

In order to achieve the better outcome, the timing of referral and diagnosis of early arthritis should be optimized. We examine the time to referral of patients with joint symptoms, and diagnosis delay of RA and SpA in a rural community medical center in Japan.

**Methods:** A total of 556 who visited Kameda Medical Center from January 2009 to December 2010 with joint symptoms (arthralgia, joint swelling and/or morning stiffness) without any previous treatment except for NSAIDs were included. In the patients diagnosed as RA and SpA, the time intervals from the onset of symptom to primary care physician (PCP) (patient delay), from PCP referral to a rheumatologist (PCP delay), from the onset of symptoms to rheumatology visit (total delay) were determined.

**Results:** Ninety-one patients were diagnosed as RA, 32 patients were diagnosed as SpA (17 Psoriatic arthritis, 8 SAPHO syndrome, and 7 Reactive Arthritis). The median patient, PCP, total delays [interquartile range [IQR]] were 8.9 weeks [2.6-27.9], 5 weeks [2-19.2], 27 weeks [11.4-60.1] for RA patients and 18.7 weeks [3-61.3], 4 weeks [1.4-9], 27.4 weeks [6.6-87.2] for SpA patients, respectively. The total delay was similar in both groups and the patient delay was longer than PCP delay, which was significant only for SpA patients ( $p = 0.04$ ), but not for RA patients ( $p = 0.1682$ ). When analyzed in subgroups, the median total delay for reactive arthritis patients ( $n = 7$ ) was 4.3 weeks [3.7-7.7], which was shorter than for RA patients.

**Conclusion:** In a rural community medical center in Japan, the patient delay is longer than the PCP delay. Although the total delay was similar, the patient delay for SpA was longer than RA. This study indicates the key delay in early arthritis diagnosis in Japan.

**Disclosure statement:** The presenting author and all the other authors declared no conflicts of interest.

#### PP64.

Abstract withdrawn.

#### PP65.

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#### PP66. SEXUAL FUNCTIONS IN MALE WITH ANKYLOSING SPONDYLITIS

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**Background:** There are numerous studies investigating the impact of Ankylosing Spondylitis (AS) on sexual functions in male patients with the disease. However, results are contradictory. New studies on this area are still necessary. Using International Index of Erectile Function (IIEF), the aim of this study was to determine the impact of AS on sexual functions in male patients, to compare with healthy controls and to identify the associations with demographic, disease-related variables and the level of depression in these patients

**Methods:** A total of 40 male patients with AS and 27 healthy were included in the study. Bath Metrology Index, Bath AS Functional Index, Bath AS Disease Activity Index, Short Form-36 (SF-36), AS Quality of Life (ASQoL), IIEF and Beck Depression Inventory (BDI) were applied to the study population.

**Results:** Prevalence of ED in patients and healthy controls were 43.6% and 51.9%, respectively ( $p: 0.512$ ). No statistically significant differences were found between male patients and controls in the demographic characteristics, IIEF and BDI scores ( $p > 0.05$ ). When we compared patients according to tumor necrosis factor (TNF) usage, no statistically significant difference was found between TNF naive patients and patients receiving TNF according to demographic characteristics, IIEF and BDI. TOTAL IIEF was correlated with C-reactive protein levels, chest expansion and BDI. Overall Satisfaction subscale of IIEF was correlated with ASQoL, Intercourse Satisfaction with Pain subscale of SF-36, Orgasmic Function with Social Function subscale of SF-36.

**Conclusions:** Sexual function are common, but not different in male AS patients when compared with healthy controls. Sexual problems in male patients with AS seem to be associated with higher depression level, decreased quality of life, decreased chest expansion and C-reactive protein levels. However, to achieve a better results of sexual functioning in AS patients, it might be better to evaluate the issue in the longitudinal follow-up.

**Disclosure statement:** The authors have declared no conflicts of interest.

#### PP67. NOVEL THERAPIES DERIVED FROM ORIENTAL MEDICINE FOR ANKYLOSING SPONDYLITIS

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**Background:** Ankylosing spondylitis (AS) is an autoimmune disease with chronic inflammation in joints that affects mainly axial skeleton with eventual fusion of the spine. There are no cures available but only treatments to relieve pain and symptoms, mainly through medications such as anti-inflammatory drugs, steroids or TNF- $\alpha$  blockers. Unfortunately, there are some patients whose symptoms did not alleviate with current treatments. Our study was to investigate novel therapies to treat the symptoms of AS and reduce the inflammation.

**Methods:** The novel therapies were developed by combinatorial treatment derived from oriental medicine, including herbal tea and acupuncture to reduce pain and inflammation. The intensity of pain and stiffness were recorded based on patients' score. The level of inflammation was determined by measuring C-reactive protein level in blood samples of patients. The treatments were performed on 3 AS patients for approximately 12 months.

