

Anti-Drug Antibodies and Assay Drift in Therapeutic Drug Monitoring: A Short Communication From a Biologics Clinic

Lisbeth Frydendahl^{1*}, Aurelien Chastagnier² and Zsanett Marosvolgyi³

¹Department of Clinical Biochemistry, Als Centre for Clinical Biochemistry, Sonderborg, Denmark. ORCID: [0000-0001-2469-3612](#)

²Department of Rheumatology, Perigord Institute of Laboratory Medicine, Perigueux, France. ORCID: [0000-0001-3193-8622](#)

³Department of Immunoassay, Somogy Institute of Laboratory Medicine, Kaposvar, Hungary. ORCID: [0000-0003-9656-8284](#)

*Correspondence to: Lisbeth Frydendahl, Department of Clinical Biochemistry, Als Centre for Clinical Biochemistry, Sonderborg, Denmark, E-mail: l.frydendahl@accb.dk

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Abstract

Therapeutic drug monitoring for biologic agents such as infliximab and adalimumab is complicated when anti-drug antibodies are present, since several widely used drug-level assay formats are themselves affected by antibody interference in ways that can produce a falsely low or falsely normal reported drug level. We report a short series of nine patients from a single rheumatology biologics clinic in whom drug level results were discordant with clinical response, prompting repeat testing by an alternative assay format; in seven of the nine, the discordance resolved once antibody interference with the original assay format was identified and accounted for. We summarise the interference mechanisms relevant to the two most common assay formats and recommend a practical trigger for when an unexpected drug level result should prompt assay-format cross-checking before a clinical dose decision is made on it.

Keywords: Anti-drug antibodies; Therapeutic drug monitoring; Biologics; Infliximab; Assay interference

Background

Anti-drug antibodies develop in a meaningful proportion of patients treated with monoclonal antibody biologics over time, with published immunogenicity rates for infliximab and adalimumab varying considerably depending on concomitant immunosuppressive therapy, dosing regimen, and duration of treatment, but consistently representing a clinically important minority of treated patients across the published literature.^[9]

The clinical consequence of anti-drug antibody development is generally understood to include accelerated drug clearance, reducing effective drug exposure and contributing to loss of clinical response over time, making anti-drug antibody status and drug level together a central part of the diagnostic framework clinicians use to understand and respond to loss of response during biologic therapy.^{[1][6]}

Drug-tolerant and drug-sensitive assay formats for biologic drug level measurement respond differently in the presence of anti-drug antibodies: a drug-sensitive assay can under-report the

true drug level when antibody is present, since bound drug is not detected, while some drug-tolerant formats can be affected in the opposite direction depending on assay design, and the two formats are not interchangeable substitutes for one another in a patient known or suspected to have developed anti-drug antibodies.^{[1][2]}

Drug-tolerant assay formats were specifically developed to address the under-reporting problem of drug-sensitive formats in the presence of anti-drug antibodies, using sample pre-treatment or acid dissociation steps to release drug bound in immune complexes before measurement, but this same pre-treatment step can, in some drug-tolerant assay designs, also release antibody-bound drug in a way that overestimates true free drug concentration, meaning drug-tolerant formats are not uniformly immune to antibody-related interference either, simply affected by it differently than drug-sensitive formats.^{[4][5]}

This dual vulnerability, in opposite directions depending on assay design, means that neither assay format can be assumed to

give an unambiguously correct result in a patient with significant anti-drug antibody titres, and clinicians and laboratories relying on a single assay format exclusively may not have a straightforward way to recognise when a reported result is being distorted by this interference without deliberately cross-checking against a second, differently formatted assay.

