Effects of Attitudes of Patients with Epilepsy Towards Their Disease on Mental Health and Quality of Life

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Objective: The study investigates the effects of attitudes displayed by patients with epilepsy toward their disease on their mental health and quality of life.

Materials and Methods: This descriptive cross-sectional study was conducted in the neurology outpatient clinic at Hafsa Sultan Hospital, Manisa Celal Bayar University between April 2015 and April 2016. The study sample comprised 182 patients. The study data were collected using the Personal Information Form for Patients with Epilepsy, Impact of Epilepsy Scale, Epilepsy Knowledge Scale, Epilepsy Attitude Scale, Short Form-36 (Quality of Life Scale), and Brief Symptom Inventory. In the analysis of the data, the t-test, ANOVA, Scheffé’s post-hoc test, and Pearson’s correlation coefficient were used.

Results: In the Epilepsy Attitude Scale, the participants obtained a mean score of 48.6±13.13, suggesting that they displayed negative attitudes toward epilepsy. In the subscales of the Short Form-36 (Quality of Life Scale), the participants’ scores were low. Of the participants with epilepsy, those with a significantly positive attitude toward epilepsy had a high quality of life perception. Psychological symptoms decreased in patients with epilepsy who have a positive attitude toward their disease.

Conclusion: The results of this study demonstrated that the participants’ “attitudes toward epilepsy” was significantly correlated to their “psychological symptoms and quality of life.” The fact that the negative attitudes of patients with epilepsy are related to their psychological symptoms and quality of life indicates the importance of recognizing and understanding patients’ attitudes toward their disease.

Keywords: Epilepsy, quality of life, attitude, psychological symptom
of coping with seizures should be discussed with the patient. Patients are afraid that their brains can be damaged or they might die during seizures, that they can lose self-control when they have seizures in front of other people, and that they can lose their friends and jobs.

Women suffer from fear of being unsafe during the seizure more intensely, and they are concerned about giving birth to and raising a child. Patients with epilepsy often experience feelings of anger, denial, shame, and frustration. If these feelings are not overcome and become chronic, patients experience decreased self-esteem, social isolation, addiction, and social disruption. Patients feel angry and rejected and blame others for their problems (5, 6). Studies indicate that if patients are more knowledgeable about epilepsy, their compliance to epilepsy management increases and the negative effects of stigma and epilepsy decrease. These data demonstrate the importance of providing patients with information.

In addition, as the education levels of patients with epilepsy increase, so does their knowledge about epilepsy (4, 7). The results of several studies have demonstrated that epilepsy has important social and psychological effects (8).

This study is expected to contribute to the assessment of the mental health of patients diagnosed with epilepsy and their attitudes toward the disease, to reveal the changes and deficiencies caused by the disease in their quality of life, and to create a draft in the training plans to be made in this regard.

MATERIALS and METHODS

This descriptive cross-sectional study was conducted in the neurology outpatient clinic at Hafsa Sultan Hospital, Manisa Celal Bayar University between April 2015 and April 2016. This study investigates the effects of attitudes displayed by patients with epilepsy toward epilepsy on their mental health and quality of life.

Population and Sample of the Study

The study population comprised 320 patients with epilepsy who were followed up at the Neurology outpatient clinic at Hafsa Sultan Hospital, Manisa Celal Bayar University in 2015. The minimum sample size of the study was 175 patients, determined using Epi Info™ (Centers for Disease Control and Prevention, Atlanta, Georgia, USA) with 95% confidence interval, 5% error margin, and 1.0 pattern effect. The study sample consisted of 182 patients who were selected using the simple random method and agreed to participate in the study.

Ethical Issues

Before the study was conducted, approval from the Faculty of Medicine Health Sciences Ethics Committee, Manisa Celal Bayar University (date: April 13, 2015; number: 164), and permission from the Chief Physician of Hafsa Sultan Hospital, Manisa Celal Bayar University, where the study was conducted (date: April 13, 2015; number: 61804347-100/2560) were obtained. Moreover, written informed consent, indicating that they agreed to participate in the study was obtained from the participants. For the scales used in the study, permissions were obtained from their authors.

