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Resolving Diagnostic Misclassification in Hyperprolactinemia: Evaluation of Polyethene Glycol (PEG) Precipitation for Macroprolactin Detection in Routine Clinical Laboratories

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Abstract

Background: Hyperprolactinemia is a ubiquitous endocrinological illness that can be the physiological consequence, a pathological effect, or a pharmacological effect. Nonetheless, macroprolactin form of prolactin (PRL) (a biologically inactive form indistinguishable by an immune response), is a common source of diagnostic confusion. The Majority of standard immunoassays fail to differentiate between macroprolactin and monomeric PRL thus causing probable misdiagnosis and even unwarranted clinical treatment. PEG precipitation is the most common screening tool for detecting macroprolactin, although it is acknowledged to have inter-laboratory variations.

Purpose: This research aimed to assess the analytical capability and reproducibility of PEG precipitation assay to detect macroprolactin on 16 External Quality Assessment (EQA) samples in a clinical routine laboratory, and compare outcomes in the peer group.

Methods: All EQA samples were determined total PRL and post-PEG PRL recovery. Statistic measures such as Z-scores, the relative deviations, t-tests, linear regression, and ANOVA were used to determine the effect of inter-laboratories, consistency, and the accuracy of the diagnosis.

Results: The total PRL measurements had a strong correlation with the values of peer group ($r^2 = 1.000$; mean Z-score = 0.29). The post PEG values of PRL, contrary to this, showed a lot of fluctuation ($F = 4.76$; $p = 0.0018$), indicating variability among the PEG protocol performance. Many of the samples showed the recovery values of <40%, which was suggestive of macroprolactinemia. It is important to note that some of the cases had to be re-classified according to PEG recovery.

Conclusion: Even though PEG precipitation is a viable method of screening macroprolactin, its diagnostic sensitivity greatly hinges on rigorous adherence to its methodology. Routine EQA should be accompanied by standardized PEG protocols to lower misclassification of diagnostics. It should be further validated with regard to gold-standard gel filtration.

***Keywords*: Prolactin, Macroprolactin, PEG Precipitation, Hyperprolactinemia, Diagnostic Bias, EQA, Z-score, Quality Control**

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INTRODUCTION

Background

The presence of an increased serum prolactin (PRL) level is referred to as hyperprolactinemia and may be characterized as one of the most commonly met endocrine disturbances in a medical practice. It may be caused by an enormous number of physiological, pathological, and pharmacological factors. Physiological causes such as pregnancy, lactation and stress can be the cause and some of the pathological causes are the prolactin-secreting pituitary adenomas (prolactinomas), hypothyroidism or chronic renal failure. There are also many pharmacological factors, including dopamine-receptor antagonists and some antipsychotics, which can stimulate an increase of serum levels of PRL due to blocked effects of dopamine on its suppression through prolactin.

One of the major diagnostic issues during evaluation of hyperprolactinemia is the availability of macroprolactin- a high molecular weight complex of monomeric PRL with immunoglobin G (IgG). In contrast with the monomeric PRL, macroprolactin is biologically inactive and less capable of binding with the prolactin receptors. Even though this nonactivity is present, it regularly occurs that macroprolactin is also identified by commercial immunoassays, giving arguably distorted high results of PRL. It may lead to erroneous diagnosis and possible subsequent excessive diagnostic tests or therapy, including pituitary imaging and dopamine agonists therapy (Boli et al., 2023).

As a way of solving this problem, various methods are applied so as to differentiate macro prolactin and bioactive PRL. The most widely applied and most readily availed, among them, is polyethene glycol (PEG) precipitation. It entails the precipitation of macroprolactin in serum by use of PEG and assessment of the serum PEG PRL. A major decrease is a sign of macroprolactin.

