THU0676

A SYSTEMATIC REVIEW AND META-ANALYSIS OF VIRAL EXPOSURES AS A RISK FACTOR FOR RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease with a complex and poorly understood etiology. Development of autoimmune disease stems from a combination of immune, genetic, hormonal and environmental factors. Infections are viewed as triggers of some autoimmune disorders, including RA.

Objectives: Different viral exposures have been implicated in the etiology of RA via several mechanisms of immune activation, such as molecular mimicry. The purpose of this systematic review was to summarise the evidence relating to the association between putative viral exposures and the development of RA.

Methods: A systematic literature search was conducted using MEDLINE-OVID, EMBASE-OVID, PUBMED and Cochrane library databases. Articles were included if they were case-controls, cross-sectional or cohort studies and were published in English. Case-series were included if there was a lack of other study designs.

Results: Of 6724 citations, 78 studies were selected for review, and 48 were included in meta-analysis. Studies had poor quality. Based on the IgG antibodies (n=12 studies) and viral DNA detection (n=3 studies), the odds of parvovirus B19 (PBV19) infection were increased in RA patients than in controls (odds ratio (OR) (95% CI)=1.77 (1.11; 2.80), p=0.02, OR (95% CI)=3.53 (1.00; 12.53), p=0.05 for PVB19 IgG and DNA, respectively). For Epstein-Barr virus (EBV), patients with RA had not significant OR of anti-Epstein-Barr nuclear antigen (EBNA) (n=17 studies, OR (95% CI)=1.05 (0.79; 1.39), p=0.75), but significant OR of anti-viral capsid antigen (VCA) (n=18 studies, OR (95% CI)=1.5 (1.07; 2.10), p=0.02) and anti-early antigen (EA) (n=11 studies, OR (95% CI)=2.74 (1.27; 5.94), p=0.01). Cytomegalovirus (CMV) was not associated with RA (n=13 studies, OR (95% CI)=1.24 (0.78; 1.95), p=0.36). Chronic hepatitis B (HBV) was not associated with RA in 5 case-control (OR (95% CI)=1.37 (0.83; 2.25), p=0.22) and 1 cohort studies (HR 1.09 (0.74, 1.63), p>0.05). Chronic hepatitis C (HCV) was associated with increased risk of RA in 7 case-control (OR (95% CI)=2.82 (1.35; 5.90, p=0.006) and 1 cohort studies (HR 2.03 (1.27, 3.22), p<0.01). There seem to be a risk of persistent arthritis after Chikungunya fever (CHIKV) (n=2 studies, OR (95% CI)=90 (15.2; 134.3).

Abstract THU0676 – Figure 1. Flow chart of study selection. Abstract THU0676 – Figure 2. Forest plots for cumulative odds ratio (95%CI) of serum IgG anti-PVB19 antibodies in RA cases and controls. (A) Without matching of cases and controls (B) With matching of cases and controls. Abstract THU0676 – Figure 3. Forest plot for cumulative odds ratio (95% CI) of serum anti-EBNA IgG in RA cases and controls. (A) Without matching of cases and controls (B) With matching of cases and controls. Abstract THU0676 – Figure 4. Forest plot for cumulative odds ratio (95% CI) of serum anti-CMV IgG in RA patients and controls.

Conclusions: Studies about the risk of RA after viral exposures suffer from inconsistent methodological quality. There is a risk of RA after Parvo B19 infection and possibly HCV but not EBV or HBV. There seems not to be a risk of RA after EBV infection. CHIKV is associated with the persistent inflammatory arthritis. There is not enough evidence to support an association between some viruses and RA development, but they probably lead to RA in genetically susceptible individuals.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2202

THU0677

PNEUMOCOCCAL ANTIBODY PROTECTION IN RHEUMATOLOGICAL PATIENTS RECEIVING bDMARD THERAPY – A CROSS-SECTIONAL STUDY

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Background: Severe pneumococcal infections contribute to increased mortality in patients with rheumatic diseases, and is preventable by vaccination against *Streptococcus pneumoniae*. EULAR recommends that pneumococcal vaccination should be strongly considered in patients with rheumatic diseases, however, need and timing of revaccination for this patient group remains unknown¹. Since 2009, rheumatological patients from our department have been vaccinated against *S. pneumoniae* prior to initiation of bDMARD therapy, by use of the 23-valent pneumococcal polysaccharide vaccine (PPV23). To our knowledge, we are the only centre in Denmark to vaccinate these patients routinely.

Objectives: The aim of the study was to determine the prevalence of rheumatological patients receiving bDMARD therapy with a protective level of antibodies against *S. pneumoniae*, and to identify possible factors of relevance affecting antibody production.

Methods: Antibodies against 12 pneumococcal serotypes were measured in the period of June to December 2017 in patients receiving bDMARD therapy initiated before March 1st 2017. A geometric mean level of all serotypes above 1 µg/ml was considered a protective antibody level. The patients had been diagnosed with rheumatoid arthritis, spondyloarthritis, psoriatic arthritis or juvenile idiopathic arthritis. The study group consisted of both vaccinated and unvaccinated individuals, where unvaccinated individuals initiated bDMARD therapy before vaccination occurred routinely.

Differences in protection between vaccinated and unvaccinated patients were evaluated using the χ^2 test. We included the following variables in a logistic regression model, to analyse factors of possible significance to the protective level of antibodies: age, sex, diagnosis, methotrexate (MTX) and/or prednisolone treatment at time of vaccination, and years since vaccination.

Results: A total of 319 patients were included in the study: 186 (58%) vaccinated and 133 (42%) unvaccinated patients. Among the vaccinated patients, 30% had a protective antibody level versus 0% of the unvaccinated patients (p<0.0001).

Logistic regression analysis showed that a significantly smaller proportion of patients treated with MTX at time of vaccination had a protective antibody level compared with patients not treated with MTX (p=0.03; odds ratio: 2.3; 95% CI [1.1;4.7]). The same applied for advanced age at time of vaccination (p=0.04), whereas years since vaccination did not decrease antibody protection significantly (p=0.12).

Conclusions: Only one third of PPV23 vaccinated rheumatological patients treated with bDMARD were observed with a GML of pneumococcal antibodies above 1 µg/ml. This suggests that a majority of these patients are not protected adequately against pneumococcal disease in spite of vaccination. MTX treatment at time of vaccination and advanced age were both independently associated with lack of protective antibody level.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3657

THU0678

TREND OF VENOUS THROMBOEMBOLISM AMONG SELECT RHEUMATOLOGIC DISEASES: AN AUDIT OF LARGE NATIONAL US DATABASE

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Background: Venous thromboembolism (VTE) is 3rd commonest cause of cardiovascular deaths and encompasses deep-venous thrombosis (DVT) and pulmonary embolism (PE). Rheumatologic diseases have been found to be associated with an increased risk of VTE among hospitalised patients.

Objectives: To describe the trend of VTE among select rheumatologic diseases over 15 years.

Methods: We used National Inpatient Sample (NIS) database for years 2000–2014 to identify adults ≥18 years with select rheumatologic diseases and VTE based on ICD-9 codes. Prevalence was age-sex adjusted against US census population data. STATA was used for querying database and Joinpoint regression