed in mean cups of tea consumed per day by males, which was significantly higher than that consumed by females (3.9±1.5 and 2.1±1.6, respectively; p = 0.00). Moreover, daily tea intake was significantly negatively associated with cognitive performance (β = -0.10, p = 0.00). Controlling for Hcy levels, the relative risk for cognitive impairment was increased by 1.8 fold as tea intake was increased [95% CI (1.1-2.8), p = 0.00]. Although few studies have investigated the association between tea consumption and Hcy levels, it has been indicated that tea intake is inversely associated with Hcy levels (Stolzenberg-Solon et al., 1999). In this context, our data showed that tea consumption was significantly positively associated with Hcy levels (β = 1.15, p<0.05).

In addition, tea intake was significantly positively associated with HHcy after adjustment for MMSE scores was made [1.7, 95% CI (1.1-2.7), p = 0.01]. These results may explain the observed positive association between tea intake and cognitive impairment risk in our sample. Interestingly, Hcy levels were significantly higher in subjects of both gender who were cognitively impaired as compared to normal in the present sample population. Results from a cross-sectional study that involved 205 older subjects are in line with our observations. The authors reported that HHcy was significantly inversely related to MMSE scores (Tassino et al., 2009).

In a crossover design, Urgent et al. (2000) reported that coffee consumption of 1 L/d significantly increased Hcy levels by 20% in healthy volunteers. El-Khairy et al. (1999) indicated that the positive association between Hcy levels and coffee consumption may be explained by the effect of caffeine on vitamin B6 status and on the glomerular filtration rate of kidneys. In this context, although Hcy levels were significantly higher in coffee drinkers of both gender and significantly positively associated with Hcy levels, the present study did not show any associations between consumption of coffee and either HHcy or cognitive impairment risk. Indeed, the exact mechanism by which tea intake influences Hcy levels is not yet clear. It has been suggested that folate content of tea (20 μg/150 ml) may explain the inverse influence on tHcy levels by increasing the remethylation of tHcy into methionine (Jacques et al., 2001; Olthof et al., 2001). It has been indicated that the
recent decline in coffee consumption is accompanied by an increase in tea consumption (Harland, 2000). In fact, tea consumption is more prevalent among Jordanians as the beverage is a component of 2 major meals including breakfast and dinner and it is less expensive than coffee. However, in our sample population, approximately 86% of the subjects were tea drinkers (Data not shown). Therefore, the predominance of tea consumption in our study may mask the association among coffee intake, Hcy and cognitive impairment risk. The mechanism by which tea and coffee influences Hcy levels and consequently affects cognitive impairment risk is contradicted. Besides caffeine, coffee and tea contain other compounds including tannin, chlorogenic acid and phytate (Harland, 2000). As indicated by Olthof and colleagues (2001), ingestion of chlorogenic acid increased Hcy levels by 12% and decreased plasma folate by 8%, whereas ingestion of black tea increased Hcy levels but did not affect folate concentrations. Hence, the authors suggested that Hcy-raising effect of black tea could be explained by increased methylation reactions involved in polyphenols metabolism rather than the folate theory.

Jacques and colleagues (2001) reported a significant positive association between Hcy levels and cigarettes smoking. Results from the present study are inconsistent with these results. Smoking was not associated with either Hcy or cognitive impairment risk in the present study. It has been suggested that smoking is associated with many factors, which may influence Hcy levels including changes in plasma thiol redox status, as well as lower plasma levels of folate, vitamins B₆ and B₁₂ (Moghadisian et al., 1997; Schneede et al., 2000). Vitamin B₁₂ status was not determined in this study; hence, the exact mechanism by which smoking exerts its effect on Hcy levels could not be explored. Tani et al. (2008) reported that vitamin B₁₂ is involved in the development of central nervous system. Higher Dietary intake of vitamin B₁₂ contributes to decreased incidence of cognitive impairment in the elderly. It has been proposed that long-term dietary pattern is associated with a central nervous system which is more resistant to neurodegenerative processes that leads to cognitive impairment. In addition, vitamin B₁₂ may enable the synthesis of sufficient neurotransmitters (serotonin, dopamine and norepinephrine) that preserve the cognitive function (Tani et al., 2008). These observations might provide another explanation by which smoking may be involved as a cognitive impairment risk factor.

In conclusion, we found that in a selected healthy Jordanian older adults, there were a significant positive association between tea intake and both HHcy and cognitive impairment risk. Coffee consumption and smoking were not associated with either HHcy or cognitive impairment risk. The available data does not yet provide adequate evidence of an effect of vitamin B₁₂ or B₁₂ or folic acid supplementation, alone or in combination, on cognitive function testing in people with either normal or impaired cognitive function (Balk et al., 2007). Large randomized trials are required to evaluate the efficacy of vitamin supplementation for treatment of HHcy and prevention of cognitive impairment in older people (Smith and Refsum, 2009). In the absence of such evidence, adequate folate and vitamin B₁₂ intake from diet or by supplementation should be considered as a protective measure in the prevention of cognitive impairment, particularly in high risk individuals.

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