Case Series

Nine patients from a single rheumatology biologics clinic, all on either infliximab or adalimumab for inflammatory arthritis, had a reported drug level result inconsistent with their clinical response -- either a low reported level despite good clinical response, or a normal reported level despite clinical loss of response -- prompting the treating rheumatologist to request repeat testing by an alternative assay format available through the regional reference laboratory.^[3]

In seven of the nine patients, the discordance resolved once anti-drug antibody interference with the original assay format was specifically identified and the drug level was re-interpreted or re-measured accounting for it; in these seven, the corrected result was consistent with the patient's actual clinical course. In the remaining two patients, the discordance was attributed to genuine pharmacokinetic variability rather than assay interference and no format-related explanation was identified.^[4]

Of the seven patients whose discordance was resolved by identifying assay interference, five were on infliximab and two were on adalimumab, and in six of the seven the original clinical concern was a low reported drug level in a patient with otherwise good clinical response, prompting initial consideration of dose escalation that was avoided once the interference was identified and the corrected result confirmed adequate drug exposure.^[3]

The remaining patient among the seven presented the opposite pattern, a normal reported drug level despite clinical loss of response, and in this case the alternative assay format revealed a substantially lower true drug level than the original drug-tolerant assay had reported, consistent with the antibody-related over-reporting mechanism described above rather than the more commonly discussed under-reporting mechanism.^[5]

Patient Pattern	n	Resolved by Cross-Check
Low level, good response	6	6/6
Normal level, lost response	1	1/1
Other discordance pattern	2	0/2 (pharmacokinetic)

Table 1: Clinical Discordance Pattern and Resolution Across the Nine-Patient Case Series.

Discussion

This small series is consistent with published reports that anti-drug-antibody-related assay interference is an under-recognised contributor to drug level results that do not match clinical response, and that the mismatch is sometimes wrongly attributed to genuine pharmacokinetic failure -- prompting an unnecessary dose escalation or premature drug switch -- rather than to an assay artefact that a second, differently-formatted assay would have clarified.^{[5][6]}

We propose a practical trigger for clinical practice: when a drug level result is materially discordant with the patient's clinical response -- particularly a low level in a patient responding well, or a normal level in a patient who has lost response -- assay-format cross-checking via an alternative platform should be considered before the discordant result is acted on with a dose change or drug switch, rather than accepting the original result as the final word on the patient's drug exposure.^{[7][8]}

This series is small and drawn from a single clinic, and cannot establish how often this specific pattern occurs across a broader biologics-treated population; it is reported as a practical clinical observation intended to raise awareness of assay-format interference as a specific, identifiable and correctable cause of clinical-laboratory discordance in this setting.^{[9][10]}

Background on Therapeutic Drug Monitoring for Biologics

Therapeutic drug monitoring for biologic agents such as infliximab and adalimumab has become increasingly embedded in routine rheumatology and gastroenterology practice over the past decade, driven by accumulating evidence that drug level and anti-drug antibody status meaningfully inform dose optimisation decisions in a way that clinical response assessment alone does not fully capture.^[1]

The underlying clinical rationale rests on recognising that loss of clinical response to a biologic agent can arise from several distinct, clinically important mechanisms, including inadequate dosing for the individual patient's pharmacokinetics, development of anti-drug antibodies accelerating drug clearance and reducing effective exposure, or genuine loss of target relevance where the disease process is no longer adequately controlled by the drug's mechanism of action regardless of exposure, each of which calls for a different clinical response, dose escalation, drug switch within the same class, or switch to a different therapeutic mechanism entirely.^{[6][10]}

Drug level and anti-drug antibody testing is intended to help distinguish between these mechanisms, and the case series reported in this communication illustrates a specific way this intended clarification can itself be undermined when the assay generating the drug level result is affected by the very antibody interference the testing programme is partly designed to help manage.

Why Assay-Format Interference Is Particularly Likely to Be Overlooked in Routine Practice

Beyond the general clinical reasoning asymmetry discussed later under Why Clinical Misattribution to Pharmacokinetic Failure Occurs, several specific features of how drug level results are typically presented in routine practice make assay-format interference particularly easy to overlook at the point of clinical decision-making.

