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Abdul Abyad

Original Contribution / Clinical Investigation

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From the Editor

A paper from Turkey looked at weight and antisocial personality disorder. The authors took consecutive check up patients between the ages of 18 and 70 years to be able to catch cases with ASPD and to avoid debility induced weight loss in elders. Patients with a history of eating disorders in their lives and patients with devastating illnesses were excluded to avoid their possible effects on weight. The study included 2,428 cases, the prevalences of ASPD were 8.4%, 13.7%, 14.9%, and 11.5% in the underweight, normal weight, overweight, and obesity groups, respectively, and there was no significant difference between them (p>0.05 for all). The authors concluded that ASPD may be a common psychopathology with terrible consequences on population, even on physicians and other patients.

A paper from Egypt looked at the use of Mini Mental State Examination and Clock-drawing Test for screening of patients with Dementia. The early and quick identification of dementia is desirable to improve overall care to affected persons in developing countries. The study was designed to evaluate patients with varied types and severity of dementia diagnosed using the Clinical Dementia Rating (CDR) scale. All patients completed the MMSE and simplified CDT. The study included 197 patients with an age range of 43-79 years. Total MMSE score of enrolled patients was significantly lower compared to control subjects with non-significant difference between varied diagnoses. Total CDT scores were significantly lower in patients compared to controls with significantly lower scores in the PDD group compared to the AD group. The authors concluded that application of both MMSE and CDT could identify persons with the least cognitive affection, but could not effectively and definitely discriminate between different types of dementia.

A paper from the USA looked at the Relationship of Age and Gender to “Diabetes Distress” and Postprandial Hyperglycemia: Impact of a Multidisciplinary Supportive, Dietary, and Pharmacologic Approach. Dietary habits associated with DD can affect postprandial hyperglycemia (PPH). This study explored the association between age, gender, DD and PPH, and the impact of a short-term multidisciplinary intervention. Therefore in conclusion the, associations between DD and PPH vary by age and gender, being highest in younger women and lowest in older men, and respond well to multi-pronged management strategy. Research into the dynamics of psychological stressors and meal-related glycemia could help in optimizing individualized treatments in patients with diabetes.
Abstract

**Objectives:** The high prevalence of posttraumatic stress disorder (PTSD) among Kuwaiti First Gulf War veterans (FGWV) necessitated the search for its biological correlates. We assessed PTSD, depression and anxiety among a sample of Kuwaiti FGWV, and correlated thyroid function levels with psychopathological indices.

**Design:** cross-sectional

**Setting:** Kuwait office for FGWV in 2003

**Subjects:** 123 registered injured FGWV (121m)

**Main outcome measures:** Prevalence of PTSD and correlation with blood levels of fT3, fT4 and TSH

**Results:** Twelve years after the FGW, 37(30.1% of 123) had PTSD by DSM-IV criteria. When grouped by clinical thyroid status using thyroid levels, 4(3.3% males) had clinically pathological thyroid conditions (3 with subclinical hypothyroidism, 1 with biochemical hyperthyroidism), compared with 1% of Kuwaiti males in the general population. Among those with PTSD, fT3 was negatively correlated with age (r = -0.20, p= 0.025). TSH level was significantly correlated with positive symptom distress index (r = 0.20, p=0.004) and negatively with PTSD avoidance scores (r = -0.41, p=0.011). Anxiety/depression co-morbidity tended to increase the values of fT3 and fT4.

**Conclusion:** These findings widen the cross-cultural base of evidence of possible enduring thyroid system alterations in chronic combat-related PTSD, and call for sustained clinical interventions for veterans.

**Key words:** PTSD, Thyroid Function, Kuwait, Gulf war, Veterans
Introduction
It is important to study the biological correlates of posttraumatic stress disorder (PTSD) among Kuwaiti First Gulf War Veterans (FGWV) because of the magnitude of the disorder in this group. Studies of representative samples of Kuwaiti FGWV reported that 31.5% of the men and 28.4% of their wives fulfilled DSM-IV criteria for PTSD, while 14% to 17% of their children had abnormal test scores for anxiety, depression and deviant behaviour (1-3).

The first association between traumatic stress and thyroid function (TF) abnormalities is said to have been reported in 1825 (4). Endocrine changes in response to stress depend on various factors, in particular, the duration and the type of stressor (5). The results of studies on stress-induced changes in the hormones of the hypothalamic-pituitary-thyroid (HPT) axis reported that thyroid stimulation hormone (TSH) levels seem to rise in acute stress and fall in chronic stress (5). In the standard thyroid releasing hormone (TRH) stimulation test, an exaggerated TSH response has been reported in PTSD patients in contrast to the blunted TSH response observed in depression (6). In acute stress, reduction of both total and free T4 (fT4) and of total and free T3 (fT3) was observed, as opposed to increases in TSH (7).

Olff et al examined the levels of hypothalamic-pituitary-adrenal (HPA) and HPT-axes hormones in 39 civilians with chronic PTSD and 44 healthy volunteers (8). Their results showed that individuals with PTSD had significantly lower plasma cortisol, prolactin and TSH levels compared with the control group. However the TSH results emerged after controlling for background variables. Haviland et al studied 22 adolescent girls with PTSD due to sexual abuse shortly after the trauma; and found that fT3 and total T3 (tT3) were correlated negatively with PTSD, indicating that lower fT3 and tT3 were associated with an increased prevalence of PTSD (9).

A significant correlation (r = -0.50, p < .05) was found between fT3 and PTSD total score. Other studies reported a positive relationship (i.e. elevated T3 levels) with PTSD in combat veterans (10). Wang et al argued that different adaptive survival strategies in the civilian and combat environments could explain the discrepancy of these results, and there could be stages in responding to overwhelming stress in PTSD in which thyroid hormones are first suppressed and then become elevated (11). Osuch et al observed lower serum T4 in patients with chronic PTSD that was raised with treatment involving repetitive magnetic stimulation combined with exposure therapy (12). Bauer et al found that TSH and all thyroid hormone concentrations were significantly reduced in patients with prolonged stress with PTSD, which they interpreted as a reflection of severe chronic stress rather than specific psychiatric disorders (5).

PTSD has been associated with a high prevalence of comorbidity of psychiatric disorders, up to 80% (13). With this high rate of comorbidity, it may be expected that controlling for these comorbid disorders in interpreting results of TF in chronic PTSD findings may affect the results. In a study of World War II veterans that involved the exclusion of those with psychoses, organic mental disorders and substance abuse disorders, it was found that those with PTSD had elevated tT3 and fT3, with no significant changes in T4 or TSH (10).

In a review of the literature, we found no published studies that controlled for the presence of comorbid depression, generalised anxiety disorder, panic attacks, and obsessive compulsive disorder in assessing the relationship of TF with combat-related PTSD. It is important to control for the presence of these disorders because they belong to the same diagnostic group of mood and anxiety disorders, and are the conditions most commonly comorbid with PTSD. Our study was designed to investigate this association. The specific objectives of the study were to: (i) assess PTSD, depression and anxiety among a sample of injured Kuwaiti FGWV (ii) assess thyroid function levels (IT3, IT4 and TSH) among the veterans, and correlate thyroid function with psychopathological indices. We hypothesized that the presence of these disorders may explain the observed changes in thyroid functions associated with chronic PTSD.

Methods
The subjects in this study were clinically examined including physical examination and face-to-face interviews by one of us, using standard psychological test instruments. In addition, blood was taken for thyroid function tests.

Subjects and setting: After the FGW in 1991, the Kuwaiti government set up a Social Development Office (SDO) to care for injured war veterans. Subjects for this study were recruited from that office. In 1998, all the registered veterans in SDO (N=234) were approached and agreed to participate in a clinical study of PTSD. This report concerns 123 (41.9%) subjects who were available for a biological study of PTSD in 2003.

Instruments: In 2003, they were interviewed with the following instruments: the Clinician Administered PTSD Scale (CAPS) (14), to quantify the severity of PTSD, Symptoms Check List-90R (SCL-90R) to ascertain psychiatric comorbidity (15), and the Composite International Diagnostic Interview (CIDI), World Health Organization (16). Scoring and interpretation of SCL-90R results was done using Global Severity Index (GSI) which shows the level or severity of disorder, and Positive Symptom Distress Index (PSDI) which measures the number of symptoms that are reported positive by the veterans. A psychologist was trained to apply the CIDI. The interviews with the CAPS and SCL-90R were done by a psychiatrist. The severity of physical injury was assessed by giving a score based on number, site and degree of disability using the Kuwait “Wergild” rule, which the government uses to quantify
disability for compensation. Injury scores based on this instrument range from mild (<100), moderate (160-230) to severe (>230). In order to qualify for full compensation for physical injury, a subject needs to score a minimum of 100 on that scale. Life Events Scale (LES) includes 46 life events that veterans may have gone through one year prior to the interview; a score of ≥ 300 is significant (17).

