Sex differences in patients with obesity hypoventilation syndrome: Do they really exist?

Nissim Arish1 | Tom Mackay2 | Ruzanna Frangulyan2 | Renata L Riha2

1Pulmonary Institute, Shaare Zedek Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel
2The Department of Sleep Medicine, Royal Infirmary of Edinburgh, Edinburgh, UK

Correspondence
Nissim Arish, Department of Sleep Medicine, Shaare Zedek Medical Center, Jerusalem, Israel.
Email: narish@szmc.org.il

1 | INTRODUCTION

The International Classification of Sleep Disorders (ICSD-3) defines obesity hypoventilation syndrome (OHS) as the triad of obesity (body mass index [BMI] >30 kg/m²), daytime hypoventilation (PaCO₂ levels >45 mmHg), and sleep-disordered breathing in the absence of other neuromuscular, mechanical, and metabolic reasons for hypoventilation. Several studies have assessed the differences between male and female OHS patients. A study involving 144 patients revealed that OHS was more prevalent in women. Moreover, women had significantly more comorbidities, such as diabetes mellitus, hypertension, and hypothyroidism, than men. In another large, longitudinal cohort study from Sweden involving 1527 OHS patients under home mechanical ventilation, the female patients were reportedly older, more obese, and more hypercapnic than males. Emergency noninvasive ventilation (NIV) was more frequently performed for female than male patients. The 5-year survival rates of both sexes were similar. However, 21% of the male patients and 28% of the female patients were initially diagnosed with chronic obstructive pulmonary disease (COPD). Ideally, they should have been excluded from the cohort (according to ICSD-3).

This study aimed to assess the differences in clinical presentation, comorbidities, adherence to NIV, and prognosis between male and female OHS patients.

2 | METHODS

This was a retrospective, cross-sectional, and longitudinal review of OHS patients under an established cohort of “NIV patients” at the Department of Sleep Medicine at the Royal Infirmary of Edinburgh, Edinburgh (2004-2017). OHS was defined as obesity (BMI > 30 kg/m²) and daytime hypoventilation (PaCO₂ > 45 mmHg) on arterial blood gas breathing room air. Patients with other causes of type 2 respiratory failure, such as COPD (FEV1/FVC ratio < 70%), neuromuscular disorders, and chest wall disorders, were excluded.

The baseline demographics, clinical characteristics, and comorbidities, including diabetes mellitus, hypertension, cancer, and smoking history, were obtained from the records. Coronary vascular disease was defined as a history of angina pectoris or myocardial infarction. Heart failure was defined as having echocardiogram abnormalities or clinical symptoms consistent with heart failure, treated with two medications, such as diuretics and beta-blockers. Sleep parameters included the apnea-hypopnea index and Epworth sleepiness score questionnaire. The causes and number of hospital admissions and all-cause mortality were also recorded.

All procedures performed in this study, which involves human participants, were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

2.1 | Statistical analysis

Standard statistical analysis was performed using SPSS v. 22 (IBM). All tests were two-tailed, and the significance was set at P < .05.
RESULTS

The cohort consisted of 99 OHS patients, including 55 men and 44 women. The mean age at diagnosis was 54.7 (53.9 years for men; and 55.8 years for women). The characteristics of OHS patients according to sex are shown in Table 1. There were no significant differences between men and women regarding age, BMI, smoking history, baseline blood gas analysis on room air, cardiovascular comorbidities, number of hospitalizations, polysomnography results, and compliance with NIV. More males had coronary vascular disease, but this was not statistically significant. Women had more documented thromboembolic disease at presentation and during follow-up (P = .021). Seventeen patients died during the follow-up period. There was no significant difference in mortality between men and women during the follow-up (P = .15; see Figure 1).

DISCUSSION

Our study suggested no significant differences in OHS prevalence and clinical presentation between male and female patients. Reports in the literature regarding sex differences in OHS prevalence have been contradicting. BaHammam et al\textsuperscript{2} reported that OHS was approximately 3.5 times greater in women than men. However, our study and a previous study involving a Swedish cohort\textsuperscript{4} recorded similar prevalence rates. The patients in our cohort, particularly the females, were significantly younger than those of the other two studies (64.4, SD 11.2 years in the Swedish cohort\textsuperscript{4}; and 61.5, SD 11.9 years in the Saudi Arabian cohort).\textsuperscript{2} This likely contributed to the differences between the studies. Women diagnosed at an older age may have presented with more severe clinical parameters, such as greater obesity, more deranged blood gases, and more emergency admissions, as reported in the Swedish cohort, and more comorbidities reported in the cohort from Saudi Arabia.

