FRI0373

LONG-TERM FOLLOW-UP OF 320 CHILDREN BORN TO MOTHERS WITH SYSTEMIC AUTOIMMUNE DISEASES: A MULTICENTRE ITALIAN SURVEY FROM 24 RHEUMATOLOGY CENTRES

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Background: Rheumatic Diseases (RD) frequently affect women during reproductive age, therefore counselling on family planning is crucial for their quality of life. Children's outcome is a major topic, but no large studies are available.
Objectives: To assess the long-term health conditions of children born to women with RD in a large multicentre cohort.
Methods: 24 Rheumatology Centres distributed the questionnaire (65 multiple-choice and 12 open-answer questions) to consecutive patients (18–55 years) in September 2015. Data were analysed dividing children upon maternal diagnosis: Chronic Arthritides (CA) and Connective Tissue Diseases (CTD).
Results: Data were collected for 320 children (166 males, 52%) born to 184 mothers (63 CA and 121 CTD). At the time of interview, children had a mean age of 17.1±9.6 years. Preterm delivery (<37 w) was observed in 72 cases (22.5%), including 13 (4%)<34 w. Data on autoimmune/inflammatory disease (AIID) and/or neurodevelopmental disorders (ND)/learning disabilities (LD) is reported in table 1. 12 children (3.7%) had a diagnosis of AIID, mostly coeliac disease (8/12, 67%) and 11 children (3.4%) of a ND and/or LD by a Paediatric Neuropsychiatrist. To rule out the possible effects of *in utero* exposure to maternal autoantibodies and/or anti-rheumatic drugs in the pathogenesis of ND, these data were retrieved for 280 children (88%) and a comparison was performed between 11 affected and 269 not-affected children (table 2).

Abstract FRI0373 – Table 1. DM: diabetes mellitus; LD: learning disorder; ADHD: attention deficit hyperactivity disorder

NEURODEVELOPMENTAL/ LEARNING DISORDERS	Present (n=11)	Absent (n=269)	p-value
Male	7 (64%)	140 (55%)	0.55
Preterm birth			
<37 weeks	3 (27%)	56 (22%)	0.44
<34 weeks	1 (9%)	10 (3.7%)	0.36
Maternal diagnosis			
Chronic Arthritides	2 (18%)	95 (37%)	0.34
Connective Tissue Diseases	9 (82%)	174 (63%)	
Birth weight (mean Kg)	2.958	3.218	0.09
***In utero* exposure to anti-rheumatic drugs**	5 (45%)	63 (24%)	0.14
Prednisone	5 (45%)	46 (17%)	0.22
Hydroxychloroquine	0 (0%)	23 (9%)	0.61
Azathioprine	1 (9%)	1 (0,4%)	0.08
***In utero* exposure to maternal auto-antibodies**	4 (36%)	54 (20%)	0.99
Anti-nuclear	4 (36%)	46 (17%)	0.64
Anti-dsDNA	3 (27%)	14 (5%)	0.06
Anti-Ro/SSA	2 (18%)	24 (9%)	0.99
Anti-cardiolipin	2 (18%)	15 (6%)	0.28
Anti-beta2gpI	0 (0%)	12 (4%)	0.99
Lupus Anticoagulant	0 (0%)	8 (3%)	0.99

Abstract FRI0373 – Table 2

NEURODEVELOPMENTAL/ LEARNING DISORDERS	Present (n=11)	Absent (n=269)	p-value
Male	7 (64%)	140 (55%)	0.55
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<37 weeks	3 (27%)	56 (22%)	0.44
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Conclusions: In this long-term follow-up of children born to mothers with RD in this large, multicenter study of randomly interviewed women each AIID did not display a significantly increased frequency as compared to the literature; only coeliac showed a mild increased frequency. Children with LD had a tendency to cluster in the group of mothers with CTD, especially after maternal diagnosis (4/63, 6.3%), with a higher frequency as compared to general paediatric population. No significant relationships between ND/LD and prematurity, intrauterine drug exposure or maternal autoantibodies were identified.
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FRI0374

MILDER CLINICAL PRESENTATION OF LUPUS NEPHRITIS AND IMPROVED RENAL SURVIVAL DURING THE LAST 50 YEARS: A MULTICENTRIC STUDY

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Background: Lupus nephritis (LN) presentation changed over time following earlier diagnosis and treatment.
Objectives: To evaluate changes in LN clinical and histological presentation in the last 5 decades.
Methods: This is a retrospective multicentric study on prospectively collected data in four Italian hospital centres. Patients diagnosed between 1970 and 2016 were recruited provided they had a biopsy-proven LN that was retrospectively reclassified according to the ISN/RPS classification criteria. Follow-up was subdivided into three periods (P) based on the year of LN diagnosis: P1:1970–1895; P2:1986–2000; P3:2001–2016. Predictors of patient and renal survival were investigated by univariate and multivariate analysis; survival curves were compared by log-rank test. Clinical pictures at presentation included isolated urinary abnormalities, nephrotic syndrome, nephritic syndrome, rapidly progressive renal failure. Outcome at last observation was defined as complete renal remission or

