Contribution of the family environment to depression in Korean adults with epilepsy

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ABSTRACT

Purpose: Depression is common in adults with epilepsy and an important factor that affects quality of life in these individuals. However, there are few studies on the interactions between epilepsy and family factors in adults and we here investigate this association.

Methods: This cross-sectional, multicenter study collected data on 391 adults with epilepsy and their caregivers recruited from 27 hospitals throughout Korea. The Beck Depression Inventory (BDI), Stigma Scale, and Caregiver Burden Inventory (CBI) were used to evaluate the study population. Multivariate analysis was conducted using hierarchical linear regression. The Sobel test and structural equation modeling were used to examine interrelationships among the potential factors.

Results: The mean patient BDI score was 16.3 (SD = 11.1). Depressive symptoms (BDI $\geq$ 10) were in 68.3% and 57.0% in patients and their caregivers, respectively. Hierarchical linear regression analysis only identified caregiver BDI (β = 0.219; $p < 0.001$) as an independent factor related to patient BDI. The mediational model suggested that caregiver BDI mediated the effects of other family factors on patient BDI: caregiver's educational level ($p = 0.002$), caregiver's CBI score ($p < 0.001$), caregiver's Stigma Scale score ($p < 0.001$), and family APGAR score ($p < 0.001$). In addition, structural equation modeling showed that the relation between caregiver and patient BDI was unidirectional.

Conclusion: Caregiver depression is the most important contributor to depression in adults with epilepsy. The other family factors such as caregiver's perception of burden and the level of family function are indirectly correlated with patient depression via the mediating effects of caregiver depression.

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1. Introduction

Depression is the most common psychiatric comorbidity with epilepsy. The point prevalence of depression is substantially higher among patients with epilepsy than the general population, ranging from 13 to 35% according to large population-based studies.[1–3] This prevalence can be as high as 50% among patients with medically refractory epilepsy.[4,5] The pathogenic mechanisms of depression in patients with epilepsy result from the complex interactions between neurobiological (including genetic), iatrogenic, and psychosocial pathogenic factors.[6] Furthermore, several studies suggest a bidirectional relationship between depressive disorders and epilepsy.[7]

Depression significantly impacts quality of life (QoL) in patients with epilepsy. In patients with uncontrolled seizures in particular, depression causes greater QoL reductions than the seizures themselves.[8] Several factors, including demographic, seizure-related, treatment-related, and psychosocial factors, can contribute to depression in patients with epilepsy.[9] The impact of epilepsy is not limited to patients who experience seizures, but also affects all members of the family to a certain degree. Most studies in this regard have focused on childhood epilepsy when assessing the relationship between the family environment and depression, and found that the family environment is predictive of the psychological well-being of children and adolescents with epilepsy.[10] For example, parental perception of epilepsy stigma is associated with depression in children with epilepsy,[10] and maternal depression negatively correlated with QoL in children with new-onset epilepsy.[11]

In contrast, there have been few studies of family members of adults with epilepsy. Poor social support (which mostly comes from the family) is a significant predictor of depression in adults

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with epilepsy.[12] In a recent study, QoL in adults with epilepsy was reportedly significantly related to the QoL of family members,[13] and negative family reactions may be detrimental to the QoL of adults with epilepsy.[14] In addition, family life dissatisfaction is an established factor that affects the QoL and psychosocial well-being of adults with epilepsy.[15] These findings suggest the need for further research into the family factors that affect adults with epilepsy. We have here investigated the relationship between family factors and depression in adults with epilepsy.

2. Materials and methods

2.1. Patients

This cross-sectional, multicenter study collected data from adults with epilepsy and their caregivers who attended the neurological outpatient clinics of 22 university hospitals in Korea. Individuals >18 years of age who had been diagnosed with any type of epilepsy and had been treated for >1 year were allowed to participate. Patients were excluded if they had experienced a seizure in the 48 h prior to answering any questionnaires, were mentally disabled, had neurological deficits that affected daily living activities, or had major medical, surgical, or psychiatric illnesses. Demographic and clinical data were collected by interview and by reviewing each patient's medical files. All patients and their caregivers were asked to fill out questionnaires on the day they visited their neurologists at the outpatient clinic. Written informed consent was obtained from all patients.

