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Serum selenium levels and asthma among seafood processing workers in Greenland

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ABSTRACT
Selenium levels in the Inuit population of Greenland have been declining during the last decades. The association between Selenium and asthma has been investigated previously, but with conflicting results. The objective was to measure human serum Se (s-Se) in Greenlandic seafood processing workers, to compare with levels recorded in previous decades and to establish if s-Se is associated with asthma or lung function. Data, including questionnaire answers, spirometry, skin-prick test and s-Se from 324 seafood processing workers in Greenland were collected during 2016–2017. Mean s-Se values were compared by t-test and one-way ANOVA. Associations between s-Se and asthma, symptoms from the lower airways at work and lung function were assessed using linear regression. The mean s-Se was 96.2 µg/L. S-Se was higher among non-smokers and workers living in settlements. Workers with asthma did not have s-Se levels significantly different from those of non-asthmatics. We found a positive association between s-Se levels and FEV_1 values. Selenium levels appear to continue declining in Greenland, presumably because of a more Westernised lifestyle. The health effects of declining Selenium levels remain unclear. We did not establish an association between s-Se and asthma, but we did record a positive association between s-Se and FEV_1.

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Introduction

Selenium (Se) is a mineral found naturally in the soil and thereby in several vegetables and grains. It is also found in fish and entrails [1]. Food of marine origin and meat from reindeer and polar bears have traditionally contributed a considerable proportion of the Inuit Se intake [2]. Se levels in humans were previously assessed in Greenland showing high Se levels [3–5]. Furthermore, Se levels have been declining in humans in Greenland from 1986 to 2004 while levels in the marine environment have remained stable. Thus, the reason for the declining Se levels in humans should be found in Inuit lifestyle changes with less intake of traditional marine food [3]. Se has been thought to protect against asthma [1]. The pathophysiology of asthma involves reactive oxygen species (ROS), normally scavenged by enzymatic antioxidants, e.g. glutathione peroxidase 1 (GPX-1) in the lungs. Se serves as a cofactor in GPX-1, thereby playing an essential role for GPX-1 [6]. For this reason, several studies have investigated this potential association between asthma and Se, but the findings have been inconsistent [6–15]. Several studies have supported a protective role of Se in asthma [16–24], but just as many have not [25–34]. Moreover, one study found higher Se levels among asthma cases [35]. In the 1940s, asthma was extremely rare in Greenland [36], whereas 4.2% of Greenlandic children aged 0–14 years in 1991 and 10.9% of Greenlandic children aged 0–14 years in 2001 were prescribed anti-asthmatics [37]. This indicates that the asthma incidence is increasing among the Inuit population in Greenland [37–39], a change that has co-occurred with the adoption of a more Westernised lifestyle [4,40]. These findings are supported by Backer et al., who found that Inuit living in Denmark adapts to a modern lifestyle and probably because of this develops patterns of respiratory illness similar to those of Danes in Denmark. Concurrently, Inuit living in

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Uummannaq, a small town with a more traditional Inuit lifestyle, were found to have a lower frequency of asthma than Inuit living in Nuuk, the capital of Greenland with a more Westernised lifestyle [41]. Besides lifestyle, another possible explanation, which might partly explain a rising asthma incidence among Inuit in Greenland, is the hygiene hypothesis in which asthma incidence is believed to be rising concurrently with people being less exposed to microbes [42].

The objective of the study was to measure human serum Se (s-Se) in Greenlandic seafood processing workers in Western Greenland, to compare with levels recorded in previous decades and to establish if s-Se is associated with asthma or lung function.

Materials and methods

Study population

In 2016, all employees at several seafood processing factories in the Disco Bay region of Greenland were invited to participate in a study on respiratory health. Data were collected from factories, both large and small, as well as from trawlers. Three large factories with approximately 60–118 employees were located in the largest towns in Greenland, the capital of Nuuk with 17,984 residents [43], and Ilulissat and Sisimiut with 4,630 and 5,498 residents, respectively [44,45]. The smaller factories located in four small settlements had approximately 12–40 employees. The three factory trawlers had approximately 11–34 employees. All trawlers set off from the larger towns of Nuuk and Sisimiut. Hence, most of the workers on these trawlers probably originated from larger towns, though this information was not included in the questionnaire. Some of the trawler employees originated from other parts of Greenland and the Faroe Islands, where some were flown in to work on the factory trawlers. The number of eligible workers could not be determined precisely because several workers were seasonal workers or were in the process of being hired or leaving their jobs. Based on employment lists and talks with the daily leaders on the factories, we estimated that approximately 415 people were potentially employed. Of these potential employees, we examined 324 equalling a participation rate of approximately 78%. Among the workers present at the examination day, nearly 100% participated in the study. The final study population consisted of 336 workers, of whom 12 had missing data, i.e. lacking s-Se levels. Hence, 324 workers aged 16–68 years were included in the analyses. The study was approved by The Regional Ethics Committee in the Central Denmark Region (2012–58-006) and the Ethics Committee for Medical Research in Greenland (2015–11317). Written and oral informed consent was obtained from each participant.