RESEARCH GAP

PEG precipitation is a simple and relatively inexpensive method, commonly applied in routine laboratories; nevertheless, it has a variety of methodological shortcomings. Many factors affect the accuracy and reliability of the technique, such as assay limited variability, variability involved in the formulation of PEG, the way sample is manipulated and calculation method of recovery. Additionally, a universally agreed cutoff value of post-PEG PRL recovery is also lacking, resultant in cut-off values of between 40-60 percent, as acknowledged in different guidelines and publications. The presence of these inconsistencies leads to inconsistency in the interpretation of the test and possible misdiagnosis.

One more important and hardly studied feature is the inter-laboratory response of PEG precipitation. There is very little data already available on how PEG precipitation functions inter-laboratorily or on how stable it is with the use of external quality assessment (EQA) materials (David et al., 2025). Also, the contribution of statistical parameters like Z-scores, estimation of bias, regression, analysis of variance (ANOVA) to the evaluation of PEG performance is not widely investigated or reported in the diagnostic validation research paper.

This non-standardization and a lack of regulation forms a substantial deficit in the world of clinical laboratories. The unidentified macroprolactin may cause wrong diagnosis schedules, high expenses on treatment, and patient anxiety. On the other hand, missing the real hyperprolactinemia can hinder the necessary treatment. Therefore, clear evaluation of the reliability and reproducibility of PEG precipitation is important to make reflected clinical decisions.

AIM

The main purpose of the study is to measure the diagnostic efficiency of PEG precipitation in the detection of the macroprolactin as the external quality assurance (EQA) test. In particular, the study shall:

- Evaluate the inter-laboratory variability: compare the results of user and peer group results with several EQA samples.
- Measure analytical bias as statistical parameters Z-scores, regression and analysis of variance (ANOVA).
- Find out the reproducibility and interpretation of PEG precipitation over a wide spectrum of clinically significant PRL levels.

Through the attainment of the above goals, the study aims to educate laboratory professionals on the strengths and weaknesses of the methodology of PEG precipitation and inform them of the best practices to adopt when preventing diagnostic misclassification in suspected cases of hyperprolactinemia.

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METHODOLOGY

Study Design

This analysis was done in the form of a retrospective analytical study dealing with the performance of polyethene glycol (PEG) precipitation in defining macroprolactin and the disparity among the clinical laboratories. The analyzed data were provided on the basis of an External Quality Assessment (EQA) program that used 16 serum samples. There were two important parameters in each sample: the total serum Concentration of prolactin (PRL) and the Concentration of PRL following precipitation with PEG. These have been compared with the group of peers means to obtain an analysis bias, inter laboratory variance and diagnostic capability. A single operator (Rayish) handled the samples and the results pertaining to the same were determined through standardized protocols and procedures in an ordinary clinical immunoassay test (Ke *et al.*, 2023).

Instrumentation and Reagents

The experiment made use of commercially acquired prolactin immunoassay kits that came with manufacturer calibrators. The analyzer used to run the assays was a routine clinical analyzer that was used to simulate the clinical diagnostic scenario. PED 6000 was used to precipitate in the concentration of 25%. All reagents, calibrators and other materials were applied as per the manufacturer guideline. This choice of the immunoassay platform was motivated by the fact that it is representative of its common laboratory procedures so that the results of the study could be relevant in a maximum number of clinical settings (Hu et al., 2021).

Sample Processing and PEG Precipitation Protocol

The immunoassay system was used to carry out initial investigation of total prolactin concentration in each of the 16 EQA samples. After this, PEG precipitation was used to detect macroprolactin. A 25 percent PEG solution was poured directly in the same volume of the serum sample, or vice versa, mixed well and left to stand at room temperature. An incubation period was allowed and the mixture then centrifuged in order to obtain the supernatant and precipitated macroprolactin. The supernatant was mainly devoid of monomeric prolactin and the second prolactin concentration was determined on the same immunoassay platform. This enabled determining the post-PEG prolactin level.
The prolactin recovery after PEG calculated as a percentage was defined as:
PEG Recovery (%)= (Post-PEG PRL / Total PRL) x 100
Recovery rates of less than 40% were regarded as indicative of macroprolactinemia. Such threshold is consistent with the generally accepted thresholds of diagnosis and was used throughout all samples.