**Procedure:** The protocol for this study was approved by the research and ethical committees of Kuwait University and University of Adelaide, Australia (supervisor's center). Participation was voluntary and the subjects did not receive any monetary rewards for participating in the study. Veterans were given the choice to withdraw at any time during the study. A written informed consent was taken from each participant.

The thyroid hormones measured were fT3, fT4 and TSH levels. Blood samples (5 ml) in red-topped (untreated) vacuum tubes for thyroid hormones were collected at 11 am from the veterans. The analysis was performed at the main endocrinology laboratory at Mubarak Al-Kabeer Teaching Hospital, Kuwait University, Kuwait. To reduce the possibility that anxiety related to psychometric and medical assessments could affect thyroid levels, thyroid samples were obtained immediately after signing the informed consent form. Thereafter, the psychiatric interviews and physical examination were performed. The blood samples were then sent to the laboratory where they were centrifuged for 2 minutes and stored at -20°C. Thyroid hormones were measured using direct labeled antibody competitive radioimmunoassay technique. Using the criteria of Al-Awadhi et al's (18) study of Kuwaiti general population, subjects were classified into the following five thyroid groups: (a) euthyroid overt hypothyroidism: low FT4 ( <9.2 pmol/l) and normal TSH; and (e) biochemical hyperthyroidism: normal or high FT4 (> 23.8 pmol/l) and low TSH (< 0.23 U/l).

**Statistical Methods:** Statistical analysis was done using SPSS version 15. Since the psychopathological scale scores (PTSD and SCL-90R) were fairly normally distributed, we used parametric statistics (t-tests) to assess differences in subscale scores between groups (PTSD vs. no PTSD). For the analyses involving thyroid function tests, however, we used non-parametric statistics (Mann-Whitney U-test and Spearman’s correlation) because the data were not normally distributed. Chi square tests were used to analyze prevalence data and other categorical variables. PTSD severity was calculated by adding the sum of frequency multiplied by intensity of the 17-item CAPS; the maximum total score is 136, and was classified as mild-moderate score (68-102) and severe PTSD score (103-136) (14).

**Results**

There were two female (1.6%), and 121 (98.4%) male veterans. Kuwaiti females joined the resistance during the FGW. Subjects were aged 42.0 (SD 9.0) years, range 28-72 years. Judging by the injury score, 61 (50%) had mild, 31 (25%) had moderate and 31(25%) had severe injury score, with a mean score of 130 (SD 104). The CAPS PTSD severity score of 101.16 (SD 41.5) indicated that those diagnosed with PTSD had moderately intense symptomatic experience (Table 1 - next page).

1. **PTSD outcome and differences in TF levels:**

   The point prevalence rate of PTSD was 37 (30.1%). Table 1 shows that, subjects with PTSD had significantly higher scores for anxiety, depression and global severity index than those without PTSD (P < 0.001). An examination of the frequency distribution of the TFs showed that, while the fT3 levels (3.5-6.4 pmol/l) were largely within the normal range for the Kuwait general population (3.95-6.8 pmol/l), 3 (0.9%) subjects had high fT4 and 2 (0.6%) had high TSH outside of the range for the Kuwait general population (Table 1). Using MWU tests, there was no significant difference in TF levels between those with PTSD and those without PTSD (P > 0.05).

   However, when the subjects were grouped by clinical biochemical thyroid status, it was found that the only subjects with pathology by biochemical measures were three men (N=3 or 2.5% of men) with subclinical hypothyroidism, and one man (N=1 or 0.85 men%) with biochemical hyperthyroidism (Table 2 - next page).

2. **Comorbidities, TF levels and PTSD (Table 3 - next page)**

   For the total sample (n = 123), in correlation analysis, using Spearman’s coefficient, the fT4 level was not significantly correlated with any of the psychopathological measures. However the fT3 level was negatively correlated with PSDI (r = -0.192, p = 0.033). Also, fT3 level was negatively correlated with age (r = -0.20, p = 0.025) and PSDI (r = -0.192, p = 0.033); and TSH level was significantly correlated with PSDI (r = 0.26, p = 0.004). But TSH’s correlation with SCL-90 depression scores (p=0.08), SCL-90 somatization scores (p = 0.056), and GSI (p = 0.09) just failed to reach significance. TSH was significantly correlated with PSDI (r = 0.35, p = 0.035). Among those with PTSD, fT3 was negatively correlated with age (r = -0.31; P < 0.18), while TSH was negatively correlated with PTSD avoidance score (r = -0.41; P < 0.01), and positively correlated with SCL-90 depression score (r = 0.35; P < 0.035). Among those without PTSD, fT3 was negatively correlated only with PSDI (r = 0.27, p = 0.04), while TSH was correlated with PSDI (r=0.22, p=0.04) and somatization (r=0.22, p=0.045) (Table 3).

   Using the CIDI interview, we found that the six veterans with major depressive disorder (MDD) also had PTSD. However, the fT3 levels of five were in the upper range of normal (4.9-6.3) while one subject had value (3.8) that was just below normal. With regard to fT4, the depressed
Table 1: Comparison of mean psychopathological scores and mean thyroid function values by PTSD status

<table>
<thead>
<tr>
<th>Variable</th>
<th>No PTSD N = 86 (69.9%) Mean(SD)</th>
<th>PTSD N = 37 (30.1%) Mean(SD)</th>
<th>T or MWU Statistic</th>
<th>P</th>
<th>All subjects N = 123 (SD) Actual range for our sample</th>
<th>Kuwait reference range for thyroid functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>43.28 (9.1)</td>
<td>39.11 (8.24)</td>
<td>5.739</td>
<td>0.018</td>
<td>42.0 (9)</td>
<td>28-72</td>
</tr>
<tr>
<td>Injury Score</td>
<td>129.1 (103.4)</td>
<td>132.0 (107.3)</td>
<td>0.019</td>
<td>0.892</td>
<td>130 (104.2)</td>
<td>10-460</td>
</tr>
<tr>
<td>LES</td>
<td>225.3 (152.36)</td>
<td>380.5 (201.6)</td>
<td>21.9</td>
<td>0.001</td>
<td>272 (182.4)</td>
<td>0-777</td>
</tr>
<tr>
<td>FT3 pmol/l</td>
<td>4.98 (0.581)</td>
<td>4.84 (0.635)</td>
<td>1.319</td>
<td>0.253</td>
<td>4.9 (0.59)</td>
<td>3.6-6.4</td>
</tr>
<tr>
<td>FT4 pmol/l</td>
<td>15.52 (2.55)</td>
<td>15.50 (2.53)</td>
<td>0.003</td>
<td>0.955</td>
<td>15.62 (2.54)</td>
<td>9.5-25</td>
</tr>
<tr>
<td>TSH UI</td>
<td>1.39 (1.1)</td>
<td>1.3 (0.59)</td>
<td>0.202</td>
<td>0.654</td>
<td>1.36 (0.97)</td>
<td>0.1-8.8</td>
</tr>
<tr>
<td>Depression SCL-90</td>
<td>1.11 (0.322)</td>
<td>1.59 (0.49)</td>
<td>40.33</td>
<td>0.001</td>
<td>0.83 (0.84)</td>
<td>0-3.62</td>
</tr>
<tr>
<td>Anxiety SCL-90</td>
<td>1.11 (0.322)</td>
<td>1.43 (0.50)</td>
<td>17.46</td>
<td>0.001</td>
<td>0.69 (0.86)</td>
<td>0-3.6</td>
</tr>
<tr>
<td>PSDI SCL-90</td>
<td>22.51 (20.59)</td>
<td>49.16 (27.86)</td>
<td>34.73</td>
<td>0.001</td>
<td>0.69 (0.86)</td>
<td>1-3.5</td>
</tr>
<tr>
<td>GSI SCL-90</td>
<td>0.479 (0.49)</td>
<td>1.26 (0.95)</td>
<td>36.12</td>
<td>0.001</td>
<td>0.716 (0.755)</td>
<td>0-3.43</td>
</tr>
<tr>
<td>Intrusions CAPS</td>
<td>4.82 (8.08)</td>
<td>24.4 (15.07)</td>
<td>88.1</td>
<td>0.001</td>
<td>10.7 (13.9)</td>
<td>0-54</td>
</tr>
<tr>
<td>Avoidance CAPS</td>
<td>10.58 (13.2)</td>
<td>39.1 (16.86)</td>
<td>101.1</td>
<td>0.001</td>
<td>19.1 (19.4)</td>
<td>0-777</td>
</tr>
<tr>
<td>Arousal CAPS</td>
<td>10.25 (10.41)</td>
<td>37.56 (16.26)</td>
<td>124.58</td>
<td>0.001</td>
<td>18.47 (17.6)</td>
<td>0-72</td>
</tr>
<tr>
<td>Total PTSD Severity score</td>
<td>25.66 (22.69)</td>
<td>101.16 (41.53)</td>
<td>268.5</td>
<td>0.001</td>
<td>48.37 (46.57)</td>
<td>0-136</td>
</tr>
</tbody>
</table>

