ORIGINAL ARTICLE

UDC: 613.86-055.26::[616-053.2::616.8-053.2
DOI: 10.2298/VSP1309842S

Health-related quality of life and depression in Rett syndrome caregivers

Kvalitet života i depresija kod roditelja dece obolele od Retovog sindroma

Adrijan Sarajlija*, Milena Djurić*†, Darija Kisić Tepavčević‡

***Mother and Child Health Institute of Serbia "Dr Vukan Čupić", Belgrade, Serbia; †Pediatrics Cathedra, ‡Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia**

Abstract

Background/Aim. Rett syndrome (RTT) is a severe neurodevelopmental disorder primarily affecting females with an estimated incidence of 1 : 10,000–15,000 female births. Currently, there is no specific treatment that halts or reverses the progression of RTT. Therefore, management was mainly symptomatic, focussed on optimising patient's abilities. The aim of this study was to investigate factors influencing health-related quality of life (HRQoL) and depression in mothers who care for children with Rett syndrome (RTT) in Serbia. **Methods.** The cross-sectional study was conducted on 49 mothers giving care to females with RTT. Caregivers` HRQoL was assessed by using the SF-36 questionnaire. Clinical severity score (CSS) of RTT patients and Beck Depression Inventory II (BDI -II) scale were used to quantify RTT severity and mothers` depression, respectively. Statistical assessment included descriptive statistics, *t*-test, Pearson correlation coefficient and multiple logistic regression. **Results.** The age of mothers ranged from 22 to 55 years and of their affected children from 3 to 29 years. Severe depression was observed in 15 (30.6%) participants. CSS and BDI – II scores correlated negatively with all SF-36 domains and composite scores. Lowest scoring domains of HRQoL in mothers giving care to RTT children were mental health, vitality and role functioning emotional. Multiple linear regression analysis revealed that severity of RTT patients` disability (CSS) and caregivers` age are factors with strongest influence to HRQoL and depression in care giving mothers. **Conclusion.** Mothers giving care to children with RTT are at high risk of severe depression and lower HRQoL scores of domains that reflect mental well-being. Results of this study can help in planning subsequent interventions directed at families dealing with Rett syndrome.

Key words:
rett syndrome; caregivers; mothers; depression; quality of life.

Apstrakt

Uvod/Cilj. Retov sindrom (RTT) je težak neurorazvojni poremećaj koji prvenstveno pogađa devojčice. Incidencija se procenjuje na 1 : 10 000–15 000 živorođene dece ženskog pola. Trenutno ne postoji specifična terapija koja bi mogla da promeni tok ove bolesti. Stoga je tretman uglavnom simptomatski sa naglaskom na unapređenje pojedinih sposobnosti bolesnika. Cilj ove studije bio je ispitivanje faktora koji utiču na kvalitet života (HRQoL) i depresiju majki koje brinu o deci oboleloj od RTT u Srbiji. **Metode.** Studija preseka je obuhvatila 49 majki koje brinu o deci oboleloj od RTT. Kvalitet života je ispitivan pomoću SF-36 upitnika. Skor težine kliničke slike (CSS) bolesnika sa RTT i Bekova skala depresije II (BDI – II) upotrebljeni su u proceni težine bolesti kod dece, odnosno stepena depresije kod majki. Statistička analiza je uključila deskriptivne metode, *t*-test, Pirsonov koeficijent korelacije i multiplu linearnu regresiju. **Rezultati.** Starost majki kretala se u rasponu od 22 do 55 godina, a uzrast bolesnika od 3 do 29 godina. Teška depresija je zapažena kod 15 (30,6%) učesnica u studiji. Skorovi CSS i BDI – II negativno su korelisali sa svim SF-36 dimenzijama i zbirnim skorovima. Najniže ocenjene dimenzije kvaliteta života kod majki koje brinu o deci sa Retovim sindromom su mentalno zdravlje, vitalnost i emocionalno funkcionisanje. Multipla linearna regresija pokazala je da godine majke i težina kliničke slike deteta imaju najsnažnije dejstvo u pravcu pojave depresije i lošijeg kvaliteta života u ovoj populaciji. **Zaključak.** Majke koje brinu o deci sa RTT imaju visok rizik za pojavu teške depresije i nižih skorova HRQoL u domenima koji odražavaju mentalno stanje. Rezultati ove studije mogu pomoći u planiranju adekvatne podrške porodicama koje imaju članove obolele od RTT.

