Heliyon 10 (2024) e29270

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

# A case-control study on asthma and obese patients: Influence of lifestyle patterns, serum trace elements, heavy metals, and total antioxidants

Aswathi Pootheri [a], Wilner Martinez lopez [b], Radha Saraswathy [a,*]

[a] Department of Biomedical Sciences, School of Biosciences and Technology, Vellore Institute of Technology, Vellore, India
[b] Genetics Department, Instituto de Investigaciones Biológicas Clemente Estable, Avenida Italia 3318, 11600, Montevideo, Uruguay

ARTICLE INFO

*Keywords:*
Asthma
Obesity
Trace elements
Heavy metals
Oxidative stress
Total antioxidant status
Lifestyle

ABSTRACT

*Background and aim:* Asthma is a chronic airway hyperresponsiveness disorder and Obese people have greater rates of asthma incidence and prevalence. Obesity, a complex condition, can cause nutritional metabolic problems that change trace elements and minerals. Trace element and antioxidant levels affect asthma aetiology. In this study, we aim to determine the serum levels of trace elements Zn, Fe, Cu, Mg, Co, Ni, Pb, Cd, and Cr, total antioxidants (TAS), and lifestyle that determine specific clinical conditions in asthma and obesity patients from Vellore City (Tamil Nadu, India).

*Methods:* A case-control study to determine the level of the serum trace elements with 838 subjects (n = 242 asthma patients, n = 140 asthmatic obese, n = 185 obese patients, and n = 271 controls) between the ages of 20 and 60 years was carried out. Asthma was diagnosed based on the clinical examination and pulmonary function tests. Trace element levels were determined by atomic absorption spectrophotometry (AAS) in serum, and a DPPH-free radical scavenging assay was used to determine the total antioxidant capacity level in serum.

*Result:* In asthma male patients, serum levels of Zn, Fe, Cu, Mg, and TAS were significantly lower and Pb, Cd, and Cr significantly higher, whereas in female asthma patients, serum levels of Zn, Fe, Mg, and TAS were significantly lower and Pb significantly higher. In asthmatic obese male patients, Fe, Cu, and TAS were significantly lower, and Pb, Cd, and Co were significantly higher; in asthmatic obese female patients, Zn, Fe, Cu, Mg, and TAS were significantly lower, and Ni was significantly higher. In obese male patients, Zn, Fe, Cu, and TAS were significantly lower and Cd was significantly higher, and in obese female patients, Zn, Fe, Cu, Mg, and TAS were significantly lower.

*Conclusion:* The influence of the level of trace elements, heavy metal, total antioxidant, and the lifestyle patterns, may increase the risk of asthma and obesity.

## 1. Introduction

Asthma is a chronic respiratory condition. The respiratory symptoms like wheeze, chest tightness, cough and shortness of breath that vary in intensity with reduced expiratory airflow is said to be asthma [1]. The most frequent co-morbidity of asthma is obesity,

* Corresponding author.
*E-mail address:* radhasaraswathy@vit.ac.in (R. Saraswathy).

https://doi.org/10.1016/j.heliyon.2024.e29270
Received 25 December 2023; Received in revised form 28 March 2024; Accepted 3 April 2024

which has been linked to a higher risk of asthma attacks, severe respiratory symptoms, and inadequate management [2].

Recent years have shown an increase in the incidence of asthma [3], and having frequent asthma attacks can lower the quality of life [4]. Around 350 million people worldwide suffer from asthma, which accounts for about 350,000 fatalities annually [5]. The impact of various factors such as family history, occupation, climate change and pollution are possible risk factors for asthma. A lot of prospective research demonstrates that obesity is an asthma risk factor and has shown a connection between body mass index and the emergence of asthma. Obesity may impact asthma in two different ways. Initially, pro-inflammatory adipokines in the blood of obese people may cause or exacerbate airway inflammation, which in turn can lead to airway hyperresponsiveness or asthma. Secondly, the extra accumulation of tissue in the thoracic wall and abdominal area puts pressure on the respiratory tract, which might change how sensitive the airways were or directly worsen symptoms [6,7].

Asthma symptoms are managed through a range of medications and lifestyle measures, and attacks may be prevented by using inhaled corticosteroids and avoiding specific asthma triggers. Meanwhile, asthma was frequently associated with other co-morbidities such as allergic rhinitis [8]. It is well-documented that the impact of oxidative stress, environment, and specific genetic characteristics are possible risk factors for developing asthma [5,9].

Trace elements are the essential micronutrients that exist or present in human in a very low concentration. They play a vital role in physiological and biochemical processes and is a key for actual functioning of immune system and acts mainly as components of enzymes and vitamins [10–12]. Trace element imbalances negatively affect biological process and are associated with diseases such COPD [13,14]. Studies reported that the deviation of trace elements may be involved in the pathogenesis of asthma patients. Currently, many studies have been conducted to investigate the serum concentration of trace elements antioxidant mechanisms in asthma patients in comparison to controls [3,8].

Obesity is a chronic disease that affects millions of people worldwide. It is characterized by an abnormal or excessive accumulation of fat in the body, which can lead to various health problems. However, the relationship between trace element exposure levels and obesity is still inconclusive. For instance, some studies have shown that obese patients have a low intake of iron and zinc in their diets. Although several studies have shown that obesity alters micronutrient status, characterized by an increased accumulation of toxic elements and deficiencies of essential micronutrients, the existing evidence is still contradictory [15]. Demands for trace elements and minerals change with sex, age, metabolic demand, and lifestyle. Due to excessive energy consumption and a resulting insufficient dietary intake of trace elements and minerals, micronutrients in obese individuals are being analysed. Hidden hunger refers to this discrepancy between the intake of trace elements and minerals and the use of energy. As a result, the overweight population is the major demographic impacted by hidden hunger, since some studies have previously shown that the trace elements and minerals in the obese population alter because of poor food quality consumption [16,17].

The trace elements influence the antioxidant defence with the help of enzymes. The effect of free radicals is reduced by antioxidants [10,11,18]. The occurrence of oxidative stress is mainly in the support of oxidants when there is an imbalance. Oxidative stress may cause lung damage by exceeding to secondary metabolic ROS (Reactive oxygen species) [12,19,20]. Recent studies indicate that disturbances in pro-oxidant/antioxidant balance play a critical role in the pathogenesis of obesity and its related complications. Overproduction of reactive oxygen (ROS) and nitrogen (RNS) species alters cellular metabolism and signalling pathways Moreover, oxidative stress leads to the development of chronic inflammation in the adipose tissue [21].

Trace elements can damage blood vessel walls and indirectly contribute to hypertension by affecting the synthesis of certain enzymes and proteins, such as Nitric oxide synthase (NOS**)** and Superoxide dismutase (SOD). It is still debatable, nevertheless, how certain components affect blood pressure regulation. The intricate relationships between these trace elements and blood pressure require more investigation to be completely understood. The incidence and development of cerebral blood vessels in the heart have been linked to an imbalance of metals including cobalt, zinc, copper, and magnesium, according to some studies [22].

Previous studies have reported that environmental heavy metals' potential health hazards are well known and the adverse effects of exposure to lead, mercury and cadmium have been of concern for more than twenty years. Asthma risk is increased by hazardous environmental factors and poor socioeconomic position, as well as by substandard housing's increased potential of toxic heavy metals [8].

The aim of this study is to determine the trace elements levels of Zinc (Zn), iron (Fe), copper (Cu), magnesium (Mg), Nikel (Ni), Lead (Pb), cadmium (Cd), chromium (Cr), Cobalt (Co) and Total antioxidant status (TAS), and lifestyle habits that determine specific clinical conditions in asthma and obesity patients. This study is to understand the function of various trace elements significance in the pathophysiology of asthma by examining their presence in the serum levels of asthma patients. This will provide differences between individuals with asthma and healthy individuals.

## 2. Materials and methods

### *2.1. Subjects*

The samples for case-control study were recruited from the Department of Asthma and Allery, Nalam Medical centre and Hospital, Vellore, Tamil Nadu, India between January 2021 to May 2023. Total 838 Subjects (n = 121 asthma male patients and n = 121 asthma female patients; n = 61 asthmatic obese male patients and n = 79 asthmatic obese female patients; n = 99 obese males and n = 86 obese females; n = 151 control males and n = 120 control females) between the ages of 20 and 60 years were included for this study. All recruited participants are belonging to Asian ethnic backgrounds.

The study protocol was approved by Nalam medical centre and hospital (NMCHEC0006) and Vellore Institute of Technology (VIT/IHCH/X/2021/03) Institutional Human Ethical committees. The signed informed consent written in the local language was obtained

**Table:1**
Working conditions (Variable) of air-acetylene flame-atomic absorption spectrophotometry.

| Trace elements | Working condition Variables | | | Atomic absorption | | | | Flame emission | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Wavelength nm | Slit width nm | Optimum working range ul/ml | Lamp current | Fuel | Support | Flame stoichiometry | Wave length nm | Slit width | Fuel | Support |
| Zn | 360.1 | 0.2 | 10–2000 | 20 mA | Acetylene | Nitrous oxide | Reducing; red cone 1.5–2 cm | 360.1 nm | 0.1 nm | acetylene | Nitrous oxide |
| Fe | 248.3 | 0.2 | 0.06–15 | 5 mA | acetylene | Air | Oxidizing | 372.0 nm | 0.1 nm | acetylene | Air |
| Cu | 324.7 | 0.5 | 0.03–10 | 4 mA | acetylene | Air | Oxidizing | 327.4 nm | 0.1 nm | acetylene | Nitrous oxide |
| Mg | 285.2 | 0.5 | 0.003–1 | 4 mA | acetylene | Air | Oxidizing | 285.2 nm | 0.1 nm | acetylene | Nitrous oxide |
| Ni | 232.0 | 0.2 | 0.1–20 | 4 mA | acetylene | Air | Oxidizing | 341.5 nm | 0.1 nm | acetylene | Nitrous oxide |
| Pb | 217.0 | 1.0 | 0.1–30 | 5 mA | acetylene | Air | Oxidizing | 4.5.8 nm | 0.1 nm | acetylene | Nitrous oxide |
| Cd | 228.8 | 0.5 | 0.02–3 | 4 mA | acetylene | Air | Oxidizing | 326.1 nm | 0.1 nm | acetylene | Nitrous oxide |
| Cr | 357.9 | 0.2 | 0.06–15 | 7 mA | acetylene | Air | Reducing | 425.4 nm | 0.1 nm | acetylene | Nitrous oxide |
| Co | 240.7 | 0.2 | 0.05–15 | 7 mA | acetylene | Air | Oxidizing | 345.nm | 0.1 nm | acetylene | Nitrous oxide |

from both the patients and controls were obtained before sample collection.

