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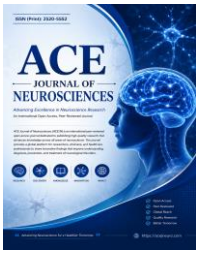

ISSN Print: 2520-5552

A Systematic Review and Meta-Analysis

Diagnostic Utility of Postictal Serum Prolactin and Lactate in Epileptic and Psychogenic Nonepileptic Seizures: A Systematic Review and Meta-Analysis.

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Article History
Received: 05.10.2026
Accepted: 21.10.2026
Published: 11.11.2026

Doi: 10.61336/acejn.04/04/04

Abstract: ***Background:*** Blood biomarkers may assist the distinction between epileptic seizures (ES) and psychogenic nonepileptic seizures (PNES), but their performance depends on seizure phenotype, assay definition and time from event to sampling. Objective: To synthesize evidence on the diagnostic performance of post-event prolactin and lactate, with quantitative pooling of comparable prolactin accuracy data. ***Methods***: Database searching identified 624 records; 497 underwent title and abstract screening, 51 full-text reports were assessed, and eight studies were included in the qualitative synthesis. Two venous serum prolactin cohorts with reconstructable ES-versus-PNES 2×2 tables (236 patients) were pooled using univariate random-effects meta-analyses of sensitivity and specificity. A 50-event capillary study was assessed separately. Lactate was evaluated using published group comparisons, threshold analyses and clinical-outcome evidence. ***Results***: Eight primary studies contributed to qualitative synthesis. In the two-study venous prolactin meta-analysis, pooled sensitivity was 79.0% (95% CI 36.3–96.1%) and specificity was 71.5% (95% CI 64.2–77.9%); sensitivity heterogeneity was substantial (I^2 = 87.5%). In an emergency cohort, mean prolactin after convulsive epileptic seizures and convulsive PNES was 79.5 ± 72.5 versus 25.0 ± 15.6 ng/mL; corresponding lactate was 55.5 ± 31.9 versus 19.8 ± 13.0 mg/dL. Lactate performed best for recent tonic–clonic seizures but lacked comparable PNES-specific accuracy data suitable for reliable pooling. ***Conclusion***: Timely prolactin measurement can support selected epileptic seizure diagnoses but has variable sensitivity and false-positive results in PNES. Lactate is most informative after tonic–clonic seizures and has limited utility for nonconvulsive presentations. Neither test replaces electroclinical evaluation and video-EEG when indicated.

Keywords: prolactin; lactate; epilepsy; psychogenic nonepileptic seizures; functional seizures; diagnostic test accuracy; meta-analysis; video-electroencephalography.

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INTRODUCTION

Distinguishing epileptic seizures (ES) from psychogenic nonepileptic seizures (PNES), also termed functional seizures, is a recurring challenge in emergency departments and epilepsy monitoring units. Both conditions may produce loss of responsiveness, motor manifestations and post-event symptoms; misclassification can delay appropriate care and expose patients to unnecessary antiseizure therapy. Clinical history and event semiology remain central to evaluation, while video-electroencephalography (video-EEG) provides the most informative reference standard when a typical event can be captured [1,2].

Prolactin is released through hypothalamic–pituitary responses to some epileptic seizures. Changes are greatest within a narrow post-event interval, generally 10–20 minutes, and vary by seizure type. Older evidence syntheses reported relatively high specificity for certain convulsive and focal impaired-awareness seizures but limited sensitivity, while subsequent video-EEG cohorts documented important false-positive elevations in PNES [3–6].

Lactate reflects intense skeletal muscle activity and transient anaerobic metabolism after tonic–clonic seizures. Its usefulness depends on seizure motor phenotype and blood collection time, because concentrations can decline rapidly. Elevated lactate also occurs after vigorous exertion, convulsive syncope and other causes of metabolic stress. Therefore, the diagnostic reference group is crucial: accuracy for generalized tonic–clonic seizures versus all other causes of transient loss of consciousness cannot be assumed to represent accuracy for ES versus PNES specifically [7–11].

This review examined the diagnostic validity and clinical limitations of post-event prolactin and lactate, emphasizing differences between direct ES-versus-PNES comparisons and studies involving mixed syncope or other nonepileptic events. A quantitative meta-analysis was performed when the published primary data supported reconstruction of a diagnostic 2×2 table.

