Section: Biochemistry

Original Research Article

REPORTED DIFFICULTY IN INTERPRETATION OF BIOCHEMICAL TESTS AND ITS ASSOCIATION WITH PREANALYTICAL, ANALYTICAL AND POST ANALYTICAL FACTORS

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ABSTRACT

Background: Biochemical tests are essential for clinical diagnosis and patient management; however, their interpretation remains challenging due to pre-analytical errors, analytical variability, inconsistent reference ranges, and limited clinical context. Despite advances in laboratory automation, misinterpretation persists and may lead to diagnostic errors and inappropriate treatment. Communication gaps between clinicians and laboratories further complicate interpretation.

Objectives

1. To estimate the prevalence of reported difficulty in interpreting biochemical test results among clinicians.
2. To assess the association of pre-analytical, analytical, and post-analytical factors with reported difficulty.

Materials and Methods: A cross-sectional study was conducted over 3 months at Government Medical College, Thrissur, among 105 clinicians with more than 6 months of experience. Data were collected using a structured, pre-validated questionnaire assessing demographic details and challenges related to pre-analytical, analytical and post-analytical factors. Responses were analyzed using descriptive statistics. **Results:** Among participants, 63.8% reported difficulty in interpretation. No significant association was found with professional role, experience, or specialty ($p>0.05$). Pre-analytical factors were not significantly associated with difficulty. However, analytical factors including method variability ($p=0.008$), analytical interferences ($p=0.003$), and lack of internal quality control ($p=0.002$) showed significant association. Post-analytical factors such as interpretative comments and reporting delays were not significant, whereas integration with electronic medical records ($p=0.039$) and critical alerts ($p=0.034$) significantly improved interpretation. **Conclusion:** Interpretation of biochemical test results remains a significant challenge. Analytical factors are the major contributors, while improved post-analytical communication enhances interpretation. Strengthening standardization, quality control, and clinician–laboratory communication can improve diagnostic accuracy and patient care.

INTRODUCTION

Biochemical tests form the cornerstone of modern clinical diagnosis and management, providing objective data that guide therapeutic decisions across diverse patient populations.[9,10] However, their interpretation remains fraught with challenges, often leading to diagnostic errors, suboptimal patient outcomes, and clinician frustration.[2,7] In complex cases like Evans syndrome, atypical biochemical patterns can confound even experienced practitioners, underscoring the need for nuanced interpretive skills.[1] Interpretative comments from clinical biochemists have emerged as a vital tool to bridge this gap, enhancing diagnostic accuracy and clinical utility, as evidenced by practitioner reports emphasizing their role in real-world decision-making.[2,8]

These interpretive difficulties are inextricably linked to errors across the total testing process. Preanalytical factors—such as improper sample collection,

handling, and patient preparation—account for up to 60-70% of laboratory errors and directly impact result reliability, yet awareness remains low among trainee doctors in tertiary settings.[3,11] Analytical phase issues, including interlaboratory variability (e.g., in HER2 testing concordance) and postanalytical challenges, like integrating results with clinical context using likelihood ratios, further complicate interpretation.[4,5] Pediatric cases highlight age-specific reference ranges as an additional layer of complexity.[6]

In Kerala, a state with high disease burdens like diabetes, tropical infections, and nutritional deficiencies, tertiary care centres manage diverse caseloads where biochemical misinterpretation can exacerbate healthcare disparities. This study, conducted at a tertiary care centre in Kerala, investigates the reported difficulties in interpreting biochemical tests and their associations with preanalytical, analytical, and postanalytical factors. By quantifying these challenges and identifying key contributors, we aim to inform targeted quality improvement strategies, ultimately enhancing diagnostic precision and patient safety in resource-constrained settings.

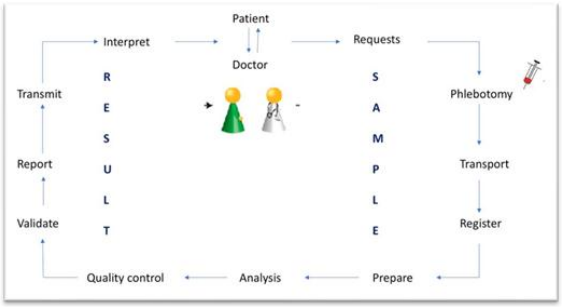

Figure 1: Key steps in requesting, delivering and using a diagnostic test result

Objectives

1. To estimate the prevalence of reported difficulty in interpreting biochemical test results among clinicians.
2. To assess the association of preanalytical, analytical and post analytical factors with reported difficulty

MATERIALS AND METHODS

Study Design: Cross-sectional study

Study Setting: Government Medical College Thrissur

Study Participants

Inclusion Criteria

- Clinicians (physicians, residents) who routinely order and interpret biochemical tests with more than 6 months experience
- Willingness to participate and provide informed consent.