### 2.2. Questionnaires

The diagnosis of bronchial asthma was established in the presence of clinical symptoms when pulmonary function test showed a reversible airflow obstruction or a positive unspecified bronchial provocation test. For allergy skin test, the substances contributing to asthma and allergy symptoms which is clinically confirmed were included. In Anthropometric measurement, Body Mass Index (BMI) was calculated using the formula weight in kilograms divided by square of height in meter. According to the Asia Pacific Guidelines for BMI Classification, those with a BMI of more than 25 were classified as obese (WHO, 2000).

The controls are free from asthma with no background of asthma and family history. Inclusion criteria, clinically confirmed asthma cases, age of above 20–60 years. Exclusion criteria, HIV patients, unwilling to give consent, pregnant and breast-feeding women, patients who are in antibiotics and patients with other diseases were excluded from the study. From each participant such as gender, age duration of disease, onset age of diseases, Blood pressure (BP) occupation, habitant, clinical characteristics and family history, triggers, medication, physical activities, diet, and lifestyle habits of the individuals was recorded. In lifestyle.

In addition, the questionnaires on smoking habits, quantities of consumed cigarettes, drinking habits, quantities of consumed alcohol beverages, tobacco use, dietary pattern and physical activity were performed. The consumed quantities of alcohol, smoking, tobacco, dietary intake, and physical activities were calculated based on daily, weekly, and monthly.

### 2.3. Sample collection and separation of serum

Approximately 2 ml of human peripheral blood sample was collected in Ac Cuvet Clot Activator tube from each individuals (patients and controls). The tubes were centrifuged at 1000 rotating per minute (RPM) 5 min (REMI Centrifuge C 854/8). Serum was extracted from the collected samples after centrifugation and then the serum samples kept at - 20°C in metal-free plastic test tubes for assay. The serum samples were then brought at room temperature prior use for analysis.

### 2.4. Analytical methods used in this study

#### 2.4.1. Flame-atomic absorption spectrophotometry

The concentrations of trace elements were measured using an atomic absorption spectroscopy method. As soon as the sample is in the right form, elemental determination is quick and precise. It is a delicate, precise technique that only allows for the simultaneous detection of one element. In this study serum trace elements levels Zn, Fe, Cu, Mg, Ni, Pb, Cd, Cr, and Co was analysed by air-acetylene flame-atomic absorption spectrophotometry (AAS; VARIAN AA240) working conditions (Variable) tabulated in Table 1.

Standard concentrations of metals prepared in 100 ml of standard flask as follows by serial dilution from 1000 parts per million ppm and added 1 mL of high purity nitric acid. Then the working standard solution were prepared from stock by the serial dilution technique,2 ppm 4 ppm,6 ppm,8 ppm, 10 ppm for each element. Serum metal analysis was done by dilution 0.5 ml of serum mixed with 9.5 ml of sterile MilliQ Water and total serum metal levels were estimated by AAS [14] in Technology Business Incubator (TBI) Laboratory, Vellore Institute of Technology, Vellore. The unknown concentration of the trace elements was determined from the standard curve.

### 2.5. DPPH free radical scavenging assay

Total antioxidant status (TAS) was determined with 2,2-Dipheny 1-1-picryl-hydrazyl (DPPH) free radical scavenging assay. The method was developed by Blois in the year 1958 to determine the antioxidant activity [23]. Working concentration of Ascorbic Acid standards of 1–10 $\mu$ M was prepared make up to 100ul with milliqu water and was treated with 0.1 mM 900ul DPPH and negative controls standard without ascorbic acid. Ascorbic acid (potent antioxidant) of different concentration was considered as standard to calculate percentage of free radical scavenging capacity. Deproteinization of serum sample 200ul of acetonitrile should be added to 100ul of serum and incubate for 5mins at room temperature. The tubes were centrifuge at 1500 rpm for 5mins.Supernatant should be collected in fresh tube and triplicates were made supernatant should be used for DPPH assay and then 100ul of serum sample was added with 900ul of 0.1 mM DPPH solution in a 2 ml micro-centrifuge tube and incubate the sample for 30mins in dark at room temperature and negative control 100ul of acetonitrile and 900ul of DPPH without serum sample. Measurements of TAS were performed on UV spectrophotometer, absorbance at 517 nm the antioxidant activity was determined by monitoring the decrease in the absorbance. Result can be reported as the percentage scavenging potential or in ascorbic acid equivalent. Percentage of scavenging potential is calculated by the mentioned formula, % of scavenging potential = (1-(sample absorbance/negative control absorbance) *100.

### 2.6. Statistical analysis

The statistical analysis for case-control study was performed by GraphPad and Pearson's correlations coefficient calculator. serum level trace elements were analysed by Unpaired student's t-test. Test of normality were Shapiro-Wilk. Subjects were classified into four groups like asthma, asthmatic obese, obese, controls, and analysed further among same genders for each group, compared with control males and females. Difference in age, height, weight BMI, serum levels of trace elements and TAS were analysed by unpaired student's

t-test.

Pearson's correlations were used for correlation studies to correlated parameters such as Systolic BP, Diastolic BP, BMI, and TAS with trace elements. Linear regression analysis was performed to examine the relationship of serum trace elements with clinical characteristics such as Systolic BP, Diastolic BP, BMI, and TAS in patients, with baseline characteristics as dependent variable and serum trace elements as independent variables. Systolic and Diastolic BP, BMI, duration of disease, and TAS were considered as confounding factors when examining association among patients, serum levels of trace elements. All the p-value of $<0.05$ was considered as statistically significance.

## 3. Results

### 3.1. Demographics characteristics and anthropometric measurements

Table 2, represent the demographic characteristics and anthropometric measurements of asthma patients, asthmatic obese patients, and obese patients compared with the control group. In asthma patient males mean age and height showed statistically significant differences when compared to control males, and in asthma patient females, the height was statistically significant when compared to control females and asthma patient male and females Systolic BP showed statistically higher when compared controls ($p < 0.05$). In asthmatic obese, male patients mean age, weight, and BMI showed statistically significant differences when compared to control males, and in females, all four factors showed significance ($p < 0.05$). All four factors in obese male patients showed a statistically significant difference ($p < 0.05$), and in obese female patients, the mean age showed no significant difference ($p > 0.05$).

Table 3 shows the lifestyle habits of asthma, asthmatic obese, obese patients, and controls. Most of the patients and controls belong to urban communities. The quantities of cigarettes, tobacco use, and alcohol consumption were greater in male patients when compared to control males. In occupation, control males and females involved in professional careers, and in patients, most of them were housewives, company workers, and laborers. Males tended to be more physically active than females in both control and patients.

Table 4 shows the serum levels of trace elements in asthma patients and controls. In asthma patient males, the serum levels of Zn, Fe, Cu, Mg, and TAS were significantly lower than control males, $p = 0.0050$, $p = 0.0457$, $p = 0.006$, $p = 0.008$, and $p = 0.0001$ ($p < 0.05$). The serum levels of Pb, Cd, and Co were found to be statistically higher $p = 0.009$, and $p = 0.026$ ($p < 0.05$) when compared to control males. In asthma patient females, serum levels of Zn, Fe, and Mg $p = 0.001$ $p = 0.003$ $p = 0.000$ and $p = 0.0001$ were found to be significantly lower than control females ($p < 0.05$). The serum levels of Pb were significantly higher, than in asthma patient females $p = 0.002$ ($p < 0.05$). There was no significant difference in the serum levels (Ni and Co) in asthma patient males and (Cu, Ni, Cd, Cr and Co) in asthma patient Females ($p > 0.05$).

Table 5 presents the serum levels of trace elements in asthmatic obese patients and controls. In asthmatic obese patient males, the serum levels of Fe, Cu, and TAS were significantly lower than control males $p = 0.037$ $p = 0.002$ and $p = 0.003$($p < 0.05$). Serum levels of Pb, Cd, and Co were significantly higher than in control males $p = 0.004$, $p = 0.000$ and $p = 0.025$, ($p < 0.05$). In asthmatic obese patient females, Zn, Fe, Cu, Mg, and TAS were found to be significantly lower than in control females $p = 0.000$ $p = 0.008$ $p = 0.001$ p

**Table 2**
Demographics characteristics and Anthropometric measurements of asthma, asthmatic obese, obese patients, and controls.

| Factors | Asthma patient Males n = 121 | Control Males n = 151 | P value | Asthma patient Females n = 121 | Controls Females n = 120 | P value |
|---|---|---|---|---|---|---|
| Mean Age (yrs) | 39.63 ± 16.13 | 34.50 ± 11.44 | 0.002* | 33.81 ± 13.57 | 32.95 ± 10.16 | 0.578 |
| Weight (Kg) | 58.33 ± 11.63 | 60.09 ± 10.46 | 0.1910 | 54.95 ± 8.59 | 54.47 ± 8.14 | 0.656 |
| Height (m) | 137.68 ± 59.57 | 163.20 ± 8.49 | 0.0001* | 129.86 ± 61.24 | 158.31 ± 7.58 | 0.000* |
| BMI (kg/m2) | 21.81 ± 3.34 | 22.49 ± 3.05 | 0.0809 | 22.08 ± 3.28 | 21.75 ± 3.15 | 0.429 |
| Systolic BP | 126.39 ± 15.25 | 121.17 ± 12.74 | 0.002* | 124.03 ± 14.18 | 120.33 ± 13.02 | 0.033* |
| Diastolic BP | 80.88 ± 9.92 | 79.35 ± 10.72 | 0.222 | 79.51 ± 10.84 | 79.99 ± 9.05 | 0.705 |
| Factors | Asthmatic obese Males n = 61 | Control Males n = 151 | P value | Asthmatic obese patient Females n = 79 | Controls Females n = 120 | P value |
| Mean Age (yrs) | 41.39 ± 13.39 | 34.50 ± 11.44 | 0.0004* | 37.24 ± 10.73 | 32.95 ± 10.16 | 0.004* |
| Weight (Kg) | 85.00 ± 14.07 | 60.09 ± 10.46 | 0.0001* | 74.80 ± 12.12 | 54.47 ± 8.14 | 0.000* |
| Height (m) | 161.36 ± 8.85 | 163.20 ± 8.49 | 0.179 | 154.23 ± 7.72 | 158.31 ± 7.58 | 0.000* |
| BMI (kg/m2) | 32.76 ± 5.41 | 22.49 ± 3.05 | 0.0001* | 31.42 ± 5.16 | 21.75 ± 3.15 | 0.000* |
| Systolic BP | 123.77 ± 18.47 | 121.17 ± 12.74 | 0.249 | 122.29 ± 13.59 | 120.33 ± 13.02 | 0.301 |
| Diastolic BP | 81.96 ± 11.69 | 79.35 ± 10.72 | 0.1275 | 80.21 ± 13.07 | 79.99 ± 9.05 | 0.680 |
| Factors | Obese Males n = 99 | Control Males n = 151 | P value | Obese Females n = 86 | Controls Females n = 120 | P value |
| Mean Age (yrs) | 38.17 ± 10.41 | 34.50 ± 11.44 | 0.0102* | 32.94 ± 7.45 | 32.95 ± 10.16 | 0.996 |
| Weight (Kg) | 87.96 ± 16.71 | 60.09 ± 10.47 | 0.0001* | 81.74 ± 17.16 | 54.47 ± 8.14 | 0.000* |
| Height (m) | 159.40 ± 9.48 | 163.20 ± 8.49 | 0.0010* | 154.71 ± 7.37 | 158.31 ± 7.58 | 0.001* |
| BMI (kg/m2) | 34.82 ± 8.06 | 22.49 ± 3.05 | 0.0001* | 34.22 ± 7.97 | 21.75 ± 3.15 | 0.000* |
| Systolic BP | 121.33 ± 14.19 | 121.17 ± 12.74 | 0.928 | 122.47 ± 13.62 | 120.33 ± 13.02 | 0.278 |
| Diastolic BP | 78.83 ± 11.34 | 79.35 ± 10.72 | 0.722 | 79.42 ± 11.32 | 79.99 ± 9.05 | 0.957 |

Student's *t*-test $P < 0.05$.