2.2. Measures

Adults with epilepsy in the current study series filled out questionnaires on depression and perceived stigma. Depressive symptoms were assessed using the Beck Depression Inventory (BDI), which consists of 21 items rated on a 4-point scale. Higher scores represent higher levels of depression. Perceived stigma was measured using the Stigma Scale for epilepsy,[16,17] which consists of the 3 items and requires simple yes/no responses. Patients were asked to say if they felt other people were uncomfortable with them, treated them as inferior, or preferred to avoid them because of their epilepsy. Patients scored 1 point for each item they agreed with, and their overall score was the sum of their positive responses; thus, a higher score indicates that the patient felt more likely to face stigma.

Caregiver depression, perceptions of stigma, and burden for caring for patients were evaluated and assessed using BDI, Stigma Scale, and Caregiver Burden Inventory (CBI), respectively. CBI is a 22-item inventory that evaluates the effects of disease on caregiver QoL, psychological suffering, financial difficulties, shame, guilt, and difficulty in social and family relationships. Scores range from 0 to 88, and a higher score indicates a higher burden.[18] The Stigma Scale was modified to assess the caregiver's perception of stigma in our current analyses. For example, the question "Because of your epilepsy, do you feel that other people are uncomfortable with you?" was modified for the caregiver to read: "Because of your offspring's epilepsy, do you feel that other people are uncomfortable with him/her?" Family function constructs were assessed using the family APGAR (Adaptation, Partnership, Growth, Affection, and Resolve) questionnaire,[19] which uses 5 questions to assess the components of family functioning. Three possible answers are allowed ("almost always", "sometimes", "almost never"), and the score varies between 0 and 2 points. Therefore, the sum ranges between 0 and 10 points, and families are characterized as functional (7–10) or dysfunctional (≤6). A dysfunctional family can be classified as mild (3–6) or severely dysfunctional (≤2).

2.3. Statistical analysis

The relationship between patient BDI and family factors was determined after controlling for demographic and clinical variables. The patient's BDI score was considered a dependent variable. Independent variables included the caregiver BDI score, Stigma Scale score, CBI score, educational level and family APGAR. Adjusted variables included age, sex, employment status, education, perceived stigma, and epilepsy-related variables such as age at onset, epilepsy duration, seizure frequency, generalized tonic-clonic (GTC) seizure frequency, and receiving polypharmacy. In univariate analysis, Pearson correlation analysis was used to assess numeric and ordinal variables and Student's t test was used to assess nominal variables. Multivariate analysis using hierarchical linear regression analysis was used to further assess variables with p values <0.05 according by univariate analysis. Significance was set at $p < 0.05$. IBM SPSS 21.0 software (IBM Inc., Armonk, NY) was used to perform these statistical analyses.

We also employed the mediational model, which proposes that some family factors affect patient depression via mediators such as caregiver depression. Evidence for mediation is considered sufficient if the relationship between some family factors and patient BDI is reduced when the effects of the mediators are controlled. Mediation effects were assessed using the Sobel test, which was performed using the R statistics program (version 2.14.2) and the "bda" package.

Lastly, using the structural equation modeling, we evaluated interrelationships among the potential factors affecting patient BDI, which were identified based on multiple linear regression analysis and Sobel test. Structural equations shown in Fig. 1 were conducted by AMOS 22.0 (SPSS Inc., Chicago, IL) based on the Maximum Likelihood Method. Standardized path coefficients were presented. For fitted model evaluation, chi-square with the degrees of freedom, the normed fit index (NFI), and the relative fit index (RFI) were measured and all the measures were acceptable.

3. Results

The demographic and clinical characteristics of the 391 study patients and their caregivers are listed in Table 1. The mean age of the adults with epilepsy in the current study series was 38.8 years (SD = 14.5; range 18–79) and 187 patients (47.8%) were female. The mean age at seizure onset was 24.7 years (SD = 16.8), and
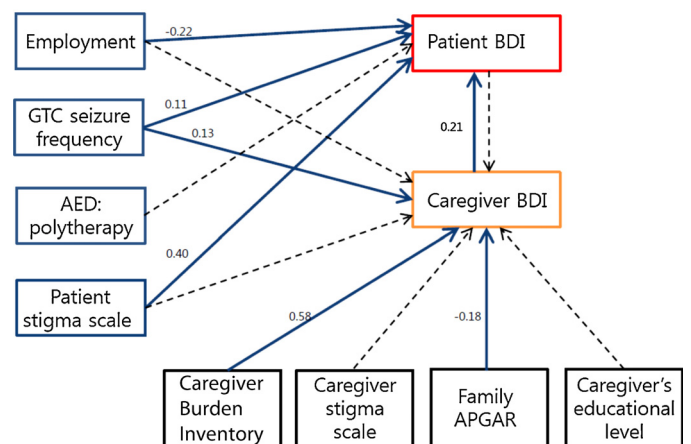
Fig. 1. Structural model used to explore the inter-relationships between patient depression (BDI) and the clinical variables. A continuous arrow represents a direct relationship from one variable to another. A dashed arrow represents a non-significant correlation between the two variables. Numbers are standardized path coefficients.

