New-onset asthma among soldiers serving in Iraq and Afghanistan

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ABSTRACT

Since June 4, 2004, asthma diagnosed and symptomatic after the age of 12 years has been an exclusion criterion for military enlistment unless exempted via *medical waiver. The Department of Defense determined that 13% of U.S. Army Medic visits in Iraq are for new-onset acute respiratory illness; case reports of veterans with asthma that began in Iraq and Afghanistan War zones have surfaced. This prompted our study to determine whether new asthma is diagnosed more frequently among Iraq/Afghanistan War troops versus stateside-based troops. Retrospective review of asthma diagnoses among computerized charts for military personnel discharged from active duty and examined between March 1, 2004 and May 1, 2007, at the Veterans Affairs Medical Center (VAMC), Northport, NY, classified soldiers by (1) deployment status—whether they were stationed in Iraq/Afghanistan for a 1-year tour of duty or stationed in the United States, and (2) VA diagnosis of asthma per International Classification of Disease codes. Associations between deployment and asthma statuses were evaluated/stratified by gender/age group. Eligibility criteria entailed (1) residence in Long Island, (2) aged 18–45 years, and (3) both U.S. military service and discharge dates between March 1, 2004 and May 1, 2007. Out of 6233 patients who served between 2004 and 2007 and were followed at the Northport VAMC, 290 new-onset/prevalent asthma cases were identified. Deployment to Iraq was associated with a significantly higher risk of asthma compared with stateside soldiers (6.6% versus 4.3%; with a crude odds ratio, 1.58; 95% CI, 1.18, 2.11). These associations persist when stratified by gender and age group. Deployment to Iraq and Afghanistan is associated with new-onset asthma. Etiologic studies, surveillance, incidence, epidemiology, and assessing response to therapy are recommended.*

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Since June 4, 2004, asthma diagnosed and symptomatic after age 12 has been an exclusion criterion for military enlistment unless exempted *via* medical waiver (<2% of requests granted).[1] Iraq/Afghanistan deployment exposes soldiers to harsh environmental conditions.[2,3] Extremes of temperature and humidity range from 120°F (summer) to below freezing (January). Rainfall occurs from December to April and can reach 100 cm annually. Spring flash floods affect the Tigris–Euphrates delta. During summer, wind prevails: dry soil and dust fill the air.[2] The local language uses terms "shamal" for northern seasonal dust storm and "sharqi" for eastern seasonal dust storm.[3] Inhalation of fine particulate matter with a diameter <2.5 μm (PM2.5) or a diameter <10 μm (PM10) in size, in the absence of allergic sensitization, may cause lung injury that mimics asthma.[4]

Exposure to indoor dust in Army trailers during the rainy season may lead to IgE-mediated allergic sensitization to dust-mite antigens, a risk factor for asthma.[5] IgE is the *sine qua non* of allergy. Conditions faced by soldiers are unprecedented because they live in confined spaces (trailers) unless on patrol.

The Department of Defense determined that 13% of U.S. Army Medic visits in Iraq are for new-onset acute respiratory illness (Michael E. Kilpatrick, M.D., Deputy Director for Force Health Protection and Readiness Programs in the Office of the Assistant Secretary of Defense for Health Affairs, personal communication).

Roop *et al.* reported that active-duty soldiers and Department of Defense contractors—both nonasthmatic and asthmatic patients—had increased respiratory symptoms of wheezing, cough, and sputum production; chest pain/tightness; and allergy symptoms during deployment to Iraq compared with predeployment.[6] In the Israeli Army, service in combat units is associated with increased frequency of asthma among not only those with prior diagnoses but also *de novo* cases, with 25% relative excess for maintenance unit workers versus clerical workers.[7] There is a precedent for considering someone to be at risk for new-onset asthma rather than at risk for reactivation or aggravation of asthma. The National Institute for Occupational Safety and Health SENSOR surveillance case definition for work-related asthma considers someone with a history of asthma who has neither had symptoms nor

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used asthma medications in the previous 2 years to be at risk for new-onset asthma.[8]

HYPOTHESIS

We hypothesized U.S. military personnel returning home from a tour of duty in Iraq and Afghanistan will have higher asthma odd ratios (ORs) when compared with soldiers who did not serve in these regions.

