A nomogram to predict the risk of lupus enteritis in systemic lupus erythematosus patients with gastroinestinal involvement

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ABSTRACT

Background: Lupus enteritis (LE), a main cause of acute abdominal pain in systemic lupus erythematosus (SLE) patients, is a serious and potentially fatal complication. This study aimed to identify clinical serological indicators to establish a nomogram to assess LE in SLE patients with gastrointestinal manifestations.

Methods: The clinical and laboratory data of SLE patients with gastrointestinal manifestations that were hospitalized in the West China Hospital from January 2010 to January 2020 were retrospectively analyzed. The least absolute shrinkage and selection operator logistic regression model was used to select potentially relevant features. Subsequently, a nomogram was developed using multivariable logistic analysis. The performance of the nomogram was evaluated using a receiver operating characteristic curve, a calibration curve, and decision curve analysis (DCA).

Findings: We included a total of 8,505 SLE patients, of which 251 had experienced gastrointestinal manifestations. The patients were randomly divided into training (n = 176) and validation (n = 75) groups. The LRA (LE Risk Assessment) model consisted of 11 significantly associated variables, which included complement 4, antineutrophil cytoplasmic antibody, albumin, anion gap, age, D-dimer, platelet, serum chlorine, anti-Sjögren’s-syndrome-related antigen A, anti-ribosomal P protein, and anti-ribonucleoprotein. In the training and validation cohorts, the areas under the curve were 0.919 (95% confidence interval [CI]: 0.876–0.962) and 0.870 (95% CI: 0.775–0.964), respectively. The nomogram demonstrated excellent performance in the calibration curve and DCA.

Interpretation: The LRA model exhibits good predictive ability in assessing LE risk in SLE patients with gastrointestinal manifestations.

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Lupus enteritis (LE) is a rare but fatal complication in patients with systemic lupus erythematosus (SLE). We searched PubMed for articles published in English on LE and found that although abdominal CT can bring some hints to the diagnosis of lupus LE, it still lacks effective and convenient diagnostic tools, and this difficulty poses a challenge for the development of clinical work.

**Evidence before this study**

Lupus enteritis is a rare but fatal complication in patients with systemic lupus erythematosus (SLE). We searched PubMed for articles published in English on LE and found that although abdominal CT can bring some hints to the diagnosis of lupus LE, it still lacks effective and convenient diagnostic tools, and this difficulty poses a challenge for the development of clinical work.

**Added value of this study**

We established a prediction model of LE by LASSO regression analysis and a total of 11 variables were included in this model, of which complement 4 (OR: 0.2, 95% CI: 0.07–0.56), anti-Sjogren's-syndrome-related antigen A (OR: 1.29, 95% CI: 1.09–1.51), anti-ribosomal P protein (OR: 1.38, 95% CI: 1.18–1.61), and anti-ribonucleoprotein (OR: 1.49, 95% CI: 1.31–1.70) contributed most to the prediction model. These variables are all common tests for patients with SLE and are easy to obtain clinically and convenient to use.

**Implications of all the available evidence**

Clinically, the diagnosis of LE is often easily delayed. However, our model has a good predictive ability and provides clues and rationale for the development of LE in patients with SLE.

**2. Methods**

**2.1. Data sources**

The corresponding authors (YL and FZ) had full access to all the data in the study, and individual participant data that underlie the results reported in this article, after de-identification can be obtained from the corresponding author upon reasonable request. We conducted a retrospective study of 8505 SLE patients who were hospitalized in West China Hospital from January 2010 to January 2020. SLE patients with the following criteria were included in the analysis: meet the 1997 American College of Rheumatology and/or the 2012 Systemic Lupus Erythematosus International Clinical Assistance Group classification criteria; [18,19]. have gastrointestinal symptoms and signs such as abdominal pain, diarrhea, nausea, vomiting, black stool, bloody stool, and fatigue as well as completed one or more abdominal CT examinations; and have complete inspection data.

