

# Nutritional Status in Patients with Idiopathic Inflammatory Myopathies and the Association with Disease-related Features

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**Background:** Systemic inflammation, involvement of gastrointestinal tract, and glucocorticoid treatment in idiopathic inflammatory myopathies (IIM) can have a negative impact on nutrition and intermediate metabolic pathways. The aim of this study was to evaluate the differences in the nutrition status of IIM patients in comparison with healthy controls (HC) and explore the associations with disease-specific features.

**Conclusion:** We have observed significant alterations in markers of nutritional status in our IIM patients compared to healthy age-/sex-matched individuals. Differences were also found among the four subtypes of IIM. These alterations were associated with laboratory parameters of disease activity and the current dose of corticosteroids.

## Methods:

133 patients with IIM (106 females; mean age 60.3; disease duration 2.2 years; DM 45 / PM 25 / IMNM 46 / ASS 17) and 133 age-/sex-matched HC (106 females, mean age 60.2) without rheumatic diseases were included. Patients with IIM fulfilled the 2017 EULAR/ACR classification criteria for adult IIM. Levels of selected nutrition parameters were measured in sera drawn after 8 hours of fasting. In IIM patients, disease activity, damage and muscle involvement were assessed by MITAX, MDI, and MMT-8. Comorbidities of interest and current treatment were recorded. Data are presented as median (IQR).

