Elevated neutrophil to lymphocyte ratio in older adults with cocaine use disorder as a marker of chronic inflammation

Supplemental material: Full medical exclusionary criteria materials

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**Inflammatory Marker Checklist**

**Requirement**

- No current or past TB
- HIV negative per self-report
- No hepatitis C diagnosis per self-report

No other significant medical conditions (see “Exclusionary Criteria for Borderline Conditions”)

Common concerns:
- Any type of arthritis
- Asthma
- GERD
- COPD

- Not pregnant, breastfeeding, or currently taking oral contraceptives
- No prescribed anti-inflammatories or regular over-the-counter anti-inflammatory use
- No schizophrenia or other psychotic disorder diagnosis

Other disorders included:
- generalized anxiety disorder
- major depressive disorder

- Cocaine dependence diagnosis

**Exclusionary Criteria for Borderline Conditions**

For conditions which have spectrums of inflammation are Diabetes Mellitus (DM), Hypertension, and Hyperlipidemia, clinical judgement was used per the following criteria.

Cases were excluded if:

- Client reports DM and they are taking DM medications
- Glucose from LabCorp is ≥ to 126, regardless of treatment
- Client reports Hypertension and they are taking an anti-hypertensive
  - If no medication for Hypertension then the Metabolic Syndrome Criteria was assessed (see below)
- Client reports any type of Hyperlipidemia and they are taking medication
If no medication for Hyperlipidemia then the Metabolic Syndrome Criteria was assessed (see below)

**Metabolic Syndrome Criteria from ATPIII**

Below is the official criteria for Metabolic Syndrome. As our dataset did not have all the required numbers, such as waist circumference, we used working definitions, noted underneath the official criteria. Meeting 3 out of the 5 criteria defined someone as having metabolic syndrome.

- Abdominal obesity, defined as a waist circumference in men ≥102 cm (40 in) and in women ≥88 cm (35 in)
  - We used BMI ≥ 30.
- Serum triglycerides ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides
  - We only used the LabCorp triglyceride values as being part of the criteria as drug treatment is an automatic exclusion.
- Serum high-density lipoprotein (HDL) cholesterol <40 mg/dL (1 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women or drug treatment for low HDL cholesterol
  - We only used the LabCorp Total Cholesterol values > 200 as we did not have HDL values. Drug treatment for hyperlipidemia was an automatic exclusion.
- Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure
  - We only used the blood pressure values as drug treatment was an automatic exclusion.
  - Either the systolic or diastolic can be elevated for meeting this criteria.
- Fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose
  - We only used the LabCorp Glucose values as drug treatment is an automatic exclusion. Here a value between 100 and 125 inclusive met the criteria. A value greater than or equal to 126 was automatically exclusionary.
Exclusion Criteria for Medications

The following table lists medications that were exclusionary for the current study. An M.D. and medical student reviewed potential medications and determined which should be excluded. Note that MISC = miscellaneous.

