FRI0065

DHCR7 AND GENETIC POLYMORPHISMS IN THE ASSOCIATION BETWEEN VITAMIN D AND LIPID PROFILE IN RA: NEW PLAYERS IN CARDIOVASCULAR DISEASE?

J. Rodríguez-Carrio^{1,2,3}, M. Alperi-López^{2,4}, M. Naves-Díaz^{1,2}, A. Dusso^{1,2}, P. López^{2,3}, F.J. Ballina-García^{2,4}, J.B. Cannata-Andía^{1,2}, A. Suárez^{2,3}. ¹Bone Mineral and Research Unit, Instituto Reina Sofía de Investigación Nefrológica, Redinren Isciii, Hospital Universitario Central de Asturias; ²Instituto de Investigación Sanitaria del Principado de Asturias (ISPA); ³Area of Immunology, University of Oviedo; ⁴Department of Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain

Background: rheumatoid arthritis (RA) is associated with increased cardiovascular (CV) risk. Although vitamin D deficiency has been linked to CV disease in other conditions, studies in RA have yielded contradictory results and pointed to the involvement of additional factors. On the one hand, several genetic polymorphisms have been linked to vitamin D levels. Moreover, emerging evidence suggests a role for the enzyme DHCR7 in the crosstalk between cholesterol and vitamin D synthesis.

Objectives: to evaluate the effect of genetic polymorphisms and DHCR7 levels in the interaction between vitamin D and lipid profile in RA.

Methods: serum levels of vitamin D and DHCR7 were measured in 212 RA patients (2010 EULAR/ACR criteria) and 104 matched healthy controls (HC) by chemiluminescence and immunoassays, respectively. VDR rs2228750 and DHCR7 rs12785878 SNPs were studied by TaqMan Assays. The effect of vitamin D deficiency on clinical features was assessed by linear regression analyses adjusting for age, gender, seasonality, vitamin D supplementation and DMARD usage.

Results: decreased vitamin D was found in RA compared to HC ($p<0.001$), vitamin D deficiency (<20 ng/ml) being more prevalent in winter/spring (58/151, 38.4%) than in summer/autumn (12/61, 19.6%; $p=0.010$). Vitamin D levels were positively correlated to those of HDL ($r=0.217$, $p<0.001$), this association being restricted to patients with the rs2228750 AG/AA genotype ($r=0.287$, $p=0.003$) but not in those with the GG one ($r=0.082$, $p=0.531$). Equivalent results were obtained for total/HDL-cholesterol ratio. Vitamin D deficiency was associated with lower HDL ($p=0.040$), higher tender joint count ($p=0.003$), swollen joint count ($p=0.005$), DAS28 ($p=0.028$) and HAQ ($p=0.030$) in AG/AA-patients but not in those with the GG status (all $p>0.050$). Decreased DHCR7 levels were found between RA and HC in winter/spring ($p=0.008$) but not in summer/autumn ($p=0.116$). RA patients with CV disease exhibited lower DHCR7 levels ($p=0.012$) than their CV-free counterparts. Moreover, the associations among DHCR7, vitamin D and HDL levels followed a seasonal pattern: DHCR7 was correlated to vitamin D levels in summer/autumn ($r=0.441$, $p=0.004$), where vitamin D was associated with both HDL levels ($r=0.354$, $p=0.009$) and total/HDL ratio ($r=-0.393$, $p=0.003$). A DHCR7 rs12785878-driven effect was observed for these associations. On the contrary, a weak correlation between HDL and vitamin D was found in winter/spring ($r=0.215$, $p=0.014$), where decreased DHCR7 was associated with age at onset ($r=-0.285$, $p=0.006$) and RF titre ($r=-0.326$, $p=0.013$).

Conclusions: the effect of vitamin D on the lipid profile is dependent on genetic polymorphisms. DHCR7 has a pivotal role in the interaction between vitamin D and lipid profile in RA. Seasonality and DHCR7-HDL axis may be novel mediators in the CV disease in RA.

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FRI0066

IMPACT OF SERUM ADIPOKINES IN EARLY STAGES OF RHEUMATOID ARTHRITIS

J.A. Chaparro^{1,2}, J.M. Bello-Gualtero^{1,2}, W. Bautista-Molano^{2,3}, L. Chila³, M. A. Cano³, R. Valle-Oñate¹, P. Chalem⁴, C. Romero-Sánchez^{1,2,3}. ¹Rheumatology and Immunology, Hospital Militar Central; ²Clinical Immunology Group, Universidad Militar Nueva Granada; ³Unit of Oral Basic Investigation, Universidad El Bosque; ⁴Fundación Instituto de Reumatología Fernando Chalem, Bogotá D.C., Colombia

Background: Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease. Adipose tissue is regarded as an active endocrine organ producing adipokines such as leptin and adiponectin, and some proinflammatory cytokines which have proinflammatory properties that account for chronic low-grade systemic inflammation