Ključne reči:
retov sindrom; staratelji; majke; depresija; kvalitet života.

Correspondence to: Adrijan Sarajlija, Mother and Child Health Institute of Serbia "Dr Vukan Čupić", 11000 Belgrade, Serbia.
E-mail: adrijans2004@yahoo.com

Introduction

Rett syndrome (RTT) is a severe neurodevelopmental disorder primarily affecting females with an estimated incidence of 1 : 10,000–15,000 female births [1, 2]. Mutations in the X-linked gene methyl CpG-binding protein 2 (MECP2) have been found in the majority of patients [3, 4]. However, diagnosis of RTT remains a clinical one, by usage of established criteria [5]. Main clinical features of RTT include progressive psychomotor deterioration, autism, stereotypic movements of the hands, loss of acquired language and decreased cranial growth. The identification of a MECP2 mutation can support a clinical diagnosis but it is not a basis for diagnosis [5, 6]. RTT has a wide clinical variability in terms of its severity, and phenotype-genotype correlation has become more elucidated in recent large studies [7].

Currently, there is no specific treatment that halts or reverses the progression of RTT, and management is mainly symptomatic, focussed on optimising patient's abilities. Among RTT patients 50–80% develops epilepsy at a median age of 3 years [8], so anticonvulsant drugs are the mainstay of pharmacological approach to these patients.

Plethora of evidence from worldwide studies indicates proneness for depression and lower health-related quality of life in mothers caring for children with disabilities [9–12]. Apart from child disease characteristics, some sociodemographic factors (family income, marital status, mother's age etc.) were also recognized for having significant influence on these outcomes [13, 14]. However, studies addressing depression, health-related quality of life (HRQoL) and social issues in RTT caregivers remain sparse [15–17].

The aim of this study was to investigate HRQoL and depression in mothers caring for children with RTT in Serbia. A specific aim of our investigation was to assess the influence of sociodemographic factors and clinical severity of child disease to HRQoL and depression in care giving mothers.

Methods

The cross-sectional study was conducted on 49 mothers giving care to females with RTT. The study was performed during the period from January 1, 2010 to July 31, 2010 in Mother and Child Health Care Institute of Serbia in Belgrade, with a set of questionnaires being sent to a total of 60 mothers caring for RTT children regularly controlled and treated in this institution. Approval by the institution`s ethics committee was obtained. Mother and Child Health Care Institute of Serbia is a tertiary care paediatric center and represents referent hospital for RTT syndrome in Serbia. Inclusion criteria were that the diagnosis of RTT in child is established on the basis of "The Rett Syndrome Diagnostic Criteria Work Group" criteria [7], and that the residency of investigated family is in Serbia. Mothers diagnosed with major medical or psychiatric condition were excluded from the study. A set of applied questionnaires was comprised of three parts. Part 1 consisted of a sociodemographic questionnaire that addressed mothers' age, marital status, education level, employment status (employed, unemployed), family income (combined family income measuring above or below two average salaries) and the place of residency (urban/rural). Serbian translation of SF-36 [18], a generic HRQoL instrument, comprised part 2 of a questionnaires set. SF-36 measures eight domains of HRQoL calculated within eight scales: physical functioning (PF), role functioning physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role functioning emotional (RE), and mental health (MH). The domains of SF-36 are used to calculate composite scores - physical health composite score (PCS) and mental health composite score (MCS), as well as SF-36 total composite score (TCS). PCS is calculated as an average value of PF, RP, BP, GH and VT domains. The MCS is also calculated out of five domains: VT, SF, RE, MH and GH. The scores for the SF-36 are based on a 0 to 100 scale; zero represents the lowest possible score, and 100 represents the highest possible score. In general population, used as a norm-based reference group, 50 represents the mean score. HRQoL scales were presented as T-scores (mean 50, SD 10) by linear transformation of raw scores that optimize comparisons across the different scales of the SF-36. Higher values meant better domains of HRQoL. Scoring and calculation of SF-36 scales were performed according to Ware's survey manual recommendations. Part 3 measured depression with a Serbian translation of Beck Depression Inventory – II (BDI-II) [19]. Scores of BDI-II from 0 to 13 were considered as minimal, 14–20 as mild, 20–28 as moderate and 29–63 as severe depression [20]. Completed questionnaires were retrieved from 49 subjects with the response rate of 81.7%.

