reviewed with regard to indication, effect on disease activity and acute phase response, adverse events and patient global assessment.
Results: There were 43 patients with FMF (20 M/ 23 F) who were treated with Anakinra for various indications (colchicine resistant recurrent febrile attacks in 39, colchicine related side effects in 3, both in 1). The mean age of the patients was 31.73±9.56 years. The mean duration of the disease was 19.90±10.52 years. There were various co-existing pathologies among this study group like Ankylosing Spondylitis (4), Psoriasis (1), Behçet's disease (1), Gout (1), Vasculitis (1), Adult-onset Still's disease (1), Polyarthritis Nodosa (1) and Celiac disease (1). The mean colchicine dose was 1.84±0.31 mg/d. As for the dosage, 35 patients were on 100 mg/day, 6 were 100 mg on alternate days, 2 were on 200 mg/day. The mean duration of anakinra treatment was 10.76±13.64 months. After the initiation of anakinra 29 patients became attack-free, 9 patients reported more than 50% decrease, 3 patients less than 50% decrease, and 2 patients no change in the frequency of the attacks. Mean patient global assessment decreased from 7.55±2.34 to 2.82±2.63 under Anakinra treatment ($p<0.001$).
As for the adverse events, eight patients (%18) had allergic reactions under Anakinra treatment (severe disseminated rash in 1 patient and severe injection site reaction in 4 patients and tolerable injection side reaction in 3) which necessitated termination of treatment in 5 patients. Anakinra was stopped because of genital warts and urinary tract infection in one other patient. Worsening of psoriatic lesions was observed in another patient. There were no adverse events in the remaining 41 patients during the course of treatment. On the other hand, treatment was terminated due to inadequate response in 11 (25%), remission in 2 and patient preference in 3 patients. Nineteen patients are still on Anakinra treatment for 10.09±14.51 months.
Conclusions: Anakinra is an effective and relatively safe alternative treatment in FMF patients with inadequate response or intolerance to colchicine, however approximately one fourth of the patients stop anakinra for insufficient response.
Disclosure of Interest: None declared
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FRI0597 FATIGUE IN FAMILIAL MEDITERRANEAN FEVER (FMF) AND ITS RELATIONS WITH OTHER CLINICAL PARAMETERS

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Background: Fatigue is a common problem in patients with rheumatic disease. It may cause disability and poor quality of life (1). Although fatigue and its determinants are studied in several rheumatic diseases, there is no study in Familial Mediterranean Fever (FMF).
Objectives: The aim of this study is to investigate fatigue in FMF patients as a disabiling symptom and its associations with clinical and demographic variables.
Methods: FMF patients were recruited into the study according to FMF Tel Hashomer criteria (2). Control group composed of healthy individuals. Patients who were pregnant or who had concomitant medical illnesses such as cancer, fibromyalgia, or psychiatric conditions such as psychosis or bipolar disorder were excluded. Age, gender, disease duration, education, marital status were noted as demographic features. Number of attacks in the last year, type of attack, involvement of joints, dosage of colchicine, genotype, amyloidosis, and severity of FMF was assessed with PRAS score, visual analogue score of pain (VAS-pain) and VAS-fatigue were used as clinical parameters. Pittsburgh Sleep Quality Index (PSQI), Multidimensional Assessment of Fatigue (MAF), Nottingham Health Profile (NHP), Fatigue Severity Scale (FSS), Fatigue Impact Scale (FIS) and Hospital Anxiety and Depression Scale (HADS) were filled out by both control and study group. Assessment of normality was analyzed with Shapiro-Wilk test. Differences in the mean scores of control and study group were compared with independent samples Mann-Whitney U and Kruskal-Wallis test. Relationship between continuous variables was assessed with Spearman's correlation coefficient (rho).
Results: 61 FMF patients and 61 age, gender (44 female, 17 male in each group) matched controls were enrolled into the study. Mean age of FMF and control group were 35.5±11.8 and 35.8±11.7 years, respectively. The mean disease duration was 82.5±81.7 months. Difference between mean of VAS-pain, VAS-fatigue, PSQI total score, MAF, all subsets of NHP, FSS, FIS, HADS scores of FMF patients were significantly higher than control group ($p<0.0001$). The correlations between scales assessing fatigue and other outcome measures in FMF patients was shown in Table.