METHODS

Study Samples

This study was approved by the Northport Veterans Affairs Medical Center (VAMC) Research and Development Committee. We retrospectively analyzed anonymous age and gender-matched data from the Northport VAMC and compared asthma proportions of Iraq/Afghanistan War veterans with veterans deployed stateside. Since June 4, 2004, asthma diagnosed and symptomatic after the age of 13 years has been an exclusion criterion for military enlistment unless exempted *via* a medical waiver.[1] Entry exams include review of past medical records and physical exams. We retrospectively reviewed Northport VAMC data from all soldiers deployed and discharged from military service during March 1, 2004–May 1, 2007. Data included age, gender, deployment location, discharge date, clinic dates, and International Classification of Disease (ICD) diagnosis codes. We studied soldiers who attended the VA Operation Enduring Freedom (OEF) Clinic, which comprises soldiers who have served in Iraq/Afghanistan, and the Operation Iraqi Freedom (OIF) Clinic, comprising Iraq War veterans. The computer database was unable to separate OEF versus OIF patients and lumped OEF + OIF versus neither. In 2004, there were 17,900 U.S. troops in Afghanistan; there were 130,000 forces in Iraq.

Diagnoses and Measurements

All patients were examined by VAMC physicians. All primary care internal medicine staff are licensed teaching faculty at the State University of New York at Stony Brook School of Medicine. The asthma ICD codes used are listed in Table 1. The clinical guidelines at the VAMC clinic for a diagnosis of asthma include recurrent episodes of respiratory symptoms (cough, wheeze, dyspnea, and exercise-induced shortness-of-breath) with spirometric evidence of airway obstruction based on the forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) or forced expiratory flow at 25–75% at rest, with improvement of symptoms after bronchodilators. All Iraq-deployed asthma patients were episodically symptomatic with cough, wheeze, and/or dyspnea on exertion. The asthma ICD codes used are listed in Table 1. Clinical course and available spirometric data were summarized. Given the absence of a comparison group, the primary motivation is to provide a full description of the cases.

Table 1 **International Classification of Diseases (ICD) diagnosis codes used for asthma**

ICD Code*	ICD Diagnosis
493.00	Extrinsic asthma not otherwise specified
493.01	Extrinsic asthma with status asthmaticus
493.02	Extrinsic asthma with acute exacerbation
493.10	Intrinsic asthma not otherwise specified
493.11	Intrinsic asthma with status asthmaticus
493.12	Intrinsic asthma with acute exacerbation
493.20	Chronic obstructive asthma not otherwise specified
493.21	Chronic obstructive asthma with status asthmaticus
493.22	Chronic obstructive asthma with acute exacerbation
493.81	Exercise induced bronchospasm
493.82	Cough variant asthma
493.90	Asthma not otherwise specified
493.91	Asthma with status asthmaticus
493.92	Asthma not otherwise specified with acute exacerbation

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PM10 measurements were collected from April 2004 to May 2006 in Balad, Iraq (Balad Air Base/Logistics Support Area or LSA Anaconda), which is the location of one of the largest military bases in Iraq. Troops were deployed there for 1 year. The climate is representative of the dusty zones affected by sandstorms.

Individuals were classified according to deployment status (deployed to the Iraq versus stationed in the United States). The standard deployment time frame to Iraq is 1 year. Categorical variables were summarized by frequencies and percentages. These included whether the veteran had visited OIF/OEF clinics (yes/no), gender (male/female), and asthma (yes/no). Age of the veteran was grouped into the following five categories: 18–25 years, 26–30 years, 31–35 years, 36–40 years, and ≥41 years. Contingency tables for categorical values were generated and associations were evaluated using Fisher's exact test.

For asthma, crude ORs and their 95% CIs were calculated for veterans with versus veterans without visits to the OIF/OEF clinics—first for all veterans, and

Table 2 **Summary of associations between asthma and deployment to the Persian Gulf**

Age group (yr)	Deployment Status	Women (n = 1453)			Men (n = 4780)		
		Asthma	No Asthma	OR (95% CI)	Asthma	No Asthma	OR (95% CI)
≤25	Persian Gulf	1	21	0.91 (0.11, 7.34)	14	272	1.67 (0.82, 3.41)
	United States	12	229		18	585	
26–30	Persian Gulf	1	16	1.96 (0.24, 16.24)	15	242	2.22 (1.13, 4.34)
	United States	10	313		22	787	
31–35	Persian Gulf	1	11	1.74 (0.21, 14.63)	6	97	1.49 (0.60, 3.73)
	United States	12	230		25	603	
36–40	Persian Gulf	1	5	7.06 (0.73, 68.63)	10	87	2.44 (1.17, 5.07)
	United States	7	247		37	784	
≥40	Persian Gulf	1	9	1.54 (0.19, 12.67)	11	99	1.74 (0.89, 3.41)
	United States	22	304		64	1002	
Homogeneity test (across different age groups)			p = 0.71			p = 0.90	
				p = 0.96			
Crude OR (all age groups)			1.69 (0.66, 4.36)			1.60 (1.17, 2.18)	
				1.58 (1.18, 2.11)			
Mantel-Haenszel Common OR (95% CI)			1.70 (0.66, 4.40)			1.90 (1.37, 2.63)	
				1.88 (1.38, 2.56)			

