

REVIEW ARTICLE

Diagnostic Accuracy of End-Tidal Carbon Dioxide for Assessing Diabetic Ketoacidosis: A Systematic Review and Meta-Analysis

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Abstract: **Introduction:** Diabetic ketoacidosis (DKA) is one of the complications of diabetes mellitus that requires rapid and accurate diagnosis. End-tidal carbon dioxide (EtCO₂) has been used for diagnosing DKA, however, there is uncertainty about the predicting value of this tool. In the current systematic review and meta-analysis, we purposed to assess the predictive value of EtCO₂ in diagnosing DKA. **Methods:** We conducted a comprehensive search in PubMed, Scopus, and Web of Science for relevant studies and after screening based on the inclusion criteria, we extracted data. DKA diagnosis in the included studies was based on a composite clinical reference standard, including arterial blood gas (ABG) analysis and ketone testing. We used the Joanna Briggs Institute (JBI) checklist for diagnostic test accuracy studies for quality appraisal. Meta-analysis was performed based on the methods of the Cochrane DTA Handbook using the MetaDTA: Diagnostic Test Accuracy Meta-Analysis v2.1.3. **Results:** A total of 13 studies were included in the systematic review, eight of which were proceeding to meta-analysis. The pooled sensitivity and specificity of EtCO₂ for diagnosing DKA were 0.96 (95% confidence interval (CI): 0.85-0.93) and 0.88 (95% CI: 0.79-0.93), respectively. The pooled diagnostic odds ratio (DOR) was 211.07 (95% CI: 38.3- 1162.1). The positive and negative likelihood ratios were 8.27 (95% CI: 4.6-14.7) and 0.03 (95% CI: 0.009-0.18), respectively. The results of the quality appraisal of include studies indicated moderate to low risk of bias. **Conclusion:** The findings of this systematic review and meta-analysis show the high sensitivity and specificity of EtCO₂ in diagnosing DKA, which indicates its potential as a reliable diagnostic tool in emergency settings. However, the overall quality of the included studies, which were assessed to have medium to high risk of bias, should be considered when using EtCO₂ in clinical practice. Further high-quality research is needed to confirm the diagnostic value of EtCO₂ in emergency settings.

Keywords: Diabetic ketoacidosis; Capnography; Diagnosis; Systematic review; Meta-analysis

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1. Introduction

Diabetic ketoacidosis (DKA), mainly manifesting by hyperglycemia, metabolic acidosis, and ketonemia, is a serious complication of diabetes, which mainly affects type 1 diabetic patients. Based on the American Diabetes Association (ADA), DKA is categorized into mild, moderate, and severe, which can assist in management and prediction of patient outcomes (1). In recent decades, the prevalence of DKA has increased, being responsible for rise in hospital admissions of diabetic patients, which consequently leads to high

healthcare costs in the world (2, 3).

Due to the nature of DKA, it is vital to promptly assess the condition, albeit in an accurate way (4). Standard diagnostic tools for DKA include blood gas analysis, anion gap assessment, measurement of serum ketones, and capnography. Capnography, specifically measurement of end-tidal carbon dioxide (EtCO₂), is a non-invasive diagnostic tool that can facilitate fast decision-making, especially in emergency departments and critical care setting (5). EtCO₂ provides valuable information regarding compensatory mechanisms during metabolic imbalances that are prevalent in DKA. A significant decrease in EtCO can act as an early indicator of metabolic acidosis (6).

Although several studies support the use of EtCO as a safe, non-invasive, and inexpensive tool for diagnosing DKA, there is a variety among cutoff values among studies, ranging from 21 to 36 mmHg, which reflects inconsistency in diagnostic

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thresholds (7, 8). To better understand the diagnostic value of EtCO₂, it is essential to evaluate its sensitivity and specificity, the key measures for indicating diagnostic test accuracy. Sensitivity refers to the percentage of actual cases that the test correctly detects, while specificity indicates the percentage of non-cases that the test correctly identifies (9). Evaluating these two measures for EtCO₂ is necessary to understand its predictive value in diagnosing DKA. Although several studies have been conducted to assess the predictive value of EtCO₂ for diagnosing DKA, the diagnostic efficacy of this tool remains uncertain. Therefore, this systematic review and meta-analysis aimed to comprehensively evaluate the predictive performance of EtCO₂ in diagnosing DKA.

