Research Article

Relationship between abnormal laboratory results and recorded clinical diagnoses in tertiary hospital settings: A retrospective observational study

Kay Weng Choy[1*], Guilherme Saffi Franco[2], Mirela Prgomet[2], Getiye Dejenu Kibret[2], Andrew Georgiou[2], Tze Ping Loh[3]

[1]*Department of Pathology, Northern Health, Epping, Australia*
[2]*Australian Institute of Health Innovation, Macquarie University, Sydney, Australia*
[3]*Department of Laboratory Medicine, National University Hospital, Singapore*

Article Info

Kay Weng Choy
Department of Pathology, Northern Health
185 Cooper Street, Epping, Victoria 3076, Australia
E-mail: kayweng.choy@nh.org.au
Fax: +(61)3 8405 2098

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Abstract

Background: The relationship between laboratory results and clinical decisions, including diagnoses, is not always clear. This study aims to determine the association between abnormal laboratory test results and diagnoses recorded by the clinicians within the electronic medical records in tertiary hospital settings.

Method: We conducted a retrospective observational study using anonymised linked hospital data of 223,789 adult admissions between January 2020 and December 2021 in two Local Health Districts in New South Wales, Australia. Data extracted from hospital information systems included patient demographics, recorded clinical diagnoses and laboratory test results. We analysed correlations between abnormal results from common laboratory tests (nasopharyngeal/oral swab SARS-CoV-2 PCR, serum/plasma total prostate-specific antigen (PSA) antigen [PSA], free thyroxine [free T4], thyroid stimulating hormone [TSH], cardiac troponin T, and cortisol) and their respective recorded diagnoses.

Results: We observed the following Spearman correlation coefficients between abnormal laboratory test results and their corresponding recorded clinical diagnoses: positive SARS-CoV-2 PCR and COVID-19 (ρ=1.00), total PSA >10 µg/L and prostate cancer (ρ=0.66), free T4 >25.0 pmol/L and hyperthyroidism (ρ=0.58), TSH >5.00 mIU/L and hypothyroidism (ρ=0.56), TSH <0.30 mIU/L and hyperthyroidism (ρ=0.55), cardiac troponin T >20 ng/L and acute coronary syndrome (ρ=0.51), free T4 <8.0 pmol/L and hypothyroidism (ρ=0.42), and cortisol <80 nmol/L and adrenal insufficiency (ρ=0.33).

Conclusions: This study demonstrates that abnormal laboratory results play an important but varied role in clinical diagnoses. The weaker associations highlight that laboratory tests may be utilised differently in different clinical pathways, underscoring the complex relationship between laboratory

results and clinical diagnoses, and the importance of considering abnormal test results in the appropriate clinical context.

Introduction

The ultimate goal of laboratory medicine is to improve health outcomes [1]. Studies focusing on health outcomes should be prioritised to provide evidence-based insights to inform appropriate test utilisation and clinical decision-making [2]. Historically, it has been claimed that 'laboratory data influences 70% of clinical decisions' but the evidence for this claim remains debated and was initially anecdotal [3]. Well-designed, and appropriately powered, studies are needed to provide an evidence base of the value added by laboratory medicine in improving health outcomes [3]. Outcome studies should be distinguished from those centred on clinical validation and predictive or prognostic evaluations [1].

The utility of laboratory results is a key element of value proposition for a laboratory investigation [4]. Studies are needed to determine how a laboratory result leads to better patient outcomes, including their role in informing clinical diagnosis. Evidence from such studies could then inform healthcare funding decisions. As laboratory medicine is one of the largest producers of structured healthcare data [5], there is ample opportunity for large-data analysis when pathology test results are linked to electronic medical records (EMRs). An EMR contains clinical data that can help address complex research questions, such as those concerning laboratory result utility [6]. Correlation (regression) analyses are commonly used in laboratory medicine to derive adjustment factors or risk scores, as these relationships can predict certain outcomes and help refine diagnostic and therapeutic approaches. Laboratory-based prediction models for a specific clinical outcome have been developed, such as one for chronic kidney disease progression [7]. Adopting such an approach to analysing the relationship between test results and clinical diagnoses could, likewise, aid in the development of prognostic models.

In the current study, using a large data source, we aimed to determine the degree of association between an abnormal laboratory result and a patient's subsequently recorded clinical diagnosis by the clinician within the EMR in tertiary hospital settings.

Method

This was a retrospective observational study of adult patients (aged ≥18 years) admitted to participating hospitals in two Local Health Districts (LHDs) in New South Wales (NSW), Australia, between 1 January 2020 and 31 December 2021. The study utilised routinely collected longitudinal data from these hospitals, all of which operate an EMR which enables clinicians to create electronic laboratory test orders and record clinical diagnoses. Ethics approval was obtained from the Human Research Ethics Committee of the South Eastern Sydney Local Health District (HREC/16/POWH/412) and the New South Wales Population and Health Services Research Ethics Committee (2022/ETH0209). This work was funded by an International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Task Force on Outcome Studies in Laboratory Medicine (TF-OSLM) Grant and the National Health and Medical Research Council (NHMRC) Partnership Projects 1111925 and 2006755. The funders played no role in designing, executing, or interpreting this study.

