

**Fatigue and subjective complaints in patients with active and controlled acromegaly: a cross sectional multi-center study**Anca Zimmermann<sup>1</sup>, Rüdiger Zwerenz<sup>2</sup>, Michael Droste<sup>3</sup>, Christof Schöfl<sup>4</sup>, Christian J. Strasburger<sup>5</sup>, Ursula Plöckinger<sup>6</sup>, Jürgen Honegger<sup>7</sup>, Bledar Millaku<sup>1</sup>, Manfred E. Beutel<sup>2</sup>, Matthias M. Weber<sup>1</sup><sup>1</sup>Dept. of Endocrinology and Metabolic Diseases, 1. Medical Clinic, University of Mainz, Germany, <sup>2</sup>Clinic and Polyclinic for Psychosomatic Medicine and Psychotherapy, University of Mainz, Germany, <sup>3</sup>Endocrinology and Diabetology Praxis, Oldenburg, Germany, <sup>4</sup>Dept. of Endocrinology and Diabetology, 1. Med. Clinic, University of Erlangen, Germany, <sup>5</sup>Clinical Endocrinology, Charité Campus Mitte, Berlin, Germany, <sup>6</sup>Endocrinology, Interdisciplinary Metabolic Center, Charité Campus Virchow-Clinicum Berlin, Germany, <sup>7</sup>Neurosurgery Clinic, University of Tübingen, Germany**Introduction:** Acromegalic patients (AP) often report fatigue and chronic subjective complaints. We aimed to investigate in more detail these aspects in AP, dependent on disease activity, age, gender, medication and pituitary insufficiency (PI).**Results:****Patients characteristics**

| Parameters                                 | Distribution            |
|--|-------------------------|
| Age (years)                                | 58.3+/-14.7 (19-86)     |
| Time since diagnosis (years)               | 13.4+/-8.1 (0-23)       |
| M (males) /F (females)                     | 51/73                   |
| GH/GH and prolactin                        | 115/9                   |
| Active disease / biochemical control       | 49 (39.5%) / 75 (60.5%) |
| Complete / partial pituitary insufficiency | 10 (7.8%) / 37 (28.7%)  |

**Age- and gender-specific differences between patients and controls based on the MFI-20 inventory**

| Age (years)             | < 39              | 40-59             | > 60              |
|-------------------------|-------------------|-------------------|-------------------|
| Patients (Pat.) (n=124) | 32.3+/-3.9 (n=15) | 51.4+/-5.3 (n=52) | 71.5+/-6.9 (n=57) |
| M pat. (n=51)           | 30.3+/-3.6 (n=7)  | 53.4+/-4.3 (n=22) | 71.5+/-7.4 (n=22) |
| F pat. (n=73)           | 34.1+/-3.3 (n=8)  | 49.9+/-5.4 (n=30) | 71.6+/-6.6 (n=35) |
| P (M,F)                 | p = 0.06          | p=0.02            | p = 0.95          |
| GF M patients           | 11+/-6.3          | 12.8+/-4.2        | 13.5+/-4.3        |
| GF M controls           | 6.6+/-2.7         | 8.0+/-3.2         | 10.1+/-3.7        |
| GF F patients           | 13.3+/-3.3        | 11.1+/-4.6        | 13.1+/-4.5        |
| GF F controls           | 7.7+/-3.2         | 8.7+/-3.5         | 10.8+/-3.7        |
| PF M patients           | 11.1+/-5.9        | 12+/-3.9          | 11.3+/-4.5        |
| PF M controls           | 6.1+/-2.9         | 7.8+/-3.5         | 10.3+/-4.3        |
| PF F patients           | 14.3+/-2.6        | 11.4+/-4.8        | 12.7+/-5.0        |
| PF F controls           | 6.8+/-3           | 8.2+/-3.8         | 11.1+/-4.2        |
| MF M patients           | 14.1+/-4.7        | 12.7+/-4.2        | 14.5+/-3.8        |
| MF M controls           | 6.4+/-2.7         | 7.1+/-3.2         | 8.7+/-3.5         |
| MF F patients           | 14.7+/-2.9        | 14.1+/-3.5        | 14.3+/-4.6        |
| MF F controls           | 7.1+/-3.1         | 7.8+/-3.1         | 9.2+/-3.4         |
| DA M patients           | 12.1+/-6.1        | 13.8+/-4.1        | 13.3+/-3.6        |
| DA M controls           | 6.4+/-2.9         | 7.6+/-3.2         | 10.3+/-4          |
| DA F patients           | 15.3+/-1.6        | 13.4+/-5.1        | 13.8+/-4.9        |
| DA F controls           | 7.1+/-3.0         | 8.2+/-3.7         | 10.5+/-4.0        |
| DM M patients           | 14.6+/-4.8        | 15.2+/-2.9        | 15.4+/-2.8        |
| DM M controls           | 6.2+/-2.4         | 7.6+/-2.9         | 9.1+/-3.3         |
| DM F patients           | 17.4+/-3.1        | 15.2+/-3.9        | 15.3+/-4.0        |
| DM F controls           | 6.7+/-2.7         | 8.0+/-3.2         | 9.9+/-3.5         |

