Article published online: 2023-05-05

Understanding the Constraints and Optimization of Serum Immunofixation Electrophoresis and Serum Free Light Chains for Detecting Monoclonal Proteins: A Single-Center Experience

Malvika Shastri[1] Pankaj Malhotra[2] Harvinder Kaur[3] Ritu Aggarwal[3]

[1] Department of Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[2] Department of Clinical Hematology and Medical Oncology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[3] Department of Immunopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence Ritu Aggarwal, MD, DNB, Department of Immunopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, 160012, India (e-mail: ritu_immunopath@yahoo.co.in).

J Lab Physicians 2023;15:518–523.

Abstract

Introduction Serum immunofixation electrophoresis (SIFE) and serum free light chain (SFLC) assay are imperative investigations in diagnosis and follow-up of multiple myeloma (MM). SFLC assays are reported to have higher sensitivity than SIFE. However, discrepancies have been reported between them. The current study was aimed at assessing concordance and discordance between SIFE and SFLC results in MM.

Methods A total of 450 observations of both SIFE and SFLC were obtained from treatment-naive and follow-up MM patients.

Results One hundred and twenty-nine (28.7%) values were observed as discordant, that is, positive SIFE with normal SFLC ratio or negative SIFE with abnormal SFLC ratio (p-value < 0.00001). Proportion of discordance was higher in SIFE positive-SFLC normal cases than SIFE negative-SFLC abnormal cases. Discordance was more frequent in follow-up cases.

Conclusion Negative SFLC alone may not be reliable for MM follow-up. Algorithm may be based on SFLC measurements on each follow-up till attainment of normal SFLC ratio. Once SFLC normalizes, follow-up may be done with SIFE. If SIFE is positive, further follow-up with SIFE may be initiated.

Keywords
- serum immunofixation
- serum free light chain
- multiple myeloma
- concordance
- discordance

Introduction

The International Myeloma Working Group (IMWG; 2014) has elaborated criteria for evaluation of multiple myeloma (MM). According to which, for any suspected case, the initial investigation includes serum protein electrophoresis (SPEP) and serum immunofixation electrophoresis (SIFE), 24-hour urine sample for urine protein electrophoresis and urine immunofixation electrophoresis (UIFE), and estimation of serum free light chains (SFLCs).[1] Of these, SIFE has been

received
December 27, 2022
accepted after revision
March 13, 2023
article published online
May 5, 2023

DOI https://doi.org/10.1055/s-0043-1768684.
ISSN 0974-2727.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

designated as the "gold standard" for confirming the presence of monoclonal protein (M protein).[2]

While SPEP is utilized as a screening test for the presence of M protein, SIFE determines both monoclonality and isotype. SFLC assay is utilized to estimate the levels of free κ and λ light chains in the serum. A ratio of κ and λ further aids in the diagnosis of monoclonal plasma cell disorders.[3]

The SFLC assays have been reported to be more sensitive than SIFE or SPEP in detecting FLC M proteins. Interestingly, the disease is detected earlier with SFLC than IFE and patients are followed-up with SFLC ratio.[4] Although it is speculated that negative SIFE plausibly have normal SLFC ratio as well, however, we observed a significant discrepancy between SIFE and SFLC in MM patients at our center. Recent studies have divulged sporadic reports with similar observations.[2–4]

Thus, the current study was undertaken to assess the concordance and discordance between SIFE and SFLC at our center. In addition, the present study determines the sensitivity and specificity of the turbidimetry-based SFLC assay as compared to electrophoretic techniques.

Materials and Methods

This was a retrospective observational study for an 18-month period, from January 2021 till June 2022. All treatment-naive and follow-up cases of MM were based on SPEP results, which were retrieved from the archival database of the Department of Immunopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India. SIFE was performed for confirmation and characterization of isotype of M proteins. SPEP was performed using serum protein 6 band Agarose gel by Helena Biosciences platform using SAS-1 SP-24 SB kit. SIFE was performed using Agarose gel-based electrophoresis kit by Helena Biosciences (SAS-1 IFE-4 kit) that utilizes monospecific antisera for immunoglobulin (Ig) G, IgM, and IgA heavy chains and κ and λ light chains. SFLC estimation was carried out by turbidimetry using Optilite Freelite kappa free kit (LK016.OPT) and Optilite Freelite lambda free kit (LK018.OPT) (The Binding Site Group Limited). The measuring range for kappa and lambda free light chains are 0.6 to 127000 mg/L and 1.3 to 139000 mg/L, respectively.