2. Methods

2.1. Study design and setting

This study was a diagnostic test accuracy (DTA) systematic review and meta-analysis that was conducted to assess the predictive value of EtCO₂ in diagnosing DKA. We have registered the protocol for this systematic review and meta-analysis in the International Prospective Register of Systematic Reviews (PROSPERO), with the registration number of CRD42025638994. This systematic review was prepared based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

This study was registered in Tabriz University of Medical Sciences (Code No: 73613). The ethics committee of Tabriz University of Medical Sciences approved the study (IR.TBZMED.REC.1403.752).

2.2. Inclusion and exclusion criteria

We adhered to Joanna Briggs Institute (JBI) methodology for diagnostic test accuracy systematic review and meta-analysis (10), according to which, the mnemonic PIRD was used to structure the inclusion criteria: P (Population): studies that included individuals with diabetes mellitus (Type 1 or Type 2), I (Index test): studies that assessed the predictive value of EtCO₂ in identifying DKA were included in this systematic review, R (Reference test): this is not applicable for the purposes of this review, since our systematic review focused primarily on the predictive performance of EtCO₂, rather than comparing it with a gold standard, and D (Diagnosis of interest): The target condition was diabetic ketoacidosis.

Studies that did not evaluate EtCO₂ as a diagnostic tool for DKA or used EtCO₂ for other purposes were excluded. Furthermore, studies that did not provide sufficient data, such as true positive (TP), false positive (FP), true negative (TN), and false negative (FN), to enable calculation of performance metrics were not considered for inclusion in the meta-analysis, however these studies were included in the systematic review and their data were extracted. In addition, we excluded narrative reviews, editorials, conference papers and non-English language papers.

2.3. Search strategy

We searched PubMed, Scopus, Web of Science, and Google Scholar on January 2025, using Medical Subject Headings (MeSH) and free-text vocabulary. The search strategy for PubMed is provided in the following:

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(((((("Capnography"[Mesh]) OR ("Carbon Dioxide"[Mesh]) OR (Capnograph*[Text Word])) OR (Etco2[Text Word])) OR (End-trial co2[Text Word])) OR (End-trial carbon dioxide[Text Word])) OR (Carbonic Anhydride[Text Word])) AND (((("Diabetic Ketoacidosis"[Mesh]) OR (Diabetic Ketoacidosis*[Text Word])) OR (Diabetic Acidosis*[Text Word])) OR (Diabetic Ketosis*[Text Word])) OR (DKA[Text Word]))).
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2.4. Study selection

Two reviewers (KJ and NK) independently screened all retrieved studies on titles and abstracts, and consequently full-texts. Any disagreements during the screening or data extraction phases were resolved through discussion with the third reviewer (HS).

2.5. Data extraction and quality assessment

Two independent reviewers extracted data from the included studies using pre-determined items including study ID, country, setting, design, sample size, mean age, DKA cases, mean EtCO₂ (mmHg), and cut-off value of EtCO₂. Also, we used Joanna Briggs Institute (JBI) checklist for diagnostic test accuracy studies (11) for assessing quality of included studies, which was conducted by the same two reviewers. To better contextualize the results, we mapped the JBI items onto the QUADAS-2 domains as follows: patient selection: Q1 (sampling method), Q2 (case-control avoidance), and Q3 (inappropriate exclusions); index test: Q4 (blinding of index test) and Q5 (pre-specified threshold); reference standard: Q6 (validity) and Q7 (blinding of reference standard); and flow and timing: Q8 (interval between tests), Q9 (reference standard consistency), and Q10 (inclusion in analysis).

2.6. Statistical analysis

We performed meta-analysis based on the methods of the Cochrane DTA Handbook (12) using the MetaDTA: Diagnostic Test Accuracy Meta-Analysis v2.1.3, a web-based tool specifically designed for diagnostic test accuracy meta-analysis (13, 14). Bivariate random-effects analysis was employed in computing pooled test accuracy estimates. The primary outcomes measured were the sensitivity and specificity of EtCO₂ test in diagnosing DKA. The numerical data including true positive (TP), true negative (TN), false negative (FN), false positive (FP), predictive values, and likelihood ratios were calculated using their formula in Excel. Forest plots and summary receiver operating characteristic (SROC) curves were used to visually represent the sensitivity and specificity for individual studies.

