MORTALITY AND MULTIPLE CAUSES OF DEATH IN CYTOKINE ACTIVATION AND FORMATION OF NEPHROPATHY IN EARLY RHEUMATOID ARTHRITIS: CLINICAL AND PATHOPHYSIOLOGICAL PARALLELS

D. Rekalov1, P. Prykova1, R. Kulynych1, 1Rheumatology, Zaporizhzhia Regional Clinical Hospital, Zaporizhzhia, Ukraine

Background: RA is characterized by not only joints destruction, but also of other organs and systems, particularly, lungs, heart, blood vessels, kidneys, etc. Nephropathy is currently the leading symptomatic complex of Rheumatoid Arthritis (RA), with up to 73% frequency, being identified as a prognostic criterion of diseases severity and outcome. The development of renal insufficiency, as a rule, is the main cause of the fatal outcome of RA without possibility of regular hemodialysis to such patients.

Objectives: of the study are to determine pathophysiological relation between cell-mediated immunity (tumornecrosis factor-alpha (TNF-α)) activation and renal dysfunction in the patients with early RA (eRA).

Methods: We analyzed the data from 35 early RA patients of average age of 50.71±2.25 years (ranged 18 - 76 years, 80% of women) with 9.21±0.43 months mean duration of the disease by the time of the study initiation. Urine and blood tests were performed to verify the main indicators of kidney function and inflammation cytokines significant interaction.

Results: All signs of renal dysfunctions at the baseline in the patients with eRA were associated with glomerular filtration rate decrease and excretion of urine protein increase. Dynamics of albumin urine, according to the analysis of variance for one-factsore models, were significantly determined by the state of disease activity, reflecting the severity of joint damage. High urine β2-microglobulin level was significantly associated with the expression rate of main inflammatory cytokines as per binary regression analysis.

Table 1. Differences in the renal function features in the patients with early RA depending on the TNF-α expression (Mm (95% confidence interval)).

<table>
<thead>
<tr>
<th>TNF-α expression level</th>
<th>Patients with RA (n=35)</th>
<th>Patients without RA (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt;7 pg/mL)</td>
<td>0.10 ±0.02</td>
<td>0.91 ±0.05</td>
</tr>
<tr>
<td>Medium (7-10 pg/mL)</td>
<td>0.63 ±0.03</td>
<td>0.80 ±0.04</td>
</tr>
<tr>
<td>High (&gt;10 pg/mL)</td>
<td>0.86 ±0.02</td>
<td>0.73 ±0.03</td>
</tr>
</tbody>
</table>

Conclusions: The obtained dependence showed the dynamics of expression of tubular disorders in early RA with a progressive deterioration which did associate with the levels of TNF-α expression, and variety of the urine microglobulin rates in the interval 200-350 μg/L. Reliable correlation (r=0.51, p<0.05) between β2-microglobulinuria and TNF-α levels was clearly shown, revealing the relationship described by the formula MGU = – 481 + 937 x log10 (TNF-α) as per regression analysis. The severity of tubular damage in early RA is associated with TNF-α expression, especially in the patients with TNF-α above 250 pg/mL, where microalbuminuria and TNF-α levels were significantly higher (p<0.00043). We identified robust data that in the early RA patients with high TNF-α, the number of reported cases of microalbuminuria was significantly higher than in those with low levels.

Disclosure of Interest: None declared


SAT0135

MORTALITY AND MULTIPLE CAUSES OF DEATH IN RHEUMATOID ARTHRITIS PATIENTS. RESULTS FROM A LARGE POPULATION-BASED COHORT IN THE VENETOREGION, 2010-2015.

1Department of Medicine - DIMED, University of Padova; 2Epidemiological Department, Veneto Region; 3Department of Medicine - DIMED, University of Padova, Padova, Italy

Background: Mortality rates in patients with rheumatoid arthritis (RA) are 1.5-1.6 fold higher than in the general population.1,2. No recent data on mortality in large cohorts of RA patients in Italy are available.

Objectives: The aim of this study was to assess standardized mortality ratios (SMRs) and multiple causes of death in RA subjects living in the Veneto Region between 2010 and 2015.

Methods: We identified in the electronic archive of the Veneto Region a cohort of patients aged 20-89 years who were exempt from copayment for RA in January 2010, and linked them with the archive of causes of deaths of the period 2010-2015. The record-linkage was performed on previously anonymized records. In the Veneto Region, a copy of all death certificates is transmitted to the Regional Epidemiology Service for coding of causes of death according to the International Classification of Diseases, 10th Edition. Each subject was followed from 1st January 2010 either until death, or 90 years of age, or 31st December 2015, whichever came first.

In the Veneto Region, the archive of causes of death include all diseases mentioned in the death certificate, and the selection of the underlying cause of death (UCOD) is performed by means of the Automated Classification of Medical Entities, a computer program developed by the US National Center for Health Statistics. SMRs with 95% confidence intervals, were computed as the ratios between deaths observed in the cohort, and those expected according to age- and gender-specific regional mortality rates.

Results: Overall 16,098 residents diagnosed with RA and aged 20-89 years were enrolled in the cohort. Follow-up was complete for above 99% of study subjects. The overall follow-up amounted to 88,599 person-years, with 2,142 registered decedents. The most common causes of death were circulatory diseases (36.6%), neoplasms (24.2%), and respiratory diseases (8.3%). SMR in RA subjects was 1.42 (1.36-1.48). Mortality was significantly increased from circulatory, respiratory, digestive, infectious, hematological diseases and falls (figure 1).

