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Temporal changes in blood biomarkers associated with sleep apnoea severity: a retrospective cohort study in Finland

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ABSTRACT

Introduction Obstructive sleep apnoea (OSA) is a common sleep disorder associated with breathing interruptions during sleep, often leading to oxygen level drops and sleep disturbances. OSA is known to impact various physiological parameters, including haematological and lipid profiles. This study aims to investigate the effect of continuous positive airway pressure (CPAP) therapy on laboratory values in patients with OSA.

Methods A retrospective study was conducted using data from Finland's largest hospital district, including 30 722 adult OSA patients treated between 2005 and 2020. A text search algorithm was implemented within the patient chart data to extract the apnoea-hypopnoea index (AHI) and the usage of CPAP therapy, along with identifying patients who had declined treatment. Haematological and metabolic laboratory values were collected 3 years before and after the first OSA diagnosis. Analysis of covariance was employed to compare parameter variations across severity levels, adjusted for age, sex and body mass index (BMI). T-test for repeated measurements was used to analyse the differences between data, 3 years prior and 3 years after the first OSA diagnosis.

Results The study of 30 722 OSA patients showed varying severity levels: 14.8% mild, 32.6% moderate and 52.6% severe, with an average diagnosis age of 55.0 years and a mean BMI of 32.4. The most clinically significant changes were observed in lipid profile markers, with improvements in cholesterol and low-density lipoprotein (LDL) levels (p value<0.05), measured before CPAP treatment initiation and after the treatment began. Conversely, glucose levels increased during the follow-up period. Similarly, haematocrit and haemoglobin decreased significantly after initiation of the CPAP treatment. In sex-specific analyses, significant improvements in cholesterol and LDL levels were found in both sexes. Triglyceride levels improved in male patients, in contrast with female participants, whose triglyceride levels increased during the follow-up period.

Conclusions CPAP therapy significantly improves cholesterol and LDL levels in both sexes and reduces haematocrit and haemoglobin levels. This study highlights the systemic effects of OSA and underscores the importance of evaluating haematological and lipid profiles in OSA management.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study includes a large cohort of over 30 000 obstructive sleep apnoea patients, with data available over a 15-year period.
⇒ The study used International Classification of Diseases and procedure codes and laboratory values in addition to a text search algorithm, ensuring data extraction on obstructive sleep apnoea severity, continuous positive airway pressure therapy use and comorbidities.
⇒ Apnoea-hypopnoea index and body mass index were measured only at the time of diagnosis.
⇒ The study design does not account for other interventions or medications that may influence laboratory values over time.

INTRODUCTION

Obstructive sleep apnoea (OSA) is a common sleep disorder marked by repeated interruptions in breathing due to the collapse of the airway during sleep, often leading to significant drops in oxygen levels and sleep fragmentation. The prevalence of OSA varies from 9% to 38% and is higher in men compared with women.[1 2] Nearly one billion people worldwide suffer from OSA, and a large proportion of patients remain undiagnosed and untreated, even in developed countries.[2 3]

OSA is not only a major cause of daytime sleepiness and cardiovascular risk but also implicated in systemic alterations that extend to haematological parameters,[4 5] along with lipid profile abnormalities.[6] Understanding how these parameters vary with different severity levels of OSA is important for elucidating the disorder's pathophysiology and clinical implications.

Studies have investigated how haematological parameters change across different severity levels of OSA showing that OSA severity, as measured by the apnoea-hypopnoea index (AHI), was negatively correlated with mean corpuscular volume

(MCV) and mean corpuscular haemoglobin (MCH), suggesting a dose-response relationship between hypoxia severity and erythropoietic responses.[7] Similarly, elevated red blood cell (RBC) count and haemoglobin levels were observed in individuals with more severe OSA, indicating a potential compensatory mechanism to enhance oxygen-carrying capacity.[8]

Moreover, OSA severity was associated with increased leucocytes and neutrophil count, indicating heightened systemic inflammation and immune activation in more severe cases of OSA.[9] Additional haematological parameters such as platelet count, MCH concentration (MCHC), haematocrit, red cell distribution width (RDW) and differential leucocyte counts (eg, basophils, eosinophils, monocytes and lymphocytes) have also been shown to vary across different OSA severity levels, further highlighting the systemic inflammatory and haematological changes associated with the disorder.[9–11]

Similarly, lipid profile abnormalities have been found to vary with OSA severity. Drager *et al* demonstrated that more severe OSA is associated with dyslipidaemia characterised by elevated total cholesterol, low-density lipoprotein (LDL), and triglycerides, as well as reduced high-density lipoprotein (HDL) levels.[12] Furthermore, haemoglobin A1c (HbA1c) levels, indicative of long-term glycaemic control, were found to increase with OSA severity, suggesting a potential link between OSA severity and metabolic dysfunction.[12]

