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POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

Increased Risk of Monoclonal Gammopathy of Undetermined Significance in US Military Service Members: A Case-Control Study of 1,068 Service Members Deployed to Either Europe or Iraq, with or without Reported Burn Pit and Toxic Smoke Exposure

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*Background:*Monoclonal Gammopathy of Undetermined Significance (MGUS) is a plasma cell disorder which may lead to and in all cases precedes multiple myeloma (MM). Although, the etiology of MGUS is unknown, multiple studies have shown an association between MGUS and pesticide exposure (Kachuri et al, Int. J. Cancer 2013). Furthermore, soldiers and First Responders may be at higher risk of developing MGUS as evidenced by a 2.4-fold increased risk for MGUS in Vietnam Veterans exposed to Agent Orange (Landgren et al, JAMA Oncol. 2015) and a 1.8-fold higher risk in World Trade Center (9/11 attacks)-exposed fire fighters compared to reference populations (Landgren et al, JAMA Oncol. 2018). US Service Members deployed to the Southwest Asia theater of military operations (e.g., Iraq and Afghanistan) may have been exposed to various airborne hazards including smoke and fumes from open burn pits (chemical, paint, munitions, petroleum, plastic, rubber, medical, human, and food waste), oil well fires, and aircraft fuel/exhaust. Researchers are currently investigating the long-term consequences from these exposures. We were motivated to determine whether US Service Members deployed to Iraq were at increased risk of developing MGUS.
Methods: Serum samples and clinical data (N=1,068) were attained from the Armed Forces Health Surveillance Division (AFHSD), the central epidemiologic health registry and biorepository for the US Military after IRB exemptions were granted. A total of 534 US Service Members who deployed to Iraq between January 1, 2005 and June 30, 2007 and reported burn pit exposure, smoke, burning trash, etc. on their post-deployment health assessment form (exposed cases) were matched 1:1 to 534 Members deployed to Germany (matched controls) who were never deployed to Southwest Asia and denied toxic exposure. All cases were deployed ≥ 6 months, were ≥ 35 years old at time of deployment, remained in the military ≥ 10 years and had serum available in the AFHSD repository 10 years after deployment. Matched criteria included deployment year (+/- 10 years), age (+/- 3 years), sex, service branch, military rank, and occupation category. The 10-year post-deployment samples underwent laboratory testing to screen for monoclonal protein by immunofixation (IFE) using pentavalent antisera with positive samples confirmed and typed using IFE gels (Sebia) and for serum free light chains (sFLC; Sebia) performed on the DYNEX Agility platform. IFE-positive samples underwent serum protein electrophoresis (SPEP) quantification by capillary electrophoresis (Sebia).
*Results:*The median age of exposed Service Members was 37 years (range: 35-52) and 37 years (range: 35-55) for controls (Table 1). In both cohorts, the frequency of White (64.8%), Black (18.7%), Hispanic (7.5%), and male (89%) patients were the same as was the distribution of military occupation, rank, and service branch. The median number of days deployed for exposed vs controls was 243 and 852, respectively.
There was no statistically significant difference between burn pit exposed and controls in the combined prevalence of MGUS (IFE+ monoclonal protein) and light chain (LC) MGUS (abnormal sFLC ratio), 6.7% (95% Confidence Interval (CI): 4.8-9.2%) vs 5.4% (95% CI: 3.7-7.7%), respectively (p=0.22). Similarly, there was no difference in prevalence when assessing IFE+ or sFLC+ cases separately (Table 2). The prevalence of MGUS or LC-MGUS for all 1,068 Service Members was 6.1% (95% CI: 4.7-7.7%).

