National Health and Nutrition Examination Survey

2013-2014 Data Documentation, Codebook, and Frequencies

Methylmalonic Acid (MMA_H)

Data File: MMA_H.xpt

First Published: October 2018

Last Revised: NA

Component Description

These data will be used to estimate deficiencies and toxicities of specific nutrients in the population and subgroups, to provide population reference data, and to estimate the contribution of diet, supplements, and other factors to serum levels of nutrients. Data will be used for research to further define nutrient requirements as well as optimal levels for disease prevention and health promotion.

Eligible Sample

Examined participants aged 19 years and older were eligible.

Description of Laboratory Methodology

MMA is analyzed by LC-MS/MS as dibutylester (Mineva et al.). MMA is extracted from serum (75 µL) along with an added internal standard (d_3-MMA) via liquid-liquid extraction with tert-butylmethylether/H^+. The extracted acid is then derivatized with butanol to form a dibutylester. The butanol is evaporated under vacuum and the derivatized sample is reconstituted in acetonitrile/water. The sample preparation takes ~4 h for a run containing 96 samples (calibrators, QC's and unknowns). MMA is chromatographically separated from other compounds as well as the isobaric succinic acid (same molecular mass as MMA), using isocratic mobile phase conditions within 5.9 min and measured by LC-MS/MS using multiple reaction monitoring. Quantitation is based on peak area ratios interpolated against a six-point aqueous calibration curve.

Increased concentrations of MMA in plasma or serum and excessive urinary excretion of MMA are believed to be direct measures of tissue stores of cobalamin (vitamin B12) and to be the first indication of cobalamin deficiency. The concentration of MMA in plasma or serum was found to be a useful indicator of cobalamin deficiency, especially in patients with few or no hematological abnormalities, normal results for the Schilling test, or normal or only slightly depressed serum cobalamin concentrations. In folate deficiency, MMA is normal. MMA may be elevated due to impaired renal function and as a result of an inborn error of metabolism (methylmalonic aciduria).

Refer to the Laboratory Method Files section for a detailed description of the laboratory methods used.

There were no changes to the lab method, lab equipment, or lab site for this component in the NHANES 2013-2014 cycle.

Laboratory Method Files

Methylmalonic Acid (October 2018)

Laboratory Quality Assurance and Monitoring

Serum samples are processed, stored, and shipped to the Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA for analysis.

Detailed instructions on specimen collection and processing are discussed in the NHANES Laboratory Procedures Manual (LPM). Vials are stored under appropriate frozen (–30°C) conditions until they are shipped to National Center for Environmental Health for testing.

The NHANES quality assurance and quality control (QA/QC) protocols meet the 1988 Clinical Laboratory Improvement Act mandates. Detailed QA/QC instructions are discussed in the NHANES LPM.

Mobile Examination Centers (MECs)

Laboratory team performance is monitored using several techniques. NCHS and contract consultants use a structured competency assessment evaluation during visits to evaluate both the quality of the laboratory work and the quality-control procedures. Each laboratory staff member is observed for equipment operation, specimen collection and preparation; testing procedures and constructive feedback are given to each staff member. Formal retraining sessions are conducted annually to ensure that required skill levels were maintained.

Analytical Laboratories

NHANES uses several methods to monitor the quality of the analyses performed by the contract laboratories. In the MEC, these methods include performing blind split samples collected during "dry run" sessions. In addition, contract laboratories randomly perform repeat testing on 2% of all specimens.

NCHS developed and distributed a quality control protocol for all CDC and contract laboratories, which outlined the use of Westgard rules (Westgard, et al. 1981) when running NHANES specimens. Progress reports containing any problems encountered during shipping or receipt of specimens, summary statistics for each control pool, QC graphs, instrument calibration, reagents, and any special considerations are submitted to NCHS quarterly. The reports are reviewed for trends or shifts in the data. The laboratories are required to explain any identified areas of concern.

All QC procedures recommended by the manufacturers were followed. Reported results for all assays meet the Division of Laboratory Sciences' quality control and quality assurance performance criteria for accuracy and precision, similar to the Westgard rules (Caudill, et al. 2008).

Data Processing and Editing

The data were reviewed. Incomplete data or improbable values were sent to the performing laboratory for confirmation.

Analytic Notes

Refer to the 2013-2014 Laboratory Data Overview for general information on NHANES laboratory data.

Please refer to the NHANES Analytic Guidelines and the on-line NHANES Tutorial for details on the use of sample weights and other analytic issues.

Demographic and Other Related Variables

The analysis of NHANES laboratory data must be conducted using the appropriate survey design and demographic variables. The NHANES 2013–2014 Demographic File contains demographic data, health indicators, and other related information collected during household interviews; as well as the sample design variables. The recommended procedure for variance

estimation requires use of stratum and PSU variables (SDMVSTRS and SDMVPSU, respectively) in the demographic data file.

The Fasting Questionnaire File includes auxiliary information, such as fasting status, length of fast, and the time of venipuncture.

This laboratory data file can be linked to other NHANES data files using the unique survey participant identifier (i.e., SEQN).

Detection Limits

The detection limits were constant for all of the analytes in the data set. Two variables are provided for each of these analytes. The variable name ending "LC" (ex., LBDMMALC) indicates whether the result was below the limit of detection: the value "0" means that the result was at or above the limit of detection, "1" indicates that the result was below the limit of detection. The other variable prefixed LBX (ex., LBXMMASI) provides the analytic result for that analyte. For analytes with analytic results below the lower limit of detection (ex., LBDMMALC=1), an imputed fill value was placed in the analyte results field. This value is the lower limit of detection divided by the square root of 2 (LLOD/sqrt[2]).

The lower limit of detection (LLOD in nmol/L) for LBXMMASI:

Variable Name	SAS Label	LLOD
LBXMMASI	Methylmalonic Acid	22.1 nmol/L

Methylmalonic Acid Method Change in NHANES 2011-2014

The same MMA LC-MS/MS method was used in 2013-2014 as in 2011-2012 (Mineva et al.). However, a different GC/MS method was used from 1999–2004. The LC-MS/MS method showed excellent correlation (n=326, r=0.99) and no bias (Deming regression, Bland-Altman analysis) compared to the GC/MS method (Mineva et al.).

References

- Caudill SP, Schleicher RL, Pirkle JL. 2008. Multi-rule quality control for the age-related eye disease study. Stat Med 27:4094-4106.
- Mineva EM, Zhang M, Rabinowitz DJ, Phinney KW, Pfeiffer CM. An LC-MS/MS method for serum methylmalonic acid suitable for monitoring vitamin B12 status in populations surveys. Anal Bional Chem (2015) 407:29555-64.
- Westgard J.O., Barry P.L., Hunt M.R., Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. Clin Chem (1981) 27:493-501.

Codebook and Frequencies

SEQN - Respondent sequence number

Variable Name:	SEQN
SAS Label:	Respondent sequence number
English Text:	Respondent sequence number.
Target:	Both males and females 19 YEARS - 150 YEARS

LBXMMASI - Methylmalonic Acid (nmol/L)

Variable Name: LBXMMASI

SAS Label: Methylmalonic Acid (nmol/L)

English Text: Methylmalonic Acid (nmol/L)

Target: Both males and females 19 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
26.6 to 5540	Range of Values	5444	5444	
.	Missing	292	5736	

LBDMMALC - Methylmalonic Acid comment code

Variable Name: LBDMMALC

SAS Label: Methylmalonic Acid comment code

English Text: Methylmalonic Acid comment code

Target: Both males and females 19 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	5444	5444	
1	Below lower detection limit	0	5444	
.	Missing	292	5736	