Continuous positive airway pressure (CPAP) therapy is an effective treatment modality for OSA, and it has been shown to have various effects on patients' laboratory parameters. Studies have demonstrated that the use of CPAP therapy can impact haematological parameters, such as RBC counts, haematocrit and haemoglobin levels.[5 13] These earlier studies, including a meta-analysis of circulating lipids in 18 116 individuals[14] and the effect of CPAP treatment on lowering the circulating lipids in 1958 individuals, have provided insights into the detrimental effects of OSA on biomarkers and the possible mechanistic effects of CPAP, as it has been shown to lower total cholesterol and LDL levels while increasing HDL levels.[15]

Moreover, understanding how haematological and lipid profile parameters vary across different severity levels of OSA, and how these values change before and after initiating CPAP treatment, provides valuable insights into the pathophysiology of the disorder and its systemic effects. While previous research on the relationship between OSA and haematological/lipid profile parameters has often used small sample sizes and focused primarily on male participants, these studies have laid a solid foundation for further exploration. Moving forward, larger scale studies with diverse participant demographics are needed to thoroughly elucidate the associations between OSA severity, treatment with CPAP and these parameters across different population groups. This study aims to investigate the variations in haematological and metabolic laboratory parameters among patients diagnosed with OSA, correlating with the severity of the condition and before and after CPAP therapy in 30 722 individuals.

MATERIALS AND METHODS

A retrospective study was conducted using data from Finland's largest hospital district, HUS Helsinki University Hospital, encompassing 30 722 adult patients diagnosed with OSA treated between 1 January 2005 and 31 December 2020. Specifically, all relevant International Classification of Diseases (ICD) and procedure codes were retrieved from the hospital registry data during the follow-up period. OSA diagnosis was based on ICD-10 code G47.3 or E66.2 (Finnish version of the ICD-codes).

OSA diagnosis was based on polysomnography or polygraphy, as validated earlier.[16] As the registry data did not directly provide information of the severity of OSA, a text search algorithm was implemented within the patient chart data to extract the AHI, a metric endorsed by the American Academy of Sleep Medicine for categorising OSA severity into mild (5–15 events/hour), moderate (15–30 events/hour) and severe (>30 events/hour). Similarly, the text search algorithm was used in determining which patients had initiated CPAP therapy, along with identifying those who had declined treatment. Based on the procedure codes individuals whose treatment modality was an oral appliance for OSA were identified. Individuals who had declined CPAP treatment or had been treated with an oral appliance were excluded from the cohort. Consequently, the study population consisted of 30 722 individuals for whom CPAP therapy had at least been initiated and the severity of OSA could be determined. In addition, no information was available if patients were following a particular diet, so no inclusion or exclusion criteria were included based on diet. The demographic characteristics of the study population are presented in table 1.

In addition to ICD-code based data and data mining, laboratory values were collected from participants during the follow-up period (figures 1–2, online supplemental table 1). Laboratory values for cholesterol, LDL, HDL, triglycerides and glucose were collected at fasting state whereas other laboratory values also included non-fasting measurements.

The first OSA diagnosis was used as a reference point, and laboratory values 3 years before and 3 years after the date of diagnosis were examined. Given that measurements were not necessarily obtained precisely 3 years before and after, values spanning 1–5 years prior to diagnosis and 1–5 years postdiagnosis were collected, resulting in an average period of 3 years before and after diagnosis. In case of multiple measurements within this timeframe, their average was computed. The Tukey's IQR test was employed to identify outliers ensuring that the findings are not influenced by extreme values, thus providing a more