Exclusion Criteria

- Interns and trainees with less than 6 months experience

Sample Size: $n=z\ \alpha 2P(1-P)/d2$

proportion of clinicians reporting difficulty in interpreting test results (e.g., 62.5% from Kulkarni etal,[11]) as expected proportion (p) for sample size calculation.

z α=1.96, p=0.625, d= 0.10; substituting, value=91; adjusting for drop outs approximated to 100

Total sample size=100

Sampling technique: Convenience sampling

Study Period: 3 months after approval from IRC and IEC

Study Procedure

A questionnaire is developed based on literature review and expert input. The questionnaire will cover:

- Demographics (age, gender, role, years of experience)
- Frequency and types of biochemical tests ordered/interpreted
- Reported difficulties in interpretation of biochemical test results and their association with preanalytical, analytical and post -analytical factors.

Questionnaire validation was done by conducting a pilot study among population including 10% of sample size. After obtaining informed consent, questionnaire (google form) was sent to 105 participants (clinicians and residents). Responses were collected and anonymized.

RESULTS

This cross-sectional study included 105 healthcare professionals from a tertiary care Centre in Kerala. Of these, 63.8% (67/105) reported difficulties in interpreting biochemical tests, while 36.2% (38/105) did not.

Demographic characteristics

No significant associations emerged between reported difficulties and professional role ($\chi^2 = 16.1$, df = 9, p = 0.064), years of experience ($\chi^2 = 2.13$, df = 3, p = 0.545), or clinical specialty ($\chi^2 = 36.1$, df = 27, p = 0.113). Residents (49/105) and physicians (34/105) formed the largest groups.

Preanalytical factors

All preanalytical variables lacked significant associations: inadequate patient preparation ($\chi^2 = 3.28$, df = 4, p = 0.513), sample collection errors ($\chi^2 = 6.36$, df = 4, p = 0.174), transport delays ($\chi^2 = 9.25$, df = 4, p = 0.055), storage variability ($\chi^2 = 8.69$, df = 4, p = 0.069), prior error notes ($\chi^2 = 0.753$, df = 1, p = 0.385), and perceived impact ($\chi^2 = 7.01$, df = 3, p = 0.072). Although not statistically significant, delay in transport and storage variability approached significance, suggesting a possible contributory role.

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Analytical Factors

Three factors showed significance: differences in lab methods/instruments ($\chi^2 = 13.8$, df = 4, p = 0.008), analytical interferences ($\chi^2 = 16.0$, df = 4, p = 0.003), and lack of quality control ($\chi^2 = 17.4$, df = 4, p = 0.002). Instrument malfunctions were not significant ($\chi^2 = 7.56$, df = 4, p = 0.109).

Table 1

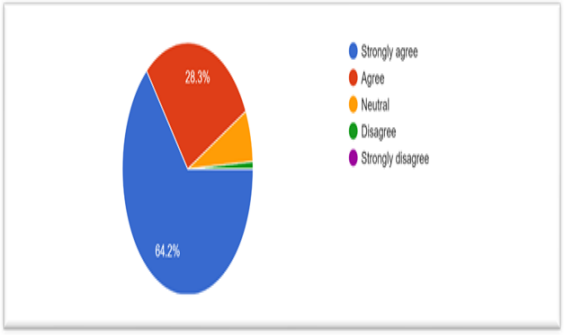
Analytical Factor	χ^2 Value	df	p-value
Methods/Instruments	13.8	4	0.008
Interferences (e.g., hemolysis)	16.0	4	0.003
Lack of Quality Control	17.4	4	0.002

Postanalytical Factors

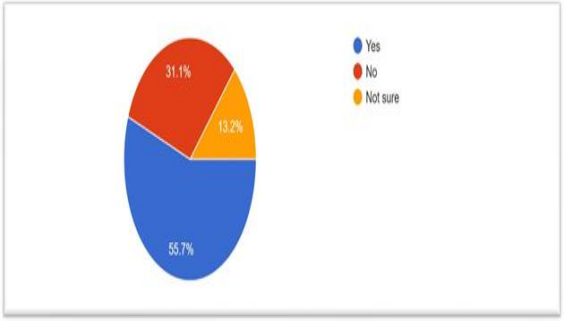
Significant links included electronic medical record integration ($\chi^2 = 8.37$, df = 3, p = 0.039) and prompt critical alerts ($\chi^2 = 6.74$, df = 2, p = 0.034). Others were non-significant: interpretive comments ($\chi^2 = 4.04$, df = 4, p = 0.400), report delays ($\chi^2 = 0.406$, df = 1, p = 0.524), and requisition completeness ($\chi^2 = 0.152$, df = 2, p = 0.927).