Data were extracted from two hospital clinical information systems: the patient administration system (PAS), which contains data on hospital admissions, and the laboratory information system (LIS), which contains data on test utilisation. Information recorded in these databases included patient demographics, recorded clinical diagnoses (using International Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification [ICD-10-AM] codes), and laboratory test results. The relevance of diagnoses was determined by one of the authors, a qualified pathologist, based on their professional judgment. (It should be noted that the diagnoses were not made by the pathologist; rather, they were the recorded clinical diagnoses made by the attending clinicians.) After linkage, pathology data were de-duplicated to one test result per admission, either the lowest or the highest (most 'severe' or 'significant') result, according to pre-determined pathology test thresholds (Supplemental file – Table 1). These thresholds were determined based on published literature [8-16] and one of the author's judgment as a qualified pathologist. In the absence of common thresholds in clinical practice guidelines, these thresholds may vary among clinicians in their clinical decision-making.

We focused on several commonly utilised laboratory tests: SARS-CoV-2 polymerase chain reaction (PCR), serum/plasma cortisol, free thyroxine (T4) and thyroid stimulating hormone (TSH), total prostate-specific antigen (PSA) and cardiac troponin T. These tests were chosen due to their widespread usage, and they generally have a clear corresponding clinical diagnosis (COVID-19, adrenal insufficiency, hyperthyroidism/hypothyroidism, prostate cancer, and acute coronary syndrome, respectively).

A rigorous data quality assessment process was employed for each dataset to evaluate the accuracy, completeness, consistency, relevance, timeliness, uniqueness, and validity of the data sources. This process included the identification of missing data, duplicates, formatting issues, and logic compliance. The linkage of hospital inpatient and pathology data was undertaken using non-identifiable patient medical record number (common to all datasets). Records were considered 'linked' if there was an exact match on all identifiers. As a given patient could have multiple visits at the same or different sites over time, only results for laboratory tests performed between the admission and discharge dates were considered.

Baseline patient characteristics, including age at admission and sex were presented for each included test. Deciles of continuous test results (excluding SARS-CoV-2 PCR positivity) and the proportion of diagnoses recorded by the clinicians falling in each

decile were calculated to descriptively evaluate the association between abnormal test results and diagnoses recorded.

Non-parametric Spearman's rank correlation coefficients were used to evaluate the correlation between the weekly volume of abnormal test results and the number of diagnoses recorded by the clinicians within the EMRs. Correlation coefficients of up to six weeks were calculated. Sensitivity and specificity of tests were assessed using a logistic regression model estimation method. Data analyses were conducted using SAS software version 9.4 (SAS Institute Inc, Cary, NC) and a P-value of 0.05 was set to declare statistical significance.

Results

A total of 223,789 distinct admissions were linked to the pathology data between 1 January 2020 and 31 December 2021 (Table 1). The number of admissions in which a test was performed, the number of abnormal tests (based on pre-defined thresholds) and the number of diagnoses recorded by the clinicians within the EMRs are described in Table 2.

Table 1: Baseline Characteristics of Patients Included for Each Laboratory Test.

		Age (years)			Sex (%)	
Test	**No. of Admissions**	**Median**	**IQR***		**Female**	**Male**
Cardiac Troponin T	52,034	71	56	81	46	54
SARS-CoV-2 PCR	50,798	70	52	81	49	51
TSH	42,150	75	58	84	56	44
Free T4	9,808	74	58	84	61	39
Cortisol	4,964	72	59	82	54	46
Total PSA	1,886	77	69	84	0	100

*IQR: Interquartile range (25th percentile – 75th percentile)

PCR: Polymerase chain reaction; T4: Thyroxine; PSA: Prostate-specific antigen; TSH: Thyroid stimulating hormone.

Table 2: Descriptive Statistics of Pathology Test Utilisation, Abnormal Results and Recorded Diagnoses.

Test (Abnormal Result Threshold)	**No. of Tests**	**No. of Abnormal Tests**	**No. of Diagnoses Recorded**	**No. with Both Diagnosis and Abnormal Test**	**% Diagnosed Among Abnormal Tests**
Cardiac Troponin T (>20 ng/L)	52,034	24,175	5,827	4,901	20.3%
SARS-CoV-2 PCR (Positive)	50,798	867	864	809	93.3%
TSH (>5.00 mIU/L)	42,150	3,974	1,118	770	19.4%
TSH (<0.30 mIU/L)	42,150	1,819	624	486	26.7%
Free T4 (>25.0 pmol/L)	9,808	588	601	286	48.6%
Free T4 (<8.0 pmol/L)	9,808	258	1,066	148	57.4%
Cortisol (<80 nmol/L)	4,964	345	191	99	28.7%
Total PSA (>10 µg/L)	1,886	510	294	232	45.5%