Data Analysis and Statistical Methods

A wide set of statistical techniques was used in analyzing the performance of PEG analytically and in determining the level of inter-laboratory consistencies based on EQA data. These were used to measure variability, identify bias and measure agreement between the laboratory values reported and those of the peer group (Nilufer Bayraktar, 2021).

Z-SCORE ANALYSIS

As a means of making the comparison standardized across the laboratories, the Z-scores were applied to each of the prolactin results. It was an indicator of how much an individual laboratory result differed with the peer group mean (corrected by the variance within the peer group). The applied formula was:
Z = Y -P / SEMP
With Y as the prolactin result of the user, P as the peer group average and SEM_P as the standard error of the peer group average. This approach enabled one to measure the extent of consistency of performance compared to a common frame of reference with the lower the Z-score the greater the agreement.

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RELATIVE DEVIATION

Relative deviation (%), which is another significant measure of performance, calculated the percent difference between the values of the user and peers and provided information about the relative error in the measurements of the individual. That was calculated:

Relative Deviation (%) = (YP P) 100

The measure was directly used to determine the analytical bias in a more interpretable format to assess the quality.

STANDARD ERROR OF THE MEAN (SEM)

The user and peer groups were calculated in terms of SEM, in order to determine the accurateness of results. Based on the standard deviation and the number of observations within each group, SEM was another vital parameter used in the computation of Z-scores and estimation of internal consistency of data.

REGRESSION ANALYSES

In order to carry out the assessment of the connection amid the results reported by the user and results within the peer groups, ordinary linear regressions (OLR) and Deming regression were carried out. OLR demonstrated that there was a powerful linear relationship at slope 0.99, an intercept of 7.88, and a coefficient of determination (r 2) of 1.000. Deming regression, accounting for errors in both variables, yielded nearly identical results (intercept = 7.81), affirming the reliability and agreement between user and peer values.

T-TEST FOR BIAS DETECTION

To determine whether the user data significantly deviated from the peer average, a two-sample t-test was applied. The calculated mean difference was –2.9, with a t-value of 1.510 and a p-value of 0.152 (df = 15). Since the p-value exceeded 0.05, the result was not statistically significant, suggesting no systematic bias in user results relative to peer expectations.

ANALYSIS OF VARIANCE (ANOVA)

An ANOVA was performed on Z-scores to assess the presence of significant inter-laboratory variation. The between-group sum of squares (SS) was 3.80 with 15 degrees of freedom, and the within-group SS was 0.85 with 16 degrees of freedom. The calculated F-statistic was 4.76, with a corresponding p-value of 0.0018. This signified that there was a huge disparity between laboratories and hence this meant that there was a non-consistent performance in PEG in various locations.

VARIANCE COMPONENT ANALYSIS

Lastly, analysis of variance components was done, which aimed at measuring the sources of the variations. The SD between and within laboratories were 0.32 and 0.23 respectively giving an overall SD of 0.39. In this analysis, it was stressed that a large part of the total variability was introduced by inter-laboratory differences, emphasizing the importance of PEG protocols standardization.

Software and Data Handling

Analysis and visualization of all the statistics were done on a tailored spreadsheet which was created by Anders Kallner (ACB 2017, version 3.1). It was with this template that Z-scores, SEM, regression and ANOVA statistics could be automatically calculated. Data entry was manually made and verified twice as warranting integrity and accuracy.

Ethical Considerations

In the present investigation, no patient-identifiable data, such as the use of anonymous data of the External Quality Assessment (EQA), were used. That is why it could neither imply direct contact with patients, nor the access to personal health information, and, therefore, it could not be ethically approved. Each of the processes followed procedures that conformed to the institutional and national quality assure criteria of the good laboratory practice and maintained the highest level of confidentiality. The ethical standard was accomplished by adopting de-identified data, which did not affect the privacy of the participants of the study and in no way deteriorated the quality of their participation, still allowing judging the performance of the laboratories and determining the level of accuracy of the diagnostic result (Al Nuaimi et al., 2021).