Spearman'sCorrelation (rho)	VAS.fatigue	MAF	FSS	FIS
PSQI.TotalScore	0.49***	0.53***	0.38**	0.50***
NHP.EnergyLevel	0.43***	0.65***	0.54***	0.55***
NHP.Pain	0.58***	0.66***	0.56***	0.67***
NHP.EmotionalReaction	0.40**	0.54***	0.48***	0.65***
NHP.Sleep	0.32*	0.24	0.12	0.31*
NHP.SocialIsolation	0.27*	0.39**	0.50***	0.54***
NHP.PhysicalAbilities	0.51***	0.64***	0.56***	0.69***
HADS.Anxiety	0.43***	0.55***	0.52***	0.75***
HADS.Depression	0.30*	0.42***	0.42***	0.57***

***=p<0.001; **=p<0.01; *=p<0.05.

Conclusions: This study has shown that fatigue in FMF is associated with a number of psychological, sleep, quality of life and disease related factors. FMF group had increased pain, fatigue, sleep disturbance and decreased quality of life compared to control group. FMF patients with fatigue may benefit from pharmacological and psychological interventions which target these factors.
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FRI0598 CHARACTERIZATION OF PATIENTS WITH AN INITIAL DIAGNOSIS OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE. OBSERVATIONS FROM A LONGSTANDING MONOCENTRIC COHORT

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Background: Evolution from Undifferentiated Connective Tissue Disease (UCTD) to a defined Autoimmune Disease (AID) remains unexplained and usually occurs in the first 3 to 5 years.
Objectives: To determine the frequency and predictors of differentiation from UCTD to AID in a selected cohort of patients originally labelled as UCTD within the first 3 years of follow-up.
Methods: Demographic and clinical features were retrieved: (i) retrospectively, from the AID's Unit current database in December 2016 (n=195), including Systemic Lupus Erythematosus (SLE), incomplete SLE, Sjögren's Syndrome (SS), Systemic Sclerosis (SSc), VEDOSS and Mixed Connective Tissue Disease (MCTD); and (ii) from a prospectively UCTD database created in January 2012 (n=48). Inclusion criteria for the latter pertains to ANA positive patients, not fulfilling any of the existing classification criteria for AID and without severe organ involvement [1]. Patients with cutaneous lesions suggestive of lupus, inflammatory myopathies, erosive arthritis, systemic sclerosis and certain auto-antibody profiles were excluded *a priori* from the definition of UCTD as these are thought to herald defined conditions, as previously defined [2]. Definition of stable UCTD includes patients with at least one clinical manifestation of AID, positive ANA result and disease duration of at least 3 years [3]. Comparisons between stable UCTD and progressing patients were made using Wilcoxon Rank Sum and Chi square tests, p values of <0.05 were considered statistically significant.
Results: Each individual patient was analysed for differentiation into AID at yearly intervals. Overall, the main features of the prospective UCTD cohort were arthralgia (79%), rash (31%), arthritis (19%), sicca symptoms (19%), photosensitivity (17%) and Raynaud (13%). Prospective analysis in the UCTD cohort revealed differentiation in 4/48 patients (8.3%): into rheumatoid arthritis (n=2), psoriatic arthritis (n=1) and SLE (n=1). The main difference between stable UCTD and those that progressed to AID was the presence of arthritis (p=0.003). Median age of onset and symptom duration was similar between both groups. Retrospective analysis yielded very few patients presenting as UCTD (n=5/195): 2/106 SLE; 1/13 incomplete SLE; 1/43 SS; 1/19 SSc; 0/7 VEDOSS and 0/7 MCTD with no distinguishing features.
Conclusions: Very few patients differentiated in the UCTD cohort after 3 years of follow-up and in our retrospectively studied cohort, in accordance to a previous study [4]. Apart from arthritis, there were no other predicting factors for differentiation to AID. UCTD at disease onset seems to be a rare event.
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FRI0599 A RETROSPECTIVE OVERVIEW OF CLINICAL FEATURES, SEROLOGY AND HISTOLOGY OF IGG4 RELATED DISEASE IN HONG KONG: A DATASET OF 108 PATIENTS FROM FOUR REGIONAL HOSPITALS

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Background: IgG4 related disease (IgG4RD) is a spectrum of immune mediated disease with multiple organs involvement characterized by organ enlargement, function loss or obstructive symptoms (1, 2).
Objectives: In this retrospective study, clinical, serological and histological features of IgG4RD patients over the past ten years from four regional hopsitals were reviewed.