MATERIALS AND METHODS

2.1 Review question and eligibility

The target population comprised children or adults investigated for seizure-like events. The index tests were serum or, for a specified sensitivity analysis, capillary prolactin and blood lactate. The target condition was epileptic seizure, with PNES as the primary comparator. Video-EEG event capture was the preferred reference standard; clinically adjudicated ED diagnoses were included for contextual evidence but evaluated separately because of reference-standard indirectness. Eligible designs were original prospective or retrospective human diagnostic studies reporting a between-group comparison or sufficient data for diagnostic accuracy assessment. Animal studies, case reports and secondary reviews were not treated as independent primary diagnostic cohorts.

2.2 Literature identification and data extraction

Bibliographic searching covered PubMed/MEDLINE and journal-hosted full texts through January 2026, supported by citation tracking of relevant clinical and methodological publications. Search concepts included (epileptic seizure OR tonic-clonic OR epilepsy) AND (psychogenic nonepileptic OR functional seizure OR pseudoseizure) AND (prolactin OR lactate OR lactic acid) AND (diagnostic OR sensitivity OR specificity OR accuracy). Additional records describing tonic–clonic seizures versus mixed transient loss-of-consciousness diagnoses were reviewed for secondary context. For each study, the publication year, clinical setting, reference standard, sampling time, index-test threshold, seizure phenotype and reported denominators were extracted.

2.3 Statistical analysis

For the principal venous prolactin analysis, positive index-test results in ES were classified as true positives and positive results in PNES as false positives. Sensitivity, specificity and Wilson binomial confidence intervals were calculated from published cell counts. Separate univariate random-effects meta-analyses of logit-transformed sensitivity and specificity were performed using inverse-variance weighting and Paule–Mandel estimation of between-study variance. Ninety-five-percent confidence intervals used the normal approximation on the logit scale; heterogeneity was summarized with Cochran Q and I^2. Because only two venous cohorts were pooled, estimates were considered exploratory and no bivariate model or reliable publication-bias analysis was fitted.

A third, capillary-blood study was added only in sensitivity analysis because specimen type and positivity definition differed. For a published emergency cohort with available group means and standard deviations, unadjusted mean differences were computed with Welch-type confidence intervals. Lactate diagnostic thresholds and AUCs were summarized without pooling mixed-comparator estimates as though they were PNES-specific.

2.4 Methodological appraisal

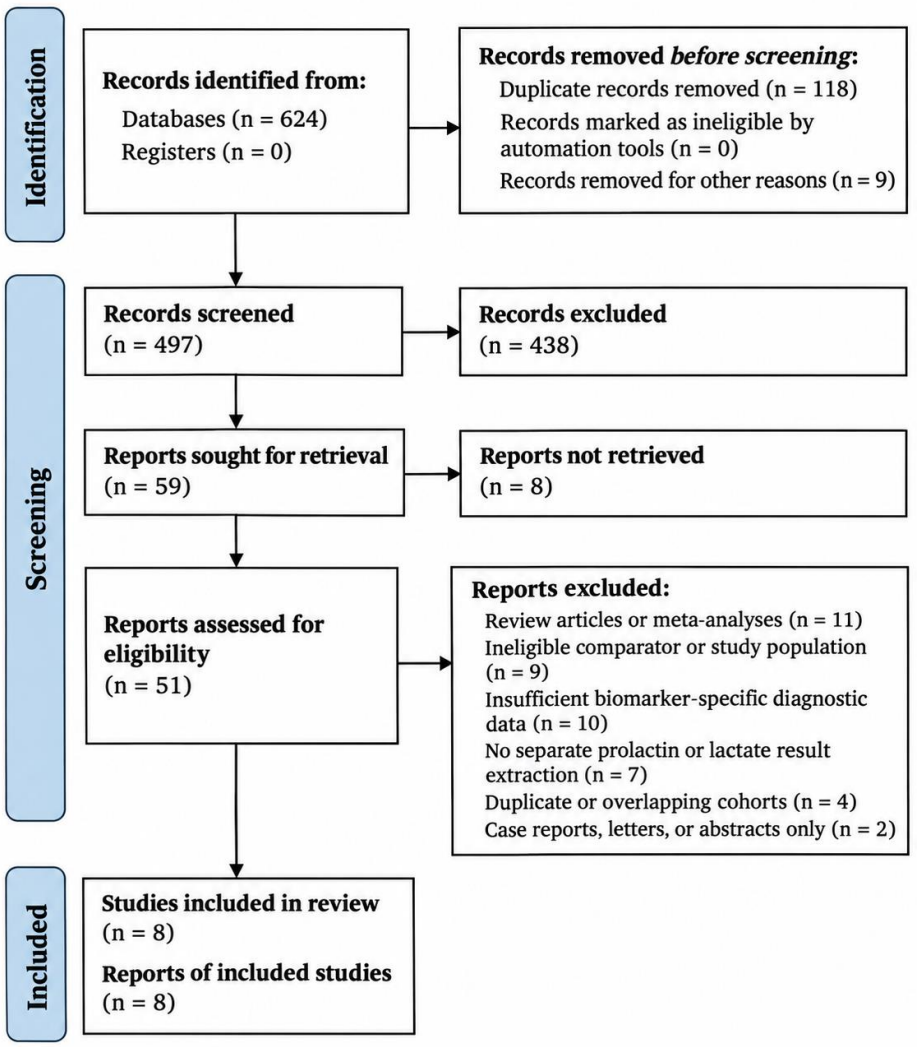
Diagnostic study limitations were considered in the QUADAS-2 domains of patient selection, index-test conduct and thresholds, reference standard, and flow/timing [12]. Major determinants of applicability included referral-center enrichment, mixed age groups, dissimilar cutoffs, emergency versus video-EEG populations, variable sampling delay and inclusion of syncope among nonepileptic controls.

