PAKISTAN SOCIETY FOR RHEUMATOLOGY

NEWSLETTER

Volume 2 June 2021

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MESSAGE FROM EDITOR-IN-CHIEF

Dear friends, we are presenting the second issue of the official newsletter of PSR. As always, I hope you will appreciate and encourage the efforts of my team.

For the new readers, I shall briefly introduce how a PSR executive member conceived the idea of publishing a newsletter. We are proud that our Pakistan society for rheumatology is now soaring on the international horizon. So, we need to meet the standards of other well-developed societies, to be compatible with the real world. All the developed societies have their publications as journals, newsletters, announcements, and many more. In the PSR council meeting, the idea of having our own publication was raised, with the objective being to have a non-cumbersome interaction with our readers. All of the executive members agreed that it is high time that PSR starts an official publication of its own to meet the demands of today. Provision will include information regarding the upcoming events in Pakistan and the latest highlights and news related to Rheumatology to our readers.

I am humbled to be chosen as the first Editor in chief for this task. My team members represent all major cities of Pakistan. It is their hard work and commitment that makes it possible for me to complete this task efficiently.

Thank you, friends, and my team.

DR. TAHIRA PERVEEN UMER
Editor in Chief-PSR Newsletter,
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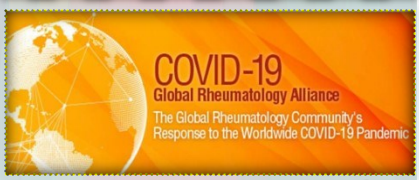

COVID-19 IN RHEUMATIC DISEASE PATIENTS

(DATA COLLECTION)

Courtesy : Dr. Babur Salim

From Pakistan Dr Babur Salim, Dr Shahida Parveen and Dr Saliha Ishaq are actively participating in collecting and sending DATA of patients with rheumatic disease and COVID infection to Global Rheumatology Alliance. Dr Babur and Dr Shahida Parveen are currently working in department of Rheumatology Fauji Foundation hospital Rawalpindi where as Dr Saliha is currently working as a Consultant Rheumatologist at south city hospital, Karachi, Pakistan. DATA of more than 90 patients have been reported to GRA.

ASIA PACIFIC LEAGUE AGAINST RHEUMATISM PEDIATRIC RHEUMATOLOGY SPECIAL INTEREST GROUP (APLAR PAEDSRHEUM SIG): BACKGROUND, INTRODUCTION & UPDATE

Courtesy : Prof. Sumaira Farman Raja

The recent 2021 ACR Pediatric Rheumatology Symposium (PRYSM) had a wonderful session on `Global Health in Pediatric Rheumatology'; however, there was no representation from Asia Pacific region where approximately 50 % or more of the estimated 6-7 million children afflicted with rheumatic diseases live!

This probably reflects the historic lack of a dedicated pediatric rheumatology association for this region.

I would like to thank the PSR Newsletter for giving me an opportunity to introduce the APLAR PaedsRheum SIG.

In most countries of the Asia Pacific region the data, although sketchy, shows a staggering shortage of trained paediatric rheumatologists (PRs).

According to `average minimum acceptable requirement' of PRs in the West, for the 31 APLAR member nations we need approximately 3,061, while the actual number is estimated around 300 only. Additionally, countries with low HDIs and low GDP, like Pakistan, have the most percentage of young population, and these are the countries with least public health spending and most shortages of PRs!

The result is that adult rheumatologists, paediatricians, general/family physicians (GPs/FPS) and orthopedics etc. are compelled to treat children with rheumatological disorders with inadequate resources to access educational and training materials. For Pakistan, we need approximately 300, and have less than 30 adult rheumatologists/ paediatricians functioning as `surrogate paeds-rheumatologists'. The credentialing of these has had to be less structured compared with the developed countries.

Recognizing the need for a collaborative regional effort, the Paediatric Rheumatology Special Interest Group (PaedsRheum SIG) was approved in April 2019 Brisbane APLAR. This took forward the stalled 2008 APAPR (Asia Pacific Association for Paediatric Rheumatology) of Prof. Yokota and Dr Prudence Manners, my mentor in Paediatric Rheumatology.

Presently we have representatives of 17 countries, and we look forward to this number growing. We are proud to have 5 members from PSR.

The SIG's single point agenda is `to improve the care of children with rheumatic diseases in APLAR region through education, research and better clinical care'.
The first APLAR Paediatric Rheumatology SIG symposium titled `Treating Children with Rheumatic Diseases in Asia Pacific: The Great Divide' was held in October 2020.

On 'World Young Rheumatic Diseases Day' a webinar was held in March 2021, and the APLAR SIG symposium will be held on 31 August 2021 during the APLAR congress. It has an exciting program and will be shared shortly. Additionally, 3 monthly webinars are scheduled to share expertise and improve care of children with rheumatic diseases in our region.

PSR has also developed a PaedsRheum SIG with 12 members presently. Both SIGs are developing a PR directory and working on collaborative research.

COVID-19 VACCINE CLINICAL GUIDANCE SUMMARY FOR PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

Developed by the ACR COVID-19 Vaccine Clinical Guidance Task Force
February 8, 2021, and updated on March 4, 2021

Courtesy : Dr. Tajvur Sabir

Recommendations

Table 1: General Considerations Related to COVID-19 Vaccination in Rheumatic and Musculoskeletal Disease Patients

Guidance Statement	Level of Task Force consensus
The rheumatology healthcare provider is responsible for engaging the RMD patient in a discussion to assess COVID-19 vaccination status and engage in a shared decision-making process to discuss receiving the COVID-19 vaccine.	Strong-Moderate
Acknowledging heterogeneity due to disease- and treatment-related factors, and after considering the influence of age and sex, AIIRD patients are at higher risk for hospitalized COVID-19 and worse outcomes compared to the general population.	Moderate
Based on their risk for COVID-19, AIIRD patients should be prioritized for vaccination before the non-prioritized general population of similar age and sex.	Moderate
Beyond known allergies to vaccine components, there are no known additional contraindications to COVID-19 vaccination for AIIRD patients.	Moderate
The expected response to COVID-19 vaccination for many AIIRD patients on systemic immunomodulatory therapies is likely to be blunted in its magnitude and duration compared to the general population.	Moderate
A theoretical risk exists for AIIRD flare or disease worsening following COVID-19 vaccination. However, the benefit of COVID-19 vaccination for RMD patients outweighs the potential risk for new onset autoimmunity.	Moderate
RMD = rheumatic and musculoskeletal disease; AIIRD=autoimmune and inflammatory rheumatic disease	

Table 2: Recommendations for Use of the COVID-19 Vaccine in RMD Patients

Guidance Statement	Level of Task Force consensus
RMD and AIIRD patients should receive COVID-19 vaccination, consistent with the age restriction of the EUA and/or FDA approval.*	Moderate
RMD patients without an AIIRD who are on immunomodulatory therapy should be vaccinated in a similar fashion as described in this guidance for AIIRD patients receiving those same treatments.	Moderate
Based on the data for the mRNA COVID-19 vaccines available in the U.S., there is no preference for one COVID-19 vaccine over another. Therefore, AIIRD patients should receive either vaccine available to them.	Moderate
For a multi-dose vaccine, AIIRD patients should receive the second dose of the same vaccine, even if there are non-serious adverse events associated with receipt of the first dose, consistent with timing described in CDC guidelines.	Strong
Healthcare providers should not routinely order any lab testing (e.g., antibody tests for IgM and/or IgG to spike or nucleocapsid proteins) to assess immunity to COVID-19 post-vaccination, nor to assess the need for vaccination in a yet-unvaccinated person.	Strong
Following COVID-19 vaccination, RMD patients should continue to follow all public health guidelines regarding physical distancing and other preventive measures.	Strong
Household members and other frequent, close contacts of AIIRD patients should undergo COVID-19 vaccination when available to them to facilitate a 'cocooning effect' that may help protect the AIIRD patient. No priority for early vaccination is recommended for household members.	Moderate
While vaccination would ideally occur in the setting of well-controlled AIIRD, except for those patients with life-threatening illness (e.g., in the ICU for any reason), COVID vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity.	Strong-Moderate
RMD = rheumatic and musculoskeletal disease; AIIRD=autoimmune and inflammatory rheumatic disease; EUA = emergency use authorization; FDA = Food and Drug Administration; mRNA = messenger RNA; CDC = Centers for Disease Control; ICU = Intensive Care Unit	

*age ≥16 as of January 2021

Table 3: Guidance Related to the Use and Timing of Vaccination and Immunomodulatory Therapies in Relation to COVID-19 Vaccination Administration in RMD Patients*