Table 1 Demographic characteristics of the study population

	All	Mild	Moderate	Severe
OSA (N)	30722	4561 (14.8%)	10011 (32.6%)	16150 (52.6%)
Age at diagnosis	55.0 (12.2)	53.2 (12.0)	55.4 (12.2)	55.3 (12.2)
BMI (mean, SD)	32.4 (6.1)	31.0 (6.0)	31.3 (5.9)	33.4 (6.0)
Male (N, %)	20612 (67.1)	2602 (12.6)	6235 (30.2)	11775 (57.1)
Age at diagnosis	53.8 (12.3)	51.9 (12.4)	53.9 (12.5)	54.12 (12.2)
BMI (mean, SD)	31.8 (5.7)	30.1 (5.4)	30.5 (5.3)	33.0 (5.7)
Female (N, %)	10110 (32.9)	1959 (19.4)	3776 (37.3)	4375 (43.3)
Age at diagnosis	57.6 (11.5)	54.9 (11.3)	57.8 (11.3)	58.6 (11.7)
BMI (mean, SD)	33.4 (6.6)	32.2 (6.6)	32.7 (6.5)	34.6 (6.6)
T1D (N, %)	474 (1.5)	81 (1.8)	147 (1.5)	246 (1.5)
T2D (N, %)	3504 (11.4)	495 (10.9)	937 (9.4)	2072 (12.8)
Hypertension (N, %)	7512 (24.5)	1038 (22.8)	2197 (21.9)	4277 (26.5)
IHD (N, %)	3672 (12.0)	529 (11.6)	1163 (11.6)	1980 (12.3)
CerebroVD (N, %)	1898 (6.2)	273 (6.0)	611 (6.1)	1014 (6.3)
Heart failure (N, %)	1731 (5.6)	250 (5.5)	467 (4.7)	1014 (6.3)
COPD (N, %)	1622 (5.3)	306 (6.7)	465 (4.6)	851 (5.3)

AHI, apnoea-hypopnoea-index; BMI, body mass index; cerebroVD, cerebrovascular diseases; COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease; OSA, obstructive sleep apnoea; T1D, type 1 diabetes; T2D, type 2 diabetes.

accurate representation of the underlying trends in the data.

The analysis of covariance (ANCOVA) was employed to compare the variation in laboratory values across different severity levels of OSA. The analysis was calculated for the full cohort and for male and female participants separately. All analyses were adjusted for sex (except sex-specific analysis) and age at OSA diagnosis. In addition to the previous covariates models adjusted for body mass index (BMI) were constructed. Additional analyses adjusted for OSA comorbidities, including type 1 diabetes, type 2 diabetes, hypertension, ischaemic heart disease, cerebrovascular disease, heart failure and chronic obstructive pulmonary disease were conducted. Continuous variables were normalised using inverse rank normalisation prior to analysis to ensure the appropriateness for the ANCOVA analyses. All p values reported are Bonferroni-adjusted (figures 1–2, online supplemental table 1).

To analyse temporal changes in haematological parameters, differences of the laboratory values were calculated 3 years prior and 3 years after the first OSA diagnosis (for individuals with available measurements for both time points), during which period the patients initiated CPAP therapy. Using a T-test for repeated measurements, analyses were calculated for the full cohort and for OSA severity levels separately and were repeated for males and female participants. All p values presented have been adjusted using the Bonferroni correction (figure 3, online supplemental table 2).

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

A total of 30722 patients with OSA were analysed with varying degrees of severity: 14.8% classified as mild, 32.6% as moderate and 52.6% as severe. The average age at the first OSA diagnosis across all severity levels was 55.0 years (SD 12.2). In terms of BMI, the mean value was 32.4 (SD 6.1). Individuals classified with severe OSA had a higher mean BMI of 33.4 (SD 6.0) compared with those with moderate or mild OSA (mean BMI 31.3, SD 5.9, mean BMI 31.0, SD 6.0, respectively, table 1).

The majority of individuals diagnosed with OSA were men, comprising 67.1% of the cohort. Male patients were generally diagnosed at a younger age, averaging 53.8 years (SD 12.3), in comparison to their female counterparts, who were diagnosed at an average age of 57.6 years (SD 11.5). Furthermore, there was a difference in BMI between the sexes, with male patients presenting a lower mean BMI of 31.8 (SD 5.7) versus a mean BMI of 33.4 (SD 6.6) observed in female patients (table 1).

Given that OSA frequently goes undiagnosed and hence untreated for years,[17] the analysis first focused on commonly measured laboratory values collected 3 years before the diagnosis was made, hypothesising that long-term undiagnosed OSA might lead to measurable changes in biochemical markers, even before