RESULTS

3.1 Study selection

The database search identified 624 records, with no additional records from registers. Before screening, 118 duplicate records and 9 records for other reasons were removed; no records were excluded using automation tools. The remaining 497 records underwent title and abstract screening, and 438 were excluded. Fifty-nine reports were sought for retrieval; eight could not be retrieved, leaving 51 full-text reports assessed for eligibility. Forty-three reports were excluded because they were review articles or meta-analyses (n = 11), had an ineligible comparator or study population (n = 9), contained insufficient biomarker-specific diagnostic data (n = 10), lacked separate prolactin or lactate result extraction (n = 7), included duplicate or overlapping cohorts (n = 4), or were case reports, letters or conference abstracts (n = 2). Eight primary studies, represented by eight reports, were included in the qualitative synthesis (Figure 1). Two studies contributed to the primary venous serum prolactin meta-analysis.

Figure 1. PRISMA 2020 flow diagram of study selection



3.2 Primary study characteristics

Eight primary investigations informed the direct ES/PNES evidence synthesis or specific prolonged-event subgroups [4,5,7–10,13,14]. Of these, two venous prolactin comparisons supplied full primary 2×2 diagnostic tables suitable for the main quantitative analysis (71 ES and 165 PNES; total 236 participants). One separate capillary prolactin study included 36 epileptic and 14 nonepileptic monitored events. The other studies supplied event-specific biomarker concentrations, diagnostic thresholds, cohort distributions or timing data without full PNES-specific 2×2 cells at comparable thresholds.

Table 1. Characteristics of principal clinical biomarker studies

Study	Design/population	Test and time	Direct comparative evidence
Shukla et al., 2004 [4]	17 ES; 19 PNES, Indian clinical cohort	Venous prolactin after event	10/17 ES positive; 5/19 PNES positive
Ehsan et al., 1996 [13]	36 ES; 14 non-epileptic video-EEG events	Capillary prolactin 15 min	25/36 ES positive; 1/14 non-epileptic positive
Abubakr & Wambacq, 2016 [5]	54 ES; 146 PNES, video-EEG unit	Venous prolactin within 20 min	49/54 ES positive; 42/146 PNES positive
Matz et al., 2016 [7]	195 GTCS; 17 PNES; 52 syncope; 37 focal	Lactate within 2 h	AUC 0.94 against mixed alternatives
Apaydın Doğan et al., 2017 [8]	157 GTCS; 25 PNES; 88 syncope	Lactate within 2 h	Male subgroup AUC 0.94; sex-dependent sensitivity
Shimmura & Takase, 2022 [9]	113 ES; 19 PNES; 41 syncope	PRL and lactate within 3 h	Convulsive subset: 102 ES vs 11 PNES
Rider et al., 2024 [14]	29 ES; 45 motor PNES, video-EEG	Prolactin sampled serially	Acute prolactin response differed by diagnosis