**Table 3**
Lifestyle habit of asthma, asthmatic obese, obese patients, and controls.

| Factors | Control Males n = 151 | Controls Females n = 120 | Asthma patient Males n = 121 | Asthma patient Females n = 121 | Asthmatic obese patient Males n = 61 | Asthmatic obese patient Females n = 79 | Obese patient Males n = 99 | Obese patient Females n = 86 |
|---|---|---|---|---|---|---|---|---|
| **Habitat** | | | | | | | | |
| Rural | 48(31.7 %) | 53(44.1 %) | 27(22.3 %) | 43(35.5 %) | 19(31.1 %) | 33(41.7 %) | 12(12.1 %) | 27(31.3 %) |
| Urban | 103(68.2 %) | 67(55.8 %) | 94(77.6 %) | 78(64.4 %) | 42(68.8 %) | 46(58.2 %) | 87(87.8 %) | 59(68.6 %) |
| **Ethnicity Group** | | | | | | | | |
| South India | 149(98.6 %) | 120(100 %) | 119(98.3 %) | 120(100 %) | 61(100 %) | 78(98.7 %) | 99(100 %) | 85(98.8 %) |
| North India | 2(1.3 %) | 0(0 %) | 2(1.6 %) | 0(0 %) | 0(0 %) | 1(1.2 %) | 0(0 %) | 1(1.1 %) |
| **Education** | | | | | | | | |
| Nil | 2(1.3 %) | 3(2.5 %) | 9(7.4 %) | 11(9.0 %) | 4(6.5 %) | 3(3.7 %) | 4(4.0 %) | 2(2.3 %) |
| Less than class 10 | 28 (18.5 %) | 18(15 %) | 36(29.7 %) | 31(25.6 %) | 16(26.2 %) | 22(27.8 %) | 20(20.2 %) | 18(20.9 %) |
| 10 + 2 | 26(17.2 %) | 19(15.8 %) | 17(14.0 %) | 39(32.2 %) | 18(29.5 %) | 14(17.7 %) | 27(27.2 %) | 22(25.5 %) |
| Graduates | 62(41.0 %) | 64(53.3 %) | 31(25.6 %) | 21(17.3 %) | 12(19.6 %) | 24(30.3 %) | 28(28.2 %) | 27(31.3 %) |
| Post Graduates | 30(19.8 %) | 12(10 %) | 18(14.8 %) | 11(9.09 %) | 9(14.7 %) | 11(13.9 %) | 14(14.1 %) | 10(11.6 %) |
| Others | 3(1.9 %) | 4(3.3 %) | 10(8.2 %) | 8(6.6 %) | 2(3.2 %) | 5(6.3 %) | 6(6.0 %) | 7(8.1 %) |
| **Cigarette Smoking** | | | | | | | | |
| Never Smokers | 110(72.8 %) | 117(97.5 %) | 66(54.5 %) | 120(99.1 %) | 28(45.9 %) | 77(97.4 %) | 65(65.6 %) | 80(93.0 %) |
| Daily(n) | 30(19.8 %) | 0(0 %) | 44(36.3 %) | 0(0 %) | 27(44 %) | 0(0 %) | 30(30.3 %) | 0(0 %) |
| Weakly (n) | 9(5.9 %) | 0(0 %) | 5(4.1 %) | 0(0 %) | 6(9.8 %) | 0(0 %) | 4(4.0 %) | 0(0 %) |
| Occasionally(n) | 2(1.3 %) | 3(2.5 %) | 6(4.9 %) | 1(0.8 %) | 0(0 %) | 2(2.5 %) | 0(0 %) | 3(3.4 %) |
| **Pan masala** | | | | | | | | |
| Never | 144(%) | 120(%) | 106(%) | 119(%) | 57(%) | 79(%) | 96(%) | 85(%) |
| Daily | 2(1.3 %) | 0(0 %) | 6(4.9 %) | 0(0 %) | 0(0 %) | 0(0 %) | 0(0 %) | 0(0 %) |
| Weakly | 3(1.9 %) | 0(0 %) | 4(3.3 %) | 0(0 %) | 3(4.9 %) | 0(0 %) | 3(3.0 %) | 0(0 %) |
| Occasionally | 2(1.3 %) | 0(0 %) | 5(4.1 %) | 1(0.8 %) | 1(1.6 %) | 0(0 %) | 0(0 %) | 1(1.1 %) |
| **Beedi** | | 120(100 %) | | | | | | |
| Never | 146(9.6 %) | 0(0 %) | 107(88 %) | 121(100 %) | 54(88 %) | 79(100 %) | 93(9.3.9 %) | 85(98.8 %) |
| Daily | 2(1.3 %) | 0(0 %) | 6(4.9 %) | 0(0 %) | 3(4.9 %) | 0(0 %) | 3(3.0 %) | 0(0 %) |
| Weakly | 3(1.9 %) | 0(0 % | 5(4.1 %) | 0(0 %) | 0(0 %) | 0(0 %) | 2(2.0 %) | 0(0 %) |
| Occasionally | 0(0 %) | | 3(2.4 %) | 0(0 %) | 4(6.5 %) | 0(0 %) | 1(1.0 %) | 1(1.1 %) |
| **Alcoholism** | | | | | | | | |
| Never alcoholism | 114(75.4 %) | 115(%) | 67(%) | 120(%) | 32(52.4 %) | 72(91.1 %) | 64(64.6 %) | 80(93.0 %) |
| Daily | 20(13.2 %) | 0(%) | 34(%) | 0(0 %) | 21(34.4 %) | 0(0 %) | 26(26.2 %) | 0(0 %) |
| Weakly | 7(4.6 %) | 0(%) | 12(%) | 0(0 %) | 5(9.2 %) | 0(0 %) | 5(5.0 %) | 0(0 %) |
| Occasionally | 8(5.2 %) | 6(%) | 3(%) | 1(0.8 %) | 3(5.5 %) | 4(5.0 %) | 4(4.0 %) | 6(6.9 %) |
| **Occupations** | | | | | | | | |
| Professional | 71(47.0 %) | 59(49.1 %) | 36(29.7 %) | 13(10.7 %) | 14(25.9 %) | 11(13.9 %) | 60(60.6 %) | 38(44.1 %) |
| Students | 19(12.5 %) | 9(7.5 %) | 27(22 %) | 24(19.8 %) | 3(5.5 %) | 5(6.3 %) | 7(7.0 %) | 2(2.3 %) |
| House wife | – | 39(32.5 %) | – | 59(48.7 %) | – | 52(65.8 %) | – | 30(34.8 %) |
| Company and factory | 28(18.5 %) | 3(2.5 %) | 13(10.7 %) | 9(7.4 %) | 16(29.6 %) | 0(0 %) | 14(14.1 %) | 6(6.9 %) |
| Labours | 32(21.1 %) | 8(6.6 %) | 42(34.7 %) | 12(9.9 %) | 25(40.9 %) | 9(11.3 %) | 17(17.1 %) | 8(9.3 %) |
| Un employed | 1(0.6 %) | 2(1.6 %) | 3(2.4 %) | 4(3.3 %) | 3(5.5 %) | 2(2.5 %) | 1(1.0 %) | 2(2.3 %) |
| **Physical activity** | | | | | | | | |
| No physical activity | 84(55.6 %) | 76(63.3 %) | 90(74.3 %) | 99(81.8 %) | 41(75.9 %) | 68(86.0 %) | 85(85.8 %) | 73(92.4 %) |
| Daily | 43(28.4 %) | 26(21.6 %) | 16(13.2 %) | 6(4.9 %) | 11(20.3 %) | 8(10.1 %) | 9(9.0 %) | 11(13.9 %) |
| Weakly | 24(15.8 %) | 19(15.8 %) | 15(12.3 %) | 16(13.2 %) | 2(3.7 %) | 3(3.7 %) | 5(5.0 %) | 2(2.3 %) |

Qualitative variable expressed as a percentage (number).

**Table 4**
Serum levels of trace element and TAS in asthma patients and controls.

| Trace elements and TAS | Males (n = 272) | | | Females (n = 241) | | |
|---|---|---|---|---|---|---|
| | Asthma Males n = 121 | Control Males n = 151 | P value | Asthma Females n = 121 | Control Females n = 120 | P value |
| Zn μg/dl | 0.090 ± 0.190 | 0.561 ± 1.843 | 0.005* | 0.107 ± 0.183 | 0.183 ± 0.182 | 0.001* |
| Fe μg/dl | 0.288 ± 0.25 | 0.390 ± 0.514 | 0.045* | 0.143 ± 0.224 | 0.233 ± 0.250 | 0.003* |
| Cu μg/dl | 0.006 ± 0.15 | 0.090 ± 0.154 | 0.006* | 0.084 ± 0.236 | 0.103 ± 0.138 | 0.452 |
| Mg μg/dl | 0.256 ± 0.38 | 0.459 ± 0.780 | 0.008* | 0.235 ± 0.336 | 0.403 ± 0.306 | 0.000* |
| Ni μg/dl | 0.038 ± 0.77 | 0.012 ± 0.307 | 0.706 | 0.072 ± 0.700 | 0.000 ± 0.217 | 0.281 |
| Pb μg/dl | 0.086 ± 0.38 | 0.002 ± 0.080 | 0.009* | 0.088 ± 0.281 | 0.005 ± 0.072 | 0.002* |
| Cd μg/dl | 0.045 ± 0.122 | 0.006 ± 0.154 | 0.026* | 0.056 ± 0.190 | 0.020 ± 0.162 | 0.120 |
| Cr μg/dl | 0.095 ± 0.49 | 0.000 ± 0.288 | 0.049* | 0.096 ± 0.516 | 0.011 ± 0.396 | 0.145 |
| Co μg/dl | 0.078 ± 0.216 | 0.035 ± 0.221 | 0.101 | 0.084 ± 0.220 | 0.062 ± 0.237 | 0.473 |
| TAS | 12.970 ± 8.499 | 23.56 ± 17.18 | 0.000* | 10.89 ± 7.300 | 20.19 ± 15.63 | 0.000* |

(Zn), iron (Fe), copper (Cu), magnesium (Mg), Nikel (Ni), Lead (Pb), cadmium (Cd), cadmium (Cd), chromium (Cr), Cobalt (Co) and Total antioxidant status (TAS).
Student's *t*-test. $P < 0.05$.

