Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.64, No.4 (2024). p.293-9; DOI: https://doi.org/10.14238/pi64.4.2024.293-9

Original Article

Prevalence and risk factors of depression in juvenile systemic lupus erythematosus

Ika Dian Puspitanza, Myrna Alia, Yudianita Kesuma, Rismarini Rismarini, Edy Novery, Erial Bahar

Abstract

Background Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organ systems, including the central nervous system. Depression is one of the neuropsychiatric manifestations of juvenile SLE .

Objective To estimate the prevalence of depressive disorders in juvenile SLE and identify its potential risk factors.

Methods This cross-sectional study was conducted in juvenile SLE patients at Dr. Mohammad Hoesin General Hospital, Palembang. Sociodemographic data and medications were recorded. Disease activity of SLE was assessed using the *Systemic Lupus Erythematosus Disease Activity Index* (SLEDAI). Physical activity was measured using the *Physical Activity Questionnaire for Children* (PAQ-C) and the *Physical Activity Questionnaire for Adolescents* (PAQ-A). All subjects were screened for depression using the *Children's Depression Inventory* (CDI) questionnaire. Multiple linear regression analyses were used to determine risk factors for depressive disorders.

Results We included 72 patients, of whom 67 (93.1%) were female. Mean age of the patients was 12 years 4 months (SD 2 years 6 months); most (67; 93.1%) were 10-18 years of age. Depression was found in 24 patients (33.3%). The SLEDAI scores of ≥3 (flare) were found in 54 patients (75%) and low physical activity was found in 62 (86.1%) patients. The prevalence of depression based on the CDI was 33.3%. A SLEDAI score of ≥3 and low physical activity were significantly associated with depression (P=0.009 and P=0.025, respectively). On multiple linear regression analysis, only SLEDAI score of ≥3 remained significantly associated with depression (P= 0.017; OR 12.6; 95%CI 1.6 to 101.7). Gender, age, family economic status, father's education, mother's education, family history of depression, and duration of illness were not associated with depression.

Conclusion A SLEDAI score indicating flare (≥3) and low physical activity are significantly associated with an increased risk of depression. A SLEDAI score is an independent risk factor for depression when all other significant risk factors are considered.

[Paediatr Indones. 2024;64:293-9; DOI: https://doi.org/10.14238/pi64.4.2024.293-9].

Keywords: *juvenile systemic lupus erythematosus; neuropsychiatric systemic lupus erythematosus; depression*

Systemic lupus erythematosus (SLE) is defined as an episodic multisystem disease characterized by extensive inflammatory processes in the blood vessels and connective tissue, as well as the presence of antinuclear antibodies (ANA) on investigations, especially antibodies to double-stranded DNA (anti-dsDNA). The difficulty of diagnosing SLE is due to the involvement of many organs, so SLE is often referred to as the "disease of a thousand faces" (masquerader or great imitator).[1,2]

The Lupus Foundation of America estimated that the number of SLE patients has reached 1,500,000 cases in America and 5,000,000 cases worldwide.[3] The prevalence of SLE in children increases by 15% to 17% a year; there are 1-6 new cases per 100,000 children annually. Pediatric SLE is more common in girls than boys, with a ratio of 4.5:1 and an interval between onset and diagnosis ranging from one to 24 months.[4-6]

The increased inflammation that occurs in autoimmune and infectious diseases can increase the permeability of the vascular and central nervous system

From the Department of Child Health, Universitas Sriwijaya Medical School/Dr. Moh. Hoesin Hosital, Palembang, South Sumatera, Indonesia.

Corresponding author: Myrna Alia. Department of Child Health, Universitas Sriwijaya Medical School/Dr. Moh. Hoesin Hospital, Palembang, South Sumatera, Indonesia. Telp. + 62-711376445. Email: e.mail.my.rna@gmail.com.

Submitted May 29, 2023. Accepted August 27, 2024.

