Glomerular Filtration Rate Estimates Based on Serum Creatinine Level in Healthy People

Conventional Jaffe Method versus Calibrated Jaffe Method at Laboratories in Rasht

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Conventional Jaffe method of serum creatinine measurement is influenced by several drugs and components of blood as well as the expertise of laboratory staffs. We obtained blood samples of 22 healthy volunteers and sent them to 23 laboratories in Rasht, Iran, in which the conventional Jaffe method would be used for serum creatinine measurement. Also, we tested the samples in 1 reference laboratory with the calibrated Jaffe method. Glomerular filtration rates were calculated using the abbreviated equation of the Modification of Diet in Renal Disease study. Eight of 23 laboratories (34.7%) reported significantly different mean serum creatinine levels from the mean values yielded in the reference laboratory. Seven of 23 laboratories (30.4%) had significantly different estimated glomerular filtration rates in comparison to those calculated in the reference laboratory. Different results for creatinine lead to wrong interpretation of patients' kidney function, and rectifications of this divergence are of utmost importance.

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Since a precise estimation of glomerular filtration rate (GFR) is critical, a veracious serum creatinine measurement would be mandatory.[1,2] Conventional methods to quantify serum creatinine level are the Jaffe method and enzymatic methods. In conventional Jaffe method, quantifying serum creatinine level is based on the reaction between creatinine and picric acid in alkaline environment and changing into orange color, which is supported by spectrophotometer measurement in 500-nm wave length. Creatinine level measurement by this method is not passably accurate because of the reaction between picric acid and some substances in blood such as glucose, protein, bilirubin, and drugs like cimetidine, cephalosporin.[3-5] On the other hand, enzymatic methods are precise but expensive. Replacing conventional Jaffe by calibrated Jaffe method which is more accurate and not expensive is more beneficial to increase accuracy of serum creatinine level measurement. In this study, we compared conventional Jaffe method used in the laboratories of Rasht, Iran, for measurement of serum creatinine level and GFR calculation with the results of calibrated Jaffe method done in the city's reference laboratory.

We collected blood samples from 22 volunteers (11 women and 11 men). They were medical students aged between 24 to 27 years. Their weight was between 60 kg and 80 kg for men and 50 kg and 70 kg for women. The participants did not have any past medical history of any specific diseases or kidney disorders. Plasma of the blood samples were separated and stored at -20°C. Every person's plasma sample (15 mL) was divided into 24 parts (0.4 mL) and to be sent to 23 laboratories and 1 reference laboratory of Rasht, all in one day. One

sample was left in the reference laboratory in order to quantify serum creatinine level using calibrated Jaffe method (Pars Azmoon, Tehran, Iran) read by Hitachi 704 autoanalyzer (Hitachi, Tokyo, Japan). In the calibrated Jaffe method, we adjusted the reader machine with control and standard serum samples for each of the 22 collected serum samples. The other laboratories used the conventional Jaffe method. Based on the measured serum creatinine levels, the GFR was calculated using the abbreviated equation of the *Modification of Diet in Renal Disease* study.[1,6] Serum creatinine levels and GFRs measured at each laboratory were demonstrated as mean ± standard deviation. Results of the 23 laboratories were compared with those reported by the reference laboratory using the sign test and the kappa statistics. For data analyses, the SPSS version 15.0 was used and a *P* value less than .05 was considered significant. The mean serum creatinine level of the participants was 0.872 ± 0.208 mg/dL based on the results at the reference laboratory. The mean values in 8 of 23 other laboratories (34.7%) were significantly different from those of the reference laboratory (Table 1 and Figure 1). Regarding the estimated GFRs, the mean value yielded at the reference laboratory was 104.0 ± 25.0 mL/min/1.73 m^2, compared to which the GFRs at 7 of 23 laboratories (30.4%) were significantly different (Table 2 and Figure 2).

Reliable serum creatinine measurements for GFR estimation and understanding factors that may affect creatinine measurement is critical for laboratory experts worldwide to increase the diagnosis accuracy of patients with chronic kidney disease. The laboratory working group of the National Kidney Disease Education Program, in collaboration with international professional organizations, has developed a plan that enables standardization and improved accuracy of serum creatinine measurements in clinical laboratories worldwide.[7]

Several studies have compared enzymatic and Jaffe methods for serum creatinine level measurement. Apple and colleagues concluded that enzymatic methods are more precise for GFR

Table 1. Mean Serum Creatinine Levels of 22 Participants Measured at 23 Laboratories and Their Mean Differences With Those of Reference Laboratory