Figure 3: Postanalytical factors

a. Electronic medical record integration



b. Prompt critical alerts



DISCUSSION

The present study demonstrates that 63.8% of clinicians reported difficulty in interpreting biochemical test results, indicating that challenges in laboratory data interpretation remain a significant issue in clinical practice. This finding is comparable to the observations of Hickner et al., who reported diagnostic uncertainty related to test interpretation in a notable proportion of clinical encounters, highlighting that interpretative challenges persist even in well-established healthcare systems.[7] The widespread nature of this difficulty across different professional roles, years of experience, and specialties in the present study further suggests that the problem is systemic rather than confined to a particular subgroup of clinicians. This observation aligns with the report by Pant and Pradhan, who emphasized that interpretation of biochemical results requires not only clinical knowledge but also effective laboratory support, including interpretative comments and communication.[2]

Although pre-analytical factors are widely recognized as a major source of laboratory error, accounting for up to 70% of total errors as described by Lippi et al., the present study did not demonstrate a statistically significant association between pre-analytical variables and reported difficulty.[3] Factors such as inadequate patient preparation, errors in sample collection, delays in transport, and improper storage did not show significant correlation, although some variables like transport delay and storage variability approached statistical significance. This apparent discrepancy may be explained by the findings of Kulkarni et al., who reported gaps in clinician awareness regarding pre-analytical processes, suggesting that clinicians may underestimate or fail to recognize the contribution of these factors to interpretative difficulty.[11] Additionally, Ríos et al. highlighted the complexity of interpreting biochemical results in clinical scenarios where pre-analytical variables may subtly influence outcomes, further supporting the notion that these factors may not always be overtly perceived by clinicians[1].

In contrast, analytical factors demonstrated a strong and statistically significant association with reported difficulty in this study. Differences in laboratory methods and instruments, analytical interferences such as haemolysis, icterus, and lipemia, and lack of internal quality control measures were all significantly associated with increased difficulty in interpretation. These findings are consistent with the work of Ivkovic-Kapic et al., who demonstrated that inter-laboratory variability significantly affects test reproducibility and can lead to inconsistencies in clinical interpretation.[4] Similarly, Fierza and Bossuyt emphasized that variability in analytical systems, including differences in measurement scales and units, complicates interpretation and advocated for approaches such as likelihood ratios to improve diagnostic accuracy.[5] The significant impact of analytical interferences observed in the present study is also supported by Lippi et al., who described how common interferences can lead to spurious biochemical results and misinterpretation.[3]

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Furthermore, the association between lack of internal quality control and interpretative difficulty reinforces the observations of Vasikaran et al., who stressed the importance of robust quality assurance systems in ensuring reliable and clinically meaningful laboratory outputs.[8]

Post-analytical factors also played a significant role in influencing interpretation. The present study found that integration of laboratory results with electronic medical records and prompt communication of critical alert values were significantly associated with reduced difficulty in interpretation. These findings are in agreement with Shine and Guha, who highlighted the importance of contextual clinical information and longitudinal data in enhancing the diagnostic utility of biochemical tests.[9] Similarly, Hickner et al. emphasized that timely communication of critical values is essential for effective clinical decision-making and patient safety.[7] However, the lack of significant association between the frequency of interpretative comments and reported difficulty in this study contrasts with the findings of Pant and Pradhan, as well as Vasikaran et al., who underscored the critical role of high-quality interpretative comments in aiding clinicians.[28] This discrepancy may be attributed to variability in the quality, clarity, or clinical relevance of the interpretative comments provided, suggesting that merely providing comments is insufficient unless they are standardized and tailored to clinical needs.

Overall, the findings of this study indicate that while pre-analytical factors are important contributors to laboratory error, analytical and post-analytical factors have a more direct and significant impact on clinicians' ability to interpret biochemical test results. Panall emphasized that accurate interpretation requires an integrated understanding of analytical reliability, biological variation, and clinical context, reinforcing the need for a holistic approach to laboratory medicine.[10] Similarly, Adeli et al. highlighted that interpretation is further complicated by patient-specific variables such as age and physiological differences, underscoring the multifactorial nature of this challenge.[6] The present study therefore supports the growing body of evidence that improving analytical standardization, strengthening quality control measures, and enhancing laboratory-clinician communication are essential steps toward reducing interpretative difficulty and improving patient care outcomes. Limitations include reliance on self-reports, single-centre design, and chi-square's inability to assess effect sizes. Future studies should use multivariate analysis and objective error audits. These results advocate quality control enhancements and digital tools to boost biochemical test utility in resource-limited tertiary care.

CONCLUSION

This study demonstrates that a significant proportion (63.8%) of clinicians experience difficulty in interpreting biochemical test results, irrespective of professional role, experience, or specialty. Among the total testing process analytical factors (method variability, interferences, quality control) showed the strongest association with interpretation difficulty. Post-analytical factors, particularly electronic medical record integration and critical alert communication, also significantly influenced interpretation. Pre-analytical factors, although important, were not significantly associated in this study. These findings highlight the need for improved standardization of laboratory methods, strengthening of internal quality control systems, enhanced laboratory-clinician communication, better integration of laboratory data with clinical systems and development of high-quality interpretative comments. Addressing these factors will improve the clinical utility of biochemical tests and ultimately enhance patient care outcomes.

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