

Correlates of Positive Thyroid Peroxidase Antibodies Among Firefighters: A Cross-Sectional Study

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Abstract

Context: Exposure to endocrine disrupting chemicals (EDCs) are associated with underactive thyroid glands, and possibly autoimmunity. Firefighters are exposed to EDCs from flame retardants; however, the prevalence and risk factor associations of thyroid antibodies among firefighters are unknown.

Context: We aimed to determine the prevalence of thyroid peroxidase antibodies (TPOAb) and associated sociodemographic and occupational risk factors among firefighters.

Methods: Firefighters attending professional health and safety conferences between November 2018 and January 2020, and with no prior diagnosis of thyroid disease were invited ($n = 278$) to submit a health survey, blood samples, and complete a thyroid ultrasound. The survey assessed for sociodemographic and occupational characteristics, including a history of familial thyroid disease, smoking, firefighter tenure, and job rank, radiation exposure, and mitigation practices of occupational exposures. Serum thyroid peroxidase antibody (TPOAb) was also assessed.

Results: Approximately 39.9% of firefighters evaluated had a positive TPOAb test. The mean age for those TPOAb positive was lower than those who tested negative (41.4 ± 7.9 vs 43.1 ± 7.9 years, $P = 0.07$) but this difference was not significant. Firefighters with a family history of thyroid disease had a statistically significant higher prevalence of TPOAb compared with those without a family history (60.0% vs 37.5%, $P = 0.02$); this association remained significant after adjusting for sociodemographic and occupational factors (odds ratio 2.99; CI, 1.31–6.85).

Conclusion: The prevalence of TPOAb is high among firefighters in our study, and family history is a significant determinant of testing positive for TPOAb. Firefighters may benefit from TPOAb and thyroid stimulating hormone tests, and screening for family history of thyroid disease at baseline employee medical check-ups. This finding suggests the need for further studies.

Key Words: thyroid, antibody, firefighters, occupation, family, history

Abbreviations: EDC, endocrine disrupting chemical; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PBDE, polybrominated diphenyl ether; PCB, polychlorinated biphenyl; PFAS, per/polyfluoroalkyl substances; SIR, standardized incidence ratio; T4, thyroxine; TPOAb, thyroid peroxidase antibody; TSH, thyrotropin (thyroid stimulating hormone).

Autoimmune thyroid disease is one of the most common types of autoimmune endocrine diseases [1]; testing positive for thyroid antibodies increases the risk of developing thyroid dysfunction [2]. Generally, autoimmune diseases are believed to be initiated by a combination of genetic predisposition and environmental triggers. In the propagation phase of autoimmune diseases, autoimmune reaction creates an inflammatory environment and a catastrophic inflammatory loop resulting in chronic disease [3]. Thyroid antibodies are positive in patients with autoimmune thyroid disease [4]. About 90% to 95% of patients with autoimmune thyroid diseases test positive for thyroid peroxidase antibody (TPOAb) [4]. TPOAb is the most common antibody frequently measured in population studies [5]. There are variations in the prevalence of

thyroid antibodies among different populations, for example, the National Health and Nutrition Examination Survey III (NHANES III) study reported the prevalence of TPOAb among disease-free populations in the United States as $11.3\% \pm 0.4\%$ [6]. A population-based study conducted in Tehran found positive TPOAb at baseline in 8.5% of men and 16.0% of women [7]. The prevalence of positive TPOAb reported by the Nordtrøndelag Health Study (HUNT) study conducted in Norway was 13.9% in females and 2.8% in males [8]. These variations may be attributed to dietary factors such as iodine intake, environmental and genetic factors, or different assay methods used to characterize TPOAb levels [9–12].

Thyroid antibodies are considered sensitive markers of autoimmune thyroid diseases [13]; in the presence of

autoimmune thyroid disease, antithyroid antibodies cause damage to thyroid tissues as a result of impairment of self-tolerance against thyroid antigens and may result in chronic lymphocytic thyroiditis (CLT), also known as Hashimoto's thyroiditis [14, 15]. The association of thyroid diseases and occupational exposure to chemicals such as polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) present in flame retardants mainly used by firefighters has been posited, but definitive evidence to support this hypothesis is limited [16]. Understanding the prevalence and pathogenesis of autoimmune antibodies is significant because of interest in using autoantibodies as a clinical tool/marker of disease. Research has shown that antibodies can predict the development of overt clinical diseases such as thyroiditis and help identify individuals with disproportionate risk, to provide opportunities for earlier interventions [17].