(CNS) barriers, which renders the brain vulnerable to infectious agents and immune components such as cytokines and brain-reactive antibodies. Increased pro-inflammatory cytokines in SLE patients cause symptoms characterized by fatigue, sleep disturbances, irritability, loss of appetite, and depression.[7]

Depression, a mood disorder, is the most common neuropsychiatric problem in SLE patients. Zhang et al. reported that depression and anxiety disorders are often found in SLE patients.[3] In SLE patients, depression has been reported in 23%, suicidal ideation in 15%, and anxiety in 27%. Risk factors for depression in children with SLE include duration of illness and a higher level of SLE disease activity.[8-10] The SLEDAI score is a measure of organ damage, signifying disease activity.[10]

Depression screening in children can be done using several instruments, such as the *Hospital Anxiety and Depression Scale* (HAD), the *Patient Health Questionnaire-9* (PHQ-9), and the *Children's Depression Inventory* (CDI). We used the CDI instrument, which has been validated in Indonesia with a reliability of 0.746 and can be used in children aged 7-17 years.[10-13]

Screening for depression in children with SLE is necessary for early treatment and prevention of complications of depression. In this study, we aimed to estimate the prevalence of depressive disorders in juvenile SLE and identify potential risk factors that influence depression.

Methods

This analytic, observational study with a cross-sectional design was done in children with SLE who sought treatment at the Pediatric Allergy Immunology Polyclinic and Inpatient Pediatric Ward at Dr. Mohammad Hoesin General Hospital, Palembang, South Sumatera, from July 2022 to February 2023.

Inclusion criteria were children with SLE aged 7 to <18 years treated at our facility who agreed to participate with written parental informed consent. Exclusion criteria were having previously been diagnosed with depression, having received treatment for depression whether pharmacologically and/or non-pharmacologically, and inability to complete the questionnaire (due to inability to read or intellectual disability).

We collected the subjects' demographic data including socioeconomic status and parental education level. Socioeconomic status was classified as low if total monthly family income was less than the 2022 South Sumatera Province minimum wage of IDR 3,144,446 (approximately USD 203), and high otherwise. Parental education level was considered low if nine years of education or less had been completed, and high otherwise.

We recorded the patient's history, performed physical examination, evaluated laboratory results from the patient's most recent visit, and calculated the SLEDAI score. The SLEDAI score, indicating lupus disease activity, was divided into 2 categories: flare (score >3) and non-flare (score <3). The CDI questionnaire and the PAQ-C/PAQ-A physical activity questionnaire were filled based on the children's reports. If a subject's CDI score was 13 or more, he or she was considered to have depression and was referred to the psychology or psychiatry divisions. A PAQ-C/PAQ-A score of ≥3 and >3 indicated low and high levels of physical activity, respectively. This study was approved by the Health Research Ethics Committee of the Faculty of Medicine at Universitas Sriwijaya/Mohammad Hoesin Hospital, Palembang.

Data were recorded and analyzed using *SPSS version 25* (*IBM*, Armonk, New York). Bivariate analysis of potential risk factors for depression in children with SLE was done using the chi-square test. Multivariate logistic regression was then employed to determine independent risk factors that were significantly associated with the occurrence of depression. Results with P< 0.05 (95%CI) were considered to be statistically significant.

Results

Subjects were mostly girls (93.1%) and had a median age of 14.2 years; most were aged 10-18 years (93.1%). The median age at SLE diagnosis was 12.6 years. Of our subjects, 47.2% had low family socioeconomic status, 25.4% had a low paternal education level, and 31.9% had a low maternal education level. Two (2.8%) patients had a history of depression in the family. The median duration of illness was 11 months (**Table 1**).