LES: Life Events Scale; SCL-90: Symptoms Checklist-90; PSDI: positive severity distress Index SCL-90; GSI: global severity index SCL-90; CAPS: Clinical Administered PTSD Scale; PTSD: posttraumatic stress disorder; T: t statistic; MWU: Mann-Whitney U statistic; p: level of statistical significance

Table 2: Prevalence of clinical biochemical thyroid groups

<table>
<thead>
<tr>
<th>Thyroid groups</th>
<th>Al-Awadhi et al (18) (Kuwait Population) N = 200</th>
<th>Kuwait injured male veterans: N = 118</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subclinical hypothyroidism</td>
<td>2 (1%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Overt hypothyroidism</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Euthyroid sick syndrome</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Biochemical hyperthyroidism</td>
<td>0</td>
<td>1 (0.85%)</td>
</tr>
<tr>
<td>Normal thyroid function</td>
<td>198 (99%)</td>
<td>114 (96.6%)</td>
</tr>
</tbody>
</table>

Table 3: Spearman’s coefficient: Thyroid functions and age, PSI, PSDI, depression, GSI, somatization and avoidance.

<table>
<thead>
<tr>
<th>Variables</th>
<th>All veterans N = 123</th>
<th>No PTSD N = 86</th>
<th>PTSD N = 37</th>
</tr>
</thead>
<tbody>
<tr>
<td>ft3 vs Age</td>
<td>-0.20</td>
<td>NS</td>
<td>-0.31</td>
</tr>
<tr>
<td>ft3 vs PSI</td>
<td>-0.192</td>
<td>0.033</td>
<td>NS</td>
</tr>
<tr>
<td>ft4</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>TSH vs Depression</td>
<td>0.157</td>
<td>0.08</td>
<td>NS</td>
</tr>
<tr>
<td>TSH vs PSDI</td>
<td>0.259</td>
<td>0.004</td>
<td>NS</td>
</tr>
<tr>
<td>TSH vs Somatization</td>
<td>0.17</td>
<td>0.056</td>
<td>NS</td>
</tr>
<tr>
<td>TSH vs GSI</td>
<td>0.153</td>
<td>0.09</td>
<td>NS</td>
</tr>
<tr>
<td>TSH vs Avoidance</td>
<td>NS</td>
<td>NS</td>
<td>-0.41</td>
</tr>
</tbody>
</table>

TSH: Thyroid Stimulating Hormone, PSDI: positive severity distress Index SCL-90, GSI: global severity index SCL-90. R: Rho correlation coefficient, P: p-value significance, NS: not significant
subject with low fT3 also had low fT4. The TSH values of the subjects with depression were all within the Kuwait reference range. Using the CIDI interview, four subjects who had generalized anxiety disorder, also had PTSD. Of these, four subjects, three (75 %) had fT3 levels above the group mean (i.e., >= 4.9 pmol/l), while another 3 (75 %) had fT4 levels above the group mean (i.e., >= 15.5 pmol/l).

Discussion

We interviewed 123 injured Kuwaiti FG WV using standard instruments, and investigated the association of TF (fT3, fT4 and TSH) with PTSD among them. In particular, we assessed the contribution of anxiety/depression co-morbidity to TF levels among subjects with PTSD. We found that 12 years after the war, 37 (30.1%) had PTSD by DSM-IV criteria. Although the TF levels were generally within the normal range for the Kuwaiti general population (18), the mean scores were mostly at the higher end of the normal range, especially for subjects with co-morbid anxiety and depression (10,13). Also, the subjects with abnormal thyroid values were those who had had PTSD.

1. Differences in TF levels that are related to PTSD outcome

In line with the majority of the literature, the TF values of our subjects were mostly within the reference range of the general population (19-21), although there are a few reports of lower TSH levels in chronic PTSD (5,8). However, the veterans with abnormal TF levels were those who had ever had PTSD, and this seemed to be particularly related to the avoidance score (9).

There are conflicting reports in the literature on this issue. Bauer et al, in a study of a sample of East German refugees found low levels of TF in chronic PTSD patients, which was explained as an adaptation toward conservation/withdrawal and a resetting of the metabolic system toward conservation, and anabolism (5). While Mason et al found no significant difference in total T4 (fT4) level observed over time, there was a persistent moderate elevation of T4 levels which was attributed to the greater PTSD symptom severity (4). In another report, Mason’s group found that total T3 (fT3) in the PTSD group was significantly elevated (22). They attributed this finding to “episodic fluctuation” in fT4, possibly associated with the noted fluctuation in PTSD symptoms (22).

2. Relationship of TF levels with co-morbidity among those with PTSD

In only a few of our subjects, the presence of anxiety/depression comorbidity was associated with fT3 and fT4 levels above the group mean. There are conflicting reports in the literature on this issue. Although Friedman et al (23) found that comorbid depression had no impact on tT3, Goenjian et al (24) reported a positive correlation of depressive symptoms with TSH. These differences could be attributed to methodology, age of subjects, duration of PTSD, severity, and the presence of other factors such as nicotine or alcohol use disorders.

Some of the literature suggested that the presence of comorbidity was an indication of greater severity of psychic distress, which could further exacerbate the condition of an already distressed thyroid state (5).

Limitations of the study:

The major limitation of the study is the relatively small sample size. Furthermore, only injured veterans were studied, and there was no control group of veterans without injury. However, we studied a national population of injured veterans in a non-compensation setting, our sample size was similar to those of many reports in the literature, and we tried to relate TF levels with anxiety/depression co-morbidity ascertained in a standard manner.

Conclusion

Within the limitations of the study, the findings widen the cross-cultural base of evidence of possible enduring thyroid system alterations in chronic combat - related PTSD, and call for sustained clinical interventions for veterans.

References

The use of Mini Mental State Examination and Clock-drawing Test for screening of patients with Dementia

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Abstract

Introduction: The early and quick identification of dementia is desirable to improve overall care to affected persons in developing countries. The aim of this study is to evaluate the discriminative ability of the Mini Mental State Examination (MMSE) and Clock Drawing Test (CDT) in differentiating demented patients from controls and also for differentiation between different types of dementia.

Patients and Methods: The study was designed to evaluate patients with varied types and severity of dementia diagnosed using the Clinical Dementia Rating (CDR) scale. All patients completed the MMSE and simplified CDT.

Results: The study included 197 patients with an age range of 43-79 years. Fifty-one patients (25.9%) were diagnosed with Alzheimer dementia (AD), 37 patients (18.8%) with Vascular (VD), 23 patients (11.7%) with Parkinson’s disease dementia (PDD) and 86 patients (43.6%) with other variants of dementia. Total MMSE score of enrolled patients was significantly lower compared to control subjects with non-significant difference between varied diagnoses. Total CDT scores were significantly lower in patients compared to controls with significantly lower scores in the PDD group compared to AD group. Patients who had AD showed non-significantly higher CDT scores compared to patients who had vascular and other types of dementia.

Conclusion: Application of both MMSE and CDT could identify persons with the least cognitive affection, but could not effectively and definitely discriminate between different types of dementia.

Keywords: Dementia, Mini Mental State Examination score, Clock-drawing test

Introduction

Dementia is a clinical syndrome whose main element is memory impairment. Dementia is due to Alzheimer’s disease in more than 75% of cases. Alzheimer’s disease, on the other hand, is a neuropathological entity that is characterized by a protracted preclinical phase followed by the onset of slowly progressive dementia. About 60% of demented patients manifest the typical pathological findings of Alzheimer’s disease, amyloid deposits and neurofibrillary tangles, without any other abnormalities in the brain, while a further 15% have these findings accompanied by brain damage of vascular origin. Dementia due to vascular lesions alone accounts for fewer than 15% of cases. Lewy-body dementia that is usually accompanied by Parkinsonism and marked fluctuations of consciousness and frontotemporal lobar degeneration (FTLD) each account for about 5% of cases of dementia. According to epidemiological data, dementia is secondary to another disease in fewer than 5% of cases; causes in this category include endocrine disorders such as hypothyroidism and hyperparathyroidism (1, 2).