Objectives: To investigate the levels of adipokines in eRA and establish their association with the state of rheumatic condition

Methods: Cross sectional study was conducted. 51 patients with eRA according to the ACR/EULAR 2010 criteria and 51 healthy controls matched by age and gender, were included. A complete medical history was obtained. Adiponectin levels measured by Luminex technology, IL6 by chemiluminescence and Iptin by Enzyme-linked immunosorbent assay. Serum markers of RA such as rheumatoid factor, erythrocyte sedimentation rate(ESR), C reactive protein(CRP), and anticitrullinated protein antibodies-APCA IgG/IgA. Disease activity was evaluated by

DAS28CRP, DAS28ESR, CDAI, SDAI and RAPID3, the functional status using Multidimensional health assessment questionnaire(MDHAQ) and radiological status by Simple Erosion Narrowing Score(SENS). An association analysis was made to evaluate the relationship between adipokines levels and rheumatologic conditions using X2 test, Mann Whitney and logistic regression model was performed to confirm this associations. All the results were performed with a level of significance of 95%

Results: In the eRA group, 80.39% were women, the mean age was 48.54 ± 10.93 years. 37.25% had overweight and 13.72% had obesity Among the controls, 80.39% were women, with the mean age of 48.55 ± 11.07 years. 27.45% had overweight and 5.88% had obesity. 45.09% moderate activity and 17.64% high activity by DAS28ESR. High leptin levels were found in 64.7% vs 23.5% in healthy controls ($p=0.001$). High adiponectin levels was found associated to BMI <25 ($p=0.017$) and high leptin level to BMI >25 ($p=0.038$) and disease activity by RAPID3 ($p=0.039$). The presence of joint space narrowing in hands was associated with low adiponectin levels ($p=0.044$). The association of leptin levels >1.67 ng/mL with the diagnosis of RA was maintained in the model adjusted for the presence of *P. gingivalis*, DAS28-ESR, CRP >3 mg/L, economic status and BMI >30 , OR=2.79 95% CI (1.54–5.07). The presence of high leptin and IL6 levels and low level adiponectin at the same time were more frequently found in the female gender ($p=0.047$), primary schooling ($p=0.050$), BMI >30 ($p=0.023$), patients with radiological damage SENS >3 ($p=0.047$) and were found associated at the same time to MDHAQ >3 , BMI >25 and RAPID3 >12 (OR 5.03 95% CI 1.05–24) adjusted to clinical variables

Conclusions: The role of adipokines as the leptin could be considered to be the bridge between immune tolerance, metabolic function and autoimmunity and suggests the possibility to use circulating levels of adipokines as potential biomarkers of disease activity and functional status in early stage of rheumatoid arthritis

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FRI0067

TRENDS IN THE INCIDENCE OF FELTY'S SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN: AN OBSERVATIONAL COHORT STUDY OF HOSPITAL DISCHARGES FROM 1999 TO 2015 (TREND-AR STUDY)

J.L. Morell¹, R. Mazzucchelli², E. Perez Fernandez³, J. Quiros⁴, C. Macia Villa⁵, N. Crespi⁶, M. Peña⁷, C. Barbadillo⁸, M. Espinosa⁸, H. Godoy⁸, M. Fernandez-Prada⁹, M. Galindo¹⁰, A. Garcia Vadillo¹¹, O. Guzon Illescas⁴, A. Herranz¹², C. Martinez Prada¹³, C. Morado Quiñoa¹³, V. Villaverde¹⁴, on behalf of TREND-AR. ¹Rheumatology, Hospital Universitario Ramón y Cajal; ²Rheumatology, Hospital Universitario Fundación Alcorcón; ³Rheumatology, Hospital Universitario Fundación Alcorcón; ⁴Rheumatology, Hospital Universitario Fundación Alcorcón; ⁵Rheumatology, Hospital Universitario Severo Ochoa; ⁶C.S La Rivota; ⁷Rheumatology, Hospital Universitario Fundación Alcorcón; ⁸Rheumatology, Hospital Universitario Puerta de Hierro, Madrid; ⁹Rheumatology, Hospital Universitario de Guadalajara, Guadalajara; ¹⁰Rheumatology, Hospital Universitario doce de octubre; ¹¹Rheumatology, Hospital Universitario La Princesa; ¹²Rheumatology, Hospital del Henares; ¹³Rheumatology, Hospital Clínico San Carlos; ¹⁴Rheumatology, Hospital Universitario de Mostoles, Madrid, Spain

Background: Felty's syndrome (FS) is an unfrequent entity related to Rheumatoid Arthritis (RA) but it's unknown the trend of FS in Spain.

Objectives: To analyze the incidence and trend of hospital admissions for FS in RA patients in Spain from 1999 to 2015.