Additionally, flame retardants are implicated in autoimmunity and thyroid disease [18, 19]. Firefighters are exposed to flame retardants and other hazards in the course of their work [20]. Occupational and sociodemographic factors may increase or decrease hazards and chemical occupational risk exposure among firefighters; the chronic long-term effects of these exposures are unclear [21, 22]. While several studies have examined the prevalence and risk of autoimmune thyroid antibodies among occupational groups such as nurses, technicians, and other hospital workers [23], and in the general population [6], there is a paucity of information among firefighters. In this study, we examine the prevalence of TPOAb and associated sociodemographic and occupational correlates among a study population of firefighters.

Methods

Study Population

This cross-sectional study consists of 278 career firefighters in the Firefighter Cancer Initiative (FCI) Polybrominated Diphenyl Ether (PBDE) and Thyroid Function Study. Firefighters were recruited from 2 national firefighter conferences held in Tennessee and Florida between the period November 2018 and December 2020. Firefighters were informed about the study and individuals who wished to participate were screened for study eligibility using a questionnaire and subsequently gave consent. Eligibility criteria were currently active firefighters between the ages of 18 to 65 years, with no history of thyroid conditions including cancer, not on medications for thyroid disease, and not pregnant. Eligible firefighters completed the electronic survey questionnaires using smart forms on electronic tablets to provide sociodemographic, occupational, and health data. Firefighters also underwent ultrasound scans of the thyroid gland by qualified technicians and blood samples taken by qualified phlebotomists for thyroid hormone analysis. Both ultrasound and thyroid function test results were interpreted by endocrinologists. None of the firefighters presented with clinical symptoms of thyroid disorders; however, those found to have suspicious thyroid ultrasound or serum analysis results were contacted and referred to the endocrinology clinic for further investigation ($n = 2$). The research protocol was approved by the University of Miami Institutional Review Board (IRB).

Data Collection and Risk Factor Definitions

Sociodemographic measures, medical and smoking history

Firefighter age at the time of the study, gender (male or female), race (Black, White, American Indian/Alaskan Native, Asian American, Hawaiian/Pacific Islander, and 2 or more races), and ethnicity (Hispanic or non-Hispanic) were assessed. The highest level of educational attainment was categorized into college graduate or higher and some college or less. Respondents were asked if there was a family history of thyroid disease in a first-degree relative i.e., father, mother, or sibling (yes/no) and if they ever smoked 100 cigarettes in their lifetime (yes/no). Participants were asked if they have ever been diagnosed with a sleep disorder (yes/no) and were asked if they had any existing medical conditions (yes/no).

Occupational risk factors

Survey questionnaires were used to collect data on known and potential occupational risk factors. Firefighters were asked to report the number of years they were employed as a firefighter, which we later categorized into < 10 years and ≥ 10 years in the logistic regression. Current job rank was assessed (chief, captain, driver/operator/engineer, lieutenant, firefighter/EMT) which was later categorized into 2 groups: those who performed more administrative roles (chief, captain, and lieutenant) vs those who are more frequently involved in fire calls (driver/operator/engineer, and firefighter). Firefighters were asked if they responded to a fire call in the past 7 days (yes or no). Duration of work shift was assessed (24 hours on/24 hours off, 24 hours on/48 hours off, 24 hours on/72 hours off, or other schedules) and later dichotomized as follows: 1) 24 hours on/24-48 hours off and 2) 24 hours on/72 hours off/others. Additional employment outside of firefighting was assessed by asking if the firefighter had a second job (yes or no). Exposure to hospital ionizing radiation was assessed by asking respondents if they assisted in procedures using x-rays, or CT-scans in the last 12 months (yes or no). Fire station location zip code was categorized using the United States regions of Midwest/West, Northeast/South, and not mentioned for those firefighters who skipped this question.

Firefighter responses to several occupational risk exposure/mitigation questions were combined to form a simple risk score based on whether the respondent owns their protective hood for limiting chemical exposures around the neck and head region (yes or no); whether they engaged in hood swaps following fire incident activities (yes or no); and if they washed their turnout gear in the last month (yes/no). The risk score variable was scored as follows: "0" if firefighters answered no to all 3 questions, "1" if they answered yes to 1 question, "2" if they answered yes to 2 questions, and "3" if they answered yes to all 3 questions.

