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Rom J Diabetes Nutr Metab Dis. **24**(2):137-148
doi: 10.1515/rjdnmd-2017-0018

THE ROLE OF NEUROTICISM AND PSYCHOLOGICAL FLEXIBILITY IN CHRONIC FATIGUE AND QUALITY OF LIFE IN PATIENTS WITH TYPE 2 DIABETES

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received: April 23, 2017 *accepted*: June 05, 2017
available online: June 15, 2017

Abstract

Background and Aims: *The purpose of this study was to identify the role of neuroticism and psychological flexibility (PF) in quality of life (QOL) and chronic fatigue (CF) in patients with Type 2 Diabetes Mellitus (T2DM).* ***Materials and Methods:*** *We considered the all of the patients with T2DM over aged 30 years and living in the province of Hamadan, Iran in 2014 that were referred to the Hamadan Diabetes Center. A sample size of 170 patients was selected by the simple random sampling method. The measuring tools were completed by the patients. To test assumptions, the Pearson correlation and structural equation modeling were used.* ***Results:*** *The results showed that the correlation coefficient between neuroticism, with CF ($r=0.579$; $p<0.001$) and QOL ($r=-0.242$; $p<0.001$), and also correlation between PF and CF ($r=0.287$; $p<0.001$) are significant. There is no significant relationship between QOL and PF ($r= -0.098$; $p=0.203$). Structural equation modeling showed that neuroticism has a direct positive effect in CF ($p<0.001$) and a negative effect on QOL ($p<0.001$), and the PF has a significant direct effect on CF ($p=0.014$) and an indirect effect on QOL. The CF affects negatively on the QOL ($p<0.001$).* ***Conclusion:*** *It could be concluded that neuroticism and PF play important roles in QOL and CF and with effective intervention can help patients with diabetes to improve them QOL.*

key words: *Quality of life; chronic fatigue; Psychological flexibility; Neuroticism; Diabetes*

Background and Aims

Diabetes as a chronic disease has multiple symptoms and it affects by abnormalities in the metabolism of carbohydrates, proteins and fats. Although, the 40-59 years age group has the maximum frequency of people with diabetes in the worldwide, the highest age-specific prevalence of diabetes is in the 60-79 years aged group [1]. Among aged 20–79 years, a study estimated the worldwide prevalence of diabetes about 6.4% (285 million adults) in 2010, and it is

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expected that will increase to 7.7% (439 million adults) by 2030. The number of adults with diabetes will increase in developing countries and a corresponding 20% in developed countries, between 2010 and 2030 [2]. In Iran, a developing country, the prevalence of diabetes is about 24% of the population over 40 years old and it increases by 0.4% with each year after 20 years of age. The risk of T2DM in women is with 1.7% greater than in men [3,4].

Over the past two decades, psychological status and quality of life (QOL) has been an important issue in the clinical research and patient care. The QOL is momentous in the patient diagnosis, prediction of disease outcome and treatment evaluation [5]. The WHO defines QOL as 'an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns' [6]. The diabetes disease has significant negative effects on QOL and the QOL of diabetic patients is associated with glycemic control and the patient's daily behavior and a diagnosis of type 2 diabetes affects on QOL [7] while controlling diabetes by patients is associated with their sense of the QOL [8].

Another symptom that may be important in diabetic patients is chronic fatigue (CF). A review study concludes that because of symptoms such as CF, diabetic patients are at greater risk for chronic complications associated with diabetes [9]. The CF, a symptom that is often observed in persons with chronic problems (such as diabetes), is an illness which lasts for more than 6 months and not relieved by rest [10]. According to factors such as the diagnostic criteria of CF syndrome, the prevalence of CF syndrome varies in between 0.01% and 2.6% in general population samples [11]. The CF is reported by at least 20% of patients seeking medical care [12]. The fatigue affects physical, psychological and cognitive tasks that are necessary in successful self-management of diabetes [9]. The fatigue is indirectly related to glucose control and in persons with adequate glucose control; fatigue is mainly influenced by the presence of diabetes symptoms and distress [13].