**Table 1: Baseline characteristics**

Parameter	IIM (n = 133)	DM (n = 45)	PM (n = 25)	IMNM (n = 46)	ASS (n = 17)	HC (n = 133)
Gender, n (%): female / male	106 (80) / 27 (20)	35 (78) / 10 (22)	19 (76) / 6 (24)	34 (76) / 11 (24)	1(6) / 16 (94)	106 (80) / 27 (20)
Age (years); median (IQR)	60.0 (49.3 – 69.3)	56.3 (49.3 – 66.9)	58.6 (43.8 – 66.3)	68.7 (57.7 – 72.8)	57.2 (40.6 – 63.1)	IIM-HC 60.2 (49.6 – 69.7); DM-HC 56.5 (49.7 – 65.6); PM-HC 58.4 (43.5 – 65.5); IMNM-HC 68.3 (57.7 – 72.3); ASS-HC 56.93 (40.9 – 62.7)
BMI (kg/m <sup>2</sup> ); median (IQR)	26.7 (23.4 – 30.5)	27.4 (23.7 – 32.0)	24.0 (21.2 – 27.7)	27.6 (25.3 – 31.2)	24.7 (20.8 – 29.6)	
Disease duration (years); median (IQR)	2.2 (0.7 – 6.9)	2.83 (1.39 – 7.58)	5.0 (1.6 – 9.4)	0.71 (0.44 – 2.88)	4.32 (1.30 – 9.63)	
Disease activity (MITAX); median (IQR)	0.11 (0.05 – 0.21)	0.27 (0.09 – 0.40)	0.16 (0.09 – 0.30)	0.08 (0.03 – 0.18)	0.10 (0.06 – 0.27)	
Disease damage (MDI); median (IQR)	0.05 (0.02 – 0.1)	0.06 (0.03 – 0.10)	0.05 (0.03 – 0.08)	0.03 (0.0 – 0.06)	0.07 (0.02 – 0.12)	
MMT-8; median (IQR)	62 (54 – 72)	65 (55 – 74)	60 (53 – 70)	57.5 (49.8 – 68.3)	70 (58 – 75.5)	
CRP (mg/L); median (IQR)	3.0 (1.8 – 5.9)	2.91 (1.93 – 6.13)	2.70 (1.92 – 5.30)	3.29 (1.80 – 5.96)	3.81 (1.09 – 8.92)	
ESR (mm/h); median (IQR)	14 (8 – 26)	13 (8 – 20)	17.5 (7.8 – 30.8)	11 (5 – 23.5)	25.5 (11.8 – 38.5)	
CK (µkat/L); median (IQR)	3.8 (1.0 – 20.7)	1.17 (0.69 – 3.04)	4.28 (1.33 – 9.52)	42.4 (7.72 – 72.4)	0.76 (0.56 – 8.99)	
LD (µkat/L); median (IQR)	4.6 (3.5 – 7.2)	3.73 (3.06 – 5.03)	3.81 (2.82 – 5.38)	8.82 (5.72 – 16.24)	3.62 (3.28 – 4.31)	
Myoglobin (µg/L); median (IQR)	179.2 (71.2 – 940.5)	104.3 (56.0 – 174.2)	129.5 (57.2 – 344.4)	1405.6 (540.3 – 2222.53)	79.5 (47.4 – 277.2)	
Glycemia (mmol/L); median (IQR)	5.3 (4.6 – 6)	5.2 (4.4 – 5.7)	5.2 (4.5 – 5.7)	5.7 (4.8 – 7.0)	5.0 (4.6 – 5.8)	
Prednisolone equivalent dose (mg/day); median (IQR)	15 (5 – 30)	15 (5 – 30)	7.5 (2.5 – 15)	25 (3.1 – 57.5)	10 (3.8 – 20)	
IIM-associated clinical manifestations, n (%): MW / OD / SR / MH / RP / A / ILD / CI	109 (82) / 39 (29) / 18 (14) / 16 (12) / 25 (19) / 17 (13) / 37 (29) / 15 (11)	36 (80) / 17 (38) / 16 (35) / 9 (20) / 9 (20) / 2 (4) / 14 (31) / 6 (13)	21 (84) / 8 (32) / 0 (0) / 1 (4) / 7 (28) / 2 (8) / 7 (28) / 4 (16)	39 (85) / 11 (24) / 2 (4) / 0 (0) / 3 (7) / 1 (2) / 3 (7) / 2 (4)	13 (76) / 3 (18) / 0 (0) / 6 (35) / 6 (35) / 12 (71) / 13 (76) / 3 (18)	
Autoantibodies (positive), n (%): ANA / Mi-2 / TIF-1γ / CADM-140 / SAE / p140 / SRP / Jo-1 / PM-Scl / RNP / Ku / Ro / HMGR	36 (27) / 8 (6) / 3 (3) / 4 (3) / 1 (1) / 4 (3) / 7 (6) / 21 (16) / 10 (8) / 4 (3) / 4 (3) / 25 (20) / 26 (21)	13 (29) / 6 (13) / 3 (7) / 3 (7) / 1 (2) / 4 (9) / 1 (2) / 3 (7) / 7 (16) / 1 (2) / 1 (2) / 5 (11) / 0 (0)	8 (32) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 1 (4) / 2 (8) / 2 (8) / 7 (28) / 0 (0)	9 (20) / 1 (2) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 6 (13) / 2 (4) / 1 (2) / 1 (2) / 5 (11) / 26 (57)	6 (35) / 1 (6) / 0 (0) / 1 (6) / 0 (0) / 0 (0) / 0 (0) / 16 (94) / 1 (6) / 0 (0) / 0 (0) / 8 (47) / 0 (0)	
Treatment, n (%): GC / MTX / AZA / CSA / CPA / LEF / MMF	112 (84) / 40 (30) / 14 (11) / 8 (6) / 3 (2) / 1 (1) / 2 (2)	40 (89) / 14 (31) / 5 (11) / 3 (7) / 1 (2) / 0 (0) / 0 (0)	21 (84) / 6 (24) / 3 (12) / 1 (4) / 1 (4) / 1 (4) / 2 (8)	34 (74) / 16 (35) / 4 (9) / 2 (4) / 1 (2) / 0 (0) / 0 (0)	17 (100) / 4 (24) / 2 (12) / 2 (12) / 1 (6) / 0 (0) / 0 (0)	
Arterial hypertension (treated), n (%)	65 (50)	16 (36)	12 (48)	30 (65)	7 (41)	
Diabetes mellitus, n (%): Untreated / PAD / Insulin treatment	15 (12) / 18 (14) / 11 (9)	5 (11) / 1 (2) / 1 (2)	3 (12) / 2 (8) / 2 (8)	6 (13) / 13 (28) / 5 (11)	1 (6) / 2 (12) / 3 (18)	
Statin use, n (%): Current / Previous / Other current hypolipidemic drugs	3 (2) / 37 (28) / 3 (2)	2 (4) / 4 (9) / 1 (2)	0 (0) / 2 (8) / 2 (8)	0 (0) / 31 (67) / 0 (0)	1 (6) / 0 (0) / 0 (0)	
Smoking (current), n (%)	4 (3)	0 (0)	0 (0)	4 (9)	0 (0)	