$= 0.012$ and $p = 0.003$ ($p < 0.05$). Serum levels of Ni and Pb were significantly higher than in asthmatic obese patient females $p = 0.028$ and $p = 0.002$ ($p < 0.05$). No significant difference in serum levels (Zn, Mg Ni and Cr) in asthmatic obese males and (Cd, Cr and Co) in asthmatic obese patient females ($p > 0.05$).

Table 6 shows serum level of trace elements in obesity and controls in obese patient males' serum levels Zn, Fe, Cu, Mg and TAS significantly was lower than control males $p = 0.032$, $p = 0.000$, $p = 0.000$, $p = 0.019$ and $p = 0.015$ ($p < 0.05$) and serum level cd was significantly higher $p = 0.0001$ ($p > 0.05$). In serum levels Zn, Fe, Cu and TAS was significantly lower when compared to controls females $p = 0.027$, $p = 0.020$, $p = 0.031$ $p = 0.003$ and $p = 0.019$ ($p < 0.05$), respectively. In obese patient males (Mg, Ni Pb, Cr and Co), obese patient females showed no significant association in serum levels of trace elements ($p > 0.05$).

The Pearson correlation framework of our dataset was shown in our study using a heatmap. All variables in our dataset are represented by the x and y axes of the heatmap, and the Pearson correlation between each pair of variables is shown by the colour gradient, which goes from blue to yellow. After analysing the heatmap, a particular group of variables that were positively associated appeared, indicating that there could be an underlying cause affecting these variables. The upcoming study will now have a new focus attributable to this result.

Fig. 1 shows the correlations of serum trace elements with baseline characteristics and TAS in controls. TAS is showed positive correlation with Cd, in control male and with Cr in controls females. Systolic BP showed a positive correlation with Co in female asthma patients. Fig. 2 shows the correlations of serum trace elements with baseline characteristics and TAS in asthma patients. TAS is showed positive correlation with Zn, Ni, and negative correlation with Cd. Cr is showed positive correlation BMI in asthma patient males. In asthma patient females, TAS is showed positive correlation with Fe and Cr. Cr showed a positive correlation with TAS in female asthma patients. Systolic BP showed a positive correlation with Co in male asthma patients, and systolic BP showed a positive correlation with Zn in female asthma patients. Fig. 3 shows Correlations of serum trace elements with baseline characteristics and TAS in asthmatic obese patients. The BMI showed positive correlation with Zn in asthmatic obese patient males. In asthmatic obese patient females TAS showed negative correlation with Pb, and duration is shows positive correlation with Cr. Systolic BP showed a negative correlation with Ni in asthma with obese males, and diastolic BP showed a negative correlation with Zn and Ni in asthma with obese males. Systolic BP showed a negative correlation with Cu and Cd in asthma with obese female patients and Ni showed a positive correlation. Fig. 4 presents Correlations of serum trace elements with baseline characteristics and TAS in obese patients. The BMI is

**Table 5**
Serum levels of trace element and TAS in asthmatic obese and controls.

| Trace elements and TAS | Males (n = 205) | | | Females (n = 199) | | |
|---|---|---|---|---|---|---|
| | Asthmatic obese Males n = 54 | Control Males n = 151 | P value | Asthmatic obese Females n = 79 | Control Females n = 120 | P value |
| Zn μg/dl | 0.176 ± 0.307 | 0.561 ± 1.843 | 0.106 | 0.093 ± 0.152 | 0.183 ± 0.182 | 0.000* |
| Fe μg/dl | 0.223 ± 0.554 | 0.390 ± 0.514 | 0.037* | 0.114 ± 0.385 | 0.233 ± 0.250 | 0.008* |
| Cu μg/dl | 0.016 ± 0.160 | 0.090 ± 0.154 | 0.002* | 0.030 ± 0.186 | 0.103 ± 0.138 | 0.001* |
| Mg μg/dl | 0.320 ± 0.418 | 0.459 ± 0.780 | 0.189 | 0.208 ± 0.762 | 0.403 ± 0.306 | 0.012* |
| Ni μg/dl | 0.089 ± 0.697 | 0.012 ± 0.307 | 0.264 | 0.068 ± 0.209 | 0.000 ± 0.217 | 0.028* |
| Pb μg/dl | 0.052 ± 0.170 | 0.002 ± 0.080 | 0.004* | 0.048 ± 0.122 | 0.005 ± 0.072 | 0.002* |
| Cd μg/dl | 0.142 ± 0.340 | 0.006 ± 0.154 | 0.000* | 0.045 ± 0.220 | 0.020 ± 0.162 | 0.358 |
| Cr μg/dl | 0.075 ± 0.682 | 0.000 ± 0.288 | 0.260 | 0.037 ± 0.767 | 0.011 ± 0.396 | 0.732 |
| Co μg/dl | 0.106 ± 0.173 | 0.035 ± 0.221 | 0.025* | 0.077 ± 0.193 | 0.062 ± 0.237 | 0.648 |
| TAS | 16.28 ± 10.83 | 23.56 ± 17.18 | 0.003* | 14.41 ± 8.59 | 20.19 ± 15.63 | 0.003* |

(Zn), iron (Fe), copper (Cu), magnesium (Mg), Nikel (Ni), Lead (Pb), cadmium (Cd), cadmium (Cd), chromium (Cr), Cobalt (Co) and Total antioxidant status (TAS).
Student's *t*-test $P < 0.05$.

**Table 6**
Serum levels of trace element and TAS in obesity and controls.

| Trace elements and TAS | Males (n = 250) | | | Females (n = 206) | | |
|---|---|---|---|---|---|---|
| | Obese Males n = 99 | Control Males n = 151 | P value | Obese Females n = 86 | Control Females n = 120 | P value |
| Zn μg/dl | 0.162 ± 0.160 | 0.561 ± 1.843 | 0.032* | 0.131 ± 0.133 | 0.183 ± 0.182 | 0.027* |
| Fe μg/dl | 0.167 ± 0.300 | 0.390 ± 0.514 | 0.000* | 0.154 ± 0.225 | 0.233 ± 0.250 | 0.020* |
| Cu μg/dl | 0.018 ± 0.117 | 0.090 ± 0.154 | 0.000* | 0.060 ± 0.141 | 0.103 ± 0.138 | 0.031* |
| Mg μg/dl | 0.236 ± 0.309 | 0.459 ± 0.780 | 0.019* | 0.174 ± 0.750 | 0.403 ± 0.306 | 0.003* |
| Ni μg/dl | 0.010 ± 0.336 | 0.012 ± 0.307 | 0.962 | 0.014 ± 0.363 | 0.000 ± 0.217 | 0.728 |
| Pb μg/dl | 0.070 ± 1.202 | 0.002 ± 0.080 | 0.488 | 0.005 ± 0.598 | 0.005 ± 0.072 | 0.999 |
| Cd μg/dl | 0.093 ± 0.158 | 0.006 ± 0.154 | 0.000* | 0.031 ± 0.063 | 0.020 ± 0.162 | 0.575 |
| Cr μg/dl | 0.071 ± 0.702 | 0.000 ± 0.288 | 0.266 | 0.019 ± 0.609 | 0.011 ± 0.396 | 0.879 |
| Co μg/dl | 0.000 ± 0.353 | 0.035 ± 0.221 | 0.338 | 0.006 ± 0.415 | 0.062 ± 0.237 | 0.220 |
| TAS | 18.19 ± 16.79 | 23.56 ± 17.18 | 0.015* | 15.09 ± 14.34 | 20.19 ± 15.63 | 0.019* |

(Zn), iron (Fe), copper (Cu), magnesium (Mg), Nikel (Ni), Lead (Pb), cadmium (Cd), cadmium (Cd), chromium (Cr), Cobalt (Co) and Total antioxidant status (TAS).
Student's *t*-test $P < 0.05$.

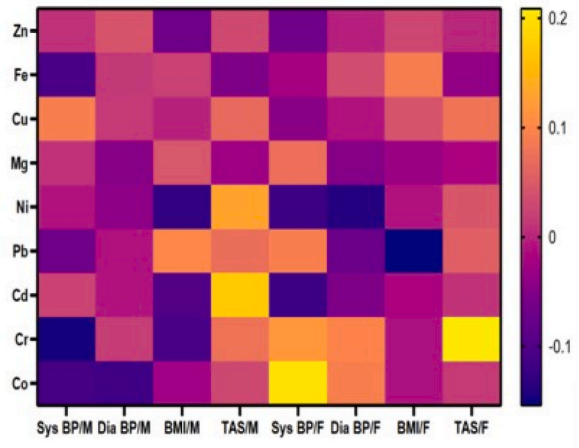


**Figure:1.** Heat map of Pearson'Correlations of serum trace elements with baseline characteristics and TAS in control.

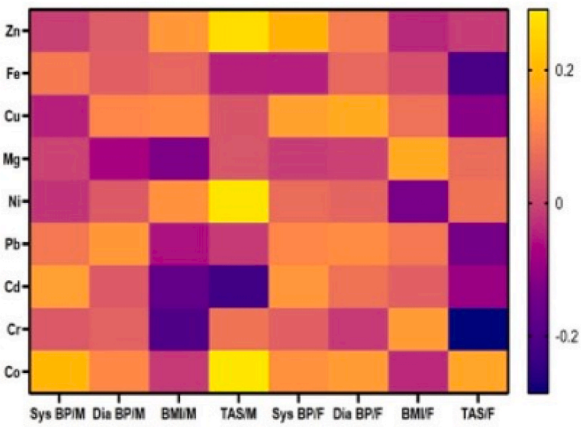


**Figure:2.** Heat map of Pearson'Correlations of serum trace elements with baseline characteristics and TAS in asthma.

showed positive correlation with Fe and Co and TAS is showed positive correlation with Cu in obese patient males. In obese patient females TAS showed a positive correlation with Co. Systolic BP showed a negative correlation with Pb in obese males, and systolic BP showed a negative correlation with Ni in obese females.