Data collection

Data were collected from 2016 to 2017 in the factories and trawlers by physicians specialised in occupational medicine. They were assisted by native medical students who were fluent in Greenlandic language. The participants received a questionnaire in both Danish and Greenlandic with questions on ethnicity, work, health, smoking and diet. Regarding diet, the participants were asked to state for how many times a month they ingested different food items, both traditional Greenlandic food items and imported foods. The participants were offered help by the researchers or by a Danish-Greenlandic medical student if they were unable to fill in the questionnaire themselves.

Subsequently, the participants underwent clinical examinations with spirometry, skin-prick test and venous blood samples.

Spirometry was performed using a spirometer (MIR Spirobank II spirometer), using the predicted values for Caucasians by GLI2012 [46,47]. Weight and height were measured without shoes and wearing light indoor clothes. Lung function was measured by forced expiratory volume in the first second of expiration (FEV_1) and forced vital capacity (FVC). If FEV_1/FVC was reduced by 20% or more in proportion to the expected value, lung function was measured again 15–20 minutes after inhalation of 0.2 mg salbutamol. The best FEV_1 and FVC from a minimum of three acceptable blows from each participant were included in the study according to European Respiratory Society/American Thoracic Society (ERS/ATS) guidelines [48]. A dataset with the spirometry data was created; and predicted values, lower limits of normal and z-scores for spirometric indices were calculated using the Quanjer GLI-2012 regression equations for Caucasians using the SPSS macro [46,49].

Participants underwent skin-prick test with a standard prick test panel, including birch, grass mix, mug wort, horse, dog, cat, house-dust mite and mould, and 5–9 specifically designed seafood preparations, including extracts from Northern prawn (raw meat, cooked meat, cooking water), Snow crab (mashed entire crab with entrails, shell, mouth, etc., raw meat, cooked meat, cooking water), Greenland cod (raw meat) and Greenland turbot (raw meat).

Asthma diagnosis

Three outcomes were defined: asthma, allergic asthma and symptoms from the lower airways at work.

Participants were categorised with asthma based on answers to the questionnaire regarding lower airway symptoms and history of asthma diagnosed by a doctor. Participants were diagnosed as having asthma if they reported at least two symptoms of cough, shortness of breath or wheezing within the previous 12 months and/or a previous diagnosis of asthma by a doctor. If those categorised as having asthma also reported positive answers regarding the symptoms of chronic bronchitis (cough with sputum for at least 3 months in the previous year), they were re-categorised to not having asthma. If these individuals performed a positive reversibility test with a more than 12% improvement in lung function after the inhalation of β_2-agonist, they were re-categorised as having asthma, despite symptoms of chronic bronchitis. A total of 30 participants were asked to observe their lung function for 2 weeks by peak flow monitoring. Due to the lack of compliance, these measurements were not included in the analyses. Participants were categorised as having allergic asthma if they were categorised as having asthma in combination with a positive skin prick test. Participants were categorised as having symptoms from the lower airways at work if they reported at least two symptoms from the lower airways during working hours (cough, wheezing, shortness of breath).

Blood samples

The serum samples were analysed at Odense University Hospital, Denmark. Se in serum samples was measured using inductively coupled plasma – mass spectrometry (ICP-MS) on an iCAP-Qc ICP-MS instrument (Thermo Fisher, Winsford, UK) [50–52]. The performance of the instrument was tested daily using a tune solution (Tune B solution, Thermo Scientific). The most abundant selenium isotope is ^{80}Se; however, due to polyatomic interference from ^{40}Ar^{40}Ar, measurements were performed on ^{78}Se. Analyses on the instrument were run in standard (STD) mode with interference-correction using mathematical correction from the ^{83}Kr signal: ^{78}Se – 0.0304348 × ^{83}Kr. The running conditions were sample uptake time 40 s, a wash step of 45 s and a dwell time of 0.01 s. All samples, calibrators and controls were diluted (1:15) in buffer containing Gallium (^{71}Ga, 5 µmol/L), 0.5% HNO_3, 0.1% Triton-X 100 and 1% propanol. ^{71}Ga was included as an internal standard to ensure that there was no drift during analysis and to be able to compensate for potential uptake variation and/or minor drift during the runs. As internal, daily control, we used Seronorm Trace Elements serum controls (Sero, Billingstad, Norway) at two different levels. As calibrator, a serum pool was spiked with increasing concentrations of a certified selenium standard for ICP solution (#50,002, Sigma-Aldrich, St. Louis, MO, USA). The calibrators were tested using certified reference material from BCR® at three different levels; BCR®637, 638, 639. The calibrators were analysed at the beginning of every run, followed by the two Seronorm controls (L1 and L2); for every 10th sample, a verification control was included (calibrators); and every series was finalised by the two Seronorm controls. This was to certify no drift during the daily runs.

Smoking

Participants were categorised as smokers if they answered *yes* to smoking in the questionnaire and as non-smokers if they answered *no* to smoking or *yes* to former smoking.

Statistical analyses

S-Se showed a normal distribution. Mean values were compared by t-test and one-way ANOVA. Associations between s-Se and asthma, allergic asthma, symptoms from the lower airways at work and lung function measurements, including FEV_1, FVC and FEV_1/FVC were assessed using linear regression analyses with adjustment for smoking and workplace. Statistical analyses were performed with Stata version 15.1 (StataCorp LLC, College Station, Texas). For all analyses, $p < 0.05$ was considered the level of significance. IBM SPSS Statistics version 25 was used for the predicted lung function value calculations [53].