Age remains the single most important risk factor for developing dementia. Epidemiological studies have shown that dementia affects one in twelve persons over age 65 and one in three over age 90. Beyond age 65, the prevalence of dementia doubles for every 5 years of life; early-onset dementia is encountered especially in those susceptible or harbouring predisposing factors, or who have developed any type of central affections (3, 4). Considering the progressive aging of the general population, increasing prevalence of early-onset dementia,
and increasing percentage of literacy and weak medical knowledge about symptoms of dementia, screening tests of susceptible persons assume significance. Neuropsychometric assessment seems to be the best method to screen individuals, however, the lack of standardisation of screening tools has to be recognised as a major issue in the estimation of the true burden. Standardisation might not be readily achieved because of diversity of language, culture, and levels of literacy. In certain communities, more than 80% of elderly people do not read or write. The Mini Mental State Examination (MMSE) has been translated into many languages and its use as an initial screening tool was settled (5, 6).

The Clock Drawing Test (CDT) has been extolled as an inexpensive, fast, “non-threatening” and easily administered measure of cognitive function, especially in the elderly. CDT is a multifaceted and multidimensional measure test thought to test visuoconstructive and visuospatial skills, symbolic and graphomotor representation, auditory language skills, hemi-attention, semantic memory, conceptual abilities, and executive function including organization, planning, and parallel processing (7, 8).

The current prospective study aimed to evaluate the discriminative ability of MMSE and CDT for differentiation of demented patients from controls and for differentiation between types of dementia.

Patients and Methods
This prospective study was conducted at the Neurology Department, King Fahd Hospital Hufof, Saudi Arabia from June 2007 to June 2011. All dementia patients with varied types and severity attending the Neurology outpatient clinic were included in the study. Patients were diagnosed with regard to type and severity of dementia using the Clinical Dementia Rating (CDR) scale (9). All patients underwent routine laboratory investigations including complete blood count, random blood glucose levels, renal function and liver function tests and thyroid hormone profile. Other investigations like CT or MR imaging were done according to need.

All patients underwent evaluation of the following demographic and social variables: age assessment including 5-year age grouping, gender, marital status, and level of education (illiterate or educated), occupation and living arrangements. Smoking status was categorized as “non-smoker,” “ex-smoker,” and “current smoker.” General health status was evaluated with emphasis on past and present history of chronic diseases especially cardiac disease, cerebrovascular diseases, Parkinson’s disease, diabetes mellitus and cancer.

All patients were assessed for neuropsychiatric manifestations including presence of signs of extra-pyramidal, pyramidal, cerebellar affection. Presence of paranoid or other delusional ideation, hallucinations, psychomotor activity disturbances, aggressiveness or affective disturbances was assessed. All clinical and radiological data were evaluated for categorization of dementia patients according to type of dementia.

All patients completed a Mini Mental State Examination; total and sub-scores were calculated and the final score determined according to the guidelines for the standardized MMSE (10, 11). Clock-drawing test (CDT): to minimize the effect of education a simple scoring system (12) was used and all patients were allowed see a large-sized wall clock prior to drawing and turn away from it to start drawing. The following three items were evaluated: Correctly drawn clock shape, all numbers in the correct position and hands of the clock set to the correct time, a score of 1 was assigned for each of these items; thus, the score could range from 0 (all items incorrect) to 3 (all items correct). The presence of bizarre drawings was scored 0 and 1 otherwise. Therefore, final possible scores ranged between 0 (the worst) and 4 (the best).

The study also included 30 control subjects for evaluation of results of MMSE and CDT. Age-matched controls were selected from patients admitted to General Surgery Department for minor surgical procedures with CDR rate ranging between 0 and 0.5 and were neurologically free.

Statistical analysis
Obtained data were presented as mean±SD and ranges. Results were analyzed using Wilcoxon ranked test for unrelated data (Z test) and Chi-square test (X2 test). Statistical analysis was conducted using the SPSS (Version 15, 2006) for Windows statistical package. P value <0.05 was considered statistically significant.

Results
The study included 197 patients; 115 males (58.4%) and 82 females (41.6%) with mean age of 68.6±7.6; 43-79 years. Fifty-four patients (27.6%) were free of medical co-morbidities, while 142 patients (82.4%) had additional medical co-morbidities and diabetes mellitus was the most frequent among these co-morbidities. Sixty-three patients (32%) had good-excellent general health, 95 patients (48.2%) had good general health, while 39 patients (19.8%) had poor-fair general health. Patients’ enrollment criteria are shown in Table 1 - next page.

Clinical and radiological evaluation defined 51 patients (25.9%) as having AD, 37 patients (18.8%) having VD, 23 patients (11.7%) having PDD and 86 patients (43.6%) having other variants of dementia. Total MMSE score of enrolled patients (19.2±2.8) showed significantly (p<0.05) lower scores compared to control subjects (28.8±0.9). Differentially according to type of dementia, the recorded MMSE estimates were significantly lower (p<0.05) compared to control group, but with non-significant (p>0.05) difference among patients of varied diagnoses, (Figure 1 - page 11).
Total CDT scores were significantly (p<0.05) lower in patients compared to control subjects, with significantly (p<0.05) lower scores in the PDD group compared to the AD group. Patients who had AD showed non-significantly (p>0.05) higher CDT scores compared to patients who had vascular and other types of dementia with non-significant (p>0.05) difference between both latter groups. Also, the PDD group showed non-significantly (p>0.05) lower CDT scores compared to patients who had vascular and other types of dementia, (Figure 2). As regards patients’ distribution among CDT scores, patients who had AD showed significantly higher frequency of higher scores compared to those who had VD (X2=3.416, p<0.05), PPD (X2=7.153, p<0.05) and other types (X2=9.221, p<0.05) with non-significant (p>0.05) difference among other groups but in favor of VD group, (Table 2, Figure 3, Page 12).

**Discussion**

The current study reported a high frequency of co-morbidities among the studied dementia patients reaching up to about 82% of studied patients. This finding illustrated a coincidence of systemic co-morbidities and dementia and this surely will intensify the burden on the caregiver, consumes resources and requires frequent inpatient management. These findings also emphasize the necessity for proper control of systemic co-morbidities to allow improvement of general health. In support of this, only 63 patients (32%) had good-excellent general health, 95 patients (48.2%) had good general health, while 39 patients (19.8%) had poor-fair general health. Phelan et al. (13) tried to determine whether dementia onset is associated with higher rates of, or different reasons for, hospitalization, particularly for ambulatory care-sensitive conditions (ACSCs), and found that the adjusted admission rates were significantly higher in the dementia group and adjusted admission rates for all types of ACSCs, including bacterial pneumonia, congestive heart failure, dehydration, duodenal ulcer, and urinary tract infection, were significantly higher among those with dementia.

One of the interesting findings of the current study is the complaint of fatigue and easy fatigability of dementia patients who had Parkinsonism, compared to other dementia patients who did not make such a complaint. This could be
Figure 1: MMES of studied patients categorised according to type of dementia

Figure 2: CDT scores of studied patients categorised according to type of dementia
Data are presented as numbers & mean±SD; percentages are in parenthesis
*: significant versus control group
†: significant versus AD group

Table 2: Results of MMSE and CDT of studied patients categorized according to type of dementia and compared to control subjects

<table>
<thead>
<tr>
<th>Number</th>
<th>Control</th>
<th>AD</th>
<th>VD</th>
<th>PDD</th>
<th>Other types</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28.8±0.9</td>
<td>19.9±2.6*</td>
<td>18.4±3.3*</td>
<td>18.9±3*</td>
<td>19.3±2.7*</td>
<td></td>
</tr>
<tr>
<td>CDT Scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
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<td>13</td>
<td>5</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>22</td>
<td>14</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>6</td>
<td>10</td>
<td>9</td>
<td>29</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>7</td>
<td>6</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.5±0.5</td>
<td>1.98±1.09*</td>
<td>1.65±1.09*</td>
<td>1.35±1.07†</td>
<td>1.65±1.2*</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3: Patients’ distribution according to CDT scores

attributed to the inherent character of Parkinson’s disease and may not be related to dementia itself. Friedman et al. (14), (2011), reported that non-motor symptoms of Parkinson’s disease have become increasingly recognized as central to the disease and include somatic symptoms, such as pain and autonomic dysfunction and behavioral problems, such as dementia, depression, fatigue, sleep disorders and psychosis and concluded that fatigue is a common and severe problem in Parkinson’s disease.