Blood Collection and Processing

Blood samples were collected in 8.5-mL vacutainer Serum Separator Tubes (SST) and centrifuged onsite at 2400 rpm for 15 minutes to isolate the serum. The resulting 4- to 6-mL serum samples were transferred into aliquots of 2 mL, labeled, and shipped on dry ice through overnight shipping to the laboratory at the University of Miami Miller School of Medicine, for storage and thyroid hormone analysis. TPOAb, thyroid stimulating hormone (TSH), and free thyroxine (T4) were assessed. TPOAb was measured on Immulite

2000 (Siemens Cat#L2KT02, RRID:AB_2756380) platform. TPOAb was reported as positive or negative [24]. The laboratory reference range for TSH and free T4 were given as follows: TSH (0.4-4.0 mIU/L), and (0.8-1.8 ng/dL). Subclinical hypothyroidism is defined as serum TSH concentration above the upper limit of the reference range when serum free T4 concentration is within its reference range. Subclinical hyperthyroidism is defined as a serum TSH concentration below the lower limit of the reference range, when serum free T4 concentration is within the laboratory reference range [25]. There was no case of overt thyroid dysfunction noted in the present study. Of note, thyroid function tests can differ between laboratories and clinic visits, and a single test alone does not relate to a clinical diagnosis.

Statistical Analysis

Statistical analysis was done using SAS 9.4 software (SAS Institute Inc., Cary, NC). Chi-squared test for categorical variables and Student's *t* test for continuous variables were used to compare sociodemographic, clinical, and occupational characteristics among participants positive vs negative for TPOAb. We reported the frequency distribution of categorical variables, means, and SD for numeric variables. Logistic regression models were used to analyze the association between sociodemographic and occupational variables and antithyroid antibodies; unadjusted and adjusted odds ratios (OR) and corresponding 95% CI for the effects of the risk factors are reported. Our model included variables known to be relevant to antithyroid antibodies from literature reviews namely age, gender, family history, smoking history, and ionizing radiation exposure [26, 27]. Age was included in our model as a continuous variable, and our variable on occupational risk prevention practices was dichotomized to represent the number of preventive practices the respondents engage in (engaging in 0-1 or 2-3 preventive practices). We tested a post hoc alternative model which included an interaction term between family history and occupational risk prevention practices given the possibility that firefighters with a family history of the disease might be particularly sensitive to occupational exposures [28]. A value of $P < 0.05$ was considered statistically significant for all analyses. This study was approved by the University of Miami Institutional Review Board (IRB).

Results

This study consisted of 278 firefighters, the mean age (\pm SD) at baseline was 42.4 ± 7.9 years. Most of the firefighters were men (259 of 278 [93.1%]), and most were White (252 of 278 [90.7%]) and non-Hispanic (241 of 278 [86.7%]). A history of ever-smoked cigarettes was reported by 54 (19.4%), and 30 (10.8%) reported a family history of thyroid disease in a first-degree relative. Overall, the number of years employed as a firefighter was 18.0 ± 7.9 years (Table 1).

The prevalence of a positive TPOAb test was 39.9% (111 of 278) among participants. The mean age among those who tested positive to TPOAb was younger than those who tested negative (41.4 ± 7.9 vs 43.1 ± 7.9 years, $P = 0.07$) but this difference was not significant. The proportion of men who tested positive to TPOAb compared with women was similar (40.2% vs 36.8%, $P = 0.78$). Of those who have ever smoked cigarettes, 44.4% tested positive compared with 38.8% of never smokers; this difference was not significant. Firefighters

with a family history of thyroid disease had a statistically significantly higher prevalence of TPOAb compared with those without a family history (60.0% vs 37.5%, $P = 0.02$). High TSH above the reference range (subclinical hypothyroidism) was found in 3.2% of participants (9 of 278), while low TSH/subclinical hyperthyroidism (TSH below the laboratory reference range) was observed in 0.7% (2 of 278) of the overall population. Among those who had high TSH, 66.7% ($n = 6$) were TPOAb positive while 33.3% ($n = 3$) were TPOAb negative. Two firefighters with low TSH tested positive for TPOAb; however, there was a marginal significant difference in TSH tests among TPOAb positive compared to TPOAb negative firefighters ($P = 0.05$) Table 1.

