



# Effects of Arsenic on White Blood Cell, Neutrophil and Lymphocyte Count

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## Background

Arsenic, a metalloid found in soil and groundwater, exists in the environment in organic and inorganic forms. Arsenic is primarily excreted in the urine; therefore, the concentration of total arsenic and individual arsenic metabolites in the urine is used as an indicator of arsenic exposure. The effects of arsenic on the human body are mainly through its modulation of cell growth and apoptosis particularly in high cell turnover tissues, such as bone marrow. The data from cellular and animal studies demonstrating an association between arsenic and white blood cells is compelling; however, epidemiological studies examining such association are lacking.

## Study Aim

Therefore, the purpose of the study was to examine the association of arsenic and its species with total white blood cell (WBC) counts and subtypes of WBCs in adults.

## Methods

National Health and Nutrition Examination Survey (NHANES) data from 2003-2016 (14-year data; 7 cycles) were used. We excluded participants younger than 20 years. Urinary arsenic metabolites values were normalized using urinary creatinine excretion and log-transformed for analysis due to right-skew of their distributions. The relationship between total WBC count, neutrophil count, and lymphocyte count with urinary arsenic metabolites was examined using survey-weighted linear regression models without and with adjustment for age, gender, race, hypertension, diabetes mellitus, smoking status, and alcohol use.

## Results/Discussion

Of the 11,628 participants, 5941 (51.1%) were females, 1264 (11.9%) were heavy drinkers, 2379 (20.5%) were current smokers. The participants' mean (SD) age was 49.9 (17.7) years, WBC count  $7.3(2.4) \times 10^9$  cell/liter, neutrophils  $4.3(1.8) \times 10^9$  cells/liter, and lymphocytes  $2.1(1.1) \times 10^9$  cell/L. Median (interquartile range) of the creatinine-normalized total urinary arsenic was 49(29) ug/gm of creatinine.