The chronic pain disease study suggests utilizing acceptance and commitment therapy (ACT) for a range of conditions associated with severe pain and distress or other similar symptoms, for example CF [14]. Psychological flexibility (PF), the primary target for improvement in ACT [15] is defined as 'contacting the present moment as a conscious human being, and, based on what that situation affords, acting in accordance with ones chosen values' [16]. Persons with a high score of PF have more satisfaction with life and higher mental health compared to those with a low score of PF. They have also more commitment to receive consistent behaviors with their values [17,18]. The ACT is essential in the behavioral and health outcomes such as depression, anxiety, smoking, diabetes, epilepsy, and work-related stress, chronic pain treatment and weight management [19-21]. In addition, the psychological inflexibility predicts of higher anxiety and lower QOL, and the acceptance predicts higher QOL [22].

Neuroticism, as a salient personality variable that decreases the emotional and physical well-being over time [23,24] explains the relationship between depression and interpersonal chronic as life stress [25]. In Parkinson's disease patient, after disease severity, neuroticism was reported the second most important variable associated with QOL [26]. A prospective longitudinal study suggested that neuroticism predict QOL among Chinese gynecologic cancer survivors [24]. An investigation in patients with CF syndrome for illness acceptance and neuroticism in cognitive

behavior therapy showed that an acceptance changes QOL beyond the effect of neuroticism [27]. In another study, the indirect effects of neuroticism via shame, psychological inflexibility, and emotion dysregulation on anxiety symptoms were evaluated [28].

As seen, the studies show the negative and positive effects of neuroticism on QOL and CF, respectively. Also, many studies have been manipulated to identify and evaluate the effect of PF and neuroticism in patients QOL without considering the role of CF as intermediate variable. Neither PF nor neuroticism effects have been investigated in diabetic 2 patients with QOL or CF. To assess whether either of PF or neuroticism may affect on QOL, we must first examine whether those are accurate predictors of CF and so patients QOL with diabetes 2. In other words, the purpose of this study is to examine the relationship of neuroticism and PF on QOL and so the significant role of these variables in patient's CF and QOL by considering the CF as mediator variable in type 2 diabetic patients.

Material and Methods

Design

In this cross-sectional study, we considered the patients with Type 2 Diabetes living in Hamadan province, Iran (652 persons), which follow treatment of the disease in Hamadan Diabetes Center in 2014. This center is referral and under supervision of the Hamadan University of Medical sciences. We considered the list of patients and then selected the samples (172 patients) with simple random sampling method from the list. We considered the accident or congenital disability, chronic diseases such as cancers, multiple sclerosis (MS) and recent heart surgery as exclusion criteria. With these criteria two patients were excluded from the study.

Measurements

QOL: a general QOL instrument is SF-36 that measures eight health related concepts: physical functioning (10 items), role limitations due to physical problems (4 items), bodily pain (2 items), general health perceptions (5 items), vitality (4 items), social functioning (2 items), role limitations due to emotional problems (3 items), and perceived mental health (5 items). A single item that indicates a perceived change in general health status in duration of a one-year period is also in the SF-36 [29]. The Persian translated questionnaire obtained the internal consistency for all SF-36 scales in which the Cronbach's a coefficient ranging from 0.77 to 0.90 except for vitality scale 0.65. Each item correlation with its hypothesized scale has been reported ranging from 0.58 to 0.95 and satisfactory convergent validity [30]. We obtained Cronbach's coefficient ranging from 0.62 to 0.91 for eight SF-36 scales.

CF: The fatigue severity scale (FSS) is a 9-item questionnaire with response categories ranging from 1 'strongly dis-agree' to 7 'strongly agree' for each inquiry. The sum score of the nine inquiries ranges from 9 ('no signs of fatigue') to 63 ('most disabling fatigue'). The Cronbach's alpha coefficient and the interclass correlation coefficient test were reported 0.96 and 0.93 respectively, which show the good repeatability of the Persian version of the FSS [31]. In the current study the alpha Cronbach's coefficient obtained 0.90.

Neuroticism: We used the neuroticism measure part of the Eysenck personality questionnaire-revised short scale that is self-report questionnaire to assess three dimensions of personality: neuroticism, extraversion and psychoticism [32]. The concurrent and construct validity of questionnaire reported in several languages [33]. The Persian version with 24 items scale measuring neuroticism was used to

assess the degree of trait neuroticism. Each item has binary answers (yes=1, no=0). The score of neuroticism obtains of the sum of 24 questions. The alpha Cronbach's coefficient for a measure of internal consistency obtained 0.84.