The average number of years employed as a firefighter was statistically significantly different comparing those who tested positive to TPOAb with those who tested negative (16.8 ± 8.2 vs 18.8 ± 7.8 years, $P = 0.03$; Table 2). A similar proportion of firefighters who respond to fire calls vs firefighters with more administrative job duties tested positive for TPOAb (41.8% vs 37.9%, $P = 0.51$). A higher proportion of firefighters whose fire stations were in the Midwest/West of the United States tested positive for TPOAb, compared with those in the Northeast/South and those who did not report their location (48.1 vs 37.4 vs 28.6 , $P = 0.05$) but these findings were not significant. There was no significant difference in TPO-positive tests among firefighters who practice less than 1 compared with 2 or 3 of the prevention practices mentioned previously (40.8% vs 39.8%, $P = 0.94$).

The significance in testing positive for TPOAb observed among those reporting a family history vs those reporting no family history of thyroid disease in our descriptive analysis (60.0% vs 37.5%) remained even after adjusting for sociodemographic and occupational factors (Table 3). The unadjusted odds of testing positive for TPOAb was higher among those who reported a positive family history of thyroid disease in a first-degree relative (OR 2.50; CI, 1.15-5.42) and significantly lower among those who have been employed as a firefighter for 10 years or more compared with those who have been employed less than 10 years (OR 0.50; CI, 0.27-0.91); all other covariates were not significant. The adjusted odds of testing positive for TPOAb remained significant (approximately 3-fold higher) among participants who reported a family history of thyroid disease in first-degree relatives compared with those who did not have a family history (OR 2.99; CI, 1.31-6.85). Age was not a significant predictor of testing positive for TPOAb (OR 0.99; CI, 0.95-1.04); those who reported they had ever smoked cigarettes had a 33% higher likelihood of testing positive for TPOAb, but this was not significant (OR 1.33; CI, 0.69-2.59). Occupational risks such as the average number of years employed as a firefighter were significantly different in our descriptive statistics among those who tested positive for TPOAb compared with those who tested negative (16.8 vs 18.8 years) and in our unadjusted logistic regression. However, the odds were not significant after adjusting for other sociodemographic and occupational variables of participants (OR 0.51; CI, 0.24-1.12). Firefighters stationed in the Midwest/West zones had 43% higher, but nonsignificant odds of testing positive for TPOAb compared with those in the Northeast/South zones of the United States. (OR 1.43; CI, 0.81-2.54). Those firefighters who reported radiation exposure had 16% higher odds of testing positive for TPOAb, but this finding was not significant (OR 1.16; CI, 0.63-2.13). Responding to a fire call in

Table 1. Distribution of thyroid peroxidase antithyroid antibody and baseline sociodemographic characteristics of participants (2018 – 2019)

Characteristics	TPO-antibody						P value
	Overall (N = 278)		No (n = 167)		Yes (n = 111)		
	N	%	N	%	N	%	
Age in years (mean ± SD)	42.4 ± 7.9		43.1 ± 7.9		41.4 ± 7.9		0.07
Age group (years)							0.60
18-29	12	100.0%	6	50.0%	6	50.0%	
30-39	91	100.0%	51	56.0%	40	44.0%	
40-49	126	100.0%	78	61.9%	48	38.1%	
50-64	49	100.0%	32	65.3%	17	34.7%	
Gender							0.78
Male	259	100.0%	155	59.8%	104	40.2%	
Female	19	100.0%	12	63.2%	7	36.8%	
Race ^a							0.79
Other	26	100.0%	15	57.7%	11	42.3%	
White	252	100.0%	152	60.3%	100	39.7%	
Ethnicity							0.42
Hispanic	37	100.0%	20	54.1%	17	45.9%	
Non-Hispanic	241	100.0%	147	61.0%	94	39.0%	
Highest level of education							0.11
College graduate or higher	139	100.0%	77	55.4%	62	44.6%	
Some college or less	139	100.0%	90	64.7%	49	35.3%	
Ever smoked ^b							0.45
No	224	100.0%	137	61.2%	87	38.8%	
Yes	54	100.0%	30	55.6%	24	44.4%	
Sleep disorder							0.69
No	199	100.0%	121	60.8%	78	39.2%	
Yes	79	100.0%	46	58.2%	33	41.8%	
Medical condition ^c							0.43
No	211	100.0%	124	58.8%	87	41.2%	
Yes	67	100.0%	43	64.2%	24	35.8%	
Family history ^d							0.02
No	248	100.0%	155	62.5%	93	37.5%	
Yes	30	100.0%	12	40.0%	18	60.0%	
TSH							0.05 ^e
High	9	100.0%	3	33.3%	6	66.7%	
Low	2	100.0%	0	0.0%	2	100.0%	
Normal	267	100.0%	164	61.4%	103	38.6%	

Bold data are statistically significant at $P < 0.05$.