Data Collection Tools

The following six forms were used to collect the study data:

- Personal Information Form for Patients with Epilepsy
- Impact of Epilepsy Scale
- Epilepsy Knowledge Scale
- Epilepsy Attitude Scale
- Short Form-36 (Quality of Life Scale)
- Brief Symptom Inventory (BSI)

Personal Information Form for Patients with Epilepsy

The form includes items regarding the participants’ sociodemographic characteristics (sex, age, educational status, marital status, employment status, etc.) and disease-related characteristics (whether the patient has a chronic illness, how long the patient has had epilepsy, whether the patient had seizures, how often the patient had seizures, etc.).

Impact of Epilepsy Scale

The scale consisting of 10 questions was developed by Aydemir (2007) to measure the effect of epilepsy in a Turkish community (9). The Cronbach’s alpha value of the scale is 0.82. The Cronbach’s alpha value of the scale in this study is 0.85. The lowest score that can be obtained from the scale is 10, and the highest score is 40. The higher the score obtained from the scale, the greater the effect of epilepsy (9).

Epilepsy Knowledge Scale

The scale was developed by Aydemir (2007) for a Turkish population (9). The scale consists of 16 items regarding the following: causes of epilepsy, treatment methods, triggers of seizure, social restrictions due to epilepsy, and appropriate seizure interventions. The lowest and highest possible scores are 0 and 16, respectively. The higher scores mean that the person’s knowledge of epilepsy is high. The responses have three options: “true,” “false,” and “I do not know.” The reliability value of the scale was 0.72 (9). The Cronbach’s alpha value of the scale in this study is 0.78.

Epilepsy Attitude Scale

The scale consisting of 14 items was developed by Aydemir (2007) to determine the attitudes of Turkish people toward epilepsy and individuals with epilepsy (8). The minimum and maximum possible scores of the scale are 14 and 70, respectively. The higher scores mean that the attitude displayed toward the person with epilepsy is positive. The reliability value of the scale was α=0.84 (9). The Cronbach’s alpha value of the scale in this study is 0.93.

Short Form-36 (Quality of Life Scale)

The scale was developed by Ware et al. in 1992 (10). A study on the validity and reliability of the Turkish version of the scale was conducted by Koçyiğit et al. (11). The scale consists of 36 items and 8 subscales and is a self-assessment scale.

The 8 subscales are as follows:

1. Physical functioning (10 items)
2. Social role functioning (2 items)
3. Role limitations due to physical health (4 items)
4. Role limitations due to emotional problems (3 items)
5. Mental health (5 items)
6. Energy/vitality (4 items)
7. Bodily pain (2 items)
8. Perceptions of general health (5 items)

The items of the scale are rated using a Likert-type scale. The items assessing health are scored between 0 and 100 for each subscale. While a score of 100 indicates good health, a score of 0 indicates bad health. The Cronbach’s alpha value of the scale in this study is 0.72.

BSI
Şahin and Durak conducted three studies to adapt the BSI into Turkish (2002) (12). The BSI includes 53 items rated on a five-point Likert-type scale ranging between 0 and 4 corresponding to “not at all” and “extremely,” respectively. The subscales included in the scale are as follows: “somatization,” “obsessive-compulsive disorder,” “interpersonal sensitivity,” “depression,” “anxiety,” “hostility,” “phobic anxiety,” “paranoid thoughts,” and “psychoticism.” A scoring key was prepared for each subscale based on the items in the subscales, additional items, and subscales of the severity index. The Cronbach’s alpha value of the scale in this study is 0.98.