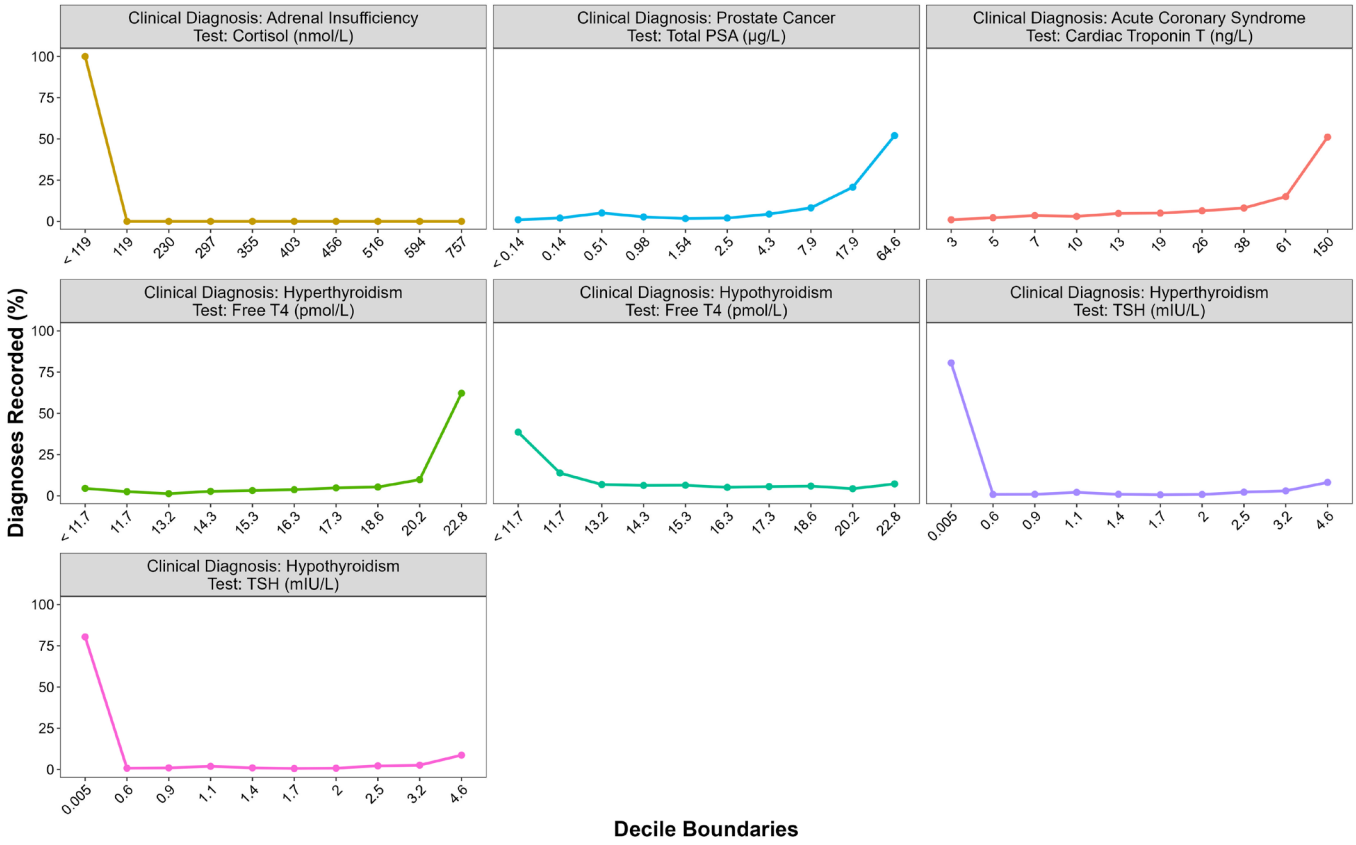
PCR: Polymerase chain reaction; T4: Thyroxine; PSA: Prostate-specific antigen; TSH: Thyroid stimulating hormone.

All tests, except for the SARS-CoV-2 PCR (nasopharyngeal/oral swab), were performed on serum or plasma.

There were 4,964 linked admissions in which a serum/plasma cortisol test result was available. Out of these, 345 (7.0%) tests were 'abnormal' (<80 nmol/L) and just over a quarter (n = 99 [28.7%]) had a recorded diagnosis of adrenal insufficiency. Similarly, 'abnormal' cardiac troponin T, TSH and free T4 were associated with less than 60% of recorded acute coronary syndrome and hyperthyroidism/hypothyroidism diagnoses. On the other hand, there was a recorded diagnosis (by the clinicians within the EMRs) of COVID-19 in 93.3% of cases of a positive SARS-CoV-2 PCR test.