Medication	Timing Considerations for Immunomodulatory Therapy and Vaccination*	Level of Task Force Consensus
Hydroxychloroquine; apremilast; IVIG; glucocorticoids, prednisone-equivalent dose <20mg/day	No modifications to either immunomodulatory therapy or vaccination timing	Strong-Moderate
Sulfasalazine; Leflunomide; Mycophenolate; Azathioprine; Cyclophosphamide (oral); TNFi; IL-6R; IL-1; IL-17; IL-12/23; IL-23; Belimumab; oral calcineurin inhibitors; Glucocorticoids, prednisone-equivalent dose ≥ 20mg/day**	No modifications to either immunomodulatory therapy or vaccination timing	Moderate
Methotrexate	Hold MTX 1 week after each vaccine dose, for those with well-controlled disease; no modifications to vaccination timing	Moderate
JAKi	Hold JAKi for 1 week after each vaccine dose; no modification to vaccination timing	Moderate
Abatacept SQ	Hold SQ abatacept both one week prior to and one week after the first COVID-19 vaccine dose (only); no interruption around the second vaccine dose	Moderate
Abatacept IV	Time vaccine administration so that the first vaccination will occur four weeks after abatacept infusion (i.e., the entire dosing interval), and postpone the subsequent abatacept infusion by one week (i.e., a 5-week gap in total); no medication adjustment for the second vaccine dose	Moderate
Cyclophosphamide IV	Time CYC administration so that it will occur approximately 1 week after each vaccine dose, when feasible	Moderate
Rituximab	Assuming that patient's COVID-19 risk is low or is able to be mitigated by preventive health measures (e.g., self-isolation), schedule vaccination so that the vaccine series is initiated approximately 4 weeks prior to next scheduled rituximab cycle; after vaccination, delay RTX 2-4 weeks after 2nd vaccine dose, if disease activity allows	Moderate
RMD = rheumatic and musculoskeletal disease; IVIG = intravenous immunoglobulin; TNFi = tumor necrosis factor inhibitor; IL = interleukin; JAKi = janus kinase inhibitor; CYC = cyclophosphamide; RTX = rituximab; IV = intravenous; SQ = subcutaneous		

**guidance to 'hold' a therapy was made based on the assumption that the patient had well-enough controlled disease to allow for a temporary interruption; if not, decision-making should be determined on a case-by-case basis, considering the circumstances involved*

***consensus was not reached for vaccination timing in patients receiving prednisone-equivalent doses ≥ 20mg/day; see full guidance document, when published, for additional details*

IL-6R = sarilumab; tocilizumab; IL-1R = anakinra, canakinumab; IL-17 = ixekizumab, secukinumab; IL-12/23 = ustekinumab; IL-23 = guselkumab, rizankizumab; JAKi = baricitinib, tofacitinib, upadacitinib

COVID VACCINE GUIDELINES:

Courtesy : Dr. Tajvur Sabir

Most vaccines are equally effective. These reduce the chance of developing Covid 19 by 95% and the disease severity. Protection starts at 10-14 days.

The mRNA vaccine seems to be as effective as the best performing vaccines in clinical trials such as the measles vaccines.

Prevention of transmission: As 40% patients don't have any symptoms this will reduce transmission to others. Vaccines cannot reduce the risk by 100% and thus for now wearing a mask in public is very important as a safety strategy.

SAFETY:

The commonest side effect is pain at the injection site. Fatigue and headaches are possible. These settle with Paracetamol or a nonsteroidal anti-inflammatory drug.

LONG TERM SAFETY:

As long term side effects of vaccines are rare, it is unlikely that the Covid vaccine will cause long term problems.

Age group: All trials have been for over 18 year old with no upper limit. A first preference is given by older age and the presence of comorbidities.

CONTRAINDICATIONS:

None for immunocompromised patients except allergy to vaccine components.
If previous allergy to another vaccine or injectable observe patient for 30 minutes.

Immunocompromised and clinically vulnerable patients are at increased risk of severe Covid 19 and thus should receive the vaccine first, irrespective of disease activity and severity.

Contraindications Include:

- Cancer
- Bone marrow transplant
- Solid organ transplant
- Stem cell for cancer treatment
- Genetic immune deficiencies
- HIV

Vaccines do not usually cause an increased risk of rejection or autoimmune disease, the same is expected of the Covid vaccines. Where possible give the vaccine 2 weeks before starting immunosuppressants and continue to wear a mask. A second dose should be given even if there is a non-serious reaction to a first dose of the vaccine.

No concerns were found regarding the use or timing of immunomodulatory therapies in patients with autoimmune inflammatory rheumatic diseases. The response to COVID-19 vaccination for AIIRD patients on systemic immunomodulatory therapies may be blunted compared to the general population. There is a theoretical risk of a flare of the disease but the potential benefit far outweighs the risk of potential new onset autoimmunity. Family members should be vaccinated to help protect the patient where possible.

No modification is needed for the following drugs:

- Hydroxychloroquine;
- Apremilast
- IVIG
- Glucocorticoids, prednisone-equivalent dose <20 mg/day
- Sulfasalazine
- Leflunomide
- Mycophenolate
- Azathioprine
- Cyclophosphamide (oral)
- TNFi
- IL-6R; all interleukins
- Belimumab
- Calcineurin inhibitors
- Glucocorticoids, prednisone-equivalent dose ≥ 20mg/day

The following drugs should be stopped for one week after the vaccine :

- Methotrexate
- JAKi

The following drug should be stopped one week before and one week after only the first dose of the vaccine.

- Abatacept subcutaneous

For Abatacept IV the first dose should be given after 4 weeks of the dose and the next dose should be delayed by a week. No adjustment needed for the second dose.
Cyclophosphamide IV should be given one week after each vaccine dose where feasible

RITUXIMAB:

Assuming that patient's COVID-19 risk is low or can be mitigated by preventive health measures (e.g., self-isolation), schedule vaccination so that the vaccine series is initiated approximately 4 weeks prior to next scheduled rituximab cycle; after vaccination, delay RTX 2-4 weeks after 2nd vaccine dose, if disease activity allows.

PREGNANCY:

Pregnant and breastfeeding patients were not enrolled in the trials but if they choose to be vaccinated this should be encouraged. A trial in pregnancy is currently under way. Immunization during pregnancy may aid transplacental transfer of maternal antibodies to the baby.

REFERENCES:

- NEJM Covid-19 vaccine frequently asked questions

- COVID-19 Vaccine Clinical Guidance Summary for Patients with Rheumatic and Musculoskeletal Diseases Developed by the ACR COVID-19 Vaccine Clinical Guidance Task Force This draft summary was approved by the ACR Board of Directors on February 8, 2021, and updated on March 4, 2021.

- Society for Maternal-Fetal Medicine (SMFM) Statement: SARS-CoV-2 Vaccination in Pregnancy 12-1-20

- Arthritis and Musculoskeletal Alliance, UK: Principles for COVID-19 Vaccination in Musculoskeletal and Rheumatology for Clinicians (Version 3, 10 March 2021)

- EULAR View-points on SARS-CoV-2 vaccination in patients with RMDs.

HIGHLIGHTS FROM EULAR 2021

Courtesy : Dr. M. Haroon

UPDATES ON COVID-19 VACCINES IN PATIENTS WITH RHEUMATIC DISEASE

Summary: Rituximab is associated with severely impaired immunogenicity of the Pfizer BioNTech vaccine in autoimmune inflammatory rheumatic diseases (AIIRDs). Glucocorticoids, abatacept, mycophenolate mofetil, and methotrexate undermine the immunogenicity of this vaccine as well in this population1. A second study investigated the safety profiles of COVID-19 vaccines in patients with rheumatic and musculoskeletal diseases (RMD). The results demonstrated that COVID-19 vaccines are safe and well tolerated in these patients2.

In a prospective, observational, open-label, controlled multicentre study, presented by Dr Victoria Furer (Tel Aviv Sourasky Medical Center, Israel), immunogenicity, safety, and efficacy of the Pfizer BioNTech vaccine were investigated in an adult AIIRD population (n=686, mean age 59) 2-6 weeks after the second vaccine dose was administered. The control group consisted of 121 healthy individuals1. A value of >15 binding antibody units (BAUs) was considered as a cut-off of seropositivity. The seropositivity rate was 86% in the AIIRD group versus 100% in the control group. Patients treated with rituximab showed the lowest seropositivity rates (41.4%). Other DMARDs that were associated with reduced seropositivity rates were glucocorticoids (66.2%), abatacept (62.5%), mycophenolate mofetil (64.3%), and to a lesser extent methotrexate (84.1%). In addition, lower seropositivity rates were more often observed in patients >65 years (79.3%) and for certain AIIRD diagnoses (rheumatoid arthritis 82.1%; idiopathic inflammatory myopathies 36.8%; and ANCA-associated vasculitis 30.77%). Authors argued that in order to improve immunogenicity of the Pfizer BioNTech vaccine, postponing treatment with rituximab or holding treatment with mycophenolate mofetil or abatacept, particularly when combined with methotrexate, should be considered.