Monoclonal gammopathy was defined by the presence of a discrete monoclonal (M) band in the gamma region or prominent bands in regions of other proteins in the serum. Concordance between SIFE and SFLC was defined as similar results on both SIFE and SFLC, that is, if SIFE was positive, SFLC ratio was also abnormal (< 0.26 or > 1.65) and if SIFE was negative, SFLC ratio was also in normal range (0.26–1.65). Discordance was defined as positive SIFE with normal SFLC ratio or negative SIFE with abnormal SFLC ratio.

Statistical Analysis

Statistical analysis was done using IBM SPSS 20 (SPSS Inc, Chicago, United States). The results were expressed as mean ± standard deviation (SD) for all continuous variables and as percentages for categorical variables. To obtain the association of categorical variables, chi-square test was applied. To find out the efficacy of two methods, McNemar test was used. A p-value of < 0.05 was considered as statistically significant.

Results

The current study included a cohort of 377 patients, which contributed to 450 values of both SIFE and SFLC. Their age ranged from 24 to 90 years with mean ± SD of 58.6 ± 9.1 years and median age of 59 years. The male-to-female ratio was 1.4:1. Majority values (279/450, 62%) were patients on follow-up. The cohort included 39 patients with light chain MM. Of these, 21 (53.8%) patients had lambda-associated MM and 18 (46.2%) patients had kappa-associated MM.

Of the 450 values for SIFE and SFLC, there were 129 (28.7%) values which were discordant, that is, positive SIFE with normal SFLC ratio or negative SIFE with abnormal SFLC ratio. These cases with discordant values were further segregated into two groups: SIFE positive-SFLC normal and SIFE negative-SFLC abnormal for further analysis (►**Table 1**).

SIFE positive-SFLC normal cases: This subgroup included 91/450, 20.2% values. Of these, majority (61, 67.1%) occurred in follow-up cases. The dominant finding in 51/61, 83.6% of the follow-up cases was M band on SPEP, while in 10/61 (16.4%) cases although SPEP was normal but monoclonal bands were noted on SIFE. Similarly, in treatment-naive cases too, 28/30, 93.3% had positive SPEP.

SIFE negative-SFLC abnormal cases: This subgroup accounted for 8.4% (38/450) values. On further analysis, 32 (84.2%) values were observed in follow-up cases.

A higher proportion of discordance was observed in the subgroup SIFE positive-SFLC normal cases as compared to SIFE negative-SFLC abnormal cases. Taking SIFE as a standard for presence of M protein, the two methods were compared (►**Table 2**).

Discussion

IMWG defines complete response (CR) in MM as "negative SIFE and UIFE with absence of soft tissue plasmacytomas and bone marrow plasma cells less than 5%" and stringent CR (sCR) as "normal SFLC ratio along with absence of clonal bone marrow plasma cells, demonstrable by immunohistochemistry or immunofluorescence."[5,6] Thus, SIFE and SFLC have distinct roles in assigning response criteria in MM. To

Table 1 Results of SIFE and SFLC in study cohort ($n = 450$)

Test results	SIFE positive (%)	SIFE negative (%)	Total
κ/λ ratio abnormal	237 (52.7)	***38 (8.4)***	275 (61.1)
κ/λ ratio normal	***91 (20.2)***	84 (18.7)	175 (38.9)
Total	328 (72.9)	122 (27.1)	450

Abbreviations: SFLC, serum free light chain; SIFE, serum immunofixation electrophoresis.

