Prevalence and Predictors of Sleep Disturbances in an Italian Cohort of Patients with Myasthenia Gravis

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Background

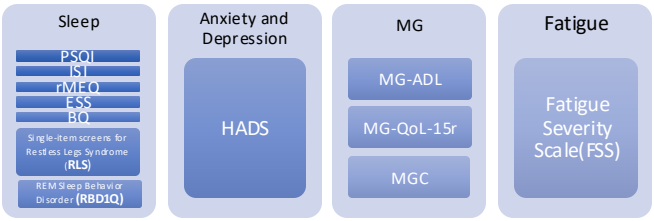
Myasthenia gravis (MG) is an autoimmune neuromuscular disorder caused by impaired neuromuscular transmission[1]. Previous studies have reported a variable prevalence of sleep disturbances among MG patients (24–64%), while the relationship between sleep parameters and disease outcomes remains unclear.[2-3].

Objectives

- investigating the prevalence of self-reported sleep disturbances in an Italian cohort of MG patients;
- exploring possible associations between such disturbances and MG outcome measures.

Materials

Cohort: 100 patients with AChRAb or MuSKAb-positive MG, who are being followed at the MG Clinic of Pisa University Hospital. Self-report questionnaires and following scales were administered:



Demographic and clinical data—including MG subtype and MGFA classification—were extracted from the medical records.

Methods

Descriptive statistics

Multivariate, linear or binomial modelling

- *To explore possible associations between sleep and circadian parameters (the dependent variables) and MG outcome measures.*

Analysis of only one MG outcome measure per model, alongside potential confounders

- *To avoid multicollinearity*
- *Potential confounders, such as severity of anxiety and depression, daily steroid dosage, age, and BMI*

Results

The **mean age** was 50 years (SD = 13), and the **mean BMI** was 28.9 (SD = 3.1). The cohort included 64 **females** (64%) and 46 **males** (46%).

Regarding the **immunological profile**, **87%** of patients were positive for anti *AChR* antibodies and **13%** for anti *MuSK* antibodies.

The MGFA clinical classification scores of our patient cohort at disease onset were as follows: Class I (9%), Class IIa (13%), Class IIb (28%), Class IIIa (1%), Class IIIb (32%), Class IVa (0%), Class IVb (11%), and Class V (6%)

A total of 43% of patients was **TAMG.**

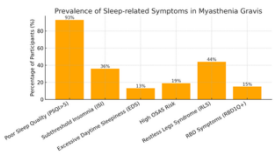
The **mean age at disease onset** was 41 years (SD = 15), and the **mean disease duration** was 10 years (SD = 9), indicating a middle-aged population with a long-standing disease course.

Specifically, EOMG patients accounted for 65%, LOMG for 32%, and JMG for 3% of the cohort.

The MGFA PIS at the last follow-up showed the following distribution: CSR in 3% of patients, PR in 5%, MM0 in 20%, MM2 in 1%, MM3 in 3%, I in 57%, U in 7%, and E in 3%. No patient experienced worsening or death

Clinical outcome measures reflected mild to moderate disease activity: the **mean MG-ADL score** was 2.59 (SD = 2.64), the **mean MG-QoL-15r score** was 4.9 (SD = 4.7), and the **mean MGC** score was 5.6 (SD = 5.0).

Treatment Type	% of Patients
Glucocorticoid	93%
Pyridostigmine	42%
Immunosoppressant	27%
Biological treatment	14%
IVIG chronic therapy	4%



In multiple regression model

- **Fatigue severity (FSS)** showed the strongest associations across all outcomes. Higher FSS scores were related to increased MG-QoL-15r ($p < 0.001$), MG-ADL ($p = 0.006$), and MGC ($p = 0.001$) scores.
- Higher **Epworth Sleepiness Scale (ESS)** scores were associated with higher MG-ADL ($p = 0.024$) and MGC ($p = 0.014$) values, suggesting that daytime sleepiness is linked to reduced functional performance and disease severity.
- Measures of **sleep quality (PSQI)** and **insomnia symptoms (ISI)** were related to higher MG-QoL-15r scores ($p = 0.045$ for both), but not to MG-ADL or MGC, implying that disrupted or insufficient sleep primarily affects perceived quality of life rather than objective or functional outcomes.
- A higher **risk of obstructive sleep apnea (OSAS)** was associated with increased **MG-ADL** scores ($p = 0.021$) and with **BMI** across all regression models ($p = 0.002$). The **presence of restless legs syndrome (RLS)** was also related to MG-ADL impairment ($p = 0.005$).
- The **daily glucocorticoid** dose was not predictive of variations in sleep-related measures (all $p > 0.05$)