*Conclusion:*In our cohort of 534 Service Members deployed to Iraq and exposed to burn pits and other airborne toxic hazards (cases) there was no statistically significant difference in the prevalence of MGUS compared to 534 deployed to Germany (matched controls). Interestingly, the overall prevalence of MGUS/LC-MGUS in this combined deployed population was 6.1%. When taking into account that the median age at deployment was 37 years and samples were attained 10 years later (approximately at an age of 47 years), the observed prevalence is 3-fold higher than that reported in the Icelandic iStopMM study (2% in the 41-50 -year age group). Future studies are needed to further elucidate causes for the increased prevalence of MGUS/LC-MGUS in deployed US Military Service Members.
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Disclosures Kazandjian: *Curio Science:* Ended employment in the past 24 months, Honoraria; *Bristol Myer Squibb:* Consultancy, Honoraria; *MJH Life Sciences:* Current Employment, Honoraria; *Karyopharm Therapeutics:* Current Employment, Speakers Bureau; *Arcellx:* Consultancy, Current Employment, Honoraria; *Aptitude Health:* Consultancy, Honoraria; *MMRF:* Ended employment in the past 24 months, Honoraria; *Bridger Consulting Group:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria; *Plexus Communications:* Ended employment in the past 24 months, Honoraria; *Aperture Medical Technology, LLC:* Consultancy, Honoraria; *Alphasights:* Consultancy, Honoraria. **Thoren:** *Binding Site:* Research Funding; *Sebia:* Research Funding. **Landgren:** *Merck:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Adaptive:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Theradex:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees.

Table 1. US Service Member Demographics

	All Service Members (N=1,068)	Exposed Cases (N=534)	Matched Controls (N=534)
Median age at deployment, years (range)	37 (35-55)	37 (35-52)	37 (35-55)
Deployment duration, median days	320	243	852
Race:			
White	692 (64.8%)	346 (64.8%)	346 (64.8%)
Black	200 (18.7%)	100 (18.7%)	100 (18.7%)
Hispanic	80 (7.5%)	40 (7.5%)	40 (7.5%)
Other	96 (9.0%)	48 (9.0%)	48 (9.0%)
Male sex	950 (89%)	475 (89%)	475 (89%)
Occupation			
Repair/Engineering	294 (27.5%)	147 (27.5%)	147 (27.5%)
Communications/Intelligence	238 (22.3%)	119 (22.3%)	119 (22.3%)
Infantry/Artillery/Combat engineering	164 (15.4%)	82 (15.4%)	82 (15.4%)
Healthcare	104 (9.7%)	52 (9.7%)	52 (9.7%)
Pilot/Aircrew	48 (4.5%)	24 (4.5%)	24 (4.5%)
Motor transport	46 (4.3%)	23 (4.3%)	23 (4.3%)
Other	174 (16.3%)	87 (16.3%)	87 (16.3%)
Rank:			
Enlisted	670 (62.7%)	335 (62.7%)	335 (62.7%)
Officer	398 (37.3%)	199 (37.3%)	199 (37.3%)
US Military Service Branch:			
Army	1016 (95.1%)	508 (95.1%)	508 (95.1%)
Air Force	52 (4.9%)	26 (4.9%)	26 (4.9%)

Table 2. Prevalence of MGUS in US Service Members Exposed to Burn Pits Compared to Those Not Exposed During Their Deployments

Monoclonal Gammopathy	All Members (N=1,068)	Exposed Cases (N=534)	Matched Controls (N=534)	P-value (Fisher's Exact Test)
Serum Immunofixation Positive, n (95% Confidence Interval (CI):)	48 (4.5%: 3.3-5.9%)	27 (5.1%: 3.4-7.3%)	21 (3.9%: 2.5-6.0%)	0.23
Isotype:				
IgG, n (n/N)	36 (75%)	20 (74.1%)	16 (76.2%)	
IgA, n (n/N)	7 (14.6%)	3 (11.1%)	4 (19.0%)	
IgM, n (n/N)	2 (4.2%)	2 (7.4%)	0	
Lambda Light Chain, n (n/N)	2 (4.2%)	2 (7.4%)	0	
Biclonal IgG/IgM, n (n/N)	1 (2.1%)	0	1 (4.8%)	
Serum Free Light Chain Ratio Abnormal, n (95% CI:)	17 (1.6%: 0.9-2.5%)	9 (1.7%: 0.8-3.2%)	8 (1.5%: 0.7-2.9%)	0.50
Serum Immunofixation Positive or Serum Free Light Chain Ratio Abnormal, n (95% CI:)	65 (6.1%: 4.7-7.7%)	36 (6.7%: 4.8-9.2%)	29 (5.4%: 3.7-7.7%)	0.22

Figure 1

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