Figure 1 shows the decile boundaries for the test results for each test and the proportion of associated diagnoses recorded by the clinicians at each decile. All recorded diagnoses related to adrenal insufficiency had a random serum/plasma cortisol result of less than 119 nmol/L. Not surprisingly, the majority of diagnoses associated with acute coronary syndrome were recorded in the highest decile of cardiac troponin T concentrations. Similarly, over half of the total cases of prostate cancer diagnosis were documented by the clinicians in the highest decile of total PSA levels.

Figure 1: Distribution of Test Results and Associated Diagnoses by Decile.



Proportion of abnormal test results and corresponding clinician-recorded diagnoses are shown across deciles of test result values.

In an assessment of the correlation between weekly number of abnormal test results at baseline and the number of recorded diagnoses (by the clinicians within the EMRs) over the following five weeks, the strongest correlations were observed at baseline (week zero) (Table 3). The correlation remained significant over the next five weeks for SARS-CoV-2 PCR positivity.

Table 3: Correlation Between Abnormal Test Results at Week Zero and Diagnoses Recorded Over the Following Five Weeks.

Test (Abnormal Result Threshold)	Week						Interpretation Based on Week 0
	0	1	2	3	4	5	
SARS-CoV-2 PCR (Positive)	**1**	**0.92**	**0.78**	**0.65**	**0.51**	**0.37**	Strong
Total PSA >10 µg/L	**0.66**	0.14	0.19	-0.02	-0.03	0.16	Moderate
Free T4 >25.0 pmol/L	**0.58**	0.12	0.19	0.14	0.1	0.15	Moderate
TSH >5.00 mIU/L	**0.56**	**0.34**	0.09	0.17	0.09	0	Moderate
TSH <0.30 mIU/L	**0.55**	**0.34**	0.1	0	0.06	0.14	Moderate
Cardiac Troponin T >20 ng/L	**0.51**	**0.35**	0.15	0.11	0.05	0.01	Moderate
Free T4 <8.0 pmol/L	**0.42**	0.11	0.07	0.09	0.01	-0.06	Weak
Cortisol <80 nmol/L	**0.33**	0.03	0.18	-0.05	-0.01	-0.11	Weak

PCR: Polymerase chain reaction; T4: Thyroxine; PSA: Prostate-specific antigen; TSH: Thyroid stimulating hormone.

Spearman's rank correlation coefficient (ρ) is used to assess correlation. Statistically significant correlations ($p < 0.05$) are shown in bold. All tests, except SARS-CoV-2 PCR (nasopharyngeal/oral swab), were performed on serum or plasma.

In a clinical sensitivity-specificity analysis of admissions linked to a SARS-CoV-2 PCR test, a recorded diagnosis of COVID-19 was associated with a higher likelihood of an abnormal PCR test result (Table 4). An abnormal SARS-CoV-2 PCR test result was observed in 93.6% of admissions with a recorded COVID-19 diagnosis. The model demonstrated strong performance in predicting a COVID-19 diagnosis, with an area under the receiver operating characteristic curve [AUC] of 0.968. For several abnormal test results (TSH <0.30 mIU/L, total PSA >10 µg/L, TSH >5.00 mIU/L, cortisol <80 nmol/L, free T4 >25.0 pmol/L, cardiac troponin T >20 ng/L), the models showed high predictability (AUC, >0.7). Excellent specificity but poor sensitivity for serum/plasma TSH >5.00 mIU/L and cortisol <80 nmol/L indicate that the models are useful in predicting the absence of the associated conditions (as recorded by the clinicians) but not in identifying true cases.

Table 4: Diagnostic Performance of Selected Laboratory Tests.

Test (Abnormal Result Threshold)	Sensitivity (%)	Specificity (%)	AUROC
SARS-CoV-2 PCR (Positive)	93.6	99.9	0.968
TSH <0.30 mIU/L	77.9	96.8	0.873
Total PSA >10 µg/L	78.9	82.5	0.807
TSH >5.00 mIU/L	68.9	92.2	0.805
Cortisol <80 nmol/L	51.8	94.8	0.733
Free T4 >25.0 pmol/L	47.6	96.7	0.722
Cardiac Troponin T >20 ng/L	84.1	58.3	0.712
Free T4 <8.0 pmol/L	13.9	98.7	0.563

AUROC: Area under the receiver operating characteristic curve; PCR: Polymerase chain reaction; T4: Thyroxine; PSA: Prostate-specific antigen; TSH: Thyroid stimulating hormone.

All tests, except for the SARS-CoV-2 PCR (nasopharyngeal/oral swab), were performed on serum or plasma.

Discussion

Outcome studies of the utility of laboratory results in related clinical pathways are key to demonstrating the value of laboratory medicine [1]. One such example is a prospective cohort study involving outpatient cases attending the emergency department due to clinically suspected pulmonary embolism (PE). The prospective cohort study found that integrating pre-test clinical probability assessment with age-adjusted D-dimer cut-off, when compared with a fixed D-diner cut-off of 500 µg/L, was associated with an increased number of patients in whom PE could be excluded with a low likelihood of subsequent clinical venous thromboembolism [17]. Another study conducted at six rural health centres in Kenya demonstrated that the effective use of basic laboratory tests within primary care settings significantly improves clinical diagnosis and patient care [18].