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partial renal remission, or poor renal outcome, including chronic kidney disease (CKD) or end stage renal disease (ESRD).
Results: 499 patients were included (85.6% females) with a median follow-up of 10.6 years (IQR 4–18). We observed an increase in both age at diagnosis of LN (P1 28.4±10.4; P2 29±11.5; P3 34.4±13.3 years) and disease duration before LN diagnosis (P1 1.3±1.3; P2 2.6±4.5; P3 4.6±6.3 years) from 1970 to 2016 (p<0.001 for both). At clinical presentation, renal insufficiency and acute nephritic syndrome became less common (P1 14.2%; P2 3.9% ; P3 3.4% and P1 29%, P2 20.3%; P3 12.4%, respectively, p<0.0001) while isolated urinary abnormalities became significantly more prevalent from P1 to P3 (P1 26.4%; P2 38%; P3 48.9%; p<0.0001). Outcome was available in 95.8% of patients. Frequency of partial and complete renal remission progressively increased (P1 6.9%; P2 28%; P3 32% and P1 49.6%; P248% ; P3 58.5%; p<0.001 and p=0.01, respectively) while CKD, ESRD and death decreased (P1 7.9%; P2 8.5%; P3 4.5% ; P1 24.8% P2 9%; P3 1.3%; P1 19.8%; P2 5.9%; P3 3.6%, respectively. p<0.001 for all). Survival without ESRD at 10 and at 20 years was 87% and 80% in P1, 94% and 90% in P2% and 99% in P3 (p=0.0019). Induction therapy with immunosuppressants was more frequently performed over time (P1 71%; P2 82%; P3 94.6%, p<0.0001) and use of MMF significantly increased both as induction and maintenance treatment (P1 0, P2 2.7%; P3. 33.8% and P1 1%; P2 15%; P3 54.8%, respectively; p<0.0001). At multivariate analysis, logarithm of serum creatinine (RR:2.72), male gender (RR:3.34), activity index (RR:1.1), chronicity index (RR:1.29), arterial hypertension (RR:5.95), and lack of maintenance immunosuppressive therapy (RR:3.04) predicted ESRD. No significant changes in histological classes or active lesions at the time of renal biopsy were observed, while chronicity index significantly decreased from P1 to P3 (p=0.023).
Conclusions: The clinical presentation of LN apparently became less severe in the last decades, likely due to earlier diagnosis and proper treatment, leading to an improved renal survival.
Disclosure of Interest: None declared
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FRI0375 DELAYED LUPUS NEPHRITIS IN THE COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS PREDICTS A POORER RENAL RESPONSE TO INDUCTION THERAPY, RENAL FLARES, AND WORSE LONG-TERM RENAL OUTCOMES: A MULTICENTER, RETROSPECTIVE COHORT STUDY

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Background: Some prognostic factors for lupus nephritis (LN) have been mentioned such as nephrotic syndrome, class 4 and chronicity on histology. In a previous single-centre study, we reported a potentially poorer renal response to induction therapy in LN that developed later after SLE onset (delayed, D-LN) compared with LN manifesting at SLE onset (early, E-LN) [1]. However, our study was limited by a small sample size and lack of long-term observation.
Objectives: This multicenter study aimed to validate whether D-LN was a useful predictor of a poor response to induction therapy with more detailed clinical and pathological parameters. Furthermore, we investigated whether D-LN was also a predictor of flares and long-term renal outcomes in addition to the established prognostic factors.
Methods: We retrospectively examined 215 biopsy-proven LN patients (136 E-LN, 79 D-LN) who attended 3 hospitals above between 1997 and 2014 and who were observed for 3–20 (median: 10.8) years from LN onset. We compared baseline clinical, pathological features and treatment options at LN onset between E-LN and D-LN. Then we compared the cumulative complete response (CR) rates, renal/extra-renal relapse rates, and the rates of renal insufficiency between the two groups. Renal insufficiency was defined as follows:[1] serum creatinine (SCr) doubling or ESRD for severe insufficiency, and[2] SCr increasing by 1.5 times and also >1.0 (female) or >1.2 mg/dl (male) for mild insufficiency. Moreover, we evaluated predictors of the response, flares and long-term renal outcomes with multivariate analysis.
Results: Anti-Sm/RNP antibodies and mixed proliferative and membranous nephritis (class 3+5 or 4+5) were significantly more prevalent in D-LN than E-LN (48.1 vs. 32.4%, 68.8 vs. 40.4%, 40.5 vs. 18.4%, respectively). Log-rank test showed that significantly lower cumulative CR rates over 3 years (65.8 *vs.* 83.1% at 12 months, 83.5 *vs.* 92.6% at 36 months, p*<0.01*) and significantly higher relapse rates (both renal and extra-renal) over 20 years in D-LN than E-LN. Mild renal insufficiency was significantly more likely to occur in D-LN over 20 years (21.5 *vs.* 12.5%, p=*0.04*). We performed multivariate Cox regression analysis for the response, flare, and renal outcomes including significant variables on univariate analysis. As independent predictors of CR, D-LN, nephrotic syndrome and chronicity index were identified. As those of renal flares, D-LN was detected. Although D-LN was not associated with severe renal insufficiency, D-LN was identified as an independent predictor of mild renal insufficiency as well as some other factors (table 1).