Another study presented by Dr Pedro Machado (University College London, UK) analysed the safety data of COVID-19 vaccines (Pfizer BioNTech 78%, Moderna 5%, AstraZeneca 16%, other 1%) used in rheumatic and musculoskeletal diseases (RMD) patients (n=1519, mean age 63, 68% women) from the COVAX registry2. The results demonstrated that the safety profile of the vaccines among patients with RMD was similar to that of the general population. Adverse events (AEs) occurred in 31% of the patients. Pain at the injection site, fatigue, headache, and generalised muscle pain were the most common AEs. Systemic/ organ side effects were reported in 33 cases. These AEs were diverse and mostly mild or moderate. Severe AEs were reported in two cases: one case of transient hemiparesis in a patient with systemic sclerosis and systemic lupus erythematosus, and a case of giant cell arteritis in a patient with osteoarthritis.

Reference:

- Furer V et al. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in adult patients with autoimmune inflammatory rheumatic diseases (AIIRD) compared to the general population: a multicenter study. LB0003, EULAR 2021 Virtual Congress, 2-5 June 2021
- Machado P M. COVID-19 vaccine safety in patients with rheumatic and musculoskeletal disease. LB0002, EULAR 2021 Virtual Congress, 2-5 June 2021

RITUXIMAB or JAKi THERAPIES IN RHEUMATOID ARTHRITIS INCREASE THE RISK OF SEVERE COVID-19

Summary: The risk of severe COVID-19 outcomes in patients with rheumatoid arthritis (RA) is four times higher for rituximab users and two times higher for JAK inhibitor users compared with TNF inhibitor users. This association was not found for abatacept and IL-6-inhibiting DMARDs. This was concluded from a large study comparing COVID-19 severity in RA patients on different classes of DMARDs. These results demonstrated the importance of risk-mitigation strategies in RA patients on rituximab or JAK inhibitors.

Authors in this study examined the effect of baseline use of different DMARD classes on COVID-19 severity in RA. 2,869 patients with resolved COVID-19 were selected from the global rheumatology alliance physician registry. Treatment with rituximab, JAK inhibitors, abatacept, or IL-6 inhibitors was compared with TNF inhibitors (reference group) on an ordinal COVID-19 severity scale (1: not hospitalised; 2: hospitalised without oxygen; 3: hospitalised with oxygen or ventilation; 4: death). Data was analysed via ordinal logistic regression analysis. The results demonstrated that patients treated with rituximab or JAK inhibitors had a four-fold or two-fold increased risk of severe COVID-19 outcomes, respectively, compared with the reference group. In 85.4% of the cases, TNF inhibitor users were not hospitalised as a consequence of COVID-19. These percentages were significantly smaller in patients on rituximab (57.7%) or JAK inhibitors (72.6%). Baseline users of abatacept or IL-6 inhibitors were not hospitalised in 76.4% and 85.5% of the cases. In addition, rituximab or JAK inhibitor use at COVID-19 onset resulted more often in hospitalisation with oxygen or ventilation (rituximab 22.0%; JAK inhibitors 15.3%; TNF inhibitors 7.4%) or death (rituximab 14.8%; JAK inhibitors 7.1%; TNF inhibitors 2.6%) than TNF inhibitor use. This study highlights the importance of COVID-19 risk management in RA patients on rituximab or JAK inhibitors, such as prioritising them for vaccination.

Reference:

- Associations of baseline use of biologic or targeted synthetic DMARDs with COVID-19 severity in rheumatoid arthritis: results from the COVID-19 Global Rheumatology Alliance Physician Registry. OP0006, EULAR 2021 Virtual Congress, 2-5 June 2021

AIR POLLUTION PREDICTS DECREASED RESPONSE TO BIOLOGICAL TREATMENT IN RHEUMATIC DISEASES

Summary: A poor response to biological disease-modifying anti-rheumatic drugs (bDMARDs) in patients with chronic inflammatory arthritis (CIA) is associated with environmental air pollution. This was the main result of a case-crossover study among Italian CIA patients, and it adds to the increasing evidence that air pollution is a relevant factor in rheumatic diseases.

For this study, data was collected from the registry of biological therapies of the University of Verona. Daily air pollution data (2013–2018) from the Verona area and data on CIA patients within this area was examined. Included in the case-crossover analysis were patients who had experienced a stable period of ≥6 months of bDMARD therapy with ≥1 low disease activity (DA) visit plus a treatment switch or swap visit (flare visit) due to drug inefficacy (n=280). Patients who switched or swapped bDMARDs due to adverse events or drug intolerance were excluded from further analysis. Air pollution concentrations of the 60 -day periods prior to the low DA visit and the flare visit were compared.

The results demonstrated that air pollution concentrations were significantly higher prior to the flare visit compared with the low DA visit. In addition, receiving operating characteristics (ROC) curves demonstrated that the combination of DA and air pollution was a better predictor for therapy switch or swap than DA alone. Dr Giovanni Adami (University of Verona, Italy) emphasised that these results show a direct association between environmental air pollution and a poor response to bDMARDs in CIA patients.

Reference:

- Adami G et al. Air pollution is a predictor of poor response to biological therapies in chronic inflammatory arthritides. POS0644, EULAR 2021 Virtual Congress, 2-5 June 2021

PROGNOSTIC FACTORS FOR MINIMAL DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS REVEALED

Summary: Minimal disease activity (MDA) following a treat-to -target (T2T) strategy in early psoriatic arthritis (PsA) can be predicted by a combination of factors, including Tender Joint Count (TJC), patient global assessment (PGA) of disease activity, pain, and the absence of enthesitis and dactylitis. As a consequence, these prognostic factors could be useful in predicting therapy outcomes and managing patient expectations in early PsA patients.

Authors emphasised that this is the first study to investigate prognostic factors for MDA in early PsA following a T2T strategy. Early PsA patients (n=77, mean age 36.9) were given methotrexate therapy for 12 months. Biologic disease-modifying anti-rheumatic drugs (DMARDs) were added for 29 patients between 3 and 9 months due to therapy ineffectiveness. At baseline and after 12 months of therapy, disease activity and the disease characteristics PsA duration and psoriasis duration were evaluated. Logistic regression

analysis was conducted to compare patients who had achieved MDA (n=45) at 12 months with patients who had not reached MDA (n=32) at this point in time.

The results showed that baseline scores of TJC, Swelling Joint Count (SJC), pain, PGA, C-reactive protein, dactylitis, enthesitis (Leeds Enthesitis Index [LEI] and plantar fascia), body surface area, Health Assessment Questionnaire (HAQ) and fatigue were significantly associated with achieving MDA at 12 months of therapy. In combination, these features were predictive of reaching MDA in early PsA patients (OR 9.68). The prognostic factors can help us to predict treatment outcomes in clinical practice.

Reference:

- Loginova EY, et al. Prognostic factors associated with achieving minimal disease activity in early psoriatic arthritis patients treated according to treat to target strategy. POS0192, EULAR 2021 Virtual Congress, 2-5 June.

PET/CT IS A RELIABLE OUTCOME MEASURE OF DISEASE ACTIVITY IN LARGE-VESSEL VASCULITIS

Summary: PET/CT showed a discriminating value in measuring disease activity in large-vessel vasculitis (LVV). This finding was consistent in giant cell arteritis (GCA) and Takayasu's arteritis (TAK) subgroups. Therefore, PET/CT could be a reliable tool in the assessment of disease activity in LVV. Surprisingly, higher PET Vascular Activity Score (PETVAS) scores during clinical remission were not predictive of future relapses.

Disease activity assessment in LVV lacks validated scoring systems. PET/CT might be the imaging biomarker that is needed. PETVAS has shown promising results in recent studies. The current study assessed whether PETVAS can discriminate between clinically active and inactive LVV (both GCA and TAK) in a single-centre cohort study. LVV patients (n=100) were followed from 2007 until 2020 and received complete assessments (clinical, laboratory, imaging) at baseline, annually, and when relapse was suspected. PETVAS was calculated for each PET/CT scan and compared to the clinical examination of disease activity status. Dr Elena Galli (University of Modena and Reggio Emilia, Italy) presented the results. Logistic regression analysis demonstrated that higher PETVAS scores were associated with clinically active LVV (OR 1.15; P<0.0001). This result was consistent in the GCA (OR 1.12; P<0.0001) and TAK (OR 1.22; P<0.0001) subgroups. The computed ROC curves demonstrated acceptable predictive values in the total population (AUC 0.73) and in the GCA (AUC 0.70) and TAK (AUC 0.79) subgroups. Nevertheless, higher PETVAS scores during low clinical disease activity were not associated with a higher risk of relapse. Authors acknowledge that this finding is not well understood and needs to be unravelled in future research.

Reference:

- Galli E et al. The role of positron emission tomography/computed tomography (PET/CT) in disease activity assessment in patients with large vessel vasculitis. OP0069, EULAR 2021 Virtual Congress, 2-5 June 2021

NO EFFECT OF FAECAL MICROBIOTA TRANSPLANTATION IN ACTIVE PERIPHERAL PSORIATIC ARTHRITIS

Summary: Faecal microbiota transplantation (FMT) as an add-on therapy to methotrexate was inferior in the treatment of active peripheral psoriatic arthritis (PsA) compared with sham in the proof-of-concept, randomised, placebo-controlled FLORA trial.