^aOther race includes Black, Native Hawaiian or Pacific Islander, American Indian or Alaskan Native, other, and don't know/not sure.

^bEver smoked 100 cigarettes in your lifetime?

^cEver been diagnosed with any chronic medical condition?

^dDo you have a first-degree relative (father, mother, brothers, or sisters) with history of thyroid disease?

^eFisher's exact test.

the last 7 days (OR 1.05; CI, 0.59-1.86) and engaging in 2 to 3 vs 0 to 1 preventive activities such as owning your hood, hood swapping after fire calls, or washing of gear in the past month were not significant (OR 1.05; CI, 0.59-1.86. The test of interaction between family history and engaging in occupational preventive practices was also not significant (OR 0.75; CI, 0.13-4.31; full model results not shown).

Discussion

In this study of 278 firefighters, our major finding is the substantially higher prevalence of TPOAb (39.9%) compared

with the prevalence reported in the general United States population ($13.0 \pm 4\%$) from analysis of NHANES data [6]. This prevalence is also notably higher than that reported for middle-aged men (14.9%) and women (22%) in a study conducted in Tehran [7]. Epidemiologic studies have shown several factors are associated with the presence of TPOAb in individuals. Some of the factors examined in this study include age, gender, race/ethnicity, family history of thyroid diseases, cigarette smoking, and ionizing radiation exposure. Age in our study was not a significant predictor of TPOAb; however, most (95%; 266 of 278) of our study participants are in a relatively restrictive age range (30-64 years) where TPOAb

Table 2. Distribution of thyroid peroxidase antibody by occupational characteristics of participants (2018 – 2019)

Characteristics	TPO-antibody						P value
	Overall (N = 278)		No (n = 167)		Yes (n = 111)		
	N	%	N	%	N	%	
Number of years employed ^a (mean ± sd)	18.0 ± 7.9		18.8 ± 7.8		16.8 ± 8.2		0.03
Job rank							0.51
Administrative	132	100.0%	82	62.1%	50	37.9%	
Fire response	146	100.0%	85	58.2%	61	41.8%	
Fire Department USA location^b							0.05
Midwest/West	106	100.0%	55	51.9%	51	48.1%	
Northeast/South	123	100.0%	77	62.6%	46	37.4%	
Not mentioned	49	100.0%	35	71.4%	14	28.6%	
Fire run in the last 7 days							0.94
No	196	100.0%	118	60.2%	78	39.8%	
Yes	82	100.0%	49	59.8%	33	40.2%	
Practice prevention^c							0.94
0-1	87	100.0%	52	59.2%	35	40.8%	
2-3	191	100.0%	115	60.2%	76	39.8%	
Work shift							0.79
24hrs on/24hrs/48hrs off	140	100.0%	83	59.3%	57	40.7%	
24hrs on/72hrs off/other	138	100.0%	84	60.9%	54	39.1%	
More than 1 job							0.94
No	186	100.0%	112	60.2%	74	39.8%	
Yes	92	100.0%	55	59.8%	37	40.2%	
Ionizing radiation exposure^d							0.61
No	205	100.0%	125	61.0%	80	39.0%	
Yes	73	100.0%	42	57.5%	31	42.5%	

^aThe average number of years employed as an active firefighter.

^bGeographic location of participant's fire station in the United States.

^cEngage in the following prevention practices 1. Wash gear in the last month, 2. Hood swap, or 3. Own hood.

^dExposure to ionizing radiation from routine diagnostic x-ray, CT scan, or portable x-ray machines, in the past 12 months.

are the highest levels compared to the extreme of ages [23, 27, 29]. A preponderance of TPOAb and autoimmune diseases is found among females than among males [13, 29], and risk is increased by occupational exposure such as radiation [29]. But in our study, female firefighters compared to male firefighters had a lower prevalence of TPOAb (OR = 0.58), although this difference was not statistically significant. It is important to note that most firefighters are men and hence the sample size of women was small (6.8%; 19 of 278) in this study. The proportion of career female firefighters was 4% nationally as reported by the National Firefighter Protection Association (NFPA) in the year 2020 [30]. In our study, White firefighters had an 13% higher odds of TPOAb than non-Whites; also results by ethnicity showed that non-Hispanic firefighters had a 27% lower odds of TPOAb than Hispanic firefighters. Findings from a study by Spencer et al, using the NHANES data showed that the Non-Hispanic White population had a higher prevalence of TPOAb, 17.4% (23.2% women, 12.3% men) compared with Black 5.6% (8.0% women, 3.1% men), or Mexican American 13.1% (18.7% women, 8.2% men) individuals [31].