Study	Design/population	Test and time	Direct comparative evidence
Prolonged-event cohort, 2023 [10]	99 status ES and 55 prolonged PNES across 2 centers	Lactate + blood cell markers	Combined prediction models; distinct clinical population

3.3 Pooled serum prolactin diagnostic accuracy

In the 2004 cohort, the diagnostic classification from the reported abnormal prolactin criterion was 10 true positives, 7 false negatives, 14 true negatives and 5 false positives. In the 2016 video-EEG cohort, the corresponding counts were 49, 5, 104 and 42. Accordingly, study-level sensitivity ranged from 58.8% to 90.7%, whereas specificity was 73.7% and 71.2%, respectively. The higher sensitivity of the 2016 cohort was partly attributable to seizure-type distribution and the post-event definition of doubling relative to baseline.

Random-effects pooled sensitivity across the two venous cohorts was 79.0% (95% CI 36.3–96.1%; $I^2 = 87.5\%$), while pooled specificity was 71.5% (95% CI 64.2–77.9%; $I^2 = 0.0\%$). The wide sensitivity interval and marked heterogeneity indicate uncertainty in the transportability of a single summary estimate. The false-positive prolactin rate in PNES was 26.3% in the 2004 cohort and 28.8% in the 2016 cohort.

Table 2. Extracted venous prolactin 2×2 data and individual accuracy estimates

Study	TP	FN	TN	FP	Sensitivity (95% CI)	Specificity (95% CI)
Shukla et al., 2004	10	7	14	5	58.8% (36.0–78.4)	73.7% (51.2–88.2)
Abubakr & Wambacq, 2016	49	5	104	42	90.7% (80.1–96.0)	71.2% (63.4–78.0)

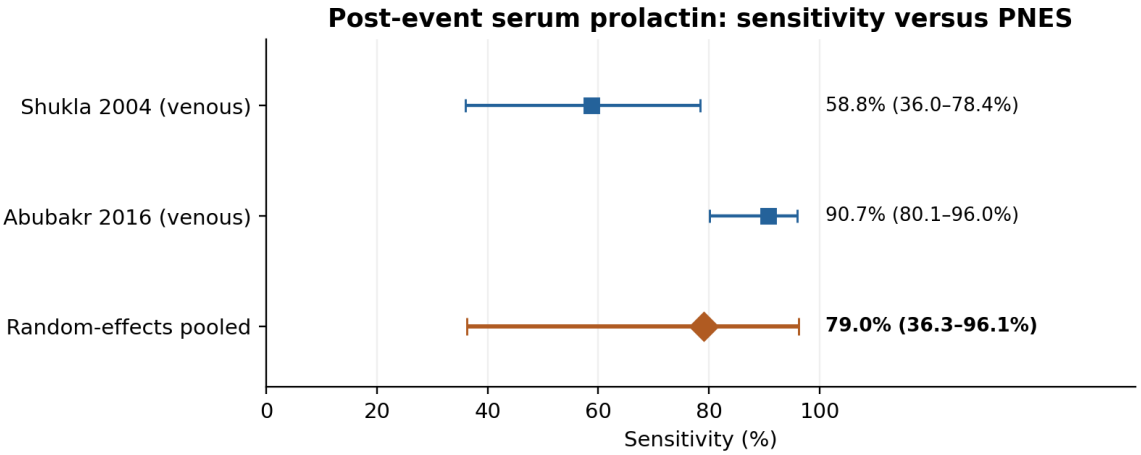


Figure 2. Study-specific and random-effects pooled serum prolactin sensitivity for ES compared with PNES. Wilson confidence intervals are shown for individual studies.