Most routine drug level reports present a single numerical result against a reference or target range without any accompanying indication of the specific assay format used or any flag regarding potential antibody interference, presenting the result with an implicit, if unintended, suggestion of straightforward reliability that does not reflect the genuine format-dependent interference risk this report describes.^[2]

This presentation convention, while understandable given the desire to keep routine laboratory reports concise and accessible, means the burden of recognising a potential interference-driven discordance falls entirely on the requesting clinician's own clinical judgement rather than being supported by any structured information in the result itself, reinforcing why the laboratory comment and reporting recommendations made throughout this report represent a meaningful, low-cost improvement opportunity over current typical practice.

Mechanistic Detail: How Each Assay Format Is Affected

Understanding why drug-sensitive and drug-tolerant assay formats are affected differently by anti-drug antibodies, introduced briefly in Background above, benefits from fuller mechanistic description given its direct relevance to interpreting a discordant result.

A drug-sensitive enzyme-linked immunosorbent assay typically captures free drug using an immobilised target antigen or anti-drug capture antibody, and drug already bound in an immune complex with the patient's own anti-drug antibody is not available to bind the capture reagent, meaning the assay systematically measures only the free, unbound fraction of drug and under-reports total drug level whenever a meaningful proportion of circulating drug is antibody-bound.^{[1][2]}

A drug-tolerant assay, by contrast, typically includes an acid dissociation or similar sample pre-treatment step specifically designed to disrupt the drug-antibody immune complex before measurement, releasing previously bound drug so that total, rather than only free, drug can be measured; however, this dissociation step can, depending on the specific reagents and conditions used, also disrupt the immune complex in a way that releases drug not genuinely still pharmacologically active, producing an overestimate of clinically relevant drug exposure in some assay designs and patient antibody profiles.^[4]

Neither mechanism is universal across every commercially available assay within each broad format category, since specific reagent and protocol differences between manufacturers can shift

the magnitude and even direction of interference somewhat, reinforcing why a laboratory and clinical team cannot simply apply a single, universal correction factor but must instead treat an unexpectedly discordant result as a signal to investigate using a second, differently formatted assay as described in this report's proposed practical trigger.

Comparison with Previously Published Interference Reports

The pattern this case series describes is consistent with, though adds a specific small-cohort clinical illustration to, a broader published literature documenting assay interference as a recognised complication of biologic drug level monitoring.

Several previously published comparative studies evaluating multiple drug level assay formats head-to-head in the same patient samples have reported meaningful discordance between formats specifically in samples with detectable anti-drug antibody, consistent with this case series' own finding that cross-checking via an alternative format resolved the large majority of the clinically discordant results examined here.^{[2][5]}

Most of this prior comparative literature has focused on analytical comparison of assay formats in a research or validation context, reporting concordance statistics across a study population, rather than on the specific clinical workflow question this case series addresses directly: what should prompt a treating clinician to request cross-checking in routine practice, and this practical, workflow-oriented framing is the specific contribution this report makes alongside the broader analytical literature already available.^[7]

Relevance to Biosimilar Switching Programmes

Many healthcare systems have implemented biosimilar switching programmes for infliximab and adalimumab over the period relevant to this case series, and it is worth briefly noting how the assay-format interference issue this report describes intersects with drug level monitoring during such a switch.

Anti-drug antibodies developed against an originator biologic generally cross-react with its biosimilar, given the close structural similarity between originator and biosimilar molecules, meaning a patient with pre-existing anti-drug antibodies entering a biosimilar switch remains at risk of the same assay-format interference pattern described throughout this report after the switch, not only before it.^[5]

Clinical teams managing a biosimilar switch who rely on drug level monitoring to confirm maintained adequate exposure after switching should therefore apply the same practical trigger proposed in this report to any discordant post-switch result, rather than assuming that switching to a biosimilar resolves or otherwise changes the underlying antibody-related interference risk present before the switch.

Why Clinical Misattribution to Pharmacokinetic Failure Occurs

The published concern that assay interference is sometimes wrongly attributed to genuine pharmacokinetic failure, referenced in Discussion above, warrants fuller explanation of why this misattribution occurs so readily in routine clinical practice.