We found significantly higher odds of testing positive for TPOAb among participants with a family history of thyroid disease (adjusted OR 2.99). Post hoc testing of the interaction between family history and occupational prevention practices

was not significant. Similarly strong family history associations have been reported in a nationwide study in Sweden for Graves and Hashimoto thyroiditis respectively (standardized incidence ratio [SIR] 3.85 and 4.75 respectively [32]. These increased risks were higher for men (SIR = 4.37 and 6.68, respectively) than for women (SIR = 3.75 and 4.36, respectively). A study of parents of children with thyroiditis found a much higher incidence of thyroid antibodies in the parent than in the general population [33]. Up to 50% of the siblings of patients with autoimmune thyroid disease are thyroid antibody-positive [34, 35], in contrast to about 12% to 15% reported in the general population [36, 37]. Furthermore, specific susceptibility genes for autoimmune thyroid diseases have been identified [38]. A study of euthyroid twins from the Danish twin registry examining the importance of genetic and environmental effects on the presence of thyroid antibodies measured TPOAb in 283 monozygotic and 403 dizygotic pairs and found that genetic influences explained 61% (95% CI, 49%-70%) of the variation in TPOAb concentration in males and 72% (95% CI, 64%-78%) in females [39]. Brix et al also concluded in their study that genetic predisposition is necessary for developing autoimmune thyroid diseases, such as Graves disease, and that environmental factors possibly have a predominant role in controlling whether a genetically predisposed subject progresses to clinical or overt disease [40].

Table 3. Logistic modeling of sociodemographic and occupational characteristics associated with positive thyroid peroxidase antibody test among study participants (2018-2019)

Characteristics	Unadjusted OR	95% CI	P value	Adjusted OR	95% CI	P value
Age	0.97	0.94 – 1.00	0.07	0.99	0.95 – 1.04	0.87
Race						
Other ^a	-	-	-	-	-	-
White	0.90	0.40 – 2.03	0.79	1.09	0.42 – 2.78	0.86
Gender						
Male	-	-	-	-	-	-
Female	0.87	0.33 – 2.28	0.78	0.58	0.20 – 1.70	0.32
Ethnicity						
Hispanic	-	-	-	-	-	-
Non-Hispanic	0.75	0.37 – 1.50	0.42	0.72	0.32 – 1.65	0.44
Education level						
Some college or less	-	-	-	-	-	-
College graduate or more	1.48	0.91 – 2.40	0.11	1.41	0.83 – 2.39	0.21
Ever smoked^b						
No	-	-	-	-	-	-
Yes	1.26	0.69 – 2.30	0.45	1.33	0.69 – 2.59	0.40
Medical condition^c						
No	-	-	-	-	-	-
Yes	0.80	0.45 – 1.41	0.43	0.84	0.44 – 1.60	0.59
Sleep disorder						
No	-	-	-	-	-	-
Yes	1.11	0.66 – 1.89	0.69	1.13	0.63 – 2.06	0.68
Family history^d						
No	-	-	-	-	-	-
Yes	2.50	1.15 – 5.42	0.02	2.99	1.31 – 6.85	0.01
Job rank						
Administrative	-	-	-	-	-	-
Firefighting	1.18	0.73 – 1.91	0.51	0.94	0.53 – 1.67	0.83
Station location^e						
Northeast/South	-	-	-	-	-	-
Midwest/West	1.55	0.92 – 2.63	0.10	1.43	0.81 – 2.54	0.22
Not mentioned	0.67	0.34 – 1.38	0.27	0.61	0.27 – 1.39	0.24
Fire run						
No	-	-	-	-	-	-
Yes	1.02	0.60 – 1.72	0.94	1.05	0.59 – 1.86	0.92
Preventive practices^f						
0-1	-	-	-	-	-	-
2-3	0.98	0.59 – 1.65	0.94	1.05	0.59 – 1.86	0.88
Shift						
24hrs on/24/48hrs off	-	-	-	-	-	-
24hrs on/ 72hrs off/other	0.94	0.57 – 1.51	0.79	1.20	0.70 – 2.06	0.52
More than 1 job						
No	-	-	-	-	-	-
Yes	1.02	0.61 – 1.70	0.94	0.96	0.55 – 1.67	0.87
Radiation exposure^g						
No	-	-	-	-	-	-
Yes	1.15	0.67 – 1.98	0.61	1.16	0.63 – 2.13	0.63
Years employed^h						
<10 years	-	-	-	-	-	-
≥10 years	0.50	0.27 – 0.91	0.02	0.51	0.24 – 1.12	0.09

Bold is statistically significant at $P < 0.05$.