3. Results

3.1. Study Selection

The initial search in databases yielded 123 results after removing duplicates, from which, 25 were assessed by full-text. After excluding 12 at this stage (6 didn't meet inclusion criteria, 2 were non-English, and 4 were narrative reviews), 13 met our inclusion criteria and were included in the study. Since not all of these 13 studies had quantitative data to be included in the meta-analysis, the final meta-analysis was conducted with eight studies. Figure 1 illustrates the PRISMA flow diagram for the study selection process.

3.2. Characteristics of included studies

We included 13 studies in this systematic review, 8 of which were eligible for meta-analysis. Among the included studies, two were case reports. These case reports were included only in the qualitative synthesis to provide supplementary descriptive information and were not entered into the quantitative meta-analysis due to their inherent limitations in estimating diagnostic accuracy. The total sample size was 1859 patients.

Studies were published between 2003 and 2024. Four investigations were conducted in the United States (5, 15-17), three in Turkey (7, 8, 18), one in Iran (19), one in India (20), one in Australia (21), and one in Belgium (22). Two studies had not specified where they were conducted (23, 24). All included studies were conducted in emergency departments except one, which was in intermediate care unit (15). Five studies were conducted on the pediatric population. Study designs were cross-sectional, cohort, and case reports. The main characteristics of included studies are summarized in Table 1.

Results of the quality appraisal of included studies are depicted in Table 2. The overall risk of bias was moderate, with several domains rated as unclear. When excluding case reports, the risk of bias in the remaining studies tends to be moderate to low, indicating generally acceptable study quality.

3.3. Meta-analysis

Meta-analysis was conducted on eight studies (5, 8, 16, 19-21, 23, 24). Case reports by Eyler et al. (18) and Redant et al. (22) and studies for which TP, FP, TN, TP values could not be calculated from the given data (7, 15, 17) were not included in the meta-analysis. The diagnostic summary estimates were calculated with random effects model using MetaDTA software (Table 3).

The pooled sensitivity was 0.96 (95% confidence interval (CI): 0.85-0.93) and the pooled specificity was 0.88 (95% CI: 0.79-0.93). The pooled diagnostic odds ratio (DOR) was 211.07 (95% CI: 38.3-1162.1). Two forest plots, separately to indicate the sensitivity and specificity, and a summary ROC curve are depicted in Figures 2A, 2B, and 2C.

4. Discussion

This systematic review and meta-analysis was performed to assess the diagnostic value of EtCO₂ in DKA. Findings show that the pooled sensitivity across eight included studies was 0.96 (95% CI: 0.85-0.93), and the pooled specificity was 0.88 (95% CI: 0.79-0.93), which exhibits the good diagnostic accuracy of this tool. However, it should be emphasized that EtCO₂ alone cannot definitively diagnose DKA but can serve as a useful adjunct for ruling out the condition.

Traditional diagnostic tools for DKA rely on blood glucose levels, arterial pH, bicarbonate concentration, and the anion gap (25). However, the use of other diagnostic tools, especially those measuring blood ketones, has increased. Blood ketone measurement, assesses metabolic derangements related to DKA, which primarily detects acetoacetate. There are point-of-care tests for blood ketones and urine ketones, which measure beta-hydroxybutyrate and acetoacetate, respectively, are FDA-cleared and considered the current standards for diagnosing DKA. While EtCO₂ monitoring offers a non-invasive and rapid adjunctive tool, it cannot replace these confirmatory biochemical tests. Instead, EtCO₂ can serve as a complementary method to help rule out DKA, particularly in settings where blood ketone testing is not readily available or feasible. On the other hand, urine testing does not accurately reflect the severity of ketoacidosis, especially in patients with severe dehydration and little amount of urine (26). EtCO₂ is a rule-out adjunct tool requiring confirmatory tests. A narrative review by Aminiahidashiti et al. showed that EtCO₂ can usefully rule out the DKA, when the patient's glucose level is above 550 mg/dl (27). On the other hand, results of a study conducted by Pishbin et al. in Iran indicated that although EtCO₂ may not be useful in estimating all variables of arterial blood gas (ABG), it is a prompt and non-invasive method with a reasonable cost, which can be used in the emergency settings (28). So, it can be implied that in limited-resource countries such as Iran using EtCO₂ can be a good alternative to high-cost diagnostic tools.