Laboratory	Creatinine Level, mg/dL	Difference, mg/dL	*P*
1	0.93 ± 0.04	0.064 ± 0.035	.08
2	0.98 ± 0.03	0.100 ± 0.039	.01
3	0.91 ± 0.03	0.043 ± 0.023	.07
4	0.88 ± 0.03	0.012 ± 0.015	.43
5	0.98 ± 0.05	0.114 ± 0.036	.006
6	0.86 ± 0.03	-0.008 ± 0.029	.77
7	0.90 ± 0.03	0.032 ± 0.023	.18
8	0.88 ± 0.04	0.012 ± 0.018	.50
9	0.83 ± 0.04	-0.033 ± 0.034	.35
10	0.93 ± 0.04	0.064 ± 0.021	.006
11	0.87 ± 0.03	0.000 ± 0.027	.99
12	0.86 ± 0.05	-0.012 ± 0.060	.84
13	0.97 ± 0.04	0.102 ± 0.028	.002
14	0.51 ± 0.04	-0.355 ± 0.072	< .001
15	0.66 ± 0.05	-0.204 ± 0.040	< .001
16	0.90 ± 0.05	0.027 ± 0.043	.53
17	0.92 ± 0.04	0.051 ± 0.019	.02
18	0.89 ± 0.03	0.025 ± 0.021	.24
19	0.89 ± 0.03	0.022 ± 0.016	.18
20	0.89 ± 0.04	0.019 ± 0.032	.55
21	0.68 ± 0.05	-0.191 ± 0.068	.01
22	0.88 ± 0.04	0.010 ± 0.030	.75
23	0.91 ± 0.04	0.045 ± 0.032	.17

Table 2. Mean Glomerular Filtration Rate (GFR) Estimated Based on Serum Creatinine Levels of 22 Participants Measured at 23 Laboratories and Their Mean Differences With Those of Reference Laboratory*

Laboratory	GFR, mL/min/1.73 m^2	Difference, mL/min/1.73 m^2	*P*
1	93.23 ± 3.25	-10.45 ± 5.67	.08
2	88.45 ± 3.99	-15.22 ± 6.31	.03
3	94.77 ± 2.38	-8.90 ± 4.42	.06
4	99.22 ± 2.77	-4.45 ± 3.82	.26
5	91.22 ± 4.91	-12.45 ± 4.58	.01
6	103.09 ± 4.34	-.59 ± 5.31	.91
7	96.90 ± 3.00	-6.77 ± 3.95	.10
8	99.81 ± 3.22	-3.86 ± 4.10	.36
9	107.95 ± 5.16	4.27 ± 6.28	.50
10	93.13 ± 3.53	-10.54 ± 4.65	.03
11	100.45 ± 2.70	-3.22 ± 4.88	.52
12	110.22 ± 7.33	6.54 ± 8.56	.45
13	89.18 ± 3.13	-14.50 ± 4.95	.008
14	212.27 ± 20.78	108.59 ± 23.32	< .001
15	151.86 ± 12.41	48.18 ± 10.44	< .001
16	103.90 ± 7.80	0.22 ± 8.54	.98
17	95.81 ± 4.09	-7.86 ± 4.60	.10
18	97.31 ± 2.82	-6.36 ± 3.99	.13
19	97.77 ± 2.69	-5.90 ± 3.86	.14
20	99.13 ± 3.70	-4.54 ± 5.88	.45
21	159.50 ± 20.10	55.81 ± 22.48	.02
22	96.72 ± 3.22	-10.45 ± 5.67	.19
23	96.00 ± 3.47	-7.68 ± 4.87	.13

*The GFR was measured according to the abbreviated equation of the Modification of Diet in Renal Disease study.