The study relied on estimation of the Mini Mental State and Clock-drawing tests; both are validated tests for evaluation of cognitive changes accompanying dementia and impact of different types of dementia on their outcome. In the context of validity of both tests for the defined target, de Guise et al. (15) compared the performances of patients with mild, moderate, and severe traumatic brain injury on the CDT and MMSE and reported that the CDT and MMSE in combination have the potential for prediction of outcome in the traumatic brain injury population.
The recorded MMSE estimates were significantly lower among dementia patients compared to the control group, but with a non-significant difference among patients of varied dementia types. These data are comparable with the study by Oh et al. (16) who conducted cognitive screening using MMSE with repeated evaluations at 6-month, 1 year, and 2 years after initial baseline assessment and found no difference between the three dementia subtypes; AD, VD and PDD with respect to baseline MMSE scores and cognitive decline was not obvious up to 6 months of the follow-up, but by 12 months of follow-up was significant regardless of the dementia subtype.

Total CDT scores were significantly lower in patients compared to control subjects with significantly higher scores in the AD group compared to the PDD group and non-significantly higher CDT scores compared to patients who had vascular and other types of dementia. These data indicated the ability of CDT for differentiation between patients having AD from those who had other types of dementia and considering identification of these patients using MMSE combination of both tests allowed proper differentiation between AD from other types of dementia. Comparable data was shown in the study by Umidi et al. (17) which documented that during screening; administration of both CDT and MMSE can be useful to identify precocious subjects with possible MCI.

Aprahamain et al. (18) reported that CDT is a robust screening test when compared with the MMSE, independent of the scale used for its interpretation and the combination with the MMSE improves its performance significantly, becoming equivalent to the Cambridge Cognitive Examination. Thereafter, Aprahamain et al. (19) tried to discriminate illiterate elderly with and without Alzheimer’s disease (AD) in a clinical sample using varied tests and reported that the best specificity was observed with the combination of the MMSE and CDT (89%).

Through the current study, considering the high percentage of literacy among the Saudi population, simple CDT requests were applied and all patients were allowed to view a large wall clock prior to drawing so as to imitate it according to the requests. These precautions allowed achievement of success with all enrolled patients irrespective of their educational level. Cacho et al. (20) documented that the Mini-clock is highly sensitive and specific in the detection of mild AD and reasonably accurate when attempting to separate MCI from healthy controls, and it has a high interrater and test-retest reliability, and can also be quickly administered, not requiring major training. Moreover, in support of these precautions, Kim & Chey (21) reported that the CDT performance in older people who are either illiterate or with 6 or less years of education should be interpreted with caution and conceptual errors in the CDT can be the result of not only dementia but also lack of education.

It could be concluded that combined application of both MMSE and CDT could identify persons with the least cognitive affection, but could not definitely discriminate types of dementia, apart from the reported lower scores of CDT in PDD. However, a wider scale study was advocated for proper assignment of cutoff values for both tests to be tested as discriminative points.

References


Relationship of Age and Gender to “Diabetes Distress” and Postprandial Hyperglycemia: Impact of a Multidisciplinary Supportive, Dietary, and Pharmacologic Approach

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Sallie Areford (2)
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Abstract

“Diabetes Distress” (DD) is a patient’s persistent feeling of being overwhelmed by the emotional burden from attention to self-management issues. Dietary habits associated with DD can affect postprandial hyperglycemia (PPH). This study explored the association between age, gender, DD and PPH, and the impact of a short-term multidisciplinary intervention. 124 patients, 78 female and 46 male, mean age 51 years, were administered a validated screening instrument (DDS2). PPH was measured by plasma 1,5-anhydroglucitol (1,5-AG). Average DD score was higher in women than men (6.4 vs. 4.9), and in patients <50 than in those ≥ 50 (5.9 vs. 5.1). In women, the average DD score was 7.2 in those <50 (n= 39) and 6.0 in those ≥ 50 (n=39), while the 1,5-AG was 3.5 and 8.8 ug/ml respectively. In men, the average DD score was 4.6 in those <50 (n=16) and 4.3 in those ≥ 50 (n=30), with the 1,5-AG being 4.8 and 9.4 ug/ml respectively. A subset of 13 subjects (8 women and 5 men, mean age 49.5 yrs) was managed with a combined supportive, dietary, and pharmacologic intervention. Average DDS2 score was 7.08 at baseline and 5.85 post-intervention, average 1,5-AG increased from 4.2 to 5.2 ug/ml, and average HbA1c changed from 8.2% to 7.9%. Thus, associations between DD and PPH vary by age and gender, being highest in younger women and lowest in older men, and respond well to a multi-pronged management strategy. Research into the dynamics of psychological stressors and meal-related glycemia could help in optimizing individualized treatments in patients with diabetes.
Introduction and Background
Living with a chronic disease such as diabetes mellitus (DM) is a daily challenge that requires patients to address diverse aspects of self-care. They include attention to lifestyle factors, diet amount and composition, physical activity, self-monitoring of blood glucose, recording and communicating readings to the health care provider, adjusting medications and insulin as necessary, and keeping up with physician appointments (1,2). The economic burden on individuals with diabetes can be considerable, and feelings of guilt and inadequacy can supervene to a varying degree (3,4). These issues are magnified in patients who are insulin-treated (all type 1 and a significant proportion of type 2) (5,6). It can also create stress and feelings of inadequacy and being overwhelmed, especially in patients treated with insulin ("diabetes distress" or DD) (7). These responses are found in a substantial number of diabetic patients, are distinct from true depression/anxiety, and can lead to diminished quality of life (8,9,10). They may impact post-meal elevations and excursions of blood glucose, because of the close connection between food and emotions, leading to postprandial hyperglycemia (PPH). Fortunately, there are validated methods of assessing both DD and PPH. We attempted to investigate the possible association between DD score and PPH with gender and age in patients with suboptimal glycemic control (those with HbA1c level >7%), which has not been done previously. Further, we evaluated the impact of a combined supportive, dietary, and pharmacologic intervention on postprandial and overall glucose control.

Diabetes, Depression, and “Diabetes Distress”
Compared with patients with diabetes alone, patients with diabetes and co-morbid depression display higher functional impairment and work loss and poorer self-management behavior, and they have more co-morbidities (11,12). Although frank depression and other psychiatric problems can manifest more commonly in patients with diabetes, more often a low-grade and consistent feeling of being overwhelmed is seen. Recent findings, however, have suggested that high levels of diabetes-specific distress, not depression, may account for many of the reported findings. This so-called “diabetes distress” (DD) is defined as patient concerns about disease management, support, emotional burden, and access to care and is an important condition distinct from depression (13).

Assessment of “Diabetes Distress”
Several experts have researched the area of the individual burden of diabetes and have devised objective methods of estimating the amount of DD and its impact on quality of life in the diabetic population (14,15,16). A brief diabetes distress screening instrument developed by Fisher et al. is the DDS2. (13) This is a validated 2-item diabetes distress screening instrument (Figure 1) asking respondents to rate on a 6-point scale the degree to which the following items caused distress: (1) feeling overwhelmed by the demands of living with diabetes, and (2) feeling that I am often failing with my diabetes regimen. A DDS2 score of either 1) an average of the 2 screening items ≥3, or 2) sum of the 2 items ≥6 is significantly high, pointing to diabetes-specific distress, with higher scores denoting increased DD.

Estimation of Postprandial Hyperglycemia
The traditional method of assessing PPH is asking the patient to perform ‘fingersticks’ 2 hours after meals, at the point of peak glucose elevation (17,18). However, when combined with pre-prandial and bedtime checks, as well as other times as necessary, the total number of daily readings amounts to 7 or more. For many patients this frequency of fingerstick readings poses a significant burden that is difficult to sustain over the long-term. Nevertheless, evaluation of PPH is important, because many patients who are otherwise well controlled by glycated hemoglobin (HbA1c), the current standard indicator of overall glycemia, also have significant PPH, which may be an independent risk factor for the development of macrovascular complications (19,20).