Results

Study group

A total of 324 workers (mean age [SD], 39.6 years [13.7]) were enrolled in the study and agreed to give blood. Of these, 72% were men and 28% women. As far as origin was concerned, 97% considered themselves of Inuit origin, whereas 3% were of other origin, mainly Danish. Among participants, 72% were smokers and 28% were non-smokers, including former smokers. Most of the participants worked at large factories (Table 1).

Table 1. Characteristics of the study population.

	Study cohort (n = 324)
Proportion answering questions on diet (% (n))	33 (108/324)
Gender (% ♂/♀)	72/28
Age (mean [SD] years)	39.6 [13.7]
Age range (years)	16–68
Ethnicity (% Inuit/other)	97/3
Workplace (%)	
Large factory	68
Trawler	14
Small factory	18
Smoking (% yes/no)	72/28
FEV_1 (% predicted) (mean (95% CI))	107.64 (105.76–109.53)
FVC (% predicted) (mean (95% CI))	111.44 (109.78–113.09)
FEV_1/FVC (% (95% CI))	78.96 (78.14–79.77)
FEV_1 z-score (mean (95% CI))	0.63 (0.49–0.78)
FVC z-score (mean (95% CI))	0.89 (0.77–1.02)
FEV_1 LLN (mean (95% CI))	2.86 (2.80–2.92)
FVC LLN (mean (95% CI))	3.51 (3.43–3.58)
$FEV_1 < FEV_1$ LLN (% (95% CI))	1.86 (0.83–4.08)
Asthma (% yes/no)	28/72
Symptoms from lower airways at work (% yes/no)	18/82
s-Se (mean [SD] μg/L)	96.22 [14.58]

Selenium

S-Se levels ranged from 66.50 μg/L to 164.94 μg/L. S-Se levels were significantly higher among non-smokers than among smokers (Figure 1a). The workers employed in large factories and thereby living in large towns had significantly lower s-Se levels than workers employed in smaller factories and thereby living in settlements. Workers at the trawlers had significantly higher s-Se levels than workers at large factories. S-Se levels among workers at trawlers were not significantly different from s-Se levels among workers at small factories (Figure 1b).

S-Se levels were the same in workers with asthma and workers without asthma (Figure 1c). Furthermore, we failed to find a difference in s-Se levels when analysing only asthma cases divided into allergic asthma and non-allergic asthma (Figure 1d).

Workers reporting symptoms from the lower airways at work had significantly lower s-Se levels than workers not reporting symptoms at work (Figure 1e). This association was statistically significant when adjusting for age, gender, smoking and workplace by linear regression (Table 2).

When comparing s-Se levels to lung function measurements, specifically to FEV_1, we found a positive association

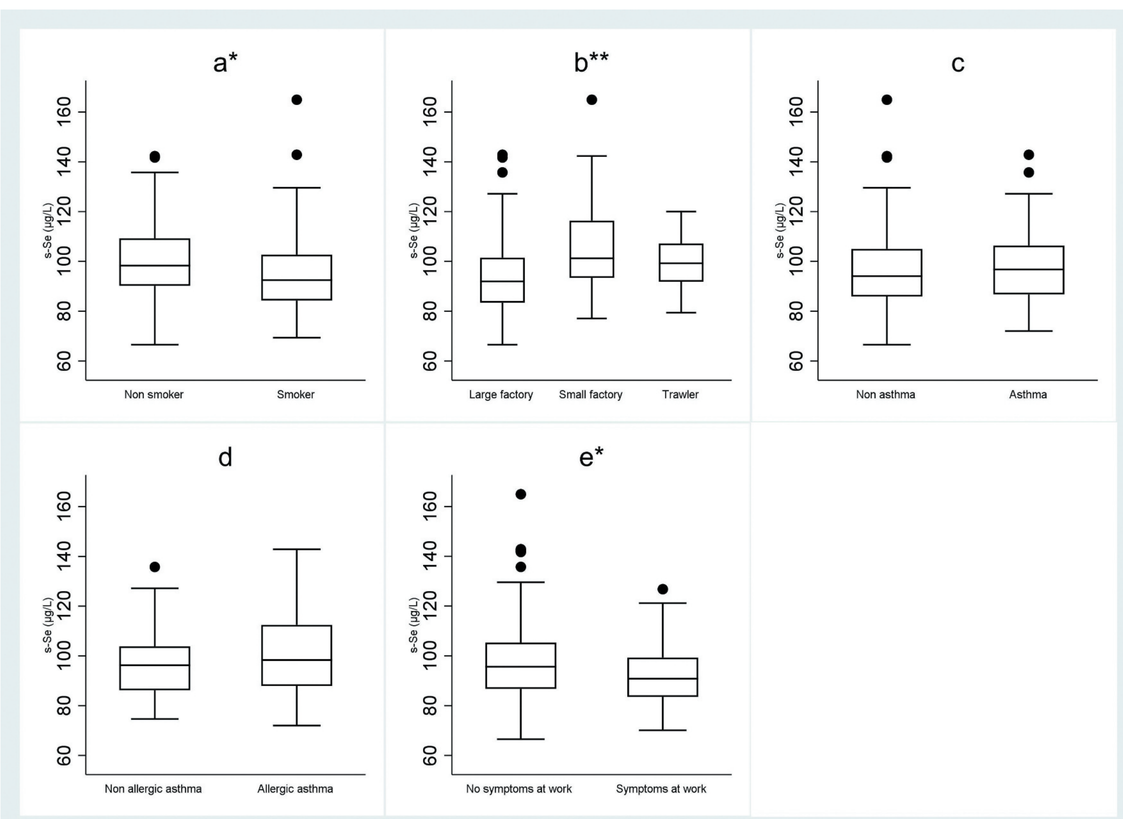

Figure 1. Boxplots of s-selenium levels among non-smokers and smokers (a), workers in the large factories, small factories and trawlers (b), non-asthma cases and asthma cases (c), non-allergic asthma cases and allergic asthma cases (d) and workers with and without symptoms from the lower airways at work (e).