In our study, the results of common laboratory tests were interpreted against pre-defined clinical thresholds and correlated with the diagnoses recorded by the clinicians within the EMRs utilising a retrospective observational study design, a scientifically valid approach for identifying correlations between variables. However, such designs are insufficient for establishing causal relationships due to inherent limitations, including the lack of randomisation, which is critical for isolating the effect of the exposure on the outcome [19]. Thus, we cannot infer causality, though the goal of our study is to identify statistical relationships via correlation. The presence of strong correlations between abnormal laboratory test results and diagnoses recorded by the clinicians within the EMRs supports the clinical relevance of these tests, even if causation is not implied [20].

For example, a positive COVID-19 PCR test is strongly correlated with a COVID-19 diagnosis, underscoring its diagnostic utility. These correlations support hypothesis generation for future research and can aid in developing prognostic models. Quantifying the correlation between the tests and disease is clinically insightful, whether for diagnosis or monitoring purposes. The growth and automation of clinical laboratories have enhanced the generation and availability of real-world data. Big laboratory datasets, used effectively with robust consideration of data quality and validity, can provide strong evidence in clinical and research settings. For instance, statistical correlation can help identify relationships between pathology markers and clinical decision-making and outcomes, with implications for disease diagnosis, treatment efficacy and risk assessment.

While the value of laboratory tests should ideally be judged in the context of patient history and physical examinations, our study aims to examine the overall relationship between abnormal test results and diagnoses recorded by the clinicians across a large inpatient population, not to replace comprehensive clinical evaluations. We included various uses of tests, including rule-out scenarios, and it should be emphasised that we are examining associations rather than causative links. It should also be highlighted that the recorded diagnoses are based on coded diagnoses (using ICD-10-AM codes), which can differ from biochemical diagnoses (e.g., TSH above the upper reference limit). This difference motivates us to examine whether biochemical abnormalities are associated with actual coded clinical diagnoses in the EMRs, serving as a proxy for how doctors use laboratory results. Potential pre-analytical problems include ordering the wrong tests (either wrong indication or wrong test for the clinical question). This may contribute to lower correlation for some tests, particularly if they are more complex or often misused.

Detecting the SARS-CoV-2 virus through reverse transcription PCR testing is a method for diagnosing COVID-19. However, false-negative test results may occur in a significant proportion of patients, ranging from 20% to 67%, with the quality and timing of testing being important factors [21]. In a systematic review of the effectiveness of tests to detect the presence of SARS-CoV-2 virus, pooled analysis of 16 studies (3,818 patients) estimated a clinical sensitivity of 87.8% (95% confidence interval [CI], 81.5-92.2%) for an initial reverse-transcriptase PCR test [22]. In our study, a perfect correlation ($\rho = 1.00$) between SARS-CoV-2 PCR positivity and recorded COVID-19 diagnosis was observed. Furthermore, the high sensitivity (93.7%) and specificity (99.9%) of SARS-CoV-2 PCR observed in our study is corroborated by previous reports [22].

A moderate correlation ($\rho = 0.66$) between elevated serum total PSA and prostate cancer diagnosis was observed in the present study. An elevated serum total PSA can be caused by non-malignant conditions, including benign prostate hyperplasia and prostatitis [23]. A tissue biopsy is the standard of care for the diagnosis of prostate cancer [23]. When serum total PSA concentration is above 10 µg/L, the probability of prostate cancer is high and a prostate biopsy is generally recommended [24]. There are other limitations associated with serum total PSA as a screening tool. Most males with non-elevated PSA values would not have undergone biopsy unless they had a digital rectal examination that was simultaneously abnormal. This workup bias may explain the overestimation of the sensitivity (78.9% in our study) and the underestimation of the specificity (82.5% in our study) of PSA for the detection of prostate cancer. In terms of the utility of a total PSA of >10 µg/L for the recorded diagnosis of prostate cancer, our study has lower sensitivity because we are using actual coded clinical diagnoses, not systematic biopsy of all subjects. A major possibility for the lower sensitivity is that the diagnosis was not recorded (by the clinician) or was recorded differently. Another possibility is the timing of the tests versus the diagnoses. The interval between tests and diagnoses might have been cut too finely, such that for cancer, which requires further follow-up tests (e.g., imaging, biopsy), the diagnosis might be missed because it has a longer diagnostic lag compared to something diagnosed faster (e.g., COVID-19, acute coronary syndrome).

Similarly, causes of an elevated high-sensitivity cardiac troponin are not limited to acute coronary syndrome [25]. Hence, the moderate correlation ($\rho = 0.51$) between abnormal cardiac troponin levels and a recorded diagnosis of acute coronary

syndrome observed in our study is not unexpected.

