



**Article:**

Ahmad Charifa, Dustin R. Bunch, and Joe M. El-Khoury.

*Practical Approach to Eliminate Bilirubin Interference in Icteric Samples for Creatinine Measurement.*

J Appl Lab Med 2019; 4: 477-9.

<http://jalm.aaccjnls.org/content/4/3/477>

**Guest:** Dr. Joe El-Khoury is Assistant Professor of Laboratory Medicine at Yale University, and Director of Clinical Chemistry and Co-director of the Clinical Chemistry Fellowship Program at Yale New Haven Health.

Randye Kaye:

Hello, and welcome to this edition of "JALM Talk," from the *Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

Clinical chemistry assays are widely impacted by inherent interferences in patient blood samples such as hemolysis, icterus, and lipemia. These interferences can cause inaccurate laboratory results and may even prevent the laboratory from releasing test results to ordering health care providers. In particular, the interference of bilirubin in various creatinine assays is common. Inaccurately reported creatinine, or the inability to report creatinine, can have adverse implications in the management of patients. Accurate creatinine results are important for assessing kidney function in many clinical contexts such as imaging procedures and the dosing of therapeutic drugs. Therefore, mechanisms to overcome bilirubin interference and creatinine assays would be beneficial to patient care.

The November 2019 issue of *The Journal of Applied Laboratory Medicine* includes a Laboratory Reflections article entitled, "A Practical Approach to Eliminate Bilirubin Interference in Icteric Samples for Creatinine Measurement." The senior author of the article is Dr. Joe El-Khoury, who is our guest on this podcast. Dr. El-Khoury is an Assistant Professor of Laboratory Medicine at Yale University as well as the Director of Clinical Chemistry and Co-director of the Clinical Chemistry Fellowship Program at Yale New Haven Health. Welcome Dr. El-Khoury. Let's begin with this, how prevalent is bilirubin interference with creatinine assays?

Dr. Joe El-Khoury:

So, bilirubin is a significant source of interference for creatinine assays and it affects both the Jaffe and the enzymatic methods. And for our particular method, the icteric index, which is a measure of how icteric the sample is, it is about 15, which is really low. That correlates with about 15 milligrams per deciliter of total bilirubin. And now, that is not an exact concentration in terms of the measure

itself versus the concentration but in general, it reflects that amount of bilirubin and it's important to note that that varies by method. So, it's important that labs also look at their particular method and what the product in such data and interference. But in general, it is low.

Randy Kay: All right thank you. So, how are the labs currently dealing with the samples that are containing high levels of bilirubin?

Dr. Joe El-Khoury: So, most will generally just attach a comment that says, "Sample icteric" and then release the result and recommend that the clinical team interpret within clinical context. Others can take an approach where they just do not result because it basically exceeds their criteria for what's acceptable as is recommended by the manufacturer. And in some extreme cases I have seen some reference labs that actually developed mass spectrometry-based assays so that they're able to provide values for these patients.

Randy Kay: I see, all right. So, in your letter you describe a new practical approach that you recommend. Can you describe it for us now?

Dr. Joe El-Khoury: Absolutely. So, it's based on an old concept which is the diluting out interferences. However, I have not seen that applied in this way for creatinine assays specifically as it comes to interferences from icteric samples and also, it's an automated process. So, what we are doing essentially is we have built a rule that triggers onboard the analyzers, that when it sees the sample with this icteric index that is greater than 15, which is our threshold for acceptability, it automatically runs on a diluted sample which is a fourfold dilution. So, by doing that fourfold dilution, we are essentially diluting that sample and diluting out the icteric interferences. So, now we would be able to release results with an icteric index up to 60. So, we're multiplying that 15 by 4 and for those patients that we couldn't give a result before. And again, the best part is it's all automated. So, the analyzer takes care of the whole process with little manual intervention.

Randy Kay: Wow, that does sound like a practical approach. How about limitations, are there any limitations to your approach that the audience should be aware of?

Dr. Joe El-Khoury: Yes. So, it's very important to remember that when you do a fourfold dilution on a sample that has essentially a low concentration of analyte, you have to multiply your limit of quantitation for that assay by that same fold of dilution. In other words, for creatinine my lower limit of quantitation is 0.06 milligrams per deciliter. So, if I do a fourfold dilution and I see a less than 0.06 on the analyzer, I actually have to multiply that by four, so it's actually the reported value

would be less than .24 milligrams per deciliter. So, same as when you're diluting a high value and running it on the analyzer and then you multiply it by four, you have to remember to do the same thing with the limit of quantitation. And what that means in clinical practice for creatinine is some of the pediatric patients that can run typically on the low 0.1 to 0.2 may not be measured using this method, but at least it's still clinically useful for over 99% of the patients we see.

Randy Kay: Okay, I see. Thank you, that's a nice percentage as well. Now, do you think that your approach to bilirubin interference in creatinine measurement has the potential to work for other clinical laboratory measurements as well?

Dr. Joe El-Khoury: Absolutely. This was a proof of concept study and we choose creatinine because that was one of the ones that are most defected by icteric interference but we do think that this can be validated for other analytes as well. Another example that comes to mind with a low threshold is total protein. So, at least for us. So, it's important that labs who are interested in adopting this for other analytes to remember that: a) the analyte has to have an approved diluent and also b) to take into context when you raise LOQ, the limit of quantitation, after the dilution that you're doing is that still clinically useful. So, if those two cases are met, you can then validate and do this and I think it should work for other analytes as well.

Randy Kay: That's wonderful. Thank you so much for your time today, doctor.

Dr. Joe El-Khoury: Thank you.

Randy Kay: That was Dr. Joe El-Khoury from Yale University, discussing his Laboratory Reflection entitled "A Practical Approach to Eliminate Bilirubin Interference in Icteric Samples for Creatinine Measurement," from the November 2019 issue of JALM. Thanks for tuning in to this episode of "JALM Talk." See you next time and don't forget to submit something for us to talk about.