한국 노인의 임상 화학 검사치에 관한 단일기관 연구

서 보 영[1] · 함 지 연[1] · 김 유 경[2] · 송 정 흡[3] · 송 경 은[1*] | [1]경북대학교 의학전문대학원 임상병리학교실, [2]영남대학교 의과대학 진단검사의학교실, [3]경북대학교병원 산업의학과

Clinical chemistry values in elderly Korean people: single institutional study

Bo-Young Seo, MD[1] · **Ji Yeon Ham, MD**[1] · **Yu Kyung Kim, MD**[2] · **Jung Hup Song, MD**[3] · **Kyung Eun Song, MD**[1*]

[1]Department of Clinical Pathology, Kyungpook National University School of Medicine, [2]Department of Laboratory Medicine, Yeungnam University College of Medicine, [3]Department of Occupational Medicine, Kyungpook National University Hospital, Daegu, Korea

*Corresponding author: Kyung Eun Song, E-mail: kesong@knu.ac.kr

Laboratory values change with age and interpreting laboratory results from elderly people using the reference intervals for younger adults may not be appropriate. The authors investigated the distribution patterns of routine chemistry values from elderly people to determine whether current reference intervals are also valid for elderly people. A total of 1,215 persons older than 65 years and 1,827 healthy adults below 65 years of age were evaluated. Blood samples were collected after an overnight fast and analyzed for chemistry tests. Computing the central 95th percentile showed that the total protein, albumin, ALP, LD, creatinine, uric acid, triglyceride, HDL-cholesterol, and electrolytes of elderly people were within the standard reference intervals used in our laboratory. For AST and ALT, the upper range of the central 95th percentile in the elderly population was found to be outside the common reference interval. However, the central 90th percentile values of AST and ALT were compatible with the common reference intervals. GGT, BUN, total cholesterol, LDL-cholesterol, and glucose showed higher values than the upper limits of the reference intervals. For common clinical chemistry tests, the common reference values in general should be applicable to elderly people, even though some parameters showed wider distributions in the elderly.

Keywords: Clinical chemistry tests; Reference values; Aged

Introduction

The population older than 65 years of the Korea was about 11.3% of the total population last year [1], and is expected to reach 24.3% and 38.2% in the year 2030 and 2050, respectively [2]. The proportion of elderly people to visit the hospital is increasing and laboratory tests are performed to screen them for many pathological conditions. The chemistry tests can be very important in diagnosis, especially for elderly people, in

Table 1. Analytical brief in clinical chemistry tests

Test item	Method	Unit
Total protein	Biuret method	g/dL
Albumin	Dye (BCG) binding method	g/dL
AST	IFCC without pyridoxal phosphate without sample blank	U/L
ALT	IFCC without pyridoxal phosphate without sample blank	U/L
ALP	PNPP/AMP buffer/IFCC	U/L
LD	UV method (pyruvate → lactate)	U/L
GGT	Szasz (γ-glutamyltransferase)	U/L
BUN	Urease with GLDH (coupledenzyme)	mg/dL
Creatinine	Jaffe method, kinetic colorimetric assay (ID–GC/MS, traceable)	mg/dL
Uric acid	Uricase method	mg/dL
Sodium	Ion selective electrode	mmol/L
Potassium	Ion selective electrode	mmol/L
Chloride	Ion selective electrode	mmol/L
Total cholesterol	Enzymetic colorimetric assay	mg/dL
Triglyceride	Enzymetic colorimetric assay	mg/dL
HDL–cholesterol	Homogenous enzymatic colorimetric assay	mg/dL
LDL–cholesterol	Homogenous enzymatic colorimetric assay	mg/dL

BCG, bromocresol green; AST, aspartate transaminase; IFCC, International Federation of Clinical Chemistry; ALT, alanine transaminase; ALP, alkaline phosphatase; PNPP/AMP, p-nitro-phenylphosphate/amino-methyl-propanol; LD, lactate dehydrogenase; UV, ultraviolet; GGT, gamma-glutamyl transpeptidase; BUN, blood urea nitrogen; GLDH, glutamate dehydrogenase; ID-GC/MS, isotope dilution gas chromatography–mass spectrometry; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

terns of routine chemistry values from elderly people to younger adults to investigate if chemistry values change with aging and if present reference intervals are also valid to elderly people.