Table 1. Demographic characteristics of subjects

Characteristics	(N=72)
Gender, n (%)	
Female	67 (93.1)
Male	5 (6.9)
Age, n (%)	
10 to <18 years	67 (93.1)
<10 years	5 (6.9)
Mean (SD)	13 years 10 months (2 years 6 months)
Mean onset age (SD)	12 years 4 months (2 years 6 months)
Family economic status, n (%)	
Low	34 (47.2)
High	38 (52.8)
Paternal education, n (%)	
Low	19 (26.4)
High	53 (73.6)
Maternal education, n (%)	
Low	23 (31.9)
High	49 (68.1)
History of depression in the family, n (%)	
Yes	2 (2.8)
No	70 (97.2)
Duration of sickness, n (%)	
≥ 1 year	35 (48.6)
< 1 year	37 (51.4)
Median dian (range)	11 mo (1 mo - 6 yr 9 mo)

Our subjects' median SLEDAI score was 6 (0-38). Most children with SLE (75%) had a SLEDAI score ≥3 (flare). The median PAQ-C/A score was 1 (range 1-4). Most subjects had low physical activity (62/72; 86.1%). The incidence of depression based on CDI results was 33.3% (**Table 2**).

The subjects' overall median CDI score was 9 (range 0-32). The CDI questionnaire measured five dimensions that influence depression in children with SLE; the most common was ineffectiveness (20.7%), followed by negative self-esteem (20.3%), anhedonia (19.7%), negative mood (16.5%), and interpersonal problems (10.1%). Subjects with CDI scores of ≥13 were referred to psychiatrists and psychologists, and underwent examinations according to the Indonesian *Guidelines for Classifying Diagnostics of Mental Disorders-III* (PPDGJ-III) and the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5). These examinations found that the patients' psychological and mental conditions were still within normal limits. Family psychoeducation was provided to our patients who screened positive for depression; no patient received pharmacological therapy for depression.

Bivariate analysis results of potential risk factors for depression in children with SLE are shown in **Table 3**. A SLEDAI score of ≥3 (P=0.009) and low physical activity (P=0.025) were significantly associated with depression. Gender, age, family economic status, paternal and maternal education, history of depression in the family, and duration of illness were not significantly associated with depression.

Table 2. Clinical characteristics and the incidence of depression

Characteristics	(N=72)
SLEDAI score, n (%)	
≥3 flare-up	54 (75)
<3 no flare	18 (25)
Median (range)	6 (0-38)
PAQ-C/A physical activity, n (%)	
≤3 (low)	62 (86.1)
>3 (high)	10 (13.9)
Median PAQ-C/A score (range)	1 (1-4)
CDI score, n (%)	
Depression present	24 (33.3)
Depression absent	48 (66.7)
Mean CDI score (SD)	9.61 (6.22)

Table 3. Potential risk factors for depression in children with SLE

Risk factors	Depression (n=24)	No depression (n=48)	OR (95%CI)	P value
Gender, n(%)				
Female	23	44 (91.7)	2.1 (0.2 to 19.8)	0.659*
Male	1	4 (8.3)		
Age, n(%)				
10 to <18 years	23	44 (91.7)	2.1 (0.2 to 19.8)	0.659*
<10 years	1	4 (8.3)		
Family economic status, n(%)				
Low	10	24 (50.0)	0.7 (0.3 to 1.9)	0.676
High	14	24 (50.0)		
Paternal education, n(%)				
≤9 years	8	11 (22.9)	1.7 (0.6 to 4.9)	0.508
>9 years	16	37 (77.1)		
Maternal education, n(%)				
≤9 years	8	15 (31.35)	1.1 (0.4 to 3.1)	1.000
>9 years	16	33 (68.75)		
History of depression in the family, n (%)				
Yes	1	1 (2.1)	2.0 (0.1 to 34.2)	1.000*
No	23	47 (97.9)		
Duration of sickness, n (%)				
≥1 year	11	24 (50.0)	0.8 (0.3 to 2.3)	0.934
< 1year	13	24 (50.0)		
SLEDAI score, n (%)				
≥3 flare-up	23	31 (64.6)	12.6 (1.6 to 101.7)	-0.009
<3 non-flare	1	17 (35.4)		
PAQ-C/A physical activity, n (%)				
≤3 (low)	24	38 (79.2)		0.025*
>3 (high)	0	10 (20.8)		