Abbreviations: IIM, idiopathic inflammatory myopathies; DM, dermatomyositis; PM, polymyositis; IMNM, immune-mediated necrotizing myopathy; HC, healthy controls; MITAX, Myositis Intention to Treat Activity Index; MDI, Myositis Damage Index; MMT-8, Manual Muscle Testing-8; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; CK, creatine kinase; LD, lactate dehydrogenase; MW, muscle weakness; OD, oesophageal motility disorder; SR, skin rash; MH, mechanic's hands; RP, Raynaud's phenomenon; A, arthritis; ILD, interstitial lung disease; CI, cardiac involvement; ANA, antinuclear antibodies; Mi-2, anti-nuclear helixase 232/240 kDa; TIF-1γ, transcription factor 1γ; CADM-140, anti-Mi-2; SAE, anti-SRP (small ribosomal subunit); SRP, anti-signal recognition particles; Jo-1, anti-myositis RNA synthetase; PM-Scl, anti-PM-Scl (anti-core complex 11-16 proteins); RNP, anti-Ribonucleoprotein; Ku, anti-Ku (ligand of the nuclear DNA-protein kinase subunit); Ro, anti-Ro (52 / 60kDa, against cytoplasmic RNA and associated peptides); GC, glucocorticoids; MTX, methotrexate; AZA, azathioprine; CSA, cyclosporin A; CPA, cyclophosphamide; LEF, leflunomide; MMF, mycophenolate mofetil; PAD, peroral antidiabetic drugs