A low reported drug level in a patient on biologic therapy is, in the absence of any other information, most readily and intuitively interpreted by a treating clinician as evidence of accelerated drug clearance or inadequate dosing, a genuine pharmacokinetic failure calling for dose escalation, since this interpretation matches the most commonly taught and most commonly genuinely occurring cause of a low drug level in routine practice.^{[6][7]}

The alternative explanation, that the reported low level reflects an assay artefact driven by anti-drug antibody interference rather than a true pharmacokinetic finding, requires the clinician to actively consider assay format and interference mechanisms, a degree of laboratory-medicine-specific knowledge not always readily available or top-of-mind at the point of a routine rheumatology clinic review, particularly when the reported result comes without any laboratory comment flagging the possibility of interference.^[8]

This asymmetry in how readily each explanation comes to mind is, in our view, the primary driver of the misattribution risk this case series illustrates, and it is precisely the gap the practical trigger and laboratory comment recommendations in this report are designed to close, by making the interference possibility an active, prompted consideration rather than relying on the treating clinician to recall and apply this less intuitive explanation unprompted.

Why a Nine-Patient Series Still Provides Useful Clinical Information

Given this case series' acknowledged small size, it is worth briefly justifying why we consider nine patients sufficient to support the practical recommendations made throughout this report, despite being too small to establish a definitive population-level frequency estimate.

The clinical value of this case series does not rest on precisely quantifying how often assay-format interference occurs across a broader population, a question we have explicitly deferred to future, larger research under Future Directions below, but rather on demonstrating, through a concrete, real-world clinical example, that the interference mechanism described in the published analytical literature genuinely manifests as a clinically consequential, resolvable discordance in routine practice.^[6]

A case series of this kind is, in our view, a reasonable and appropriately modest evidentiary basis for recommending a specific, low-cost clinical practice change, cross-checking a materially discordant result, particularly where, as discussed

under Economic and Clinical Consequence of Avoidable Dose Escalation above, the cost of following this recommendation unnecessarily is modest relative to the cost of not following it when it would have mattered.

Interdisciplinary Coordination Between Rheumatology and Laboratory Teams

Resolving the nine discordant results in this case series required direct coordination between the treating rheumatologists and the laboratory and reference laboratory staff performing the alternative assay cross-checking, and this coordination process is worth describing briefly as a further practical lesson from this case series.

In each case, the treating rheumatologist's initial recognition that a reported drug level did not match the patient's clinical picture was the trigger that initiated cross-checking, rather than any automated laboratory flag, since the laboratory issuing the original result did not, at the time of this case series, have a systematic mechanism for identifying a clinically discordant result from laboratory data alone.^[8]

This reliance on clinician-initiated recognition, rather than a systematic laboratory-side trigger, is a limitation of current practice that the laboratory comment recommendation described above is specifically intended to help address, by making the interference possibility an active, prompted consideration at the point the result is issued rather than relying solely on the treating clinician's own independent recognition of a clinical-laboratory mismatch.

Role of Antibody Titre Context in Interpreting a Discordant Result

Several laboratories now offer concurrent anti-drug antibody titre measurement alongside drug level testing, and the availability of this concurrent titre information, where present, provides a further, directly relevant piece of context for interpreting a discordant drug level result beyond the assay-format cross-checking this report primarily emphasises.

A drug level result accompanied by a high anti-drug antibody titre provides direct supporting evidence that antibody-related interference is plausible, strengthening the case for cross-checking via an alternative assay format before the original drug level result is acted on clinically, whereas a drug level result accompanied by an undetectable or low antibody titre somewhat reduces, though does not entirely exclude, the likelihood that interference explains an observed discordance.^{[9][10]}

In this case series, seven of the nine patients had a concurrently measured antibody titre available at the time of the initial discordant result, and in six of these seven the titre was elevated, consistent with the subsequently confirmed interference-related explanation; the remaining patient with an elevated titre available at presentation was among the two ultimately attributed to genuine pharmacokinetic variability,

illustrating that antibody titre elevation, while supportive, does not deterministically confirm that interference, rather than a separate genuine pharmacokinetic process, explains a given discordant result.

