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ORIGINAL ARTICLE

Effect of Virus Inactivation by Heating on Routine Clinical Laboratory Indicators in Serum

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SUMMARY

Background: **Highly infectious viruses such as SARS-CoV-2, MERS-CoV, and Ebola virus represent a threat to clinical laboratory workers. We aimed to investigate how virus inactivation by heating at 60°C for 1 hour affects routine clinical laboratory indicators.**
Methods: **Each collected serum sample was separated into two aliquots, and various indicators were measured in first aliquot after inactivation by heating at 60°C for 1 hour and in the second after room-temperature incubation for 1 hour.**
Results: **Serological test results for 36 indicators remained mostly unaffected by heat inactivation, with a mean estimated bias of < 10%. By contrast, the results for alanine transaminase, pseudocholinesterase, creatine kinase, lactate dehydrogenase, cardiac troponin I, and myoglobin were affected by heat inactivation, with the mean estimated bias here being > 20%, which was further increased in the case of the results for alkaline phosphatase, lipase, and creatine kinase isoenzyme MB. Immunological serological measurements showed good agreement according to Kappa consistency checks after heat inactivation of serum. The results for alanine transaminase, pseudocholinesterase, creatine kinase, lactate dehydrogenase, cardiac troponin I, and myoglobin were significantly correlated (r > 0.95) after heat inactivation, and after correction by using a regression equation, the results for the indicators still retained a clinical reference value.**
Conclusions: **Inactivation by heating at 60°C for 1 hour exerts no marked effect on numerous routine biochemical and immunological indicators in serum, but the detection values for certain items are significantly decreased. Our method could serve as reference strategy for routine serological diagnostics in patients with suspected or confirmed infection with highly pathogenic viruses.**
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Supplementary Tables and Figures

Table S1. Statistical description of 53 biochemical and immunological serological tests between non-inactivation and inactivation group.

	Statistical description					Percentage deviation (%)	Between-run CV (%)		CAP evaluation criteria
	Baseline values	n	Non-inactivation	Inactivation	p-value		Low level	High level	
Enzymatic activity indicators									
Alanine transaminase	3.00 - 224.00 IU/L	10	20.50 (7.75, 92.25)	12.50 (5.75, 32.5)	0.014	-66.67 - 66.67	5.04	3.47	± 20%
Aspartate transaminase	9.00 - 100.00 IU/L	10	23.50 (13.75, 53.50)	22.5 (10.75, 53.75)	0.040	-75.00 - 22.22	3.59	2.57	± 20%
Gamma-glutamyl transpeptidase	7.00 - 126.00 U/L	10	19.00 (8.75, 59.75)	15.50 (9, 48.75)	0.036	-31.58 - 28.57	1.69	1.34	± 3SD
Alkaline Phosphatase	29.00 - 192.00 U/L	10	87.6 ± 55.51	6.20 ± 3.39	0.001	-94.40 - -77.78	3.09	2.77	± 30%
Pseudocholinesterase	2.63 - 12.39 KU/L	10	6.23 ± 2.89	4.18 ± 2.51	< 0.001	-59.70 - -16.86	3.51	2.14	± 30%
Creatine Kinase	12.00 - 2437.00 IU/L	10	96.00 (27.00, 412.25)	3.00 (2.00, 8.50)	0.005	-99.47 - 83.33	1.89	1.78	± 30%
Lactate Dehydrogenase	102.00 - 528.00 IU/L	10	183.00 (117.75, 370.25)	149.00 (91.25, 324.75)	0.005	-41.32 - -10.06	2.15	1.92	± 20%
Amylase	15.00 - 1813.00 U/L	10	54.50 (29.50, 431.25)	53.50 (28.75, 388.75)	0.007	-11.73 - 0.00	2.91	2.45	± 30%
Lipase	2.40 - 722.00 U/L	10	21.50 (11.00, 87.00)	9.00 (4.50, 11.00)	0.011	-98.20 - 40.00	6.55	4.00	± 30%
Protein and ion indicators									
Protein, Total	49.60 - 91.70 g/L	10	72.24 ± 13.47	70.49 ± 11.90	0.147	-10.47 - 3.12	1.95	2.09	± 10%
Albumin	27.60 - 47.00 g/L	10	40.57 ± 6.58	40.85 ± 6.62	0.272	-1.50 - 3.57	2.47	2.03	± 10%
Prealbumin	52.00 - 402.00 mg/L	10	235.6 ± 101.09	230.6 ± 97.15	0.239	-7.99 - 42.31	1.78	2.44	NA
Total bile acid	0.62 - 24.05 μmol/L	10	5.46 (2.46, 11.40)	5.13 (2.55, 11.08)	0.878	-9.76 - 26.66	6.81	6.40	NA
Bilirubin, Total	7.70 - 174.30 μmol/L	10	36.1 (11.55, 50.1)	35.4 (11.78, 50.48)	0.444	-5.76 - 3.23	2.42	2.51	± 0.4 mg/dL or 20%
Bilirubin, Direct	2.30 - 28.00 μmol/L	10	4.65 (3.48, 11.48)	4.45 (3.58, 10.08)	0.135	-15.71 - 4.35	2.62	3.21	± 0.4 mg/dL or 20%
Carbon dioxide	20.40 - 33.43 mmol/L	10	25.71 ± 3.79	24.54 ± 4.21	0.048	-13.80 - 2.98	4.83	4.34	± 3SD
Creatinine	34.00 - 639.00 μmol/L	10	61.00 (50.00, 238.50)	61.50 (50.50, 244.75)	0.031	-2.00 - 3.33	2.71	1.78	± 0.3 mg/dL or 15%
Glucose	3.55 - 18.50 mmol/L	10	4.95 (4.31, 10.14)	4.87 (4.42, 10.18)	0.109	-3.86~2.91	2.20	2.16	± 6.0 mg/dL or 10%
Urea	1.71 - 23.74 mmol/L	10	8.24 ± 6.97	8.27 ± 7.00	0.173	-0.92~2.26	2.21	2.61	± 2.0 mg/dL or 9%
Uric Acid	127.00 - 606.00 μmol/L	10	316.00 ± 173.04	317.40 ± 175.92	0.285	-2.15 - 1.29	2.91	2.57	± 17%
Beta-hydroxybutyric acid	0.03 - 0.57 mmol/L	10	0.18 (0.04, 0.49)	0.16 (0.04, 0.51)	0.064	-33.33 - 8.33	5.88	2.21	NA
Sodium	132.60 - 166.60 mmol/L	10	144.99 ± 11.8	144.78 ± 10.97	0.709	-2.90 - 1.18	0.78	0.80	± 4.0 mmol/L