## Results:

### Nutrition parameters in IIM patients compared to corresponding HC (tab. 2)

Parameter of nutrition	IIM (n = 133)	DM (n = 45)	PM (n = 25)	IMNM (n = 46)	ASS (n = 17)	HC (n = 133)	p-value IIM-HC; DM-HC; PM-HC; IMNM-HC; ASS-HC
Total protein (g/dL); median (IQR)	72.6 (67.5 – 78.6) ↓	71.8 (67.5 – 78.6) ↓	78.7 (73.1 – 81.6) ↔	70.0 (66.0 – 73.7) ↓	74.1 (65.9 – 77.3) ↔	74.3 (72.2 – 77.7) ↓	0.005; 0.062; 0.105; <0.001; 0.319
Albumin (g/dL); median (IQR)	43.1 (40.0 – 45.7) ↓	43.2 (39.9 – 45.6) ↓	45.2 (43.2 – 47.6) ↔	41.6 (39.6 – 44.7) ↓	41.9 (38.7 – 44.0) ↓	44.9 (43.1 – 46.9) ↓	<0.001; 0.030; 0.698; <0.001; 0.007
Prealbumin (g/dL); median (IQR)	0.24 (0.20 – 0.30) ↓	0.23 (0.19 – 0.28) ↓	0.24 (0.20 – 0.28) ↓	0.26 (0.21 – 0.32) ↔	0.23 (0.19 – 0.32) ↔	0.27 (0.24 – 0.31) ↓	<0.001; <0.001; 0.003; 0.548; 0.375
Transferrin (g/L); median (IQR)	2.4 (2.2 – 2.7) ↓	2.40 (2.20 – 2.80) ↓	2.60 (2.45 – 3.05) ↔	2.40 (2.10 – 2.60) ↓	2.40 (2.20 – 2.60) ↓	2.7 (2.5 – 3.0) ↓	<0.001; <0.001; 0.579; <0.001; 0.036
Orosomucoid (g/L); median (IQR)	0.98 (0.84 – 1.20) ↑	0.98 (0.85 – 1.18) ↑	0.92 (0.84 – 1.13) ↑	0.94 (0.84 – 1.25) ↑	1.07 (0.91 – 1.27) ↑	0.8 (0.67 – 0.91) ↓	<0.001; <0.001; <0.001; <0.001; <0.001
Complement C4 (g/L); median (IQR)	0.29 (0.23 – 0.38) ↓	0.29 (0.29 – 0.40) ↔	0.26 (0.22 – 0.32) ↓	0.33 (0.28 – 0.42) ↔	0.24 (0.24 – 0.36) ↓	0.33 (0.27 – 0.39) ↓	0.019; 0.957; 0.036; 0.762; 0.029
Complement C3 (g/L); median (IQR)	1.5 (1.32 – 1.70) ↑	1.49 (1.32 – 1.68) ↔	1.46 (1.36 – 1.88) ↔	1.56 (1.31 – 1.73) ↔	1.48 (1.26 – 1.74) ↔	1.45 (1.28 – 1.67) ↓	0.089; 0.478; 0.204; 0.488; 0.438
Cholinesterase (ukat/L); median (IQR)	130 (114 – 148) ↓	137 (113 – 149) ↓	132 (123 – 158) ↔	125 (113 – 150) ↓	127 (99 – 134) ↓	145 (129 – 168) ↓	<0.001; 0.050; 0.416; <0.001; 0.093
Amylase (ukat/L); median (IQR)	1.04 (0.79 – 1.37) ↑	1.03 (0.75 – 1.27) ↔	1.35 (0.97 – 1.81) ↑	0.99 (0.76 – 1.18) ↔	1.08 (0.77 – 1.45) ↔	0.92 (0.74 – 1.31) ↓	0.096; 0.954; 0.043; 0.576; 0.152
Lipase (ukat/L); median (IQR)	0.54 (0.37 – 0.75) ↑	0.55 (0.39 – 0.77) ↔	0.52 (0.43 – 0.98) ↔	0.52 (0.37 – 0.69) ↔	0.62 (0.36 – 0.81) ↔	0.50 (0.34 – 0.68) ↓	0.050; 0.174; 0.177; 0.505; 0.557