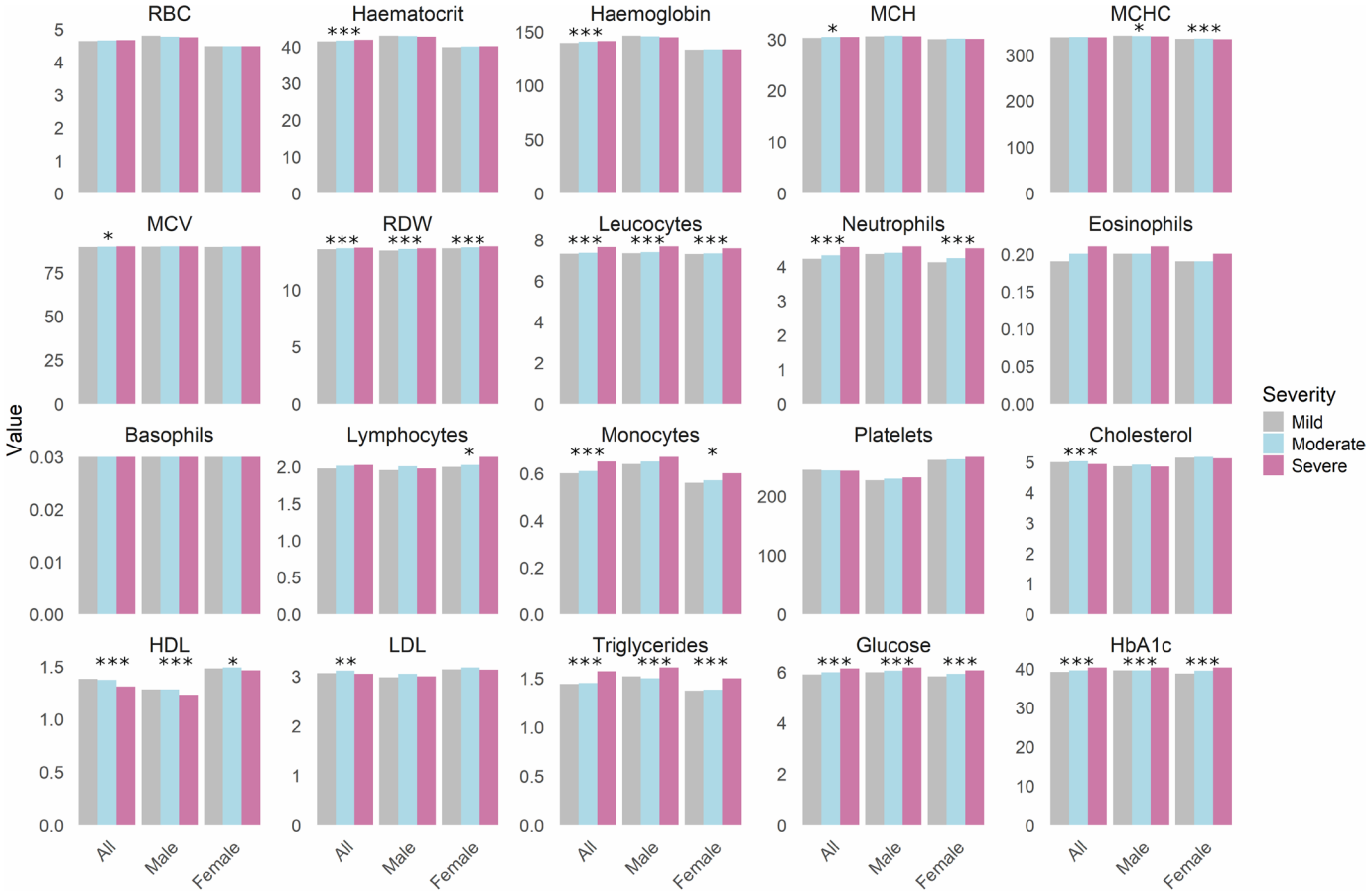

Figure 1 Measurements of haematological parameters 3 years prior to the first obstructive sleep apnoea (OSA) diagnosis. The analysis compares the differences between OSA severity groups per each laboratory value and has comparisons for the full cohort and for male and female participants separately. *Indicates if the result was statistically significant; Bonferroni-corrected p values; ***p value<0.001, **p value<0.01, *p value<0.05. HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MCH, mean corpuscular haemoglobin; MCHC, MCH concentration; MCV, mean corpuscular volume; RBC, red blood count; RDW, red cell distribution width.

diagnosis. Therefore, 20 laboratory values were examined including haematological and metabolic markers such as RBC (10^{12}/L), haematocrit (%), haemoglobin (g/L), MCH (picograms per cell), MCHC (g/L), MCV (fL), RDW (%), leucocytes (10^9/L), neutrophils (10^9/L), eosinophils (10^9/L), basophils (10^9/L), lymphocytes 10^9/L, monocytes (10^9/L), platelets (10^9/L), cholesterol (mmol/L), HDL (mmol/L), LDL (mmol/L), triglycerides (mmol/L), glucose (mmol/L) and HbA1c (%) obtained 3 years prior to the diagnosis of OSA to identify potential variations across different severity levels of the condition. Additionally, sex-specific analyses were conducted to explore potential differences in these associations (figure 1, online supplemental table 1). All analyses were adjusted for age and sex (unless sex-specific) and additionally a separate model was computed to include further adjustment for BMI, following a model adjusted for comorbidities (figure 1, online supplemental table 1).