Design of a Laboratory Comment Supporting the Practical Trigger

The practical trigger proposed in Discussion above, cross-checking via an alternative assay format when a drug level result is materially discordant with clinical response, is best supported by a laboratory comment accompanying any drug level result where the local laboratory information system or requesting clinician has flagged a potential discordance, and we describe the recommended content of such a comment here.

An effective comment should note the specific assay format used to generate the reported result, state explicitly that anti-drug antibody interference can affect this format in a specific direction, under-reporting for a drug-sensitive format or, potentially, over-reporting for some drug-tolerant formats, and recommend that a result materially inconsistent with the patient's clinical response be cross-checked via an alternative assay format before a dose change or drug switch decision is made on the original result alone.^[9]

Where the laboratory has access to anti-drug antibody titre measurement alongside drug level measurement, as is increasingly common for infliximab and adalimumab monitoring, the comment should also note whether a concurrently measured antibody titre is available and, where elevated, specifically flag this as supporting evidence that interference should be considered before the drug level result is acted on.^[10]

Age and Disease Duration Characteristics of This Case Series

The nine patients in this case series spanned a range of disease duration and prior biologic exposure, and briefly noting these characteristics provides further useful context for readers assessing how this series' findings might apply to their own patient population.

Patients who had been on their current biologic agent for a longer duration at the time of the discordant result were somewhat over-represented among the seven cases ultimately attributed to assay interference, consistent with the expectation that anti-drug antibody development, and therefore the risk of antibody-related assay interference, tends to accumulate over the duration of exposure to a given biologic agent rather than appearing immediately upon treatment initiation.^[9]

This pattern suggests that the practical trigger proposed in this report may be particularly relevant for patients later in their treatment course with a given biologic agent, though we would not recommend restricting consideration of cross-checking only to this group, given that the remaining cases in this series, including patients earlier in their treatment course, also benefited

from the same cross-checking approach.

Regional Reference Laboratory Access as a Practical Enabler

The practical trigger proposed in this report depends on having timely access to an alternative assay format, a requirement that, as in this case series, is often met through referral to a regional reference laboratory rather than through in-house availability of multiple assay formats at every individual biologics clinic or local laboratory.

Most individual clinics and local laboratories do not maintain more than a single drug level assay platform in-house, given the comparatively modest volume of biologic drug level testing relative to routine chemistry or haematology testing, making referral to a regional or specialist reference laboratory offering an alternative assay format the practical route to cross-checking for most clinical teams, as it was for the nine patients in this series.^[2]

We would recommend that clinics managing patients on biologic therapy establish, in advance of needing it, a known referral pathway to a reference laboratory offering an alternative assay format specifically for this cross-checking purpose, rather than needing to identify such a laboratory reactively at the point a discordant result first arises, since establishing this pathway in advance would be expected to reduce the turnaround time between identifying a discordant result and obtaining the cross-check needed to resolve it.

Regulatory and Professional Guideline Context

Several professional gastroenterology and rheumatology society guidelines addressing therapeutic drug monitoring for biologics now acknowledge assay-format interference as a recognised limitation, and briefly situating this report's recommendations relative to that existing guidance is useful context.

Existing guidance generally recommends awareness of assay-format-dependent interference as a general principle without always specifying the concrete clinical workflow trigger, cross-checking when a result is materially discordant with clinical response, that this report proposes, representing a practical operationalisation of the general principle already endorsed in the broader professional guidance literature.^{[8][10]}

We would encourage professional society guidance to consider incorporating a more specific, operational trigger along the lines proposed in this report, since a general awareness statement alone, without a concrete prompting rule, risks leaving individual clinicians to decide ad hoc, and potentially inconsistently, when a discordant result genuinely warrants cross-checking versus when it can be accepted at face value.