In our study, we applied a linear regression analysis to investigate the relationship between the dependent variable and the

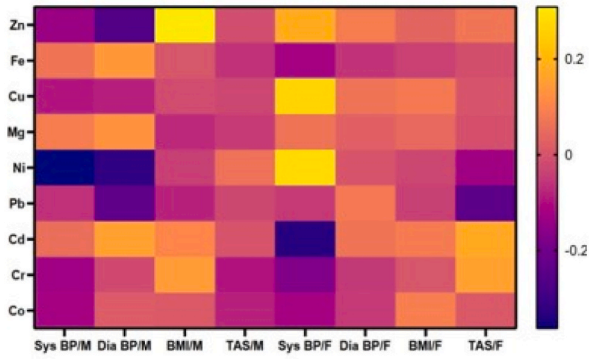


**Figure:3.** Pearson'Correlations of serum trace elements with baseline characteristics and TAS in asthmatic obese patients.

independent variables with trace elements. Systolic BP, diastolic BP, BMI, and TAS was chosen as dependent variables. Zn, Fe, Cu, Mg, Ni, Pb, Cd, Cr, and Co were independent variables in the linear regression analysis. In linear regression analysis, the correlation is significant at the 0.05 level (2-tailed), as shown in Table 7. A report of the overall statistical significance of the linear regression include the R-squared value, Beta (β) value and p-value.

## 4. Discussion

The incidence of asthma has been progressively rising over the past several years on a global scale. A lung disease with persistent inflammation is known as asthma. It is characterized by a production of mucous, airway smooth muscle (ASM) hypertrophy and hyperplasia [24]. Asthma incidence and prevalence are higher in obese individuals [6,25].

As per numerous studies, trace elements may have a role in both acute and chronic inflammatory disorders, including asthma [26]. Endogenous reactive oxygen species [ROS], as well as free radicals, which are important in the development of asthma, were created by inflammatory cells an harm tissues. [3], The lung's antioxidant defence systems against block these harmful oxidants [27]. The most important antioxidant systems are the superoxide dismutase (SOD) which contains zinc and copper in their structures, and hence zinc is essential for the optimal functions of immune system [28]. Trace elements are vital in preventing damage from oxidative stress [3, 29].

Studies reported concentrations of some elements in excess (above optimum) or deficient amount can progress to some types of metabolic abnormalities which could lead to obesity [16,17]. Gizela et al., 2023 reported obesity can have harmful consequences such as nutritional metabolic disturbance, accumulation of adipose tissue, which harms the subject health [17].

In the present study, we aimed to determine the trace element levels of Zn, Fe, Cu, Mg, Co, Ni, Pb, Cd, Cr, and TAS in asthma and obese patients and compared with controls in the Vellore population. Patients had lower serum trace element levels of Zn, Fe, Cu, Mg, and TAS. markedly higher levels of Ni, Pb, Cd, Cr, and Co when compared with controls. In this study, we found a significant difference between patients and controls in serum element levels ($p < 0.05$). The current study has several strengths. To the best of our knowledge, this is the first study to assess the relationship between trace element levels and antioxidant potential in asthma, asthmatic obese and obese individuals in South Indian. Also, there is lack of research in serum levels of nickel, lead, cadmium, and chromium in asthma and obesity individuals in Indian population.

The levels of trace elements have been proposed as potential biomarkers for assessing susceptibility to asthma and obesity. The status of trace elements is contingent upon various factors, including dietary patterns and the distribution of indicated elements within the body. In the present study, the dietary pattern of asthma, asthmatic obese, obese and controls, food habits non-vegetarians were

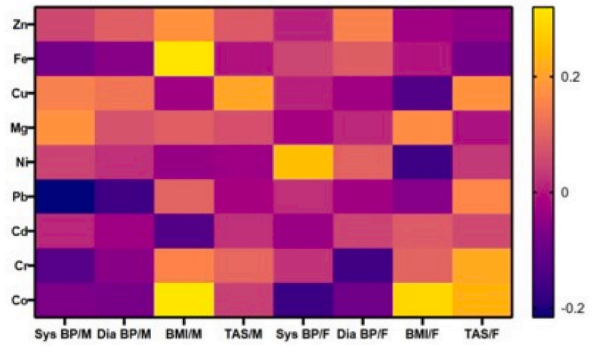


**Figure:4.** Pearson'Correlations of serum trace elements with baseline characteristics and TAS in obese patients.

**Table 7**
Linear regression analysis of Systolic BP, Diastolic BP, BMI, and total antioxidant status (TAS) as dependent variable in Asthma, Asthmatic obese and obese patients, and controls.

| Trace elements | R2 | β | P value |
|---|---|---|---|
| **Control Males** | | | |
| Cd/TAS | 0.03 | 19.06 | 0.035[a] |
| **Control Females** | | | |
| Co/Systolic BP | 0.04 | 11.08 | 0.028[a] |
| Cr/TAS | 0.044 | 8.22 | 0.022[a] |
| **Asthma patient Males (n=121)** | | | |
| Zn/TAS | 0.022 | 2.58 | 0.099 |
| Ni/TAS | 0.083 | 3.15 | 0.001[a] |
| Cr/BMI | 0.042 | −1.36 | 0.023[a] |
| Co/Systolic BP | 0.014 | 8.46 | 0.187 |
| **Asthma patient Females (n=121)** | | | |
| Fe/TAS | 0.046 | −6.98 | 0.020[a] |
| Cr/TAS | 0.082 | −4.07 | 0.002[a] |
| Zn/Systolic | 0.012 | 8.75 | 0.231 |
| **Asthmatic obese patient Males (n=61)** | | | |
| Zn/BMI | 0.095 | 5.28 | 0.016[a] |
| Pb/TAS | 0.000 | −1.52 | 0.852 |
| Ni/Systolic BP | 0.13 | −9.31 | 0.004[a] |
| Zn/Diastolic BP | 0.073 | −10.24 | 0.035[a] |
| Ni/Diastolic BP | 0.082 | −4.78 | 0.025[a] |
| **Asthmatic obese patients Females (n=79)** | | | |
| Fe/BMI | 0.001 | −0.52 | 0.741 |
| Co/BMI | 0.007 | 2.44 | 0.435 |
| Cu/Systolic BP | 0.07 | 19.29 | 0.016[a] |
| Ni Systolic BP | 0.078 | 18.05 | 0.011[a] |
| Cd/Systolic BP | 0.11 | −20.49 | 0.002[a] |
| **Obese patient Males n=99** | | | |
| Cu/TAS | 0.043 | 29.89 | 0.039[a] |
| Co/TAS | 0.001 | 1.99 | 0.682 |
| Pb/Systolic BP | 0.048 | −2.52 | 0.030[a] |
| **Obese patient Females n=86** | | | |
| Co/TAS | 0.05 | 9.78 | 0.039[a] |
| Ni/Systolic BP | 0.062 | 9.18 | 0.021[a] |

Dependent Variable: duration, BMI, and total antioxidant status (TAS).
Zn), iron (Fe), copper (Cu), magnesium (Mg), Nikel (Ni), Lead (Pb), cadmium (Cd), cadmium (Cd), chromium (Cr), Cobalt (Co) and Total antioxidant status (TAS).
[a] Correlation is significant at the 0.05 level (2-tailed).

higher in all groups. Intake of fruits, vegetables, chicken, mutton, and fish are less in patients when compared to controls. The fast-food consumption was higher in the weekly basis of obese males when compared to other groups. Lower dietary intake may alter the trace elements concentration.

Most of the enrolled asthma and obesity patients were labourers and factory workers whose work area could be related to exposure change in trace elements. A large proportion of asthma patients suffer from severe, long-term conditions, which may interfere with body homeostasis and change the amounts of certain trace elements. Trace elements play a significant role in the pathogenesis of asthma, and a variety of factors, including age, time span, cardiovascular condition, inheritance, profession, surroundings, harmful substances report, metallic substances in food and water, polluted air and soil, and way of life determine the disease's overall course [30].

Our results agree with results obtained by others [1, 3, 7 17]. The onset and progression of asthma may be influenced by blood trace element levels, as evidenced by the previously documented substantial reduction in Zn, Fe, Cu, Mg, and TAS in asthma patients compared to controls Song Mao et al., [3]. By the same token, Hyun et al., and Wu, Ke et al. [31,32], reported that higher levels of heavy metals are leading to asthma, coincident with an increase in serum Pb levels in asthma patients compared with controls.

A few past studies reported an association between serum trace element levels and antioxidant mechanisms [33]. Esra et al., [34] assumed that the molecular makeup of the antioxidant enzymes contains trace elements. By controlling the host immune system, these enzymes function as a component of the immune response and can change the viral genome. Reactive oxygen species can make a person more susceptible if they consume inadequate antioxidants. The current study shows patients have significantly lower antioxidant capacity when compared to controls.

Zinc (Zn), a constituent of Superoxide Dismutase (SOD), exhibited a protective effect against oxidative stress [35]. Zn is an essential nutrient that plays a special role in the conductive airways and partly contributes to the structure and function of many biological enzymes [36,37]. Changes in the level of serum zinc level has a negative effect on the activity of antioxidant systems leading to hyperreactivity and inflammation in the respiratory [14]. Zn also inhibits inflammatory and apoptotic processes [3]. Findings on the connection between zinc and asthma vary. Studies frequently discovered low blood zinc levels in asthmatics [38,39], and they also established links between zinc deficiency as well as overweight and accumulation of fat [17,40].

Our finding with respect to serum Zn levels were significantly lower in asthma patient males, asthma patient females and asthmatic obese patient females than in the control group, we concluded that zinc deficiency may be reduce antioxidant function and tend to play a role in the onset of asthma. In Pearson corelation analysis, Zn is positively corelated with TAS in asthma patient males and in female zinc is positively correlated with systolic blood pressure and in asthmatic obese negatively corelated with diastolic blood pressure and Zn is positively corelated with BMI. In obese male and female patients' serum Zn levels were significantly lower in this study.

Previous research suggested a link between a lower dietary Zn intake and a greater chance of acquiring asthma [41]. Also, Yousef et al., and Rajkumar et al., both authors, concluded that taking zinc supplements can be beneficial in the management of people with asthma [28,42]. Zinc supplements need to be taken properly to control asthmatic individuals.

