Evaluation of Cystatin C Ordering Trends in a Quaternary Care Health System

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ABSTRACT

Background: Cystatin C is an alternative and adjunct kidney biomarker to creatinine in the estimation of glomerular filtration rate (eGFR). The National Kidney Foundation and American Society of Nephrology have called for increased use of cystatin C in the evaluation of kidney function. Our institution brought cystatin C testing in-house in August 2021. The goal of this study was to evaluate the utilization and longitudinal ordering trends of cystatin C within our quaternary care health system.

Methods: Cystatin C is measured on a Roche cobas® c502 using an assay traceable to IFCC-certified reference material. The electronic health record system (Epic) was queried using Epic SlicerDicer to identify ordering trends within the Johns Hopkins Health System between July 2021 and March 2024. The frequency of unique (one-time) cystatin C orders and concomitant orders with creatinine was also conducted. An in-depth analysis and chart review was performed over a three-month period to evaluate ordering locations, underlying clinical conditions, including previous diagnosis of kidney disease, and correlations between cystatin C and creatinine measurements.

Results: Between July 2021 and March 2024, 10,471 tests were performed from 8,098 unique patients. Cystatin C orders remained stable since April 2022, with an average 370 orders (363-378) placed per month. Sixty nine percent of cystatin C test requests were accompanied with creatinine testing within a 24-hour timeframe from January 2024 to March 2024. In a detailed analysis of a three month period, cystatin C testing was primarily performed in patients with a kidney-related disease (66%) and in the management of patients with a cancer diagnosis (27%).

Conclusion: There has been sustained adoption of cystatin C by providers at our institution. The majority of orders have occurred in patients with an underlying renal diagnosis, as well as comorbid or chronic conditions that may affect kidney function.

WORKFLOW

Electronic Health Record(EHR) data queried for number of cystatin c specimens resulted between July 2021 to March 2024 from Johns Hopkins Health System entities.

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Total number of cystatin C specimens by entity over a thirty-two month period among hospitals within the Johns Hopkins Health System.

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Distribution of cystatin C specimens ordered over a thirty-two month period by Johns Hopkins Hospital inpatient services and patient age stratification among inpatient cystatin C orders

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Correlation of paired creatinine and cystatin C specimens resulted within a 24-hour timeframe from January 2024 to March 2024. Both creatinine and cystatin C were measured on Roche cobas instruments using enzymatic (sarcosine oxidase) and immunoturbidimetric (standardized against ERM-D471/IFCC reference material) assays respectively.

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Raw data extraction, filtering and analysis was performed using R studio with the R programing language. All plots were performed with Microsoft Excel.

RESULTS AND DISCUSSION

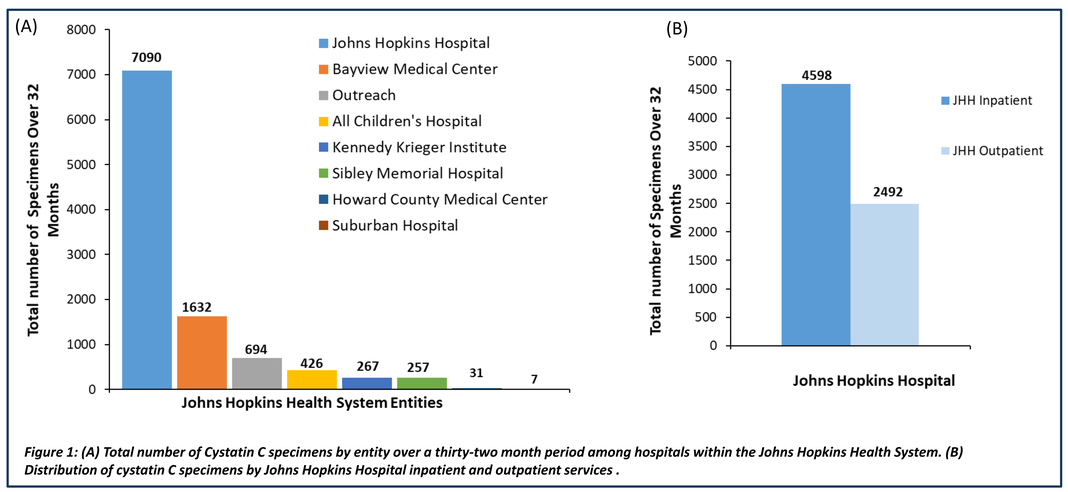


Figure 1: (A) Total number of Cystatin C specimens by entity over a thirty-two month period among hospitals within the Johns Hopkins Health System. (B) Distribution of cystatin C specimens by Johns Hopkins Hospital inpatient and outpatient services .