Severity of RTT was determined by using a Clinical Severity Score (CSS) developed specifically for this disease [21]. The CSS is a composite score based on thirteen individual categories measuring clinical features of RTT. All the scores range from 0 to 4 or 0 to 5 with 0 representing the least severe and 4 or 5 representing the most severe finding, while a total score ranges from 1 to 58. The CSS score was assigned and evaluated by the paediatric neurologist.

Descriptive statistics, such as mean ± standard deviation (SD) on the collected data were calculated. Pearson correlation coefficients were used to examine the relation between SF-36 domains, composite and total scores to scores of BDI-II, CSS and age of mothers giving care to children with RTT. We used *t*-test to compare SF-36 domains, composite and total scores of the studied group to general population. Assessing the difference of SF-36 scores and BDI-II score between the group of mothers giving care to less severely affected children with RTT (CSS $\leq$ 20) and the group with more severely affected children (CSS > 20) was also performed by *t*-test. This cut-off value for CSS was used since it represents median CSS in our group of patients.

We used multiple linear regression to investigate the influence of sociodemographic factors of care giving mothers and the presence of epilepsy in RTT patients on SF-36 composite scores (PCS, MCS and TCS) and BDI-II scores in our study group. Mothers educational, employment and marital status, family income, place of residency (village or city), number of children in family and the presence of epilepsy in RTT children were the factors selected for testing. The statistically significant level was set at $p < 0.05$.

Results

The demographic characteristics of 49 mothers caring for children with RTT are presented in Table 1, while clinical features of 49 female children with RTT are summarized in Table 2. Age of mothers ranged from 22 to 55 years and of their affected children from 3 to 29. In RTT patients, mean CSS was 21.5 (range from 10 to 39) with 23 (46.9%) patients scoring ≤ 20 on CSS.

Table 1
Characteristics of the participant mothers giving care to children with Rett syndrome (N = 49)

Variable	Values
Age (years), $\bar{x}$ ± SD	37.5 ± 7.5
Marital status, n (%)	
married	41 (83.7)
divorced	8 (16.3)
Education, n (%)	
elementary school	4 (8.2)
high school	33 (67.3)
university	12 (24.5)
Place of residency, n (%)	
urban	37 (75.5)
rural	12 (24.5)
Employment status, n (%)	
employed	35 (71.4)
unemployed	14 (28.6)
Family income, n (%)	
below average	19 (38.8)
above average	30 (61.2)
Number of children in family, n (%)	
1	10 (20.4)
≥ 2	39 (79.6)

Table 2
Characteristics of the children with Rett syndrome (N = 49)

Variable	Values
Age (years), $\bar{x}$ ± SD	12.2 ± 6.7
Clinical Severity Score (CSS)), $\bar{x}$ ± SD	21.5 ± 7.9
Epilepsy, n (%)	
present	32 (65.3)
absent	17 (34.7)