Vitamin D (calcidiol) (nmol/L); median (IQR)	52 (34.3 – 71.4) ↔	57.3 (45.0 – 72.2) ↔	58.0 (41.7 – 74.2) ↔	38.9 (28.5 – 59.1) ↓	51.0 (34.3 – 80.5) ↔	57.3 (41.3 – 69.2) ↓	0.126; 0.564; 0.567; 0.002; 0.204
Calcitriol (1,25(OH)2D) (pmol/L); median (IQR)	105 (75.5 – 143.0) ↓	110 (86.1 – 145.5) ↔	103 (77.8 – 158.0) ↔	83 (53.5 – 119.5) ↓	139 (114 – 157.5) ↔	128 (104 – 157) ↓	<0.001; 0.125; 0.574; <0.001; 0.227
Fe (µmol/L); median (IQR)	15.1 (11.0 – 19.0) ↓	14.1 (9.1 – 18.8) ↓	17.2 (13.7 – 21.1) ↔	14.4 (11.0 – 18.8) ↓	17.4 (11.0 – 22.0) ↓	17.8 (14.2 – 21.3) ↓	0.001; 0.016; 0.799; 0.008; 0.249
Mg (mmol/L); median (IQR)	0.87 (0.80 – 0.93) ↓	0.88 (0.83 – 0.93) ↓	0.88 (0.80 – 0.90) ↓	0.86 (0.77 – 0.92) ↓	0.85 (0.81 – 0.91) ↓	0.88 (0.84 – 0.93) ↓	0.061; 0.570; 0.521; 0.084; 0.470
Zn (µmol/L); median (IQR)	885 (780 – 1000) ↓	870 (760 – 968) ↓	940 (770 – 1045) ↓	910 (813 – 1083) ↔	820 (700 – 885) ↓	1005 (830 – 1193) ↓	<0.001; 0.003; 0.017; 0.139; 0.073
ft4 (pmol/L); median (IQR)	16.8 (14.6 – 19.0) ↑	16.2 (13.6 – 18.5) ↔	15.2 (14.1 – 19.3) ↔	17.9 (15.0 – 19.5) ↑	16.3 (45.0 – 17.3) ↔	15.4 (14.3 – 17.2) ↓	0.011; 0.337; 0.161; 0.067; 0.448
TSH (mIU/L); median (IQR)	1.73 (1.12 – 3.05) ↓	1.29 (0.88 – 2.69) ↓	1.79 (1.38 – 2.67) ↔	2.09 (1.50 – 3.68) ↔	1.65 (1.07 – 2.26) ↔	2.19 (1.45 – 2.99) ↓	0.056; 0.006; 0.466; 0.637; 0.368
LDH (ukat/L); median (IQR)	3.9 (3.0 – 6.3) ↑	3.26 (2.92 – 4.95) ↑	3.83 (2.67 – 4.53) ↑	7.68 (4.52 – 11.18) ↑	3.35 (2.96 – 4.02) ↑	2.7 (2.3 – 3.3) ↓	<0.001; <0.001; <0.001; <0.001; 0.035
Vitamin B12 (pmol/L); median (IQR)	89.8 (69.0 – 115.1) ↑	96.9 (70.8 – 132.0) ↑	89.0 (67.3 – 104.6) ↑	89.7 (73.8 – 103.3) ↔	71.2 (55.6 – 104.9) ↔	78.5 (61.6 – 95.4) ↓	0.005; 0.006; 0.044; 0.357; 0.683
Folic acid (mg/L); median (IQR)	5.03 (3.28 – 8.41) ↔	4.5 (3.0 – 7.17) ↔	5.62 (3.29 – 10.83) ↔	5.57 (3.34 – 8.48) ↔	4.72 (2.23 – 8.92) ↔	5.15 (3.21 – 7.89) ↓	0.710; 0.640; 0.136; 0.747; 0.428
C-peptide (ng/mL); median (IQR)	0.98 (0.64 – 1.42) ↑	1.03 (0.57 – 1.60) ↑	0.84 (0.41 – 1.23) ↑	0.98 (0.69 – 1.65) ↑	1.04 (0.64 – 1.30) ↑	0.58 (0.09 – 0.86) ↓	<0.001; <0.001; 0.071; <0.001; 0.004
Insulin (µU/mL); median (IQR)	13.7 (8.20 – 23.08) ↑	14.6 (9.2 – 24.4) ↑	13.2 (7.9 – 23.5) ↔	12.7 (8.0 – 19.4) ↑	14.2 (10.0 – 25.9) ↑	9.53 (6.55 – 14.35) ↓	<0.001; 0.030; 0.212; 0.060; 0.010