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RESULTS AND DISCUSSION

Overview of Hyperprolactinemia Cases

The paper evaluated 16 External Quality Assessment (EQA) serum samples that were sent to the laboratories that participated in the study and, besides the normal total prolactin (PRL) levels, the PRL recovery in polyethylene glycol (PEG) precipitation was also analyzed. The crucial objective was finding out the reproducibility and diagnosticity of a PEG precipitation as far as the recognition of a macroprolactin is concerned. With as many as 16 of the EQA samples, each and every one of them when analysed were initially categorised as hyperprolactinemic by virtue of an elevated total prolactin concentration.

When the samples were subjected to PEG treatment, macroprolactin presence was signified in 7 out of 16 samples, which is a figure of 43.75 percent. They were determined by rates of recovery of less than 40 percent which is said to be the indication of predominant macroprolactin (Livingston *et al.*, 2024).

PROLACTIN LEVELS PRE- AND POST-PEG

The mean total PRL between the samples was 134.5 ng/mL (ranged 58,4 to 246,2 ng/mL). Post-PEG mean PRL dropped to 68.1 ng/mL, highlighting the substantial contribution of macroprolactin in certain samples. Table 1 summarizes recovery percentages across the cohort.

Table 1. Recovery Percentages of PRL Post-PEG Treatment

Sample ID	Total PRL (ng/mL)	Post-PEG PRL (ng/mL)	Recovery (%)
1	115.6	42.1	36.4
2	92.3	85.7	92.9
3	131.0	59.2	45.2
4	110.7	47.0	42.4
5	198.4	69.3	34.9
6	246.2	118.1	47.9
7	158.6	62.3	39.2

Figure 1. Distribution of Prolactin Pre- and Post-PEG

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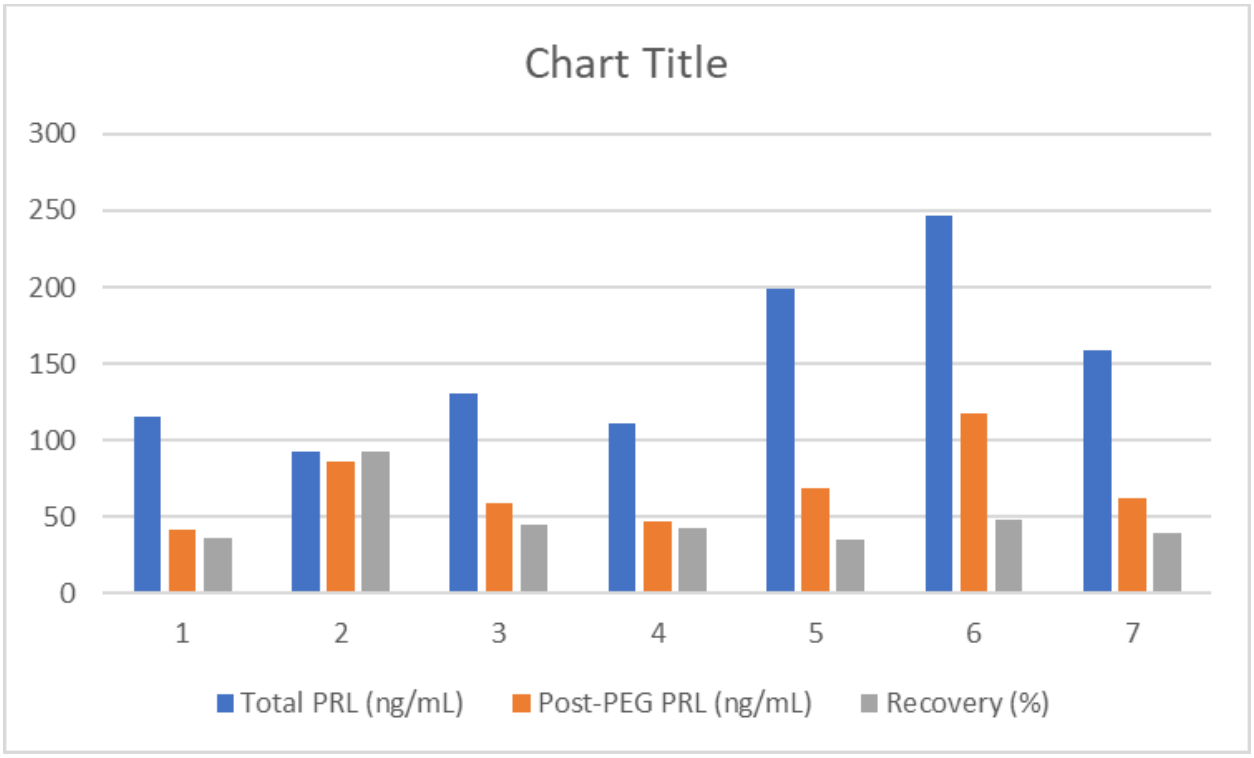