Table 1
Characteristics of the adults with epilepsy and their caregivers.

Patient	
Age (years), mean ± SD	38.8 ± 14.5
Female, n (%)	187 (47.8%)
Marital status, n (%)	
Married	177 (45.9%)
Employed, n (%)	246 (62.9%)
Education, n (%)	
Elementary school	26 (6.6%)
Middle school	49 (12.5%)
High school	139 (35.5%)
University	149 (38.1%)
Seizure onset (years), mean ± SD	24.7 ± 16.8
Duration (years), mean ± SD	13.6 ± 12.5
Epilepsy syndrome, n (%)	
Idiopathic generalized epilepsy	33 (8.4%)
Symptomatic partial epilepsy	187 (47.8%)
Cryptogenic partial epilepsy	146 (37.3%)
Undetermined	22 (5.6%)
Predominant seizure type, n (%)	
Absence seizure	18 (4.6%)
Partial seizure	247 (63.2%)
Generalized seizure	122 (31.2%)
Seizure frequency, n (%)	
Remission (>1 year)	109 (27.9%)
1–11 years	177 (45.3%)
Monthly	105 (26.9%)
Number of AEDs, n (%)	
Monotherapy	147 (37.6%)
Polytherapy	240 (61.4%)
Caregiver	
Relation to the patient, n (%)	
Mother	151 (38.6%)
Father	40 (10.2%)
Spouse	164 (41.9%)
Other	20 (5.1%)
Education, n (%)	
Elementary school	38 (9.7%)
Middle school	70 (17.9%)
High school	151 (38.6%)
University	107 (27.4%)
Economic status, n (%)	
High	7 (1.8%)
Middle	232 (59.3%)
Low	121 (30.9%)

AEDs, antiepileptic drugs; SD, standard deviation.

Table 2
Results of the questionnaire given to adults with epilepsy and their caregivers.

Questionnaire	Patient	Caregiver
Beck Depression Inventory, mean ± SD	16.3 ± 11.1	13.7 ± 11.1
No depression (<10), n (%)	124 (31.7%)	168 (43.0%)
Mild depression (10–18), n (%)	120 (30.7%)	105 (26.9%)
Moderate depression (19–29), n (%)	98 (25.1%)	81 (20.7%)
Severe depression (≥30), n (%)	49 (12.5%)	37 (9.5%)
Stigma Scale, mean ± SD	0.7 ± 1.1	0.7 ± 1.1
0 (i.e., no stigma), n (%)	254 (65.6%)	246 (65.1%)
1, n (%)	43 (11.1%)	47 (12.4%)
2, n (%)	36 (9.3%)	29 (7.7%)
3, n (%)	54 (14.0%)	56 (14.8%)
Caregiver Burden Inventory, mean ± SD		43.8 ± 26.7
Little or no burden (≤20), n (%)		95 (24.4%)
Mild to moderate burden (21–40), n (%)		84 (21.5%)
Moderate to severe burden (41–60), n (%)		99 (25.4%)
Severe burden (>60), n (%)		112 (28.7%)
Family APGAR, mean ± SD		6.0 ± 2.6
Functional family (7–10), n (%)		152 (39.3%)
Dysfunctional family (≤6)		
Mildly dysfunctional (3–6), n (%)		202 (52.2%)
Severely dysfunctional (≤2), n (%)		33 (8.5%)

APGAR, Adaptation, Partnership, Growth, Affection, and Resolve; SD, standard deviation.

were noted in 235 families (60.7%). Detailed information about the scores measured using these questionnaires are provided in Table 2.