**Results:** All three patients with AS were presented severe pain and stiffness around their axial joints, including spine and pelvis before treatments. Their initial CRP levels were ranged from 5 to 300 mg/L. After the combination of treatments, the CRP levels were reduced dramatically to normal level at 0~1 mg/L. The patients also experienced reduced pains where pain scores reduced from 10 to 0 or 1. The pain and stiffness of their joints of spines, knees and ankles disappeared after the treatments.

**Conclusions:** The study demonstrated a novel therapy derived from oriental medicine that can treat the symptoms of AS, suggesting alternative treatments for AS patients who did not experience any effect from conventional therapies.

**Disclosure statement:** The presenting authors have declared no conflicts of interest.

#### NATURE AWARDS NA01-NA02

##### NA01. RHEUMATOLOGIC BACKGROUND IN CANDIDATES OF VALVULAR HEART SURGERY: A SINGLE CENTER SURVEY

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**Background:** Valvular heart diseases are among the frequent causes of cardiac surgery. Some of the patients have a well known rheumatic condition. Heart valves are fragile connective tissues which are vulnerable to any systemic autoimmune disease.

**Material and method:** We selected 120 patients who were candidates for valvular heart surgery who had not any known rheumatologic diagnosis. Careful history and physical examination undertaken from rheumatologic stand point. The most sensitive screening serologic tests were also assayed.

**Results:** 53.3% were male and 46.6% were female with mean of 48.18 years old. 45.8% of patients had history of non-mechanical joint disease, 14.2% had history of rheumatologic conditions in their family, 30% had history of constitutional symptoms. 29.8% had positive joint findings in their physical exam. 25.8% had anemia of chronic disease. Rheumatoid factor, antiCCP, abnormal urine, elevated ESR, CRP, ANA in 34%, 2.5%, 5%, 36.7%, 26.7%, 4.2% respectively. ANCA, APA was positive in a few cases.

**Conclusion:** Above findings may show immunologic bases for most valvular heart diseases candidates for surgery. Undifferentiated connective tissue diseases may have an important role in pathophysiology of valvular damage.

## NA02. PREGNANCY OUTCOME IN LUPUS PATIENTS WITH PREVIOUS ADVERSE OUTCOMES: EXPERIENCE WITH PROTOCOL-BASED, MULTIDISCIPLINARY CARE FROM KERALA, SOUTH INDIA

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**Background:** In patients with SLE with previous adverse obstetric outcome the risk of an adverse outcome in subsequent pregnancy rises. In this prospective cohort of such patients the primary objective was to assess the impact of a protocol based care.

**Methods:** Between March and September 2010 all patients with SLE fulfilling the ACR classification criteria with previous at least one adverse obstetric outcome (maternal; preterm labour, pre eclampsia or previous medical termination of pregnancy (MTP) in view of SLE flare, foetal; miscarriage, IUGR, preterm birth, low birth weight (LBW), intrauterine death or still birth) desirous of having more children were prospectively enrolled. Briefly the protocol comprised of pre natal counselling, pre-natal drug and disease status review, risk stratification, periodic ante-natal visits for the monitoring of pregnancy (including with obstetric ultrasounds) and disease, 2D echocardiogram at weeks 18 and 32 if Ro/La were positive and post natal disease and drug review and contraception advice. Therapeutic changes were made as necessary at each stage.

**Results:** Fourteen patients (age mean  $\pm$ SD years;  $29 \pm 3$ ) were enrolled. Previous poor obstetric outcomes were: miscarriage(s) in 6, MTP in 3, preterm labour with IUGR in 2, intrauterine death, still birth and pre eclampsia in 1 each. Four patients had secondary APS and 6 had both or either Ro/La positive. Three had lupus nephritis (LN); > 6months ago in 2. There were 10 (71%) live births (2 LBW, instrumentation or caesarean section in 3). Three patients had miscarriages (one had ongoing LN). One decided against becoming pregnant after initial counselling. Five patients (35%) had lupus flare (2 mild, 2 moderate and 1 severe based on SLEDAI).

**Conclusions:** Majority of patients in our cohort had acceptable pregnancy outcome. This highlights that for high risk lupus pregnancies a multidisciplinary input with protocol based care offers a good chance of improved pregnancy outcome.

**Disclosure statement:** The authors have declared no conflicts of interest.

## ABSTRACTS FROM EIR SCHOOL ES01-ES25

### ES01. THE EFFECTIVENESS OF MONOCLONAL ANTIBODIES TO TUMOR NECROSIS FACTOR ALPHA: INFlixIMAB IN JUVENILE ANKYLOSING SPONDYLITIS

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**Background:** Juvenile ankylosing spondylitis (JAS) is a type of arthritis that affects the spine and the sites where the muscles, tendons, and ligaments are attached to bone, with frequent onset before 15 years of age preferably in boys. Currently, besides standard schemes of immunosuppressive therapy, administration of biological agents, influencing on various components of pathogenesis is most perspective. One of them consists in administration of monoclonal anti-TNF- $\alpha$  antibodies, consisting in variable area of murine highly affinitive neutralizing monoclonal antibodies to TNF- $\alpha$ (A2), combined to fragment of human IgG – infliximab.