Analysis of the Study Data
In the analysis of the study data, Statistical Package for the Social Sciences (version 21.0; IBM Corp., Armonk, NY, USA) was used. The demographic data of the participating patients with epilepsy were presented as frequency and percentage analysis. The skewness coefficient was used to test the normality of the scale scores. That the skewness coefficient used in the normal distribution of the scores obtained from a continuous variable was within the limits of ±1 can be interpreted as that the scores did not significantly deviate from the normal distribution (13). Because the normality test indicated that the scores for the scale and its subscales had a normal distribution, the independent samples t-test was used to compare the scores according to the demographic variables between two groups, and an analysis of variance (ANOVA) was conducted to compare the scores according to demographic variables between more than two groups. When a significant difference was observed in the ANOVA, Scheffé’s post-hoc test was used to determine from which group(s) the difference stemmed. Pearson’s correlation technique was used to analyze the relationship between the scores for the Impact of Epilepsy Scale, Epilepsy Knowledge Scale, Epilepsy Attitude Scale, the subscales of the Short Form-36 (Quality of Life Scale), and psychological symptoms. P values of <0.05 were used to denote statistical significance.

RESULTS
Of the 182 patients with epilepsy who participated in the study, 54.9% were women, 40.7% were ≤30 years old, 41.8% were high school graduates, 49.5% were married, 50.5% were single, 46.7% were employed at a paid job, and 45.1% lived in a metropolitan area (Table 1).

Furthermore, among the participants, 35.2% had comorbidities with epilepsy, 84.6% perceived their life as stressful, 68.7% presented for follow-up care regularly, and 83.5% received support to cope with the disease (Table 2).

According to the frequency of seizures, no significant difference
was observed between the scores in the Epilepsy Knowledge Scale (p>0.05) (Table 3); however, a significant difference was found between the scores in the Impact of Epilepsy Scale (F=8.19; p<0.05).

Scheffé’s post-hoc test performed to determine from which group the difference stemmed showed that the participants who had seizures every day had significantly higher positive scores than those who had seizures once a year (Table 3).

Furthermore, a significant difference was observed between the scores in the Epilepsy Attitude Scale according to the frequency of seizures (F=5.55; p<0.05).

Moreover, Scheffé’s post-hoc test revealed that the participants who had seizures once a year had significantly higher positive scores than those who had seizures once a week (Table 3).

In the Short Form-36 (Quality of Life Scale), significant differences were found between the scores in the physical functioning (t=3.92; p<0.05), social role functioning (t=3.11; p<0.05), role limitations due to physical health (t=3.56; p<0.05), role limitations due to emotional problems (t=2.47; p<0.05), mental health (t=2.54; p<0.05), energy/vitality (t=3.57; p<0.05), bodily pain (t=4.91; p<0.05), and perceptions of general health (t=5.64; p<0.05) subscales in terms of presenting for follow-up care regularly.

The participants who presented for follow-up care regularly had higher scores in the Short Form-36 (Quality of Life Scale) than those who did not present for follow-up care regularly.

Furthermore, in the BSI, significant differences were observed between the scores in the somatization, obsessive–compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid thoughts, and psychoticism subscales than those who were employed. A negative significant relationship was observed between the scores in the Impact of Epilepsy Scale and those in the Short Form-36 (Quality of Life Scale) (p<0.05). Moreover, the scores in the Impact of Epilepsy Scale were positively significantly related to psychological symptom scores (p<0.05). The participants whose perception of the impact of epilepsy was significantly negative had poorer quality of life and more psychological symptoms (Table 4). The scores in the Epilepsy Knowledge Scale were positively significantly related to the scores in the role limitations due to emotional health, bodily pain, and perceptions of general health subscales of the Short Form-36 (Quality of Life Scale) (p<0.05).

The relationship between the scores in the Epilepsy Knowledge Scale and psychological symptom scores was insignificant (p<0.05). In addition, the participants, those whose Epilepsy Knowledge Scale scores were high had significantly high scores in the physical functioning, role limitations due to emotional health, bodily pain, and perceptions of general health subscales of the Short Form-36 (Quality of Life Scale). No significant relationship was found between the scores in the Epilepsy Knowledge Scale and psychological symptom scores (Table 4).