Methods: Four regional hospitals participated with study period from 1/1/2006 to 30/6/2016. IgG4RD patients were classifed into definite, probable and possible IgG4RD according to Japanese Comprehensive Diagnostic Criteria for IgG4RD (3).
Statistical analysis: Association between the individual categorical covariates and the different organ involvement were analyzed by Fisher's exact test.
Results: 108 patients were included. There were 81 male patients and 27 female patients and the male to female ratio is 3:1. The mean age of diagnosis was 62.8 year old. 57 patients were diagnosed as definite IgG4RD (53%), 14 patients as probable IgG4RD (13%) and 37 patients as possible IgG4RD (34%). Salivary glands involvement was the commonest, (M=45.7% vs F=33.3%), followed by pancreas (M=28.4% vs F=18.5%) and biliary system in male (M=24.7% vs F=11.1%) and orbital in female (M=23.5% vs F=18.5%). 53% patients also had multi organ involvement.
104 patients had serum IgG4 level checked and it was raised in 94 patients (90.4%). 77 patients (74.0%) had IgG4 level above twice upper limit of normal. IgG4 level was normal in 10 patients. 98% and 86.3% patients with multi organ involvement had IgG4 level >135mg/dL (p=0.016) and >270mg/dL (p=0.007) respectively. In the hepatobiliary group (n=36), 30 patients had blood checked for Ca19.9 level and it was raised in 17 patients (56.7%), with the highest level 14127 U/ml.
71 histological reports were available. Lymphoplasmacytic infiltration was a consistent features in all specimens (100%). Eosinophilic infiltration was seen in 19 specimen (27%). Fibrosis was seen in 44 specimens (63%). Sialadenitis and dacryoadenitis were associated with dense fibrosis. Obliterative phlebitis was seen in 7 specimens (10%). IgG4/IgG ratio was reported in 61 specimens. 53 specimens had IgG4/IgG ratio greater than 40% per high power field which accounted for 86.9% of the specimens.
Conclusions: Most patients were male with the peak diagnosis at age 50 to 70. Salivary gland and pancreas were the most common organ involved. Most patients had a raised IgG4 level and most histological specimens showed a raised IgG4/IgG ratio on immunostaining. IgG4 level twice the upper limit of normal was quite specific for the disease and was associated with multi organ involvement.
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FRI0600 THE EFFICACY OF DIFFERENT COLCHICINE DOSES IN TREATMENT OF FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Background: Recommended colchicine dose in familial mediterranean fever (FMF) is 1–1.5 mg/day in adults. If necessary it can be increased up to 3 mg/day by clinical monitoring. In the final FMF recommendation report of the EULAR, it was reported that after 5 years of stable disease, in appropriate patients, the dose of colchicine may be reduced by close follow-up. However, the number of clinical trials supporting this recommendation is not enough.
Objectives: In this study, demographic and clinical characteristics of FMF patients whose disease under control and treated with different doses of colchicine were compared.
Methods: Among the all FMF patients attending to the rheumatology outpatient clinic between April and September 2016, only the patients in non-attacks period at least for the last 1 month were included to the study. Clinical and laboratory findings, MEFV gene mutations, drug compliance of the patients and duration and doses of the colchicine treatment were recorded. The 'international severity scoring system for familial mediterranean fever' (ISSF) score was calculated to determine disease severity. The patients who were under the control (less than 4 attacks per year and ISSF score ≤2) divided to three gruops. These gruops were the patients taking low dose (average daily dose of colchicin <1 mg), median dose>1 mg/day and<1.5 mg/ day and standard dose ≥1.5 mg/colchicine treatment at least for 3 years. Patients treated with DMARDs or biological therapy were excluded from the study.
Results: Of the 162 FMF patients enrolled into the ongoing cohort, 86 patients were excluded from the study due to 57 patients had active disease, 19 had not yet completed 3 years of colchicine treatment and 10 patients received biological or DMARD treatment. The remaining 76 patients (25 male, 51 female) met the study criteria. The mean age was 32±11.5 years and the disease duration was 18.2±10.9 years. Amyloidosis or organ failure was not detected in any of these patients. Because of various reasons (drug side effect, treatment incompatibility, physician advice), 16 patients (21%) were treated with low dose colchicine (group A), 30 patients (39%) with moderate dose of colchicine (group B) and the remaining 30 patients (39%) with standard dose colchicine (group C). There were no statistically significant differences in demographic, clinical or laboratory data among these 3 subgroups.
Conclusions: Disease control in FMF is important to prevent amyloidosis and improve the quality of life. Recent studies contribute to the determination of treatment goals. Reducing the colchicine dose may increase drug compliance in this lifelong treatment. In our study, there was no difference between the treatment groups in amyloidosis, MEFV gene mutation or subclinical inflammation. These findings suggest that the dose of colchicine maybe reduced in inactive patients who determineted by the number of annual episodes and the ISSF score.
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FRI0601 HYPERFERRITINEMIC SYNDROME IN A GENERAL UNIVERSITARY HOSPITAL