*Fisher's exact test

On bivariate analysis, subjects with SLEDAI scores ≥3 (flare) had an odds ratio (OR) of 12.6 (95%CI 1.6 to 101.7; P=0.009) to experience depression compared to those with SLEDAI score <3 (non-flare). None of the ten subjects with high physical activity experienced depression, while 24 (38.7%) subjects with low physical activity experienced depression (P=0.025). Multivariate logistic regression analysis revealed that the only factor that remained independently associated with depression was SLEDAI score ≥3 (OR 12.6; 95%CI 1.6-101.1; P=0.017).

Discussion

Most of our subjects were female (93.1%). Similarly, a study in Bandung, West Java, another major city in Indonesia, noted that 82.1% of their subjects were female.[14] Relative deficiency of androgens and increased levels of estrogens are hallmarks of SLE. Estrogen activates polyclonal B cells, resulting in excessive production of autoantibodies in SLE patients. Sex hormones also play a role in the predisposition and severity of the disease.[1,2,15,16]

The mean age of our subjects was 13 years 10 months (SD 2 years 6 months). This finding is in line with that of a previous study, in which the majority of SLE patients were adolescents aged 10-18 years (93.1%), and children aged 11-15 years had a higher frequency of SLE compared to other age groups.[14] Another study showed that the average age of SLE sufferers among children was 12-13 years.[2]

The majority of our subjects had low family socioeconomic status (47.2%). Parental education level of ≤9 years was noted in 26.4% of fathers and 31.9% of mothers. Two subjects (2.8%) had a family history of depression. A study on 815 girls aged 9-15 years reported that in 30% of cases, depression in children was associated with genetic factors.[17]

A total of 54 children with SLE (75%) had a SLEDAI score ≥3 (flare-up). A modification of SLEDAI currently widely used due to its ease of completion is the SELENA-SLEDAI developed in the Safety of Estrogen in Lupus Erythematosus National Assessment (SELENA) trial. The SELENA-SLEDAI score divides flare into two categories, namely, mild-moderate flare (score 3-11) and severe flare (score ≥12).[1] A cohort study on 525 SLE patients reported that 45% patients had flares, with a significant proportion of both early and late organ damage attributable to corticosteroid therapy, although the majority of damage occurred at 15 years.[18] In addition, another study reported that 56% of pediatric SLE patients had a high SLEDAI score indicating flare, which was significantly associated with pyuria, high ANA titers, and increased erythrocyte sedimentation rates.[19] In the present study, we found that SLEDAI score was not associated with age and duration of illness.

Most of our subjects had low physical activity (86.1%). Another cohort study reported that the average physical summary (Phs) score of SLE children was significantly lower thatn that of healthy children (P<0.001).[20]

We found that 24/72 children (33.3%) experienced depression. The median CDI score of our subjects was 9 (range 0-32). A previous study reported that the majority of their subjects experienced depression; some of them had a risk of suicide and were referred to a psychologist.[21] In another study, depression was found in 23% of subjects and was accompanied by suicidal ideation in 15% and anxiety in 27% of subjects.[10]

Our subjects who screened positive for depression using the CDI were found to have normal psychological and mental condition on further examination by psychiatrists and psychologists. This highlights the nature of the CDI as a screening instrument, which is geared at finding individuals who may have depression or are at risk for depression, and should be followed up by further assessment to ascertain the diagnosis. Nevertheless, the screening made it possible to provide early psychoeducation before pharmacologic treatment was necessary.

