Demographic Variability of Newborn α-L-iduronidase (IDUA) and acid α-glucosidase (GAA) Enzyme Activities in Michigan

2019 APHL Newborn Screening and Genetic Testing Symposium (NBSGTS)

4/7/19

Mike Sarzynski
Conflict of Interest Disclaimer

I have no identified conflicts of interest to disclose associated with this presentation
Data Source

• Michigan full population LSD screening for MPS I and Pompe disease began 8/7/17
• 2-plex IDUA and GAA digital microfluidic fluorimetry platform
• 125,571 samples received 8/7/17-8/23/18 used for demographic analysis
Demographics

• Demographic information recorded on NBS sample card
• Demographics and DBS linked with unique accession # and entered into LIMS
• IDUA and GAA activity merged with Demographic information for analysis
Statistical Analysis

• *Microsoft Excel*-preliminary calculations

• *Minitab* statistical analysis software-confidence intervals for demographic subpopulations
Statistical Analysis

• Log transformation (ln) performed on entire data set of IDUA and GAA activity values.
  • Population distribution closely approximated by a normal fit that improves for each subpopulation as confounding variables are removed.
  • Descriptive statistics (mean, s.d., etc.) for each of the subpopulation demographic groups calculated after log transformation.
Statistical Analysis

• Confidence intervals
  • The calculated mean activity values and confidence intervals of each sub-group were back-transformed by calculating the natural exponential of each value to allow for the use of the normal activity scale.
  • Overlap of the confidence interval bars indicates that the means of subgroups are not statistically different from each other.
Gestational Age

• 111,580 total samples
  • ~91% within 37-42 weeks gestation

• Excluded samples:
  • Collected < 24 hrs or > 71 hrs after birth as age at sample collection was determined to be a confounding variable
  • Categories with very small number of samples
    • Gestational age < 23 wks n=12
    • Gestational age > 42 wks n=19
  • Gestational age missing on demographic form
Gestational Age-IDUA

>50% increase in mean IDUA activity at 23 weeks vs full term

Mean IDUA activity decreases with each week of gestation until stabilizing at ~32 weeks through full term/late term
Gestational Age-GAA

~20% increase in mean GAA activity at 23 weeks vs full term

Mean GAA activity decreases with each week of gestation until reaching a minimum at ~33 weeks

Sigmoidal increase in mean GAA activity from 33 to 40 weeks

Mean GAA activity then decreases late term (>40 weeks)
Birth Weight

- 111,890 total samples
- ~9% LBW/VLBW (<2500 g/<1500 g)
- Excluded samples:
  - Collected < 24 hrs or > 71 hrs after birth as age at sample collection was determined to be a confounding variable
  - Categories with very small number of samples
    - < 500 g (n=50)
    - > 5250 g (n=54)
  - Birth weight missing on demographic form
- Birth weight was rounded down to nearest 250 g
Birth Weight

The trends of mean IDUA and GAA activity observed for birth weight are very similar to those for gestational age due to the relationship between the two demographics.
Birth Weight-IDUA

Mean IDUA activity for VLBW samples is elevated with activity decreasing as birth weight increases.

Mean IDUA activity remains relatively constant from $\sim 1750$ g - 4500 g
Mean GAA activity for VLBW samples is elevated with activity decreasing as birth weight increases until reaching a minimum at $\sim 1750$ g. Mean GAA activity then increases nearly 20% as birth weight increases towards the data set median birth weight (3320 g).
Ethnicity

• 90,396 total samples

• Excluded samples:
  • Collected < 24 hrs or > 71 hrs after birth as age at sample collection was determined to be a confounding variable
  • Gestational age < 37 wks or > 41 wks as gestational age was determined to be a confounding variable
  • Transfused
  • NICU
  • Ethnicity missing on demographic form
Ethnicity

- Michigan NBS demographics:
  - 67% White/Caucasian
  - 18% Black/African-American
  - 6.8% Multi-Racial
  - 4.7% Arab Descent
  - 3.2% Asian/Pacific Islander
  - 0.4% Native American
Ethnicity-IDUA

Significantly lower mean IDUA activity for newborns of Arab descent compared to other ethnic groups as a whole.
Ethnicity-GAA

Significantly lower mean GAA activity for newborns of Arab descent compared to other ethnic groups as a whole.
Age at Sample Collection

- 123,772 total samples
- Age at sample collection was rounded down to the nearest full day
- > 90% samples collected on day 1 of life (24-47 hours)
- Excluded samples:
  - Collected > 30 days of age
  - Date/time of sample collection missing on demographic form
Age at Sample Collection-IDUA

Mean IDUA activity:
- Decreases by ~20% between day 0 and day 1
- Decreases by 11% between day 1 and day 2
- Stable from day 2 through day 10
- Gradual decrease day 10 through day 30
- Day 30 mean activity ~20% lower than day 1
Age at Sample Collection-GAA

Mean GAA activity:
- Decreases by $\sim 10\%$ between day 0 and day 1
- Decreases by 15% between day 1 and day 2
- Steady decrease of 1-2% per day from day 2 through day 26
- Day 26 mean activity $\sim 45\%$ lower than day 1
- Day 26 through day 30 mean activity increases to $\sim 35\%$ lower than day 1
Demographic Findings Summary

• Premature births display increased mean IDUA and GAA activity compared to full term births.
• Sigmoidal increase in GAA activity from 33 to 40 weeks gestation followed by slightly lower GAA activity in late term newborns.
• Significantly lower IDUA and GAA mean activity for newborns of Arab descent compared to other ethnic groups as a whole.
• IDUA and GAA mean activity significantly higher for samples collected on day 0 of life.
“This work is supported by the Association of Public Health Laboratories through the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number # UG9MC30369 New Disorders Implementation Project for $4,000,000. This information or content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S. Government.”
Questions?