*Significant differences in s-Se levels ($p < 0.05$). **s-Se levels were significantly higher among workers at small factories and trawlers than among workers at large factories. No significantly different s-Se levels were observed among workers at trawlers compared with workers at small factories. Significant differences in s-Se levels ($p < 0.05$).

Table 2. Multiple linear regression analyses for associations between s-selenium (dependent variable) and asthma, allergic asthma, symptoms from the lower airways at work and pulmonary function tests adjusted to age, gender, smoking and workplace. A detailed overview of the multiple linear regression analyses is available online in a supplementary table.

	N	Coefficient	95% confidence interval
Asthma	76	−0.72	−3.64–3.49
Allergic asthma	29	4.50	−2.35–11.34
Symptoms at work	57	−6.00	−9.82- −2.17
FEV_1 z-score	-	1.27	0.14–2.40
FVC z-score	-	0.30	−1.01–1.62
FEV_1/FVC z-score	-	2.65	1.13–4.18

between s-Se levels and FEV_1 values ($p = 0.002$) (Figure 2). We also found a significant association between s-Se levels and FEV_1/FVC z-score. These positive associations remained statistically significant when adjusting for smoking and workplace by linear regression (Table 2). A detailed overview of the linear regression analyses is available online in a supplementary table.

Only 108 out of 324 participants answered the questions regarding diet. Of these 108 participants, a high percentage ingested seafood a minimum of once a month. Most ingested fish (94%) followed by shrimp (97%), seal (88%), whale (76%), crab (72%) and walrus (28%). On the contrary, 95% to 99% ingested western food once a month (meat, potatoes, grain, vegetables and fruit) and 84% ingested fast-food minimum once a month. All but two participants, who answered the questions regarding diet, worked in the large cities. When comparing s-Se levels between workers reporting intake of traditional food more than once a week to those reporting intakes of traditional food once a week or less, we found no difference in s-Se level ($p = 0.393$). When comparing s-Se levels according to intake of fish, which constituted the majority of the traditional food intake, we found an association between fish intake and s-Se. Participants ingesting fish once a week or more had a significantly higher s-Se level than participants ingesting fish more rarely. We found no significant association between s-Se levels and FEV_1 z-score by linear regression in this part of the study population. The lack of association between s-Se levels and FEV_1 z-score among those answering the diet questions remained absent when adjusting the linear regression for fish intake and workplace (results not shown).

Discussion

The mean s-Se level was 96.22 µg/L, ranging from 66.50 µg/L to 164.94 µg/L. This is slightly higher than