Iron (Fe) plays several vital roles in human beings and is an important element [34]. Falah S et al., [43] theorised that majority of Fe in the body is contained within haemoglobin, an erythrocyte protein that transfers oxygen from the lungs to the tissues. Both excessive and inadequacies of this mineral are acknowledged as serious health issues [34]. Fe, on the contrary, is an essential component in a variety of oxidative processes. Free radicals were created in part by Fe [3]. Fe is a necessary component of all living forms' diets however excessive Fe can lead to several illnesses. High body Fe reserves have been linked to a higher risk of developing asthma, according to certain research [44,45]. Song et al., reported that Asians and the general population both reported significantly greater levels of Fe in asthma than in controls. Lower levels Fe values in obese people have also been identified in other studies [46].

Ali, Md et al., conclude that complementing clinical and experimental investigations demonstrate a substantial association between the level of iron and regulation of asthma [47]. In this study we find significantly lower serum Fe levels in asthma, asthmatic obese, and obese. In Pearson corelation analysis, Fe is negatively corelated with TAS in asthma patient females. In obesity male, Fe is positively corelated with BMI.

Copper (Cu) a crucial trace element, is necessary for maintaining cellular homeostasis [3]. The inclusion of Cu in sodium dismutase may theoretically impact antioxidant status and lung function [48]. H. Vural et al., [49] reported that excessive intakes or excessive releases of free iron and copper from bound form result in increase of free radicals' production and consequently increase risk of asthma onset. According to the third National Health and Nutrition Survey [50], an adult's recommended daily dietary intake of copper ranges from 1.0 to 1.6 mg. These investigations have shown that the loss of tightly controlled levels of copper and copper-dependent enzymes in tissues and circulatory may lead to decreased whole-body metabolism [51,52]. Yang et al., 2019 observed greater levels of copper in obese individuals [53]. Zajac et al. theorized that Copper excess and deficiency can both cause oxidative stress and chronic inflammation, which may be linked to the risk of development asthma [54]. However, we found that significantly asthma patient males, asthmatic obese male and female patients, obese male and female patients had significantly lower level of Cu than in controls. In Pearson corelation analysis, Cu is negatively correlated with diastolic blood pressure in asthmatic obese female. In obesity male, Cu is positively corelated with TAS.

Magnesium (Mg), a significant intracellular cation, participates in the mineralization of bones. Mg also participates in a variety of physiological procedures, including the folding of proteins and enzymatic activities [55]. The effects of Mg on the bronchial smooth muscles and respiratory tract might lessen asthma symptoms. The phagocytosis, ROS generation, and proinflammatory activities brought on by decreased Mg intake might compromise pulmonary function [56]. we found that asthma patient males, asthma patient females, asthmatic obese patient females had markedly lower level of Mg than in the control. However, Song Mao et al., [3] and Falah et al., (1) reported the significant difference in asthma patients had markedly decreased level of Mg and Ahmed et al., [57] reported that lower levels Mg in asthma patients with comparison with the controls. Indeed, the National Health and Nutrition Examination Survey (NHANES) 3 study demonstrates that $Mg2+$ deficiency is more common in obese people [58]. Al Shammaa et al., reported that obese people have decreased levels of magnesium in their bloodstream [59]. In this study, serum levels of Mg were significantly lower in obese males and females. Magnesium deficiency has been shown to play a vital role in the pathogenesis of asthma. Song et al., found that routine MgSO4 medication may be effective in the treatment of adult patients with severe or life-threatening exacerbations [60].

Nickel (Ni) allergy is the most prevalent contact allergy. It belongs to a different hypersensitivity type to asthma and rhino-conjunctivitis [61]. Humans are susceptible to ambient nickel exposure and nickel absorption through their skin, dietary intake, and respiratory systems [62]. Alveoli inflammation and reactive oxidative stress are linked to chronic nickel inhalation [63]. Novey et al., [64] reported that occupational asthma due to nickel in metal plating. The present study shows serum level of Ni was significantly higher in asthmatic obese patient females. Mikiko et al. reported that Ni allergy was associated with significantly higher obesity patients and toxic and immune-mediated effects of Ni may synergistically play a role in the genesis of obesity and hormonal impairment [65]. Syurin et al., reported Occupational bronchitis and occupational asthma have been associated with increased nickel exposure concentrations [66]. In this study Ni was higher in obese male and female patients but no statistically significant difference was found when compared to controls. In Pearson corelation analysis, Ni is positively corelated with TAS in asthma patient males and in asthmatic obese males Ni is negatively corelated with systolic and diastolic blood pressure and in Ni is positively corelated with systolic blood pressure in asthmatic obese females and obese females. There are few studies updated in different countries [67], and none in the Indian population.

Lead (Pb), a heavy metal that is very hazardous and has grown in the environment due to a variety of causes, has a detrimental effect on several human organs. Even through Pb can be absorbed from skin, it is mostly absorbed from raspatory system [68]. The relationship between lead exposure and asthma is unknown because there are many research studies investigating this issue. Bronchial hyperresponsiveness and total IgE are linked to elevated Pb blood levels [69–71]. Asthma patients exhibited considerably higher blood levels of lead, as reported by Mohammad et al., [72]. The current study found a significantly increased level of Pb in asthma and asthmatic obese patients when compared to controls. Héctor et al., 2022 highlight the effect of environmental Pb exposure and health risk on humans and the significant positive association between Pb levels in obese individuals [73]. According to research by Raddam et al., there is a significant relationship between lead levels, asthma and total IgE levels [74]. In this study, Pb was higher in obese

patients, but no significant difference was found when compared to controls. In Pearson corelation analysis, Pb is negatively corelated with TAS in asthmatic obese females. Not many studies have looked at the serum lead level among individuals with asthma.

Heavy metal cadmium (Cd) has cumulative harmful effects [75]. Exposure to inhaled Cd may be linked to asthma, however, smoking obscures this link because cigarettes contain cadmium, and smoking is linked to asthma. There were more smokers in the current research. As reported by Ge Yang et al., 2019, high blood cadmium levels were substantially linked to asthma patients [76]. According to research by S. Songül et al., non-smokers' lung function may be adversely affected by exposure to greater concentrations of heavy metals, especially cadmium [77]. In our study, serum concertation of Cd was statistically significant higher in asthma patient males, asthmatic obese patient males and obese patient males when compared to controls males and in Pearson corelation analysis, Cd is negatively corelated with TAS in asthma patient males and in asthmatic obese females showed Cd is negatively corelated with systolic blood pressure. In obesity, Cd is negatively corelated with systolic blood pressure in obese male. The association of Cd with BMI and obesity remains controversial. Studies have reported both negative and positive associations. The inverse relationship of Cd exposure with BMI and obesity has been observed by some researchers [78] Meiduo et al., reported Exposure to cadmium may be correlated with BMI and abdominal circumference [79].

Due to the frequent usage of chromium (Cr) in several industrial sectors, workers might be regarded as the population that is most at risk for acquiring asthma since Cr is a naturally existing metallic component in industrial processes [68]. Individuals who smoke actively or passively may be exposed to chromium because it is a significant toxin found in tobacco smoke S. Songül et al., [77]. Mar et al., 2022 reported a exposure to chromium salts is a poorly characterized cause of occupational asthma [79]. The present study shows that most of the asthma and obesity patients are laborers and factory workers, whose serum Cr levels was significantly higher in asthma patient males when compared to controls males and in Pearson corelation analysis, Cr is negatively corelated with BMI in asthma patient males and in females Cr is negatively corelated with TAS in asthma patient females. We could not find any statistical difference in obese patients. Many occupations background was also major risk factor for asthma development. Researchers have reported people who live in areas where Cr pollution has been present for a long time may have Cr exposure that affects how their bodies process glucose and lipids [80]. Tinkov et al., 2021 have documented inconsistent associations between Cr exposure and obesity [81].

Metals such as cobalt (Co)are elements naturally found in the environment. Cobalt can be found in air, water, and tobacco smoke, though vegetables account for the majority of human intake [82]. Cobalt is essential as a metal constituent of vitamin B12 but its toxic potential from excessive exposure is well known [83]. R. Sauni et al., [84] reported that the mean exposure levels to inhaled cobalt higher the level of risk of occupational asthma and even small levels of Co might be dangerous for vulnerable workers. Co serum levels was significantly higher in asthmatic obese patient males, but we could not find any statistical difference on the group of asthma patients. In Pearson corelation analysis, Co is positively corelated with systolic blood pressure in asthma patient males. In obese male, Co is positively corelated with BMI and Co is positively corelated with TAS in obese female. Jianwei et al., (2022) reported relationships between Co exposure and obesity, insulin resistance, and metabolic-related disorders [85]. In this study Co serum levels was higher in obese male and female patients, but no significant difference was observed when compared to controls.

There are certain limitations of the study, as we could not get equal number of males and females' samples and there is also a lack of sample in asthmatic obese (in both males and females). In the near future, more investigation on trace elements and their concentration in serum will be carried out to further clarify its association with asthma and obesity.

## 5. Conclusion

Our study showed that deviation in the serum trace element and TAS levels may increase the health risk of asthma and obese patients. Patients had low level Zn, Fe, Cu Mg and, TAS and higher level of Ni, Pb, Cd, Cr and Co when compared with the control group. Quantitative determination of trace elements and TAS may help in the early detection of the disease and evaluation of an appropriate therapy. Diet and nutrition, life style are important modifiable risk factors for the progression and management of chronic disease such as asthma and obesity.

## Data availability statement

Data presented in this article is not deposited into a publicly available repository. It will be presented in conferences.

## CRediT authorship contribution statement

**Aswathi Pootheri:** Writing – original draft, Visualization, Validation, Investigation. **Wilner Martinez lopez:** Writing – review & editing, Supervision. **Radha Saraswathy:** Writing – review & editing, Validation, Supervision.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

The authors acknowledge VIT University Vellore, Tamil Nadu, India. A.P. is grateful to VIT for providing a Teaching Cum Research Assistant (TRA) Fellowship.

The authors acknowledge Dr. John Joseph at the Technology Business Incubator (VITTBI) for helping in analysing the samples.

We would like to thank Dr. Sathya Narayanan Sharma at the Vellore Institute of Technology for helping with the statistical analysis of the data.

All the authors were thankful to the Nalam medical center and hospital, and the patients participated in the study.