Our study revealed that a slight majority of mothers had minimal scores of BDI-II (53.2%), 8 (16.4%) of them had mild to moderate depression, while severe depression was observed in 15 (30.6%) of the investigated participants. Furthermore, we found statisticly significant correlation between CSS, BDI-II, mother's age and all domains of SF-36 (Table 3.). Patients` age did not show a significant correlation with CSS scores. The CSS scores had significantly negative correlation with all SF-36 domains and composite scores with highest correlation coefficients found for VT, GH and all composite scorres. We demonstrated a high statistical significance of negative correlation between BDI-II and all SF-36 domains with highest correlation coefficients for SF, VT and PCS domains. Mother`s age correlated negatively to all SF-36 domains and composite scores with high statistical significance, particularly for SF, PF, VT and PCS (Table 3).

We found that the lowest scoring domains of HRQoL in mothers giving care to RTT children were mental health (47.3 ± 29.6), vitality (43.6 ± 27.8) and role functioning emotional (42.1 ± 42.4), but none of domains differed significantly to general population norms. However, when we compared HRQoL scores between two groups of mothers divided on the basis of CSS (≤ 20 and > 20) we found significantly lower values of MH, PF, PCS and TCS in the group caring for more severely affected children (Table 4). Other

Table 3
Correlation between each of 8 domains and 3 composite scores of SF-36 health-related quality of life instrument and Clinical Severity Score (CSS), maternal depression (measured by Beck Depression Inventory-II – BDI-II) and maternal age (AoM)

Variable	PF	RP	BP	GH	VT	SF	RE	MH	MCS	PCS	TCS
CSS	-0.354[a*]	-0.398[**]	-0.343[*]	-0.423[**]	-0.519[**]	-0.335[*]	-0.408[**]	-0.478[**]	-439[**]	-463[**]	-441[**]
BDI-II	-0.744[**]	-0.687[**]	-0.836[**]	-0.832[**]	-0.891[**]	-0.903[**]	-0.728[**]	-0.862[**]	-855[**]	-900[**]	-880[**]
AoM	-0.526[**]	-0.339[*]	-0.408[**]	-0.441[**]	-0.485[**]	-0.519[**]	-0.407[**]	-0.446[**]	-464[**]	-492[**]	-482[**]

The values presented as Pearson correlation coefficients. CSS – Clinical Severity Score; BDI-II – Beck Depression Inventory-II; AoM – age of mothers; PF – physical functioning; RP – role functioning physical; BP – bodily pain; GH – general health; VT – vitality; SF – social functioning; RE – role functioning emotional; MH – mental health; MCS – mental composite score; PCS – physical composite score; TCS – total composite SF-36 score; *$p < 0.05$; **$p < 0.01$

Table 4
Mean scores for SF-36 health-related quality of life domains and composite scores and Beck Depression Inventory-II (BDI-II) in the mothers giving care to the children with Rett syndrome

Variable	Total group ($\bar{x}$ ± SD)	Clinical severity score ($\bar{x}$ ± SD)		*t*-test (*p*-value)
		≤ 20 (n = 23)	> 20 (n = 26)	
BDI-II	17.0 ± 13.3*	14.1 ± 10.7	19.6 ± 14.9	0.001
PF	73.1 ± 27.4	79.1 ± 20.9	67.7 ± 31.5	0.001
RP	52.0 ± 37.4	61.9 ± 32.7	43.3 ± 39.7	0.104
BP	51.5 ± 32.9	57.1 ± 29.9	46.5 ± 35.2	0.421
GH	49.7 ± 27.7	57.9 ± 23.8	42.3 ± 29.3	0.06
VT	43.6 ± 27.8	53.5 ± 22.8	34.8 ± 29.3	0.089
SF	47.9 ± 32.1	52.2 ± 30.5	44.2 ± 33.6	0.369
RE	42.1 ± 42.4	55.0 ± 40.9	30.7 ± 41.0	0.73
MH	47.3 ± 29.6	56.5 ± 22.6	39.2 ± 32.9	0.008
MCS	46.1 ± 29.6	55.04 ± 24.9	38.2 ± 31.6	0.064
PCS	54.2 ± 28.4	62.1 ± 22.7	47.1 ± 31.4	0.009
TCS	50.9 ± 29.4	59.1 ± 24.2	43.7 ± 32.2	0.021