Economic and Clinical Consequence of Avoidable Dose Escalation

Six of the seven resolved cases in this series involved an initial concern about a low drug level prompting consideration of dose escalation, and it is worth stating explicitly the economic and clinical consequence of proceeding with an unnecessary dose escalation that this report's practical trigger is designed to help avoid.

Biologic therapy dose escalation carries a direct and often substantial drug acquisition cost, and an escalation prompted by an assay artefact rather than genuine pharmacokinetic failure represents an avoidable cost with no corresponding clinical benefit, since the patient's true drug exposure was already adequate before the escalation.^[6]

Beyond direct cost, an avoidable dose escalation also exposes the patient to a higher drug dose than clinically necessary, with whatever modestly increased risk of dose-related adverse effects that higher exposure carries, and may also delay recognition of the true underlying cause of any genuine clinical concern that prompted the original drug level testing, if the clinical team incorrectly attributes an unrelated symptom or sign to inadequate drug exposure rather than investigating it independently.

For the single resolved case showing the opposite pattern, a normal reported level despite lost clinical response, the consequence of not cross-checking would have been the reverse: a missed opportunity to recognise genuine pharmacokinetic failure and appropriately escalate dose or switch therapy, potentially prolonging a period of inadequate disease control for the patient, illustrating that the practical trigger proposed in this report protects against both directions of potential clinical harm, not only the more commonly discussed over-escalation direction.

Why This Communication Was Reported as a Short Communication Rather Than a Larger Study

This report is deliberately framed as a short communication rather than a full original research article, reflecting both the small sample size available from a single clinic and the primarily practice-alerting, rather than definitively quantifying, purpose this report serves.

A short communication format is, in our view, the appropriate vehicle for raising clinical awareness of a specific, under-recognised pattern based on a focused case series, while explicitly flagging, as this report does throughout, that a larger prospective study would be needed to establish population-level frequency estimates with the kind of statistical confidence a full original research article would be expected to provide.^[7]

We would encourage readers to treat this report's practical trigger recommendation as a reasonable, low-cost clinical practice to adopt pending that larger confirmatory evidence, rather than waiting for definitive population-level frequency data before considering cross-checking a materially discordant drug level result, given the asymmetry between the modest cost of an unnecessary cross-check and the potentially substantial cost of

an avoidable dose escalation or missed genuine pharmacokinetic failure discussed earlier in this report.

Patient Communication Considerations

Communicating the resolution of a discordant drug level result to a patient, once assay interference has been identified as the explanation, requires some care, particularly for the six patients in this series whose initial low drug level result had raised the prospect of dose escalation before the interference explanation was identified.

For these patients, clear explanation that the originally reported low level reflected a laboratory assay limitation specific to their antibody status rather than a true deterioration in their drug exposure helps avoid the impression that their treatment was inadequately monitored, while also explaining why a dose escalation, briefly considered, was ultimately not needed once the corrected result became available.^[7]

For the single patient whose normal reported level was found, on cross-checking, to reflect a true lower drug exposure than initially reported, communication should instead focus forward-looking on the subsequent dose or therapy adjustment this corrected finding supports, framing the cross-check as having identified a genuine clinical issue that the original result had masked rather than dwelling on the delay this masking introduced before the correct explanation was found.

Study Limitations

This case series' limitations should be stated plainly given its small size and single-centre origin.

Nine patients from a single rheumatology biologics clinic cannot establish the true population frequency of clinically significant assay-format interference among patients on infliximab or adalimumab therapy, and the proportion resolved by cross-checking in this series, seven of nine, should not be interpreted as a generalisable population-level estimate of how often this specific pattern occurs.

The two patients whose discordance was attributed to genuine pharmacokinetic variability rather than assay interference were not subjected to further mechanistic investigation beyond the alternative assay format cross-check, and it remains possible, though considered less likely by the investigating clinicians, that some more subtle or incompletely characterised interference mechanism contributed to these two cases as well.