Table S1. Statistical description of 53 biochemical and immunological serological tests between non-inactivation and inactivation group (continued).

	Statistical description					Percentage deviation (%)	Between-run CV (%)		CAP evaluation criteria
	Baseline values	n	Non-inactivation	Inactivation	p-value		Low level	High level	
Potassium	3.11 - 6.33 mmol/L	10	4.44 ± 1.09	4.47 ± 1.10	0.015	-0.26 - 1.73	0.84	0.89	± 0.5 mg/Dl
Chloride	92.50 - 126.90 mmol/L	10	106.84 ± 11.34	106.64 ± 10.96	0.666	-3.12 - 1.49	0.78	0.81	± 5%
Calcium	1.66 - 3.04 mmol/L	10	2.30 ± 0.41	2.26 ± 0.39	0.028	-4.49 - 1.18	1.91	2.01	± 1.0 mg/dL
Phosphorus	0.49 - 4.80 mmol/L	10	1.12 (0.72, 1.71)	1.16 (0.71, 1.62)	0.798	-7.19 - 10.20	3.20	2.24	± 0.3 mg/dL or 10.7%
Magnesium	0.59 - 1.30 mmol/L	10	0.90 ± 0.23	0.91 ± 0.22	0.309	-2.67 - 5.63	2.82	2.46	± 25%
Lipid indicators									
Triglyceride	0.39 - 6.81 mmol/L	10	1.11 (0.58, 2.55)	1.11 (0.60, 2.58)	0.288	-2.06 - 15.38	1.18	1.28	± 25%
HDL Cholesterol	0.71 - 2.12 mmol/L	10	1.36 ± 0.49	1.30 ± 0.54	0.039	-23.38 - 2.11	2.19	2.64	± 30%
LDL Cholesterol	1.70 - 4.99 mmol/L	10	3.15 ± 1.22	3.12 ± 1.19	0.248	-2.94 - 3.41	4.22	4.78	± 30%
Cholesterol	1.54 - 6.75 mmol/L	10	4.22 ± 2.04	4.28 ± 2.07	0.032	-0.67 - 3.00	1.49	1.90	± 10%
Inflammatory indicators									
C-Reactive Protein	0.79 - 175.23 mg/L	10	4.27 (1.03, 38.23)	4.24 (1.06, 38.42)	0.374	-2.25 -3.88	5.07	5.07	± 3 SD
Procalcitonin	0.05 - 4.74 ng/mL	10	0.18 (0.06, 0.93)	0.17 (0.04, 0.94)	0.080	-46.94 - 6.98	4.37	3.29	NA
Interleukin-6	2.16 - 222.12 pg/mL	10	60.18 (11.68, 112.06)	34.89 (11.14, 94.87)	0.013	-64.93 - 0.40	2.11	4.38	NA
Myocardial injury indicators									
B-type natriuretic peptides	3.00 - 1219.00 ng/L	10	197.50 (36.75, 268.50)	172.50 (48.5, 219)	0.037	-29.85 - 35.56	2.70	3.43	± 3 SD or 10%
Cardiac troponin I	0.01 - 7.88 ug/L	10	0.07 (0.03, 0.53)	0.06 (0.03, 0.23)	0.049	-65.00 - 3.33	4.20	3.81	NA
Myoglobin	11.9 - 611.9 ug/L	10	23.95 (14.30, 113.63)	21.55 (10.38, 93.53)	0.005	-58.39 - -6.63	3.79	3.14	NA
Creatine kinase isoenzyme MB	0.40 - 78.00 ug/L	10	1.60 (0.40, 11.90)	0.05 (0.00, 0.10)	0.005	-99.87 - -100.00	3.15	3.04	NA
Thyroid function indicators									
Thyroid Stimulating Hormone	1.26 - 8.17 mU/L	10	4.01 ± 2.49	3.83 ± 2.52	0.023	-13.53 - 0.75	3.46	4.94	± 3 SD
Triiodothyronine (T3 Total)	0.50 - 3.21 nmol/L	10	1.70 ± 0.75	1.58 ± 0.66	0.024	-14.44 -16.00	3.97	5.23	± 3 SD
Thyroxine, Total (T4 Total)	80.30 - 168.17 nmol/L	10	122.7 ± 28.27	131.93 ± 29.83	0.003	0.96 - 16.87	3.96	3.28	± 1.0 µg/dL or 20%
Triiodothyronine Free (T3 Free)	2.57 - 7.87 pmol/L	10	5.22 ± 1.35	5.60 ± 1.38	0.083	-7.99 - 21.29	3.22	3.02	± 3 SD
Thyroxine, Free (T4 Free)	3.46 - 20.13 pmol/L	10	10.53 ± 4.63	12.39 ± 5.54	< 0.001	-6.07 - 23.85	6.32	6.69	± 3 SD