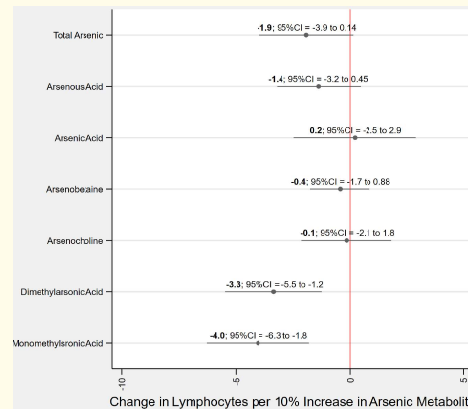


Figure 1: Change in Lymphocyte per 10% Increase in Arsenic Metabolite

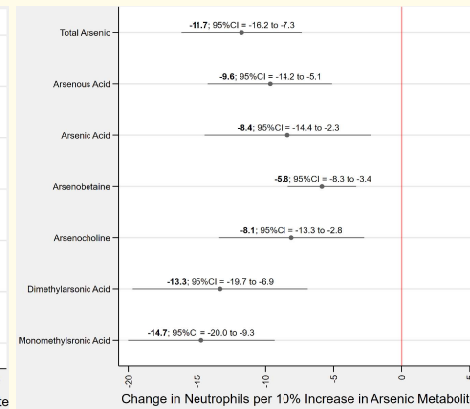


Figure 2: Change in Neutrophils per 10% Increase in Arsenic Metabolite

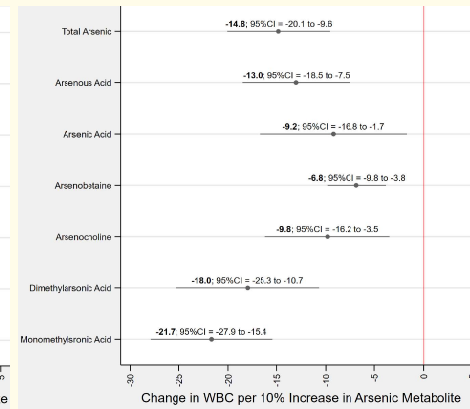


Figure 3: Change in WBC per 10% Increase in Arsenic Metabolite

Decrease in lymphocyte count was associated with only dimethylarsonic acid ( $-3 \times 10^6$ , 95%CI= $-5 \times 10^6$ ,  $1 \times 10^6$ ;  $P=0.002$ ) and monomethylarsonic acid ( $-4 \times 10^6$ , 95%CI= $-6 \times 10^6$ ,  $-2 \times 10^6$ ;  $P=0.001$ ) in adjusted analyses and not with other urinary arsenic metabolites. On the other hand, decrease in neutrophil count was associated with all normalized urinary metabolite species in adjusted analysis: total arsenic acid  $-12 \times 10^6$  ( $-16 \times 10^6$ ,  $-7 \times 10^6$ ;  $P<0.001$ ), arsenous acid  $-10 \times 10^6$  (95%CI= $-14 \times 10^6$ ,  $-5 \times 10^6$ ;  $P<0.001$ ); arsenic acid  $-8 \times 10^6$  (95%CI= $-14 \times 10^6$ ,  $2 \times 10^6$ ;  $P=0.007$ ), arsenobetaine  $-6 \times 10^6$  (95%CI= $-8 \times 10^6$ ,  $3 \times 10^6$ ;  $P<0.001$ ), arsenocholine  $-8 \times 10^6$  (95%CI= $-13 \times 10^6$ ,  $-3 \times 10^6$ ;  $P=0.003$ ), dimethylarsonic acid  $-13 \times 10^6$  (95%CI= $-20 \times 10^6$ ,  $-7 \times 10^6$ ;  $P<0.001$ ), and monomethylarsonic acid  $-15 \times 10^6$  (95%CI= $-20 \times 10^6$ ,  $-9 \times 10^6$ ;  $P<0.001$ ).

In unadjusted analysis, each 10% increase in normalized total arsenic was associated with a  $19 \times 10^6$  (95%CI= $-24 \times 10^6$ ,  $-15 \times 10^6$ ;  $P<0.001$ ) cells/L decrease in WBC. The results remained similar after adjusting for potential confounders; each 10% increase in normalized total arsenic was associated with  $14 \times 10^6$  (95%CI= $-20 \times 10^6$ ,  $-9 \times 10^6$ ;  $P<0.001$ ) cells/L decrease in WBC. Similarly, adjusted analysis showed following decrease in WBC count/L with 10% increase respective normalized urinary arsenic species: arsenous acid  $-13 \times 10^6$  (95%CI= $-18 \times 10^6$ ,  $-7 \times 10^6$ ;  $P<0.001$ ); arsenic acid  $-9 \times 10^6$  (95%CI= $-17 \times 10^6$ ,  $2 \times 10^6$ ;  $P=0.02$ ), arsenobetaine  $-7 \times 10^6$  (95%CI= $-10 \times 10^6$ ,  $4 \times 10^6$ ;  $P<0.001$ ), arsenocholine  $-10 \times 10^6$  (95%CI= $-16 \times 10^6$ ,  $-3 \times 10^6$ ;  $P=0.003$ ), dimethylarsonic acid  $-18 \times 10^6$  (95%CI= $-25 \times 10^6$ ,  $-11 \times 10^6$ ;  $P<0.001$ ), and monomethylarsonic acid  $-22 \times 10^6$  (95%CI= $-28 \times 10^6$ ,  $-15 \times 10^6$ ;  $P<0.001$ ).

## Conclusion

The results suggest that arsenic has distinct effects on white blood cells. We found a higher intake of arsenic, as measured by creatinine-normalized urinary metabolite levels, were associated with decrease in total WBC count and neutrophil counts. We also found that only methylated arsenic metabolites were associated with a decrease in lymphocyte count. Whether the decrease in WBC counts is associated with immunosuppression and higher risk of infections needs to be explored in future studies.

## Conflicts of Interest

Authors have no conflicts of interest to declare.