Univariate analysis	Hazard ratio	P-value	Multivariate analysis	Hazard ratio	P-value
Predictors of CR					
D-LN	0.66(0.49-0.89)	0.006	D-LN	0.50(0.36-0.69)	<0.001
Serum creatinine	0.61(0.46-0.81)	0.001			
Nephrotic syndrome	0.54(0.40-0.73)	<0.001	Nephrotic syndrome	0.51(0.37-0.70)	<0.001
Class Ⅳ	0.66(0.49-0.87)	0.004			
Activity Index	0.94(0.90-0.97)	0.001			
Chronicity index	0.75(0.66-0.84)	<0.001	Chronicity index	0.81(0.70-0.92)	0.002
Predictors of renal flare					
D-LN	2.50(1.55-4.03)	<0.001	D-LN	2.17(1.30-3.65)	0.003
Anti-RNP antibodies	1.71(1.05-2.78)	0.030			
Non-CR at 12months after induction therapy	2.05(1.25-3.37)	0.005			
Predictors of extra-renal flare					
D-LN	1.92(1.05-3.52)	0.035	D-LN	1.64(0.88-3.05)	0.122
Anti-Sm antibodies	2.49(1.34-4.65)	0.004	Anti-Sm antibodies	2.31(1.23-4.34)	0.009
Predictors of severe renal insufficiency					
D-LN	2.31(0.89-5.99)	0.085			
Anti-RNP antibodies	9.41(2.14-41.3)	0.003	Anti-RNP antibodies	10.1(2.27-44.6)	0.002
Chronicity index	1.42(1.03-1.97)	0.032			
Non-CR at 6months after induction therapy	4.38(1.54-12.4)	<0.001	Non-CR at 6months after induction therapy	3.21(1.06-9.75)	0.039
Predictors of mild renal insufficiency					
D-LN	2.00(1.02-3.92)	0.044	D-LN	2.12(1.03-4.34)	0.041
Male	2.14(1.02-4.48)	0.044	Male	2.87(1.31-6.27)	0.008
Serum creatinine	1.97(1.45-2.67)	<0.001	Serum creatinine	1.97(1.30-2.99)	0.002
Nephrotic syndrome	2.48(1.26-4.88)	0.009			
Activity index	1.14(1.04-1.24)	0.003			
Chronicity index	1.77(1.42-2.19)	<0.001	Chronicity index	1.61(1.25-2.09)	<0.001
Non-CR at 6months after induction therapy	5.24(2.50-11.0)	<0.001	Non-CR at 6months after induction therapy	3.29(1.46-7.41)	0.004

Conclusions: D-LN might be a novel predictor of a poorer treatment response, renal flares and long-term renal outcomes independent of the established prognostic factors. The distinct differences in the autoantibody profiles between E-LN and D-LN groups suggest that D-LN patients might reflect a refractory SLE subset with a specific immunological profile.

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FRI0376 DYSLIPIDEMIA AS A NEWLY RECOGNISEDFACTOR ASSOCIATED WITH DAMAGE ACCRUAL IN EARLY DIAGNOSED SLE: RESULTS FROM THE MULTICENTER EARLY LUPUS PROJECT INCEPTION COHORT

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Background: Preventing organ damage is a major challenge in Systemic Lupus Erythematosus (SLE).
Objectives: To evaluate factors associated with development of damage in a prospectively followed cohort of early diagnosed SLE patients.
Methods: The Early Lupus Project[1] encompasses 9 Italian centres recruiting, from the 1 st January 2012, an inception cohort of consecutive patients diagnosed with SLE within 12 months from appearance of four or more 1997 ACR classification criteria. At study entry and then every 6 months a large panel of data was recorded.
Here, we report on factors associated with the development of damage assessed by the SLICC/ACR Damage Index (SDI). Using univariate analysis, we assessed the contribution of covariates collected at baseline (demographic, comorbidities, serological, clinical by BILAG2004 domains, disease activity by ECLAM, HRQoL by visual analogic scale) in the development of damage (SDI from 0 to $\geq$1). Forward-Backward Cox-regression models were fitted with covariates with p<0.05 to identify factors independently associated with increased risk of damage development.
Results: Overall, 279 patients were enrolled in the Early Lupus Project inception cohort up to the 31th of December 2017; 230 patients (89.6% Caucasians, 13.4% males) were eligible for this study having SDI=0 at enrolment and at least 6

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