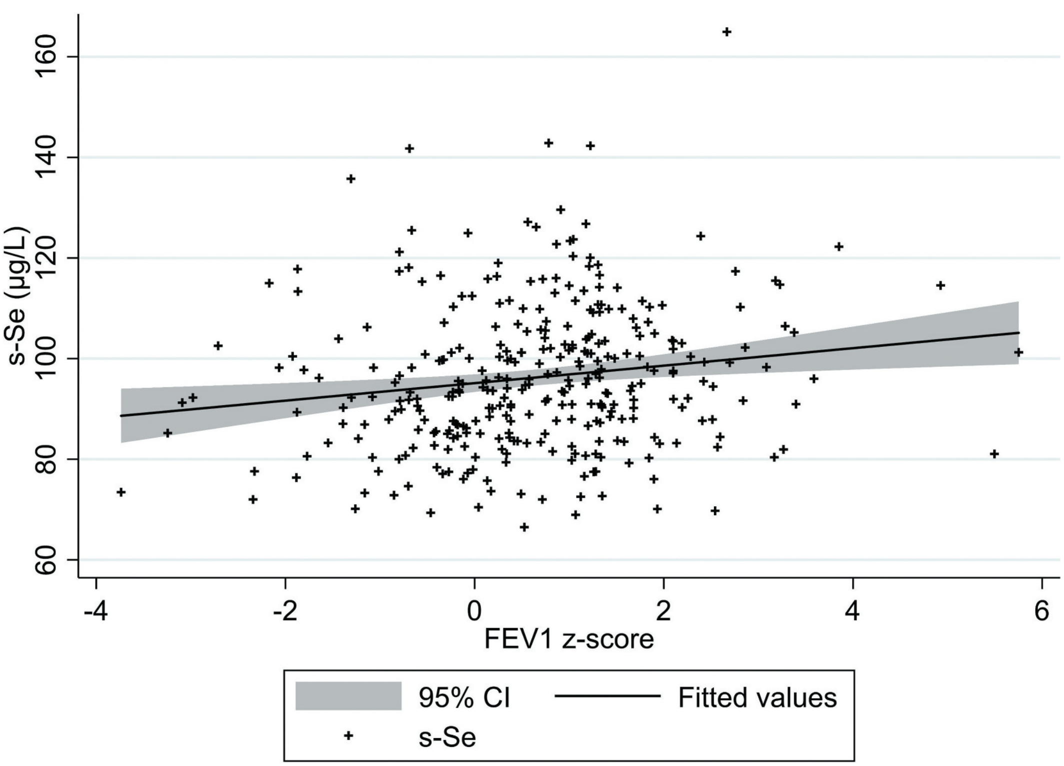

Figure 2. Relationship between s-selenium and FEV_1 z-score. S-selenium levels showed a positive association with FEV_1. The mean FEV_1 z-score was above 0, indicating that the mean Inuit lung function was higher than the predicted Caucasian lung function used as a reference.

measurements in European countries in a study from 2008 (plasma Se, 85.4 µg/L and 85.7 µg/L) [28]. By comparison, Se levels were measured among pregnant women in Greenland in 2010–2015. The mean plasma Se was 72.9 µg/L in the Disco Bay region, i.e. lower than the mean Se level in the present study, presumably as a result of different lifestyles among pregnant women and adult men [5]. Earlier measurements in Greenland showed whole-blood Se levels ranging from 803 to 3,100 µg/L in Qaanaaq (north-west coast) in 1986, 198 µg/L (mean) in Ittoqqortoormiit (east coast) in 1999, 180 µg/L (mean) in Tasiilaq (east coast) in 2000–2001, 149 µg/L (mean) in Sisimiut (west coast, Disco Bay Region) in 2002–2003, 483 µg/L (mean) in Qaanaq in 2003 and 354 µg/L (mean) and 743 µg/L (mean) in Uummannaq (north-west coast) in 1999 and 2004, respectively [2,3]. Compared with these earlier measurements of Se in blood in Greenland, the Se level appears to continue declining. As measurements in the marine environment from 1986 to 2004 have shown steady Se levels, the reason for declining Se levels in humans should be found in Inuit lifestyle changes [3]. Lifestyle may also explain why participants working and living in the settlements had higher s-Se levels. The supply of food in the supermarkets is inadequate in some periods, especially in the settlements, where people rely more on their own catch from hunting and fishing [54]. Furthermore, people living in larger towns tend to have a more Westernised lifestyle in general [55]. We tried to establish if s-Se levels were associated with a more traditional diet. We found no difference between those who ingested traditional food more than once a week and those who ingested traditional food to a lesser extent. Even so, we did find higher s-Se levels among those ingesting fish once a week or more compared with those eating fish more rarely. Since only a third answered the diet-related questions, the estimates are likely not representative of the population and should be considered with caution.

The s-Se level among participants with asthma and non-asthmatics was the same and in line with the level reported in other studies [25–34]. Still, we found lower s-Se levels among seafood factory workers with symptoms from the lower airways at work and a positive association between FEV_1/FVC and s-Se. A possible explanation could be that Se level reflects the degree of ongoing inflammation in the lungs rather than the asthma diagnosis alone. Adequately treated asthmatics might not be inflamed, leading to less activity of the oxidative defence.

A possible explanation that results on asthma and Se have been conflicting so far and that the s-Se levels were not associated with asthma in our population of adults may be that dietary antioxidants are particularly important during childhood when airways are growing, as stated by Devereux et al. [9]. Hence, Se levels would be more important in childhood when the asthma disease is developing than among adults. Additionally, the effect of dietary factors on the development of asthma may be important already in organogenesis [35].

We found a positive association between s-Se level and FEV_1 as shown previously by Hu et al. and Pearson et al. [56,57]. Again, these findings indicate that the s-Se level is associated with the degree of inflammation in the lungs. Guo et al. found an association between Se status and inflammatory responses in the lungs [17], supporting our findings. It is known that eating fish more than once a week is associated with a higher FEV_1, probably because of the effect of fish oil on arachidonic acid metabolism and thereby inflammatory processes [58]. We tried to establish if fish intake among the participants could explain some of the association between FEV_1 and s-Se. Among the participants answering the questions regarding diet, we found a high percentage eating fish more than once a week. In this small part of the study population, we found no association between FEV_1 and s-Se. The absence of association between FEV_1 and s-Se among those answering the diet questions remained absent when adjusting for fish intake and workplace. Since it was not possible to adjust for fish intake in the entire population because we did not have data regarding diet, we cannot exclude the possibility that fish intake in general may explain some of the association between Se and FEV_1 in the entire study population. On the other hand, if workers in the settlements ingest more fish than workers in larger towns, we have adjusted for fish intake indirectly by adjusting for workplace in our analyses. Since all but two participants, who answered the questions regarding diet, worked and lived in large towns, it was not possible to compare fish intake to workplace location and thereby test the hypothesis that fish intake reflect living places.

The mean s-Se level was higher than 90 µg/L in our study, a concentration that has previously been shown to be sufficient for near optimal activity of the plasma GPX-1 [29,33]. Thus, for a substantial proportion of the participants, the s-Se level may have been adequate for plasma GPX-1 expression. Hence, we might not have seen an association between s-Se level and asthma in our study because GPX-1 was functioning adequately.