The FLORA study investigated the safety and efficacy of a single-donor FMT in active peripheral PsA patients (n=31). In addition to methotrexate treatment, participants were randomised to FMT (n=15) or sham (n=16). Primary endpoint was the proportion of patients with treatment failure at 26 weeks of therapy. Safety was assessed by comparing the number of treatment-induced serious adverse events (AEs).

The results demonstrated that treatment failure at 26 weeks of therapy had occurred more often in the FMT group (60%) than in the sham group (19%). Compared with baseline, Health Assessment Questionnaire Disability Index (HAQ-DI) scores, a key secondary efficacy endpoint, had decreased significantly more in the sham group (-0.30) than in the FMT group (-0.07). A similar difference was observed for the SPARCC Enthesitis Index score (FMT -1.9 vs sham -4.3). No serious AEs were detected with FMT therapy in the safety analysis. Although FMT was inferior to sham in this trial, authors argued that other trials should investigate the efficacy and safety of FMT, and described that the most important finding of this study is the feasibility of FMT. There are no preliminary safety issues and patients reacted positively to the application of this therapy. Authors also described that we have to learn more about the immunological effects of FMT and thoroughly analyse the composition of microbiota in donors and recipients to find the right donor for each patient.

Reference:

- Skov Kragsnaes M et al. Safety and efficacy of faecal microbiota transplantation for active peripheral psoriatic arthritis: an exploratory randomised placebo-controlled trial. OP0010, EULAR 2021 Virtual Congress, 2-5 June 2021

SLE IS ASSOCIATED WITH INCREASED RISK OF SEVERE INFECTION CONTRIBUTING TO 21% OF THE MORTALITY

Summary: Patients with systemic lupus erythematosus (SLE) have an increased risk of developing severe infections compared with non-SLE cases. Moreover, 21% of the mortality in SLE is related to these infections. These were the main outcomes of a first large population-based incident SLE cohort study.

Previous studies investigating the infection risk in SLE have been prevalent cohort studies with small sample sizes. The current study is a large retrospective 1:5 matched incident cohort study based on 25 years of administrative data of 2,000,000 randomly selected Canadian citizens and 5,169 confirmed incident SLE cases (mean age 47, 90% women). Participants were matched for age and sex. Outcome measures were: first severe infection (defined by the need for professional medical care), the number of severe infections, and infection-related death. The results demonstrated that SLE patients had an 82% increased risk of developing a severe infection compared with their matched non-SLE counterparts. Furthermore, SLE patients had twice as many severe infections and a 61% increased risk of infection-related death. Mr Kai Zhao (Simon Fraser University, Canada) argued that early SLE patients often have more disease activity and use more glucocorticoids. According to Mr Zhao, these features could explain why these patients have an increased risk of severe infections. He suggested that a tailored treatment, including increased use of immunosuppressants, could provide a solution for this problem. In addition, further analysis of infection type (bacterial, viral) might give more insight into how to tackle severe infections in SLE in the future.

Reference:

- Zhao et al. Increased risk of severe infections and mortality in patients with newly diagnosed systemic lupus erythematosus: a population-based study. OP0043, EULAR 2021 Virtual Congress, 2-5 June 2021

EVEN PASSIVE SMOKING IS ASSOCIATED WITH AN INCREASED RISK OF RHEUMATOID ARTHRITIS

Summary: Exposure to passive smoking in childhood and/or adulthood is associated with an increased risk of rheumatoid arthritis (RA). This was found in the large prospective E3N-EPIC cohort study of French women. The effect is more pronounced in women who have actively smoked during their lives. Furthermore, passive smoking during childhood could lead to an earlier onset of RA.

Active smoking is an established risk factor for RA. The role of passive smoking in the development of RA has not been studied thoroughly. The current analysis of the E3N-EPIC cohort study, presented by Dr Yann Nguyen (Université Paris-Saclay, France) aimed to fill this gap in the literature. The study included 79,806 women (mean age at baseline 49.0) and 698 incident RA cases have been identified since the initiation of the project in 1990. At baseline, participants were asked whether they were exposed to passive smoking in their childhood or adulthood. A cox proportional hazards model was used to analyse the data.

Passive smoking in childhood (non-cases 13.5% vs RA cases 16.3%) and adulthood (non-cases 53.6% vs RA 57.45%) were significantly associated with an increased risk of RA. Among the participants exposed to passive smoking, the effect was larger for ever-smokers compared with never-smokers (absolute risk 53.67/100,000 per year vs 47.59/100,000 per year). Participants who were not exposed to passive smoking and never smoked had a later age of disease onset (mean age 66.5) compared with participants who were exposed to passive smoking (mean age 63.7), had actively smoked (mean age 63.4), or had been exposed to passive smoking and had actively smoked (mean age 62.3). In addition, in the childhood passive smoking subgroup, ever-smokers had an earlier age of RA onset than never-smokers (mean age 60.6 vs 64.2). Dr Nguyen suggested that these results could be explained by a citrullination effect of passive smoking in genetically predisposed individuals.

Reference:

- Nguyen Y et al. Association between passive smoking in childhood and adulthood and rheumatoid arthritis: results from the French E3N-EPIC cohort study. OP0010, EULAR 2021 Virtual Congress, 2-5 June 2021

REMOTE MANAGEMENT OF RA IS A FEASIBLE ALTERNATIVE FOR USUAL OUTPATIENT FOLLOW-UP VISITS

Summary: Considering the limited access to healthcare facilities due to the current pandemic, remote patient management has become a topic of particular interest. Remote management of rheumatoid arthritis (RA) provides a feasible alternative for routine outpatient follow-up. This is the main conclusion of a prospective, longitudinal real-world study among RA patients in the UK.

Dr Mwidimi Ndosi (University of the West of England, UK) and colleagues investigated to what extent remote management and routine outpatient monitoring decisions are interchangeable. The patients selected for this study (n=72, mean age 57.8, 87% women) continued usual care and clinical assessments, each

Continued on page 06....

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month, every 3 months, or every 6 months, depending on disease activity. In addition, they performed a monthly self-assessment at home, including patient-reported outcome measures (PROMs) and the self-assessment questionnaires patient global assessment (PGA), Arthritis Self-Efficacy Scale (ASES), pain visual analogue scale, and fatigue visual analogue scale, as well as the self-reported components joint stiffness and flares. An independent health professional had access to the PROMs, questionnaires, and data considering medical history, ongoing therapy, and adverse events (AEs). Hospital-assessed clinical data was not provided (joint assessment, blood monitoring). Possible remote decisions were the addition or removal of a drug, to bring the patient in for review, or to not change therapy. Remote decisions and usual outpatient follow-up decisions demonstrated fair agreement in the 252 performed assessments. This result was observed for overall changes to RA therapy (kappa=0.24) and changes to bDMARD therapy (kappa=0.23). The self-assessment questionnaires identified 34 flares and one patient had to stop treatment due to an AE. This was recognised by remote and clinic-based evaluation. Dr Ndosi argued that future studies should investigate if the addition of blood test monitoring adds value to remote decision making.

Reference:

- Ndosi M et al. Remote management of rheumatoid arthritis vs routine outpatient follow-up: a prospective, longitudinal real-world study. OP0155, EULAR 2021 Virtual Congress, 2-5 June 2021

EFFICACY AND SAFETY OF SECUKINUMAB IN JUVENILE IDIOPATHIC ARTHRITIS

Summary: Secukinumab significantly increased the time to flare and reduced the number of flares in children with enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) compared with placebo. The safety profile of secukinumab in this population is congruent with the known safety profile of the drug. These were the main results of the phase III randomised, double-blind JUNIPERA trial 104 weeks after treatment initiation.

Efficacy and safety of secukinumab, a human monoclonal antibody targeting IL-17, has been demonstrated in adult PsA and radiographic and non-radiographic ax ial spondyloarthritis patients. The current study aimed to evaluate the efficacy and safety of secukinumab in ERA and JPsA patients (aged 2-18) with a history of inadequate response or intolerance to ≥1 NSAID or ≥1 DMARD. If patients (n=86) reached juvenile idiopathic arthritis (JIA) ACR 30 at the end of a 12-week open-label secukinumab 75/150 mg subcutaneous first treatment period (TP) (qw first 4 weeks, then q4w), they were randomised to secukinumab q4w (n=37) or placebo (n=38). After the occurrence of a flare in the second TP, the patient was moved to another open-label secukinumab TP. The primary endpoint was time to disease flare of patients on secukinumab versus placebo in the second TP. Time to flare was significantly longer in the secukinumab arm compared with the placebo arm (HR 0.28; 95% CI 0.13-0.63; p<0.001). The number of flares was lower in the treatment arm (secukinumab 10 vs placebo 21) and JIA ACR 30 was maintained more often for secukinumab-treated patients (89.2%) than for placebo patients (64.9%) after the second TP. Dr Nicola Ruperto (IRCCS Istituto G. Gaslini, Italy) argued that the median time to flare of 453 days in the placebo arm indicated a prolonged biological effect of the first TP. Complete resolution of enthesitis occurred in 73.9% of the ERA patients after TP 1. Adverse events (AEs) were reported in 91.7% of the secukinumab patients and 92.1% of the placebo patients, including seven and four non-fatal serious AEs, respectively.