PF: The central mechanism of the ACT model is PF. This model has two main components: acceptance and mindfulness processes (acceptance, defusion, the present moment, and a transcendent sense of self), and the commitment and behavioral change processes (values, committed action, the present moment and a transcendent sense of self) [34]. Palladino et al. (2013) applied three overlapping measures, AAQ-II, CFQ and mindful attention and awareness questionnaires to evaluate PF [35]. This ACT process is often equated to mindfulness, engaged living scale (ELS) and cognitive fusion questionnaire (CFQ) [34]. On the other hand, the acceptance and action questionnaire-II (AAQ-II) is a seven-item, holistic measure of PF [17,19]. We used the sum of AAQ-II, ELS, mindfulness and CFQ scores to obtain a PF score as a center of ACT parts. In this study, we obtained the PF internal consistency (alpha Cronbach's coefficient) equal to 0.71. So, we follow these four components.

Acceptance and action questionnaire: We used AAQ-II, which has a Likert scale and runs from 1 (never true) to 7 (always true), with higher scores indicating greater levels of PF. The alpha Cronbach's coefficient was reported in the acceptable range (0.78–0.88). The 3- and 12-month test–retest reliabilities for the AAQ-II were very acceptable at 0.81 and 0.79 respectively, and illustrated incremental validity [17,36]. For Persian version, the alpha Cronbach's coefficient was reported 0.89 and test-retest reliability 0.71 [37]. We obtained the alpha Cronbach's coefficient = 0.86.

ELS: We used the 16-item questionnaire that rated a 7-point Likert scale (1- never true, 7-always true). The Cronbach's alpha for the test scores of both subsection and the total scale of the ELS have been reported good to excellent internal consistencies, ranging from 0.86 to 0.90. The internal consistency and construct validity of the 16 items by assessing relationships with other theoretically related were investigated [38]. In this study, the alpha Cronbach's coefficient was obtained 0.88.

Mindfulness: The mindfulness was measured using the 24-item mindfulness questionnaire [39]. The respondents were asked to rate how true given statements are for themselves on a five-point Likert scale. The 12 questions have direct (1 = rarely to 5 = always) and 12 questions, indirect (1 = always to 5 = rarely) scores. Gillanders et al. (2014) reported the questionnaire internal reliability equal to 0.87. The mindfulness questionnaire received the highest possible rating in multiple studies for internal consistency and construct validation [40]. We obtained the alpha Cronbach's coefficient=0.74 for internal reliability of Persian version.

CFQ: a brief, self-report measure of cognitive fusion that participants complete a paper-and-pencil form of the CFQ, containing 7 items. They answer with a 7-point Likert scale (1=never to 7=always). The CFQ demonstrated excellent internal consistency (Cronbach's $\alpha \geq 0.88$) in different samples and good test-retest reliability r=0.80. Also, the preliminary evidence of the CFQ's constructs and incremental validity was reported [41]. In this study, the alpha Cronbach's coefficient was obtained 0.87 for internal reliability.

Procedure

We excluded diabetic 1 and pregnant diabetic patients. All patients completed consent form. The questionnaires were completed by self-reporting by patients in the clinical center in waiting for treatment or at home. We completed,

the incomplete or corrupted data by telephone interviewing or revisiting the patients. The illiteracy patients were interviewed and then completed questionnaires.

Statistical analysis

We used the descriptive statistics for characterizing the sample data and the correlation coefficients and structural equation modeling (SEM) to find the variable's relationship. Data were analyzed in SPSS software version 16.0 and the SEM was conducted using AMOS. Standardized direct and indirect path coefficients were calculated and several indices were used to assess the model goodness of fit; goodness-of-fit statistic (GFI), normed-fit index (NFI), the comparative fit index (CFI), incremental fit index (IFI), the root-mean-square error of approximation (RMSEA) and the Chi-square test [42].

We considered a p-value less than 0.05 for statistically significant. Also, the Pearson (or Spearman) correlation coefficient was performed in the assessment of the relationship between variables. The Bonferroni correction was used to decide a statistical significance cutoff for the correlation coefficient to account for the many analyzes. A total of 69 correlation analyzes were performed. So, individual analyzes with P<.0007 were considered statistically significant.