Conclusions: Overall, a 42% excess risk of death could be observed among patients with RA in the Veneto Region. These data confirm results from previous studies in large cohorts of RA subjects.[1,2].

REFERENCES:

Disclosure of Interest: None declared


SAT0134

CLINICAL AND PATHOPHYSIOLOGICAL PARALLELS OF NEPHROPATHY IN EARLY RHEUMATOID ARTHRITIS: INCREASED RENAL TUBULAR DAMAGE AND EXPRESSION OF PROINFLAMMATORY CYTOKINES IN EARLY RHEUMATOID ARTHRITIS PATIENTS. RESULTS FROM A LARGE POPULATION-BASED COHORT IN THE VENETOREGION, 2010-2015.

1Department of Medicine - DIMED, University of Padova; 2Epidemiological Department, Veneto Region; 3Department of Medicine - DIMED, University of Padova, Padova, Italy

Background: No recent data on mortality in large cohorts of RA patients in Italy are available.

Objectives: The aim of this study was to assess standardized mortality ratios (SMRs) and multiple causes of death in RA subjects living in the Veneto Region between 2010 and 2015.

Methods: We identified in the electronic archive of the Veneto Region a cohort of patients aged 20-89 years who were exempt from copayment for RA in January 2010, and linked them with the archive of causes of deaths of the period 2010-2015. The record-linkage was performed on previously anonymized records. In the Veneto Region, a copy of all death certificates is transmitted to the Regional Epidemiology Service for coding of causes of death according to the International Classification of Diseases, 10th Edition. Each subject was followed from 1st January 2010 either until death, or 90 years of age, or 31st December 2015, whichever came first.

In the Veneto Region, the archive of causes of death include all diseases mentioned in the death certificate, and the selection of the underlying cause of death (UCOD) is performed by means of the Automated Classification of Medical Entities, a computer program developed by the US National Center for Health Statistics. SMRs with 95% confidence intervals, were computed as the ratios between deaths observed in the cohort, and those expected according to age- and gender-specific regional mortality rates.

Results: Overall 16,098 residents diagnosed with RA and aged 20-89 years were enrolled in the cohort. Follow-up was complete for above 99% of study subjects. The overall follow-up amounted to 88,599 person-years, with 2,142 registered decedents. The most common causes of death were circulatory diseases (36.6%), neoplasms (24.2%), and respiratory diseases (8.3%). SMR in RA subjects was 1.42 (1.36-1.48). Mortality was significantly increased from circulatory, respiratory, digestive, infectious, hematological diseases and falls (figure 1).

Conclusions: Overall, a 42% excess risk of death could be observed among patients with RA in the Veneto Region. These data confirm results from previous studies in large cohorts of RA subjects.[1,2].

REFERENCES:

Disclosure of Interest: None declared

Methods:
The study population included 127 non-diabetic subjects (90 RA pts and 37 matched controls). We determined body mass index, waist circumference (WC), and presence of metabolic syndrome (MetS). All pts were on disease modifying antirheumatic drugs, 65.6% on steroids (none on steroids >10 mg/day), and 27.8% on biologic therapy. Laboratory analyses included hsCRP, glucose, insulin, and C-peptide (as a marker of insulin secretion). Insulin resistance (IR) was calculated using the updated Homeostasis Model Assessment (HOMA2-IR), based on fasting plasma glucose and specific insulin concentrations. The output of the HOMA2 model was calibrated to give IR of 1 as normal. HOMA2-B indicates the potential of β-cells to compensate increased IR. Lack of compensatory rise of HOMA2-B implied impaired β-cell function.

Results:
IR was detected in 74.4% of RA pts and in 54.2% controls, p=0.025. RA pts had significantly higher concentration of specific insulin, C peptide, and HOMA2-IR than controls, while HOMA2-B was not statistically different. Both groups were comparable regarding all other factors known to affect glucose metabolism (age, WC, presence of MetS). We found significant differences in inflammation markers between RA pts and controls: ESR 29.5 (14–44) vs. 16.0 (10.0–20.0); hsCRP 5.5 (2.8–15) vs. 3.0 (1.8–3.9); p<0.000 for both, as well as in lipids, especially HDL concentration 1.50±0.4 vs 1.60±0.3, p=0.027 and a number of the pts with low HDL (37.8 vs 13.5%, p=0.007). Univariate regression analysis revealed significant positive effect of HDL on logHOMA2-B (β 0.099, 95%CI 0.029–0.169, p=0.006) and negative, but not significant effect on HOMA2-IR. In the logistic regression, after adjustment for HDL concentration, significant differences for HOMA2-IR and insulin became less important but still persisted (Table), while significance for C peptide became more prominent. When we added the influence of inflammation, this favourable effect of HDL-cholesterol on C-peptide disappeared.

Conclusions: RA pts had higher IR and impaired β-cell function in comparison to healthy controls. The augmentation of statistical significance for C peptide, as a marker of insulin secretion, after adjustment for low HDL-cholesterol and significant effect of HDL on logHOMA2-B implicate its important role in disturbances of glucose metabolism in RA.

Disclosure of Interest: None declared