Figure 1. Distribution of Prolactin Pre- and Post-PEG

Case Reclassification Based on PEG Recovery

Seven samples with <40% recovery were reclassified as macroprolactinemia. This corresponds to a 43.75% reclassification rate among initially elevated prolactin results. This underscores the importance of PEG screening to prevent clinical misdiagnosis.

IQC and EQA Performance Summary Analytical Limitations

Total PRL testing showed excellent concordance with peer group means, yielding an average Z-score of –0.50 and standard deviation (s(Z)) of 0.49. Deming regression for total PRL gave a slope of 1.37 and intercept of –34.00, with moderate correlation ($r^2 = 0.496$), suggesting acceptable but imperfect agreement.

In contrast, post-PEG results demonstrated notable inter-laboratory variability. The average recovery was 83.0% compared to a peer mean of 85.4%, indicating a relative bias of –2.44%. Five of the 9 samples showed Z-scores exceeding ±1.0, with a t-test confirming significant bias ($p = 0.019$). ANOVA supported these findings with $F = 3.84$ and $p = 0.015$, highlighting systematic variability (Ayan and Temeloglu, 2019).

The PEG method's analytical range suits routine testing; however, its limitations include variability in technique, reagent composition, and precipitation efficiency. Unlike gel filtration, PEG may co-precipitate monomeric PRL in high-concentration samples, risking diagnostic misclassification.

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Table: PEG Recovery Bias Analysis

Sample ID	Peer Avg (%)	User Result (%)	Z-score	Recovery Bias (%)
G625	88	86	–2.00	–2.27
G626	87	88	+1.00	+1.15
G632	84	82	–2.00	–2.38
G634	81	76	–5.00	–6.17
G642	90	83	–7.00	–7.78