^aOther race includes Black, Native Hawaiian or Pacific Islander, American Indian or Alaskan Native, other, and don't know/not sure.

^bEver smoked 100 cigarettes in your lifetime?

^cEver been diagnosed with any chronic medical condition?

^dFirst degree relative with history of thyroid disease?

^eGeographic location of participant's fire station in the United States.

^fEngage in 2 or more of: wash gear in the last month, hood swap, or own hood.

^gExposure to ionizing radiation, e.g., diagnostic x-ray, or CT scan, in the past 24 months.

^hThe average number of years employed as an active firefighter.

A cross-sectional study by Zhang et al, across 10 cities in China, showed that current smokers had lower levels of TPOAb than former smokers, while former smokers showed lower levels of TPOAb compared with never smokers [41]. On the contrary, in our study, we found 31% higher odds of positive TPOAb among firefighters reporting current smoking or who reported a history of smoking compared to never smokers. We reran our multivariable model reported in Table 3 replacing our ever-smoker variable with a current smoking variable (yes vs no). There was a higher odds of positive TPOAb among current smokers compared with nonsmokers, although this finding was not significant (3.78; 0.84-17.03), in part due to the relatively small number of current smokers in the analysis (n = 9). This increased risk of TPOAb among ever smokers is supported by findings in another study by Effraimidis et al, carried out among subjects from the Amsterdam autoimmune thyroid disease cohort, where they found that discontinuation of smoking was associated with increased risk for occurrence of thyroid antibodies [42]. In addition, Effraimidis et al found that discontinuation of smoking increases the risk of TPOAb. A study in China found that regular smokers had a lower concentration of TPOAb than occasional smokers, former smokers, and never smokers [41]. Several other studies also show a decrease in TPOAb associated with smoking suggesting a protective effect of smoking [42, 43]. The increased odds of TPOAb seen among firefighters who are former smokers suggests the possibility that other firefighter-specific exposures may be affecting autoimmunity. Overall, the association of smoking on thyroid disease is controversial and the underlying mechanisms of action are still unclear [41].

Reported occupational radiation exposure increased the odds of being TPOAb positive by 16% in our study population, but this finding was not significant. Several studies have shown an association between radiation exposure including medical radiation and increased risk of autoimmune thyroid disorder [13, 23, 44]. A dose-effect relation between the high dose of radiation exposure and autoimmune thyroid disease has been reported; however, firefighters are not typically exposed to high doses of radiation.

Firefighters' occupational risk includes exposure to endocrine disrupting chemicals (EDCs), also called forever chemicals because they do not break down and persist in the environment after being released. Some examples are per- and polyfluoroalkyl substances (PFAS), polychlorinated biphenyls (PCBs) polybrominated diphenyl ethers (PBDEs) [18, 45]. Their mechanisms of action are broad and converge upon the endocrine system, including the thyroid [46]. Studies have found an association between EDCs and thyroid autoimmunity, possibly increasing autoantibodies [18]. PFAS and PBDEs are used as flame retardants in firefighting protective gear as well as in consumer goods, while PCBs are used in electrical equipment, hydraulic fluids, heat transfer fluids, lubricants, and plasticizers. Firefighter studies have shown that to reduce exposure to these chemicals, firefighters should practice preventive activities such as gear cleaning practices [47], hood swap, hood ownership and cleaning practices, onsite decontamination, showering immediately after fires [47], and the use of wipes on the skin to wipe the neck and hands [48]. Our measures of occupational risk prevention practices were likely imprecise assessments covering the span of their careers, as best practices have evolved over time in response to emerging research and modified training practices.

For example, recently published reports indicate that the use of wipes can reduce polycyclic aromatic hydrocarbon contamination on the neck by a median of 54% following firefighting activities [48], while in another study there was a 76% reduction in contamination observed after laundering of hoods [49]. Firefighters currently report positive attitudes, beliefs, and perceived norms about decontamination, but the use of hand wipes and routine cleaning of gears are reported to occur less frequently [50]. However, in this study population, we did not find any significant association of TPOAb with the preventive practices measured.