Table 2 Comparison of SIFE and SFLC in new and follow-up cases of MM ($n = 450$)

Test	SIFE positive	SIFE negative	Sensitivity (%)	Specificity (%)	Accuracy (%)	*p*-Value	PPV (%)	NPV (%)
κ/λ ratio abnormal	237	38	72.3	68.9	71.3	< 0.00001[a]	86.2	47.9
κ/λ ratio normal	91	84						

Abbreviations: MM, multiple myeloma; NPV, negative predictive value; PPV, positive predictive value; SFLC, serum free light chain; SIFE, serum immunofixation electrophoresis.
[a]The chi-square statistic is 63.2324. The *p*-value is < 0.00001 (*p*-value < 0.05 is significant).

simplify, SIFE negativity is required for CR and SFLC normalization is favored for sCR in MM. On the other hand, the minimal residual disease (MRD) analysis requires detection of very low levels of persistent or reemergent neoplastic plasma cells by highly sensitive multicolor/next-generation flow cytometry and/or next-generation sequencing on bone marrow aspirates in patients who have achieved CR.[7,8] However, there are no specified time intervals for MRD testing.[8,9]

SIFE is the most sensitive method for identification and characterization of M proteins. It is a unique technique integrating the resolution offered by SPEP with specificity of antigen-antibody reaction.[7] In initial "electrophoresis" phase, the serum gamma globulins are separated based on their electrophoretic mobility under an electric field, followed by "fixation," whereby specific antisera are individually added to each migration lane to precipitate out the heavy and light chains from gamma globulins in form of visible precipitin band.[10,11] Turbidimetry-based measurement of SFLCs utilizes polyclonal and monospecific anti-κ and anti-λ antibodies.[11,12] The relative sensitivities of SPEP, SIFE, and abnormal SFLC ratio have been estimated as 77, 95, and 96%, respectively.[13] The turbidimetry-based FLC assays are reported to be 50 to 100 times more sensitive than SIFE or SPEP in detecting M proteins, which enables detection of SFLC earlier than SIFE.[4] Further, SFLC performed along with SPEP and SIFE is claimed to improve the overall sensitivity for screening and prognostication of MM disease spectrum.

Previous studies attempted to compare these highly sensitive turbidimetry-based SFLC assays with standard electrophoresis techniques (►**Table 3**). The discordance rates between results of SIFE and SFLC in these studies are quite variable, ranging from approximately 17% to as high as 50% (►**Table 3**).[3,4,14–17] Our study revealed a discordance rate of 28.7%, which is comparable to the rates reported by Wood at el and Singhal et al, respectively.[4] The normal range of SFLC ratio is 0.3 to 1.2; an abnormal ratio outside the acceptable reference range is considered to favor monoclonal over polyclonal elevations of SFLC.[18,19] In MM, the reference range of diagnostic ratio is taken to be 0.26 to 1.65. However, an exception to this reference ratio is made for patients with renal failure, where the SFLCs are more retained and the ratio is revised to 0.37 to 3.17.[20]

Several plausible causes have been put forth in the literature to explain the discordance between the two testing modalities. According to Böer and Deufel, not just MM but non-neoplastic conditions such as infections, autoimmune disorders, chronic liver disease, and neurological disorders as well as certain malignancies produce hypergammaglobulinemia or elevated serum levels of κ and λ.[21] Bhole et al and Heaton et al attributed issues such as excess antigen, nonlinear antigen-antibody reaction, and polymerization of FLC molecules, which lead to falsely elevated or diminished values of SFLC.[22,23] Associated renal dysfunction and aggregator property of SFLC can also yield erroneous results which do not correspond to SIFE as mentioned by Singh.[2] Further, Udd et al in their study concluded that the FLCs need to be sufficiently elevated to be able to be detected via FLC assays.[24] Since discrepancy was more in follow-up cases, it may also be reflective of the effect of stage of disease, individual heterogeneity in disease progression, and disease biology on the estimation of SFLC as demonstrated by Habib et al.[25] It has been observed that approximately 36% of patients may demonstrate abnormal SFLC ratio even without monoclonal gammopathy, which is mainly κ-associated.[26] Normal SFLC ratio despite positive SIFE is ascribed to shorter half-lives of κ and λ light chains.[4] Also, false negative SFLC ratios are encountered more frequently with λ-light chain disorders owing to underproduction and/or underdetection of excess λ FLC.[2] In the current study, we noted an increased number of λ-associated MM cases on follow-up when SFLC was within normal limits, however, SIFE reported positive (►**Table 4**).[2–4,15–17] Interestingly, κ-associated SFLC ratios may be seen in λ chain–associated MM postautologous stem

Table 3 Isotype distribution of follow-up cases of MM where SFLC was within normal limits but SIFE was positive ($n = 58$)

Isotype	No. of cases
IgG κ	21
IgA κ	6
IgG λ	22
IgA λ	6
κ light chain disease	1
λ light chain disease	2
Total	58

Abbreviations: Ig, immunoglobulin; SFLC, serum free light chain; SIFE, serum immunofixation electrophoresis.
Note: Total λ-associated cases: 30; Total κ-associated cases: 28.