High-sensitivity cardiac troponin tests may improve the diagnosis of acute coronary syndrome but increase the detection of elevated cardiac troponin in patients without this condition [25]. Of note, the criteria for acute myocardial infarction include the detection of a rise and/or fall of cardiac troponin values with at least one value above the 99th percentile upper reference limit and at least one of five other clinical features [26]. An elevated cardiac troponin level in patients with low pre-test probability for acute myocardial infarction predominantly reflects myocardial injury rather than myocardial infarction [27]. This is reflected in the relatively low specificity (58.3%) of high-sensitivity cardiac troponin in our study. In one study, elevations in high-sensitivity cardiac troponin concentration were observed in approximately one in eight consecutive patients attending the emergency department without suspected acute myocardial infarction [27]. The study found that elevated cardiac troponin levels were associated with older age, multiple morbidities, adverse physiological indicators, and mortality [27].

Thyroid function tests should be interpreted within the overall clinical management of each patient [28]. Relying solely on biochemical markers is insufficient; instead, the individual's history and clinical presentation should also be considered [28]. Treatment decisions integrate clinical evaluations alongside careful consideration of both TSH and free T4 results [29]. In this context, the moderate correlation (ρ = 0.42-0.58) between thyroid function tests (TSH/free T4) and the recorded diagnosis (by the clinicians) of hyper- and hypothyroidism observed in the present study is expected.

The diagnosis of adrenal insufficiency depends on the demonstration of inappropriately low cortisol production. Basal (early morning) serum cortisol concentration has been demonstrated as a viable first line investigation in the evaluation of patients with suspected adrenal insufficiency. Several studies have reported a threshold above which adrenal insufficiency is unlikely and an adrenocorticotropic hormone (ACTH) stimulation test is rarely indicated [30, 31]. However, the utility of baseline or random serum cortisol to diagnose adrenal insufficiency remains uncertain. A meta-analysis by Kazlauskaite et al. [32] reported that in the absence of exogenous glucocorticoids, a basal morning (0600-1000 hours) cortisol concentrations of <140 nmol/L is suggestive of adrenal insufficiency. However, Mathara Diddhenipothage and colleagues looked at random cortisol concentrations measured at any time of the day (0440-2355 hours) and did not ascertain a lower threshold below which there was adrenal insufficiency [31]. These factors may explain the high specificity (94.5%) but low sensitivity (51.8%) for a serum/plasma cortisol of <80 nmol/L in diagnosing adrenal insufficiency (as recorded by the clinicians within the EMRs) observed in our study. In patients with suspected low cortisol-binding globulin due to sepsis or cirrhosis, "subnormal" morning cortisol levels may be seen in the absence of adrenal insufficiency [33, 34].

The strength of the current study design is its large data covering a two-year period, with relatively minimal data removal. However, potential study limitations include missed recording of diagnosis, clinician discretion and subjectivity in pathology test requesting and interpretation, and the absence of a true underlying diagnostic 'reference'. We have not focused on patient admission sources (emergency versus scheduled) and pre-admission testing. While such details could provide additional context, our study's focus is on the overall association between laboratory results and clinical diagnoses, aiming for broad generalisability.

While the recorded diagnoses should ideally reflect the current admission or presentation (i.e., an acute illness resulting in a new diagnosis), it is possible that they may be influenced by pre-existing or historical diagnoses. Such misclassification represents a potential limitation and source of confounding in our analysis. This may partly explain the association of certain diagnoses with laboratory values that fall within reference intervals or pre-defined thresholds.

Regarding thyroid function tests and associated diagnoses, one limitation of our study is the inability to determine whether patients were receiving thyroid-related treatment such as thyroxine replacement or anti-thyroid therapy. Similarly, some cortisol results may reflect values obtained during stimulation or suppression testing rather than baseline levels. For example, cortisol suppression following dexamethasone or elevation following ACTH stimulation may lead to results that differ from routine, random testing. These factors could affect the observed distributions and confound the interpretation of our findings. Consequently, these results should be interpreted with caution. Future studies should aim to exclude such confounders and thereby provide more definitive insights.

Regarding the interpretation of raised biomarkers, such as cardiac troponin and PSA, and their association with myocardial infarction and prostate cancer, respectively, we acknowledge that these biomarkers can be elevated due to conditions other than the ones mentioned. However, it is important to note that our study was based on the clinical diagnoses recorded by the attending clinicians whom we assumed considered the complete clinical picture, including the potential impact of illness on biochemical tests. Our study's objective was not to determine the definitive cause of each biochemical abnormality but to explore how abnormal results align with the clinical diagnoses made in practice. The diagnostic codes used in the current study were directly entered by attending clinicians and represent the actual recorded diagnoses within the electronic medical record. These codes reflect the clinical team's evaluation of the patient's condition at the time of diagnosis (clinician-centred diagnostic codes), thus serving as an accurate representation of clinical practice. Future big-data research into the value of laboratory tests in clinical diagnoses or differential diagnoses should consider incorporating the patient's history including an understanding of the chief complaint and presenting symptoms, and the results of a physical examination (where relevant).