We found no association between depression and gender, age, age of onset, family socioeconomic status, paternal and maternal education, or history of depression in the family. Similarly, a study in South Korea also found no association between gender and depression in physically healthy children.[22] In contrast, a study China, also in healthy children, noted that depression was present and more common in boys, possibly due to the traditionally higher expectations that Chinese parents place on their sons, leading to pressure to perform well.[23] The South Korean study reported a higher mean CDI score in children aged 9 years compared to other age groups, with the lowest score found in children aged 11 years.[22] However, the Chinese study showed a higher rate of depressive symptoms in children aged 11-12 years.[23] In our study, children ager 10 to <18 years had a higher proportion of depression compared to their younger counterparts.

The study in China showed an association between socioeconomic status and the occurrence of depression. Families with low socioeconomic status are more prone to depression. The presence of depression in parents has genetic and environmental effects on children's behavior and the incidence of depression.[23] The majority of our study subjects had low family socioeconomic status, but no significant association with depression was found. This finding differed from other studies that reported that higher education and economic status more often led to a tendency toward mental disorders, as well as greater life pressures.[24-26]

Low paternal and maternal education was also not associated with the incidence of depression in our study. This finding contrasts with that of previous studies reporting that depressive symptoms increased in line with low family income due to limitations in meeting daily needs.[22,23]

Two children with SLE (2.8%) had a family history of depression, but there was no significant association between depression in children with SLE and family history of depression. In previous studies, children with a family history of depression reportedly had a three times higher risk of developing depression.[8,10] Other research stated that one of the strongest predictors of adolescent-onset depression is family history. The risk of becoming depressed has been reported to be at least three times greater in adolescents whose parents have had major depressive disorder (MDD) compared to those whose parents have never been depressed.[27]

The median duration of illness in our study was 11 months (range 1 month to 6 years and 9 months),

and was not associated with depression, in similarity to other reports.[21,28] In contrast, one study noted that patients with longer duration of illness and poor disease control had a higher risk of depression.[10]

A SLEDAI score ≥3 had a significant association with depression. Pediatric SLE patients with flares were 12.6 times more likely to experience depression than those without flares (OR 12.6; 95%CI 1.6 to 101.1; P=0.017). Similarly, a previous study reported an increased incidence of depression with increased disease activity indicated by SLEDAI score (OR 1.1; 95%CI 1.1 to 1.2; P< 0.001).[10]

Low physical activity was found in most subjects (86.1%), and was significantly associated with the incidence of depression in the bivariate analysis (P=0.09). Physical activity was assessed using the PAQ-C/A questionnaire, which has good validity and calculates scores by considering activities carried out in the previous seven days. None of our subjects with high activity were depressed. Low physical activity has been associated with mood disorders, especially depression, due to increased pro-inflammatory cytokines and disruption of the balance of hormones and neurotransmitters in the brain, including serotonin and dopamine.[9,29,30]

In conclusion, the incidence of depression in children with SLE in our population was 33.3%. SLEDAI score > 3 is the only independent risk factor for depression in children with SLE. There is a trend towards an increased incidence of depression in SLE children with low physical activity.

Conflict of interest

None declared.