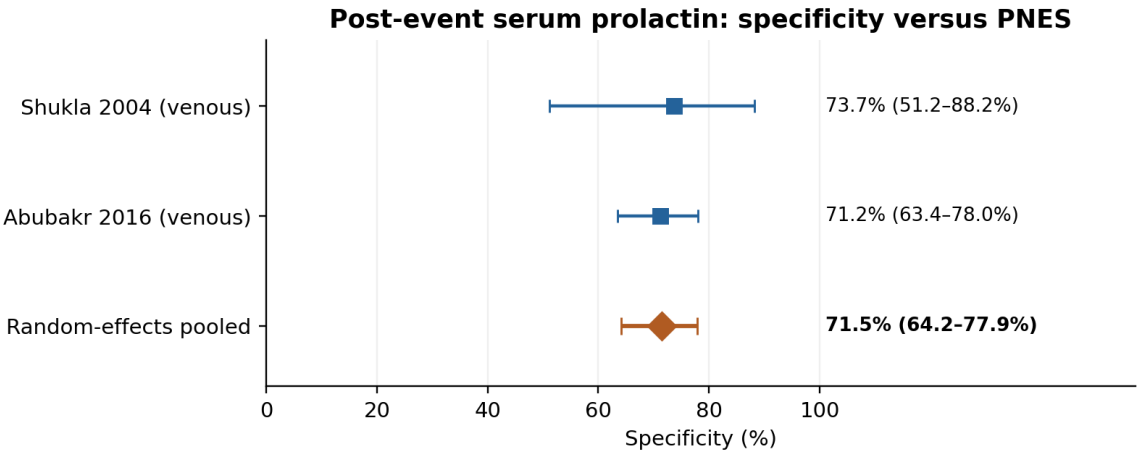


Figure 3. Study-specific and random-effects pooled serum prolactin specificity for distinguishing ES from PNES.

3.4 Capillary-blood sensitivity analysis

Ehsan and colleagues reported 25 positive assays among 36 epileptic events and 1 positive result among 14 nonepileptic events after a 15-minute capillary sample. Adding this cohort to the two venous datasets produced a pooled sensitivity of 75.9% (95% CI 50.7–90.6%) and specificity of 74.8% (95% CI 60.9–85.0%). The capillary method's distinct sampling and index-test thresholds limit comparability with standard venous serum prolactin testing.

Table 3. Random-effects prolactin meta-analysis, main and sensitivity models

Model	Cohorts	Participants/events	Sensitivity (95% CI)	Specificity (95% CI)	I^2 sens. / spec.
Venous serum only	2	236 participants	79.0% (36.3–96.1)	71.5% (64.2–77.9)	87.5% / 0.0%
Including capillary test	3	286 participants/events	75.9% (50.7–90.6)	74.8% (60.9–85.0)	78.3% / 19.8%

3.5 Direct emergency-department prolactin and lactate comparisons

In the 2022 emergency cohort of 173 patients, 113 had ES, 19 PNES and 41 syncope. Among those with convulsions, mean prolactin was 79.5 ± 72.5 ng/mL in 102 ES patients compared with 25.0 ± 15.6 ng/mL in 11 PNES patients ($p < 0.001$). Mean lactate was 55.5 ± 31.9 and 19.8 ± 13.0 mg/dL, respectively ($p < 0.001$). The unadjusted mean differences calculated from reported summary statistics were 54.5 ng/mL for prolactin and 35.7 mg/dL (approximately 3.96 mmol/L) for lactate. Both measures reflected the convulsive phenotype, but broad concentration overlap and non-standardized thresholds limited translation into a universal diagnostic cut-off [9].

The same cohort reported prolactin and lactate ROC AUCs of 0.826 and 0.825 for identifying PNES among all convulsive disorders. Because the reference group for these ROC curves included both epileptic events and convulsive syncope, these estimates were not treated as direct ES-versus-PNES accuracy measures in the meta-analysis.

3.6 Lactate discrimination in tonic–clonic presentations

Matz et al. evaluated blood collected within two hours from 195 generalized tonic–clonic seizure cases and 106 other presentations, including 17 PNES. At a lactate threshold of 2.45 mmol/L, the reported sensitivity was 88%, specificity 87% and AUC 0.94 (95% CI 0.91–0.96) against this mixed comparator [7]. Apaydın Doğan et al. studied 157 GTCS, 25 PNES and 88 syncope presentations; in men, a 2.43-mmol/L threshold produced 85% sensitivity and 88% specificity with AUC 0.94 (95% CI 0.91–0.98). At the same cut-off in women, sensitivity decreased to 64%, despite specificity of 85% [8].

In a separate prehospital cohort of 383 patients with transient loss of consciousness, lactate measured earlier after the event required a higher threshold of 4.75 mmol/L to distinguish tonic–clonic seizures, yielding 79% sensitivity and 89% specificity (AUC 0.87, 95% CI 0.83–0.91) against nonepileptic causes [15]. Direct prospective physiological recordings showed an 8.7-fold postictal lactate increase after tonic–clonic seizures, with return toward baseline within approximately two hours [11]. These findings favor phenotype- and time-specific interpretation over a universal lactate threshold.