PF – physical functioning; RP – role functioning physical; BP – bodily pain; GH – general health; VT – vitality; SF – social functioning; RE – role functioning emotional; MH – mental health; MCS – mental composite score; PCS – physical composite score; TCS – total composite SF-36 score.

HRQoL domains showed reduced values in the group caring for children with CSS > 20, but theres was no statistically significant difference. A significant statistical difference was found between these two groups in BDI-II scores (Table 4).

Multiple regression analysis identified CSS and mothers` age as factors significantly influencing depression level and all HRQoL composite scores. Multivariate model showed also that employment status significantly affected mothers` depression level (Table 5).

Table 5

Multiple linear regression model using significant values to predict health-related quality of life and depression of caregivers

Variable	β coefficient	*p*-value
PCS		
age of mothers	-1.803	0.001
CSS	-1.164	0.040
MCS		
age of mothers	-1.738	0.002
CSS	-1.205	0.041
TCS		
age of mothers	-1.817	0.002
CSS	-1.171	0.049
BDI-II		
age of mothers	1.034	0.000
employment status	10.13	0.019
CSS	0.509	0.034

PCS – physical composite score; MCS – mental composite score; TCS – total composite SF-36 score; BDI-II – Beck Depression Inventory-II; CSS – Clinical Severity Score.

Discussion

Challenges of caring for children with RTT are only sparsely reported in the literature. A substantial number of studies have found that HRQoL is significantly worse in mothers caring for a disabled child compared with mothers of children without disability [22–24]. Rett syndrome is a severe neurodevelopmental disorder, so our study aimed to confirm impact of debilitating disease on psychological and the physical functioning of care giving mothers. We assessed HRQoL and presence of depression in 49 mothers caring for children with RTT. We also analyzed possible correlations of HRQoL, depression level, clinical severity of RTT and sociodemographic characteristics of mothers. Clinical severity and BDI-II scores were found to be significantly related to all the domains and composite scores of SF-36. These findings are in accordance with investigations of caregivers for patients with different chronic diseases [25–27]. Thus, more severe clinical manifestations of RTT in children were correlated to higher level of depression and lower HRQoL of their mothers. Also, significantly lower BDI-II, MH, PF, PCS and TCS in group caring for more severely affected children (CSS ≤ 20) further pointed out the impact of clinical severity of child`s disease on parental well-being.

The presence of severe depression (BDI-II score ≥ 29) in 30.6% of care giving mothers is similar to findings of studies involving primary caregivers of children with disabilities [15, 28]. Most of studies investigating mental health of parents with disabled children have found higher scores for maternal depression compared to control groups [29]. We decided to address only maternal HRQoL and depression since a number of research consistently reported that fathers of children with disabilities show normal depression scores [30, 31]. Observation that mothers experience more distress than fathers could be caused by the fact that mothers take on a larger part of care and practical work that children with disabilities require. More proper burden measures could substantiate this hypothesis for RTT caregivers in future studies.

A significant negative correlation of BDI-II scores to CSS that we proved in our study also corresponds to findings that severity of clinical manifestations in children with disability is closely related to parental psychosocial stress [32–34]. However, some studies that addressed depression in parents with children affected with cerebral palsy did not find a significant correlation of depression and clinical severity of child's disease [27, 34].