Table 4 Studies on discordance between SIFE and SFLC

Serial no.	Authors	Country	Cohort	Methodology	Results	Conclusion
1	Singhal et al (2009)	USA	No. of patients = 122 (values available = 2,648)	SFLC: Freelite, The Binding Site on Dade-Behring nephelometer	Discordance between SIFE and SFLC-33.9% No of *SIFE positive-SFLC normal* patients was much greater than *SIFE negative-SFLC abnormal* patients	Normal SFLC cannot rule out residual disease Normal SFLC more likely to be in presence of positive SIFE than negative SIFE in presence of abnormal SFLC
2	Wood et al (2010)	USA	No. of samples = 501	IFE: Paragon IFE kit (Beckman Coulter, Brea, CA); SFLC: Freelite, (The Binding Site Ltd, Birmingham) on Dade Behring BNII automated nephelometer	Discordance between SIFE and SFLC-24.6% 82% light chain disease patients had abnormal SFLC	Proportion of patients with normal SFLC similar in IgG and IgA subgroups
3	Kim et al (2014)	Korea	No. of samples = 157	SFLC: N Latex FLC assays (Siemens Healthcare Diagnostics GmbH, Marburg, Germany) and Freelite assays (The Binding Site Ltd., Birmingham) performed on Behring Nephelometer II (Siemens Healthcare Diagnostics GmbH, Germany) IFE: Agarose gel (Helena Laboratories, Beaumont, USA)	Discordance between SIFE and SFLC: 17.8% (N latex assay), 17.2% (Freelite assay)	Essential to perform SIFE with SFLC to detect M-protein in cases with very low M-protein levels, CKD, polyclonal gammopathy, biclonal gammopathy, IgM-type monoclonal gammopathy
4	Li et al (2015)	China	No. of patients = 16	SPEP: Sebia Hydragel 15 protein kit (Sebia, Lisses, France); SIFE: Sebia Hydragel 4 Immunofixation PE kit on Hydrasys system (Sebia, Lisses, France);SFLC: Immunonephelometry (Freelite, Binding Site Ltd, Birmingham)Tests were performed on Beckman Coulter Immage 800 (Beckman Coulter, Brea, CA)	50% patients with positive SIFE but normal SFLC	IFE is more sensitive than SPEP and SFLC assay in detection of relapse
5	Singh (2017)	USA	No. of patients = 468 (values available = 2,409)	SPEP: Agarose gel electrophoresis using Helena SPIFE 3000 system SFLC: Siemens ADVIA 2400 instrument, using Freelite kits and reagents from the Binding Site	Concordance rate of electrophoretic method greater than for SFLC ratio ($p << 0.00001$) Discordant rate of SPEP/SIFE:0.58% Discordance rate for SFLC ratio: 3.3%	Electrophoretic tests are superior to SFLC ratio in diagnosis and monitoring of MG Nonconcordant observations in SFLC had detectable monoclonal proteins by electrophoretic method Nonconcordance rate was nearly twice as good for electrophoretic methods compared to SFLC ratio
6	Kuriakose et al (2019)	India	No. of patients = 46	SPEP: Agarose gel zone electrophoresis on Interlab Genios fully automated Machine	19% discordance between SIFE and SFLC	Combination of SPEP, SIFE, and SFLC has more diagnostic potential in the identification

(*Continued*)

Table 4 (*Continued*)