Materials and methods

1. Populations

From January, 2009 till June, 2011, The 2,604 Korean individuals above 65 years of age were selected from the people attending general health check-ups at Kyungpook National University Hospital. They were screened by using a health questionnaire that contained questions about medical history, present illness, and present medication and excluded from the final diagnosis of cancer, hyperlipidemia, diabetes, cardiovascular disease, viral hepatitis, and any past history of confirmed disease such as stroke. And some subjects were also excluded because of strong suspicion of disease from their laboratory data [3,6]: C reactive protein >200 mg/dL, blood urea nitrogen (BUN) >42 mg/dL, creatinine >2.6 mg/dL, total proteins >90 g/dL, glucose >180 mg/dL. Finally, 1,215 elderly people (group I) then consisted of 1,003 persons (551 males and 452 females) for 65 to 74 years (group Ia) and 212 persons (110 males and 102 females) older than 75 years (group Ib). 1,827 younger healthy adults (982 males and 845 females) below 65 years of age (mean age, 52.8 years; range, 21 to 64 years) (group II) were also evaluated as a comparing group. The study was

whom clinical symptoms and signs are not typical or often absent even during an acute event. Common reference intervals are needed for adequate interpretation of these tests. Since many chemistry markers change with age and the current reference intervals are mostly based on a population in the age range from 20 to 50 years, however, interpreting laboratory results from elderly people by the reference intervals for younger adults may not be appropriate [3-5]. Defining a 'healthy' elderly population and collecting data from them are difficult because diabetes, cancer, cardiovascular diseases, and some types of medication are common in older people. Therefore, reports of laboratory reference values for elderly people are sparse in Korea.

In this study, authors compared the distribution pat-

Table 2. Comparison of clinical chemistry values in elderly people (group I) and young adults (group II)

Variable	Unit	Group I			Group II			P-value
		n	Mean	SE	n	Mean	SE	
Total protein	g/dL	1,216	7.52	0.01	1,827	7.51	0.01	0.661
Albumin	g/dL	1,216	4.47	0.01	1,827	4.47	0.01	0.722
AST	U/L	1,215	23.68	0.23	1,825	22.25	0.17	<0.0001
ALT	U/L	1,214	20.35	0.3	1,752	20.01	0.28	0.014
ALP	U/L	1,216	73.25	0.63	1,827	66.84	0.44	<0.0001
GGT	U/L	1,216	28.49	0.75	1,809	30.99	0.69	0.024
LD	U/L	217	387.2	4.08	1,192	355.56	1.74	<0.0001
Total cholesterol	mg/dL	1,138	189.85	0.87	1,753	187.42	0.7	0.021
HDL-cholesterol	mg/dL	1,216	53.64	0.38	1,827	54.61	0.32	0.038
LDL-cholesterol	mg/dL	1,106	111.62	0.77	1,648	113.29	0.61	0.155
Triglyceride	mg/dL	1,158	118.95	1.39	1,723	113.77	1.19	0.001
Total amylase	U/L	458	60.32	0.98	1,333	58.66	0.47	0.412
BUN	mg/dL	217	16.08	0.28	1,193	14.17	0.11	<0.0001
Creatinine	mg/dL	1,207	1	0	1,826	1	0	0.099
Uric acid	mg/dL	1,216	4.87	0.04	1,826	4.9	0.03	0.778
Serum glucose	mg/dL	1,116	97.03	0.32	1,740	95.32	0.25	<0.0001
Sodium	mmol/L	1,211	142.22	0.07	1,825	141.52	0.05	<0.0001
Potassium	mmol/L	1,211	4.23	0.01	1,825	4.31	0.01	<0.0001
Chloride	mmol/L	1,211	104.55	0.08	1,825	105.16	0.06	<0.0001

SE, standard error; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; LD, lactate dehydrogenase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BUN, blood urea nitrogen.

approved by the institutional review board of Kyung-pook National University Hospital and all the study participants gave written informed consent.

2. Methods

Blood samples were collected in BD Vacutainer SST (Becton Dickinson, San Jose, CA, USA) from a median cubital vein after an overnight fasting. Chemistry tests were performed on Modular Analytics (Roche Diagnostics, Mannheim, Germany). The analytic method and the reference range in our laboratory was presented (Table 1).

3. Statistics

PASW Statistics 18 ver. 18.0.0 (SPSS Inc., Chicago, IL, USA) was used for analysis. The distribution pattern was assessed using Kolmogorov-Smirnova test. Comparisons between groups were evaluated with Mann-Whitney test and Kruskal-Wallis test. Mean values, as well as the central 90th and 95th percentile, were calculated for all measurements in each group. The significance level was set at P, 0.05.

Results

Compared with young adults (group II), elderly

Table 3. Comparison of clinical chemistry values in 65- to 74-year-olds (group Ia), and ≥75-year-olds (group Ib)