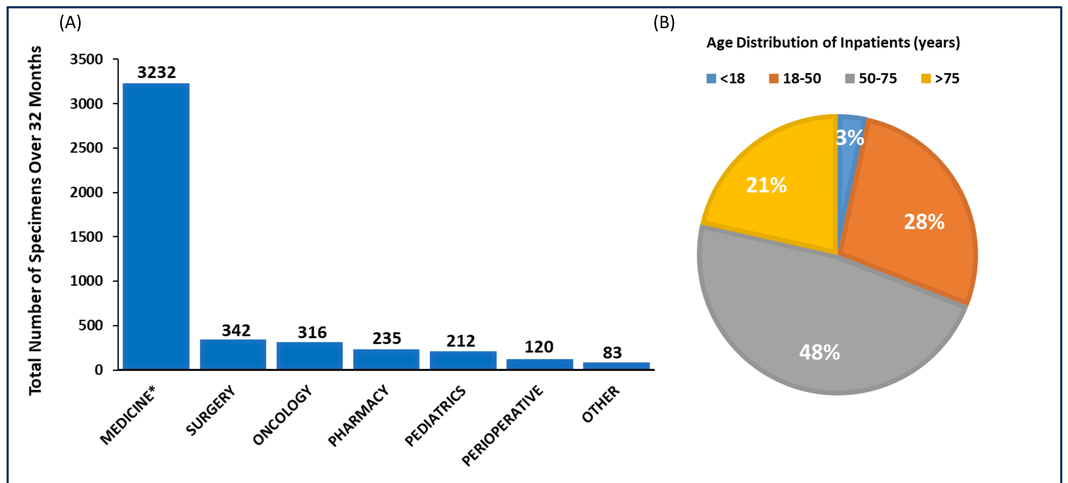
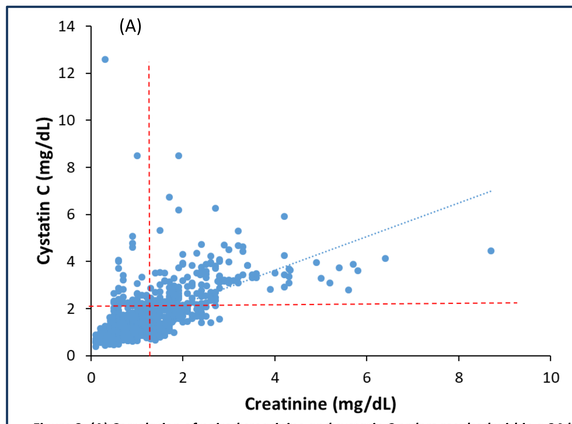


*Figure 2: (A) Distribution of 4540 cystatin C specimens ordered over a thirty-two month period by JHH Inpatient services. (B) Patient age stratification among inpatient cystatin C orders. *Inclusive of Nephrology, Hepatology, and Cardiology.*



(B)

Creatinine (mg/dL) / Cystatin C (mg/dL)	Unique Specimens Within RI	Unique Specimens Outside RI
Unique Specimens < 2x ULN	514	129
Unique Specimens ≥ 2x ULN	56	163

Figure 3: (A) Correlation of paired creatinine and cystatin C orders resulted within a 24-hour timeframe from January 2024 to March 2024 (n=862 specimens). (B) Box plot categorization of creatinine and cystatin C concentrations. The shaded area indicates 56 unique specimens from 36 patients with normal creatinine and cystatin C two times above the upper limit of normal (ULN). ULN: 1.03 mg/dL; 2x ULN: 2.06 mg/dL. Reference interval (RI)

Table 1: Diagnosis stratification for cystatin C orders (n=3 months; Jan 2024-Mar 2024)

Diagnosis of Patients Receiving Cystatin C Testing	Number of Patients
Chronic Kidney Disease	590 (47%)
Acute Kidney Injury	125 (10%)
Kidney Transplant Recipient management	114 (9%)
Transplant Donor/Recipient Evaluation	7 (1%)
Sarcopenia/Cachexia	31 (2%)
HIV Management	53 (4%)
Cancer Management including Drug Dosing	337 (27%)

Electronic Health Record overview of 1257 patients with cystatin C testing over three months to evaluate the rationale for cystatin C testing. Two-thirds (66%) of patients had kidney-related disease, including chronic kidney disease, acute kidney injury and transplant recipient management. Nearly one-third of patients (27%) had testing ordered for cancer treatment management.

Table 2: Reasons for ordering cystatin C for discordant results (n=3 months; Jan 2024-Mar 2024)

Reason For Ordering Cystatin C	Number of Patients
Chronic Kidney Disease	14 (39%)
Acute Kidney Injury	13 (36%)
Kidney Transplant Recipient management	1 (3%)
Drug Dosing	4 (11%)
Other	4 (11%)

Electronic Health Record review of 56 specimens (36 patients, median age = 68, range 3-98) with creatinine within normal limits but cystatin C ≥ 2x the upper limit of normal to ascertain rationale for cystatin C testing. More than three-quarters (78%) of patients received cystatin C testing for nephrology-related indications, including 39% with chronic kidney disease, 36% with acute kidney injury, and 3% for transplant management. The four patients in which cystatin C was performed for drug dosing were in the background of Lasix or Bactrim treatment.

CONCLUSION

- The majority of cystatin C test requests came from our academic hospital (Johns Hopkins Hospital), with 65% coming from inpatient units.
- There was variability in patient demographics, particularly age, but the most common causes for ordering cystatin C were associated with underlying kidney disease or cancer management.
- Cystatin C and creatinine levels were highly correlated in 79% of specimens tested. Notably 6.5% were associated with elevated cystatin C levels above twice the upper limit of normal (ULN) with a normal creatinine result.
- Interrogation of discordant results, where cystatin C was high and creatinine was low, suggest cystatin C test utilization for diagnosis or management of kidney-related disease.
- Cystatin C ordering has remained consistent and should be considered in individuals with underlying kidney disease, including in cases when creatinine results are inconsistent with clinical presentation.

REFERENCES

- Cynthia Delgado, Mukta Baweja, Deidra C. Crews, Nwamaka D. Eneanya, Crystal A. Gadegbeku, Lesley A. Inker, Mallika L. Mendu, W. Greg Miller, Marva M. Moxey-Mims, Glenda V. Roberts, Wendy L. St. Peter, Curtis Warfield, Neil R. Powe,A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease,American Journal of Kidney Diseases,Volume 79, Issue 2,2022,Pages 268-288.e1,ISSN 0272-6386,https://doi.org/10.1053/j.ajkd.2021.08.003.