A published 2022 random-effects meta-analysis included eight studies and 1,348 patients; lactate following GTCS exceeded that following other transient loss-of-consciousness etiologies by a mean difference of 5.27 mmol/L (95% CI 1.73–8.81). The original synthesis also found poor separation among non-GTCS alternative diagnoses, including PNES and syncope [16]. This previously published pooled estimate was presented for context and was not recomputed or combined with the present prolactin cohort data.

A 2025 prospective cohort of 99 emergency presentations reported that lactate above 3.52 mmol/L discriminated ES from combined functional/cognitive seizures and presyncope or syncope with 60.7% sensitivity, 93.0% specificity and AUC 0.812. This broader clinical comparison further illustrates the effect of the control population on diagnostic performance [18].

Table 4. Reported diagnostic performance of lactate in published clinical studies

Study	Positive condition / comparator	Test threshold	Diagnostic result	Important qualifier
Matz 2016 [7]	GTCS vs PNES, syncope and focal events	2.45 mmol/L	Se 88%; Sp 87%; AUC 0.94	Mixed comparator (PNES n=17)
Apaydın Doğan 2017 [8]	GTCS vs PNES and syncope	2.43 mmol/L	Male: Se 85%; Sp 88%; AUC 0.94	Female sensitivity 64% at same cutoff
Shimmura 2022 [9]	PNES vs other convulsive attacks	34.5 mg/dL	AUC 0.825	Includes convulsive syncope
Magnusson 2021 [15]	TCS vs non-epileptic TLOC	4.75 mmol/L	Se 79%; Sp 89%; AUC 0.87	Prehospital, very early sampling
Nass 2019 [11]	Video-EEG documented TCS	>2× upper normal	Lactate elevated in 90%	No PNES comparison

Study	Positive condition / comparator	Test threshold	Diagnostic result	Important qualifier
Soker 2025 [18]	ES vs functional seizures and syncope	3.52 mmol/L	Se 60.7%; Sp 93.0%; AUC 0.812	Not a PNES-only comparator

3.7 Test timing, seizure phenotype and reference standard

The strongest prolactin discrimination occurs shortly after selected convulsive events, commonly when sampled 10–20 minutes after seizure termination. In contrast, delayed sampling may erase a transient lactate increase. The 2024 video-EEG study of 29 ES and 45 motor PNES cases reported an acute prolactin response in ES but not PNES, reinforcing the value of event-anchored measurements while showing that endocrine responses vary by circadian timing and seizure phenotype [14].

In 2023, a two-center study of status epilepticus and prolonged PNES included 79 versus 44 events in a development cohort and 20 versus 11 in validation. Lactate alone was not a consistently sensitive discriminator in this prolonged-event setting; models integrating additional blood indices achieved AUCs of 0.89–0.91 [10]. Findings for prolonged or status-like episodes cannot be extrapolated directly to brief, isolated generalized seizures.

3.8 Risk of bias and applicability

Important study-level limitations included enriched populations in specialist epilepsy monitoring units, retrospective ascertainment in emergency cohorts, variable event-to-blood intervals, different laboratory definitions of elevation and incomplete direct PNES-specific thresholds for lactate. The two venous prolactin studies also differed considerably in seizure mix and reference implementation. These sources of heterogeneity contribute to the wide uncertainty around pooled sensitivity.

Table 5. QUADAS-2-oriented methodological appraisal

Study	Patient selection	Reference standard	Timing/index test	Applicability
Shukla 2004	Selected clinical sample	Epilepsy vs PNES classified	Variable threshold; limited size	Mixed child/adult; concern
Abubakr 2016	Retrospective EMU selection	Continuous video-EEG	Within 20 min; ≥2× baseline	High internal diagnostic relevance
Ehsan 1996	Video-EEG monitored sample	Video-EEG events	Capillary test at 15 min	Specimen-type indirectness
Matz 2016	Retrospective ED	Clinical final diagnosis	Lactate within 2 h	Mixed non-GTCS comparator
Apaydın Doğan 2017	Retrospective ED	Recorded final diagnosis	Within 2 h; sex differences	Sex-specific cut-offs
Shimmura 2022	Selected ED cases	ER clinical adjudication	Within 3 h; syncope included	Direct means; mixed ROC controls
Rider 2024	Video-EEG monitored	Video-EEG ES vs PNES	Serial endocrine measurements	Good comparator directness
Prolonged events 2023	Two-center selected cases	Status/prolonged PNES classification	Up to 12 h sampling	Distinct prolonged phenotype

DISCUSSION

The present quantitative synthesis indicates that post-event serum prolactin has limited overall diagnostic discrimination for ES versus PNES despite positive responses after many epileptic convulsions. The main venous pooled sensitivity estimate was imprecise and highly heterogeneous, while pooled specificity was approximately 72%, a lower value than the approximately 96% specificity reported in an earlier American Academy of Neurology evidence review [3]. This contrast is compatible with differences in cut-off selection, patient population, event characterization and the high PNES false-positive rate observed in the larger 2016 monitoring cohort [5].