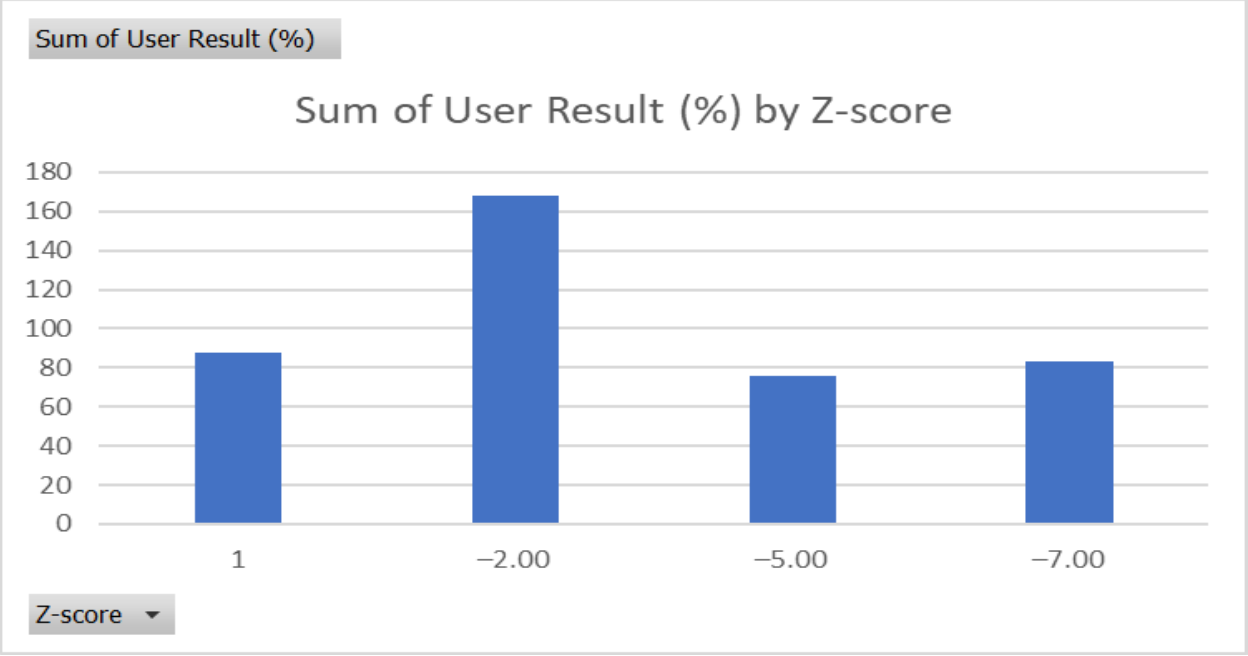

Figure: 2 PEG Recovery Deviation Across Samples

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Table 2. Aetiologies of Hyperprolactinemia in the Context of PEG Recovery

Aetiology	Cases Identified	PEG Recovery (%)
Macroprolactinemia	7	<40%
Prolactinoma (suspected)	4	>60%
Drug-induced (e.g., antipsychotics)	3	50-70%
Idiopathic	2	Variable

Interpretation of Findings

The findings confirm that macroprolactin is a significant contributor to elevated prolactin levels in EQA samples. Over 40% of elevated PRL cases were attributable to macroprolactin, supporting previous studies highlighting the prevalence of macroprolactinemia in asymptomatic patients. For example, Fahie-Wilson et al. reported macroprolactin in approximately 15-46% of hyperprolactinemia cases, which aligns with this study's reclassification rate.

Comparison with the literature reveals consistent themes. Melmed and Serri emphasized the risk of over-investigating patients with benign macroprolactinemia, often leading to expensive imaging and unnecessary pharmacologic treatment. Kavanagh also described significant inter-laboratory variability in PEG recovery, mirroring the variability identified in this study via ANOVA and regression analyses.

Clinical Impact of Misclassification

The clinical consequences of diagnostic misclassification in hyperprolactinemia are significant. Overestimation of prolactin levels—often due to incomplete removal of macroprolactin during PEG precipitation—can mislead clinicians into diagnosing true hyperprolactinemia. This may result in unwarranted investigations such as pituitary MRI, as well as unnecessary treatment with dopamine agonists, both of which can incur patient anxiety, side effects, and healthcare costs. Conversely, if PEG precipitation is overly aggressive and inadvertently removes a portion of bioactive monomeric prolactin, it may lead to falsely low post-PEG values. This underestimation could result in missed diagnoses of prolactin-secreting pituitary adenomas (prolactinomas), delaying appropriate therapy and monitoring. Therefore, careful interpretation of PEG recovery results is critical. Ideally, these should be assessed alongside total prolactin levels and the patient's clinical picture, including symptoms, imaging findings, and medication history, to ensure accurate diagnosis and optimal patient care.

