Nordic recommendation

Pneumatic Transportion System

Venous blood sampling

Hemolysis index

XXXIX NORDIC CONGRESS IN CLINICAL CHEMISTRY
17-20 SEPTEMBER 2024 STOCKHOLM

NOKLUS
sammen for god kvalitet

How to handle the haemolysis index

Validation and quality control

Gunn B B Kristensen, Noklus

Validation and QC of the H-index analysis

- Transparency between the different manufacturers' measurement principles for H-Index are poor
- The automated methods used to measure H-Index are not harmonized
- ISO standard 15189:2022 and CLSI document C65-A Hemolysis state that validation and quality control of analyses is mandatory in an accredited laboratory

Clin Chim Acta 2018;484:328-32
ISO 15189, 2022
CLSI document, C56-A Hemolysis

Differences in the management of the H-index analysis

Country	Perform IQC for H-index	Participate in EQA for H-index	Validation
Denmark (2017)	25 % (4/16)	29 % (5/17)	24 % (4/17)
Norway (2023) (not published)	19 % (8/43)	86 % (36/43)	
Finland (2020) (not published)	17 % (21/126)	49 % (58/126)	

J Appl Lab Med 2017;4:450-2

NOKLUS
sammen for god kvalitet

Due to lack of validation and QC

Erroneous results are released, or correct results are erroneously detained

NOKLUS
sammen for god kvalitet

Recommendation from the Nordic scientific preanalytical working group

Validation and quality control of the H-index analysis

A pragmatic approach

Detection of hemolysis: **Recommendation**

- Automated detection of H-index
  - Rapid, accurate and inexpensive
  - Do not impact turnaround time (TAT)
  - Enables direct transfer to the laboratory information system (LIS)

RECOMMENDED

- Visual inspection of the sample serum color after centrifugation
  - inaccurate
  - substantial inter-observed variability

STRONGLY DISCOURAGED

Ann Clin Biochem 2016;53(Pt 5):527-38

Defining H-index cut offs
(Hemolysis acceptance limits)

a) Traditional ± 10% change in concentration from baseline (± 10%Δ)

b) Analytical Change Limit (ACL) based on state-of-the-art analytical variation: ACL = $1.96 \times \sqrt{2} \times CV_A$, where CV_A is the analytical variation.

c) Analytical significant bias based on biological variation: I (%) = $0.5 \times CV_I$, where CV_I is the average within-subject variation listed by the EFLM-database (Milan model)

d) Clinically significant bias expressed as Reference Change Value (RCV) based on analytical and within-individual biological variation. RCV = $1.96 \times \sqrt{2} \times \sqrt{CV_A{}^2 + CV_I{}^2}$

Scand J Clin Lab Invest 2020;80:580-9act

Scand J Clin Lab Invest 2015;75:162-9.

Clin Chem Lab Med. 2018;56(5):718–727

Validation of H-index: **Recommendation**

H-index analysis should be validated in the same way as other analytes in your laboratory:

1. Prepare the hemolysate by use of the freeze method
2. Acquire a pool of plasma/serum free of interferences
3. Divide these into a sufficient number of tubes and add increasing amounts of hemoglobin-titrated hemolysate
4. Analyse and calculate mean positive or negative percentage change of concentration from baseline pool for the analytes potentially affected by hemolysis
5. Determine the H-Index corresponding to the Analytical significant bias based on I (%) = 0.5 × CV_I
6. Determine the allowable H-Index based on analytical and within-individual biological variation; Reference Change Value (RCV).

CLSI. Interference Testing in Clinical Chemistry - Third Edition. CLSI document EP-07. Wayne (PA): Clinical and Laboratory Standards Institute; 2018

Internal Quality control (IQC)

Recommendation

1. Prepare a pool of serum/plasma with predefined acceptance and rejection criteria from routine patient samples with clinically relevant concentrations of cell-free hemoglobin.
2. Preferably, at least 2 levels for the interfering substance should be used.
3. IQC testing for H-index should be performed at least 2 times per day.
4. IQC testing should be systematically recorded.
5. IQC should be interpreted and acted upon in the same manner as any other IQC result.

CRITICAL REVIEWS IN CLINICAL LABORATORY SCIENCES 2020, VOL. 57, NO. 1, 1–21
https://doi.org/10.1080/10408363.2019.1664391

External quality assessment (EQA):
Recommendation

The laboratory should participate in an available EQA-program for the H-Index

- The EQA of the H-index can be done by
  - **circulation of samples simulating errors** (Type II model)
  - **registration of errors/adverse events** (Type III model)

- Two Nordic EQA providers offer pre-analytical External Quality Assessment program (EQAS) including samples simulating errors:
  - **HIL-index and interference (4131 DK)**
    - Offered three times a year by **DEKS**, (*Danish EQA organisation)*
  - **Serum index (437)**
    - Offered four times a year by **Equalis***, (Swedish EQA organization*)

Biochem Med. 2014;24:114-122.

Reporting flagged or alarming test results - **Recommendation**

- Release the laboratory test result if the H-Index is below the analytical significant bias.
- Release the result with a comment describing the direction in which the result is potentially falsely altered, if the H-Index is between the analytical significant bias and the Reference Change Value (RCV).
- If the H-Index value is associated with a change that exceeds the Reference Change Value (RCV), the test result must be suppressed.
- Suppress all test results in samples with cell free Hb>10 g/L.
- Include H-Index data in the laboratory report.

Using corrective formulas for adjusting test results is strongly discouraged

Practical recommendations for managing hemolyzed samples in clinical chemistry testing. Clin Chem Lab Med. 2018;56(5):718–727
CRITICAL REVIEWS IN CLINICAL LABORATORY SCIENCES 2020, VOL. 57, NO. 1, 1–21 https://doi.org/10.1080/10408363.2019.1664391

Summary - **Practical recommendations** for managing test results in hemolyzed specimens:

1. Check sample quality (i.e. presence of hemolysis) before testing
2. Check presence and degree of hemolysis with automatic assessment of the H-index
3. Validate the H-index at the laboratory
4. When the H-index is unavailable, visual assessment of hemolysis with a color chart is advisable
5. Transfer (and store) H-index results into the laboratory information system (LIS) and consider to include it in the laboratory report
6. Convert the results of the H-index into the corresponding hemoglobin concentration (i.e. g/L)
7. Define standard operating procedures (SOPs) for standardized management of test results in hemolyzed specimens
8. Use quality control materials, both internal and external, for continuously monitoring the analytical performance of the H-index

Practical recommendations for managing hemolyzed samples in clinical chemistry testing. Clin Chem Lab Med. 2018;56(5):718–727