A positive and significant relationship was observed between the scores in the Epilepsy Attitude Scale and those in the energy/vitality, mental health, social functioning, and perceptions of general health subscales of the Short Form-36 (Quality of Life Scale) (p<0.05). The scores in the Epilepsy Attitude Scale were negatively and significantly related to psychological symptom scores (p<0.05). Moreover, of the participants, those who displayed high levels of positive attitudes toward epilepsy had high levels of positive perceptions of energy/vitality, mental health, social functioning, and perceptions of general health. In the participants whose attitudes

### Table 3. Comparison of the scores from the Impact of Epilepsy Scale, Epilepsy Knowledge Scale, and Epilepsy Attitude Scale in terms of the frequency of seizures

<table>
<thead>
<tr>
<th>Scale</th>
<th>Frequency of seizures</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>F</th>
<th>p</th>
<th>Significant difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact of epilepsy</td>
<td>A - Once a year</td>
<td>76</td>
<td>20.39</td>
<td>6.33</td>
<td>8.19</td>
<td>0.000</td>
<td>D&gt;A</td>
</tr>
<tr>
<td></td>
<td>B - Once a month</td>
<td>28</td>
<td>24.61</td>
<td>6.96</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C - Once a week</td>
<td>30</td>
<td>24.50</td>
<td>8.48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D - Every day</td>
<td>11</td>
<td>29.82</td>
<td>5.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epilepsy knowledge</td>
<td>A - Once a year</td>
<td>76</td>
<td>11.61</td>
<td>3.68</td>
<td>0.60</td>
<td>0.619</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B - Once a month</td>
<td>28</td>
<td>12.25</td>
<td>3.86</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C - Once a week</td>
<td>30</td>
<td>10.90</td>
<td>4.46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D - Every day</td>
<td>11</td>
<td>11.91</td>
<td>4.28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epilepsy attitude</td>
<td>A - Once a year</td>
<td>76</td>
<td>51.68</td>
<td>12.69</td>
<td>5.55</td>
<td>0.001</td>
<td>A&gt;C</td>
</tr>
<tr>
<td></td>
<td>B - Once a month</td>
<td>28</td>
<td>43.54</td>
<td>15.73</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C - Once a week</td>
<td>30</td>
<td>41.30</td>
<td>11.82</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D - Every day</td>
<td>11</td>
<td>46.00</td>
<td>14.72</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD: Standard deviation

The participants who were unemployed had higher scores from the somatization, obsessive–compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid thoughts, and psychoticism subscales than those who were employed. The scores in the Epilepsy Attitude Scale were negatively significantly related to psychological symptom scores (p<0.05). The participants whose perception of the impact of epilepsy was significantly negative had poorer quality of life and more psychological symptoms (Table 4). The scores in the Epilepsy Knowledge Scale were positively significantly related to the scores in the role limitations due to emotional health, bodily pain, and perceptions of general health subscales of the Short Form-36 (Quality of Life Scale) (p<0.05). The relationship between the scores in the Epilepsy Knowledge Scale and psychological symptom scores was insignificant (p<0.05). In addition, the participants, those whose Epilepsy Knowledge Scale scores were high had significantly high scores in the physical functioning, role limitations due to emotional health, bodily pain, and perceptions of general health subscales of the Short Form-36 (Quality of Life Scale). No significant relationship was found between the scores in the Epilepsy Knowledge Scale and psychological symptom scores (Table 4).
DISCUSSION

Because epilepsy affects patients' social and physical functioning, it can lead to increased psychological distress and reduced quality of life. In the present study, epilepsy symptoms significantly decreased in the participants whose epilepsy knowledge was significantly high (Table 4). These results conform to the results of this study. In a study by Aydemir in 2011, the patients whose knowledge level of epilepsy was low, those who were employed, and those who were male displayed a more negative attitude toward epilepsy (4). This difference may be due to the fact that participants were from different regions, that they experienced epilepsy-induced problems at work, and that they were exposed to stigma. In this study, as the Impact of Epilepsy Scale scores increased, the psychological symptoms increased as well. However, the negative and significant relationship was observed between the scores in the subscales of the Short Form-36 (Quality of Life Scale) and psychological symptom scores (p<0.05). Psychological symptoms decreased in the participants whose short form-36 (quality of life scale) scores were significantly high (Table 4).