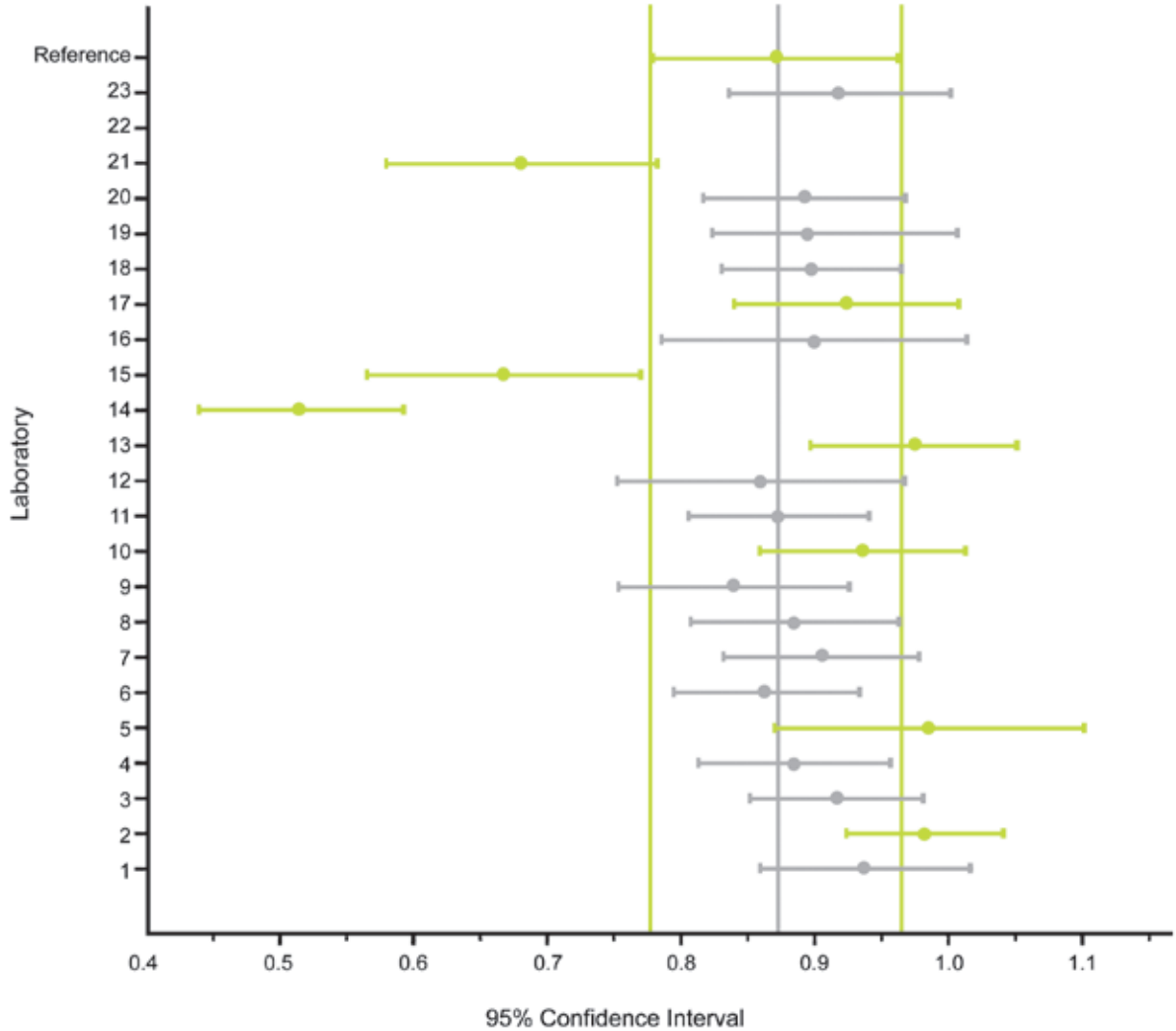

Figure 1. Comparison of mean values of serum creatinine levels at each laboratory with that in the reference laboratory. Green lines belong to the reference laboratory and those whose results were significantly different from that of the reference laboratory.

calculation, and recently, Vervoort and colleagues confirmed their results.[8,9] However, enzymatic methods are too expensive to be widely applied in practice. In this study, we showed the conventional Jaffe method for serum creatinine level measurement may present results variably different from those by the calibrated Jaffe method, which that is not more expensive than conventional method. Thus, we will have more realistic estimation of patients' kidney function.

The current variability in serum creatinine measurement renders all estimating equations for GFR, including the abbreviated equation of the Modification of Diet in Renal Disease study, less accurate in healthy individuals and slightly elevated in the those with impaired kidney function, making diagnosis of lower stages of chronic kidney disease inaccurate.[10] The interlaboratory creatinine measurement differences was also shown by Séronie-Vivien and colleagues who indicated that the discrepancies were too much to allow prediction of GFR or creatinine clearance based on serum creatinine level.[11] To elucidate the extent of this potential variability in serum creatinine measurements in Rasht, we did this study and found that 8 of 23 laboratories (34.7%) in the city had a mean serum creatinine level beyond 95% confidence interval of the reference laboratory results. This finding is fairly conceivable when GFR estimation is done. Seven of 23 laboratories of the city had a momentous difference in measurement of GFR using conventional Jaffe method in