| Supplementary Table 1. Exclusionary Medications |
|-----------------------------------------------|
| **ANTI-INFECTIVES** | MISC | ANTIFUNGALS | RIFAMYCIN DERIVATIVES | HYDRAZIDE DERIVATIVES | ADAMANTANE ANTIVIRALS | ANT-IVIRAL CHEMOKINE RECEPTOR ANTAGONIST |
| **ANTI-FUNGALS** | ANTI-MALARIAL QUINOLINES | MISC ANTI-TUBERCULOSIS AGENTS | PROTEASE INHIBITORS | PURINE NUCLEOSIDES | INTEGRASE STRAND TRANSFER INHIBITOR |
| **ANTI-MALARIAL AGENTS** | AZOLE ANTIFUNGALS | ANTI-TUBERCULOSIS COMBINATIONS | NRTIS | NEURAMINIDASE INHIBITORS | FIRST GENERATION CEPHALOSPORINS |
| **ANTI-TUBERCULOSIS AGENTS** | MISC ANTI-MALARIALS | MACROLIDES | MISC ANTI-VIRALS | ANTI-VIRAL COMBINATIONS | SECOND GENERATION CEPHALOSPORINS |
| **ANTI-VIRAL AGENTS** | ANTI-MALARIAL COMBINATIONS | KETOLIDES | NNRTIS | ANTI-VIRAL INTERFERONS | THIRD GENERATION CEPHALOSPORINS |
| **LEPROSTATICS** | PENICILLINASE RESISTANT PENICILLINS | QUINOLONES | LINCOMYCIN DERIVATIVES | LINCOMYCIN DERIVATIVES | MISC ANTI-NEOPLASTICS |
| **MACROLIDE DERIVATIVES** | ANTI-PSUEDOMONAL PENICILLINS | SULFONAMIDES | GLYCOPEPTIDE ANTIBIOTICS | OTHER IMMUNO-STIMULANTS | MITOTIC INHIBITORS |
| **MACROLIDE DERIVATIVES** | AMINO-PENICILLINS | TETRACYCLINES | ALKYLATING AGENTS | ANTINEOPLASTIC HORMONES | ANTINEOPLASTIC INTERFERONS |
| **MISC ANTIBIOTICS** | BETA-LACTAMASE INHIBITORS | URINARY ANTI-INFECTIVES | ANTI-METABOLITES | RESPIRATORY INHALANT PRODUCTS | ANTINEOPLASTIC DETOXIFYING AGENTS |
| **PENICILLINS** | NATURAL PENICILLINS | AMINO-GLYCOSIDES | ANTINEOPLASTIC HORMONES | PSYCHO-THERAPEUTIC AGENTS | MULTIKINASE INHIBITORS |
| **ANTI-NEOPLASTICS** | BCR-ABL TYROSINE KINASE INHIBITORS | CORTICOTROPIN | RESPIRATORY AGENTS | IMMUNOLOGIC AGENTS | INHALED CORTICO-STEROIDS |
| **CENTRAL NERVOUS SYSTEM AGENTS** | VEGF/VEGFR INHIBITORS | GLUCOCORTICOIDS | IMMUNOSUPPRESSIVE AGENTS | ANTIPSYCHOTICS | TGF ALFA INHIBITORS |
| **ANALGESICS** | EGFR INHIBITORS | MINERALOCORTICOID | IMMUNO-STIMULANTS | IMMUNE GLOBULINS | INTERLEUKIN INHIBITORS |
| **NONSTEROIDAL ANTI-INFLAMMATORY AGENTS** | HER2 INHIBITORS | ANDROGENS AND ANABOLIC STEROIDS | MISC ANTIPSYCHOTIC AGENTS | MISC BIOLOGICALS | SELECTIVE IMMUNOSUPPRESSANTS |
| **SALICYLATES** | PROTEASOME INHIBITORS | IMMUNOLOGIC AGENTS | PSYCHO-THERAPEUTIC COMBINATIONS | IMMUNOSUPPRESSIVE AGENTS | OTHER IMMUNOSUPPRESSANTS |
| **ANALGESIC COMBINATIONS** | COX-2 INHIBITORS | CALCINEURIN INHIBITORS | PHENOTHIAZINE ANTIPSYCHOTICS | ATYPICAL ANTIPSYCHOTICS | COLONY STIMULATING |
Variable Harmonization

Age, race, and gender were determined by standard self-report methods. For estimated income data, NHANES respondents were asked to report total family income for themselves and the other members of their family, received last month in dollars. Family monthly income was reported as a range of values in dollars. The response categories were (by upper limit): $0-$399, $400, $800, $1250, $1650, $2100, $2900, $3750, $4600, $5400, $6250, $8400 and above. CUD participant income data was obtained from the Addiction Severity Index, ASI\(^{(50)}\). Similar to the NHANES, participants reported total family/household income received from all sources. The response categories were (by upper limit): $0-$399, $800, $1250, >$1250. The NHANES data were subsequently recoded to match the CUD (ASI) data and create identical income categories for data analysis.

Data collection methods regarding substance use patterns between the NHANES and ASI datasets were sufficiently different that alcohol, nicotine, and marijuana use data required harmonization into binary response categories (current user vs. non-user). For the ASI data, alcohol use (beer, hard liquor, wine) in the past month and year were used to estimate annual usage. If the estimated number of drinking occasions per 12 months was ≥ 12 / < 12, respondents were coded as alcohol users / non-users, respectively. For the NHANES data, alcohol use was reported as frequency per week, month, or year (as appropriate). These data were used to estimate annual usage and occasions per 12 months with ≥ 12 / < 12 used to code users / non-users, respectively, to match the ASI estimates. Reports coded in the NHANES dataset as “Don’t
“Know” or “Refused” or “Missing” were coded as missing. ASI data for marijuana use frequency, times used in the past 30 days was used to code the participant as a current-user or non-user. NHANES data from use of marijuana or hashish in the past 30 days was used similarly to code the respondent as a current marijuana user or non-user. For CUD nicotine use, data were obtained from intake medical screening documents and based on number of cigarettes per day in half-pack increments. Those reporting 0 (“I never smoke cigarettes”) on the medical screen were coded as non-smokers and those reporting 1-6 (“occasionally smoke cigarettes” to “smoke 3 packs per day”) were coded as smokers. NHANES data for nicotine use was determined from reports of “Every Day”, “Some Days”, or “Not at all” to code respondents as a user or non-user. Reports coded in the NHANES dataset as “Don’t Know” or “Refused” or missing were coded as missing. Data were harmonized by categorizing individuals both datasets as 0 (non-smoker) or 1 (smoker).

Race was initially obtained in standard categories, as per NIH NOT-15-089 (https://grants.nih.gov/grants/guide/notice-files/not-od-15-089.html): American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, White. Due to 0 to < 3 observations in several categories in the CUD group, categories were collapsed into Black, White, and Other (n = 7). For the NHANES dataset, the same standard NIH categories were present in the NHANES dataset, but were collapsed into Black, White, and Other in order to harmonize the datasets for analysis.