LE patients that were included in this study met the following requirements: have a clear diagnosis of SLE; exhibit one of the following symptoms: abdominal pain, bloating, nausea and vomiting, or related clinical symptoms and signs such as diarrhea, melena, blood in the stool; and had abnormal abdominal CT scans indicating intestinal wall thickening, "target sign", "comb sign", intestinal dilatation, mesenteric vascular filling, or abnormal attenuation of mesenteric fat; and respond to glucocorticoid therapy.

Patient exclusion criteria included: gastrointestinal symptoms indirectly caused by other systems involved in SLE including nausea, vomiting, or abdominal pain; prior gastrointestinal diseases such as gastrointestinal perforation, bleeding, liver cirrhosis, or pancreatitis; infectious diseases including infectious peritonitis or acute gastroenteritis; malignant tumors of the digestive tract; adverse reactions caused by drugs; presence of other autoimmune diseases such as Sjogren's syndrome, scleroderma, Kawasaki disease, panniculitis, rheumatoid arthritis, inflammatory bowel disease, spondyloarthritis, or autoimmune hepatitis; and atypical digestive system symptoms with no objective (i.e., test, imaging) basis.

We collected the clinical and laboratory indicators of each eligible patient as potential predictors of LE risk. Details are provided in Supplementary Table 1.

This study was approved by the Ethics Committee at Biomedical Research at the West China Hospital of Sichuan University; the Ethics Committee waived the need for patients to give informed consent.

**3. Feature selection and model establishment**

Based on the split proportions in previous studies, we randomly divided the cohort into training (70%) and validation (30%) datasets [20]. To assess the risk of LE in SLE patients, we used the least absolute contraction and selection operator (LASSO) logistic regression algorithm to select LE-related feature indicators with non-zero coefficients from the laboratory test indicators [21]. Nomograms are powerful tools that, by integrating multiple risk factors, can quantify an individual's risk for a clinical disease. The risk factors selected by the LASSO regression were used to establish the model [22].

**4. Model performance**

A calibration curve was drawn to evaluate the nomogram. By quantifying the net benefits under different threshold probabilities in the LE cohort, the decision curve was analyzed to determine the nomogram's clinical effectiveness. The receiver operating characteristic curve was used to evaluate the diagnostic value of the nomogram in discriminating LE from non-LE and to determine the cutoff values for assessing accuracy, sensitivity, and specificity.
5. Statistical analysis

Continuous variables are expressed as the mean ± standard deviation, while categorical values are expressed in frequencies or percentages. The Student’s t-test and Chi-square test were used to analyze differences between variances; categorical data as frequencies were analyzed using the latter. The LASSO algorithm was used to select important relevant features with non-zero coefficients from the training set. Correlation would be assessed by Spearman’s test. All statistical tests were two-tailed, with \( P < 0.05 \) considered significant. The data were analyzed using R software (version 3.6.2) and SPSS 24.0 (IBM, USA).

6. Ethics statement

The study protocol was approved by the Ethics Committee of West China Hospital, Sichuan University with a waiver of informed consent (ethics application reference number:20,201,130).

7. Role of the funding source

This work was supported by the National Key Research and Development Program of China (Project no. 2016YFC0906201) and by the 1.3.5 Project for Disciplines of Excellence, West China Hospital, Sichuan University (Project No. ZYGJ18015). All sources of funding did not have any role in the study design, collection, analysis, or interpretation of the data, the writing of this manuscript, or the decision to submit it for publication.