Methods: We performed an observational retrospective population study analyzing the spanish administrative database that includes a Minimum Basic Data Set (MBDS) of hospital admissions of RA patients from 1999 to 2015. We selected the MBDSs for FS. Cases were identified by the presence in primary and secondary diagnosis of its ICD9 code. The population at risk was estimated with an estimated prevalence of RA of 0,5% (0,8% women and 0,2% men). Crude and adjusted rates were calculated, and the trend was analysed using the Generalised Linear Model (GLM) with the year as the analysis variable. SPSS version 20 (SPSS Inc, Chicago, IL) was used.

Results: 338.343 RA hospital admissions were detected, being 802 (0,2%) due to FS, 455 (56,7%) women and 347 (43,3%) men. Mean age was 67,94(SD 13,76). There were 61 (7,6%) deaths. Age-adjusted rate during the period was 42,19/10⁵ inhab. per year (19,76 women and 64,61 men). FS age-adjusted rate decreased from 25,90/10⁵ inhab. per year in 1999 to 17,20 in 2015, both women (12,85 in 1999 to 11,75 in 2015) and men (80,15 in 1999 to 38,75 in 2015). An annual decrease in the FS rate of 0,5% is estimated (RRI 0,995; CI 95% 0,976–1,014).

Conclusions: In Spain FS hospital admissions in patients with RA decreased between 1999–2015 with an estimation of 0.5% annual reduction not statistically significant.

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FRI0068

ULTRASONOGRAPHIC SUBCLINICAL CARDIOVASCULAR FINDINGS IN HISPANIC RA PATIENTS: A CASE-CONTROL STUDY

J.R. Azpiri-López¹, D.A. Galarza-Delgado², I.J. Colunga-Pedraza², A.H. Guillén-Lozoya², J.A. Dávila-Jiménez², E.E. Abundis-Márquez². ¹Cardiology; ²Rheumatology, Hospital Universitario "Dr José E. Gonzalez", UANL, Monterrey, Mexico

Background: Patients with RA have a 1.5–2.0 fold increased risk of developing coronary artery disease (CAD) compared with the general population. Patients with RA are typically managed by several physicians, and coordination of care may be suboptimal.¹ The leading cause of death in RA-patients is atherosclerotic cardiovascular disease (ASCVD).² Carotid artery and heart evaluation by ultrasound is a useful tool for detection of cardiovascular conditions.

Objectives: To compare the presence of subclinical cardiovascular conditions among Mexican-mestizo RA patients and matched controls.

Methods: Design: Observational, cross-sectional, case-control study. Patients of 40 to 75 years old who fulfilled the 2010 ACR/EULAR and/or the 1987 ACR classification criteria for RA were consecutively enrolled. Patients with previous ASCVD or any other rheumatic disease were excluded. Two board-certified radiologist performed and assessed all carotid ultrasounds (cUS) and two board-certified cardiologist performed and assessed transthoracic echocardiography (TTE) according to guidelines of the American Society of Echocardiography. ASE, 2016

Results: The RA patients showed higher prevalence of cardiovascular risk conditions with respect to control population, such as concentric remodelling/hypertrophy, diastolic dysfunction, valve regurgitation and Carotid intima media thickness (CIMT) (See table 1).

Abstract FRI0068 – Table 1. Ecographic cardiovascular pathological conditions among RA patients.

Ecographic findings	RA n=50 (%)	Controls n=50 (%)	P	O.R. (C.I. 95%)
Valve regurgitation, n (%)	42 (84)	32 (64)	0.023	2.95 (1.14-7.64)
Aortic, n (%)	4 (8)	3 (6)	0.999*	1.36 (0.28-6.42)
Tricuspid, n (%)	41 (82)	29 (58)	0.009	3.29 (1.32-8.23)
Mild, n (%)	37 (74)	29 (58)	0.091	2.06 (0.88-4.80)
Moderate, n (%)	4 (8)	0 (0)	0.126*	0.92 (0.84-0.99)
Mitral, n (%)	28 (56)	6 (12)	0.0001	9.30 (3.36-25.87)
Pulmonar, n (%)	8 (16)	2 (4)	0.046	4.57 (0.91-22.73)
Diastolic dysfunction, n (%)	34 (68)	16 (32)	0.003	3.46 (1.52-7.90)
LVCR, n (%)	13 (26)	6 (12)	0.074	2.50 (0.89-7.44)
LVH, n (%)	5 (10)	1 (2)	0.092	5.40 (0.61-48.39)
LVCR/LVH, n (%)	18 (36)	8 (16)	0.017	3.09 (1.19-7.99)
Mass index (g/m ²), mean ± SD	66.75±7.40	73.11±22.49	0.132	1.01 (-14.67-1.93)
LVEF (%), mean ± SD	60.14±5.12	63.42±5.67	0.004	1.12 (-5.49-1.06)
GLS (%), mean ± SD	-20.73±2.90	-21.03±2.48	0.639	0.96 (-0.96-1.56)
TAPSE (mm), mean ± SD	23.01±4.41	24.06±3.12	0.193	1.05 (-2.6-0.54)
CAWH, n (%)	21 (42)	10 (20)	0.017	2.80 (1.18-7.06)
Carotid plaque, n (%)	11 (22)	10 (20)	0.806	1.12 (0.43-2.95)