Funding acknowledgment

The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Akib AA, Soepriadi M, Setiabudiawan B. Lupus eritematosus sistemik . In: Akib AAP, Munasir Z, Kurniati N, eds. Buku ajar alergi imunologi anak. 2nd ed. Jakarta: Badan Penerbit IDAI; 2010. p. 345-72.
2. Silverman E, Allison E. Systemic lupus erythematosus. In: Cassidy JT, Ronald ML, Ross EP, Carol BL, editors. Textbook of pediatric rheumatology. 6th ed. Philadelphia: Elsevier; 2011. p. 315-41.
3. Trisnaramawati F, Satiadarma MP, Soetikno N. Gambaran kecemasan dan depresi pada orang dengan systemic lupus erythematosus (SLE) di rumah sakit x. Jurnal Mutiara Ilmu Sosial, Humaniora, dan Seni. 2019;3:457-64. DOI: https://doi.org/10.24912/jmishumsen.v3i2.3471.2019
4. Geist R, Grdisa V, Otley A. Psychosocial issues in children with chronic conditions. Best Pract Res Clin Gastroenterol.2003;17:141-52. DOI: https://doi.org/10.1016/s1521-6918(02)00142-7
5. Compas BE, Jaser SS, Dunn MJ, Rodriguez EM. Coping with chronic illness in childhood and adolescence. Annu Rev Clin Psychol. 2012;8:455-80. DOI: https://doi.org/10.1146/annurev-clinpsy-032511-143108
6. Perhimpunan Reumatologi Indonesia. Rekomendasi Perhimpunan Reumatologi Indonesia: Diagnosis dan pengelolaan lupus eritematosus sistemik. Revised ed. Jakarta: Perhimpunan Reumatologi Indonesia; 2019.
7. Raafat HA, El Refai RM, Alrasheed HA, El Din MN. Major depression and disease activity among systemic lupus erythematosus Egyptian females. Egyptian Rheumatol. 2015;37:S1-6. DOI: https://doi.org/10.1016/j.ejr.2015.09.007
8. Knight AM, Trupin L, Katz P, Yelin E, Lawson EF. Depression risk in young adults with juvenile and adult-onset lupus: 12 years of follow up. Arthritis Care Res. 2018;70:475-80. DOI: https://doi.org/10.1002/acr.23290
9. Istiqomah A, Kurniati N, Liana P. Hubungan antara tingkat aktivitas penyakit LES dan tingkat depresi pada penderita lupus eritematosus sistemik di Persatuan Lupus Sumatera Selatan dan Poliklinik Ilmu Penyakit Dalam RSUP Dr. Mohammad Hoesin Palembang. Maj Kedokt Sriwijaya. 2018;50:185-91.
10. Knight A, Weiss P, Morales K, Gerdes M, Rearson M, Vickery M, *et al*. Identifying differences in risk factors for depression and anxiety in pediatric chronic disease: a matched cross-sectional study of youth with lupus/mixed connective tissue disease and their peers with diabetes. J Pediatr. 2015;167:1397-403. DOI: https://doi.org/10.1016/j.jpeds.2015.07.048
11. Mujahidah E, Listiyandini RA. Pengaruh resiliensi dan empati terhadap gejala depresi pada remaja. Jurnal Psikologi. 2018;14:60-75. DOI: https://doi.org/10.24014/jp.v14i1.5035
12. Kovacs M. Children's Depression Inventory (CDI and CDI

2). In: Cautin RL, Lilienfeld SO, editors. The Encyclopedia of Clinical Psychology. Hoboken, NJ: John Wiley & Sons, Inc.; 2015. p. 1-5.