8. Results

8.1. Clinical characteristics

This study included 8505 SLE cases. After excluding patients who did not meet the inclusion criteria, 251 remaining cases were enrolled for the final analysis (Fig. 1). The baseline characteristics of the training and validation cohorts are listed in Table 1 and Supplementary Table S2. The training cohort consisted of 176 cases (19 males and 157 females), while the validation cohort included 75 cases (7 males and 68 females). The two cohorts did not differ in age, sex, BMI, smoking history, alcohol consumption history, diabetes, dsDNA positive rate (\( P > 0.05 \)). However, there were significant differences in the incidence of hypertension, SM antibody positivity, C3 and C4 levels in serum between the LE and non-LE groups in the training cohort (\( P <0.05 \)), but not in the validation cohort. Typical images of SLE patients with LE are shown in Supplementary Figure S1.

8.2. Feature selection and model development

Eleven potential predictors with non-zero coefficients were subsequently selected; the optimal lambda (\( \lambda \)) value was 0.054 (log \( \lambda \) = −2.912; Fig. 2A and 2B). Based on the 11 independent predictors, the nomogram, coined the “LRA (LE Risk Assessment) model”, was constructed (Fig. 2C). The 11 features were: complement 4 (C4), antineutrophil cytoplasmic antibody (ANCA), albumin (ALB), anion gap (AG), age, d-dimer, platelet (PLT), chlorine (Cl), anti-Sjögren’s-syndrome-related antigen A (SSA), anti-ribosomal P protein (Rib-P), and anti-ribonucleoprotein (RNP).

Supplementary Figure S2 and Supplementary Table 3 display the contribution of each variable in the model to the outcome variable. Among them, C4, anti-SSA, anti-Rib-P, and anti-RNP had the highest contribution. C4 was a protective factor (odds-ratio [OR]: 0.2, 95% confidence interval [CI]: 0.07–0.56), while anti-SSA (OR: 1.29, 95% CI: 1.09–1.51), anti-Rib-P (OR: 1.38, 95% CI: 1.18–1.61), and anti-RNP (OR: 1.49, 95% CI: 1.31–1.70) were risk factors. Among the indicators included in the model, C4, ANCA, ALB, AG, and age were negatively correlated with the occurrence of LE, while anti-RNP, anti-Rib-P, anti-SSA, Cl, d-dimer, and PLT were positively correlated (Supplementary Fig. S3).

8.3. Predictive ability and performance of the LRA model

The LE risk prediction model exhibited good consistency between predictions and actual observations in both the training and validation cohorts (Fig. 3). The area under the curve (AUC) were 0.919 (95% CI: 0.876–0.962) and 0.870 (95% CI: 0.775–0.964) in the training and validation cohorts, respectively. The two cohorts did not significantly differ (\( P = 0.356; \text{Fig. 4A} \)). The accuracy of the training and validation cohorts were 0.864 (95% CI: 0.862–0.865) and 0.840 (95% CI: 0.836–0.844), the sensitivity specificity of these two cohorts were 0.917 (95% CI: 0.853–0.981) and 0.783 (95% CI: 0.614–0.951), and the specificity of these two cohorts were 0.864 (95% CI: 0.754–0.900) and 0.865 (95% CI: 0.773–0.958; Table 2). The results suggest that the LRA model was consistent and had good predictive capabilities.

The results of the decision curve analysis (DCA) revealed that using the LRA model to predict LE risk in SLE patients confers a net benefit, which highlights its clinical application value in LE risk prediction (Fig. 4B), which showed when the threshold probability of a doctor or patient was in the range of 0–0.5, the model achieved more net benefits than the “full treatment” or “no treatment” strategy.

9. Discussion

LE is a serious and potentially fatal complication and is the main cause of acute or chronic abdominal pain in SLE [23]. However, due to the lack of specificity in its clinical manifestation, patients often experience a delay in diagnosis and treatment, which can result in serious complications or death. In our study, we developed a LRA model and validated its ability to predict LE based on the clinical features of SLE patients with gastrointestinal manifestations. This model may be a new method to diagnose LE. The internal validation and DCA confirmed the model’s discrimination and calibration capabilities; in particular, the AUC and matrix diagrams confirmed that the nomogram can be used clinically. Its use will increase the possibility of early intervention in high-risk patients, especially in primary hospitals in areas where medical resources are unevenly distributed.