It is plausible that the effect of Se on asthma is modified by other factors. For instance, Se has been shown to act synergistically with vitamin E in some of its biological actions [28]. Smoking has also been associated with Se in other studies [28]. We did adjust for current smoking, but it was not possible to adjust for other confounders since we did not measure these outcomes. Like other studies, we found that smokers had lower s-Se levels than non-smokers. As stated by Burney et al., Se has a protective effect against asthma in non-smokers who are exposed to environmental tobacco smoke [28]. S-Se levels appear to be lower in smokers for two reasons. First, smokers consume less selenium-rich foods than non-smokers as they tend to select diets that are low in nutrient density [59]. Second, smoking induces oxidative stress in the airways, where ROS is scavenged by antioxidants. Thereby, smokers use up their antioxidants, including selenium [60].

Finally, to explain inconsistent and conflicting findings in previous studies as well as in our study, it is possible that Se intake is not linearly related to the inflammation occurring during asthma [7,8]. Hoffman et al. found that both diets moderately deficient in Se and diets with a high Se content produced lower levels of asthma, while adequate diets resulted in high levels of asthma [7,8]. Also, Bishopp et al. suggested that the association between antioxidant level and asthma is not a simple dose-response relationship. They argued that the function and use of antioxidants in relation to asthma were factors of larger importance than the absolute deficiency of antioxidants [25]. An explanation for conflicting results may also be that studies exploring the association between asthma and Se have not adjusted for the same variables, leading to different results.

Krause et al. found that Inuit has a higher lung capacity than Caucasians of the same gender, height and age [61]. When comparing the lower 5th centile of FEV_1 LLN to the measured FEV_1, only 1.86% of the participants had FEV_1 values below the lower 5th centile of FEV_1LLN in comparison to the expected 5%. Hence, as we used Caucasian reference values, this indicates that Inuit has a higher lung function than Caucasians, as also stated by Krause et al. [61]. Additionally, mean FEV_1 and FVC values (% predicted) were above 100%, also indicating that the mean Inuit lung function was higher than the predicted Caucasian lung function.

Our study possesses some strengths including a high participation rate, where almost every worker present at the factories on the examination day participated in the study. Danish-Greenlandic medical students conducted the interviews, which reduced language barriers. This minor cross-sectional study also comes with some weaknesses. One of the weaknesses of the study is that it was not possible to adjust for exactly the same variables, such as socioeconomic status since we did not have access to this information. However, we do believe to have adjusted for the most important confounders including gender, age, smoking and geography. Some workers did not show up at work on the examination day. There may be several reasons for this. At some factories, there was not enough work on the days of our investigations for the entire workforce to be present. Some workers were said to be engaged in other social activities, but it is also possible that the ones who did not show up were those with poor health. An important weakness is that the asthma diagnosis relied on a self-reported doctor's diagnosis or symptoms in combination with spirometry and reversibility tests among those with signs of pulmonary obstruction. We did not perform a bronchial challenge test or serial peak flow monitoring. Moreover, in order to reduce the length of the questionnaire, we did not include questions regarding asthma medication in the questionnaire, thus inducing a non-differential misclassification due to both low sensitivity and specificity in the diagnosis of the disease. The risk estimate will hence move towards zero, thus blurring a potential effect.

Conclusion

Se levels appear to continue declining in Greenland, presumably because of their more westernised lifestyle. The health effects of declining Se levels remain unclear. Since we did not observe an association between s-Se and asthma, it is possible that Se levels in Greenland remain adequate to withhold sufficient physiologic effects with regard to asthma. However, an association was found between s-Se and lung function, suggesting a possible association with inflammation in the lungs. If Se levels continue to decline in Greenland, a concern may be that sufficient physiologic effects of Se might not be sustained. A continued focus on Greenlandic lifestyle and the possibility to consume traditional food is important.

