Study Protocol and Statistical Analysis Plan

Official Title:
Evaluation of Observation Periods and Biphasic Reaction Risk Factors in Pediatric Anaphylaxis Cases in the Pediatric Emergency Department: A Retrospective Study

Brief Title:
Observation Periods and Biphasic Reaction Risk Factors in Pediatric Emergency Anaphylaxis Cases

Unique Protocol ID:
ADUPEDANAPH

NCT Number:

Responsible Party / Principal Investigator:
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Ethics Approval:
Approved by the Clinical Research Ethics Committee of Adnan Menderes University Faculty of Medicine (Approval Date: 24/09/2025).

Document Date: 03 October 2025

1. Study Rationale

Anaphylaxis is a severe, rapidly developing systemic allergic reaction that poses unique challenges in pediatric emergency care. International guidelines recommend observation after treatment due to the risk of biphasic reactions (recurrence within 1–72 hours), but the optimal observation period in children is uncertain. Limited data exist from Turkey regarding pediatric anaphylaxis triggers, treatment practices, biphasic reaction frequency, and risk factors.

2. Objectives

- **Primary Objective:**
  To determine the average observation period in the pediatric emergency department for children presenting with anaphylaxis and to evaluate the frequency and timing of biphasic reactions.

- **Secondary Objectives:**

  - To analyze independent risk factors for biphasic reactions, including delayed epinephrine administration, asthma history, and severity at presentation.
  - To assess the rate of hospital admission and need for intensive care.
  - To describe treatment patterns (use and timing of epinephrine, corticosteroids, antihistamines, fluids) in the emergency setting.

3. Hypotheses

H1: Early administration of intramuscular epinephrine reduces the risk of biphasic reactions and improves clinical outcomes.

H2: A history of asthma and severe initial clinical presentation are associated with higher risk of biphasic reactions and prolonged observation requirements.

H3: Children requiring multiple doses of epinephrine are at increased risk for hospitalization and biphasic reactions.

4. Study Design

Type: Observational

Design: Retrospective analytic cohort (chart review)

Setting: Pediatric Emergency Department, Adnan Menderes University Hospital

Period: January 1, 2014 – December 31, 2024

Sample: All consecutive patients <18 years diagnosed with anaphylaxis

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5. Study Population

Inclusion Criteria:

- Children aged 0–18 years
- Diagnosis of anaphylaxis according to WAO 2020 criteria
- Complete medical records available

Exclusion Criteria:

- Incomplete or missing medical records

- Cases not meeting WAO 2020 diagnostic definition
- Isolated urticaria or localized allergic reactions

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6. Methods

Data Sources: Patient files and electronic medical records (January 2014 – December 2024).
Variables collected:

- Demographics (age, sex)
- Medical history (comorbidities such as asthma, allergic diseases)
- Triggers (food, drug, insect sting, idiopathic)
- Clinical manifestations (skin, respiratory, cardiovascular, gastrointestinal, neurological)
- Treatments (IM epinephrine, time to first dose, number of doses, IV antihistamines, IV corticosteroids, fluid therapy, inhaled therapy)
- Duration of ED observation, hospitalization, ICU stay
- Occurrence and timing of biphasic reactions
- Outcomes: discharge, readmission, mortality (if any)

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7. Statistical Analysis Plan

- **Software:** SPSS v20.0
- **Descriptive statistics:** Continuous variables will first be tested for normality (e.g., Shapiro–Wilk test). Normally distributed variables will be presented as mean ± SD, while non-normally distributed variables will be expressed as median (IQR). Categorical variables will be summarized as n (%).
- **Comparisons:** Chi-square or Fisher's exact test for categorical variables; Student's t-test or Mann–Whitney U test for continuous variables, depending on distribution.
- **Regression analysis:** Logistic regression to identify independent predictors of biphasic reactions and prolonged observation (candidate variables: time to epinephrine, asthma, severity, multiple epinephrine doses).
- **Significance level:** $p < 0.05$ considered statistically significant.

Sample size: All eligible patients.

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8. Ethical Considerations

- Approved by Adnan Menderes University Faculty of Medicine Clinical Research Ethics Committee (Approval No: 2025/266).

- Retrospective study design → no informed consent required.
- All data anonymized and stored securely.

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9. Expected Contribution

This study will provide evidence-based data for determining safe observation periods in pediatric anaphylaxis and will highlight risk factors for biphasic reactions in the Turkish pediatric population. Results are expected to guide clinical practice and support international guideline comparisons.