In an emergency setting, the rapid differentiation between DKA and other hyperglycemic conditions, especially hyperosmolar hyperglycemic state (HHS), plays an important role in management and prognosis of each condition. DKA is characterized by an uncontrolled hyperglycemia, metabolic acidosis, and ketonemia (29, 30). In contrast, HHS involves marked hyperglycemia and dehydration but does not include acidosis (31, 32). The mechanisms and clinical manifestations of these two conditions are different and impact the treatment method. For example, DKA mainly occurs in young patients with type 1 diabetes, who can deteriorate rapidly without effective insulin therapy (31). On the other hand, HHS mainly occurs in older patients, with type 2 diabetes, may present more gradually and in the presence of other comorbidities such as cardiovascular disease or renal conditions (33, 34). A study indicates that patients with HHS have higher mortality rates than DKA (34). Therefore, there is a strong need for an emergency department to adhere to ef-

fective protocols for triage and distinguish between DKA and HHS as promptly as possible.

Quick identification and appropriate treatment of DKA can also reduce hospitalization rate and enhance recovery of patients. In addition, differentiating between these states has implications for prognostic evaluation. For example, understanding that a patient with DKA is at risk of specific complications, such as acute renal failure or severe electrolyte imbalances, necessitates vigilant monitoring and may affect clinical decision-making and resource allocation in an emergency environment (31, 34). Heterogeneity across studies may be attributed to differences in patient populations (pediatric vs. adult), types of capnography devices used (nasal vs. mainstream), and variation in EtCO cut-off values (21–36 mmHg). These factors should be considered when interpreting the pooled estimates.

5. Limitations

This study has several limitations. First, the number of included studies and the total sample size in the meta-analysis was small and most included studies were single-center, which may limit the generalizability of the findings. Additionally, there were heterogeneity in different items such as EtCO cut-off values, study designs, and patient demographics. Furthermore, some studies lacked sufficient data to calculate diagnostic accuracy indices, and were therefore excluded from meta-analysis. Also, six out of eight studies did not report blinding between EtCO measurement and the reference standard, which could introduce bias. Finally, heterogeneity statistics were not provided because of the use of the (MetaDTA) software, and we did not conduct supplementary analyses with other tools to calculate these measures. However, the small number of included studies (n=8) limits the reliability of such heterogeneity estimates.

6. Conclusions

Our findings indicated that EtCO is a highly sensitive and specific, safe, and non-invasive tool for diagnosis of DKA, especially in emergency settings where prompt practice is critical. EtCO can be used as a non-invasive tool to help rule out DKA, and help in rapid decision-making, especially when blood gas analysis or ketone testing are delayed or unavailable. Future research should focus on large-scale prospective studies to validate these findings across diverse clinical contexts. In addition, standardized cut-off thresholds and comparison with gold-standard diagnostic methods are essential to establish EtCO as a reliable tool in DKA diagnosis.

7. Declarations

7.1. Acknowledgments

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7.2. Author contributions

NHK and NK supervised the whole study. NK conducted a systematic search and meta-analysis. KJ, and NK screened the articles. KJ and NHK extracted the data, and assessed the methodological quality of the studies. NK prepared the early draft of the manuscript. All authors confirmed the final manuscript.

7.3. Funding

This research was financially supported by Tabriz University of Medical Sciences, Tabriz, Iran.

7.4. Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

7.5. Using Artificial Intelligence Chatbots

We used large language models, specifically ChatGPT, to assist with editing.

7.6. Data Availability

All data are provided within the study.

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Table 1: The main characteristics of included studies