3.1. The family environment can contribute to depression in adults with epilepsy

By univariate analysis, patient BDI scores were found to be significantly correlated with all family factors, including the caregiver's educational level ($r = -0.200$; $p < 0.001$), CBI ($r = 0.279$; $p < 0.001$), BDI ($r = 0.339$; $p < 0.001$), Stigma Scale scores ($r = 0.158$; $p = 0.002$), and APGAR ($r = -0.232$; $p < 0.001$). Other statistically significant factors included patient age ($r = 0.152$; $p = 0.003$), patient's educational level ($r = -0.261$; $p < 0.001$), unemployment status (BDI scores 20.9 vs 14.3; $p < 0.001$), GTC seizure frequency ($r = 0.148$; $p = 0.004$), receiving polypharmacy (BDI scores 17.8 vs 14.1; $p = 0.001$), and patient stigma ($r = 0.466$; $p < 0.001$). Demographic and social variables (age, educational level, and employment status) were entered into the hierarchical linear regression analysis as the first step. The second step included epilepsy-related variables (GTC seizure frequency and receiving polypharmacy). The third step included psychological variables (perceived stigma). All family factors considered significant according to the univariate analysis were entered during the last step. Only caregiver BDI ($\beta = 0.219$; $p < 0.001$) was identified as an independent factor related to patient BDI after controlling for variables that demonstrated p values <0.05 according to univariate analysis (Table 3). Independent variables considered significant after the first step included employment status ($\beta = -4.785$; $p < 0.001$), which explained 12.3% of the BDI variance. GTC seizure frequency ($\beta = 1.742$; $p = 0.042$) and polypharmacy ($\beta = 2.417$; $p = 0.037$) additionally accounted for 5.6% of the variance, and patient stigma ($\beta = 3.712$; $p < 0.001$) in the third step additionally accounted for 14.5% of the variance. Caregiver BDI in the last step additionally explained 4.5% of the variance in patient BDI (Table 3).

3.2. Mediational effects of caregiver depression

To test a patient series using the mediational model, it is necessary to first prove that the predictors (caregiver's educational level, caregiver's CBI and Stigma Scale scores, and family APGAR), mediators (caregiver's BDI score), and outcomes (patient's BDI

mean epilepsy duration was 13.6 years (SD = 12.5). Most adults with epilepsy had partial epilepsy (47.8% were symptomatic; 37.3% were cryptogenic). In total, 27.9% of adults with epilepsy were in remission for >1 year. About 37.6% of adults with epilepsy were treated using monotherapy (Table 1). The primary caregivers were the spouse (n = 164; 41.9%), mother (n = 151; 38.6%), father (n = 40; 10.2%), or other person (n = 20; 5.1%).

The mean patient BDI score was 16.3 (SD = 11.1). Abnormal BDI scores (i.e., ≥10) were noted in 267 patients (68.3%). Of these, 120 (30.7%), 98 (25.1%), and 49 patients (12.5%) experienced mild-to-moderate (BDI ≥ 10), moderate-to-severe (≥19), or severe depression (≥30), respectively. Patient BDI score was significantly correlated with the caregiver BDI ($r = 0.339$; $p < 0.001$). The mean caregiver BDI score was 13.7 (SD = 11.1). Abnormal BDI scores (i.e., ≥10) were noted in 223 caregivers (57.0%), and 9.5% demonstrated severe depression (≥30). About 34.4% of adults with epilepsy reported feeling some level of stigma, and 13.8% of adults with epilepsy answered "yes" to all 3 items, thereby indicating that they felt highly stigmatized by their disorder. Patient Stigma Scale scores were significantly correlated with patient BDI ($r = 0.466$; $p < 0.001$), caregiver BDI ($r = 0.199$; $p < 0.001$), and the caregiver's perception of stigma ($r = 0.240$; $p < 0.001$). The mean score on family APGAR was 6.0 (SD = 2.6). Abnormal APGAR scores (i.e., <7)

Table 3
Hierarchical linear regression analysis of the factors associated with depression in adults with epilepsy.

