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**When Normal Isn't Normal: Reassessing the Anion Gap in the Diagnosis and Resolution of Diabetic Ketoacidosis – A Systematic Review**

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**ADMINISTRATIVE INFORMATION**

**Support** - No financial support needed.  
**Review Stage at time of this submission** - Preliminary searches.  
**Conflicts of interest** - None declared.  
**INPLASY registration number:** INPLASY202540064

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 April 2025 and was last updated on 20 April 2025.

**INTRODUCTION**

**Review question / Objective** The objective of this study is to reassess the effectiveness of using anion gap in comparison to not using it in the diagnosis and monitoring its resolution among DKA patients.

**Rationale** To best of our knowledge, we found that there is no current literature review has been conducted in regard of anion gap significance in diagnosis and resolution of DKA.

**Condition being studied** Diabetic ketoacidosis (DKA) is the most common life-threatening acute complication of diabetes mellitus (DM) and requires early detection and prompt management. It is most likely seen in patients with type 1 DM compared to those with type 2. DKA is defined by a triad of hyperglycemia, hyperketonemia, and metabolic acidosis.

**METHODS**

**Search strategy** PubMed, Ovid MEDLINE, EMBASE and GOOGLE SCHOLAR are searched using a defined search strategy adjusted for each database.

**Participant or population** DKA patients.

**Intervention** Using anion gap as a marker for diagnosis and resolution of DKA.

**Comparator** Not using anion gap as a marker for diagnosis and resolution of DKA.

**Study designs to be included** Cohort, and randomized clinical trials.

**Eligibility criteria**  
Non-DKA Patients.

Any articles that don't have our outcome, any preclinical studies, editorials, letters and non-English publications.

#### Information sources Databases:

PubMed, Ovid MEDLINE, EMBASE and GOOGLE SCHOLAR are searched using a defined search strategy adjusted for each database.

#### Hand Searching:

International Endocrine Journals  
International Emergency Journals.

**Main outcome(s)** To our knowledge, no prior systematic review has been conducted to determine the effectiveness of anion gap in the diagnosis and resolution of DKA. Our main aim in the present study is to reassess the effectiveness of using anion gap in comparison to not using it in the diagnosis and monitoring its resolution among DKA patients.

**Data management** Data will be extracted independently from the selected articles by two reviewers and stored in an electronic database. The following data will be extracted: study type, design and limitations, patient demographics, patient co-morbidities, previous diagnosis of DKA using anion gap, previous diagnosis of DKA not using anion gap, clinical outcome.

**Quality assessment / Risk of bias analysis** The study quality of cohort studies will be assessed according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. Studies that reported a complete STROBE checklist for cohort studies will be assessed as high-quality studies and we will include in our review. For RCT studies, a revised Cochrane risk-of-bias tool will be used.

**Strategy of data synthesis** A systematic assessment of the available evidence will be conducted in accordance with the GRADE methodology and PRISMA checklist, A meta-analysis will be considered if we have enough of prospective randomized trials. Our qualitative synthesis is a narrative, textual approach to summarizing, analyzing, and assessing the body of evidence included in our review, we will use the qualitative synthesis to:

- Provide a general summary of the characteristics and findings of the included studies.
- Analyze the relationships between studies, exploring patterns and investigating heterogeneity.
- Discuss the applicability of the body of evidence to the review's question within the PICO structure.

- Explain the meta-analysis (if one is conducted) and interpret and analyze the robustness of its results.
- Critique the strengths and weaknesses of the body of evidence as a whole, including a cumulative assessment of the risk of bias across studies.
- Discuss any gaps in the evidence, such as patient populations that have been inadequately studied or for whom results differ.
- Compare the review's findings with current conventional wisdom when appropriate.

**Subgroup analysis** Not applicable.

**Sensitivity analysis** Not applicable.

**Language restriction** No.

**Country(ies) involved** Saudi Arabia.

**Keywords** Diabetes Ketoacidosis, Anion gap, Acid Base Imbalance, Metabolic Acidosis.

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