| Author, year, Country | Study setting | Purpose of study | Study design | Population | Sample size | DKA cases | Age | Mean EtCO (mmHg) | AuROC | Cut-off | Authors' conclusion |
|--|---|--|------------------------------|--|-------------------------|------------|---------------------|--|------------------------------|------------------------------|---|
| Agus MSD, 2006 USA | Intermediate care unit in a large children's hospital | To evaluate whether EtCO ₂ monitoring could provide ongoing insights into a patient's acid-base status | Cross-sectional | Pediatric inpatients with DKA | 72 (37 girls/35 boys) | Not stated | Median: 12 years | Not stated | Not stated | Not stated | Continuous non-invasive EtCO ₂ monitoring is a trustworthy method to evaluate acid-base status in pediatric DKA patients. Comparable to traditional methods and can reduce the need for invasive tests. |
| Bhattaram S, 2023 India | 40-bedded emergency department in a large tertiary care university hospital | To determine the value of EtCO ₂ as a screening test for the exclusion of DKA | Cohort | Patients with blood sugar levels >250 mg/dl and moderate-to-large (≥2+) urine ketones | 123 (81 male/42 female) | 86 | Mean: 42.30 ± 17.03 | In DKA patients: 14.51±6.45 In non-DKA patients: 29.89±5.69 | 0.967 | ≤ 24 | EtCO ₂ values ≤24 must be considered a valuable addition to the diagnostic criteria of DKA (EtCO ₂ ≤24 can be used to rule in DKA in patients with blood sugars >250 mg/dl and positive urinary ketones). |
| Bou Chebl R, 2016 USA, Detroit, Michigan | Single emergency department in an urban tertiary care centre | To evaluate the effectiveness of EtCo ₂ as a diagnostic tool for identifying and ruling out DKA | Cross-sectional | Adult patients >17 years with blood glucose level >550mg/dL | 71 (39 male/32 female) | 21 | Median: 48 | Median in DKA patients: 17 Median in non-DKA patients: 37 | 0.95 | ≥35 ≤21 | In adults presenting to the emergency department with glucose levels >550mg/dL, EtCO ₂ may be useful in identifying and ruling out DKA. |
| Eyler Y, 2020 Turkey | Emergency department | To investigate the correlation between EtCo ₂ levels and metabolic parameters (PH and Hco ₃) during treatment of a patient with DKA. | Case report | A patient with type 1 diabetes and symptoms of DKA | 1 | 1 | Mean: 23 | 23 | Not applicable (case report) | Not applicable (case report) | Continuous EtCo ₂ monitoring should be considered by emergency physicians in the metabolic monitoring of the patients as it is easy to use. The study suggests that EtCO monitoring is a useful, non-invasive, and cost-effective method for assessing metabolic status in DKA patients. |
| Fearon DM, 2002 Not specified | An urban, university-affiliated pediatric emergency department | To assess the ability of capnography to predict DKA | Cross-sectional | Children with known or suspected new-onset diabetes who presented to the ED with hyperglycemia. | 42 | 6 | Range: 2-18 | In DKA patients: 22.2 ± 7.5 In non-DKA patients: 36.7 ± 3.2 | 0.95 | <29 | EtCO ₂ is linearly related to HCO ₃ and is significantly lower in children with DKA. |
| Garcia E, 2003 USA | University-affiliated children's hospital | To determine the utility of continuous non-invasive capnometry for monitoring pediatric patients with DKA as assessed by the agreement between PetCO ₂ and PCO ₂ | Observational clinical study | All children with a diagnosis of DKA as evidenced by PH of <7.3 with hyperglycemia and ketonuria | 121 | Not stated | Mean: 10.9 ± 5.2 | Initial PetCO ₂ : 18.6 ± 10.8 | Not stated | Not stated | PetCO ₂ monitoring of patients with DKA provides an accurate estimate of PCO ₂ . |