13. Widhiarso W, Retnowati S. Investigasi butir bias jender dalam pengukuran depresi melalui Children's Depression Inventory (CDI). J Penelitian Psikologi. 2011;2:99-111.
14. Ghrahani R, Ganesan PD, Ningrat RFS. Clinical manifestations of systemic lupus erythematous in children at Dr. Hasan Sadikin General Hospital Bandung, Indonesia. Althea Med J. 2018;5:187-91. DOI: https://doi.org/10.15850/amj.v5n4.664
15. Haftel HM. Penyakit rematik pada anak: Lupus eritematosus sitemik. Dalam: Sumadiono, Rahayiningsih SE, penyunting. Nelson Ilmu Kesehatan Anak Esensial. Edisi kedelapan. pISBN: 9789814666848. Singapore: Elsevier; 2021. p. 369-72.
16. Sadun RE, Ardoin SP, Schanberg LE. Systemic lupus erythematosus. In: Kliegman RM, ST Geme III JW, Blum NJ, Shah SS, Tasker RC, Wilson KM, editors. Nelson Textbook of Pediatrics. 21st ed. Philadelphia: Elsevier; 2021. p. 5232-48.
17. Hammen C, Brennan PA, Keenan-Miller D, Hazel NA, Najman JM. Chronic and acute stress, gender, and serotonin transporter gene-environment interactions predicting depression symptoms in youth. J Child Psychol Psychiatry. 2010;51:180-7. DOI: https://doi.org/10.1111/j.1469-7610.2009.02177.x
18. Thamer M, Hernán MA, Zhang Y, Cotter D, Petri M. Prednisone, lupus activity, and permanent organ damage. J Rheumatol. 2009;36:560-4. DOI: https://doi.org/10.3899/jrheum.080828
19. Nazri SKSM, Wong KK, Hamid WZWA. Pediatric systemic lupus erythematosus: retrospective analysis of clinico-laboratory parameters and their association with Systemic Lupus Erythematosus Disease Activity Index score. Saudi Med J. 2018;39:627-31. DOI: https://doi.org/10.15537/smj.2018.6.22112
20. Levy DM, Peschken CA, Tucker LB, Chédeville G, Huber AM, Pope JE, *et al.* Association of health-related quality of life in childhood-onset systemic lupus erythematosus with ethnicity: results from a multiethnic multicenter Canadian cohort: influence of ethnicity on HRQOL in Canadian cSLE patients. Arthritis Care Res. 2014;66:1767-74. DOI: https://doi.org/10.1002/acr.22363
21. Mulvihill E, Furru R, Goldstein-Leever A, Driest K, Lemle S, MacDonald D, *et al*. Targeted provider education and pre-visit planning to increase rates of formal depression screening in childhood-onset SLE. Pediatr Rheumatol. 2021;19:116. DOI: https://doi.org/10.1186/s12969-021-00576-4
22. Shin YM, Cho H, Lim KY, Cho SM. Predictors of self-reported depression in Korean children 9 to 12 years of age. Yonsei Med J. 2008;49:37-45. DOI: https://doi.org/10.3349/ymj.2008.49.1.37
23. Shang X, Wang D, Wang J, Hu X, Du S, Li Y. Prevalence and socioeconomic status correlation of depressive symptoms among children living in urban Beijing. N Am J Med Sci. 2010;3:153-9.
24. Carr F, Nicassio P, Ishimori M, Moldovan I, Katsaros E, Torralba K, *et al*. Depression predicts self-reported disease activity in systemic lupus erythematosus. Lupus. 2011;20:80-4. DOI: https://doi.org/10.1177/0961203310378672
25. Zakeri Z, Shakiba M, Narouie B, Mladkova N, Ghasemi-Rad M, Khosravi A. Prevalence of depression and depressive symptoms in patients with systemic lupus erythematosus: Iranian experience. Rheumatol Int. 2012;32:1179-87. DOI: https://doi.org/10.1007/s00296-010-1791-9
26. Mazzoni D, Cicognani E. Social support and health in patients with systemic lupus erythematosus: a literature review. Lupus. 2011;20:1117-25. DOI: https://doi.org/10.1177/0961203311412994
27. Jaffee SR, Sligo JL, McAnally HM, Bolton AE, Baxter JM, Hancox RJ. Early-onset and recurrent depression in parents increases risk of intergenerational transmission to adolescent offspring. J Child Psychol Psychiatry. 2021;62:979-88. DOI: https://doi.org/10.1111/jcpp.13356
28. Carbajal-Alonso HL, García-Moreno NP, Rodríguez-Arreola B, de Leon JCB. Depressive disorder in Mexican pediatric patients with systemic lupus erythematosus (SLE). Gac Med Mex. 2016;152:36-42. PMID: 26927642.
29. Fekadu N, Shibeshi W, Engidawork E. Major depressive disorder: pathophysiology and clinical management. J Depress Anxiety. 2017;6:1-7. DOI: https://doi.org/10.4172/2167-1044.1000255
30. Greenan-Barrett J, Doolan G, Shah D, Virdee S, Robinson GA, Choida V, *et al*. Biomarkers associated with organ-specific involvement in juvenile systemic lupus erythematosus. Int J Mol Sci. 2021;22:7619. DOI: https://doi.org/10.3390/ijms22147619