Table 4. Correlation analysis between the variables

| 2          | 3          | 4          | 5          | 6          | 7          | 8          | 9          | 10         | 11         | 12         | 13         | 14         | 15         | 16         | 17         | 18         | 19         | 20         |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 1. Impact of epilepsy | -0.01** | -0.34** | -0.18** | -0.24** | -0.29** | -0.25** | -0.27** | -0.42** | -0.17* | -0.39** | 0.36* | 0.40** | 0.45** | 0.45** | 0.47** | 0.38** | 0.40** | 0.47** | 0.46** |
| 2. Epilepsy knowledge | 1         | -0.26** | 0.21** | 0.11 | 0.19* | 0.14 | 0.07 | 0.08 | 0.16* | 0.16* | -0.08 | -0.15* | 0.03 | 0.09 | 0.01 | 0.03 | 0.03 | 0.06 | 0.04 |
| 3. Epilepsy attitude | 1         | 0.06 | 0.10 | 0.07 | 0.15* | 0.25** | 0.24** | -0.10 | 0.26* | -0.28 | -0.26 | -0.38** | -0.30** | -0.39** | -0.36** | -0.34** | -0.34** | -0.41** |
| 4. Physical functioning | 1         | 0.54** | 0.43** | 0.40** | 0.20** | 0.35** | 0.54** | 0.48** | -0.24 | -0.20** | -0.28 | -0.30** | -0.22** | -0.05 | -0.13 | -0.15* | -0.22** |
| 5. Role limitations due to physical health | 1         | 0.64** | 0.38** | 0.30** | 0.47** | 0.53** | 0.45** | -0.28 | -0.27** | -0.34** | -0.36** | -0.29** | -0.17** | -0.20** | -0.23** | -0.23** |
| 6. Role limitations due to emotional health | 1         | 0.39** | 0.30** | 0.47** | 0.39** | 0.44** | -0.28** | -0.33** | -0.30** | -0.35** | -0.23** | -0.14 | -0.16 | -0.27** | -0.23** |
| 7. Vitality | 1         | 0.69** | 0.34** | 0.31** | 0.53** | -0.30** | -0.33** | -0.40** | -0.48** | -0.38** | -0.24** | -0.29** | -0.33** | -0.35** |
| 8. Mental health | 1         | 0.36** | 0.16** | 0.42** | -0.32** | -0.30** | -0.38** | -0.43** | -0.40** | -0.32** | -0.28** | -0.38** | -0.40** |
| 9. Social function | 1         | 0.50** | 0.49** | -0.37** | -0.46** | -0.47** | -0.48** | -0.32** | -0.38** | -0.42** | -0.44** |
| 10. Pain | 1         | 0.51** | -0.36** | -0.31** | -0.38** | -0.36** | -0.31** | -0.19** | -0.23** | -0.22** | -0.27** |
| 11. Perceptions of general health | 1         | -0.43** | -0.41** | -0.52** | -0.53** | -0.45** | -0.37** | -0.35** | -0.44** | -0.45** |
| 12. Somatization | 1         | 0.70 | 0.76** | 0.75** | 0.82** | 0.68** | 0.78** | 0.71** | 0.75** |
| 13. Obsessive-compulsive disorder | 1         | 0.74** | 0.80** | 0.77** | 0.66** | 0.69** | 0.80** | 0.75** |
| 14. Interpersonal sensitivity | 1         | 0.90** | 0.88** | 0.74** | 0.79** | 0.81** | 0.85** |
| 15. Depression | 1         | 0.87** | 0.70** | 0.77** | 0.84** | 0.85** |
| 16. Anxiety | 1         | 0.85** | 0.86** | 0.84** | 0.89** |
| 17. Hostility | 1         | 0.74** | 0.74** | 0.78** |
| 18. Phobic anxiety | 1         | 0.77** | 0.87** |
| 19. Paranoid thought | 1         | 0.83** |
| 20. Psychoticism | 1         | 0.90** |