Table 1: The main characteristics of included studies

| Author, year Country | Study setting | Purpose of study | Study design | Population | Sample size | DKA cases | Age | Mean EtCO ₂ (mmHg) | AuROC | Cut-off | Authors' conclusion |
|------------------------------|--|---|-----------------|--|-----------------------------|------------|--|--|------------------------------|---------------------------------|--|
| Gilhotra Y, 2007 Australia | Emergency department of an urban tertiary referral pediatric hospital | To determine if nasal capnography can be used as a screening tool to predict DKA in children with type 1 diabetes mellitus | Cross-sectional | Children with known or suspected type 1 diabetes | 58 (33 male/25 female) | 15 | Mean: 10.7±4.7 | Median in DKA patients: 21 Median in non-DKA patients: 35 | Not stated | > 30 | Nasal capnography in conjunction with clinical assessment is predictive of DKA. |
| Hunter Ch, 2020 USA | Emergency Medical Services | To determine if EtCO ₂ is an effective diagnostic tool for identifying DKA in hyperglycaemic patients before they reach the hospital | Cohort | Adult patients with hyperglycaemia (BS level>200 mg/dL) | 118 (66 male/52 female) | 6 | ≥18 | In DKA patients: 15 In non-DKA patients: 35 | 0.96 | Not specified from the abstract | Among patients with hyperglycaemia pre-hospital levels of EtCO ₂ were significantly lower in patients with DKA compared to those without and were predictive of the diagnosis of DKA. |
| Kartal M, 2011 Turkey | Emergency department in a tertiary care university hospital | To examine the relation between EtCO ₂ measurement and Hco ₃ level reflecting the patients' metabolic status | Cross-sectional | Non-intubated patients with a suspected metabolic disturbance | 240 (144 male/96 female) | Not stated | Mean: 61.2 ±15.4 | Mean initial value: 29.5 | 0.734 | ≥36 ≤25 | EtCO ₂ should be used as a predictive tool in excluding metabolic acidosis in patients with possible metabolic disturbances. |
| Kayali A, 2024 Turkey, Izmir | Emergency Medicine Clinic of a tertiary-level Izmir Atatürk Training and Research Hospital | To assess the diagnostic utility of non-invasive end tidal carbon dioxide measurements in patients with DKA | Cross-sectional | Adults (over 18 years old) with symptoms of DKA and stable vital signs | 730 (321 males/409 females) | 120 | Women: 59.45±17.04 Men: 58.95±14.88 | In DKA patients: 18.88 ±4.71 In non-DKA patients: 26.28 ± 5.1 | 0.86 | <23.7 | DKA should be among preliminary diagnoses in patients with elevated blood glucose levels if the EtCO ₂ value is <23.7. |
| Peng P, 2024 Not stated | Emergency department in an urban tertiary care center | To examine the clinical impact of a capnograph profile in the ED triage for screening acidemia | Pilot study | Adult patients who had a serum bicarbonate level or PH value drawn during their ED encounter | 100 (42 males/58 females) | 28 | Mean: 61 ±14 | 36± 6.6 | 0.85 | <32 | Capnography can be implemented feasibly in ED triage as an adjunct to vital signs. |
| Redant S, 2019 Belgium | Emergency department | To evaluate and promote the use of non-invasive EtCO ₂ monitoring in pediatric emergency settings particularly for metabolic emergencies | Case report | Pediatric patients experiencing metabolic emergencies | 2 | Not stated | 15-year-old/ 8-month-old | Case 1: initially was 17, increased to 32 at the end of continuous IV insulin infusion Case 2: initially 23, increased to 30. | Not applicable (case report) | Not applicable (case report) | Monitoring of EtCO ₂ is uncommon in acid-base disorders but is a reliable, easy to use, non-invasive method and does not require painful repeated capillary punctures for the pediatric patients. |

Table 1: The main characteristics of included studies

| Author, year Country | Study setting | Purpose of study | Study design | Population | Sample size | DKA cases | Age | Mean EtCO ₂ (mmHg) | AuROC | Cut-off | Authors' conclusion |
|------------------------|---|--|-----------------|---|--------------------------|-----------|-------------------|--|-------|---------|---|
| Soleimani H, 2013 Iran | Emergency department of a training hospital | To introduce capnography as a screening tool for DKA diagnosis | Cross-sectional | Patients older than 18 years old with blood sugar levels higher than 250 mg/dL and probable DKA | 181 (74 male/107 female) | 62 | Mean: 57.9 ± 17.8 | In DKA patients: 17.98 ± 5.24 In non-DKA patients: 31.23 ± 5.45 | 0.963 | >24.5 | Capnography values greater than 24.5 mmHg accurately allow the exclusion of DKA in ED patients suspected of that diagnosis. |

EtCO₂/PetCO₂: End-tidal Carbon Dioxide; DKA: Diabetic Ketoacidosis; PCO₂: partial pressure of carbon dioxide; HCO₃: Bicarbonate; ED: Emergency Department; BS: Blood Sugar; IV: intravenous; AuROC: area under the receiver operating characteristic curve.