A retrospective study analyzed 62 SLE patients with gastrointestinal manifestations and found that decreases in C4 levels in LE patients may be related to active mesenteric vascular lesions and the activation of the complement pathway [13]. In our study, similar to the aforementioned results, we found that C4 was negatively correlated with LE risk.

The anti-RNP, anti-SSA, and anti-Rib-P antibodies have been reported as specific autoantibodies of SLE and are related to its diagnosis and differential diagnosis [24]. We found that anti-RNP, anti-Rib-P, and anti-SSA antibodies were positively correlated with the occurrence of LE. Among them, anti-RNP antibodies were the highest risk factor. Chen’s study revealed that the positive rate of anti-SSA and anti-RNP antibodies in SLE patients can be greater than 50% [25]. Therefore, anti-SSA and anti-RNP antibodies may be related to the condition of SLE patients with LE. Others have reported that in SLE patients, the anti-RNP antibody is related to symptoms such as Raynaud’s phenomenon, pulmonary hypertension, hemolytic anemia, leukopenia, and mental symptoms; [24,26] the association with Raynaud’s phenomenon and pulmonary hypertension suggests that it may be related to vascular disease [27]. Positive anti-RNP antibodies have also been found to be an independent risk factor for death in patients with SLE and thrombotic microangiopathy [28]. Although the anti-RNP antibody’s role in LE is unclear, it is associated with thrombosis in SLE patients, especially in the presence of lupus...
### Table 1
Characteristics of patients included in this study.

|                          | Training cohort | Validation cohort |
|--------------------------|-----------------|-------------------|
|                          | Non-LE (n = 104)| LE (n = 72)       |
| Age, mean (SD), years    | 44.15 (15.98)   | 35.39 (13.26)     | 0.08  |
| Female                   | 50.67 (16.50)   | 31.75 (19.72)     | 31.00 (15.95) |
| Male                     | 43.06 (15.72)   | 35.60 (12.96)     | 45.71 (12.72) |
| Gender, n (%)            | 0.06            | 0.07              |
| Male                     | 15 (14.42)      | 7 (13.46)         | 0 (0)  |
| Female                   | 89 (85.58)      | 98 (86.54)        | 23 (100) |
| BMI, mean (SD)           | 21.34 (4.27)    | 21.27 (4.21)      | 0.921  |
| Smoking history, n (%)   | 8 (7.7)         | 4 (5.6)           | 0.76   |
| Alcohol consumption history, n (%) | 7 (6.7) | 4 (5.6)  | 0.40   |
| Diabetes, n (%)          | 5 (4.8)         | 1 (1.4)           | 4.77   |
| Hypertension, n (%)      | 18 (17.3)       | 1 (1.4)           | 0.001  |
| ANA-positive, n (%)      | 104 (100)       | 72 (100)          | 52 (100) |
| dsDNA-positive, n (%)    | 56 (53.8)       | 35 (48.6)         | 26 (50) |
| SM-positive, n (%)       | 10 (9.6)        | 23 (31.9)         | 8 (15.4) |
| C3, mean (SD)           | 0.54 (0.22)     | 0.43 (0.22)       | 0.50 (0.24) |
| C4, mean (SD)           | 0.14 (0.07)     | 0.11 (0.07)       | 0.13 (0.08) |