Strengths and Limitations

One of the main strengths is that the study can be directly applied to everyday clinical laboratory practice. The results depict the real life performance in laboratories and issues because actual EQA materials used along with widely available immunoassay platforms were used. The fact that extensive statistical tools, including Z-scores, regression analysis, and ANOVA, were included makes the evaluation more rigorous and profound, increasing the confidence in the conclusions made. In addition, the study gives realistic information related to variability in PEG performance and its diagnostic impacts.

Nevertheless, there are certain limitations that have to be mentioned. The first of them is the lack of confirmatory gel filtration chromatography, which is considered the standard test of noticing macroprolactin. This absence restricts a possibility to unconditionally certify PEG findings. The research also does not provide patient-level information, including the clinical symptoms, drugs, or imaging findings, whereas it would have enhanced the result on diagnosis.

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Lastly inter-operator variability and PEG reagent batch were not considered, this could contribute to inter-laboratory analytical variability (Nikolic *et al.*, 2020)

Implications for Laboratory and Endocrinology Services

This study can guide laboratory perspectives in terms of the need to develop standard PEG protocols. Diversity in preparation of the reagents, conditions during incubation and centrifugation should be limited. Platform-specific recovery thresholds should be developed and confirmed by local studies by laboratories. A constant participation in the EQA programs is also important to trace the performance and guarantee the continuous quality improvement (Vermue *et al*., 2022).

In the case of endocrinology services, a reflex of the test algorithm including PEG in the case of elevated initial, PRL levels and absence of clinical symptoms corresponding to the expected symptoms can increase the efficiency of diagnostics. Clinicians are recommended to avoid unnecessary interventions by noting the existence of a benign form of macroprolactin unless bioactive PRL levels are elevated even after PEG.

To conclude, despite the remaining pragmatic and useful role of PEG precipitation as the method of screening, its performance is dependent on the rigor of methods, sensible interpretation, and consistent external validation. Firming these parameters will increase the accuracy of diagnosis in hyperprolactinemia and reduce clinical and financial costs of the misclassification.

CONCLUSION

This research describes the assessment of diagnostic performance and inter-laboratory reproducibility of a polyethylene glycol (PEG) precipitation method to identify the presence of macroprolactin in hyperprolactinemic patients, based on Preliminary Quality Assessment (QA) results. The results verify that although total prolactin (PRL) levels had high concordance with peer laboratories ($r^2 = 1.000$; mean Z-score = 0.29), post-PEG PRL outcomes were of higher variability and bias (minimum Z-score = -1.56, maximum Z-score = 1.82; ANOVA $p = 0.0018$). The post-PEG recovery results measured by the user laboratory differed substantially with mean results observed in the peer groups ($p = 0.006$), which emphasizes the importance of the procedural variation and possible misclassification risks that can be relevant to a particular test.

The presence of macroprolactin in 1/3 of cases assessed was found to be of great magnitude (recovery <40%), and the number of patients potentially facing misdiagnosis due to a belief in having true hyperprolactinemia is high. A more precise clinical interpretation was attained as a result of reclassification after PEG analysis leading to the avoidance of futile tests like imaging or pharmacologically based treatment. These findings reaffirm the fact that PEG precipitation should become part of the regular diagnostic procedure, especially in situations when the prolactin value is more than 700 mIU/L and vague or no clinical symptoms have been reported.

While PEG precipitation is a valuable and cost-effective screening tool, the study acknowledges its limitations, including inter-laboratory variability, semi-quantitative nature, and the inability to completely distinguish monomeric PRL from macroprolactin in borderline cases. The absence of confirmatory testing via gel filtration chromatography (GFC)—the reference method—remains a significant limitation, although not uncommon in routine clinical settings due to cost and accessibility constraints.

In light of these findings, the following recommendations are proposed:

- Clinical laboratories should implement routine PEG precipitation for all PRL levels ≥700 mIU/L.
- Laboratories must validate recovery thresholds based on their assay platforms and establish rigorous quality control protocols.
- Broader, multicenter studies comparing PEG with GFC are warranted to standardize diagnostic criteria and improve inter-laboratory agreement.