Variables			Patient BDI				
			B	t	p	ΔR^2	p
Step 1	Demographic factors	Employment status	−4.785	−3.958	<0.001	0.123	<0.001
		Age	0.051	1.203	0.230		
		Educational level	−0.872	−1.266	0.206		
Step 2	Epilepsy-related factors	GTC seizure frequency	1.742	2.041	0.042	0.056	<0.001
		Polytherapy	2.417	2.091	0.037		
Step 3	Psychological factors	Patient's Stigma Scale	3.712	7.537	<0.001	0.145	<0.001
Step 4	Family factors	CBI	−0.056	−1.904	0.058	0.045	0.001
		Caregiver's BDI	0.219	3.571	<0.001		
		Caregiver's Stigma Scale	−0.171	−0.305	0.760		
		APGAR	−0.396	−1.637	0.103		
		Caregiver's educational level	−0.513	−0.820	0.413		

AEDs, antiepileptic drugs; APGAR, family Adaptation, Partnership, Growth, Affection, and Resolve; BDI, Beck Depression Inventory; CBI, Caregiver Burden Inventory.

score) are interrelated.[20] We already established that (a) the mediator is related to outcomes and (b) predictors are associated with outcomes. We used Pearson correlation analysis to establish the relationship between the mediator and predictors. The caregiver's BDI score was significantly related to the caregiver's educational level ($r = -0.189$; $p < 0.001$), caregiver's CBI score ($r = 0.636$; $p < 0.001$), Stigma Scale score ($r = 0.415$; $p < 0.001$), and family APGAR ($r = -0.431$; $p < 0.001$). Mediational modeling was conducted to assess caregiver BDI score as a mediator between patient BDI and other family factors. The Sobel test showed that family factors, including the caregiver's educational level ($p = 0.002$), caregiver's CBI ($p < 0.001$) and Stigma Scale scores ($p < 0.001$), and family APGAR ($p < 0.001$) affect patient BDI mediated by caregiver BDI (Table 4).

3.3. Interrelationship among factors affecting patient BDI

Complex interrelationships were illustrated by the refined path diagram (Fig. 1). The respective contribution of the variables to a dependent variable was indicated by the standardized regression coefficient of the predictor variables. Caregiver BDI had direct (unmediated) effects on patient BDI (standardized path coefficient = 0.22). However, patient BDI did not have direct effect on caregiver BDI. The CBI and family APGAR were identified to have direct influence on caregiver BDI, and indirect effect on patient BDI mediated by caregiver BDI in accordance with Sobel test. However, caregiver stigma scale and caregiver's educational level did not have indirect relationship with patient BDI. GTC seizure frequency had direct effects on both patient and caregiver BDI. However, polytherapy did not have direct effect on patient BDI in disagreement with linear regression analysis. Table 5 presents the unstandardized and standardized coefficients of the structural equation model.

Table 4
Mediational effects of caregiver depression on the relationship between family factors and depression in adults with epilepsy.

	B	SE	Z	p
Caregiver's Burden Inventory	0.070	0.017	4.175	<0.001
Caregiver's Stigma Scale	1.281	0.259	4.940	<0.001
Family APGAR	−0.560	0.115	−4.882	<0.001
Caregiver's educational level	−0.653	0.209	−3.123	0.002

APGAR, Adaptation, Partnership, Growth, Affection, and Resolve.
Data obtained using the Sobel test.

4. Discussion

We find in our current analysis that the family environment significantly affects depressive symptoms in adults with epilepsy. Among several family factors tested, caregiver depression was found to be the most important factor that contributes to depression in adults with epilepsy. Other family factors, such as the caregiver's educational level, caregiver's perception of burden and stigma, and family functioning levels were found to be indirectly correlated with patient depression via the mediational effects of caregiver depression. In addition, unemployment, high GTC seizure frequency, polypharmacy, and a perceived stigma were identified as independent predictors of depression in adults with epilepsy.

In our current study, patients with abnormal BDI scores (i.e., ≥10) and at least moderate-to-severe depression (≥19) comprised 68.3% and 37.6% of the study population, respectively. The point prevalence and severity of depression in our current series are similar to those of previously reported studies.[3,21] In our current study also, caregivers demonstrated a high point prevalence of depressive symptoms that were comparable to those in the adults with epilepsy. Caregivers with abnormal BDI scores (i.e., ≥10) and at least moderate-to-severe depression (≥19) comprised 57.0% and 30.2% of the study population, respectively. Thompson and Upton investigated the psychological well-being of the caregivers of adults with epilepsy and reported that depression is more common among caregivers (7 of 44 caregivers; 15.9%) than the general

Table 5
Unstandardized and standardized path coefficient estimates for the final model.