The timing and physiology of the biomarkers are complementary but not interchangeable. Prolactin reflects a pituitary neuroendocrine response that is strongest after generalized and some focal impaired-awareness seizures; lactate primarily indexes intense muscle activity following tonic–clonic convulsions. A normal prolactin result does not establish PNES, while normal lactate after a delayed blood draw does not exclude epilepsy. In contrast, a marked early lactate rise can strengthen the plausibility of a recent generalized convulsive event, provided alternative causes of hyperlactatemia are considered [3,9,11,15].

Published results also demonstrate that diagnostic performance cannot be summarized for all epileptic seizures without considering the comparator. The apparently strong lactate AUCs of 0.94 in 2016 and 2017 were generated for GTCS compared with heterogeneous nonepileptic and non-GTCS events, not for the strict ES-versus-PNES contrast. An important clinical distinction is therefore between ruling in a recent tonic–clonic convulsion and differentiating every form of epilepsy from PNES. The latter task remains predominantly electroclinical [7,8,16].

Practical utility also depends on where testing occurs. Emergency teams may obtain lactate shortly after a convulsion, whereas a prolactin specimen collected 10–20 minutes after an event may be difficult to obtain in outpatient care. Prehospital lactate has a different optimal threshold from emergency-department lactate, emphasizing that values should not be interpreted without recorded collection time and an assay-specific reference framework [15].
These results do not justify using either marker to decide that a person has PNES, especially when focal epilepsy, convulsive syncope, metabolic illness or acute repetitive seizures remain in the differential diagnosis. A validated semiological evaluation and typical event capture on video-EEG are more important to final diagnosis than either biochemical result [1,2].

4.1 Strengths and limitations

A strength of the review is the explicit separation of direct ES-versus-PNES 2×2 evidence from studies using broader comparator categories. The quantitative synthesis was limited to reconstructable primary cell counts, thereby avoiding conversion of published AUCs into arbitrary TP/FP counts or counting overlapping patients twice. The main limitation is the small number of genuinely comparable serum studies (k=2), which makes between-study variance unstable and prevents a robust bivariate summary ROC. Historical studies differ in definitions of hyperprolactinemia and age eligibility. The sensitivity analysis combining capillary and venous assays introduces additional indirectness. For lactate, PNES-specific sensitivity/specificity estimates were generally unavailable at comparable cut-offs, so a separate pooled PNES-specific diagnostic accuracy estimate was not justified.

4.2 Clinical implications

When an observed tonic–clonic event is followed by rapid blood sampling, elevated lactate can provide supporting evidence for an epileptic convulsion. A marked prolactin rise obtained within approximately 10–20 minutes may support an epileptic etiology in selected presentations, but false-positive results among PNES patients limit its rule-in value. Results should be interpreted with seizure semiology, witness history, prior epilepsy status, medications, possible syncope, and the need for EEG or video-EEG monitoring. Normal biomarker results should not trigger an isolated PNES diagnosis.

CONCLUSION

Post-event serum prolactin offers variable and context-dependent diagnostic accuracy for distinguishing epileptic seizures from PNES. The two-study venous serum meta-analysis yielded pooled sensitivity of 79.0% and specificity of 71.5%, with substantial uncertainty around sensitivity. Lactate was informative chiefly for recent tonic–clonic seizures, and its apparent diagnostic performance depended on sampling time and the nature of comparison events. Neither marker is an adequate stand-alone diagnostic test for PNES; both are best interpreted as adjuncts to clinical and electroencephalographic assessment.