OR = odds ratio.

then for each gender. For asthma, age group stratified ORs were also calculated, first for each gender, and then for all veterans. If any cell frequency was 0, 0.5 was added to each cell of the 2 × 2 table before the OR was calculated. Breslow-Day tests with a conservative significance level of 0.10 were used to evaluate the homogeneity among stratified ORs. If not significant, Mantel-Haenszel common ORs were estimated, and their 95% CIs were calculated.

RESULTS

Sixty-one of 920 (6.6%) soldiers deployed to Iraq had asthma compared with only 4.3% (229 of 5313) of soldiers stationed in the United States (p = 0.003). The overall crude OR for asthma after deploying to Iraq was 1.58 (95% CI, 1.18, 2.11), with OR = 1.69 (95% CI, 0.66, 4.36) for women and 1.60 (95% CI, 1.17, 2.18) for men (Table 2). When stratified by age group, the higher risk for asthma still holds. For men, the ORs of deployment to Iraq were statistically significant in the 26- to 30-year-old age group and 36- to 40-year-old age group. The same age groups of women also showed higher risks of asthma, although the ORs were not statistically significant because of smaller sample sizes. Mantel-Haenszel estimates of the common OR were even higher: 1.88 (95% CI, 1.38, 2.56) for all soldiers, 1.90 (95% CI, 1.37, 2.63) for men, and 1.70 (95% CI, 0.66, 4.40) for women.

In the 45 with available numerical VA data, spirometric measurements were collected while patients were taking asthma medications and showed a reduced mean FVC of 4.76 ± 1 L, reduced mean FEV_1 of 3.49 ± 0.19 L, and a reduced mean FEV_1/FVC of 74 ± 5%. The mean FEV_1 is lower than expected for white male patients, 25–45 years of age.[9] The mean FEV_1/FVC is similar to the third National Health and Nutrition Examination Survey asthma population.[9,10] Two subjects were on prednisone, 20 took inhaled steroids, 7 were on leukotriene modifiers, 5 used long-acting β_2-receptor agonists, and 34 were actively using short-acting β_2-agonists. Although on asthma medications, 7 patients had a bronchodilator response of >200 mL and 12%, 1 subject had evidence of air trapping (residual volume, residual volume divided by total lung capacity increased greater than 120%), 9 subjects showed reversibility of the forced expiratory flow at 25–75% of >35%, and 10 of 12 subjects who had diffusing capacity for carbon monoxide measurements were normal, while 2 subjects were >120% predicted.

All Iraq-deployed asthma patients were episodically symptomatic with cough, wheeze, and/or dyspnea on exertion. Eighteen had supportive histories such as one with several intubations for asthma and a positive methacholine challenge conducted at an outside institution; another had Samter's triad; nine patients had multiple asthma attacks per week relieved with a bronchodilator; six patients had exercise-induced wheezing; and all patients had relief of asthma attacks with asthma medications.

Concentrations of 10-μm-sized particles/m^3 of air exceeded 120 $\mu g/m^3$ (Fig. 1) in 160/190 measure-