Recent studies have suggested that OHS is more prevalent among postmenopausal women. This is partially explained by progesterone withdrawal during menopause, which reduces respiratory drive and respiratory pathway relaxation.\textsuperscript{4}

In our study, the mortality rate was 17%. This was similar to the mortality rates of 21.7% and 18.5% reported in Spanish\textsuperscript{5} and French\textsuperscript{6} cohorts, respectively. There were no differences in mortality between men and women who complied with NIV treatment (defined as mean usage time of 4 hours per night or greater), which was consistent with the results of the Swedish cohort.\textsuperscript{7} The study was limited due to its

| TABLE 1 | Demographic, medical and metabolic characteristics of men and women in the OHS cohort |
|---------|---------------------------------|-----------------|---------|
| Age (years) | 53.85 ± 10.4 | 55.64 ± 10.8 | .5 |
| BMI (kg/m\textsuperscript{2}) | 48.45 ± 10.1 | 52.16 ± 8.02 | .2 |
| PaO\textsubscript{2} (mmHg) | 56.9 ± 13.3 | 58.02 ± 12.2 | .6 |
| PaCO\textsubscript{2} (mmHg) | 58.05 ± 12.5 | 55.48 ± 6.64 | <.001 |
| HCO\textsubscript{3} | 31.65 ± 4.4 | 31.85 ± 3.6 | .12 |
| Death | 9 (16%) | 8 (18%) | .99 |
| Apnea/Hypopnea index (AHI) (events per hour of sleep) | 61.59 ± 40 | 64.72 ± 50 | .03 |
| Epworth sleepiness score (ESS) | 14.45 ± 6.6 | 14.43 ± 6.6 | .2 |
| Current smoking history | 29 (52%) | 16 (36%) | .59 |
| Type II diabetes | 23 (41%) | 17 (38%) | .84 |
| Hypertension | 35 (63%) | 28 (63%) | .99 |
| Coronary vascular disease (CVD) | 11 (20%) | 5 (11%) | .4 |
| Heart failure | 21 (38%) | 16 (36%) | .98 |
| Asthma | 11 (20%) | 8 (18%) | .98 |
| Pulmonary embolism | 4 (7%) | 11 (25%) | .021 |
| Hospitalization after diagnosis | 26 (47%) | 18 (40%) | .54 |
| Emergency NIV | 13 (23%) | 8 (18%) | .62 |
| Oxygen requirement with NIV | 20 (36%) | 17 (38%) | .84 |
| Compliance | 6.3 ± 2.5 | 5.7 ± 2.9 | .44 |
| IPAP | 17.3 ± 3.6 | 16.8 ± 3 | .1 |
| EPAP | 7.9 ± 1.7 | 7.2 ± 2.1 | .018 |

Abbreviations: BMI, body mass index; EPAP, expiratory positive airway pressure; HCO\textsubscript{3}, bicarbonate; IPAP, inspiratory positive airway pressure; NIV, noninvasive ventilation; OHS, obesity hypoventilation syndrome.
small sample size and retrospective data. However, this was a “real-life” cohort of patients prospectively treated and followed up in a single, large referral center. The sex differences reported in previous literature were likely caused by the delayed presentation or diagnosis of OHS in women within particular health services.

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CONFLICT OF INTEREST
The authors report no conflicts of interest in relation to this study.

AUTHOR CONTRIBUTIONS
Conceptualization: Nissim Arish, Renata L. Riha.
Data Curation: Ruzanna Frangulyan, Nissim Arish.
Manuscript Writing: Nissim Arish.
Supervision: Renata L. Riha, Tom Mackay.
Writing—Review and Editing: Nissim Arish, Renata L. Riha.
Writing: Nissim Arish.

I confirm that I had full access to all of the data in the study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT
I confirm that “manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the
study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID
Nissim Arish https://orcid.org/0000-0003-2187-3831

REFERENCES
1. Mokhlesi B. Obesity hypoventilation syndrome: a state-of-the-art review. Respir Care. 2010;55:1347-1362, discussion 1363.
2. BaHammam AS, Pandi-Perumal SR, Piper A, et al. Gender differences in patients with obesity hypoventilation syndrome. J Sleep Res. 2016 Aug;25:445-453.
3. International Classification of Sleep Disorders (ICSD-3).
4. BaHammam AS, Almeneessier AS. Is obesity hypoventilation syndrome a postmenopausal disorder? Open Respir Med J. 2019;13:51-54.
5. Ojeda Castillejo E, de Lucas Ramos P, López Martín S, Resano Barrios P, Rodriguez P, Morán L. Caicedo noninvasive mechanical ventilation in patients with obesity hypoventilation syndrome. Long-term outcome and prognostic factors arch. Bronconeumol. 2015;51:61-68.
6. Priou P, Hamel J-F, Person C, et al. Long-term outcome of noninvasive positive pressure ventilation for obesity hypoventilation syndrome. Chest. 2010;138:84-90.
7. Palm A, Midgren B, Janson C, Lindberg E. Gender differences in patients starting long-term home mechanical ventilation due to obesity hypoventilation syndrome. Respir Med. 2016;110:73-78.

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