Bahi-Buisson et al. [17] indicated that the presence of epileptic and non-epileptic seizures in RTT patients had a significant impact on their family's quality of life. Multivariate regression analysis that we performed showed no significant influence of seizure presence to HRQoL domains or depression level. On the other hand, CSS of RTT patients was identified as significant factor that adversely affect all SF-36 composite scores and BDI-II score in their mothers. Calculating CSS includes the presence of epilepsy among the variety of other signs and symptoms encountered in RTT.

A recent Turkish study pointed out a significant negative correlation between BDI scores and all domains of HRQoL tested by Nottingham Health Profile with maternal educational level having strongest impact on HRQoL [35]. Maternal education was recognized as a predictor of maternal depression and lower domain scores of HRQoL in other studies [36]. Our study did not show any significant influence of maternal education to HRQoL and depression level. The most probable reason is our small study sample with only 4 mothers with college education.

Studies conducted in patients with different neurologic diseases or their caregivers (muscular dystrophies, multiple sclerosis) showed a significant negative correlation between depression and HRQoL in tested subjects [18, 37]. Similar results were obtained in our study. These findings indicate that depression associated with chronic disease significantly affects HRQoL, both in patients and their caregivers.

The largest study to date involving HRQoL in RTT caregivers observed lowest score for MCS among composite HRQoL scores [15], similarly to our study. A high prevalence of severe depression in our group could be related to lower scores in the mental health domain of SF-36. Laurvick et al. [15] also identified family income and behaviour problems in RTT affected children as the strong predictors of lower mental health scores, while age of mothers did not affect mental or physical health [15]. In our study, family income was not proved as a significant "buffer" of psychosocial stress. This finding does not correspond to a number of studies dealing with caregivers of children with disabilities [15, 36]. There are, however, researchers who, similarly to our results, did not prove significant influence of family income on care-

giver well-being [10, 12, 16]. Our study showed that age of mothers had significant impact on investigated outcomes (BDI-II score and all SF-36 composite scores), while unemployment was a significant predictor of higher depression level.

The domains of HRQoL mainly affected in our study group were RE, MH and VT scores. Other HRQoL studies with caregivers of children with disability reported similar experience [35, 38]. Dividing the study group on the basis of children`s CSS, showed significantly lower HRQoL scores and higher depression level in mothers with more severely affected children. This result strongly contributes to finding that clinical severity of the childs` disease is one one of the strongest factors influencing HRQoL and depression level. This is in accordance to the conclusions of a large Canadian study that identified care giving demands and child behaviour as significant influencing factors on emotional and physical well-being of caregivers for children with cerebral palsy [38].

Our study has few considerable limitations. A cross-sectional design limits the possibility of discerning causal relationships and relatively small number of participants implies the need for multicentric study. Future studies should include prospective repeated measurements of HRQoL and depression in order to obtain more accurate conclusions. Also, the genetic profile of patients was not analyzed as possible predictor of investigated outcomes, since only 53% of patients had been established with molecular diagnosis. However, a study with RTT caregivers did not show a correlation of genotype (MECP mutations) and caregiver HRQoL [21].

Conclusion

Our study showed a high prevalence of depression among mothers caring for children with Rett syndrome. Mostly affected domains of HRQoL in this population were role functioning emotional, vitality and mental health, all significantly influenced by maternal age and clinical severity of their children`s disease. The results of this study can help in planning subsequent interventions directed at families dealing with Rett syndrome. On the basis of our findings, future interventions should include early recognition of depression symptoms, providing better employment possibilities for mothers giving care to children with RTT and improvement of specific medical measures to alleviate clinical severity of affected children.