**Methods:** 58 patients with juvenile ankylosing spondylitis were enrolled in the study, from them there are 17 girls and 41 boys. Median age of the patients was  $12 \pm 3,1$  years, median duration of disease  $-4 \pm 3,6$  years.

Average dose of infliximab comprised to 7,5 mg/kg/administration. Administration of Infliximab was conducted in standard scheme 0, 2, 6 weeks, thereafter every 8 weeks.

**Results:** Before treatment of infliximab overall assessment score in doctor's opinion (VAS) comprised to 60(53;72), overall health assessment in patient's opinion or his parents (VAS)-72(58;82), number of

“active” joints-3,9(3;6), number of joints with function limitation-4(3;6), assessment of functional ability by using questionnaire Childhood Health Assessment Questionnaire (CHAQ)-2(1,6;2,4), ESR-40(25;58) mm/h, C-PR-3 (1,2;6)mg/%. After 9 administration (54 weeks) of the drug 89% patients achieved 90%, 100% patients – 70% improvement in criteria ACR-pedi.

**Conclusion:** infliximab is a highly effective drug in patients with juvenile ankylosing spondylitis.

### ES02. RELATIONSHIP BETWEEN FATIGUE AND IL 6, DISEASE ACTIVITY, DEPRESSION IN PATIENTS TREATED WITH TOCELIZUMAB

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**Background:** Fatigue is a symptom described as chronic prostration not relieved by appropriate sleep that causes incapacity to participate in social and professional activities as well as in rehabilitation programs. Fatigue is a common complaint in rheumatoid arthritis patients and contributes to loss of quality of life.

There are several theories to explain the appearance of fatigue in RA patients. One of them is that the fatigue is due to high levels of pro-inflammatory cytokines such as IL-6.

**Methods:** We studied 35 RA patients receiving intravenous infusions of TCZ (8 mg/kg each) at a 4-week intervals in combination steady-state therapy with disease-modifying anti-rheumatic drugs and glucocorticoids. We assessed C-reactive protein, erythrocyte sedimentation rate, serum interleukin (IL) 6 concentration, fatigue (assessed by VAS), depression level by EQ 5D scale, VAS for general health, tender joint count (TJC), swollen joint count (SJC), hemoglobin level.

**Results:** Basic level of fatigue was 5,3 (4,0; 7,0), IL6 171,3 (83,98;462,29), DAS-28 6,5(5,92;7,16), pain 66,0 (51,0;74,0), TJC 13(8;17), SJC 12 (8;18). Significant improve in IL6 level, fatigue and DAS28 was on the 4 week of therapy. The improvement continued throughout the 6 months.

In 6 month improve in fatigue was 52%, in DAS28 68%, in IL6 level 80,4%. Fatigue value did not correlated with IL6 level ( $r = -0,039$ ,  $p = 0,82$ ), hemoglobin level ( $r = -0,23$ ,  $p < 0,05$ ), pain ( $r = 0,30$ ,  $p < 0,05$ ), TJC( $r = 0,19$ ,  $p < 0,05$ ), SJC( $r = 0,11$ ,  $p < 0,05$ ). But it was associated with DAS-28 ( $r = 0,36$ ,  $p = 0,047$ ), depression ( $r = 0,45$ ,  $p = 0,02$ ) and VAS for general health ( $r = 0,52$ ,  $p < 0,05$ ).

**Conclusion:** High fatigue levels characterize activity of RA. The decrease in fatigue and depression in patients treated with TCZ is a result of reduction of disease activity, not pro-inflammatory cytokines.

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### ES03. NK CELL DEPLETION AND ITS RELATION TO ELEVATED REDOX POTENTIAL IN RHEUMATOID ARTHRITIS

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**Background:** Reactive oxygen intermediates (ROIs) attack on the mitochondrial Electron transport chain and oxidative phosphorylation and depletes the ATP levels. The cells life cycle is dependent on the level of ATPs produced during metabolism. The number of natural killer cells in the autoimmune disorders is one of the major prognostic factors. This work is comprised of the correlation between elevated ROIs with the NK cell numbers in Rheumatoid arthritis (RA) patients.

**Methods:** Peripheral blood of 15 patients of RA and 15 age and sex matched healthy volunteer with ethically approved inclusion and exclusion criteria were collected. The enzymatic activities evaluated (within 5-6 hours) in peripheral blood lymphocytes were Superoxide dismutase, Catalase and Glutathione Peroxidase. Two non-enzymatic markers Malondialdehyde (MDA) for Lipid peroxidation and Reduced Glutathione (GSH) were also analyzed. The ROS levels were measured by DCFHDA dye using Flow cytometry. The percentage population of Natural Killer (NK) cells were enumerated by flow cytometry. The results were analysed by using Student's t test.

**Results:** The levels of MDA were negatively correlated with the NK cell numbers while the GSH and antioxidant enzyme concentrations were found positively correlated with the NK cell population.