Haematocrit, haemoglobin, MCH, MCV, RDW, leucocytes, neutrophils, monocytes, cholesterol, HDL, LDL, triglycerides, glucose and HbA1c levels differed significantly between the OSA severity groups (p value<0.05) while analysing the full cohort. The results remained constant after adjusting for BMI and comorbidities. In male participants, significant differences were found in MCHC, RDW, leucocytes, HDL, triglycerides, glucose and HbA1c levels, and the results remained similar after adjusting for BMI and comorbidities. In female participants, significant differences between the severity groups were found in MCHC, RDW, leucocytes, neutrophils, lymphocytes, monocytes, HDL, triglycerides, glucose and HbA1c levels, with a similar trend observed after adjusting for BMI and further for comorbidities, except for lymphocytes, where the difference was no longer significant after adjustment for comorbidities.

In a similar manner, an analysis was conducted on laboratory values obtained 3 years after the diagnosis of OSA and initiation of CPAP therapy. While analysing the full cohort significant differences were observed in various blood parameters including haematocrit, haemoglobin, MCH, MCV, RDW, leucocytes, neutrophils, eosinophils, monocytes, platelets, cholesterol, HDL, LDL, triglycerides, glucose and HbA1c levels across different severity levels (p value<0.05). These differences remained consistent after adjusting for BMI and comorbidities. In