Fig. 1. Flowchart.
Fig. 2. Clinical feature selection and model establishment. A. Optimal parameter (lambda) selection by LASSO used tenfold cross validation via minimum criteria. The average number of predicted variables is expressed as a number along the upper x-axis. The average deviation of each model is represented by a red dot, and the upper and lower limits of the deviation are represented by vertical lines passing through the red dot. The best value of lambda is defined by a vertical black line (\(\lambda=0.054\)). B. LASSO coefficient profiles of the 71 variables plotted against the log(lambda) sequence. Drawing vertical lines by optimum lambda values of eleven nonzero coefficients through tenfold cross-validation. C. The LRA model was developed with C4, ANCA, ALB, AG, age, D-dimer, PLT, serum chlorine (Cl), anti-SSA, anti-Rib-P and anti-RNP. The scale of the line segment corresponding to each variable in the prediction model indicates the possible value range of the variable, and the length of the line segment indicates the influence of the factor on the outcome event. Point represents the individual score corresponding to each variable under different values, and the total score is obtained by adding the individual scores of all variables. Risk represents the risk of LE in SLE patients with gastrointestinal manifestations. Anti.Rib-P, anti-Rib-P antibody; anti.RNP, anti-RNP antibody; anti.SSA, anti-SSA antibody; ANCA, antineutrophil cytoplasmic antibody; C4, complement 4; ALB, albumin; AG, anion gap; PLT, blood platelet; Cl, serum chlorine; SLE, Systemic lupus erythematosus; LE, Lupus enteritis.
However, in this study, we did not find a link between lupus anticoagulant and LE. The anti-SSA antibody is associated with various autoimmune diseases, including Sjogren's syndrome, SLE, and primary biliary cirrhosis as well as with pulmonary hypertension, and neonatal heart block [24,30–32]. Anti-Rib-P antibody is a specific autoantibody that has diagnostic value for SLE and is related to disease activity and early onset [33,34]. However, the association between anti-Rib-P and LE is unclear. Anti-Rib-P antibodies can specifically bind to Rib-P antigens as well as to ribosomal proteins within cells and prevent protein synthesis [33,35]. Moreover, it can enhance the production of tumor necrosis factor and interleukin-6 and upregulate their mRNA expression in activated monocytes [36].

ANCA is an autoantibody considered to be closely related to multiple clinical small vasculitis diseases [37]. The research on the relationship between ANCA and SLE is still lacking. However, our results suggest that ANCA is negatively correlated with LE in SLE patients (Supplementary Fig. S2), which has yet to be reported in the literature.

**Table 2**

|                      | Accuracy (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) |
|----------------------|-------------------|----------------------|----------------------|
| Training cohort      | 0.864 (0.862–0.865) | 0.917 (0.853–0.981) | 0.827 (0.754–0.900) |
| Validation cohort    | 0.840 (0.836–0.844) | 0.781 (0.614–0.951) | 0.865 (0.773–0.958) |
literature. Therefore, we speculate that ANCA may be a risk factor for digestive system involvement in SLE, but this association needs further verification via basic experiments and clinical practice.

Although our study was well-designed, several limitations should be emphasized. This study was retrospective and involved a single center with a relatively small number of patients, which may result in reduced generalizability of the LRA model. Thus, to improve its performance, in future studies we plan to expand the sample size of SLE patients by using data from multiple hospitals and further optimizing the selection of clinical and serological indicators that predicts the occurrence of LE in SLE patients with gastrointestinal manifestations; this model may assist clinically in early intervention.

Author contributions

ZH-L, MG and YR-C were responsible for experiment design, data analysis, and writing the manuscript. YZ were responsible for experiment design, acquisition and analysis of data. FX-Z and YL were responsible for revising the manuscript. All authors read and approved the final manuscript.

Data sharing statement

All data will be available upon reasonable request to the corresponding author, and it will be shared according to the standards of ethical policies regulating data sharing of human subjects.

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Declaration of Competing Interest

All the authors declare that this work was supported by the National Key Research and Development Program of China (Project no. 2016YFC0906201) and by the 1.3.5 Project for Disciplines of Excellence, West China Hospital, Sichuan University (Project No. ZYGDD18015). All the authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2021.100900.