Results

Descriptive statistics for the sample

In the study sample, 125 persons (73.50%) were women. 74.70% (127) of patients were under diploma education, and others were diploma or universities graduated. 39 persons were single and lived alone or with their children. The mean (SD) age of patients was 59.13 (9.16) and in the range 33-95 years. The mean duration since the onset of the disease (years) was 11.582 (7.46). The average (range) number of children of patients was 4.18 (0-10). Table 1 shows the mean, minimum and maximum of the PF (four subsections), the QOL (sum of eight related subsections that transformed in percent), neuroticism and chronic fatigue. The mean of QOL, CF, PF and neuroticism scales are 50.91 (20.30), 43.34 (12.32), 192.68 (19.91) and 16.12 (5.08). To test the normality distribution of variables, we used Kolmogorov–Smirnov test. Except the physical function, role limitation due to physical health problems and role limitation due to emotional problems; the variables have approximately normality distribution (p>0.05). We compared mean of QOL(p=0.872), CF(p=0.711), neuroticism(p=0.423) and PF(p=0.518) in interviewing patients (53) and self-reporters (117) and t-test showed that there isn't significant differences between two groups.

PF and QOL

Table 2 shows the correlation coefficients of variables. There are negative significant correlation between PF and two subsections of physical sections of QOL; physical functioning (Pearson correlation = -0.199; p=0.009) and role limitation due to physical health problems (Spearman's correlation =-0.169; p=0.028). There are no significant correlation between PF and other QOL subsections (p=0.30). The relationship between the subsections of PF and QOL information showed that the CFQ and acceptance and action are negatively correlated with subsections of QOL (p<0.001) and are positively correlated with CF (p<0.001). The mindfulness is positively correlated with sections of QOL (p<0.018), except the role limitation due to physical health problems subsections (r=0.101; p=0.190). In addition, the ELS is correlated with subsections of QOL (p<0.009) except physical functioning (p=0.364)and role limitation due to physical health problems (p=0.517).

Table 1. Demographic and personality characteristics and QOL of the patients

Charactristic		Value*	min	max
Gender	Female	73.50%	-	-
	Male	26.50%	-	-
Education	Under diploma	74.70%	-	-
	Diploma	15.90%	-	-
	University education	16.20%	-	-
Marital status	Single	22.94%	-	-
	Married	77.04%	-	-
Age (years)		59.13(9.16)	33.00	95.00
Number of children of patients		4.18(1.98)	0.00	10.00
Time since onset of the disease (years)		11.58(7.46)	1.00	10.00
QOL subsectins	Physical functioning	50.35(29.17)	0.00	100.00
	Role limitation due to physical health problems	44.77(39.31)	0.00	100.00
	pain	53.53(28.67)	0.00	100.00
	General health	46.97(21.49)	0.00	100.00
	Social functioning	68.09(29.48)	0.00	100.00
	Role limitation due to emotional problems	48.43(36.77)	0.00	100.00
	Energy and fatique	43.32(25.17)	0.00	100.00
	Emotional well-bing	51.79(26.90)	0.00	100.00
QOL (SF-36)		50.91(20.30)	0.00	93.96
CF		43.34(12.32)	9.00	63.00
Neuroticism		16.12(5.08)	2.00	24.00
PF Subsctions	AAQ-II	27.31(11.61)	7.00	49.00
	Mindfulness	75.22(11.55)	49.00	108.00
	ELS	60.43(11.14)	30.00	80.00
	CFQ	29.73(11.04)	7.00	49.00
	PF	192.68(19.91)	124.00	254.00

*Values are presented as number (%) or mean(standard deviation).

Note: QOL=quality of life; SF-36= The Short Form Health Survey; CF=chronic fatigue; PF=psychological flexibility; AAQ-II= acceptance and action questionnaire-II; ELS= engaged living scale; CFQ= cognitive fusion questionnaire.

Neuroticism and QOL

The neuroticism is negatively correlated with subsections of QOL (P<0.001) and with increasing neuroticism of patients the QOL and subsections scores decrease.

PF, neuroticism and CF

There is a positive significant relationship between neuroticism and CF (r=0.58; p=<0.001), and between CF and PF (r=-0.29; p<0.001). The mindfulness is negatively correlated with CF (p<0.001). But, the ELS and CF aren't correlated (p=0.194).

CF and QOL

The CF is negatively correlated with QOL (r=-0.29; p<0.001) and QOL subsections (-0.49<r<-0.28; p<0.001).

Table 2. Correlations between the QOL subscales and CF with other measures.