## References

[1] F.S. Al-Fartusie, M.J. Abood, H.K. Al-Bairmani, A.S. Mohammed, Evaluation of some trace elements in sera of asthma patients: a case control study, Folia Med. 63 (5) (2021 Oct 31) 797–804.
[2] C.W. Baffi, D.E. Winnica, F. Holguin, Asthma and obesity: mechanisms and clinical implications, Asthma research and practice 1 (2015 Dec) 1–7.
[3] S. Mao, L. Wu, W. Shi, Association between trace elements levels and asthma susceptibility, Respir. Med. 145 (2018 Dec 1) 110–119.
[4] R. Dahl, Systemic side effects of inhaled corticosteroids in patients with asthma, Respir. Med. 100 (8) (2006 Aug 1) 1307–1317.
[5] A.S. Yadav, M. Saini, Evaluation of systemic antioxidant level and oxidative stress in relation to lifestyle and disease progression in asthmatic patients, J. Med. Biochem. 35 (1) (2016 Jan) 55.
[6] U. Peters, A.E. Dixon, E. Forno, Obesity and asthma, J. Allergy Clin. Immunol. 141 (4) (2018 Apr 1) 1169–1179.
[7] S.A. Shore, Obesity and asthma: possible mechanisms, J. Allergy Clin. Immunol. 121 (5) (2008 May 1) 1087–1093.
[8] K.G. Wu, C.Y. Chang, C.Y. Yen, C.C. Lai, Associations between environmental heavy metal exposure and childhood asthma: a population-based study, J. Microbiol. Immunol. Infect. 52 (2) (2019 Apr 1) 352–362.
[9] B. Ermis, F. Armutcu, A. Guerel, L. Kart, N. Demircan, R. Altin, F. Demirel, Trace elements status in children with bronchial asthma, Eur. J. Gen. Med. 1 (1) (2004 Mar) 4–8.
[10] S. Urushidate, M. Matsuzaka, N. Okubo, H. Iwasaki, T. Hasebe, R. Tsuya, R. Inoue, K. Yamai, K. Danjo, I. Takahashi, T. Umeda, Association between concentration of trace elements in serum and bronchial asthma among Japanese general population, J. Trace Elem. Med. Biol. 24 (4) (2010 Oct 1) 236–242.
[11] F.S. Al-Fartusie, S.N. Mohssan, Essential trace elements and their vital roles in human body, Indian J. Adv. Chem. Sci. 5 (3) (2017 Jan 1) 127–136.
[12] T. Attar, A mini-review on importance and role of trace elements in the human organism, Chemical Review and Letters 3 (3) (2020 May 1) 117–130.
[13] H. Vural, K. Uzun, E. Uz, A.B. Koçyigit, A. Cigli, Ö. Akyol, Concentrations of copper, zinc and various elements in serum of patients with bronchial asthma, J. Trace Elem. Med. Biol. 14 (2) (2000 Jun 1) 88–91.
[14] A.M. Yousef, E. Elmorsy, Serum zinc level in bronchial asthma, Egypt. J. Chest Dis. Tuberc. 66 (1) (2017 Jan 1) 1–4.
[15] R. Zhan, L. Liu, M. Yang, Y. Ren, Z. Ge, J. Shi, K. Zhou, J. Zhang, H. Cao, L. Yang, K. Liu, Associations of 10 trace element levels in the whole blood with risk of three types of obesity in the elderly, Environ. Geochem. Health 45 (12) (2023 Dec) 9787–9806.
[16] S. Karatela, N.I. Ward, Trace elements and human obesity: an overview, Manipal journal of nursing and health sciences 2 (2) (2016) 15.
[17] G.P. Junqueira, M.V. Junqueira-Franco, R. San Martin, C.F. Brandão, F.B. Júnior, E.M. Rocha, F.B. Chueire, J.S. Marchini, Assessment of minerals in biological fluids in people with obesity: a pilot study, Journal of Trace Elements and Minerals 3 (2023 Mar 1) 100052.
[18] L.A. Pham-Huy, H. He, C. Pham-Huy, Free radicals, antioxidants in disease and health, International journal of biomedical science: IJBS 4 (2) (2008 Jun) 89.
[19] W. MacNee, Oxidative stress and lung inflammation in airways disease, Eur. J. Pharmacol. 429 (1–3) (2001 Oct 19) 195–207.
[20] A.A. Ali, R.A. El-Wahsh, H.F. Afia, G.A. Abdelaal, Trace element and magnesium in patients with bronchial asthma, Egypt. J. Chest Dis. Tuberc. 71 (1) (2022 Jan 1) 44–50.
[21] B. Choromańska, P. Myśliwiec, M. Łuba, P. Wojskowicz, H. Myśliwiec, K. Choromańska, M. Żendzian-Piotrowska, J. Dadan, A. Zalewska, M. Maciejczyk, Impact of weight loss on the total antioxidant/oxidant potential in patients with morbid obesity—a longitudinal study, Antioxidants 9 (5) (2020 May 1) 376.
[22] M.O. Feiler, C.J. Pavia, S.M. Frey, P.J. Parsons, K. Thevenet-Morrison, R.L. Canfield, T.A. Jusko, Early life blood lead levels and asthma diagnosis at age 4–6 years, Environ. Health Prev. Med. 26 (1) (2021 Dec) 1–7.
[23] V.S. Chedea, R.M. Pop, Total polyphenols content and antioxidant DPPH assays on biological samples, in: InPolyphenols in Plants, Academic Press, 2019 Jan 1, pp. 169–183.
[24] K.P. Hough, M.L. Curtiss, T.J. Blain, R.M. Liu, J. Trevor, J.S. Deshane, V.J. Thannickal, Airway remodeling in asthma, Front. Med. 7 (2020 May 21) 191.
[25] A. Murphy, K.G. Tantisira, M.E. Soto-Quirós, L. Avila, B.J. Klanderman, S. Lake, S.T. Weiss, J.C. Celedón, PRKCA: a positional candidate gene for body mass index and asthma, Am. J. Hum. Genet. 85 (1) (2009 Jul 10) 87–96.
[26] F.S. Al-Fartusie, M.J. Abood, H.K. Al-Bairmani, A.S. Mohammed, Evaluation of some trace elements in sera of asthma patients: a case control study, Folia Med. 63 (5) (2021 Oct 31) 797–804.
[27] S.S. Yalçın, N. Emiralioğlu, S. Yalçın, Evaluation of blood and tooth element status in asthma cases: a preliminary case–control study, BMC Pulm. Med. 21 (1) (2021 Dec) 1–8.
[28] A.M. Yousef, E. Elmorsy, Serum zinc level in bronchial asthma, Egypt. J. Chest Dis. Tuberc. 66 (1) (2017 Jan 1) 1–4.
[29] S. Pucheau, C. Coudray, N. Tresallet, A. Favier, J. de Leiris, Effect of dietary antioxidant trace element supply on cardiac tolerance to ischmia—reperfusion in the rat, J. Mol. Cell. Cardiol. 27 (10) (1995 Oct 1) 2303–2314.
[30] A.A. Tinkov, P. Bogdański, D. Skrypnik, K. Skrypnik, A.V. Skalny, J. Aaseth, M.G. Skalnaya, J. Suliburska, Trace element and mineral levels in serum, hair, and urine of obese women in relation to body composition, blood pressure, lipid profile, and insulin resistance, Biomolecules 11 (5) (2021 May 4) 689.
[31] H.Y. Koh, T.H. Kim, Y.H. Sheen, S.W. Lee, J. An, M.A. Kim, M.Y. Han, D.K. Yon, Serum heavy metal levels are associated with asthma, allergic rhinitis, atopic dermatitis, allergic multimorbidity, and airflow obstruction, J. Allergy Clin. Immunol. Pract. 7 (8) (2019 Nov 1) 2912–2915.
[32] K.G. Wu, C.Y. Chang, C.Y. Yen, C.C. Lai, Associations between environmental heavy metal exposure and childhood asthma: a population-based study, J. Microbiol. Immunol. Infect. 52 (2) (2019 Apr 1) 352–362.
[33] A.B. Kocyigit, F. Armutcu, A. Gurel, B. Ermis, Alterations in plasma essential trace elements selenium, manganese, zinc, copper, and iron concentrations and the possible role of these elements on oxidative status in patients with childhood asthma, Biol. Trace Elem. Res. 97 (2004 Jan) 31–41.
[34] E.A. Özkan, A.Y. Göçmen, Y. Küçükbağriaçik, M. Akyüz, Serum levels of trace elements, vitamin d and oxidant status in children with asthma, Journal of Basic and Clinical Health Sciences 3 (2) (2019 Jan 6) 63–68.
[35] Ł. Lewandowski, M. Kepinska, H. Milnerowicz, Inhibition of copper-zinc superoxide dismutase activity by selected environmental xenobiotics, Environ. Toxicol. Pharmacol. 58 (2018 Mar 1) 105–113.
[36] Ł. Lewandowski, M. Kepinska, H. Milnerowicz, Inhibition of copper-zinc superoxide dismutase activity by selected environmental xenobiotics, Environ. Toxicol. Pharmacol. 58 (2018 Mar 1) 105–113.
[37] P.D. Zalewski, Zinc metabolism in the airway: basic mechanisms and drug targets, Curr. Opin. Pharmacol. 6 (3) (2006 Jun 1) 237–243.
[38] A. AbdulWahab, A. Zeidan, T. Avades, P. Chandra, A. Soliman, Serum zinc level in asthmatic and non-asthmatic school children, Children 5 (3) (2018 Mar 16) 42.
[39] A.M. Yousef, E. Elmorsy, Serum zinc level in bronchial asthma, Egypt. J. Chest Dis. Tuberc. 66 (1) (2017 Jan 1) 1–4.
[40] S.F. Azab, S.H. Saleh, W.F. Elsaeed, M.A. Elshafie, L.M. Sherief, A.M. Esh, Serum trace elements in obese Egyptian children: a case–control study, Ital. J. Pediatr. 40 (2014 Dec) 1–7.