References

[1] Barnett R. Systemic lupus erythematosus. Lancet 2016 Apr 23;387(10029):1711.
[2] El Dubois, DI Tuffanelli. Clinical manifestations of systemic lupus erythematosus. computer analysis of 520 cases. JAMA 1964 oct 12;190.
[3] Li Z, Xu D, Wang Z, et al. Gastrointestinal system involvement in systemic lupus erythematosus. Lupus 2017;26(11):1127–38.
[4] Tu Y, Yeh H, Chen L, et al. Differences in disease features between childhood-onset and adult-onset systemic lupus erythematosus patients presenting with acute abdominal pain. Semin Arthritis Rheum 2011;40(5):447–54.
[5] Yuan S, Lian F, Chen D, et al. Clinical features and associated factors of abdominal pain in systemic lupus erythematosus. J Rheumatol 2013;40(12):2015–22.
[6] Kwok SK, Sheo SH, Ju JH, et al. Lupus enteritis: clinical characteristics, risk factor for relapse and association with anti-endothelial cell antibody. Lupus 2007;16(10):803–9.
[7] Hellwell TR, Flook D, Whitworth J, et al. Arteritis and venulitis in systemic lupus erythematosus resulting in massive lower intestinal haemorrhage. Histopathology 1985 Oct;9(10):1103–13.
[8] Cervera R, Espinosa G, Cordoba A, et al. Intestinal involvement secondary to the antiphospholipid syndrome (APS): clinical and immunologic characteristics of 97 patients: comparison of classic and catastrophic APS. Semin Arthritis Rheum 2007 Apr;36(5):287–96.
[9] Renontov R, Laala Co Lo SK, et al. Activation of cultured vascular endothelial cells by antiphospholipid antibodies. J Clin Invest 1995 Nov;96(5):2211–9.
[10] Ju JH, Min JK, Jung CK, et al. Lupus mesenteric vasculitis can cause acute abdominal pain in patients with SLE. Nat Rev Rheumatol 2009 May;5(5):273–81.
[11] Buck AC, Sereho UH, Quinet RJ, et al. Subacute abdominal pain requiring hospitalization in a systemic lupus erythematosus patient: a retrospective analysis and review of the literature. Lupus 2001;10(7):491–5.
[12] Zicz TM, Classen JN, Stevens MB, et al. Acute abdominal complications of systemic lupus erythematosus and polyarteritis nodosa. Ann J Med 1982 Oct;73(4):525–31.
[13] Koo BS, Hong S, Kim YJ, et al. Lupus enteritis: clinical characteristics and predictive factors for recurrence. Lupus 2015 May;24(6):828–32.
[14] Endo H, Kondo Y, Kawagoe K, et al. Lupus enteritis detected by capsule endoscopy. Intern Med 2007;46(18):1621–2.
[15] Liao WC, Yuan WH, Yan WH, et al. Vomiting and diarrhea in a woman with systemic lupus erythematosus. J Chin Med Assoc 2015 Feb;78(2):133–5.
[16] Byun JY, Ha HK, Yu SY, et al. CT features of systemic lupus erythematosus in patients with acute abdominal pain: emphasis on ischemic bowel disease. Radiol 1999 Apr;211(1):203–9.
[17] Forni L, Basizi KW, French AR, et al. Mesenteric vasculitis in children with systemic lupus erythematosus. Clin Rheumatol 2016 Mar;35(3):785–93.
[18] Ruiz-Irastorza G, Khamashia MA, Castellino G, et al. Systemic lupus erythematosus. Lancet 2001 Mar;31(9962):1027–32.
[19] Petri M, Orbai AM, Alarcon GS, et al. Derivation and validation of the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012 Aug;64(8):2677–86.
[20] Fatima N, Zheng H, Maassad E, et al. Development and validation of machine learning algorithms for predicting adverse events after surgery for lumbar degenerative spondylolisthesis. World Neursurg 2020 Aug;140:627–41.