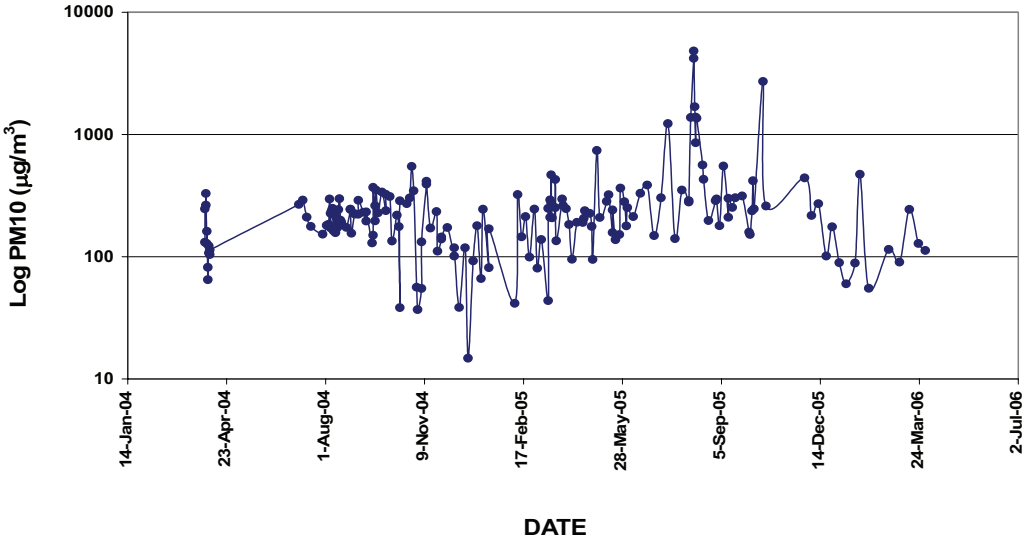

Figure 1. Concentrations of particulate matter with a diameter <10 μm (μg/m³) in ambient air in Balad, Iraq.

ments (84%) and had a maximum of 4823 $\mu g/m^3$. The mean and SD were 307 ± 526 $\mu g/m^3$. The National Ambient Air Quality Study limit for air pollution is 150 $\mu g/m^3$.[11]

EDITORIAL NOTE

Significance of Study

This study provides the first indication of new-onset asthma among U.S. military personnel deployed to Iraq and Afghanistan from 2004 to 2007. Soldiers deployed to Iraq and Afghanistan received at exit visit more diagnoses of asthma than soldiers stationed in the United States. At issue is whether this is actually a form of lung injury rather than classic extrinsic IgE asthma versus intrinsic non-IgE asthma. Lung injury and bronchiolitis are plausible because infections, irritants, and toxin exposure may be occurring on the battlefield.

Air pollution (PM10) may explain these findings.[12] A prospective study using more sensitive objective measures pre- and postdeployment, with a control group (nondeployed), will help illuminate possible ramifications of current environmental air exposure in Iraq.

Uncontrolled burning of trash in Balad "burn pits" without use of incinerators before November 2009 is concerning because plastic water bottles doused in jet fuel were lit on fire. Products of combustion from polyethylene terephthalate plastic water bottles leads to release of phthalates, a source of occupational asthma. Furthermore, carcinogens benzene and formaldehyde and aliphatic hydrocarbons are emitted.

Suggested prevention and control measures include cessation of uncontrolled burning of garbage, installation of incinerators, recycling plastic, and use of respiratory protection devices. Surveillance may be accomplished by obtaining spirometry and 2-mi run times for soldiers pre- and postdeployment, with documentation of their duty station location. Personal PM2.5 monitors may better quantify exposure risk. The practice of using jet fuel (JP-8) as an accelerant to burn trash is not recommended, because it releases benzene and *n*-hexane, a neurotoxin, when burned.

Limitations of this study entail its reliance on ICD diagnosis codes and lack of pre- and postdeployment spirometry. More sensitive measures such as methacholine challenge, cardiopulmonary exercise testing, impulse oscillometry to assess small airways, and exhaled breath condensate nitric oxide levels, as well as skin-prick testing for aeroallergens may be helpful.[13] Quantitation of indoor aeroallergens from bulk dust in trailers may separate the indoor component versus the outdoor component. Sampling of burn pit pile dust itself will enable geochemical characterization of the source. Geological characterization of endogenous dust for geometry, mineral content, porosity, and bacteriology may also be helpful, as is use of animal models with spontaneous asthma such as the vasoactive intestinal peptide knockout mouse—challenged with burn pit or endogenous dust—with and without allergic sensitization to dust-mite antigen.

Similar data are available from Operation Desert Storm and the first deployment to Kuwait and Iraq. The PM size was defined in a study by Korenyi who identified the chemical content of the sand and pigeon droppings as the amplified cause of Al Eskan disease/pneumonitis.[14]

SUMMARY

1. What is known: Increased respiratory and allergy symptoms have occurred among U.S. soldiers and contractors in Iraq. Combat status in Israeli soldiers

is associated with increased risk of *de novo* asthma and exacerbations of preexisting asthma.
2. Our study adds that: New-onset asthma diagnoses are more common among U.S. veterans returning from Iraq and Afghanistan compared with state-side-stationed troops. Even among those Iraq/Afghanistan War veterans taking asthma medications, spirometric values still showed mild airway obstruction at rest.
3. Implications: The practice of dousing discarded plastic polyethylene terephthalate water bottles with jet fuel (JP-8) and setting it on fire is to be discouraged, because phthalates are a source of occupational asthma. Additionally, release of carcinogens benzene and formaldehyde and aromatic hydrocarbons is dangerous; JP-8 itself releases benzene and neurotoxin *n*-hexane. Recycling of plastic and use of incinerators may reduce respiratory health risks of Iraq/Afghanistan War asthma.

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