The PReclampsia Early Determination for Intervention, Cure, and Therapeutics by Vasopressin (PREDICTV) Study

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What is Preeclampsia?

- Pregnancy Complication
- Symptoms
  - Headaches/Blurred Vision
  - High Blood Pressure
  - Kidney Damage
- Health Issues
  - For Child and Mother
  - Eclampsia
  - HELLP
- 20 weeks into gestation – 6 weeks postpartum
26 Weeks
0.5 Pounds
Delivered due to Severe Preeclampsia
What is PreE? Cont’d

• Diagnosis
• No Known Treatment
• No Known Direct Cause
• Biomarkers Aid in Detection
What are Vasopressin & Copeptin?

- Previous Research (Morgenthaler et al, 2006)
  - Vasopressin
    - Hormone
    - Not stable
  - Copeptin
    - Protein
    - Surrogate biomarker of Vasopressin

- High levels Vasopressin/Copeptin in Preeclamptic Women (Zulfikaroglu et al, 2011)
Why Copeptin?

- Statistically Significant in the First Trimester (Santillan et al, 2014)
  - Sensitivity
  - Specificity
  - Positive Predictive Value
  - Negative Predictive Value

- Additional Benefits
  - Easy to Measure
  - Early Detection
  - Cheap
  - Simple Blood Test
Why Study Preeclampsia?

- One of the Leading Causes of Death in Pregnancy
  - Mother and Child
  - 100,000 and 500,000 deaths respectively each year
  - 5-10% pregnancies affected
- Delay in diagnosis caused 92% of deaths (Snydal, 2014)
- If early detection is possible…
  - Helps decrease mortality and complications
Objectives

• What factors play a role in Preeclampsia?
  • Race
  • Diabetes
  • Multiple Gestation
  • Age
  • BMI
  • History of Preeclampsia

• What level of plasma copeptin is a good classifier of Preeclampsia?

• Can urine samples be a good measure early Preeclampsia detection?
  • More Efficient
  • Cheaper → Home Tests
What is Logistic Regression?

- The response variable is dichotomous (success; failure)
  - Preeclamptic or Non Preeclamptic
- Estimates the probability of success ($\pi$)
  - $1 = \text{success}; \ 0 = \text{failure}$
- Logit:
  - Log of the Odds of success $= \log\left(\frac{\pi}{1-\pi}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n = \text{logit}(\pi)$
  - Logit linearizes the problem
Logistic Regression Cont’d

- How is the logit used in fitting a logistic regression model?
  - \( \text{logit}(\pi) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k \Rightarrow \frac{e^{\text{logit}(\pi)}}{1 + e^{\text{logit}(\pi)}} = \pi \)
  - \( \pi = \frac{e^{\beta'x}}{1 + e^{\beta'x}} \)

- Three Components for a Logistic Regression Model:
  1. Data:
     - Number of successes in total number of observations
     - Has predictors
  2. Randomness:
     - Trials are independent
     - Depends on the Bernoulli distribution
  3. Fixed: \( \frac{e^{\text{logit}(\pi)}}{1 + e^{\text{logit}(\pi)}} \)
Coefficients

- Log(odds of success) = logit = $\beta_0 + \beta_1 X_1$, where $X_1 = 0$ or 1
  - If $X_1 = 0$, $e^{\beta_0} = \text{odds of success}$
  - If $X_1 = 1$, $e^{\beta_0 + \beta_1} = \text{odds of success}$

- Log(odds of success) = logit = $\beta_0 + \beta_1 X_1$, where $X_1$ is continuous
  - If $X_1$ increases by 1, $(e^{\beta_0 + \beta_1 X_1})(e^{\beta_1}) = \text{odds of success}$
Data

• Cohort of 104 women (Preeclamptic and nonpreeclamptic)
  • 68 Prognostic Variables
    • Univariate analysis
  • Success = Having Preeclampsia
Results

- Variables not Significant:
  - BMI
  - Age
  - Multiple Gestation
  - Race
  - Diabetes

- Significant Variables:
  - Copeptin
  - History of Preeclampsia
Results

Logit(\(\pi\)) = -3.19 + 0.003*Copeptin
- As copeptin level increases by 100, then the probability of getting preeclampsia increases by ~2%

Copeptin Level: 811 pg/mL
Specificity: 0.81
Sensitivity: 0.94
AUC: 0.90
Results

Logit(\(\pi\)) = -4.21 + 0.005*Copeptin – 3.23*History

With History of Preeclampsia:
As copeptin level increases by 100, then the probability of preeclampsia increases by 0.06%
AUC: 0.85
Copeptin Level with History: 1138 pg/mL

Without History of Preeclampsia:
As copeptin level increases by 100, then the probability of preeclampsia increases by 3%
AUC: 0.963
Copeptin Level without History: 684 pg/mL
Data

• Cohort of 8 women (Preeclamptic and nonpreeclamptic)
  • Urine and plasma copeptin levels
  • Interested in finding relationship between Plasma and Urine Copeptin
Results

Copeptin in Urine

Sensitivity

Specificity
Results

Urine Copeptin = 76.2 + 0.07*Plasma Copeptin

$t_7 = 3.041; p = 0.0228; R^2 = 0.6065$
Results

Monte Carlo simulation
Median = 134.9 pg/mL
Mean = 134.8 pg/mL
Discussion/Conclusion

• Conclusions
  • History of PreE and 1st Trimester Copeptin levels
    • ~800 pg/mL
  • Urine Copeptin
    • ~130 pg/mL
    • Could be used as an at-home diagnostic test

• Limitations
  • Small sample size
  • Lack of diversity
  • Lack of studies involving plasma and urine copeptin
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Bibliography