An automated assay (GlycoMark) measures plasma 1,5-anhydroglucitol (1,5-AG), a naturally occurring dietary polyol that has been proposed as a marker for PPH and is approved in the U.S. as a short-term marker for glycemic control (21,22). A similar assay has been in use in Japan for over a decade (23,24). 1,5-AG responds sensitively and rapidly to changes in serum glucose, reflecting even transient elevations of glucose within a few days (25). 1,5-AG has been shown to reflect daily glycemic excursions in patients with HbA1c at or near goal (26). Due to the rapid response of 1,5-AG to changes in glyoxylate, serial 1,5-AG measurements may be useful in assessing PPH. This may be particularly valuable in examining the effect of therapy specifically targeted to postprandial glucose control. In most patients, it may be difficult to discern whether the true barrier to perfect glycemic control lies with inadequate prandial or basal glycemic treatment. There is often insufficient self-monitoring data to make the intricate adjustments that may be necessary.

The 1,5-AG assay can prove valuable in this regard. The association between the 1,5-AG level and peak post-meal glycemic excursions is shown in Figure 2 (27).

Thus the 1,5-AG level reflects glycemic excursions, often in the postprandial state, more robustly than the HbA1c. In clinical practice, 1,5-AG may be useful in conjunction with HbA1c to assess glycemic control in patients with moderate or good control (28). The two can be used sequentially, first utilizing the HbA1c assay to identify patients who are above goal (HbA1c >7%) and then using the 1,5-AG assay to determine the extent of postprandial glycemic excursions. If the HbA1c is above target and the 1,5-AG is
Directions: Living with diabetes can sometimes be tough. There may be many problems that range from minor hassles to major life difficulties. Listed below are 2 potential problem areas that people with diabetes may experience. Consider the degree to which each of the 2 items may have distressed or bothered you DURING THE PAST MONTH and circle the appropriate number.

Please note that we are asking you to indicate the DEGREE to which each item may be bothering you in your life, NOT whether the item is merely true for you. If you feel that a particular item is not a bother or a problem for you, you would circle "1." If it is very bothersome to you, you might circle "6."

1. Feeling overwhelmed by the demands of living with diabetes.

<table>
<thead>
<tr>
<th>Feeling</th>
<th>Not a Problem</th>
<th>Moderate Problem</th>
<th>Serious Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

2. Feeling that I am often failing with my diabetes regimen.

<table>
<thead>
<tr>
<th>Feeling</th>
<th>Not a Problem</th>
<th>Moderate Problem</th>
<th>Serious Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Figure 1: The 2-Item Diabetes Distress Screening Scale (DDS2) (adapted from Fisher et al., Ann Fam Med 2008;6(3):246-252.)

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Av. DDS2 score before</th>
<th>Av. DDS2 score after</th>
<th>Change</th>
<th>Av. 1,5-AG (ug/ml) before</th>
<th>Av. 1,5-AG (ug/ml) after</th>
<th>Change</th>
<th>Av. HbA1c (%) before</th>
<th>Av. HbA1c (%) after</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=13)</td>
<td>7.08</td>
<td>5.85</td>
<td>-17%</td>
<td>4.2</td>
<td>5.2</td>
<td>+24%</td>
<td>8.3</td>
<td>7.9</td>
<td>-4.8%</td>
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<td>Women (n=8)</td>
<td>7.9</td>
<td>6.7</td>
<td>-15%</td>
<td>5.5</td>
<td>6.2</td>
<td>+13%</td>
<td>8.1</td>
<td>7.8</td>
<td>-3.7%</td>
</tr>
<tr>
<td>Men (n=5)</td>
<td>5.8</td>
<td>4.4</td>
<td>-24%</td>
<td>2.2</td>
<td>3.6</td>
<td>+64%</td>
<td>8.5</td>
<td>8.0</td>
<td>-5.9%</td>
</tr>
</tbody>
</table>

Figure 2: The relationship between 1,5-Anhydroglucitol level and postprandial hyperglycemia

*1,5-AG = 1,5Anhydroglucitol, HbA1c = hemoglobin A1c

Figure 3: Use of 1,5 Anhydroglucitol in conjunction with HbA1c to assess glycemic control in diabetes.*
normal, therapy targeting basal glucose may be more useful. On the other hand, if the HbA1c is above target and the 1,5-AG is low, targeting postprandial glucose elevations may be more productive. This may involve more intensive postprandial monitoring, as well as pharmacoc-psychotherapeutic approaches that specifically address PPH. The usefulness of 1,5-AG when used together with the HbA1c level to stratify patients in terms of their glucose control and thus guide therapy, is given in Figure 3, page 17.

Methods
Patients were seen at the Diabetes Unit, University of South Carolina School of Medicine, Columbia, South Carolina, USA. The unit is staffed by endocrinologists, endocrine fellows, and nursing personnel who specialize in the office evaluation monitoring methods, and management of diabetes, and its complications (29).

Inclusion criteria were age 18-75 years and type 1 or type 2 diabetes treated with insulin, with or without other therapeutic agents. Exclusion criteria included pregnancy, severe medical illnesses, anemia, and serum creatinine >2.0 mg/dl. Consecutive patients had point-of-care HbA1c testing using the Abbott Diagnostics Afinion AS100 Analyzer that has a 3-minute turnaround time, is National Glycohemoglobin Standardization Program (NGSP) certified, autocalibrated, and CLIA-waived. The normal reference range for HbA1c by this method is 4.5 - 5.8%. An HbA1c below the American Diabetes Association (ADA) recommended target of 7% is optimal. PPH was measured by blood draw for an automated plasma 1,5-anhydroglucitol assay (1,5-AG, commercially available as GlycoMark, LabCorp/Esoterix and Quest Diagnostics). The normal range for the 1,5-AG assay in males is 10.7-32.0 mcg/ml and in females is 6.8-29.3 mcg/ml. Lower values are correlated with higher or worse postprandial glycemic excursions. Patients were administered a previously validated diabetes distress screening instrument (DDS2, described above). Data for all patients after the application of the inclusion/exclusion criteria, was analyzed to ascertain whether a significant association exists between the Diabetes Distress score on the DDS2 instrument, the 1,5-AG level, and gender and age. In a smaller subset of patients, the impact of supportive, dietary, and pharmacologic care on glycemic control for 12 weeks was also ascertained. A follow-up 1,5-AG was drawn at 4 weeks and a HbA1c at 12 weeks. A Data Collection Instrument is shown in Figure 4. It is important to note that these adjustments are standard of care and part of the usual treatment approach for patients seen at the Diabetes Unit as well as advocated by professional societies such as the ADA. No experimental pharmacologic or non-pharmacologic treatment was employed or introduced. Details of the SDPC intervention are as follows:

*MDDS2 score = diabetes distress screening instrument score, HbA1c = hemoglobin A1c, 1,5-AG = 1,5Anhydroglucitol

Table 1: Association of Age and Gender with diabetes distress score (DDS2) and 1,5 Anhydroglucitol (1,5-AG) levels

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Av. DDS2 score before</th>
<th>Av. DDS2 score after</th>
<th>Change</th>
<th>Av. 1,5-AG (ug/ml) before</th>
<th>Av. 1,5-AG (ug/ml) after</th>
<th>Change</th>
<th>Av. HbA1c (%) before</th>
<th>Av. HbA1c (%) after</th>
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<td>7.08</td>
<td>5.85</td>
<td>-17%</td>
<td>4.2</td>
<td>5.2</td>
<td>+24%</td>
<td>8.3</td>
<td>7.9</td>
<td>-4.8%</td>
</tr>
<tr>
<td>Women (n=8)</td>
<td>7.9</td>
<td>6.7</td>
<td>-15%</td>
<td>5.5</td>
<td>6.2</td>
<td>+13%</td>
<td>8.1</td>
<td>7.8</td>
<td>-3.7%</td>
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<tr>
<td>Men (n=5)</td>
<td>5.8</td>
<td>4.4</td>
<td>-24%</td>
<td>2.2</td>
<td>3.6</td>
<td>+64%</td>
<td>8.5</td>
<td>8.0</td>
<td>-5.9%</td>
</tr>
</tbody>
</table>

*MDDS2 score = Diabetes Distress Screening instrument score, 1,5-AG = 1,5Anhydroglucitol

Table 2: Changes in average Diabetes Distress scores (DDS2) and glucose control in 13 patients before and after a 4-week multidisciplinary intervention.*

*DDS2 score = Diabetes Distress Screening instrument score, HbA1c = hemoglobin A1c
1) Support and regular communication - Communicate with patients by phone or fax was individualized, taking place between approximately twice weekly to twice monthly during the 12-week study period. Adherence to diet, answers to treatment-related questions, and general morale-boosting and encouragement was the standard part of each interaction (30,31). The connection between eating, emotions, and glucose levels was particularly emphasized. Patients were asked to do frequent self-monitoring of blood glucose, including post-meal checks, and communicate with the office staff at least twice weekly. Periodic contact, questioning, feedback, and adherence to self-care and diet recommendations through a suggestive, non-threatening, and "coaching" in a patient-centered manner, were used.