[41] A. Soutar, A. Seaton, K. Brown, Bronchial reactivity and dietary antioxidants, Thorax 52 (2) (1997 Feb 1) 166–170.
[42] S. Rajkumar, N.K. Bhat, V. Kumar, R. Bolia, P.K. Verma, M. Kumar, S. Chacham, A.A. Mirza, Association of serum zinc levels and symptom control of asthma in children and adolescents—a prospective observational study, Eur. J. Pediatr. 182 (1) (2023 Jan) 141–147.
[43] F.S. Al-Fartusie, S.N. Mohssan, Essential trace elements and their vital roles in human body, Indian J. Adv. Chem. Sci. 5 (3) (2017 Jan 1) 127–136.
[44] M. Uysalol, E.P. Uysalol, Y. Yilmaz, G. Parlakgul, T.A. Ozden, H.V. Ertem, B. Omer, N. Uzel, Serum level of vitamin D and trace elements in children with recurrent wheezing: a cross-sectional study, BMC Pediatr. 14 (2014 Dec) 1–8.
[45] L.S. Greene, Asthma and oxidant stress: nutritional, environmental, and genetic risk factors, J. Am. Coll. Nutr. 14 (4) (1995 Aug 1) 317–324.
[46] O.P. García, K.Z. Long, J.L. Rosado, Impact of micronutrient deficiencies on obesity, Nutr. Rev. 67 (10) (2009 Oct 1) 559–572.
[47] M.K. Ali, R.Y. Kim, A.C. Brown, J.R. Mayall, R. Karim, J.W. Pinkerton, G. Liu, K.L. Martin, M.R. Starkey, A.L. Pillar, C. Donovan, Crucial role for lung iron level and regulation in the pathogenesis and severity of asthma, Eur. Respir. J. 55 (4) (2020 Apr 1).
[48] A.A. Bast, G.R. Haenen, C.J. Doelman, Oxidants and antioxidants: state of the art, Am. J. Med. 91 (3) (1991 Sep 30) S2–S13.
[49] H. Vural, K. Uzun, E. Uz, A.B. Koçyigit, A. Cigli, Ö. Akyol, Concentrations of copper, zinc and various elements in serum of patients with bronchial asthma, J. Trace Elem. Med. Biol. 14 (2) (2000 Jun 1) 88–91.
[50] P. Trumbo, A.A. Yates, S. Schlicker, M. Poos, Dietary reference intakes, J. Am. Diet Assoc. 101 (3) (2001 Mar 1) 294.
[51] E. Aigner, M. Strasser, H. Haufe, T. Sonnweber, F. Hohla, A. Stadlmayr, M. Solioz, H. Tilg, W. Patsch, G. Weiss, F. Stickel, A role for low hepatic copper concentrations in nonalcoholic fatty liver disease, Official journal of the American College of Gastroenterology| ACG. 105 (9) (2010 Sep 1) 1978–1985.
[52] K. Jomova, M. Valko, Advances in metal-induced oxidative stress and human disease, Toxicology 283 (2–3) (2011 May 10) 65–87.
[53] H. Yang, C.N. Liu, R.M. Wolf, M. Ralle, S. Dev, H. Pierson, F. Askin, K.E. Steele, T.H. Magnuson, M.A. Schweitzer, G.W. Wong, Obesity is associated with copper elevation in serum and tissues, Metallomics 11 (8) (2019 Aug) 1363–1371.
[54] D. Zajac, Mineral micronutrients in asthma, Nutrients 13 (11) (2021 Nov 10) 4001.
[55] E. Bellomo, A. Abro, C. Hogstrand, W. Maret, C. Domene, Role of zinc and magnesium ions in the modulation of phosphoryl transfer in protein tyrosine phosphatase 1B, J. Am. Chem. Soc. 140 (12) (2018 Mar 7) 4446–4454.
[56] E. Bellomo, A. Abro, C. Hogstrand, W. Maret, C. Domene, Role of zinc and magnesium ions in the modulation of phosphoryl transfer in protein tyrosine phosphatase 1B, J. Am. Chem. Soc. 140 (12) (2018 Mar 7) 4446–4454.
[57] A.A. Ali, R.A. El-Wahsh, H.F. Afia, G.A. Abdelaal, Trace element and magnesium in patients with bronchial asthma, Egypt. J. Chest Dis. Tuberc. 71 (1) (2022 Jan 1) 44–50.
[58] S. Jiang, X. Ma, M. Li, S. Yan, H. Zhao, Y. Pan, C. Wang, Y. Yao, L. Jin, B. Li, Association between dietary mineral nutrient intake, body mass index, and waist circumference in US adults using quantile regression analysis NHANES 2007–2014, PeerJ 8 (2020 May 4) e9127.
[59] A. Al Shammaa, A. Al-Thani, M. Al-Kaabi, K. Al-Saeed, M. Alanazi, Z. Shi, Serum magnesium is inversely associated with body composition and metabolic syndrome, Diabetes, Metabolic Syndrome and Obesity 31 (2023 Dec) 95–104.
[60] W.J. Song, Y.S. Chang, Magnesium sulfate for acute asthma in adults: a systematic literature review, Asia Pacific Allergy 2 (1) (2012 Jan 1) 76–85.
[61] L. Kolberg, F. Forster, J. Gerlich, G. Weinmayr, J. Genuneit, D. Windstetter, C. Vogelberg, E. von Mutius, D. Nowak, H. Drexler, T. Schäfer, Nickel allergy is associated with wheezing and asthma in a cohort of young German adults: results from the SOLAR study, ERJ Open Research 6 (1) (2020 Jan 1).
[62] J.S. Joh, M.Y. Kang, J.P. Myong, Dose–response relationship between environmental exposure to nickel and pulmonary function in the Korean general population aged 40 or older, Int. J. Environ. Res. Publ. Health 18 (13) (2021 Jun 30) 7016.
[63] M.G. Ahlström, J.P. Thyssen, M. Wennervaldt, T. Menné, J.D. Johansen, Nickel allergy and allergic contact dermatitis: a clinical review of immunology, epidemiology, exposure, and treatment, Contact Dermatitis 81 (4) (2019 Oct) 227–241.
[64] H.S. Novey, M. Habib, I.D. Wells, Asthma and IgE antibodies induced by chromium and nickel salts, J. Allergy Clin. Immunol. 72 (4) (1983 Oct 1) 407–412.
[65] M. Watanabe, S. Masieri, D. Costantini, R. Tozzi, F. De Giorgi, E. Gangitano, D. Tuccinardi, E. Poggiogalle, S. Mariani, S. Basciani, E. Petrangeli, Overweight and obese patients with nickel allergy have a worse metabolic profile compared to weight matched non-allergic individuals, PLoS One 13 (8) (2018 Aug 28) e0202683.
[66] S. Syurin, D. Vinnikov, Occupational disease predictors in the nickel pyrometallurgical production: a prospective cohort observation, J. Occup. Med. Toxicol. 17 (1) (2022 Nov 5) 21.
[67] G. Genchi, A. Carocci, G. Lauria, M.S. Sinicropi, A. Catalano, Nickel: human health and environmental toxicology, Int. J. Environ. Res. Publ. Health 17 (3) (2020 Feb) 679.
[68] M. Balali-Mood, K. Naseri, Z. Tahergorabi, M.R. Khazdair, M. Sadeghi, Toxic mechanisms of five heavy metals: mercury, lead, chromium, cadmium, and arsenic, Front. Pharmacol. (2021) 227.
[69] Y.S. Pak, A. Oh, Y.L. Kho, D. Paek, Lung function decline and blood lead among residents nearby to industrial complex, Int. Arch. Occup. Environ. Health 85 (2012 Nov) 951–959.
[70] J.Y. Min, K.B. Min, R. Kim, S.I. Cho, D. Paek, Blood lead levels and increased bronchial responsiveness, Biol. Trace Elem. Res. 123 (2008 Jun) 41–46.
[71] I.J. Wang, W.J. Karmaus, C.C. Yang, Lead exposure, IgE, and the risk of asthma in children, J. Expo. Sci. Environ. Epidemiol. 27 (5) (2017 Sep) 478–483.
[72] Sherbeny MM. El, O.G. Behairy, O.I. Mohammad, A.M. Elsayed, Serum levels of lead and copper in a group of Egyptian children with bronchial asthma, Egyptian Journal of Pediatric Allergy and Immunology (The) 14 (2) (2016 Nov 16) 47–52.
[73] H. Hernández-Mendoza, M.J. Rios-Lugo, H.E. Álvarez-Loredo, E.T. Romero-Guzmán, D. Gaytán-Hernández, I. Martínez-Navarro, B.I. Juárez-Flores, C. Chang-Rueda, Serum lead levels and its association with overweight and obesity, J. Trace Elem. Med. Biol. 72 (2022 Jul 1) 126984.
[74] Q.N. Raddam, N.K. Assad, Determination of blood lead concentration in pateints with asthma, in: InJournal of Physics: Conference Series, vol. 1294, IOP Publishing, 2019 Sep 1 062071, 6.
[75] T. Mattila, T. Santonen, H.R. Andersen, A. Katsonouri, T. Szigeti, M. Uhl, W. Wąsowicz, R. Lange, B. Bocca, F. Ruggieri, M. Kolossa-Gehring, Scoping Review—the association between asthma and environmental chemicals, Int. J. Environ. Res. Publ. Health 18 (3) (2021 Feb) 1323.
[76] G. Yang, T. Sun, Y.Y. Han, F. Rosser, E. Forno, W. Chen, J.C. Celedón, Serum cadmium and lead, current wheeze, and lung function in a nationwide study of adults in the United States, J. Allergy Clin. Immunol. Pract. 7 (8) (2019 Nov 1) 2653–2660.
[77] S.S. Yalçın, N. Emiralioğlu, S. Yalçın, Evaluation of blood and tooth element status in asthma cases: a preliminary case–control study, BMC Pulm. Med. 21 (1) (2021 Dec) 1–8.
[78] R. Garner, P. Levallois, Cadmium Levels and Sources of Exposure Among Canadian Adults, Statistics Canada, Ottawa, ON, Canada, 2016 Feb 1.
[79] M. Zhao, X. Ge, J. Xu, A. Li, Y. Mei, J. Zhao, Q. Zhou, X. Liu, L. Wei, Q. Xu, Negatively interactive effect of chromium and cadmium on obesity: evidence from adults living near ferrochromium factory, Ecotoxicol. Environ. Saf. 231 (2022 Feb 1) 113196.
[80] M. Fernández-Nieto, S. Quirce, J. Carnés, J. Sastre, Occupational asthma due to chromium and nickel salts, Int. Arch. Occup. Environ. Health 79 (2006 Jun) 483–486.
[81] A.A. Tinkov, M.G. Skalnaya, O.P. Ajsuvakova, E.P. Serebryansky, J.C. Chao, M. Aschner, A.V. Skalny, Selenium, zinc, chromium, and vanadium levels in serum, hair, and urine samples of obese adults assessed by inductively coupled plasma mass spectrometry, Biol. Trace Elem. Res. 199 (2021 Feb) 490–499.
[82] F. Wahlqvist, I.L. Bryngelsson, H. Westberg, P. Vihlborg, L. Andersson, Dermal and inhalable cobalt exposure—uptake of cobalt for workers at Swedish hard metal plants, PLoS One 15 (8) (2020 Aug 6) e0237100.
[83] F. Wahlqvist, I.L. Bryngelsson, H. Westberg, P. Vihlborg, L. Andersson, Dermal and inhalable cobalt exposure—uptake of cobalt for workers at Swedish hard metal plants, PLoS One 15 (8) (2020 Aug 6) e0237100.
[84] R. Sauni, A. Linna, P. Oksa, H. Nordman, M. Tuppurainen, J. Uitti, Cobalt asthma—a case series from a cobalt plant, Occup. Med. 60 (4) (2010 Jun 1) 301–306.
[85] R. Sauni, A. Linna, P. Oksa, H. Nordman, M. Tuppurainen, J. Uitti, Cobalt asthma—a case series from a cobalt plant, Occup. Med. 60 (4) (2010 Jun 1) 301–306.