Reference:

- Ruperto N et al. Efficacy and safety of secukinumab in enthesitis-related arthritis and juvenile psoriatic arthritis: primary results from a randomised, double-blind, placebo-controlled, treatment withdrawal, phase 3 study (JUNIPERA). LB0004, EULAR 2021 Virtual Congress, 2-5 June 2021

QUIZ

Courtesy : Dr. M. Haroon

1. Based on latest Assessment of SpondyloArthritis International Society (ASAS)/European League Against Rheumatism (EULAR) recommendations, which specific non-steroidal anti-inflammatory drug (NSAID) treatment strategy should be used first line in patients with confirmed axial spondyloarthritis (AxSpA) before escalating to a biologic disease-modifying antirheumatic drug (bDMARD)?

   a. At least 1 NSAID over 2 weeks in total
   b. At least 1 NSAID over 6 weeks in total
   c. At least 2 NSAIDs over 4 weeks in total
   d. At least 2 NSAIDs over 6 weeks in total

2. A male patient, 38 years of age, presents with a history of low back pain for 5 years, with no other peripheral or extra-articular manifestations. He has developed decline in spinal mobility and is showing high level of spinal pain.; he is human leukocyte antigen (HLA)-B27 negative and x-rays show ankylosed sacroiliac joints. His C-reactive protein (CRP) is 8.2 mg/L (normal <0.5 mg/L); Ankylosing Spondylitis Disease Activity Score (ASDAS) is 2.7. Magnetic resonance imaging (MRI) of the spine shows signs of inflammation. He is on daily diclofenac at the highest dose.

   What would be the next best step in the management of this patient to achieve and maintain control of the underlying inflammation?

   a. Add another NSAID
   b. Switch treatment to local corticosteroid injections
   c. Escalate treatment to biologic therapy
   d. Switch treatment to sulfasalazine

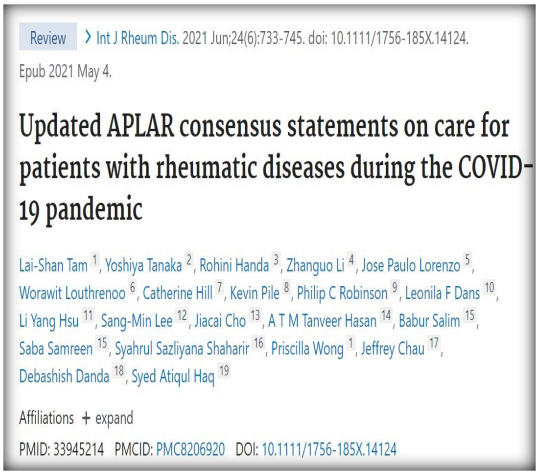
Answers on last page

Dr Shahida Parveen is one of the members from Pakistan who is running APLAR Covid facebook page along with other members of APLAR from other countries.

UPDATED APLAR CONSENSUS STATEMENTS ON CARE FOR PATIENTS WITH RHEUMATIC DISEASES DURING THE COVID-19 PANDEMIC

Courtesy : Dr. Babur Salim

The recommendations were based on evidence based randomized controlled trials, observational studies and expert opinions. The taskforce included 22 members from different countries of Asia. Dr Babur Salim and Dr Saba Samreen from Fauji Foundation Hospital Rawalpindi, Pakistan, were part of APLAR recommendations. The recommendations were made on the basis of GRADE system & Modified Delphi approach. The aim of these recommendations is to review all available new and pertinent evidence and to update the preliminary statement by developing consensus recommendations for the management of the patient with RMD during the COVID-19 pandemic.



Review › Int J Rheum Dis. 2021 Jun;24(6):733-745. doi: 10.1111/1756-185X.14124. Epub 2021 May 4.

Updated APLAR consensus statements on care for patients with rheumatic diseases during the COVID-19 pandemic

Lai-Shan Tam [1], Yoshiya Tanaka [2], Rohini Handa [3], Zhanguo Li [4], Jose Paulo Lorenzo [5], Worawit Louthrenoo [6], Catherine Hill [7], Kevin Pile [8], Philip C Robinson [9], Leonila F Dans [10], Li Yang Hsu [11], Sang-Min Lee [12], Jiacai Cho [13], A T M Tanveer Hasan [14], Babur Salim [15], Saba Samreen [15], Syahrul Sazliyana Shaharir [16], Priscilla Wong [1], Jeffrey Chau [17], Debashish Danda [18], Syed Atiqul Haq [19]

Affiliations + expand

PMID: 33945214 PMCID: PMC8206920 DOI: 10.1111/1756-185X.14124

IN YEAR 2020-21 RHEUMATOLOGY DEPARTMENT FATIMA MEMORIAL HOSPITAL, LAHORE

Courtesy : Dr. M. Haroon

POSTGRADUATE SUCCESSFUL FELLOWS:

From our department, 4 fellows appeared for FCPS final exam and all of them passed their exam in their first attempt.

1) Dr. Naveed Aslam
2) Dr. Muhammad Faiq
3) Dr. Zia Ullah
4) Dr. Asad Ullah

PUBLICATIONS:

Following articles from our department have been published in International renowned Rheumatology Journals

- Haroon M, Batool S, Asif S, Hashmi F, Ullah S. Combination of Methotrexate and Leflunomide Is Safe and Has Good Drug Retention Among Patients With Psoriatic Arthritis. J Rheumatol. 2021 May 15:jrheum.201408. doi: 10.3899/jrheum.201408. Epub ahead of print. PMID: 33993112. Factor 3.18
- Haroon M Dr, Aamer M. Elderly onset of rheumatoid arthritis is more common in males, and requires maintenance of low-dose corticosteroids along with the combination of disease modifying anti rheumatic agents. Semin Arthritis Rheum. 2020 Dec 18:S0049-0172(20)30293-6. doi: 10.1016/j.semarthrit.2020.09.017. Epub ahead of print. PMID: 33358003 Factor 4.7
- Haroon, M., Anis, K., Khan, Z. and Nawaz, N. (2020), High prevalence of the new onset or worsening of Hepatitis-C related musculoskeletal symptoms after commencing direct-acting antiviral therapies: a challenging novel observation. Arthritis and Rheumatology. Arthritis Rheumatol. 2021 Feb;73(2):355-356. doi: 10.1002/art.41496. Epub 2020 Aug 25. Impact Factor 9.58
- Haroon M, Khan Z, Aamer M. Tapering antirheumatic drugs in a resource-poor setting: real-world evidence [published online ahead of print, 2020 Aug 14]. Ann Rheum Dis. 2020;annrheumdis-2020-218703. doi:10.1136/annrheumdis-2020-218703 Impact Factor 16.1

ABSTRACT PRESENTATIONS:

EULAR 2021. From our department, we had six abstract presentations, and very brief summaries are provided here.

Abstract Number: POS0663
Safety and Efficacy of Combining Methotrexate and Leflunomide among patients with Inflammatory Arthropathies: Findings from the PRIME registry

Summary: The data of 766 inflammatory arthritis patients (RA=663, PsA=103) was reviewed. Among them, 241 patients (RA=196, PsA=45) were using combination therapy of MTX and LEF (combo MTX+LEF). Combination of MTX and LEF was well tolerated and had good drug retention time, with 94.6% of patients having ongoing treatment to date. In low-income countries, where bDMARD availability is limited, financial arguments significantly influence decision making process, and our data provides initial evidence that MTX and LEF combination therapy could be an effective treatment option..

Final Number: POS0310
Exposure to major psychological trauma or stress in the preceding one year significantly contributes to poor disease control in patients with Rheumatoid Arthritis: Single centre results from the PRIME registry cohort

Summary: The data of consecutive 507 RA patients (mean age 42.3±12.6 years, 73.6% female, disease duration of 80±22 months) was reviewed. Thirty-six percent of the cohort reported to have major psychological stress and trauma in the preceding one year. Statistical association of low education status (p=0.042), longer disease duration (p=0.044), higher DAS-28 values (p<0.001) and other markers of RA disease activity (SJC, TJC, ESR, patient global health) was found. On multiple logistic regression analysis, a significant association of major psychological stress and trauma in the preceding one year was noted with active disease (DAS-28; OR 1.67, CI 1.17-2.4, p=0.005).

Abstract number: AB0581
Nail Psoriasis among patients with psoriatic arthritis is more associated with the severity of skin psoriasis than with features of severe arthritis

Summary: The objective of this study was to examine the association of nail disease with patient demographics and features of active psoriasis and PsA. For this cross-sectional study, data from 3 PsA cohorts was studied (St Vincent's University Hospital Dublin, Ireland; University Hospital Kerry, Ireland; and Fatima Memorial Hospital Lahore, Pakistan). Data on 476 PsA patients was assessed. The presence of nail disease among patients with PsA is significantly associated with severity of skin psoriasis with only borderline associations with measures of active musculoskeletal involvement on multiple stepwise regression analysis.