Governance Recommendations for Laboratories Issuing Drug Level Results

Drawing together the preceding discussion, we propose the following governance recommendations for a laboratory issuing biologic drug level results, building on the laboratory comment design and antibody titre integration recommendations already discussed above.

First, document explicitly, in the local laboratory information system or result reporting template, which assay format, drug-sensitive or a specific drug-tolerant design, is used for each reported drug level result, so that this information is readily available to inform any subsequent cross-checking decision rather than requiring the requesting clinician to separately investigate which format generated a given result.^[2]

Second, where concurrent anti-drug antibody titre testing is available, report it alongside the drug level result by default rather than only on specific request, giving the requesting clinician the supporting context discussed above as a matter of routine practice rather than requiring them to separately request it when a discordance is first suspected.

Third, establish the referral pathway to an alternative-format reference laboratory recommended above as a standing, documented arrangement, with a defined expected turnaround time, so that a clinician identifying a discordant result can act on the practical trigger proposed in this report promptly rather than facing delay in arranging the cross-check itself.

Applicability to Other Biologic Agents Beyond Infliximab and Adalimumab

This case series focused specifically on infliximab and adalimumab, the two biologic agents most extensively studied for therapeutic drug monitoring and assay-format interference in the published literature, and it is worth briefly noting how the principles described in this report might extend to other biologic agents increasingly subject to drug level monitoring.

Other monoclonal antibody biologics used in rheumatology and gastroenterology, including other anti-TNF agents and newer biologics targeting different inflammatory pathways, share the same basic immunogenicity risk, development of anti-drug antibodies capable of interfering with drug level assays, though the specific assay formats available and their individual interference profiles have not been characterised as extensively in the published literature for these newer agents as for infliximab and adalimumab specifically.^[1]

We would recommend that clinical and laboratory teams monitoring drug levels for any biologic agent, not only the two examined in this case series, adopt the same general practical trigger proposed here, treating a drug level result materially discordant with clinical response as a prompt for assay-format cross-checking consideration, pending the development of agent-specific interference literature comparable to what currently exists for infliximab and adalimumab.

Future Directions

A larger, prospective, multi-centre study systematically applying the practical trigger proposed in this report across a broader biologics-treated population would help establish the true population frequency of clinically significant assay-format interference and would provide a more robust evidence base for the specific discordance threshold that should prompt cross-checking than this small case series alone can support.

Further research directly comparing drug-sensitive and multiple distinct drug-tolerant assay formats head-to-head in patients with varying anti-drug antibody titres would help characterise more precisely which specific assay designs are most prone to the over-reporting mechanism described above, information that would allow laboratories to select or weight assay formats more specifically informed by their own local patient population's antibody prevalence and titre distribution.

Practical Checklist for Clinics Managing Biologic Therapy

As a closing practical summary, we offer the following checklist for a rheumatology or gastroenterology clinic managing patients on infliximab, adalimumab, or other biologic agents subject to drug level monitoring.

Establish, in advance, a known referral pathway to a reference laboratory offering an alternative assay format for drug level cross-checking, rather than needing to identify one reactively once a discordant result first arises.

Treat any drug level result materially discordant with the patient's clinical response, whether a low level with good response or a normal level with lost response, as a trigger for considering cross-checking via this alternative-format pathway before a dose change or drug switch decision is made on the original result alone.

Where concurrent anti-drug antibody titre testing is available, review the titre result alongside the drug level result as additional supporting context, recognising that an elevated titre strengthens but does not deterministically confirm an interference-based explanation for a discordant result.

Request that the laboratory issuing drug level results provide an explanatory comment, along the lines described in this report, whenever a reported result is identified as potentially affected by assay-format interference, so that the clinical team receives this context directly rather than needing to seek it out independently.

Conclusion

In seven of nine patients with a biologic drug level result discordant with clinical response, the discordance was resolved by identifying anti-drug antibody interference with the original assay format. A materially discordant drug level result should prompt consideration of assay-format cross-checking before a dose change or drug switch is made on the strength of a single assay result.

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