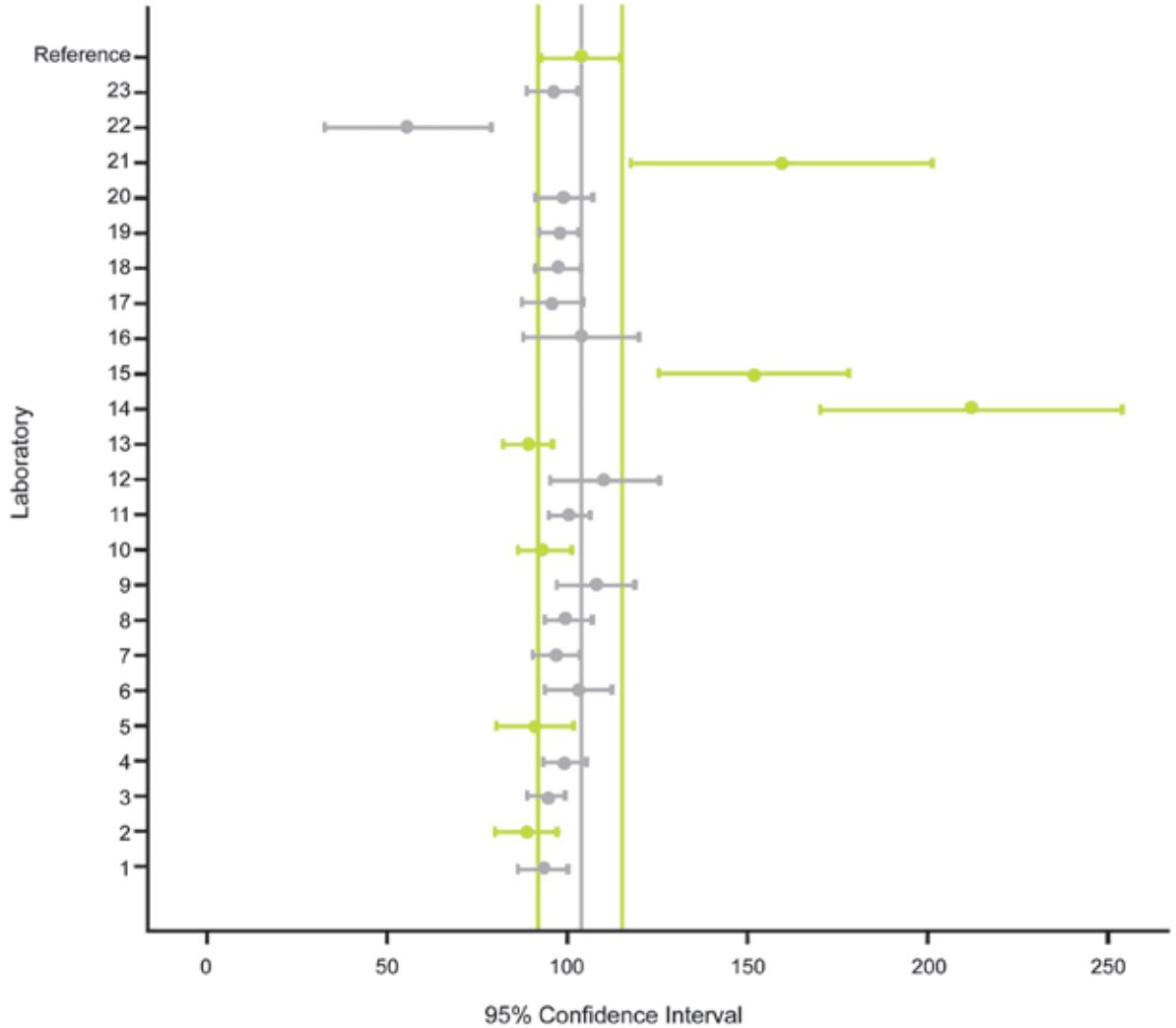

Figure 2. Comparison of mean values of glomerular filtration rates estimated based on serum creatinine levels measured at each laboratory with that in the reference laboratory. Green lines belong to the reference laboratory and those whose results were significantly different from that of the reference laboratory.

comparison to the estimated GFR using calibrated Jaffe method in the reference laboratory. Since GFR plays a fundamental role in the approach to the patients, minimizing errors in quantification of GFR would yield a more accurate GFR and a more realistic judgment about the patient's kidney function.

The participants of this study were selected from among healthy people, and if these results were for patients, it would give rise to negligence of patients' disease, and then, it would lead to more unnecessary spending of money for extra diagnostic procedures and spare treatment. This amount of laboratory errors in measurement of serum creatinine level will reduce the reliability for physicians to decide on the treatment modalities. Whereas, with some changes like removing interferential factors in serum creatinine level and calibration of laboratory kits of the Jaffe method, the results will be more exact and true. Rectifications of these divergent laboratory results are very important , and in order to achieve this goal, our laboratories should apply novel and more precise methods in assessing patients' kidney function and aged methods like the Jaffe method in creatinine measurement must be substituted with methods like enzymatic method.

CONFLICT OF INTEREST

None declared.

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