Abstract Number: POS0589
Prevalence and Severity of Stress at Home among patients with Rheumatoid Arthritis: single centre results from the PRIME registry cohort

Summary: We aimed to examine the prevalence of mental/emotional stress at home and its associations among patients with Rheumatoid arthritis. We addressed this question using real-world data from the PRIME registry. The data of consecutive 507 RA patients (mean age 42.3±12.6 years, 73.6% female, disease duration of 80±22 months) was reviewed. Forty-eight percent of patients accepted to have moderate-severe stress at home (moderate stress=29.9%, severe stress=18.3%). On multiple logistic regression analysis, a significant association of moderate-severe stress at home was observed with higher DAS-28 scores (OR 1.76, CI 1.29-2.41, p<0.001). These findings demonstrate an important need for integration of rheumatologic, social workers and mental health services

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Final Number: AB0533
Combination of Methotrexate and Leflunomide is safe and has good drug retention among patients with Psoriatic arthritis

Summary: We aimed to review our PsA cohort data especially examining the drug retention of first-line csDMARD monotherapy and combination csDMARDs. For this study, only those adult patients were included who had a follow up of at least 6 months with our rheumatology services, and were fulfilling CASPAR criteria. Moreover, only patients who were DMARD-naïve (no prior DMARD therapy for any cause, including psoriasis), and initiated DMARD as monotherapy after 1 April 2018 were included. If any patient had already been on any DMARDs prior to attending our rheumatology services was excluded. Moreover, only patients who were DMARD-naïve (no prior DMARD therapy for any cause, including psoriasis), and initiated DMARD as monotherapy after 1 April 2018 were included. If any patient had already been on any DMARDs prior to attending our rheumatology services was excluded. A total of 81 PsA patients fulfilled the inclusion and exclusion criteria. Among csDMARD naïve PsA patients, 79% of patients failed MTX monotherapy with median drug retention time of only 6 months. Combination of MTX and LEF was well tolerated and had good drug retention time, with 84% of patients having ongoing treatment to date. Our data provides initial evidence that MTX and LEF combination therapy could be an effective treatment option for PsA.

GUIDELINE FOR THE MANAGEMENT OF REPRODUCTIVE HEALTH IN RHEUMATIC AND MUSCULOSKELETAL DISEASES

Courtesy : Dr. Tajvur Sabir

Rheumatic diseases often affect women in childbearing age most commonly. As pregnancy can lead to serious maternal and fetal outcomes in these patients it needs to be planned and managed properly. Before that contraception needs to be tailored to a patient's needs.

There are effects of rheumatic disease on pregnancy and effects of pregnancy on the disease. The Ro La and Antiphotpholipid antibodies as well as renal disease cause the biggest threat.

EFFECTS OF PREGNANCY ON RHEUMATIC DISEASES:

Pregnancy often effects Rheumatoid arthritis, Lupus and Antiphospholipid syndrome most commonly. RA often, but not always, improves during pregnancy and flares after childbirth.

The relationship of Lupus and pregnancy is more complicated. The best outcomes are when the disease is under control for 6 months prior to pregnancy. Fertility may be reduced by renal disease or medication, but not otherwise. Most women have mild to moderate flare in the second and third trimester and post partum.

Antiphospholipid syndrome (APS), is associated with veinous and arterial thromboembolism and obstetric complications such as miscarriage, prematurity or hypertension during pregnancy. When pre-existing kidney disease, the possibility exists for pre-eclampsia. Pre-eclampsia and eclampsia carry a risk to the mother's kidneys and liver and also increase the risk of prematurity or death of the fetus. Thus, for women with APS, pregnancy—especially the time around delivery—is a particularly dangerous period and dictates special care.

Pulmonary hypertension, can complicates some rheumatic diseases (SLE, APS, Sjögren's and, particularly, scleroderma), this warrants mention. It frequently worsens during pregnancy—especially in the post-partum period—pregnancy is considered inadvisable.

Other diseases such as scleroderma (in the absence of pulmonary hypertension or lung fibrosis), polymyositis, dermatomyositis and vasculitis do not seem to be particularly influenced by pregnancy. However, pregnancy is only recommended when these diseases are under control and with the care of your rheumatologist.

EFFECT OF RHEUMATIC DISEASES ON PREGNANCY:

During pregnancy, problems may arise due to flare of the rheumatic disease or the necessary anti-inflammatory and/or immunosuppressive drugs can cause problems. Diseases with the potential to affect the kidney and, especially, APS are more likely to affect pregnancy outcome than others.

Patients who have or have had renal disease, due to vasculitis, scleroderma or, more frequently, lupus, are at increased risk of severe hypertension and pre-eclampsia. If renal function and blood pressure are normal prior to pregnancy, and the disease is inactive at the time of conception for at least six months, the outcome is likely to be good. Conversely, women with severely impaired renal function, uncontrolled hypertension and/or active kidney involvement usually are advised against getting pregnant.

APS probably impacts pregnancy the most. It is associated with early and late miscarriage, prematurity and low-weight babies, as well as thrombosis and pre-eclampsia. Thus, pregnancy in women with APS should always be considered as high risk, and be managed with combined medical and obstetric monitoring. Therapy includes use of low-dose aspirin and heparin. Mothers with anti-Ro antibodies (most frequently seen in patients with LUPUS and Sjögren's syndrome) carry a 2% risk of congenital heart block. Anti-Ro antibodies are of 2 types the 60 and 52 kilo-dalton. Of these the latter carries a higher risk. Fetal heart rate should be monitored from week 18-28. These babies may need a permanent pacemaker.

USE OF RHEUMATIC DRUGS DURING PREGNANCY AND LACTATION:

Antirheumatic drugs during pregnancy and lactation require special consideration. Every woman with a rheumatic disease should be counselled before conception for their specific risk.

A summary of these drugs is shown in Table 1.

	Pregnancy	Lactation
NSAID	Yes (avoid after 32 weeks)	Yes
Sulfasalazine	Yes	Yes
Hydroxychloroquine	Yes	Yes
Corticosteroids	Yes	Yes
Cyclosporin	Yes	probably yes
Azathioprine	Yes	probably yes
Mycophenolate	No, stop 3 months prior	No
Methotrexate	No, stop 1-3 months prior	No
Cyclophosphamide	No, stop 3 months prior	No
Anti-tumor necrosis factor (TNF)	Yes	Yes
Rituximab	No, use 6 months pre pregnancy	No
Warfarin	No (with caution, only after first trimester)	Yes
Heparin	Yes	Yes

A summary of these drugs is shown in Table 1.

Ideally, pregnancy should be planned and medication should be adjusted.

Several drugs (particularly sulfasalazine and cyclophosphamide) have effects on sperm cells. It is recommended that these medications be stopped for 3 months before a man fathers a child.

Indication of "high risk"?

- Previous pregnancy with complications
- Underlying renal disease
- Underlying heart disease
- Underlying lung disease (including pulmonary hypertension)
- Flare of rheumatic illness
- A history of previous thromboembolism
- the presence of SSA and SSB antibodies
- IVF (in vitro fertilization)
- pregnancy with twins, triplets, etc
- Maternal age over 40 years

Prednisone should be used at doses below 10 mg/d if possible, this will reduce complications such as high blood pressure, diabetes, excessive weight gain, infection risk and premature rupture of membranes.

Hydroxychloroquine, is an extremely safe drug for both the mother and the fetus, and should not be stopped before, during or after pregnancy. High blood pressure should be managed using medicines that are safe during pregnancy like Captopril and enalapril.

All women with APS must receive low-dose aspirin, with heparin if previous obstetric and thrombotic history. If heparin is needed it is recommended from conception upto 4-6 weeks post-partum. Those with previous blood clot should re-start warfarin as soon as possible after delivery, which is safe during lactation (Table 1).

Women with stable disease on safe drugs have a low-risk profile and should include in their usual treatment plan and have regular visits to the rheumatologist. Those with a high risk profile should be managed by a rheumatologist and obstetric team with experience in high-risk pregnancies. More frequent monitoring may be needed as pregnancy advances as the risk may increase in later pregnancy and peripartum. Doppler studies of the placenta can help assess uterine artery health. Regular blood-pressure measurements and urine dipstick will aid early detection and treatment of pre-eclampsia.

Recommendations and good practice statements for use of contraception

In patients with Rheumatic and Musculoskeletal Diseases (RMD) who are at risk for unplanned pregnancy contraception and plans for pregnancy should be discussed at an initial or early visit and when initiating treatment with potentially teratogenic medications.

Counselling about contraceptive methods for each patient should be based on efficacy, safety, and individual values and preferences.

Continued on page 9...

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In females for whom use of other, more effective forms of birth control are contra-indicated, using barrier methods of contraception as birth control over other less effective options or no contraception is suggested. IUDs and the combined pill are relatively safe for most patients. Oestrogen patches should be avoided in SLE patients.