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Background: Hyperferritinemia is associated with severe inflammatory conditions, such as rheumatic diseases with systemic inflammatory responses, and multiorgan dysfunction syndromes.
Objectives: To determine which diseases are associated with hyperferritinemia in a tertiary hospital; to compare ferritin levels between these different entities and to evaluate relationship between levels of ferritin and mortality in these patients.
Methods: A retrospective study was carried out in which all patients over 18 years with at least one determination of serum ferritin equal to or greater than 1000 ng/ml were identified in the laboratory database of our hospital between 1/1/2006 and 6/30/2016. Corresponding electronic medical records were reviewed and demographic data and clinical data were collected. Mortality was assessed at the end of follow-up. Descriptive statistical analysis and logistic regression analysis were performed in order to identify variables associated with mortality.
Results: A total of 1979 patients were included, 1235 men (62.4%) with a mean age of 63.2 years (SD 17.2). Only 36 patients (1.8%) presented a rheumatologic diagnosis as the only cause of high levels of ferritin, with Still's disease (n=8) and systemic Vasculitis (n=9) being the main diagnoses. Table 1 shows patients' characteristics grouped according to whether the elevation of ferritin was associated with a rheumatic disease or not. Median serum ferritin and transferrin saturation in both groups were similar (see Table 1). Mortality was lower for rheumatologic causes (5.9% vs 37.2%, p<0.001). Variables that were associated with mortality in multivariable logistic regression analysis were: maximum ferritin value (OR 1,0004, 95% CI 1,0003–1,0004, p<0.001) and age (OR 1.03, 95% CI 1.02–1.04, p<0.001), whereas the diagnosis of a rheumatic disease was a protective factor (OR 0.11, 95% CI 0.03–0.47, p=0.003). ROC curve for ferritin and mortality showed an area under the curve of 0.59 (95% CI 0.58–0.62). Ferritin levels greater than 3000 ng/ml showed a specificity of 89.2% and a sensitivity of 19.7% for mortality, regardless of cause of ferritin elevation.

Table 1. Patients' characteristics grouped by cause of Hyperferritininemia (Rheumatologic or not)

	Rheumatic disease (n=35)		Other causes of ferritin elevation (n=1944)		p
Female, n (%)	13 (37.1)		731 (37.6)		0.96
Mean age, years (DS)	62.5 (17.1)		52.4 (21.1)		<0.001
Diagnostic	Vasculitis	9	Solid cancer	497	
	Still's disease	8	Infections	336	
	Rheumatoid arthritis	4	Onco-hematologic disease	302	
	SLE	3	Chronic renal insufficiency	236	
	Seronegative arthritis and psoriatic arthritis	3 3	Hepatic disease	188	
	Others	3	Others	152	
	Gout	2	Hematologic disease	128	
	Juvenile idiopathic arthritis	1	Cardiovascular	57	
	Myositis	1	Sepsis	46	
	IgG 4	1	Iron overload	2	
Serum ferritin, median (IQR)	1622 (1264- 3639)		1460 (1200–2140)		0.07
Tranferrin saturation, %, median (IQR)	38 (19–50)		33 (18–55)		0.83
Follow-up time, years, median (IQR)	5.2 (1,2–10.2)		5.7 (1.2–8.9)		0.97
Mortality, n (%)	2 (5.9)		698 (37.2)		<0.001

Conclusions: Rheumatic diseases, represents a very small percentage of the causes of elevation of ferritin above 1000 ng/ml, and were associated with lower mortality than the non-rheumatic causes. Serum ferritin levels were significantly associated with increased mortality regardless of the underlying cause.
Disclosure of Interest: None declared
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FRI0602 NATIONAL RECOMMENDATIONS ON THE USE OF IMMUNOMODULATORY DRUGS IN PATIENTS WITH NON-INFECTIOUS NON-MALIGNANT ANTERIOR UVEITIS

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