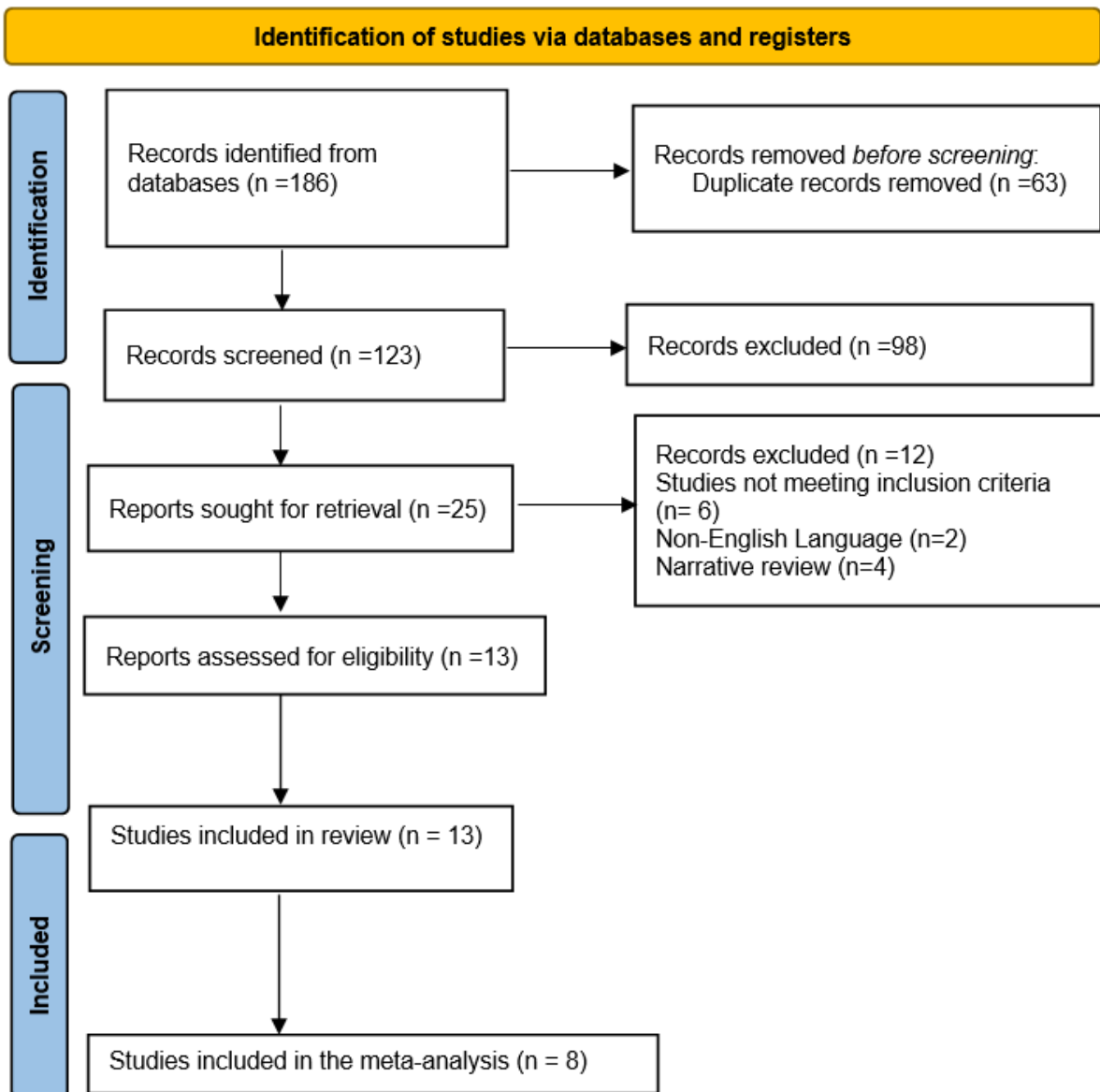


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for study selection and inclusion.