		PF subsections				PF	Neuroticism	CF
		AAQ-II	Mindfulness	ELS	CFQ			
QOL subsections	Physical functioning	-0.30**	0.27**	0.07	-0.40**	-0.20**	-0.36**	-0.49**
	Role limitation due to physical health problems [a]	-0.20*	0.10	.050	-.028**	-0.17*	-0.38**	-0.41**
	pain	-0.28**	0.32**	0.27**	-0.37**	-0.04	-0.38**	-0.38**
	General health	-0.32**	0.31**	0.35**	-0.40**	-0.03	-0.46**	-0.36**
	Social functioning	-0.35**	0.29**	0.38**	-0.38**	-0.04	-0.40**	-0.28**
	Role limitation due to emotional problems [a]	-0.19*	0.18*	0.20*	-0.17*	0.04	-0.38**	-0.36**
	Energy and fatique	-0.35**	0.39**	0.31**	-0.49**	-0.08	-0.57**	-0.42**
	Emotional well-bing	-0.42**	0.48**	0.41**	-0.51**	-0.02	-0.56**	-0.30**
QOL		-0.42**	0.42**	0.34**	-0.52**	-0.10	-0.24*	-0.29**
CF		0.41**	-0.28**	-0.10	0.48**	0.29**	0.58**	-

*p<0.05 **p<0.0001; [a] Spearman correlation calculated in relationship with other variables.
Note: QOL=quality of life; CF=chronic fatigue; PF=psychological flexibility; AAQ-II= acceptance and action questionnaire-II; ELS= engaged living scale; CFQ= cognitive fusion questionnaire.

Structural equation Modeling

In Table 3, the estimated regression weights, unstandardized and standardized coefficients (direct and indirect) of the conceptual model are provided. The neuroticism involved in CF and QOL. The PF plays a role in the CF and CF affects in the QOL. Covariance and correlation coefficient between PF and neuroticism shows that the neuroticism predicts and demonstrates PF. The correlation between these two variables is positive and significant (r=0.24; p=002). In addition, the table shows the effects (total, direct and indirect) of neuroticism and PF on CF.

Table 3. Unstandardized and standardized (direct and indirect) of structural estimation mode1 coefficient

	Unstandardized effect		Standardized effect			
	Estimate	SE	Indirect	Direct	Total	p
Neuroticism --> CF	1.31	0.15	0.00	0.54	0.54	<0.01
PF--> CF	0.10	0.04	0.00	0.16	0.16	0.01
CF--> QOL	-0.41	0.12	0.00	-0.25	-0.25	<0.01
Nneuroticism --> QOL	-1.94	0.28	-0.14	-0.49	-0.62	<0.01
PF--> QOL	-	-	-0.04	0.00	-0.04	-

Note: SE=standard error; CF=chronic fatigue; QOL=quality of life; PF=psychological flexibility

Finally, Table 4 shows the model fit criteria. Indices are in the acceptance interval for goodness of model fitting [41]. Figure 1 shows the graphical relationships of variables. As seen, an association is between neuroticism and PF. The neuroticism has a negative direct effect on

QOL and positive direct effect on CF. Additionally, CF has a significant effect on QOL. In other words, the neuroticism has an indirect effect on QOL. The PF has a direct effect on the CF and result the indirect effect on QOL. The dashed line in Figure 1 represents that PF was included in the exploratory analysis, but is not significant and it hasn't a direct effect on QOL.

Table 4. Indices of goodness of fit of the model

IFI	CFI	GFI	NFI	RMSEA	Chi-Square	df	p
0.99	0.99	0.99	0.99	0.04	2.77	1	0.10

Note: IFI=incremental fit index; CFI=comparative fit index; GFI=goodness-of-fit statistic; NFI= normed-fit index; RMSEA= root-mean-square error of approximation.

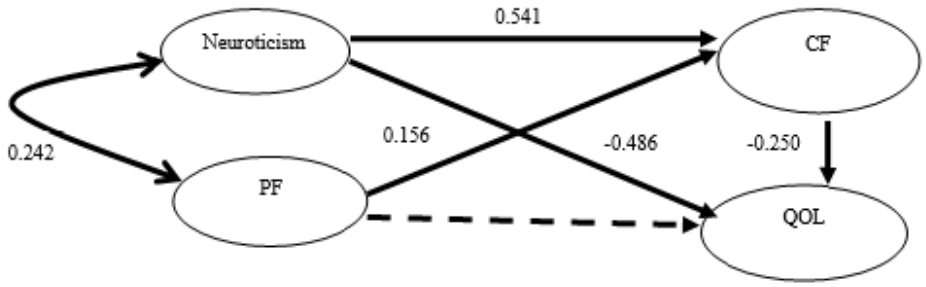

Figure 1. *Structural equation modeling of association between neuroticism and PF with CF and QOL.*

Significant standardized regression coefficients are presented as association and effect of mesures on CF and QOL; dashed line represents effect that was included in the exploratory analysis, but was not significant. Note: PF=psychological flexibility; CF=chronic fatigue; QOL=quality of life.