Conclusions

This study examined the correlation between abnormal laboratory results and the subsequently recorded diagnoses by the clinicians within the EMRs. The documented diagnosis may be considered to represent a form of clinical decision. Among the laboratory tests examined, the correlations between abnormal results and corresponding recorded clinical diagnoses were generally of moderate strength (ρ = 0.5-0.6). Our findings demonstrate that pathology results play a varied and important role in clinical diagnosis but also highlight that laboratory tests may be utilised differently in different clinical pathways. Moreover, an abnormal laboratory result may be an incidental (self-limiting) finding or is associated with other clinical conditions not examined in this study, which may weaken the strength of association with a recorded diagnosis. Finally, it should be noted that a rule-out diagnosis based on laboratory results is an equally important clinical decision as rule-in diagnosis, although the former is not usually recorded and hence, much harder to quantify.

Declaration of conflicting interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

Ethics approval was obtained from the Human Research Ethics Committee of the South Eastern Sydney Local Health District (HREC/16/POWH/412) and the New South Wales Population and Health Services Research Ethics Committee (2022/ETH0209).

Author contributions

All authors contributed to the conception and design of the study. AG and MP obtained ethical approval while GSF and GDK conducted the data analysis. KWC and TPL drafted the initial manuscript. All authors critically reviewed, revised, and approved the final version of the manuscript for submission.

Guarantor

KWC.

References

1. Gounden V, Banerjee M, Amundsen EK, Serdar MA, Suárez Sánchez CI, Strain C, et al. Linking laboratory testing to clinical outcomes: Bridging the gap through outcome-based studies in laboratory medicine. Clin Chem. 2023;69(11):1317-1321. https://doi.org/10.1093/clinchem/hvad132
2. Hallworth MJ, Epner PL, Ebert C, Fantz CR, Faye SA, Higgins TN, et al. Current evidence and future perspectives on the effective practice of patient-centered laboratory medicine. Clin Chem. 2015;61(4):589-599. https://doi.org/10.1373/clinchem.2014.232629
3. Hallworth MJ. The '70% claim': what is the evidence base? Ann Clin Biochem. 2011;48(Pt 6):487-488. https://doi.org/10.1258/acb.2011.011177
4. Price CP, St John A. The role of laboratory medicine in value-based healthcare. J Appl Lab Med. 2020;5(6):1408-1410. https://doi.org/10.1093/jalm/jfaa136
5. Hulsen T, Friedecký D, Renz H, Melis E, Vermeersch P, Fernandez-Calle P. From big data to better patient outcomes. Clin Chem Lab Med. 2023;61(4):580-586. https://doi.org/10.1515/cclm-2022-1096
6. Zhang Z. The role of big-data in clinical studies in laboratory medicine. J Lab Precis Med. 2017;2.
7. Ferguson T, Ravani P, Sood MM, Clarke A, Komenda P, Rigatto C, et al. Development and external validation of a machine learning model for progression of CKD. Kidney Int Rep. 2022;7(8):1772-1781. https://doi.org/10.1016/j.ekir.2022.05.004
8. Tosoian JJ, Carter HB, Lepor A, Loeb S. Active surveillance for prostate cancer: current evidence and contemporary state of practice. Nat Rev Urol. 2016;13(4):205-215. https://doi.org/10.1038/nrurol.2016.45
9. Gretzer MB, Partin AW. PSA levels and the probability of prostate cancer on biopsy. Eur Urol Suppl.. 2002;1(6):21-27.
10. Struja T, Briner L, Meier A, Kutz A, Mundwiler E, Huber A, et al. Diagnostic accuracy of basal cortisol level to predict adrenal insufficiency in cosyntropin testing: Results from an observational cohort study with 804 patients. Endocr Pract. 2017;23(8):949-961. https://doi.org/10.4158/ep171861. Or
11. Torpy DJ, Lim WT. Glucocorticoid-induced adrenal suppression: Physiological basis and strategies for glucocorticoid weaning. Med J Aust. 2023;219(10):444-447. https://doi.org/10.5694/mja2.52140
12. Tucker BM, Walther CP. Outcomes associated with hypernatremia at admission in hospitalized persons. Kidney360. 2022;3(7):1122-3. https://doi.org/10.34067/kid.0003052022
13. Fitzgerald RL, Hollander JE, Peacock WF, Limkakeng AT, Breitenbeck N, Rivers EJ, et al. The 99th percentile upper reference limit for the 5th generation cardiac troponin T assay in the United States. Clin Chim Acta. 2020;504:172-179. https://doi.org/10.1016/j.cca.2020.01.027
14. Giannitsis E, Mueller-Hennessen M, Zeller T, Schuebler A, Aurich M, Biener M, et al. Gender-specific reference values for high-sensitivity cardiac troponin T and I in well-phenotyped healthy individuals and validity of high-sensitivity assay designation. Clin Biochem. 2020;78:18-24. https://doi.org/10.1016/j.clinbiochem.2019.11.013

15. Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012;18(6):988-1028. https://doi.org/10.4158/ep12280.Gl
16. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. Thyroid. 2016;26(10):1343-1421. https://doi.org/10.1089/thy.2016.0229
17. Righini M, Van Es J, Den Exter PL, Roy PM, Verschuren F, Ghuysen A, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA. 2014;311(11):1117-1124. https://doi.org/10.1001/jama.2014.2135
18. Carter JY, Lema OE, Wangai MW, Munafu CG, Rees PH, Nyamongo JA. Laboratory testing improves diagnosis and treatment outcomes in primary health care facilities. Afr J Lab Med. 2012;1(1):8. https://doi.org/10.4102/ajlm.v1i1.8
19. Bosdriesz JR, Stel VS, van Diepen M, Meuleman Y, Dekker FW, Zoccali C, et al. Evidence-based medicine-When observational studies are better than randomized controlled trials. Nephrology (Carlton). 2020;25(10):737-743. https://doi.org/10.1111/nep.13742
20. Hung M, Bounsanga J, Voss MW. Interpretation of correlations in clinical research. Postgrad Med. 2017;129(8):902-6. https://doi.org/10.1080/00325481.2017.1383820
21. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A Review. JAMA. 2020;324(8):782-793. https://doi.org/10.1001/jama.2020.12839
22. Jarrom D, Elston L, Washington J, Prettyjohns M, Cann K, Myles S, et al. Effectiveness of tests to detect the presence of SARS-CoV-2 virus, and antibodies to SARS-CoV-2, to inform COVID-19 diagnosis: a rapid systematic review. BMJ Evid Based Med. 2022;27(1):33-45. https://doi.org/10.1136/bmjebm-2020-111511
23. Grossman DC, Curry SJ, Owens DK, Bibbins-Domingo K, Caughey AB, Davidson KW, et al. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. JAMA. 2018;319(18):1901-1913. https://doi.org/10.1001/jama.2018.3710
24. Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. N Engl J Med. 1991;324(17):1156-1161. https://doi.org/10.1056/nejm199104253241702
25. McCarthy CP, Raber I, Chapman AR, Sandoval Y, Apple FS, Mills NL, et al. Myocardial injury in the era of high-sensitivity cardiac troponin assays: A practical approach for clinicians. JAMA Cardiol. 2019;4(10):1034-1042. https://doi.org/10.1001/jamacardio.2019.2724
26. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). J Am Coll Cardiol. 2018;72(18):2231-2264. https://doi.org/10.1016/j.jacc.2018.08.1038
27. Lee KK, Noaman A, Vaswani A, Gibbins M, Griffiths M, Chapman AR, et al. Prevalence, determinants, and clinical associations of high-sensitivity cardiac troponin in patients attending emergency departments. Am J Med. 2019;132(1):110.e8-.e21. https://doi.org/10.1016/j.amjmed.2018.10.002
28. Koulouri O, Gurnell M. How to interpret thyroid function tests. Clin Med (Lond). 2013;13(3):282-286. https://doi.org/10.7861/clinmedicine.13-3-282
29. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022;8(1):30. https://doi.org/10.1038/s41572-022-00357-7
30. Yo WS, Toh LM, Brown SJ, Howe WD, Henley DE, Lim EM. How good is a morning cortisol in predicting an adequate response to intramuscular synacthen stimulation? Clin Endocrinol (Oxf). 2014;81(1):19-24. https://doi.org/10.1111/cen.12373
31. Mathara Diddhenipothage SAD, Beck KJ, Loo H, Amiyangoda GK, Pofi R, Tomlinson JW, et al. "A morning cortisol is the most effective clinical predictor of short synacthen test outcome": A tertiary care centre experience. Clin Endocrinol (Oxf). 2023;99(2):142-151. https://doi.org/10.1111/cen.14934
32. Kazlauskaite R, Evans AT, Villabona CV, Abdu TA, Ambrosi B, Atkinson AB, et al. Corticotropin tests for hypothalamic-pituitary- adrenal insufficiency: A metaanalysis. J Clin Endocrinol Metab. 2008;93(11):4245-4253. https://doi.org/10.1210/jc.2008-0710
33. Rauschecker M, Abraham SB, Abel BS, Wesley R, Saverino E, Trivedi A, et al. Cosyntropin-stimulated serum free cortisol in healthy, adrenally insufficient, and mildly cirrhotic populations. J Clin Endocrinol Metab. 2016;101(3):1075-1081. https://doi.org/10.1210/jc.2015-2285
34. Ho JT, Al-Musalhi H, Chapman MJ, Quach T, Thomas PD, Bagley CJ, et al. Septic shock and sepsis: a comparison of total and free plasma cortisol levels. J Clin Endocrinol Metab.