2) Diet and carbohydrate content - At the baseline visit, the diabetes nurse specialist provided each patient with a review of carbohydrate counting, the glycemic index of various foods, and the impact of various foods on postprandial control (32). A brief reinforcement of the effect of various foods, portion sizes, and carbohydrate amounts on blood glucose elevations and excursions was utilized. Methodology included written material on calorie content, carbohydrate counting, exchange sizes, and the connection between food and emotional state (33).

3) Pharmacologic intervention - Since this study involved primarily insulin-treated patients, the use of both basal and short-acting mealtime insulins, as indicated, was adjusted under physician supervision to achieve better postprandial control (34). Other medications were also adjusted in an individual manner (35).

Statistical analysis - Data was entered into an Excel Spreadsheet. All subjects who met the inclusion criteria were assessed at pre- and post-intervention times. Based on that data, estimates for HbA1c and 1,5-AG mean levels and pre-post differences were derived along with standard errors and 95% confidence intervals. Using the paired-t test at the 0.05 level of significance, pre- and post-intervention values were compared. A significant test result indicated that the intervention was effective. In order to determine whether there was an association between DDS2 scores, 1,5-AG levels, and gender/age, Pearson correlations were calculated.

Results
124 patients with diabetes, 78 female and 46 male, completed the study. They varied in age from 15 to 85 years, mean age 51 years, with 63 <50 and 61 ≥50. Results are given in Table 1 - opposite page. The average DDS2 score was higher in women than men (6.4 vs. 4.9), and in patients <50 than in those ≥50 (5.9 vs. 5.1). In women, the average DDS2 score was 7.2 in those <50 (n=39) and 6.0 in those ≥50 (n=39), while the 1,5-AG levels were 3.5 and 8.8 ug/ml respectively. In men, the average DD score was 4.6 in those <50 (n=16) and 4.3 in those ≥50 (n=30), with the 1,5-AG levels being 4.8 and 9.4 ug/ml respectively.

The results in the intervention subset are shown in Table 2. 13 subjects with type 2 diabetes (8 women and 5 men, mean age 49.5 years) completed the study. Average DDS2 score was 7.08 at baseline and 5.85 at the end of intervention. The score increased in 2 subjects, decreased in 6, and remained unchanged in 5. The average 1,5-AG went up from 4.2 to 5.2 ug/ml (increase in 11 and decrease in 2). The average A1C changed from 8.2% to 7.9% (decrease in 8, unchanged in 2, and increase in 3). Both women and men responded with improvements in all parameters.

Discussion
Individuals with diabetes can experience a considerable degree of chronic stress because of the burden of self-management activities, and also have incident glycemic variations that have multiple causes. This study points to associations between diabetes-related distress and postprandial hyperglycemia and their variation by age and gender in diabetes, both being higher in women than men, highest in younger women, and lowest in older men. Results in the smaller interventional arm show that DD and PPH are high in patients with diabetes, and both respond encouragingly well to a short-term supportive intervention strategy addressing emotional aspects and dietary characteristics of self-management. Further research can assist in understanding emotional, psychological, and meal-related characteristics of diabetes in different populations and their impact on glycemic control. Investigating the dynamics and impact of psychological stressors on diabetes management and meal-related hyperglycemia could help in optimizing individualized treatments in patients living with a chronic disease like diabetes.

Limitations of our study include the potential effect of unmeasured confounding factors on both glycemic control and distress, and the small size of the intervention group. Thus, concrete conclusions cannot be drawn and the data can only be regarded as preliminary, albeit promising and pointing to the need for further research. However, we believe that there are potential wider implications of the study. DD is a common but under-recognized barrier to achieving optimal diabetes control and alleviating quality of life, especially in insulin-treated patients. If a simple algorithm consisting of a quick DD screening instrument (DDS2) and laboratory glucose assessment testing (HbA1c and 1,5-AG) can be devised for use in the majority of primary care office settings, it can be used to identify patients prone to inadequate glycemic control, particularly that resulting from food-related or post-prandial hyperglycemia. Such patients can then be the object of a targeted and focused multipronged therapeutic approach. Such an intervention can be validated and used in similar situations. In addition, these results form the basis for larger and more elaborate trials in this area. The information thus gained should be useful when applied to similar
patient populations globally, and should serve as a stimulus for further translational research and care in this area. We feel that paying attention to psychosocial and psychological aspects of diabetes in addition to nutrition and medications forms a vital strategy that is extremely relevant to specialty and primary care to combat a burgeoning epidemic of diabetes worldwide.

Conclusion
In individuals with mainly insulin-treated diabetes, higher levels of self-reported and objectively measured diabetes-related distress seem to be associated with post-meal glycemic elevations. Both are higher in younger patients and in women, and respond well to a multidisciplinary intervention of communicative support, diet advice, and medication adjustment. Further research should elucidate the role of gender, age, and diabetes-related burden on postprandial and overall hyperglycemia and assist in devising effective management strategies.

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3. Schmitz N, Wang J, Lesage A, Malla A, Strychar I. Psychological distress and short-term disability in women, and respond well to a multidisciplinary intervention of communicative support, diet advice, and medication adjustment. Further research should elucidate the role of gender, age, and diabetes-related burden on postprandial and overall hyperglycemia and assist in devising effective management strategies.

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Abstract

Background: Excess weight has many consequences on physical health, but its association with antisocial personality disorder (ASPD) is unknown.

Methods: We took consecutive check up patients between the ages of 18 and 70 years to be able to catch cases with ASPD and to avoid debility induced weight loss in elders. All cases were evaluated by the same internist under the supervision of the same psychiatrist, and their medical histories were learnt, and a routine check up procedure was performed. Patients with a history of eating disorders in their lives and patients with devastating illnesses were excluded to avoid their possible effects on weight. Prevalences of ASPD were detected in the underweight, normal weight, overweight, and obesity groups, and compared.

Results: The study included 2,428 cases (1,384 females), totally. Prevalences of underweight, normal weight, overweight, and obesity were detected as 3.9%, 34.7%, 35.9%, and 25.3%, respectively. Prevalences of ASPD were 8.4%, 13.7%, 14.9%, and 11.5% in the underweight, normal weight, overweight, and obesity groups, respectively, and there was no significant difference between them (p>0.05 for all).

Conclusion: ASPD may be a common psychopathology with terrible consequences on population, even on physicians and other patients. After contacts with such cases, physicians cannot normalize themselves against following patients with a fear of meeting with another case. Although excess weight has many consequences on physical health, including type 2 diabetes mellitus, hypertension, coronary heart disease (CHD), perhaps certain types of cancers, and an increased all-cause mortality rate (4).

Key words: Excess weight, underweight, antisocial personality disorder

Introduction

In recent years, obesity and regulation of body weight are rapidly becoming the center of attention for public health experts. The current prevalence of obesity in the general population, is estimated at 19.9% and 24.9% in men and women, respectively (1). Certain calculations suggest that, given trends over the past 30 years, the entire United States population could be obese by the year 2230 if these trends persist (2). A more disturbing trend is the increased early onset of obesity in children. This alarming trend has prompted the World Health Organization to declare obesity a worldwide epidemic (3). Obesity is a disorder characterized by increased mass of adipose tissue that results from a systemic imbalance between food intake and energy expenditure, and is a public health challenge, because it is associated with many adverse effects on physical health, including type 2 diabetes mellitus, hypertension, coronary heart disease (CHD), perhaps certain types of cancers, and an increased all-cause mortality rate (4).
Material and Methods
The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007, prospectively. We took all consecutive check up patients between the ages of 18 and 70 years during the period to be able to catch ASPD and to avoid debility induced weight loss in elders, since according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition Text Revision (DSM-IV-TR), people with antisocial personality disorder demonstrate a pattern of antisocial behavior since age 15, but cases are diagnosed over the age of 18 years (7). All of the subjects were evaluated by the same internist under the supervision of the same psychiatrist, and their medical histories were learnt, and a routine check up procedure was performed. At least one relative or a close friend of the cases were used for help during the procedure. Patients with a history of eating disorders in their lives including anorexia nervosa, bulimia nervosa, compulsive overeating, or binge eating disorder, and patients with devastating illnesses including malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure, and metformin or insulin using diabetics were excluded to avoid their possible effects on weight (8). Body Mass Index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared, and obesity is defined as a BMI of 30 or greater, overweight as 25-29.9, normal weight as 18.5-24.9, and underweight as lower than 18.5 kg/m(2) (9). ASPD was diagnosed according to the DSM-IV-TR (7). Eventually, prevalences of ASPD were detected in the underweight, normal weight, overweight, and obesity groups, and results were compared. Independent-Samples T Test and comparison of proportions were used as the methods of statistical analyses.