R E F E R E N C E S

1. *Weaving LS, Ellaway CJ, Gecz J, Christodoulou J.* Rett syndrome: clinical review and genetic update. J Med Genet 2005; 42(1): 1–7.
2. *Bienvenu T, Philippe C, De Roux N, Raynaud M, Bonnefond JP, Pasquier L,* et al. The incidence of Rett syndrome in France. Pediatr Neurol 2006; 34(5): 372−5.
3. *Amir RE, Van den Veyver IB, Wan M, Tran CQ, Francke U, Zoghbi HY.* Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. Nature Genet 1999; 23(2): 185–8.
4. *Huppke P, Laccone F, Kramer N, Engel W, Hanefeld F.* Rett syndrome: analysis of MECP2 and clinical characterization of 31 patients. Hum Mol Genet 2000; 9(9): 1369-75.
5. *Neul JL, Kaufmann WE, Glaze DG, Christodoulou J, Clarke AJ, Bahi-Buisson N,* et al. Rett Syndrome: Revised Diagnostic Criteria and Nomenclature. Ann Neurol 2010; 68(6): 944−50.
6. *Williamson S, Christodoulou J.* Rett syndrome: new clinical and molecular insights. Eur J Hum Genet 2006; 14(8): 896–903.
7. *Bebbington A, Anderson A, Ravine D, Fyfe S, Pineda M, de Klerk N.* Investigating genotype–phenotype relationships in Rett syndrome using an international data set. Neurology 2008; 70(11): 868−75.
8. *Glaze DG, Percy AK, Skinner S, Motil KJ, Neul JL, Barrish JO.* Epilepsy and the natural history of Rett syndrome. Neurology 2010; 74(11): 909−12.
9. *Breslau N, Staruch KS, Mortimer EA.* Psychological distress in mothers of disabled children. Am J Dis Child 1982; 136(8): 682−6.
10. *Blacher J, Shapiro J, Lopez S, Diaz L.* Depression in Latina mothers of children with mental retardation: a neglected concern. Am J Ment Retard 1997; 101(5): 483−96.
11. *Brehaut JC, Kohen DE, Raina P, Walter SD, Russell DJ, Swinton M.* The Health of Primary Caregivers of Children With Cerebral Palsy: How Does It Compare With That of Other Canadian Caregivers? Pediatrics 2004; 114(2): 182−91.
12. *Bourke J, Ricciardo B, Bebbington A, Aiberti K, Jacoby P, Dyke P.* Maternal physical and mental health in children with Down syndrome. J Pediatr 2008; 153(3): 320–6.
13. *Mobarak R. Khan N, Munir S, Zaman S, McConachie H.* Predictors of Stress in Mothers of Children With Cerebral Palsy in Bangladesh. J Pediatr Psychol 2000; 25(6): 427−33.
14. *Manuel J, Naughton M, Balkrishnan R, Smith BP, Koman LA.* Stress and Adaptation in Mothers of Children With Cerebral Palsy. J Pediatr Psychol 2003; 28(3): 197−201.
15. *Laurvick CL, Msall ME, Silburn S, Bower C, de Klerk N, Leonard H.* Physical and Mental Health of Mothers Caring for a Child With Rett Syndrome. Pediatrics 2006; 118(4): 1152−64.
16. *Moore H, Leonard H, de Klerk N, Robertson I, Fyfe S, Christodoulou J.* Health Service Use in Rett Syndrome. J Child Neurol 2005; 20(1): 42−50.
17. *Bahi-Buisson N, Guellec I, Nabbout R, Guet A, Nguyen G, Dulac O,* et al. Parental view of epilepsy in Rett Syndrome. Brain Dev 2008; 30(2): 126−30.
18. *Drulovic J, Pekmezovic T, Matejic B, Mesaros S, Manigoda M, Dujmovic I,* et al. Quality of life in patients with multiple sclerosis in Serbia. Acta Neurol Scand 2007; 115(3): 147–52.
19. *Tovilović S, Novović Z, Mihić Lj. Jovanović V.* The role of trait anxiety in induction of state anxiety. Psihologija 2009; 42(4): 491−504.
20. *Beck AT, Steer RA, Brown, GK.* Beck Depression Inventory. 2nd ed. San Antonio, TX: The Psychological Corporation; 1996.
21. *Neul JL, Fang P, Barrish J, Lane J, Caeg EB, Smith EO,* et al. Specific mutations in methyl-CpG-binding protein 2 confer different severity in Rett syndrome. Neurology 2008; 70(16): 1313−21.
22. *Cadman D, Rosenbaum P, Boyle M, Offord DR.* Children with chronic illness: family and parent demographic characteristics and psychosocial adjustment. Pediatrics 1991; 87(6): 884 –9.
23. *Dyson LL.* Response to the presence of a child with disabilities: parental stress and family functioning over time. Am J Ment Retard 1993; 98(2): 207–18.