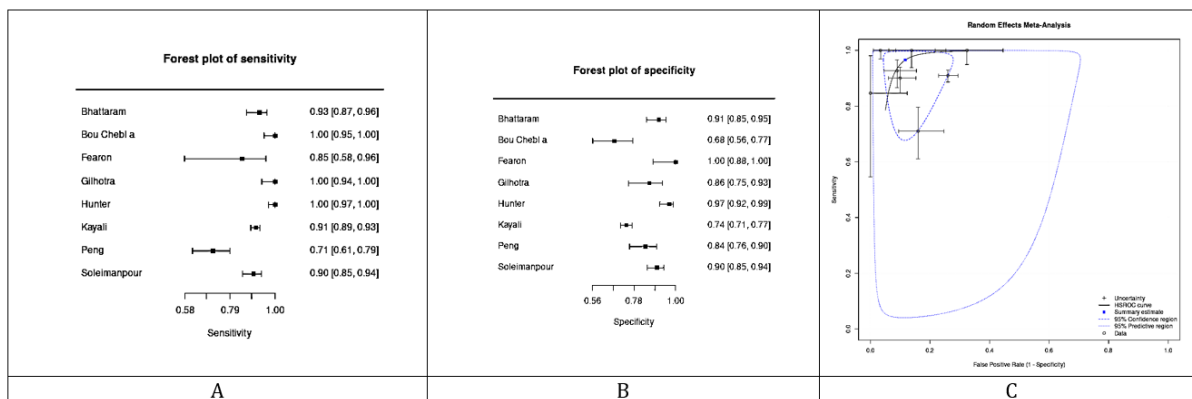


Figure 2: A: Forest plot demonstrating the sensitivity; B: Forest plot demonstrating the specificity; C: Summary receiver operating characteristic (ROC) curve.

Table 2: The quality assessment results of the included studies

| Study | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | Q10 |
|----------------------|---------|---------|-----|---------|-----|---------|---------|---------|-----|-----|
| Bhattaram S, 2023 | Unclear | Unclear | Yes | Unclear | Yes | Unclear | Unclear | Unclear | Yes | Yes |
| Bou Chebli R, 2016 | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Fearon DM, 2002 | Yes | Yes | Yes | Unclear | Yes | Yes | Unclear | Yes | Yes | Yes |
| Gilhotra Y, 2007 | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Soleimanpour H, 2013 | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Kayali A, 2024 | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Peng P, 2024 | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Hunter Ch, 2020 | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

- Q1: Was a consecutive or random sample of patients enrolled?
- Q2: Was a case-control design avoided?
- Q3: Did the study avoid inappropriate exclusions?
- Q4: Were the index test results interpreted without knowledge of the reference standard?
- Q5: If a threshold was used, was it pre-specified?
- Q6: Is the reference standard likely to correctly classify the target condition?
- Q7: Were the reference standard results interpreted without knowledge of the index test?
- Q8: Was there an appropriate interval between index test and reference standard?
- Q9: Did all patients receive the same reference standard?
- Q10: Were all patients included in the analysis?

Table 3: Diagnostic summary estimates of EtCO2 for the studies included in meta-analysis

| Study ID | TP | FN | FP | TN | Sensitivity | Specificity | PPV | NPV | LR+ | LR- | DKA prevalence | DOR |
|----------------------|-----|----|-----|-----|-------------|-------------|----------|----------|-------|------|----------------|-------|
| Bhattaram S, 2023 | 114 | 9 | 11 | 112 | 0.93 | 0.91 | 0.912 | 0.92562 | 10.33 | 0.08 | 0.70 | 128.9 |
| Bou Chebli R, 2016 | 71 | 0 | 23 | 48 | 0.99 | 0.68 | 0.755319 | 0.989691 | 3.09 | 0.01 | 0.30 | 296.3 |
| Fearon DM, 2002 | 11 | 2 | 0 | 28 | 0.85 | 0.97 | 0.956522 | 0.933333 | 28.33 | 0.15 | 0.14 | 308 |
| Gilhotra Y, 2007 | 58 | 0 | 8 | 50 | 0.98 | 0.86 | 0.878788 | 0.990099 | 7.00 | 0.02 | 0.26 | 725 |
| Hunter Ch, 2020 | 118 | 0 | 4 | 114 | 0.99 | 0.97 | 0.967213 | 0.995633 | 33.00 | 0.01 | 0.05 | 6726 |
| Kayali A, 2024 | 664 | 66 | 190 | 540 | 0.91 | 0.74 | 0.777518 | 0.891089 | 3.50 | 0.12 | 0.16 | 28.59 |
| Peng P, 2024 | 71 | 29 | 16 | 84 | 0.71 | 0.84 | 0.816092 | 0.743363 | 4.44 | 0.35 | 0.28 | 12.85 |
| Soleimanpour H, 2013 | 163 | 18 | 18 | 163 | 0.9 | 0.9 | 0.900552 | 0.900552 | 9.00 | 0.11 | 0.34 | 82 |

EtCO2: End-tidal Carbon Dioxide; TP: True Positive; FN: False Negative; FP: False Positive; TN: True Negative; PPV: Positive Predictive Value; NPV: Negative Predictive Value; LR+: Positive Likelihood Ratio; LR-: Negative Likelihood Ratio; DKA: Diabetic ketoacidosis; DOR: Diagnostic odds ratio.