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CONTRIBUTION TO PSR AND APLAR

Courtesy : Prof. Sumaira Farman Raja

I have been asked to share my contribution to PSR and APLAR.

As Assistant Professor Medicine I joined Rheumatology in 2001 and as an executive member PSR since 2003 contributed in PSR conferences as stage secretary(!) to speaker to organizer and co-convener. I served as PSR Joint and General secretary and am Immediate Past President.

Since 2006 represented PSR at several APLAR general body meetings and have been an invited speaker. Dr. Azra Ali, Prof. Abid and my mentor Prof. Nighat as PSR members were involved with APLAR at various levels and had encouraged me to do the same. Following their lead, I tried to follow this tradition of opening avenues for juniors and colleagues; during my tenure as President PSR, I proudly facilitated PSR members to become various SIG members, and actively lobbied for PSR member(s) to be selected variously as editor APLAR Pulse and Secretary AYR.

I had been an active Peer reviewer of IJRD since 2006, later selected as Associate Editor.

In 2008 in Yokohama, I was selected committee member of APAPR (Asia Pacific Association for Paediatric Rheumatology) by Dr. Prudence Manners, my mentor in PR. This initiative got revived in 2018 with the approval of an APLAR Paediatric Rheumatology (PR) Special Interest Group, with the responsibility of Convener falling on me. The SIG is in the process of developing PR provider directory, has identified training centers and is developing a hybrid PR course. Educational webinars have been initiated, while work on Registries and Treatment Guidelines is in initial stages.

I am tremendously humbled to have been elected Treasurer APLAR, and I hope that as part of the present office bearers we continue to facilitate better cooperation and coordination in various fields of education, research, and clinical care across the region, including Pakistan. Insha'Allah.

UPDATE FROM APLAR 2021 CONGRESS: EPIDEMIOLOGY AND COPCORD SESSION

Courtesy: Prof. Muhammad Ahmed Saeed

Community Oriented Programme for Control of Rheumatic Diseases (COPCORD)is a joint initiative of WHO and ILAR started in 1988. Since its inception it has generated wealth of epidemiological data on rheumatic diseases.

This year in APLAR Congress's Epidemiology and COPCORD session on Rheumatoid Arthritis (RA) I presented data on prevalence of RA from Pakistan, Bangladesh, Middle East, Indonesia, Malaysia and Australia. I highlighted in my presentation that prevalence in most of the studies from Asia pacific region have been quoted to be around 0.5 % which is less as compared to the western world.

I also compared the prevalence trends with data from Latin American countries like Argentina which has highest prevalence of RA up to 2.4 %. Other Countries like Mexico, Columbia, Ecuador have also quoted higher figures up to 1.4 %. Interestingly most of these studies have been conducted in last 5-6 years pointing towards increase prevalence rates. Now the question is whether it is the disease which has changed or improved expertise of rheumatology health professionals and diagnostic testing.

I in the session reiterated the need for conducting new Stage I surveys in the region as most of these in the region had been two decades back. We should encourage our fellows in training and young rheumatologists to pursue epidemiological research to see any changing trends in the burden of Rheumatoid Arthritis and other MSK disorders. This will help us in convincing stakeholders in allocation of resources especially in less developed countries. Then we can move to Stage II studies which focus on identifying risk factors and stage III on improved health care through preventive and control strategy.

The Pakistan Society for Rheumatology was established in 1995, with a view to enhance the knowledge about rheumatic diseases in Pakistan and to encourage further development of expertise in this field. Now there are 71 registered Rheumatologists in Pakistan and there are 8-10 registered centers for training in field of Rheumatology across the country. Annual PSR conference is an international event where renowned Rheumatologists not only from Pakistan but around the world get together to share their experiences.

Last year where the whole world was hit with covid-19 pandemic, the PSR 2020 preparations done by the team of Rheumatologists at Fauji Foundation Hospital, Rawalpindi came to a halt in the midst due to regional restrictions. Despite this set back, the team continued their planning and preparation for a hybrid conference (virtual and live sessions) whenever the conditions were suitable. To conduct this sort of event in Pakistan requires not only utmost planning and precision in execution but patience too.

PSR 2021 is an international event to be held on October 1-2 ,2021. This year the conference is going to be held in the scenic hilltop 'Bhurban'. Dr Babur Salim is the convener for this event whereas Prof. Amjad Nasim, Dr Saba Samreen and Dr Haris Gul from Fauji Foundation Hospital are working as coordinators for the event.




To ensure flawless execution of the event not only Weekly meetings are planned, but weekends are also utilized. Online group communications are done to ensure social distancing as the country is hit with the fourth wave of covid -19. Another challenge is to safeguard health of not only the organizers but also the speakers and attendees. Optimal measures are being taken, as there would be virtual presence of international speakers along with live sessions from eminent Rheumatologists from all over the country. These virtual sessions would be amalgamated with live sessions by local renowned Rheumatologist.

The conference would be preceded by a brainstorming session for trainees and young Rheumatologists titled "Interactive Rheumatology — challenge yourself" to be held on September 30th, 2021.

SPEAKERS FOR 24TH ANNUAL INTERNATIONAL PSR CONFERENCE 2021

Day 1

PROF. ABID FAROOQI
Topic : Treating Rheumatoid Arthritis in Pakistan-'Practice pearls from a senior rheumatologist'.

PROF. M. AHMED SAEED
Topic : Therapeutic updates in Rheumatoid Arthritis.

PROF. LAI SHAN TAM
Topic : APLAR Recommendations on management of rheumatic diseases in COVID.

PROF. WAJAHAT AZIZ
Topic : With Neuropsychiatric lupus, expect the unexpected.

PROF. NIGHAT AHMAD MIR
Topic : Lupus Nephritis: From basics to practice.

DR. SHABEEHA RANA
Topic : Hematological aspects of Lupus- 'Case based discussion'

DR. MUHAMMAD HAROON
Topic : PsA-From guidelines to clinical practice.

PROF. WALTER P. MAKSYMOWYCH
Topic : Radiological vs Non radiological Spondyloarthropathy (From diagnosis to treatment)

DR. JAVAID MEHMOOD MALIK
Topic : ILD in Scleroderma

DR. SULEMAN KHAN
Topic : APS: Pregnancy & fertility issues-management.

DR. EL SADEG SHARIF
Topic : Macrophage activation syndrome-Therapeutic approaches.

PROF. SUMAIRA FARMAN RAJA
Topic : JIA-What do we have & what do we want to achieve?

PROF. DAVID D'CRUZ
Topic : Approach to a patient with vasculitis & digital Ischemia

Day 2

DR. YASIR PARVIZ
Topic : Pulmonary Hypertension in Scleroderma, Role of Right Heart Catheterisation.

PROF. TAFAZZUL-E-HAQUE MAHMUD
Topic : Scleroderma mimics: Diagnostic challenges

DR. AFLAK RASHEED
Topic : Gout: A call to action

DR. CHENG YEW KUANG
Topic : AYR Updates

DR. SHAKAIB SAJID QURESHI
Topic : Myositis: Challenging cases

PROF. BHASKAR DAS GUPTA
Topic : Takayasu Arteritis : Current & emerging therapies

PROF. SARGUNAN SOCKALINGAM
Topic : ANCA Associated Vasculitis(AAV)-Landmark trials

DR. MASEM AFZAL
Topic : Sjögren's Syndrome: Beyond the dryness

DR. LILIAN KARINA JULIAN
Topic : Uveitis in Rheumatic diseases: Approach at a glance

DR. TAHIRA PERVEEN UMER
Topic : MCTD vs. Overlap: untying the knots

DR. MOHAMMAD SAEED
Topic : Behcet's—Untangling the silk threads

DR. SAMINA GHAZNAVI
Topic : Osteoarthritis in Asia-Are we different ?

DR. TAHIR MAHMOOD HASHMI
Topic : Osteoarthritis: Role of intra-articular injections. Do we have any evidence

CASE REPORT: CYCLOPHOSPHAMIDE AND TWIN PREGNANCY

Courtesy: Dr Syed Ali Rukh Pirzada & Dr Sana Zahid Choudhry

INTRODUCTION:

Cyclophosphamide is an alkylating agent widely used for the treatment of malignancies and organ or life -threatening autoimmune diseases. While being effective, Cyclophosphamide has a narrow therapeutic index and is associated with significant toxicity. Research on cyclophosphamide treated women has consistently demonstrated that the risk of sustained amenorrhea depends on the age of the patient and the cumulative dose received besides other side effects. There have been multiple case series reflecting variable outcomes of pregnancies like live births and births with teratogenic effects during and after pulse cyclophosphamide therapy in patients with autoimmune disease. So we need to know more about the drug and its behavior as for as its adverse effect on reproductive health is concerned.

In this case report, where a woman after pulse cyclophosphamide treatment for Lupus nephritis delivered alive healthy twins, we would like to emphasize, the need of better understanding of the impact of cyclophosphamide exposure on fertility and pregnancy outcome.