P (P value) O.R. (Odds ratio) C.I. (Confidence interval) LVCR (Left ventricle concentric remodeling) LVH (Left Ventricle hypertrophy) LVEF (Left ventricle ejection fraction) GLS (Global longitudinal strain) TAPSE (Tricuspid annular plane systolic excursion) CAWH (Carotid artery wall hypertrophy) SD (Standard deviation) * (Yates continuity correction)

Conclusions: This study reinforces the usefulness of cUS and TTE as a tool in the evaluation of cardiovascular conditions in RA patients. A systematic search of extra-articular and cardiovascular comorbidities should be mandatory in all RA patients.

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FRI0069

DIFFERENCE OF CLINICAL IMPLICATION REGARDING THE NUMBERS OF AUTOANTIBODIES AT PRESENTATION IN KOREAN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

J.Y. Pyo¹, C.-H. Mun², S.M. Jung², S.W. Lee², J. Song², S.K. Lee², Y.B. Park².

¹Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju; ²Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic Of

Background: Epitope spreading occurs prior to the clinical diagnosis of rheumatoid arthritis (RA), the number of peptide recognised and its titer increases remarkably as becoming close to the clinical diagnosis. However, the effect of multiple autoantibodies on the clinical outcome is not well known.

Objectives: This study is to investigate the association between the number of autoantibodies at presentation and the clinical aspects in Korean patients with early RA.

Methods: The number of baseline autoantibody (rheumatoid factor, anticitrullinated peptide antibodies (ACPA), and anti-carbamylated protein antibodies (anti-CarP)) was analysed in the Korean Intensive Management of Early Rheumatoid Arthritis (KIMERA) cohort. All patients were disease-modifying antirheumatic drug (DMARD)-naïve RA patients with symptom duration less than 1 year. They were intensively treated by adjusting medications every 4 weeks, and treated to target as DAS28 of <2.6. Patients were classified regarding the number of autoantibodies and clinical characteristics were compared between the groups.

Results: A total of 128 patients were included, seronegative patients showed higher baseline physician global VAS (7.3 vs 4.7 vs 4.6 vs 4.4, p=0.005) and DAS28-ESR (7.1 vs 4.5 vs 5.0 vs 4.7, p=0.003) than patients with 1, 2, and 3 autoantibodies. Also seronegative patients showed a trend to have higher baseline HAQ score and pain VAS. After intensive treatment, there were no differences in remission rate and DAS28-ESR at 12, 24, and 36 months.

Abstract FRI0069 – Table 1. Disease characteristics regarding number of autoantibodies

Variables	0 (n=5)	1 (n=13)	2 (n=58)	3 (n=52)	p-value
Age, years	58.2±16.2	46.4±12.4	52.8±12.9	48.2±13.5	0.104
Female sex, N (%)	5 (100%)	7 (53.8%)	44 (75.9%)	44 (84.6%)	0.062
Symptom duration, days	7.0±4.8	10.2±12.1	10.5±16.0	8.1±7.5	0.736
BMI (kg/m ²)	24.1±4.2	21.7±1.9	23.0±2.9	23.0±3.1	0.508
ESR (mm/hour)	59.0±15.8	44.4±17.6	56.8±32.0	57.9±32.2	0.543
CRP (mg/L)	20.9±17.3	13.6±26.9	19.0±29.4	12.9±15.7	0.559
HAQ score	1.4±0.5	0.6±0.6	0.7±0.6	0.7±0.6	0.092
Pain VAS	7.6±0.9	4.0±2.0	4.5±2.7	4.4±2.9	0.073
Patient global VAS	7.3±1.7	4.7±2.2	4.6±2.5	4.4±2.7	0.127
Physician global VAS	7.0±0.9	4.9±1.1	5.5±1.2	4.5±1.6	0.005
DAS28-ESR	7.1±0.6	4.5±1.2	5.0±1.4	4.7±1.4	0.003

Values are expressed as means±standard deviation or N (%). BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; HAQ: health assessment questionnaire; VAS, visual analogue scale; DAS, disease activity score

Changes in DAS28 according to number of autoantibodies

Conclusions: Seronegative patients showed higher levels of baseline inflammation than seropositive patients. However, they had favourable treatment response with rapid improvement which resulted in excellent clinical outcome.

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