Model pathways	Unstandardized path coefficient	Standardized path coefficient	p
GTC seizure frequency → caregiver BDI	2.23	0.13	0.002
CBI → caregiver BDI	0.23	0.58	<0.001
Family APGAR → caregiver BDI	−0.72	−0.18	<0.001
Employment status → patient BDI	−5.04	−0.22	<0.001
Caregiver BDI → patient BDI	0.21	0.21	<0.001
GTC seizure frequency → patient BDI	1.81	0.11	0.02
Patient stigma scale → patient BDI	3.80	0.40	<0.001

APGAR, family Adaptation, Partnership, Growth, Affection, and Resolve; BDI, Beck Depression Inventory; CBI, Caregiver Burden Inventory; GTC, generalized tonic-clonic.

population.[22] A caregiver's perceived practical and emotional support, which is derived mostly from the family, is inversely associated with depression.[22] In previous studies on childhood epilepsy, 12–49% of mothers either met or scored above the clinical cut-off values for depression according to self-reported screening measures.[23] One study measured clinical depression and found that 31.5% of mothers of children with epilepsy had a major depressive disorder.[24]

In our current investigation, caregiver depression was the most important predictor of depression in adults with epilepsy. This finding is in agreement with those of previous studies on childhood epilepsy, which have found that the children of mothers with depression are at significantly higher risk for depression.[25] In addition, Dunn and Austin[26] have suggested that a family history of depression is an important clue for diagnosing depression in children with epilepsy. However, contrasting findings were reported in another study,[27] in which no correlation was found between the level of maternal depressive symptoms and depression in children with epilepsy. In an additional study on caregivers of adults with intractable epilepsy, which used the Rand 36-item Health Survey (RAND-36),[28] the caregivers seemed to demonstrate reduced mental well-being. This was also reported to be associated with self-reported higher burdens of care, but not to be influenced by the patient's mental well-being, seizure frequency, or employment status.

Using the structural equation modeling, the relationship between patient and caregiver BDI was found to be unidirectional but not bidirectional. Only the effect of caregiver BDI on patient BDI was found, but reverse relationship was not valid. Our findings did not exclude a possibility of bidirectional relationship between depressive symptoms of patients and their caregivers. It is because interrelationship could be changeable depending on factors constructing a structural equation model. Therefore, patients' depressive mood may be a predictor of caregiver depression as stated in previous reports.[22–24]

We found that caregiver depression mediated the effect of other family factors on patient depression. On Sobel test, the caregiver's educational level, caregiver's perceived burden and stigma of epilepsy, and family functioning significantly impact depression in adults with epilepsy through caregiver depression. The structural equation modeling also showed the indirect effect of caregiver's perceived burden and family functioning on patient BDI. In studies on childhood epilepsy, however, some of these family factors were found to be directly related to psychopathology in children with epilepsy. Parental perception of epilepsy stigma reportedly contributes to depression in children with epilepsy.[29] The burden of pediatric epilepsy may be regarded as a threat to family homeostasis, to which the family responds with extreme reactions that lead to family dysfunction that exacerbates the child's illness.[30] The impact of family functioning on depressive symptoms in children with epilepsy has also been reported.[31,32] A child's satisfaction with family relationships also predicts the child's level of depression,[31] and family conflicts are correlated with child depression.[32]

In our current investigation, patients with epilepsy reported low family satisfaction by demonstrating low family APGAR scores (mean ± SD = 6.0 ± 2.6), and about 60.7% of these patients were in dysfunctional families (≤6). According to an earlier Hong Kong study that used the APGAR scale, 43.7% of families with a family member with epilepsy are dysfunctional.[33] In general, families with family members with epilepsy experience more stress, are not as close, and more likely to be dysfunctional than controls. Austin et al. have also indicated that families with children with epilepsy demonstrate lower levels of communication, family social support, and financial well-being than control families.[34] In previous studies, the APGAR scores of families with patients with epilepsy were associated with

caregiver depression, patient depression, and a poor QoL level. Family satisfaction, as measured using APGAR, demonstrates strong associations with mental health-related QoL.[33] In a recent study, Mahrer-Imhof reported that the QoL of adults with epilepsy is significantly related to the QoL of the family members,[13] and family life dissatisfaction is an established factor that affects QoL and the psychosocial well-being of adults with epilepsy.[15]