Table S1. Statistical description of 53 biochemical and immunological serological tests between non-inactivation and inactivation group (continued).

	Statistical description					Percentage deviation (%)	Between-run CV (%)		CAP evaluation criteria
	Baseline values	n	Non-inactivation	Inactivation	p-value		Low level	High level	
Immune indicators									
Anti-HBs	< 2.00 - 597.60 mIU/mL	10	8.37 (< 2.00, 108.62)	9.13 (< 2.00, 93.17)	0.138	-31.03 - 10.32	4.10	NA	NA
HBsAg	0.46 - 5801.00 S/CO	10	80.88 (0.58, 3310.25)	92.55 (0.59, 3237.00)	0.541	-9.02 - 14.46	6.25	NA	NA
Anti-Hbe	0.00 - 1.61 S/CO	10	1.00 (0.00, 1.42)	0.91 (0.00, 1.42)	0.498	-14.48 - 2.40	7.46	NA	NA
HBeAg	0.09 - 1417 S/CO	10	67.11 (0.10, 1376.25)	46.32 (0.11, 1071.50)	0.016	-35.29 - 3.03	7.46	NA	NA
Anti-HBc	0.01 - 3.34 S/CO	10	0.69 (0.01, 3.14)	0.67 (0.01, 3.2)	0.400	-7.69 - 4.11	6.60	NA	NA
Anti-HCV	0.03 - 105.30 S/CO	10	1.24 (0.04, 33.81)	1.08 (0.03, 37.88)	0.241	-27.03 - 28.39	4.44	NA	NA
Anti-HIV-1/2 Antibody, HIV-1 p24 Antigen	0.07 - 0.28 S/CO	10	0.14 ± 0.06	0.22 ± 0.06	0.005	3.57 - 120.16	4.11	2.83	NA
Syphilitic specific antibody	0.06 - 166.60 S/CO	10	17.23 (0.06, 71.42)	16.57 (0.06, 69.77)	0.386	-6.56 - 43.48	5.10	NA	NA
SARS-CoV-2 IgM	0.22-19.99 S/CO	10	4.77 (0.22, 8.08)	4.04 (0.19, 7.43)	0.005	-0.18 - -0.03	7.84	7.74	NA
SARS-CoV-2 IgG	0.14-39.03 S/CO	10	6.33 (0.30, 15.23)	6.39 (0.31, 13.52)	0.059	-0.14 -0.04	10.68	7.49	NA

CV - coefficient of variation, S/CO - signal-to cutoff ratio, HIV - human immunodeficiency virus, HCV - hepatitis C virus, HBV - hepatitis B virus, Ag - antigen, Ab - antibody, SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2, NA - not available.