CASE PRESENTATION:

A 36 years old lady with SLE (on the basis of clinical and immunological criteria), being managed with 15 mg prednisolone and leflunamide in periphery, presents with active disease along with Lupus nephritis to our rheumatology unit. At the time of presentation, she had high grade fever, high BP, alopecia, active polysynovitis, oral ulcers, and malar rash.

Her lab reports showed Hb 7.5 mg/dl rest of cell lines were normal, Coombs test –ve, normal RFTs and LFTs, ESR 80 mm/ hour, Urine DR showed RBCs 5 to 10 per HPF, +++ Albuminuria and RBC cast in urine, proteinuria of 2.3 grams in urinary volume of 2800 ml per 24 hours ,ANA by IFA +++ Homogeneous, Anti ds DNA Abs 812 IU/ml (<20 IU/ml), Serum C3 0.85 g/L (0.8 -1.6), C4 0.02 g/L (0.1- 0.4). Her family refused her renal biopsy. She was offered cyclophopsmide or Mycophenolate mofetil. Due to cost constraints and completion of family, she opted pulse cyclophosphamide as per NIH protocol. She had three Spontaneous vaginal deliveries with alive and healthy children and one C-section for twin pregnancies. She with her husband was counseled about contraception and well educated about the teratogenicity of CYC. She responded well to pulse methylprednisolone and cyclophosphamide infusions. During routine follow up visit after her 6th pulse CYC, she informed about her 4 months gestational amenorrhea. This indicated that she had conceived after receiving the 2nd dose of cyclophosphamide, and the foetuses were inadvertently exposed to the subsequent dose of cyclophosphamide. Her lab results after 6 completed pulses of CYC were, ESR 60, Hb was 10 gm/dl, normal RFTs, LFTs, few RBCs and WBC with Trace proteins in urine D/E and 24 hours Urinary proteins were 0.2 grams / 1010 ml of urine in 24 hours. She refused investigations like Anti Ro Antibodies and Complements levels as well as treatment with Azathioprine. But agreed to continue HCQ and Prednisolone 5 mg and referred to a senior Gynaecologist. On Ultrasonography, she had Diamniotic, Dichorionic pregnancy without any embryonic developmental defects. Her disease activity remained low during her pre natal visits. She had C-Section on 8 and half month of pregnancy and delivered healthy, non-identical female twins. Now a days the patient is under routine follow ups and her disease is in remission.

DISCUSSION:

Systemic lupus erythematosus a multisystem autoimmune disease, more common in females of childbearing age, may need cyclophosphamide for organ threatening manifestations like severe glomerulonephritis and Neurological involvement. Contraception is strongly recommended during treatment. It has been proven that high cumulative dose and increasing age are two major risks of premature ovarian failure. Yet pregnancy occurs with or without embryopathies. The likelihood of ovarian failure in lupus patients receiving intravenous cyclophosphamide has varied from 15.5 to 37.3% in various studies. CYC crosses the human placenta with concentration of 25% of the plasma level and is also excreted in breast milk and may result in myelotoxicity of breastfed infant. Enns et al. studied teratogenic phenotypes of CYC treated patients during pregnancy and observed severe anomalies such as microencephaly, craniosynostosis, blepharophimosis, Baraitser–Winter syndrome, cleft palate, ear and limb defects, including hypoplastic thumbs and oligodactyly. On the other hand there is data in which CYC exposed patients during gestation did not develop significant mortality and morbidity in their fetal outcomes.

Data on twin pregnancy outcomes in patients treated with CYC is scarce. In the present case report neither the mother faced high disease activity nor the intrauterine fetuses underwent abortion or any teratogenic effects of Intra Venous CYC. Hence it is concluded that we need to know more about the behavior of CYC in human being as far as its adverse effects are concerned.

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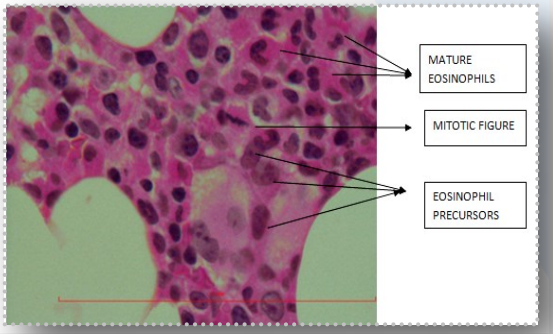
BIOPSY OF A PATIENT WITH HYPEREOSINOPHILIC SYNDROME

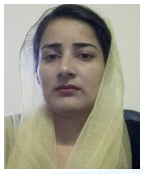
Courtesy : Dr. Lubna Nazir

Photomicrograph of bone marrow trephine biopsy at high power demonstrating many eosinophil precursor cells. A mitotic figure is also visible. (Leishmann Stain x100)



SUCCESS STORY: A LADY WHOSE PHYSICAL DISABILITY COULD NOT STOP HER TO ACHIEVE HER GOALS

Courtesy: Dr. Babur Salim



SHAHIDA PERVEEN

I met Dr Shahida Perveen in 2018. She was working in the medical department of Fauji Foundation Hospital Rawalpindi , Pakistan, as a medical registrar. She was interested in doing residency in rheumatology but could not join due to her health issues at that time. I later found out that she was born with spina bifida and neuropathy leading to charcot arthropathy of bilateral feet with recurrent osteomyelitis.

Dr. Shahida belongs to a middle class family with limited financial resources. Due to limited resources, she could not physically go to school in her early life and received homeschooling instead. Despite all the odds, she persevered and completed her schooling in 2003. In 2006 , she got admission in Rawalpindi Medical College, Pakistan . Throughout this time she faced recurrent health related issues in the form of foot ulcers, osteomyelitis and local infections but nothing could stop her. Her hard work and perseverance paid off once again when she completed her fellowship in medicine in 2017. By 2020, she joined fellowship in rheumatology at Fauji Foundation Hospital, Rawalpindi.

Presently, in her last year of residency, Dr. Shahida has waddling gate and has been advised amputation of both the feet as reconstructive surgery was not possible. Despite her debilitating health issues, she works the same hours as her fellow residents, hardly ever accepts physical aid, and completes her work on time. Moreover, she never brings up her physical disability as an excuse for missing out on some work. In fact during the peak of the COVID pandemic , Shahida actively participated in managing COVID patients as well. She is one of the investigators in a grant received from ILAR/GRA in 2021 and is also one of the coordinators of the APLAR COVID-19 facebook page and her journey still continues. Her determination and persistence is a source of inspiration not only for her fellow residents, but all the doctors who meet her. She has proven, time after time, that nothing will stand in her way from achieving her dreams.

IMPACT OF ULTRASOUND IN ASSESSING REMISSION IN RHEUMATOID ARTHRITIS

Courtesy : Dr. Masem Afzal

INTRODUCTION:

Rheumatoid Arthritis is a chronic systemic inflammatory disorder affecting small joints but can also affect large joints if not treated in time with the appropriate medicine. It may result in structural joint damages and functional disabilities of the individuals. Achieving remission is an ultimate goal in rheumatoid arthritis. Studies have shown that clinical composite scores are less sensitive in defining complete clinical remission when compared to the objective assessment conducted through ultrasound. The aim of this review is to identify standards of remission in rheumatoid arthritis thus defined by ultrasound.

METHODS:

A systemic search was conducted using PubMed and Embase using NICE Healthcare Database conducted between 2006 and 2017. Following key words: ***Rheumatoid arthritis and ultrasonography or ultrasound and remission.*** Articles were selected after reading titles and abstracts.

RESULTS:

Total of 22 out of 688 articles were identified. In all studies number of joints assessed with ultrasound, varied from 5 to 44 joint counts. Wrist and Metacarpophalangeal joints were included in all the studies. Ultrasound assessments of reduced joint sets were found to have good correlation with comprehensive joint sets. Except two recent studies (1,2); all other demonstrated the superiority of ultrasound over clinical composite scoring system for the assessment of clinical remission.

CONCLUSION:

In order to achieve true remission, modification of composite scoring system with the inclusion of ultrasound assessment is a practical solution. Moreover further studies are required towards its standardization.

NEXT ISSUE OF NEWSLETTER:

We are planning to publish the next issue in December 2021, In sha Allah Taala.

Please send us your departmental activities from June 2021 till November 2021, including titles of research papers published in National and International Journals.

The write-ups for the news and happenings in your Rheumatology department should be upto 100 words, each research highlight upto 200 words, summarized latest guidelines for any Rheumatic disease management upto 300 words and case report upto 400 words.

We would also appreciate receiving interesting quiz and images with two liner description.

Send your write-ups latest by 15 Dec, 2021 at the following addresses:

Tahira.Perveen@lnh.edu.pk
Humza.Masood@lnh.edu.pk
Drhamza84@gmail.com

Quiz Answer:

1. C: At least 2 NSAIDs over 4 weeks in total
2. C: Escalate treatment to biologic therapy

Reference:

- EULAR recommendation for SpA management.

Thank You

In case of any query regarding the newsletter, please feel free to contact us at the below mentioned emails.

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