[21] Saurerbi W, Rosyon P, Binder H, et al. Selection of important variables and determination of functional form for continuous predictors in multivariable model building. Stat Med 2007 Dec 30;26(30):5352–8.
[22] Balachandran VP, Gonien M, Smith J, et al. Nomenclar in oncology: more than meets the eye. Lancet Oncol 2015 Apr;16(4):e173–80.
[23] Yuan S, Ye Y, Chen D, et al. Lupus mesenteric vasculitis: clinical features and associated factors for the recurrence and prognosis of disease, 43. Semin Arthritis Rheum; 2014 Jun. p. 759–66.
[24] Li J, Leng X, Li Z, et al. Chinese SLE treatment and research group registry: II. association of autoantibodies with clinical manifestations in Chinese patients with systemic lupus erythematosus. J Immunol Res 2014;2014:809389.
[25] Chen SY, Xu JH, Shuai ZW, et al. A clinical analysis 30 cases of lupus mesenteric vasculitis. Zhonghua Nei Ke Za Zhi 2009 Feb;59(2):99–102.
[26] Cervera R, Espinosa G, Cordero A, et al. Intestinal involvement secondary to the antiphospholipid syndrome (APS) - a clinical review. J Rheumatol 2000;27(1):139–44.
[27] Plastiras SC, Karadimitrakis SP, Kampolis C, et al. Determinants of pulmonary arterial hypertension in scleroderma. Semin Arthritis Rheum 2007 Jun;36(6):392–4.
[28] Chen WC, Ko PS, Wang HY, et al. Difference in thrombotic microangiopathy between concurrently and previously diagnosed systemic lupus erythematosus. J Chin Med Assoc 2020 Aug;83(8):743–9.
[29] Zamaro-Medina MDC, Hinojosa-Azaola A, Nuñez-Alvarez CA, et al. Anti-RNP/Sm antibodies in patients with systemic lupus erythematosus and its role in thrombosis: a case-control study. Chin Rheumatol 2019 Mar;38(3):885–93.
[30] Gilbow IM, Kivin TK, Uhlig T, et al. Sicca symptoms and secondary Sjögren’s syndrome in systemic lupus erythematosus: comparison with rheumatoid arthritis and correlation with disease variables. Ann Rheum Dis 2001 Dec;60(12):1103–9.
[31] Reed BR, Lee LA, Harmon C, et al. Autoantibodies to SS-A/Ro in infants with congenital heart block. J Pediatr 1983 Dec;103(6):889–91.
[32] Granito A, Muratori P, Muratori L, et al. Antibodies to SS-A/Ro-52 kD and centromere in autoimmune liver disease: a clue to diagnosis and prognosis of primary biliary cirrhosis. Aliment Pharmacol Ther 2007 Sep 15;26(5):743–50.
[33] Olesińska M, Chwalicka-Sadowska H, Wiestek-Szwarc E, et al. Clinical manifestation of systemic lupus erythematosus in patients with anti-bisposomal P protein antibodies. Pol Arch Med Wewn 2010 Mar;120(3):76–81.
[34] Tzoufas AG, Tzortzakos NG, Panous-Pomonis E, et al. The clinical relevance of antibodies to ribosomal-P protein epitope in two targeted systemic lupus erythematosus populations: a large cohort of consecutive patients and patients with active central nervous system disease. Ann Rheum Dis 2000 Feb;59(2):99–104.
[35] Heilen LD, Ritterhouse LL, McClain MT, et al. Ribosomal P autoantibodies are associated with presence of SLE before SLE onset and are directed against non-C-terminal peptides. J Mol Med (Berl) 2010 Jul;88(7):719–27.
[36] Toubi E, Shoenfeld Y. Clinical and biological aspects of anti-P-ribosomal protein autoantibodies. Autoimmun Rev 2007 Jan;6(1):119–25.
[37] Kitching AR, Anders HJ, Basu N, et al. ANCA-associated vasculitis. Nat Rev Dis Primers 2020 Aug 27;6(1):71.