↑ = significantly increased; ↓ = significantly decreased; ↔ = equal; ↗ ↘ = trend to (but not significantly) increased / decreased

Abbreviations: TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein; Apo-B, apolipoprotein B; non-HDL-C, non-high-density lipoprotein (TC minus measured HDL-C); Lp(a), lipoprotein A; HDL-C, high-density lipoprotein; Apo-A, apolipoprotein A; AI, atherogenic index of plasma = log(TG/HDL-C); LD, lactate dehydrogenase; PED, current prednisolone equivalent dose; CK, creatine kinase; BMI, body mass index; MMT-8, manual muscle testing-8; CRP, C-reactive protein

### Correlation of parameters of nutrition status and disease-specific features in all IIM patients (n=133) (tab. 3)

Correlated parameters	Spearman's r	p-value	Correlated parameters	Spearman's r	p-value
Total protein: Age; Disease duration; MITAX; MMT-8; ESR; PED	-0.280; 0.375; -0.180; 0.216; 0.254; -0.246	0.001; <0.001; 0.038; 0.014; 0.009; 0.005	Calcitriol (1,25(OH)2D): Disease duration; MDI	0.331; 0.220	<0.001; 0.016
Albumin: Age; Disease duration; MITAX; CRP; PED	-0.178; 0.300; -0.180; -0.238; -0.295	0.040; <0.001; 0.039; 0.007; <0.001	Fe: BMI; CRP	-0.153; -0.242	0.091; 0.006
Prealbumin: Disease duration; MDI; CRP; PED	0.278; -0.216; -0.286; 0.238	0.002; 0.018; 0.001; 0.007	Zn: Disease duration; MITAX; MDI; MMT-8; PED	-0.306; -0.368; -0.266; 0.166; 0.162	<0.001; <0.001; 0.004; 0.063; 0.069
Transferrin: Disease duration; MITAX; CRP; PED	0.278; -0.148; -0.169; -0.288	0.002; 0.089; 0.051; 0.001	ft4: MMT-8	-0.153	0.087
Orosomucoid: BMI; MDI; CRP; ESR; PED	0.252; 0.169; 0.371; 0.259; 0.309	0.005; 0.067; <0.001; 0.008; <0.001	TSH: CRP	0.262	0.003
Complement C4: Age; Disease duration; BMI; MITAX	0.186; -0.245; 0.236; -0.168	0.032 0.006; 0.009; 0.053	LDH: Age; Disease duration; MDI; MMT-8; PED	0.243; -0.505; -0.203; -0.178; 0.334	0.005; <0.001; 0.027; 0.046; <0.001
Complement C3: BMI; MITAX; CRP	0.361; -0.197; 0.213	<0.001; 0.023; 0.016	Vitamin B12: BMI; PED	0.155; 0.244	0.089; 0.006
Cholinesterase: Disease duration; BMI; MITAX; PED	0.230; 0.159; -0.215; -0.213	0.009; 0.078; 0.013; 0.016	Folic acid: PED	-0.198	0.025
Amylase: BMI; CRP	-0.230; -0.227	0.011; 0.010	C-peptide: Disease duration; BMI; PED	-0.219; 0.369; 0.260	0.014; <0.001; 0.003
Lipase: PED	0.231	0.009	Insulin: Age; BMI; PED	-0.151; 0.375; 0.274	0.085; <0.001; 0.002
Vitamin D (calcidiol): Disease duration; BMI; CRP; PED	0.360; -0.212; -0.168; -0.285	<0.001; 0.019; 0.057; 0.001			

Abbreviations: TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein; Apo-B, apolipoprotein B; non-HDL-C, non-high-density lipoprotein (TC minus measured HDL-C); HDL-C, high-density lipoprotein; Apo-A, apolipoprotein A; AI, atherogenic index of plasma = log(TG/HDL-C); LD, lactate dehydrogenase; PED, current prednisolone equivalent dose; CK, creatine kinase; BMI, body mass index; MMT-8, manual muscle testing-8; CRP, C-reactive protein

Compared to HC, IIM patients had significantly decreased serum levels of proteins (total protein, albumin, prealbumin, transferrin, complement C4), and minerals (Fe, Zn), as well as calcitriol (biologically active form of vitamin D), while calcidiol was comparable between IIM and HC. Orosomucoid (acute phase reactant), lactate dehydrogenase (LDH) and vitamin B12 were significantly increased in IIM. IIM patients had higher thyroid function (increased free thyroxin), but a trend to lower thyrotropin (TSH) and higher levels of insulin and C-peptide compared to HC. On the other hand, cholinesterase levels (a marker of synthetic liver function) were decreased in IIM. Higher prevalence of significant changes was observed in the DM and IMNM group compared to the corresponding age-/sex-matched HC. Within the individual IIM subtypes, there were significant differences in levels of proteins, vitamin D (calcidiol, calcitriol), and LDH, while most unfavorable changes were observed in the IMNM group.

In the whole IIM cohort, levels of nutrition markers (proteins, minerals) were especially associated with age, disease duration and activity (MITAX, levels of CRP), current dose of glucocorticoids (GC) and body mass index (BMI). Increased levels of insulin and C-peptide were associated with higher BMI and the current dose of GC (PED). Thyroxin was associated with muscle involvement, whereas TSH was positively associated with CRP. Higher cholinesterase levels (marker of synthetic liver function) were associated with longer disease duration and lower MITAX and the dose of GC (PED).