*: p<0.05; **: p<0.01
with epilepsy, the one suffered most is depression (14, 15). In addition, the prevalence of depression was higher than that of other chronic diseases in patients with epilepsy (16, 17). Studies have shown that patients with epilepsy suffer from psychological problems when they experience internalized stigma (18). In a study conducted on children and adolescents with epilepsy, perceived stigma was associated with a worse self-concept and more symptoms of depression (19). In another study, stigma feelings of patients with epilepsy were associated with increased anxiety and depression (15, 20). In Jacoby et al.’s study, 21% of 168 patients with epilepsy who still had seizures were depressed. These results conform to the results of this study (21). In this study, in the participants with high levels of psychological symptoms, the perception of quality of life decreased. The perception of quality of life is worse in individuals with epilepsy than that in the general population (22, 23). In a study conducted involving 354 patients with epilepsy in Ethiopia, quality of life was low in unemployed patients with epilepsy. In this study, employed participants displayed a more favorable attitude toward epilepsy than unemployed participants, which is probably due to the fact the support the employed participants received from their social environment at their workplace improves their adaptation to work and in turn to the disease. Low socioeconomic level, difficulty in accessing health facilities, sociocultural characteristics, and incorrect knowledge about the disease can cause the person to develop negative attitudes toward the disease. In this study, the quality of life decreased as the frequency of seizures increased. In some studies, the frequency and types of seizures were the most important factors affecting the quality of life (24, 25). In a study by Leidy in 1999, the quality of life of patients without seizures was the same as that of healthy individuals and that the quality of life decreased as the frequency of seizures increased (24). This result conforms to that of this study. In patients with epilepsy, mental and cognitive disorders are among the leading factors negatively affecting the quality of life (26). Moreover, psychological symptoms affect the quality of life of patients, and therefore, health professionals should be aware of the importance of the patients’ psychosocial functioning. In studies conducted on patients with epilepsy, comorbidities, including depression and anxiety, have significantly decreased the quality of life (6, 27, 28). These results conform to those of this study. In Kwong et al.’s study conducted in 2016, the results of which are similar to those of this study, anxiety and the frequency of seizures were correlated with depression scores (29). This study revealed that the quality of life of the participants who displayed a favorable attitude toward epilepsy had better quality of life. In addition, psychological symptoms decreased in those who displayed a favorable attitude toward epilepsy. Several studies have been demonstrated that the quality of life decreases in patients exposed to stigma. Stigma restricts the personal, educational, and social opportunities of patients with epilepsy and significantly affects the quality of life of both patients with epilepsy and their family members (27, 30). Patients’ attitudes toward their illness affect their quality of life. In this regard, healthcare professionals are responsible for raising patients’ awareness, which facilitates their acceptance of the disease and the development of favorable attitudes.

CONCLUSION

The results of this study suggest that the psychiatric conditions of patients with epilepsy should be diagnosed and treated early to improve their quality of life and to treat them more successfully. It is recommended that systematic and comprehensive studies should be conducted to investigate the origins and consequences of negative attitudes displayed by patients toward their disease, how prejudices have been developed, and when and how these prejudices have been turned into negative attitudes. In addition, we believe that increasing the level of knowledge, reducing false or inaccurate information and prejudices about epilepsy in society, and sharing the disease with others and accepting it rather than hiding it will have a direct impact on patients’ negative attitudes toward the disease. We believe that patients should be informed about their diseases more. Since negative attitudes toward the disease may have a direct effect on the quality of life and psychiatric symptoms of patients with epilepsy, we think that negative attitudes toward the disease and the relationship between these attitudes and conditions affecting the disease should be routinely evaluated in neurology clinics. With the awareness that patients need more education, counseling, and support, we believe that healthcare professionals who care for patients with epilepsy should question and guide these patients within a framework of the multidisciplinary approach.

In addition, these patients should be supported when they want to work, and they should be reintegrated into society. We would like to express our sincere thanks to all the patients who participated in this research. This manuscript was obtained from master’s thesis at the Health Sciences Institute, Manisa Celal Bayar University.

Ethics Committee Approval: The Celal Bayar University Clinical Research Ethics Committee granted approval for this study (date: April 13, 2015, number: 164).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – SN, TA; Design – SN, TA; Supervision – SN; Resource – SN, TA; Materials – TA; Data Collection and/or Processing – TA; Analysis and/or Interpretation – SN, TA; Literature Search – SN, TA; Writing – SN, TA; Critical Reviews – SN.

Conflict of Interest: The authors have no conflict of interest to declare.

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