As expected, epilepsy-related factors such as high GTC seizure frequency and receiving polypharmacy were significantly related to depression in the adults with epilepsy in our present study. Especially, GTC seizure frequency did not only exert direct effect on patient depression, but also indirect effect through caregiver depression in our current study. Thapar et al.[35] reported that depression and seizure frequency mutually influence each other, both concurrently and across time. However, our present analysis and some previous studies did not suggest that overall seizure frequency influences depression in adults with epilepsy.[12,36] Seizure severity seems to be more important to causing depressive symptoms in epilepsy patients than seizure frequency.[36] A history of status epilepticus,[37] higher levels of perceived seizure severity,[36] greater problems with seizure recovery,[36] and high GTC seizure frequency were identified in our current study as factors that contribute to depression in patients with epilepsy. In the present study, receiving polypharmacy as a significant predictor for patient BDI lost its significance in structural equation modeling. Adults with epilepsy on polytherapy often have a more complicated form of epilepsy. Issues related to having a difficult-to-treat epilepsy such as uncontrolled seizures may indirectly cause depressive symptoms via the variable 'receiving polytherapy'. In addition, 34.4% of patients in this study reported feelings of stigma that were associated with their epilepsy, and they were more likely to suffer depressive symptoms.

This study had some limitations of note. First, our cross-sectional study design could not directly evaluate causal hypotheses, even though the structural equation model could provide direction of influence and show direct and indirect effects among the potential factors. Second, our study did not provide data about the psychiatric family history that would have been a moderator. Third, there was no information about treatment of antiepileptic drugs which could have significant influence on patient depression by its side effects.[4] Fourth, the family environment and its relationship to individual patients can differ considerably, especially between Western and Eastern countries with different traditions. Caution is needed when interpreting the results of our current study in different cultural environments. Lastly, our study population was recruited from university hospitals, and the enrolled patients likely had more severe seizures than patients at attending primary clinics. Hence, some of our results, such as prevalence and severity of depressive symptoms, may not be applicable to other populations. However, our main findings in terms of family factors that are most likely to influence depression in adults with epilepsy could be generally applied to all adults with epilepsy.

5. Conclusion

Caregiver depression is the most important contributor to depression in adults with epilepsy. The caregiver's educational level, caregiver's perception of burden and stigma, and family functioning level are indirectly correlated with patient depression via the mediational effects of caregiver depression. Our findings suggest that the family environment significantly impacts the depressive symptoms that present in adults with epilepsy, as is the case in childhood epilepsy, and that more appropriate family-centered care is also required when treating depression in adults with epilepsy. Further research is needed—especially prospective

studies and interventional trials—to identify the important familial factors that impact patient depression and the results of particular treatments.

Conflicts of interest

None of the authors have any conflicts of interest to disclose.

Appendix A

The Korean QoL in Epilepsy Study Group consists of the following individuals and institutions: Eun Jeong Koh and Jun Young Lee, Chonbuk National University (Chonju); Myeong Kyu Kim, Chonnam National University (Kwangju); Dong Jin Shin, Gachon University (Incheon); Ki Whan JI, Kyung-Il Park, Inje University (Pusan); Sun Ah Park, Soonchunhyang University (Pucheon); Hyunwoo Nam and Chang Ho Yun, Seoul National University (Seoul); Young Won Cho, Keimyung University (Daegu); Eun-yeon Joo, Sungkyunkwan University (Seoul); Sang Ho Kim, Dong-A University (Pusan); Dong Wook Kim, Konkuk University (Seoul); Sun Jung Han, Wonkwang University (Koonpo); Young Min Sohn, Catholic University (Seoul); Kyoung Heo, Won Joo Kim, and Yang Je Cho, Yonsei University (Seoul); Eun Mi Lee, University of Ulsan (Ulsan); Hyun Jeong Han, Kwandong University (Koyang); Kwang Ki Kim, Dongguk University (Ilsan); Won Chul Shin, Kyunghee University (Seoul); Gyu Sik Kim, National Health Insurance Corporation Ilsan Hospital (Ilsan); Jeong Ju Lee, Eulji University (Seoul); Seong Ho Koh, Hanyang University (Seoul); and Ju Yong Kim, Hallym University (Seoul).

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