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Disclosure statement

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References

[1] Selenium. Monograph. Altern Med Rev. 2003;8:63–71.
[2] Deutch B, Dyerberg J, Pedersen HS, et al. Dietary composition and contaminants in north Greenland, in the 1970s and 2004. Sci Total Environ. 2006;370(2–3):372–381. Accessed 2020 Jan 27. https://doi.org/10.1016/j.scitotenv.2006.07.015
[3] Hansen JC, Deutch B, Pedersen HS. Selenium status in Greenland Inuit, Sci. Total Environ. 2004;331(1–3):207–214.
[4] Deutch B, Dyerberg J, Pedersen HS, et al. Traditional and modern Greenlandic food - Dietary composition, nutrients and contaminants, Sci. Total Environ. 2007;384(1–3):106–119.
[5] Bank-Nielsen PI, Long M, Bonefeld-Jørgensen EC. Pregnant inuit women's exposure to metals and association with fetal growth outcomes: ACCEPT 2010–2015. Int J Environ Res Public Health. 2019;16(7):1171.
[6] Huang Z, Rose AH, Hoffmann PR. The role of selenium in inflammation and immunity: from molecular mechanisms to therapeutic opportunities. Antioxid Redox Signal. 2012;16(7):705–743.
[7] Hoffmann PR, Berry MJ. The influence of selenium on immune responses. Mol Nutr Food Res. 2008;52(11):1273–1280.
[8] Hoffmann PR, Jourdan-Le Saux C, Hoffmann FW, et al. A role for dietary selenium and selenoproteins in allergic airway inflammation, J. Immunol. 2007;179(5):3258–3267.
[9] Devereux G, Seaton A. Diet as a risk factor for atopy and asthma. J Allergy Clin Immunol. 2005;115(6):1109–1117.
[10] McKeever TM, Britton J. Diet and asthma. Am J Respir Crit Care Med. 2004;170(7):725–729.
[11] Allam MF, Lucena RA. Selenium supplementation for asthma (Review). Cochrane Database Syst Rev. 2004. DOI:10.1002/14651858.cd003538.pub2
[12] Norton RL, Hoffmann PR. Selenium and asthma, Mol. Aspects Med. 2012;33(1):98–106.
[13] Riccioni G, D'Orazio N. The role of selenium, zinc and antioxidant vitamin supplementation in the treatment of bronchial asthma: adjuvant therapy of not? Expert Opin Investig Drugs. 2005;14(9):1145–1155.
[14] Baker JC, Ayres JG. Diet and asthma. Respir Med. 2000;94:925–934.
[15] Mao S, Wu L, Shi W. Association between trace elements levels and asthma susceptibility, Respir. Med. 2018;145:110–119.
[16] Huang X, Xie J, Cui X, et al. Association between concentrations of metals in urine and adult asthma: a case-control study in Wuhan, China. PLoS One. 2016;11. DOI:10.1371/journal.pone.0155818.
[17] Guo CH, Liu PJ, Hsia S, et al. Role of certain trace minerals in oxidative stress, inflammation, CD4/CD8 lymphocyte ratios and lung function in asthmatic patients. Ann Clin Biochem. 2011;48(4):344–351.
[18] Chih Hung Guo P-C-C, Liu P-J, Lin K-P. Nutritional supplement therapy improves oxidative stress, immune response, pulmonary function, and quality of life in allergic asthma patients; an open-label pilot study. Altern Med Rev. 2012;17:42–56.
[19] Carneiro MFH, Rhoden CR, Amantéa SL, et al. Low concentrations of selenium and zinc in nails are associated with childhood asthma. Biol Trace Elem Res. 2011;144(1–3):244–252.
[20] Malling TH, Sigsgaard T, Andersen HR, et al. Differences in associations between markers of antioxidative defense and asthma are sex specific, Gend. Med. 2010;7:115–124.
[21] Kocyigit A, Armutcu F, Gurel A, et al. 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. 2004;97:31–41.
[22] Omland O, Deguchi Y, Sigsgaard T, et al. Selenium serum and urine is associated to mild asthma and atopy. The SUS study. J Trace Elem Med Biol. 2002;16:123–127.
[23] Seif PGJB, Shaheen O, Sterne JAC, et al. Dietary antioxidants and asthma in adults population-based case–control Study. Am J Respir Crit Care Med. 1823–1828;164:2001.
[24] Misso NLA, Powers KA, Gillon RL, et al. Reduced platelet glutathione peroxidase activity and serum selenium concentration in atopic asthmatic patients. Clin Exp Allergy. 1996;26(7):838–847.
[25] Bishopp A, Sathyamurthy R, Manney S, et al. Biomarkers of oxidative stress and antioxidants in severe asthma: a prospective case-control study. Ann Allergy, Asthma Immunol. 2017;118:445–451.
[26] N. Ariaee, R. Farid, F. Shabestari, M. Shabestari, F. Jabbari Azad, Trace Elements Status in Sera of Patients with Allergic Asthma. Reports Biochem Mol Biol. (2016); 5: 20–25. www.RBMB.net.
[27] Bakkeheim E, Mowinckel P, Carlsen KH, et al. Altered oxidative state in schoolchildren with asthma and allergic rhinitis. Pediatr Allergy Immunol. 2011;22:178–185.
[28] Burney P, Potts J, Makowska J, et al. A case-control study of the relation between plasma selenium and asthma in European populations: a GA2LEN project. Allergy Eur J Allergy Clin Immunol. 2008;63(7):865–871.
[29] Shaheen SO, Newson RB, Rayman MP, et al. Randomised, double blind, placebo-controlled trial of selenium supplementation in adult asthma. Thorax. 2007;62:483–490.