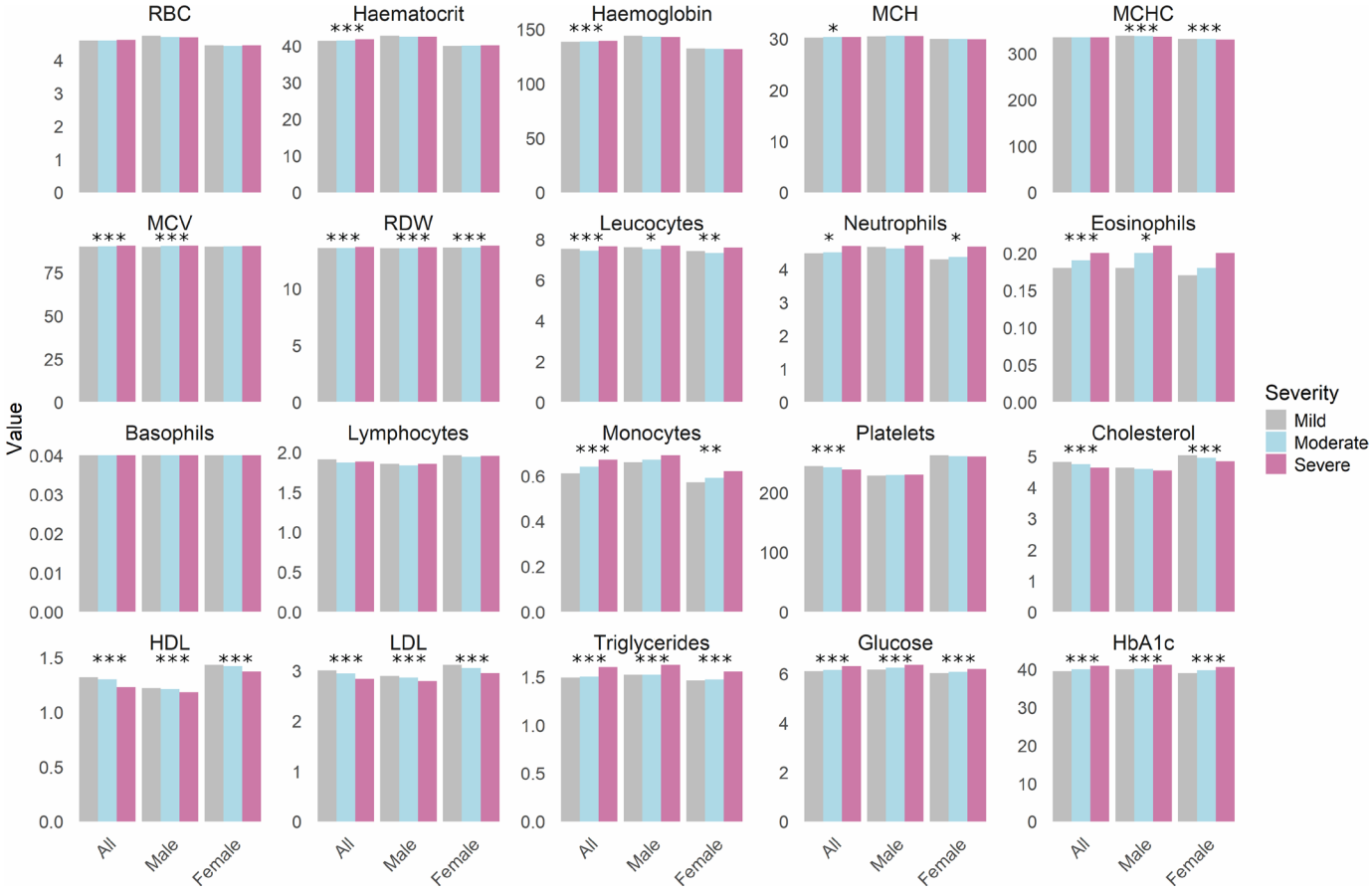

Figure 2 Measurements of haematological parameters 3 years after the first obstructive sleep apnoea (OSA) diagnosis. The analysis compares the differences between OSA severity groups per each laboratory value and has comparisons for the full cohort and for male and female participants separately. *Indicates if the result was statistically significant; Bonferroni-corrected p values; ***p value<0.001, **p value<0.01, *p value<0.05. HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MCH, mean corpuscular haemoglobin; MCHC, MCH concentration; MCV, mean corpuscular volume; RBC, red blood count; RDW, red cell distribution width.

male participants, significant differences were found in MCHC, MCV, RDW, leucocytes, eosinophils, HDL, LDL, triglycerides, glucose and HbA1c levels, and the results remained the same after adjustments. In female participants, significant differences between the severity groups were found in MCHC, RDW, leucocytes, neutrophils, monocytes, cholesterol, HDL, LDL, triglycerides, glucose and HbA1c levels with similar results after adjusting for BMI and further for comorbidities.

Differences in laboratory values were observed 3 years prior to the OSA diagnosis compared with those observed 3 years after the initiation of CPAP therapy. Furthermore, analyses were conducted separately for different severity levels of OSA followed by sex-specific analyses. When examining the full study cohort, statistically significant differences in the biomarker levels before and after OSA diagnosis for the following variables were identified: RBC, haematocrit, haemoglobin, MCH, MCHC, MCV, RDW, leucocytes, neutrophils, basophils, lymphocytes, monocytes, cholesterol, HDL, LDL and glucose levels (p value<0.05, figure 3, online supplemental table 2).

Additionally, the analysis was calculated separately for different severity groups. In the mild group, significant differences were found in RBC, haemoglobin, MCHC, MCV, RDW, leucocytes, basophils, cholesterol, HDL, LDL and glucose levels (p value<0.05). In the moderate group significant differences were found in RBC, haemoglobin, MCH, MCHC, MCV, RDW, neutrophils, basophils, lymphocytes, cholesterol, HDL, LDL and glucose levels (p value<0.05). In the severe group differences were found in RBC, haemoglobin, MCH, MCHC, MCV, basophils, lymphocytes, monocytes, cholesterol, HDL, LDL and glucose levels (p value<0.05).

A similar analysis was conducted in a sex-specific manner. Among male patients, significant differences were found in RBC, haematocrit, haemoglobin, MCH, MCHC, MCV, leucocytes, basophils, lymphocytes, monocytes, cholesterol, HDL, LDL, triglycerides and glucose levels (p value<0.05). In the mild group, significant differences were found in RBC, haematocrit, haemoglobin, MCHC, MCV, leucocytes, cholesterol, HDL, LDL and glucose levels (p value<0.05). In the moderate group significant differences were found in RBC, haemoglobin, MCHC, MCV, RDW, basophils, cholesterol, HDL, LDL and glucose levels (p value<0.05). In the severe group, significant differences were found in RBC, haemoglobin,

Figure 3 Results of a T-test for repeated measurements of the laboratory values 3 years prior and 3 years after the first obstructive sleep apnoea diagnosis. (a) The entire cohort is depicted, with different severity levels shown. (b) The male participants of the cohort are displayed alongside various severity levels. (c) The female participants are illustrated with different severity levels. The length of the bar presents the T-statistic and also shows the direction of the difference. Red colour indicates p value<0.05 and grey indicates a non-significant result. All p values are Bonferroni-corrected. HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MCH, mean corpuscular haemoglobin; MCHC, MCH concentration; MCV, mean corpuscular volume; RBC, red blood count; RDW, red cell distribution width.

MCH, MCHC, MCV, basophils, lymphocytes, monocytes, cholesterol, HDL, LDL, triglycerides and glucose levels (p value<0.05).