Multiple Regression Models (MG-ADL)

Independent Variables		MG-ADL	dGC	HADS	Age	BMI	Adjusted R2 or AIC
PSQI	Beta	0.11	-0.01	0.19	0.02	0	0.234
	p-value2	0.2	0.5	<0.001***	0.3	>0.9	
ISI	Beta	0	-0.02	0.37	-0.03	0.01	0.186
	p-value	>0.9	0.8	<0.001***	0.5	0.5	
ESS	Beta	0.33	0.02	0.13	0.04	0.01	0.107
	p-value	0.024**	0.5	0.030**	0.11	0.5	
FSS	Beta	1.3	0.08	0.7	-0.1	-0.03	0.252
	p-value	0.006**	0.4	<0.001***	0.3	0.4	
rMEQ	Beta	-0.07	-0.03	-0.02	0.04	-0.02	0.044
	p-value	0.6	0.2	0.7	0.064	0.049*	
RLS	OR	1.3	0.99	1.13	0.98	1	122
	p-value	0.005**	0.8	0.002**	0.2	>0.9	
High OSAS Risk	OR	1.28	0.99	1.05	1.01	1.15	98.9
	p-value	0.021*	0.6	0.3	0.1	0.002**	
RBD1Q	OR	1.14	1.01	1.06	1	0.98	91.5
	p-value	0.2	0.8	0.2	0.9	0.7	

Multiple Regression Models (MG-QoL-15r)

Independent Variables		MG-QoL-15r	dGC	HADS	Age	BMI	Adjusted R2 or AIC
PSQI	Beta	0.13	-0.02	0.17	0.02	0	0.255
	p-value	0.045*	0.3	<0.001***	0.2	>0.9	
ISI	Beta	0.22	-0.04	0.3	-0.02	0.01	0.221
	p-value	0.045*	0.3	<0.001***	0.6	0.5	
ESS	Beta	-0.07	0.03	0.19	0.04	0.01	0.064
	p-value	0.4	0.4	0.003**	0.13	0.6	
FSS	Beta	1.4	-0.01	0.49	-0.01	-0.03	0.376
	p-value	<0.001***	0.9	0.008**	0.7	0.4	
rMEQ	Bet	-0.03	-0.02	-0.02	0.04	-0.02	0.042
	p-value	0.6	0.3	0.7	0.08	0.05	
RLS	OR	1.06	0.99	1.14	0.99	1	129
	p-value	0.3	0.5	<0.001***	0.4	0.9	
High OSAS Risk	OR	1.13	0.98	1.05	1.01	1.16	99.5
	p-value	0.054	0.5	0.3	0.054	0.001**	
RBD1Q	OR	1.03	1	1.07	1	0.99	92.8
	p-value	0.6	0.9	0.2	>0.9	0.7	

Multiple Regression Models (MGC)

Independent Variables		MGC	dGC	HADS	Age	BMI	Adjusted R2 or AIC
PSQI	Beta	0.01	-0.01	0.2	0.02	0	0.222
	p-value	0.8	0.5	<0.001***	0.3	>0.9	
ISI	Beta	-0.01	-0.02	0.37	-0.03	0.01	0.187
	p-value	0.8	0.7	<0.001***	0.5	0.5	
ESS	Beta	0.2	0	0.15	0.05	0.01	0.116
	p-value	0.014*	0.9	0.010*	0.061	0.5	
FSS	Beta	0.86	-0.03	0.76	-0.07	-0.03	0.279
	p-value	0.001**	0.8	<0.001***	0.5	0.4	
rMEQ	Beta	0	-0.03	0.03	0.04	-0.02	0.04
	p-value	>0.9	0.3	0.5	0.068	0.053	
RLS	OR	1.06	0.98	1.15	0.98	1	127
	p-value	0.11	0.3	<0.001***	0.4	0.9	
High OSAS Risk	OR	1.05	0.98	1.08	1.04	1.15	93.6
	p-value	0.4	0.5	0.093	0.093	0.002**	
RBD1Q	OR	1.05	1	1.07	1	0.99	92.3
	p-value	0.4	>0.9	0.12	>0.9	0.7	

Discussion and Conclusions

Self-reported sleep disturbances were highly prevalent in this Italian MG cohort. Different MG outcome measures were associated with partially distinct sleep disruption patterns, independent of demographic and clinical factors (ge, BMI, daily steroid dosage, anxiety and depression symptoms). In conclusion, integrating sleep assessment into MG management may help improve patient outcomes and overall well-being.

References
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