GF-general fatigue; PF-physical fatigue; MF-mental fatigue; DM – decreased motivation; DA-decreased activity

**Patients /methods:** Cross sectional, 124 patients (M/W 51/73, age 58.3+/-14.7ys., 49/75–active/controlled disease). The patients completed the Multidimensional Fatigue Inventory (MFI-20) and the Giessen Subjective Complaints Inventory (GSI-24), after written informed consent. Age, gender, IGF-1 concentrations, comorbidities, treatment modalities and PI were documented. Means and deviation scores were calculated. T-tests for unpaired groups were used for comparisons. P<0.05 was considered significant.

The MFI-20 inventory showed higher age- and gender-specific values on all fatigue subscales compared to controls (general and mental fatigue, decreased motivation and decreased activity), except physical fatigue, which was obviously higher only in patients under 60 years of age. No differences were observed between patients, dependent on disease activity, age, gender and PI.

**Physical complaints in different patient subgroups according to the GSI-24 inventory**

|  | E          | G         | J          | H         | GC          |
|--|------------|-----------|------------|-----------|-------------|
| Total (n= 124)                             | 8.6+/-5.8  | 3.6+/-3.7 | 9.3+/-5.5  | 4.2+/-3.8 | 25.7+/-15.8 |
| M (n=51)                                   | 8,4+/-5.2  | 3,1+/-2.6 | 8.3+/-5.1  | 3.5+/-3.2 | 23.3+/-12.9 |
| F (n=73)                                   | 8,8+/-6.2  | 3.9+/-4.3 | 9.9+/-5.6  | 4.7+/-4.1 | 27.4+/-17.3 |
| p (M, F)                                   | 0.65       | 0.20      | 0.11       | 0.08      | 0.16        |
| Controlled (C) (n=73)                      | 8.3+/-6.3  | 3.4+/-3.8 | 9.3+/-5.8  | 3.8+/-2.1 | 24.7+/-17.0 |
| Active (A) (n=49)                          | 9.2+/-5.1  | 3.7+/-5.1 | 9.2+/-4.9  | 5.0+/-3.7 | 21.1+/-13.8 |
| p (C/A)                                    | 0.43       | 0.59      | 0.92       | 0.07      | 0.43        |
| Disease duration ≤ 10 yrs (n=57)           | 8.0+/-5.1  | 2.5+/-2.2 | 7.6+/-4.9  | 3.4+/-3.0 | 21.7+/-12.0 |
| Disease duration >10 yrs (n=67) *          | 9.0+/-6.3  | 4.3+/-3.2 | 10.5+/-5.5 | 4.7+/-3.1 | 28.5+/-16.9 |
| p (≤10/>10 yrs)                            | 0.33       | 0.007     | 0.003      | 0.05      | 0.01        |
| Without pituit. insufficiency (wPI) (n=76) | 7.6+/-5.5  | 2.8+/-2.2 | 8.4+/-5.2  | 3.8+/-3.5 | 22.7+/-14.3 |
| With pituitary insufficiency (PI) (n=48)   | 10.3+/-5.9 | 4.8+/-4.4 | 10.7+/-5.6 | 4.9+/-4.1 | 30.6+/-16.8 |
| p (wPI/PI)                                 | 0.01       | 0.005     | 0.02       | 0.10      | 0.006       |
| Without medication (wM) (n=56)             | 7.5+/-5.1  | 3.2+/-2.4 | 8.8+/-5.5  | 3.9+/-3.5 | 23.4+/-14.1 |
| With medication (M) (n=68)                 | 9.6+/-6.2  | 3.8+/-3.9 | 9.6+/-5.1  | 4.5+/-3.9 | 27.6+/-16.7 |
| p (wM/M)                                   | 0.03       | 0.34      | 0.41       | 0.44      | 0.14        |

E-exhaustion; G-gastric complaints; J-joint complaints; H-heart complaints; GC-general complaints

\* In this group, patients were older (62.2+/-13.6 vs. 53.3+/-14.4 ys); however, 14/67 had an active disease compared to 35/57 patients with a disease duration ≤ 10 years (p&lt;0.001).

**Conclusion:** AP display more fatigue than healthy controls. Chronic subjective complaints are more pronounced in patients with a disease duration >10 yrs., PI and medication for disease control, irrespective of the hormonal activity status.