Among female patients, significant differences were found in RBC, haemoglobin, MCH, MCHC, MCV, RDW, basophils, lymphocytes, cholesterol, HDL, LDL, triglycerides and glucose levels (p value<0.05). In the mild group, significant differences were found in MCHC, MCV, RDW, basophils, cholesterol, HDL, triglyceride levels and glucose levels (p value<0.05). In the moderate group, significant differences were found in RBC, haemoglobin, MCH, MCHC, MCV,

RDW, basophils, cholesterol, HDL, LDL, triglycerides and glucose levels (p value<0.05). In the severe group, we found significant differences in RBC, haemoglobin, MCHC, MCV, RDW, basophils, lymphocytes, cholesterol, HDL, LDL, triglycerides and glucose levels (p value<0.05).

DISCUSSION

This study examined the impact of OSA severity on a broad spectrum of laboratory values, ranging from haematological to metabolic markers, before and after the diagnosis of OSA in a large patient cohort, and assessed how CPAP treatment influenced these markers over time, with a focus on sex-specific responses. This study is currently the largest single cohort that examines biomarker association and treatment response in OSA and has data from diagnosis, laboratory values and comorbid diseases of OSA. A robust association was identified between biomarkers and OSA including OSA severity and CPAP treatment. The findings are in line with earlier clinical data and additionally provide novel insight into how registry data from one large university hospital can capture clinically relevant associations and treatment effect on modifiable biomarkers.

OSA diagnosis can often be delayed for years, which is why an initial investigation was conducted to determine whether differences between severity levels could be detected even before a diagnosis was made.[17] Such approach is used with previous studies where biomarkers have been used as a screening tool for earlier diagnosis of OSA.[4 18] This study expands these studies by using data set almost twice the size of most previous studies. Moreover, the findings support the earlier findings of the role of metabolic and immune biomarkers in the aetiology of OSA.

Specifically, when examining the entire population prior to OSA diagnosis significant differences were observed in haematocrit, haemoglobin, MCH, MCV and RDW. These values were highest in severe cases of OSA suggesting possible compensating for decreased oxygen saturation and intermittent hypoxia—common in severe OSA—by producing more red blood cells to enhance oxygen transport and retention, hence the elevated haematocrit and haemoglobin levels.[8] Additionally, variations in MCV and MCH could indicate alterations in red blood cell morphology due to prolonged nocturnal oxygen deprivation, while changes in RDW possibly reflect an increased variability in red blood cell size, which often occurs in response to the stress of chronic hypoxia.[9–11] Similarly, leucocyte counts, including neutrophils and monocytes, were highest in cases of severe OSA. This increase may be attributed to the systemic inflammatory response triggered by the chronic and intermittent hypoxia characteristics of severe OSA. The frequent reductions in blood oxygen levels and subsequent reoxygenation lead to oxidative stress, which stimulates the immune system.[19] On the other hand, total cholesterol and LDL levels did not increase in correlation with the severity of OSA. This could be due to the fact that many patients are under medical treatment, using effective cholesterol-lowering medications. However, in the case of HDL, it was observed that levels were lower in severe cases of OSA. Earlier studies have discovered a similar association between immunological and metabolic biomarkers. For example, a meta-analysis across metabolic biomarkers and 107 datasets of OSA[14] showed a similar robust decrease in HDL and increase in triglyceride levels, similar to the findings in this study, with earlier evidence also highlighting a particular effect of AHI on triglyceride levels.[12] The study aligns with these earlier results and additionally provides insight into the complex relationship between comorbidities and the biomarker levels and the role of severity in biomarker levels.

Significant differences were observed prior to OSA diagnosis in both sexes, with the MCHC showing lower values in cases of severe OSA, while the RDW, leucocytes, triglycerides, glucose and HbA1c displayed higher values as the severity of OSA increased. HDL levels were also lower in severe OSA cases for both sexes. This finding was expected and aligns with earlier literature of OSA biology and metabolic biomarkers.[20] Significant values were observed exclusively in female participants for neutrophils, lymphocytes and monocytes. This finding could indicate a sex-specific response to OSA, suggesting that women might experience a different or more pronounced inflammatory response compared with men when suffering from severe OSA.[21]

Changes in laboratory parameters were observed approximately 3 years post-apnoea diagnosis across different severity levels of OSA. Many similarities were found in the values to those measured 3 years before the diagnosis, but there were also differences. MCV was significantly higher in men with severe OSA, possibly due to sex-specific physiological responses to hypoxia. Eosinophil counts were elevated significantly across the entire cohort and particularly in men. Conversely, lymphocyte counts did not display significant variations in women postdiagnosis, perhaps due to a potential stabilisation or adaptation to long-term CPAP therapy, whereas monocyte levels were altered only in female participants. However, understanding a full clinical response and possible sex specific treatment effects would benefit from being examined in future cross cohort meta-analyses and validation studies in sufficiently powered cohorts to provide insight into robustness across cohorts, different clinical settings and regions.