Serial no.	Authors	Country	Cohort	Methodology	Results	Conclusion
				SIFE: Interlab Genios fully automated machine SFLC: Immunoturbidimetry on Beckman Coulter AU 2700 analyzer		of MG than in isolation Sensitivity, specificity, positive, and NPV of SIFE with respect to SFLC were 81.3, 78.6, 89.7, and 64.7%, respectively Accuracy of SIFE came to be 80% compared to SFLC
7	Current study (2022)	India	No. of patients = 377 (values available = 450)	SPEP: serum protein 6 band gel by Helena biosciences (SAS-1 SP-24 SB kit) SIFE: gel-based electrophoresis kit by Helena biosciences (SAS-1 IFE-4 kit) SFLC: Turbidimetry using Optilite Freelite Kappa and Lambda Free Kit by The Binding Site group	28.7% values had discordance between SIFE and SFLC ratios More follow-up cases with normal SFLC ratio but positive SIFE than abnormal SFLC ratio and negative SIFE	Normal SFLC ratio alone cannot exclude residual disease as defined conventionally by positive SIFE

Abbreviations: CKD, chronic kidney disease; Ig, immunoglobulin; SFLC, serum free light chain; SIFE, serum immunofixation electrophoresis; SPEP, serum protein electrophoresis.

cell transplantation contributing to unexpected results.[20] Thus, it can be concurred, that SFLC ratio does not always score above SIFE for diagnosis and monitoring in a subset of MM patients.[2–4,12,15–17]

For any suspected case, an abnormal SFLC ratio must be confirmed by electrophoretic studies. An electrophoretic evidence of M protein is a reliable diagnostic marker of MM. However, a substantial rate of false negative SFLC ratio, in patients with detectible M protein argues against using it as the only modality for guiding evaluation of MM, especially in follow-up phase. Furthermore, serial measurements of SFLC ratio are only appropriate and reliable when read in parallel with SIFE or bone marrow findings.[2] Several studies have upheld the use of combination or sequential tests for accurate diagnosis owing to the discrepant results of SFLC vis-a-vis electrophoresis.[3,17,21–23,25,26] In the current study, we encountered 28.9% discordance between SIFE and SFLC results. Since normal SFLC ratio heralds an impending negative SIFE, we propose a more practical laboratory-based approach to follow-up MM patients. All old cases of MM may be followed up with SFLC measurement. After attaining normal SFLC ratio, further follow-up should be done with SIFE and that may be considered as the actual, deepest response to therapy. This algorithm will help in optimizing the available resources in the laboratory in the best possible manner. Furthermore, few authors have reported SIFE to be more sensitive and useful than SFLC for detection of residual disease.[16] By adopting this algorithm, we can optimize the utilization of the tests and resources as well.[23]

However, in this laboratory-based study, long-term follow-up was not available due to limited study time period. Also, the cohort comprising of light chain multiple myeloma patients was small.

Conclusion

The current study denotes that normal SFLC ratio cannot exclude residual disease as defined conventionally by positive SIFE. Larger studies are needed to explore the temporal relation between normalization of SFLC ratio and serum/urine M protein clearance.

Authors' Contribution

All authors contributed equally in the study , conception, acquition of data for the research.

Conflict of Interest

None declared.

References

1 Rajkumar SV. Updated diagnostic criteria and staging system for multiple myeloma. Am Soc Clin Oncol Educ Book 2016;35: e418–e423
2 Singh G. Serum free light chain assay and κ/λ ratio: performance in patients with monoclonal gammopathy-high false negative rate for κ/λ ratio. J Clin Med Res 2017;9(01):46–57
3 Kuriakose E, Narayanan Unni Cheppayil S, Kuzhikandathil Narayanan S, Vasudevan A. A study on free light chain assay and