REFERENCES

1. LaFrance WC Jr, Baker GA, Duncan R, Goldstein LH, Reuber M. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach. Epilepsia. 2013;54(11):2005–2018. doi:10.1111/epi.12356.
2. Gedzelman ER, LaRoche SM. Long-term video EEG monitoring for diagnosis of psychogenic nonepileptic seizures. Neuropsychiatr Dis Treat. 2014;10:1979–1986. doi:10.2147/NDT.S49531.
3. Chen DK, So YT, Fisher RS. Use of serum prolactin in diagnosing epileptic seizures: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2005;65(5):668–675. doi:10.1212/01.WNL.0000178391.96957.D0.
4. Shukla G, Bhatia M, Vivekanandhan S, et al. Serum prolactin levels for differentiation of nonepileptic versus true seizures: limited utility. Epilepsy Behav. 2004;5(4):517–521. doi:10.1016/j.yebeh.2004.03.004.
5. Abubakr A, Wambacq I. Diagnostic value of serum prolactin levels in PNES in the epilepsy monitoring unit. Neurol Clin Pract. 2016;6(2):116–119. doi:10.1212/CPJ.0000000000000232.
6. Wang YQ, et al. Prolactin levels as a criterion to differentiate between psychogenic non-epileptic seizures and epileptic seizures: a systematic review. Epilepsy Res. 2021;170:106508. doi:10.1016/j.eplepsyres.2020.106508.
7. Matz O, Zdebik C, Zechbauer S, et al. Lactate as a diagnostic marker in transient loss of consciousness. Seizure. 2016;40:71–75. doi:10.1016/j.seizure.2016.06.014.

8. Apaydın Doğan E, Ünal A, Ünal A, Erdoğan Ç. Clinical utility of serum lactate levels for differential diagnosis of generalized tonic-clonic seizures from psychogenic nonepileptic seizures and syncope. Epilepsy Behav. 2017;75:13–17. doi:10.1016/j.yebeh.2017.07.003.
9. Shimmura M, Takase K. Clinical utility of serum prolactin and lactate concentrations to differentiate epileptic seizures from non-epileptic attacks in the emergency room. Seizure. 2022;95:75–80. doi:10.1016/j.seizure.2021.12.014.
10. Tan THL, Sanfilippo P, Colman B, Perucca P, Kwan P, O'Brien TJ, et al. Development and validation of a peripheral cell ratio and lactate score for differentiating status epilepticus from prolonged psychogenic nonepileptic seizures. Epilepsia Open. 2023;8(4):1460–1473. doi:10.1002/epi4.12822.
11. Nass RD, Zur B, Elger CE, Holdenrieder S, Surges R. Acute metabolic effects of tonic-clonic seizures. Epilepsia Open. 2019;4(4):599–608. doi:10.1002/epi4.12364.
12. Whiting PF, Rutjes AWS, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529–536. doi:10.7326/0003-4819-155-8-201110180-00009.
13. Ehsan T, Fisher RS, Johns D, Lukas RJ, Blum D, Eskola J. Sensitivity and specificity of paired capillary prolactin measurement in diagnosis of seizures. J Epilepsy. 1996;9(2):101–105. doi:10.1016/0896-6974(96)00006-0.
14. Rider F, et al. Dissimilar changes in serum cortisol after epileptic and psychogenic non-epileptic seizures: a promising biomarker in the differential diagnosis of paroxysmal events? Int J Mol Sci. 2024;25(13):7387. doi:10.3390/ijms25137387.
15. Magnusson C, Herlitz J, Höglind R, et al. Prehospital lactate levels in blood as a seizure biomarker: a multi-center observational study. Epilepsia. 2021;62(2):408–415. doi:10.1111/epi.16806.
16. Patel J, Tran QK, Martinez S, Wright H, Pourmand A. Utility of serum lactate on differential diagnosis of seizure-like activity: a systematic review and meta-analysis. Seizure. 2022;102:134–142. doi:10.1016/j.seizure.2022.10.007.
17. Yilmaz M, Oztok Tekten B. Serum prolactin level and lactate dehydrogenase activity in patients with epileptic and nonepileptic seizures: a cross-sectional study. Medicine (Baltimore). 2021;100(38):e27329. doi:10.1097/MD.0000000000027329.
18. Soker EB, Erdem M, Ozdogru D, Coddu C, Gulen M. The role of serum biomarkers in differential diagnosis of epileptic seizures, functional/cognitive seizure and syncope: a prospective cohort study. Clin Neurol Neurosurg. 2025;258:109123. doi:10.1016/j.clineuro.2025.109123.
19. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71.