Platelet levels were lower in severe OSA cases across all individuals, linked to systemic inflammation and oxidative stress that may affect platelet production.[22] In lipid profiles, total cholesterol levels were significantly lower in women with severe OSA but not in men. Both sexes exhibited reduced LDL levels as OSA severity increased, potentially influenced by the use of cholesterol-lowering medications.

Laboratory values before and after the diagnosis of OSA were compared. All patients had at least initiated

treatment with CPAP. During the follow-up period a general decrease in RBC levels was observed across all participants. Haematocrit levels also decreased across the entire cohort, and specifically in men within the mild OSA group. Haemoglobin levels decreased in all groups except for women with mild OSA. MCH levels also declined during the follow-up and RDW showed a particular decrease in women. Conversely, leucocyte counts increased, with no significant rise observed in women. These findings may suggest that while CPAP therapy could generally improve certain blood parameters, its impact on others can be variable. The decrease in RBC, haematocrit, and haemoglobin levels may reflect an improvement in OSA-induced erythrocytosis, whereas the variable responses in leucocyte counts indicate differing immune responses between sexes.

The most clinically significant changes were observed in lipid profile markers, with improvements in cholesterol and LDL levels during the follow-up period. Although no increase in absolute HDL values was observed, a decrease in total cholesterol and LDL values was noted. Elevated cholesterol and LDL levels are significant risk factors for cardiovascular disease, so their reduction represents a substantial positive outcome of CPAP therapy. Conversely, glucose levels increased during the follow-up period. In sex-specific analyses, significant improvements in cholesterol and LDL levels were found in both sexes. This consistency suggests that CPAP therapy is effective in improving lipid metabolism across sexes, further supporting its role in reducing cardiovascular risk in OSA patients. However, triglyceride levels showed a different pattern: they improved in male patients but increased in female participants during the follow-up period. This divergence may indicate that women have a different metabolic response to CPAP therapy compared with men.

Limitations

These results are consistent with previous smaller studies, yet there are some limitations to this research. First, word search algorithms were used to extract data on CPAP use and OSA severity from medical records. This method might have overlooked relevant details, if CPAP use or AHI values were documented in formats not recognisable by the algorithm, potentially introducing data omissions. Second, while comprehensive metrics on CPAP use were not captured, information was gathered regarding patients who discontinued or returned their CPAP devices. This aspect might bias the analysis, implying that the study population could include individuals who did not consistently use their prescribed treatment. Third, AHI and BMI were measured solely at the diagnosis stage, presuming these values remained unchanged during follow-up. This assumption differs from the approach to laboratory values, which were measured at two separate points in time, providing a dynamic view of biochemical changes. Fourth, no information was available on medication purchases including antihypertensive and cholesterol-lowering drugs. Therefore, it is likely that some of the lower levels with circulating measures of metabolites seen after treatment are possibly influenced or modulated by lipid-lowering medication. Finally, the definition of AHI is based on the criteria that were in use during the year AHI was measured, which may result in slight variations in the AHI definition across different years.

CONCLUSIONS

CPAP therapy significantly improves cholesterol and LDL levels in both sexes, indicating a positive impact on lipid metabolism and a potential reduction in cardiovascular risk. Additionally, CPAP therapy reduces haematocrit and haemoglobin levels, suggesting improved oxygenation and a decrease in the compensatory response to chronic hypoxia. This study highlights the systemic effects of OSA, emphasising the importance of evaluating both haematological and lipid profiles in the management of OSA.

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Contributors MH: literature review, formal analysis, writing (original draft). TR: data curation. HMO: data collection, study design, data interpretation and writing. STS: data collection, study design. TV, HRK, TM: data collection, study design, writing (original draft) and writing (review and editing). SS: literature review, data collection, study design, formal analysis, methodology, writing (original draft) and writing (review and editing). All authors had final responsibility for the decision to submit for publication. SS had final responsibility for submission and is the guarantor.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The protocol of the retrospective study was approved by the Hospital District of Helsinki and Uusimaa (HUS/237/2021, §15). Principles outlined in the Declaration of Helsinki were followed. As this study was based on registry data, written informed consent was not required, as per applicable ethical guidelines.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data that support the findings of this study are available from Helsinki University Hospital but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Helsinki University Hospital.

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