Subclinical hypothyroidism (high TSH) was seen in only n = 9 of 278 (3.2%) study participants and subclinical hyperthyroidism in n = 2 of 278 (0.7%). This is within the prevalence range in the disease-free United States population (3% to 8%) for subclinical hypothyroidism, and lower than the reported prevalence rate (2%) of subclinical hyperthyroidism [6]. Although subclinical thyroid dysfunction was higher among those who tested positive for TPOAb compared with those who tested negative, this finding was marginally significant. Thus, there may be a correlation that is not being observed due to the small sample size of firefighters with subclinical thyroid dysfunction. Other studies have shown significant correlation between abnormal TSH and positive TPOAb tests [51].

In this study population, family history is the only significant correlate of TPOAb. There was no significant relationship between TPOAb and the occupational risk prevention practices studied. The firefighters in our study had no prior history of being diagnosed with thyroid disease; published studies have shown that a significant proportion of patients with TPOAb progress to thyroid dysfunction over time [52]. The high prevalence of TPOAb seen in this study sample of firefighters attending a national occupational health conference is a cause of concern. Although currently available laboratory techniques may be more sensitive in detecting the presence of antibodies, a 13-year follow-up longitudinal study by Walsh et al showed that current immunoassay techniques also provide clinically useful estimates of the long-term risk of hypothyroidism [24]. Additionally, studies in other populations have shown that TPOAb and thyroid dysfunction are associated with cancer and cardiovascular diseases [53, 54]. It is noteworthy that among firefighters, sudden cardiac death accounted for 42% of duty-related deaths over the past decade [55], and according to data from the International Association of Firefighters (IAFF), cancer is a major cause of in line of duty deaths of career firefighters [56].

Because most patients with autoimmune disease develop symptoms well after the abnormal immune reactions begin [3], the high prevalence of firefighters testing positive for TPOAb suggests that firefighters may benefit from baseline thyroid hormone analysis at employee medical check-up conducted by clinicians, and 3- to 5-year regular medical follow-up thereafter for those testing positive. A more general study should be conducted to assess correlates of TPOAb among a larger population of firefighters, and other factors responsible for the high prevalence of TPOAb among firefighters, including parental occupation and secondary exposure to EDCs, should be examined. A longitudinal study of firefighters to examine the long-term outcome of TPOAb on thyroidal and extrathyroidal diseases (cancer and cardiovascular) may be required. None of the firefighters in this study presented with clinical symptoms of thyroid disorder and 2

firefighters with significantly abnormal serological and ultrasound findings were referred to the endocrinology clinic for further evaluation. Currently, we are also analyzing blood PBDE levels in this cohort; the association between PBDEs and thyroid dysfunction among firefighters will be addressed in a subsequent publication.

The strengths of this study are the direct measurement of thyroid antibodies from samples collected from firefighters, and physical examination by physicians for symptoms of thyroid disorder. To our knowledge, this is the first study to examine TPOAb prevalence and determinants among firefighters. Limitations include the sampling technique which is nonrandomized and prone to bias. There could be overrepresentation or underrepresentation of particular firefighters as a function of occupational exposures, since attendees were attending conferences that focused on health and safety matters in this occupational group. We therefore cannot generalize our findings to represent the general population of firefighters. Also, the cross-sectional nature of our study did not allow for repeated measurements of TPOAb among firefighters. Exclusive reliance on self-reported data prevention practices is a limitation given the possibility of reporting more socially acceptable responses.

Conclusion

To our knowledge, this is the first study to examine the prevalence of TPOAb among a study population of firefighters. The results of our study confirm that family history is a major risk factor for testing positive for TPOAb among firefighters. We did not find any significant association of testing positive with a history of cigarette smoking, radiation exposure, and the geographic location of the fire station. Additionally, age, number of years employed as a firefighter, and practicing 2 or 3 prevention practices such as owning your hood, and routine washing of gear to reduce contaminants were not associated with the odds of testing positive among firefighters. However, the fact that the prevalence of TPOAb seems high in firefighters, especially since the majority are men, means there must be other factors associated with the increased risk, and there may be a need for long-term follow-up of follow-up firefighters to monitor for thyroid failure. Firefighters with a family history of thyroid disease may require more frequent follow-up. We are conducting additional studies to examine the association of serum PBDEs and TPOAb among firefighters to address these potential health risks in this occupational group.

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Disclosures

The authors declare that there are no conflicts of interest.

Data Availability

Some or all datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

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