Results
The study included 2,428 cases (1,384 females and 1,044 males), totally. There were only 3.9% (95) of all cases in the underweight group (Table 1). Prevalences of the cases with normal weight, overweight, and obesity were detected as 34.7%, 35.9%, and 25.3%, respectively. Mean ages of the groups were 24.5 ± 8.4, 32.3 ± 13.8, 43.2 ± 13.5, and 49.6 ± 10.3 years in the underweight, normal weight, overweight, and obesity groups, respectively, and they showed a gradual increase from the underweight towards the obesity groups. The differences between the normal weight and overweight and obesity groups were statistically significant (p<0.001 for both). So probably aging is the main determinant factor of weight excess. Additionally, female ratios were detected as 61.0%, 51.2%, 47.1%, and 78.8% in the underweight, normal weight, overweight, and obesity groups, respectively. So there was a significant female predominance in the obesity group when we compared it with the normal weight group (p<0.001). Prevalences of ASPD were 8.4% (eight cases), 13.7% (116 cases), 14.9% (131 cases), and 11.5% (71 cases) in the underweight, overweight, and obesity groups, respectively. When we compared the underweight, overweight, and obesity with the normal weight groups according to the prevalence of ASPD, there was no statistically significant difference between any of them (p>0.05 for all).

Discussion
Recent studies have revealed that adipose tissue produces biologically active leptin, tumor necrosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Underweight</th>
<th>p-value</th>
<th>Normal weight</th>
<th>p-value</th>
<th>Overweight</th>
<th>p-value*</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>95 (3.9%)</td>
<td></td>
<td>843 (34.7%)</td>
<td></td>
<td>874</td>
<td></td>
<td>616 (25.3%)</td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>24.5 ± 8.4</td>
<td>ns†</td>
<td>32.3 ± 13.8</td>
<td>&lt;0.001</td>
<td>43.2 ± 13.5</td>
<td>&lt;0.001</td>
<td>49.6 ± 10.3</td>
</tr>
<tr>
<td>Female ratio</td>
<td>61.0% (58)</td>
<td>ns</td>
<td>51.2% (432)</td>
<td>&lt;0.05</td>
<td>47.1% (412)</td>
<td>&lt;0.001</td>
<td>78.8% (486)</td>
</tr>
<tr>
<td>Prevalence of ASPD†</td>
<td>8.4% (8)</td>
<td>ns</td>
<td>13.7% (116)</td>
<td>ns</td>
<td>14.9%</td>
<td>ns</td>
<td>11.5% (71)</td>
</tr>
</tbody>
</table>

*Values as a result of the comparison between normal weight and obese individuals
†Antisocial personality disorder
‡Nonsignificant (p>0.05)
Table 1: Characteristics of the study cases
factor-alpha, plasminogen activator inhibitor-1, and adiponectin, which are closely related with the development of consequences on physical health (10). For example, individuals with excess weight will have an increased circulating blood volume as well as an increased volume of cardiac output, thought to be the result of increased oxygen demand of the extra body tissue. The prolonged increase in circulating blood volume can lead to myocardial hypertrophy and decreased compliance, in addition to the common comorbidity of HT. In addition to HT, prevalences of high FPG, high serum total cholesterol, and low HDL-C, and their clustering were all raised with increases in BMI (11). Combination of these cardiovascular risk factors will eventually lead to an increase in left ventricular stroke with a higher risk of arrhythmias, cardiac failure, or even sudden cardiac death. Eventually, the risk of death from all causes including cardiovascular diseases and cancers increases throughout the range of moderate and severe excess weight both for men and women in all age groups (12).

Although the excess weight is associated with greater consequences on physical health, there are various reports about its association with psychiatric disorders. For example, mental health tended to be related with BMI in a previous study (13), and there was a higher percentage of mentally ill persons among general practice patients showing obesity than in a national population sample of England in another study (14). Similarly, obesity was related to the increased rates of mental disorders in women between the ages of 18 and 25 years (15). A telephone survey including 9,585 completed interviews in a general population sample revealed a relationship between depression and an increased risk of obesity by using the DSM-IV (16). Additionally, those with obesity showed higher odds for depression compared with those with a normal weight or overweight between the ages of 50 to 94 years (17). In another study, obesity was associated with a 37% increase in the probability of being diagnosed with major depression in women, while with a decrease of similar magnitude in men (18). Similarly, obesity was associated with significant increases in lifetime diagnosis of major depression, bipolar disorder, and panic disorder or agoraphobia (19). Additionally, a 10-unit increase of BMI increased the risk of past-year suicide thought and attempts by 22% in females, however, reduced the risk by 26% and 55%, respectively, in males (18). The interesting finding among men was the association between being underweight and having an increased probability of clinical depression and suicidal tendencies. When the authors analyzed weight status as a categorical variable, the underweight men were 81% more likely to have thought about suicide, 77% more likely to have attempted suicide, and 25% more likely to be clinically depressed than average-weight men (18). On the other hand, obesity was associated with significantly lower lifetime risk of substance abuse disorders, and subgroup analyses found no difference in these associations between men and women (19). Another survey study did not find a relationship between BMI and general psychopathology by using DSM-IV criteria, and it was conducted with a general population sample of 3,021 German persons ranging from 14 to 24 years of age, and controlled for eating disorders (20). There was no significant association between BMI and mood, anxiety, substance use, and somatoform disorders (20). Additionally, neither obesity nor underweight was significantly associated with any kind of general psychopathology (20). Similarly, although authors found a statistically significant relationship between BMI and physical health, they could not between BMI and psychosocial outcomes such as poorer emotional, school, or social functioning (21).

ASPD is a type of chronic mental illness, in which ways of thinking, perceiving situations and relating to others, are dysfunctional. In our opinion, ASPD is a common psychopathology in society, with terrible consequences on the surrounding population. For example, such cases probably are the main patience points of the physicians. After contacts with such cases, physicians cannot normalize themselves against following patients with a fear of meeting with another case of ASPD. This fear of physicians negatively affects their performance on other patients, and also the patient and doctor interactions. So ASPD cases are becoming harmful not just for the physicians but also for other patients, since such cases fail to conform to social norms. They are deceitful and manipulative of others. They are irritable or aggressive, engaging in physical fights, and exhibit reckless disregard for the safety of self or others. They are consistently irresponsible, and demonstrate lack of remorse for the harm of their behaviors. The official stance of the American Psychiatric Association as presented in the DSM-IV-TR is that psychopathy and sociopathy are obsolete synonyms for ASPD. The exact cause of ASPD is not known, and is negatively correlated with all DSM-IV Axis I disorders except substance abuse disorders (7). Robins found an increased incidence of sociopathic characteristics and alcoholism in the fathers of individuals with ASPD (22). He found that, within such a family, males had an increased incidence of ASPD, whereas females tended to show an increased incidence of somatization disorder instead (22). Bowlby saw a connection between ASPD and maternal deprivation in the first five years of life in 1944 (23). ASPD is diagnosed in approximately 3% of all males and 1% of all females according to the DSM-IV (7). The National Comorbidity Survey, which uses DSM-III-R criteria, discovered that 5.8% of males and 1.2% of females showed evidence of a lifelong chance of obtaining the disorder (24). Prevalence estimates within clinical settings vary from 3% to 30%, depending on the predominant characteristics of the populations being sampled. Prevalence of the disorder is even higher in selected populations, such as people in prisons, and about half
of the prisoners in western countries met the diagnostic criteria of ASPD in a meta-analysis of 62 surveys (n = 23,000) (25). Although, DSM-IV reported the prevalence of ASPD as 3% of in males and 1% of in females, we think it has a much higher prevalence in society, and we found its prevalence as 13.4% among the 2,428 check up cases (57.0% females) without any significant difference between the underweight, normal weight, overweight, and obesity groups in Turkey.

As a conclusion, ASPD may be a common psychopathology with terrible consequences on populations, even on physicians and other patients. After contacts with such cases, physicians cannot normalize themselves against following patients with a fear of meeting with another case of ASPD. This fear of physicians negatively affects their performance on other patients, and also the patient-doctor interactions. Although excess weight has many consequences on physical health, including type 2 diabetes mellitus, hypertension, dyslipidemia, coronary heart disease, and stroke, neither underweight nor excess weight shows a significant causative relationship with ASPD.

References