Discussion

In this study, diabetic patients who refer to diabetes center of Hamadan city were considered. Several studies were conducted in diabetes disease risk factors and complications [43,44]. In this study, we evaluated neuroticism and PF on QOL and CF.

A major finding of the present study is that neuroticism decrease QOL. This is compatible with a study in Parkinson's disease patient that showed after disease severity, the neuroticism is associated with QOL [26] and with another study among Chinese gynecologic cancer survivors that suggested the neuroticism predict QOL [24]. In addition, it agrees with a study's results in public health [45].

The finding showed that the neuroticism has a positive role in the CF and it indicated that the neuroticism is associated with the CF syndrome [46]. The neuroticism is a pervasive predictor of CF over a variety of time points. The strength of the relationship between neuroticism and fatigue, changes over the course of the weekdays and the weekend [47].

We found that PF has an indirect relation with QOL and there is a negative correlation between PF and physical functioning and role limitation due to physical health problems. Whereas, studies noted that PF is predictive of lower QOL [22] and psychological function in diabetic patients is lower than in healthy people [48]. The QOL is significantly correlated with

PF [49] and at all, the chronic disease alike depression could be a risk factor for abnormal behaviors [50,51].

The psychological stress has a role in CF [52] and we found that there is a positive direct role of PF on CF. In other words, increasing PF decreases the CF.

Furthermore, PF plays an important role in QOL of patients. This is agreement with another study, which emphasizes the psychological inflexibility predicts of higher anxiety and lower QOL, and the acceptance predicts higher QOL [22]. The ACT is a psychotherapeutic model helps to increase PF. Acceptance is an important element in coping and living with chronic illnesses such as diabetes. Increasing acceptance causes in many positive outcomes such as greater QOL.

The CF is a disabling problem and relates to weak reported QOL compared to other chronic situations. The difference in QOL between CF patients and healthy adolescents was reported larger than expected. A large sample of adolescents with CF emphasizes that CF is a disabling problem and has a strong impact on QOL [53].

The chronic and debilitating nature of diabetes affects all dimensions of life. The economic and social problems of communities related in psychological problems associated with chronic diseases. The diabetes reduces the QOL and many interventions could improve the status of disease and increase the QOL of patients [54]. Diabetes control is associated with a sense of QOL by patients [8].

We evaluated the effect of PF and neuroticism in patients QOL by considering the role of CF as mediator variable and this evaluation was done in diabetic 2 patients. To assess whether either of PF or neuroticism might be effected QOL, we find these variables are predictors of CF and CF is a mediator variable between these variables and QOL.

This study has several limitations, including, study samples were from one center, the more questionnaires were filled via self-report (0.69%) and the PF measure is new tools and should be reexamined to evolve and further refinement of instrument and construct. And further, there might be variation in PF measures, such as mindfulness that does not relate directly to PF [55] and it is necessary for more investigation.

It is an important to understand the relations among neuroticism, PF and CF and QOL with considering subsections. To fully find the etiology of each QOL subsection problem, it will be necessary to explore each of these factors and relationships. Number of QOL subsections problems (e.g. less than first each subsection quartile) is an interesting field for future study by using count data distribution modeling [56,57].

Conclusion

We found, in diabetic patients, the neuroticism and PF are correlated and are essential in CF as mediator variable. In addition, CF and neuroticism affect the QOL (Figure 1). The PF on QOL hasn't direct effect, but has a significant indirect effect on QOL. In other words, to increase the QOL, it should be taught patients to adapt the disease condition and improve somewhat the neuroticism. Although, modifying the PF improves CF and then CF affects on the QOL.

Understanding the causal pathways linking QOL and CF to the many variables associated with those will likely show a great deal about possessing common health problems. This should help the development and integrated causal models for treating the many adverse symptoms associated with CF and QOL.

Acknowledgement. This article was a part of MSc thesis of Frazaneh Momeniarbat in clinical psychology of Hamadan Branch, Azad University. We thank the Hamadan Diabetes Center personnel in cooperation to do this research.

Conflict of interest. The authors declare that they have no conflict of interest.

Ethical approval. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study. The Research Council of Hamadan Branch, Azad University approved the study.

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