24. *Friedrich WN, Friedrich WL.* Psychosocial assets of parents of handicapped and nonhandicapped children. Am J Ment Defic 1981; 85(5): 551–3.
25. *Cushner-Weinstein S, Dassoulas K, Salpekar JA, Henderson SE, Pearl PL, Gaillard WD,* et al. Parenting stress and childhood epilepsy: the impact of depression, learning, and seizure-related factors. Epilepsy Behav 2008; 13(1): 109−14.
26. *Shaligram D, Girimaji SC, Chaturvedi SK.* Quality of life issues in caregivers of youngsters with thalassemia. Indian J Pediatr 2007; 74(3): 275−8.
27. *Sajedi F, Alizad V, Malekkhosravi G, Karimlou M, Vameghi R.* Depression in Mothers of Children with Cerebral Palsy and Its Relation to Severity and Type of Cerebral Palsy. Acta Med Iranica 2010; 48(4): 250−4.
28. *Ones K, Yilmaz E, Cetinkaya B, Caglar N.* Assessment of the quality of life of mothers of children with cerebral palsy (primary caregivers). Neurorehabil Neural Repair 2005; 19(3): 232−7.
29. *Veisson M.* Depression symptoms and emotional states in parents of disabled and non-disabled children. Soc Behav Personal 1999; 271(11): 87−98.
30. *Wolf L, Noh S, Fisman S, Speechley M.* Psychological effects of parenting stress on parents of autistic children. J Autism Dev Disord 1989; 19(1): 157−66.
31. *Dagenais L, Hall N, Majnemer A, Birnbaum R, Dumas F, Gosselin J,* et al. Communicating a diagnosis of cerebral palsy: caregiver satisfaction and stress. Pediatr Neurol 2006; 35(6): 408−14.
32. *Altindag O, Iskan A, Akcan S, Koksal S, Ercin M, Ege L.* Anxiety and Depression Levels in Mothers of Children with Cerebral Palsy. Turk J Phys Med Rehab 2007; 53: 22−4.
33. *Blacher J, McIntyre LL.* Syndrome specificity and behavioural disorders in young adults with intellectual disability: cultural differences in family impact. J Intellect Disabil Res 2006; 50 (Pt 3): 184−98.
34. *Lambrenos K, Weindling AM, Calam R, Cox AD.* The effect of a child's disability on mother's mental health. Arch Dis Child 1996; 74(2): 115−20.
35. *Bumin G, Günal A. Tükel F.* Anxiety, depression and quality of life in mothers of disabled children. SDÜ Týp Fak Derg 2008; 15(1): 6−11.
36. *Fávero-Nunes MA, dos Santos MA.* Depression and quality of life in mothers of children with pervasive developmental disorders. Rev Lat Am Enfermagem 2010; 18(1): 33−40.
37. *Im SH, Lee SC, Moon JH, Park ES, Park YG.* Quality of life for primary caregivers of muscular dystrophy patients in South Korea. Chinese Med J 2010; 123(4): 452−7.
38. *Raina P, O'Donnell M, Rosenbaum P, Brehaut J, Walter SD, Russell D.* The Health and Well-Being of Caregivers of Children With Cerebral Palsy. Pediatrics 2005; 115(6): 626−36.

Received on January 16, 2012.
Accepted on March 27, 2012.