serum immunofixation electrophoresis for the diagnosis of monoclonal gammopathies. Indian J Clin Biochem 2019;34(01): 76–81
4 Jaskowski TD, Litwin CM, Hill HR. Detection of kappa and lambda light chain monoclonal proteins in human serum: automated immunoassay versus immunofixation electrophoresis. Clin Vaccine Immunol 2006;13(02):277–280
5 Singhal S, Vickrey E, Krishnamurthy J, Singh V, Allen S, Mehta J. The relationship between the serum free light chain assay and serum immunofixation electrophoresis, and the definition of concordant and discordant free light chain ratios. Blood 2009; 114(01):38–39
6 Durie BG, Harousseau JL, Miguel JS, et al; International Myeloma Working Group. International uniform response criteria for multiple myeloma. Leukemia 2006;20(09):1467–1473
7 Cedena MT, Martin-Clavero E, Wong S, et al. The clinical significance of stringent complete response in multiple myeloma is surpassed by minimal residual disease measurements. PLoS One 2020;15(08):e0237155
8 Bertamini L, D'Agostino M, Gay F. MRD assessment in multiple myeloma: progress and challenges. Curr Hematol Malig Rep 2021; 16(02):162–171
9 Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol 2016;17(08):e328–e346
10 Manasanch EE. What to do with minimal residual disease testing in myeloma. Hematology (Am Soc Hematol Educ Program) 2019; 2019(01):137–141
11 Cawley LP, Minard BJ, Tourtellotte WW, Ma BI, Chelle C. Immunofixation electrophoretic techniques applied to identification of proteins in serum and cerebrospinal fluid. Clin Chem 1976;22 (08):1262–1268
12 Optilite® Freelite® Kappa Free Kit. Birmingham, United Kingdom: The Binding Site Group Ltd.; 2018
13 Hoedemakers RM, Pruijt JF, Hol S, et al. Clinical comparison of new monoclonal antibody-based nephelometric assays for free light chain kappa and lambda to polyclonal antibody-based assays and immunofixation electrophoresis. Clin Chem Lab Med 2011;50 (03):489–495
14 Shah NN, Nooka AK, Harvey D, et al. Using serum free light chain (SFLC) ratio and serum protein electrophoresis (SPEP) as a substitute for 24-hour urine studies in myeloma patients. Blood 2013;122(21):5358
15 Beaumont-Epinette MP, Moreau C, Besnard S, et al. Heavy/light chain specific immunoglobulin ratios provides no additional information than serum proteins electrophoresis and immunofixation for the diagnosis and the follow-up of intact immunoglobulin multiple myeloma patients. Pathol Biol (Paris) 2015;63 (4-5):215–221
16 Kim HS, Kim HS, Shin KS, et al. Clinical comparisons of two free light chain assays to immunofixation electrophoresis for detecting monoclonal gammopathy. BioMed Res Int 2014;2014:647238
17 Li W, Zhou JZ, Chang HR, et al. Comparison of SPE, IFE, and FLC in monitoring patients with multiple myeloma after autologous stem cell transplantation. Cell Biochem Biophys 2015;73(03): 643–647
18 Wood PB, McElroy YG, Stone MJ. Comparison of serum immunofixation electrophoresis and free light chain assays in the detection of monoclonal gammopathies. Clin Lymphoma Myeloma Leuk 2010;10(04):278–280
19 Shaheen SP, Levinson SS. Serum free light chain analysis may miss monoclonal light chains that urine immunofixation electrophoreses would detect. Clin Chim Acta 2009;406(1-2):162–166
20 Ramasamy I. Serum free light chain analysis in B-cell dyscrasias. Ann Clin Lab Sci 2007;37(03):291–294
21 Böer K, Deufel T. Quantitation of serum free light chains does not compensate for serum immunofixation only when screening for monoclonal gammopathies. Clin Chem Lab Med 2009;47(09): 1109–1115
22 Bhole MV, Sadler R, Ramasamy K. Serum-free light-chain assay: clinical utility and limitations. Ann Clin Biochem 2014;51(Pt 5):528–542
23 Heaton C, Vyas SG, Singh G. Audit of use and overuse of serum protein immunofixation electrophoresis and serum free light chain assay in tertiary health care: a case for algorithmic testing to optimize laboratory utilization. Am J Clin Pathol 2016;145(04):531–537
24 Udd KA, Spektor TM, Berenson JR. Monitoring multiple myeloma. Clin Adv Hematol Oncol 2017;15(12):951–961
25 Habib K. Comparison of serum immunoglobulin free light chains assay and serum immunofixation electrophoresis in patient transplanted for multiple myeloma. Haematol Int J. 2020;4(01): 000152
26 Lee WS, Singh G. Serum free light chain assay in monoclonal gammopathic manifestations. Lab Med 2019;50(04):381–389
27 Singh G. Serum free light chain assay and κ/λ ratio performance in patients without monoclonal gammopathies: high false-positive rate. Am J Clin Pathol 2016;146(02):207–214