[30] Jacobson GA, Yee KC, Ng CH. Elevated plasma glutathione peroxidase concentration in acute severe asthma: comparison with plasma glutathione peroxidase activity, selenium and malondialdehyde. Scand J Clin Lab Invest. 2007;67(4):423–430.
[31] Rubin RN, Navon L, Cassano PA. Relationship of serum antioxidants to asthma prevalence in youth. Am J Respir Crit Care Med. 2004;169(3):393–398.
[32] Picado MTC, Deulofeu R, Lleonart R, et al. Dietary micronutrients/antioxidants and their relationship with bronchial asthma severity. Allergy. 2001;56(1):43–49.
[33] Fenech AG, Ellul-Micallef R. Selenium, glutathione peroxidase and superoxide dismutase in maltese asthmatic patients: effect of glucocorticoid administration. Pulm Pharmacol Ther. 1998;11:301–308.
[34] Flatt A, Pearce N, Thomson CD, et al. Reduced selenium in asthmatic subjects in New Zealand. Thorax. 1990;45(2):95–99.
[35] Oluwole O, Arinola OG, Adu MD, et al. Relationships between plasma micronutrients, serum IgE, and skin test reactivity and asthma among school children in rural Southwest Nigeria. J Biomarkers. 2014;(2014):1–9.
[36] Ehrström MC. Medical studies in North Greenland 1948-1949. III. Allergic and pulmonary emphysema. Acta Medica Scand CXL. 1951;317–323.
[37] Niclasen BVL. Changes in drug prescription over a decade in an Arctic child population. Acta Paediatr Int J Paediatr. 2006;95(11):1456–1460.
[38] Krause TG, Koch A, Friborg J, et al. Frequency of atopy in the Arctic in 1987 and 1998. Lancet. 2002;360(9334):691–692.
[39] Niclasen BVL, Bjerregaard P. Review article: child health in Greenland. Scand J Public Health. 2007;35(3):313–322.
[40] Milman N, Laursen J, Byg K-E, et al., Elements in autopsy liver tissue samples from Greenlandic Inuit and Danes. V. Selenium measured by X-ray fluorescence spectrometry, 2004. Accessed 2019 Dec 3. http://www.etsevier-deutschland.de/jtemb.
[41] Backer V, Nepper-Christensen S, Porsbjerg C, et al. Respiratory symptoms in Greenlanders living in Greenland and Denmark: a population-based study. Ann Allergy Asthma Immunol. 2004;93(1):76–82.
[42] Strachan DP Hay fever, hygiene, and household size. Br Med J. 1989;299(6710):1259–1260. https://doi.org/10.1136/bmj.299.6710.1259
[43] Statistik G. Grønland i tal 2019, 2019. Accessed 2020 Apr 24. http://www.stat.gl/publ/da/GF/2019/pdf/Grønlandital2019.pdf.
[44] Kommunia A, (n.d.). cited 2020 Apr 24. https://www.avannaata.gl/Emner/Om_kommunen/Faktaomkommunen?sc_lang=da
[45] Kommunia Q, (n.d.). cited 2020 Apr 24. http://qeqqata.odeum.com/dk/by-_og_bygdeplaner/sisimiut/
[46] Quanjer PH, Stanojevic S, Cole TJ, et al., the E.G.L.F. Initiative. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012;40(6):1324–1343.
[47] Mark LI, Fenton E, Stanojevic S, et al. Interpretation of spirometry in Saskatchewan First Nations adults. Ann Am Thorac Soc. 2012;15(10):1237–1239.
[48] Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):319–338.
[49] SPSS macro, (n.d.). cited 2020 Sept 18. https://dev.ers-education.org/lr/show-details/?idParent=138989
[50] Labat L, Dehon B, Lhermitte M. Rapid and simple determination of selenium in blood serum by inductively coupled plasma-mass spectrometry (ICP-MS). Anal Bioanal Chem. 2003;376(2):270–273.
[51] Laur N, Kinscherf R, Pomytkin K, et al. ICP-MS trace element analysis in serum and whole blood. PLoS One. 2020;15(5):1–14.
[52] Stojsavljević A, Jagodić J, Vujotić L, et al. Reference values for trace essential elements in the whole blood and serum samples of the adult Serbian population: significance of selenium deficiency. Environ Sci Pollut Res. 2020;27(2):1397–1405.
[53] IBM, (n.d.). cited 2020 Sept 18. www.ibm.com
[54] Johansen P, Pars T, Bjerregaard P. Lead, cadmium, mercury and selenium intake by Greenlanders from local marine food. Sci Total Environ. 2000;245(1–3):187–194.
[55] Bente Deutch JCH. High human plasma levels of organochlorine compounds in Greenland. Dan Med Bull. 2000;47:132–137.
[56] Guizhou Hu PAC, Cassano PA Antioxidant nutrients and pulmonary function: the Third National Health and Nutrition Examination Survey (NHANES III). Am J Epidemiol. 2000;151(10):975–981. https://academic.oup.com/aje/article-abstract/151/10/975/81833
[57] P. Pearson, J. Britton, T. McKeever, S.A. Lewis, S. Weiss, I. Pavord, A. Fogarty, Lung function and blood levels of copper, selenium, vitamin C and vitamin E in the general population. Eur J Clin Nutr. (2005); 59: 1043–1048. https://doi.org/10.1038/sj.ejcn.1602209
[58] Schwartz J, Weiss ST. The relationship of dietary fish intake to level of pulmonary function in the first National Health and Nutrition Survey (NHANES I). Eur Respir J. 1994;7(10):1821–1824.
[59] Kafai MR, Ganji V. Sex, age, geographical location, smoking, and alcohol consumption influence serum selenium concentrations in the USA: third National Health and Nutrition Examination Survey, 1988-1994. J Trace Elem Med Biol. 2003;17(1):13–18.
[60] C.D. Thomson, K. Wickens, J. Miller, T. Ingham, P. Lampshire, M.J. Epton, G.I. Town, P. Pattemore, J. Crane, and T. year six N.Z.A. and A.C.S.G. (NZAACS6). Selenium status and allergic disease in a cohort of New Zealand children. Clin Exp Allergy. (2012); 42: 560–567. https://doi.org/10.1111/j.1365-2222.2011.03924.x
[61] Krause TG, Pedersen BV, Thomsen SF, et al. Lung function in Greenlandic and Danish children and adolescents, Respir. Med. 2005;99:363–371.