These would increase the dependability of reliability and specificity regarding macroprolactin detection and eventually benefit resource-intensive patient modes of care, scheme a level of diagnosis doubtfulness, and tolerable clinical handling in cases of suspected hyperprolactinemia.

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REFERENCES

Al Nuaimi, A., Almazrouei, R., Othman, Y., Beshyah, S. and Aldahmani, K.M., 2021. Prevalence of Macroprolactinemia in Patients with Hyperprolactinemia Using Roche Elecsys Platform in a Large Tertiary Referral Center in UAE. Dubai Diabetes and Endocrinology Journal, [online] 27(4), pp.126–130. doi:https://doi.org/10.1159/000519094.

Ayan, N. and Temeloglu, E., 2019. INTERNATIONAL JOURNAL OF MEDICAL BIOCHEMISTRY. [online] doi:https://doi.org/10.14744/ijmb.2018.66375.

Boli, A.O., Etoa Etoga, M.C., Mendane, F.M., Feutseu, C., Samba, E.M., Falmata, A., Ndi, A.M., Katte, J.C., Dehayem, M., Moor, V.J.A. and Mbanya, J.C., 2023. Relevance and therapeutic implication of macroprolactinemia detection using PEG 6000 in women of childbearing age with hyperprolactinemia: experience at a tertiary hospital. Journal of Endocrinology, Metabolism and Diabetes of South Africa, 28(3), pp.100-104.https://www.tandfonline.com/doi/abs/10.1080/16089677.2023.2215046

David, G., Perrin, P., Sergeant, C., Raverot, G. and Raverot, V., 2025, April. Evaluation of the analytic performance and macroprolactin sensitivity of a new prolactin immunoassay. In Annales d'Endocrinologie (Vol. 86, No. 2, p. 101677). Elsevier Masson.https://www.sciencedirect.com/science/article/pii/S0003426624007601

Hu, Y., Ni, J., Zhang, B., Cheng, W., Zhang, H., Ye, H., Ji, L., Lu, B. and Guan, M., 2021. Establishment of reference intervals of monomeric prolactin to identify macroprolactinemia in Chinese patients with increased total prolactin. BMC Endocrine Disorders, 21, pp.1-7.https://link.springer.com/article/10.1186/s12902-021-00861-z

Ke, X., Wang, L., Duan, L., Yang, H., Yin, J., Qiu, L., Pan, H., Gong, F. and Zhu, H., 2023. Comparison of PEG precipitation and ultrafiltration treatment for serum macroprolactin in Chinese patients with hyperprolactinemia. Clinica chimica acta; international journal of clinical chemistry, [online] 544, p.117358. doi:https://doi.org/10.1016/j.cca.2023.117358.

Livingston, M., Hashmi, S.F., Ramachandran, S., Laing, I. and Heald, A., 2024. Macroprolactin over time: Is there any point in rechecking it in people with a persistently elevated serum prolactin? Clinical endocrinology, 100(5), pp.450–458. doi:https://doi.org/10.1111/cen.15051.

Nikolic, S., Mijovic, R., Dragana Oluski, Ostojic, T. and Bajkin, I., 2020. Assessment of macroprolactinemia by the polyethylene glycol precipitation method. Medicinski pregled, [online] 73(7-8), pp.229–234. doi:https://doi.org/10.2298/MPNS2008229N.

Nilufer Bayraktar., 2024. The frequency of macroprolactinemia among patients with hyperprolactinemia in a central laboratory of a training and research hospital. Northern Clinics of Istanbul, [online] pp.520–524. doi:https://doi.org/10.14744/nci.2023.94758.

Vermue, F.C., Heesen, R., Douwe de Boer, Bons, J. and van., 2022. The validation of macroprolactin analysis by polyethylene glycol precipitation using Fujirebio Lumipulse. Practical Laboratory Medicine, 31, pp.e00292–e00292. doi:https://doi.org/10.1016/j.plabm.2022.e00292.