Variable	Unit	Group I a			Group II b			P-value
		n	Mean	SE	n	Mean	SE	
Total protein	g/dL	212	7.5	0.04	1,003	7.52	0.02	0.572
Albumin	g/dL	212	4.37	0.22	1,003	4.49	0.01	<0.0001
AST	U/L	212	23.32	23.32	998	23.54	0.23	<0.0001
ALT	U/L	212	19.04	0.63	997	20.38	0.32	0.008
ALP	U/L	212	75.86	1.76	1,003	72.67	0.66	<0.00001
GGT	U/L	212	28.12	1.68	995	27.12	0.66	0.061
LD	U/L	37	381.24	7.19	176	384.31	4.31	<0.0001
Total cholesterol	mg/dL	204	187.84	2.21	934	190.29	0.94	0.037
HDL–cholesterol	mg/dL	212	54.56	0.93	1,003	53.46	0.41	0.056
LDL–cholesterol	mg/dL	197	108.99	1.92	908	112.19	0.83	0.1
Triglyceride	mg/dL	187	106.44	2.82	878	111.07	1.29	0.001
Total amylase	U/L	85	61.62	2.36	372	60.06	1.08	0.686
BUN	mg/dL	36	16.33	0.61	178	15.87	0.3	<0.00001
Creatinine	mg/dL	210	0.84	0.14	996	0.8	0.01	0.073
Uric acid	mg/dL	212	4.8	0.98	1,003	4.88	0.04	0.629
Serum glucose	mg/dL	187	96.84	0.82	928	97.06	0.35	<0.0001
Sodium	mmol/L	210	142.22	0.17	1,000	142.22	0.08	<0.0001
Potassium	mmol/L	210	4.27	0.03	1,000	4.22	0.01	<0.0001
Chloride	mmol/L	210	104.84	0.2	1,000	104.49	0.09	<0.0001

SE, standard error; AST, aspartate transaminase; ALT, alanine transaminase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; LD, lactate dehydrogenase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BUN, blood urea nitrogen.

people (group I) showed significant increases in aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), lactate dehydrogenase (LD), BUN, total cholesterol, triglyceride, and glucose, and significant decrease in high-density lipoprotein (HDL)-cholesterol (Table 2). Especially, AST, ALT, LD, total cholesterol, triglyceride, and glucose were increased with age when comparing group Ia with group Ib (Table 3). In spite of these significant differences between group I and group II, computing the central 95th percentile of group I showed that total protein, albumin, ALP, LD, creatinine, uric acid, triglyceride,

HDL-cholesterol, and electrolytes were within the common reference intervals which we generally use in our laboratory. For AST and ALT, the central 90th percentile values were compatible with the common reference intervals (Figure 1). GGT, BUN, total cholesterol, low-density lipoprotein (LDL)-cholesterol, and glucose showed higher upper 97.5th and even 95th percentile values than the upper limits of the common reference intervals (Figure 2).

Discussion

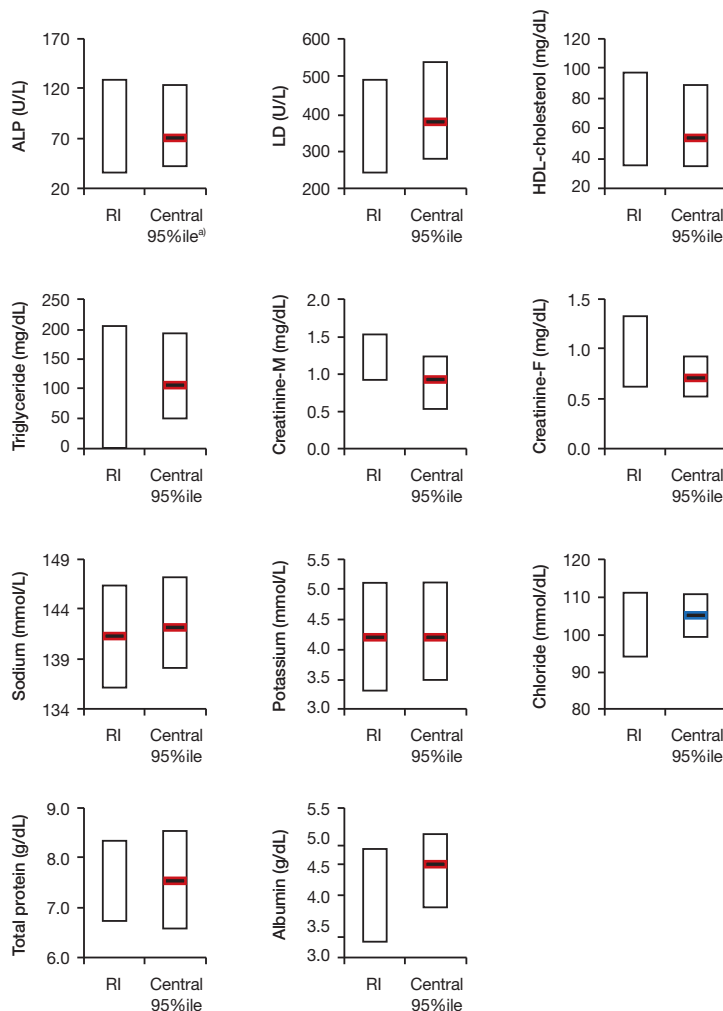Selection of an ideal reference population for the

Figure 1. Central 95th percentile of clinical chemistry values in elderly people. ALP, alkaline phosphatase; RI, common reference interval; LD, lactate dehydrogenase; HDL, high-density lipoprotein. [a]2.5 to 97.5 percentile in the age group I (65 years or above) of the research subjects. The upper and lower limits of the box are the 97.5 and 2.5 percentile and the horizontal bar is the median value (n=1,215).

age in this study was 65 years or older. As an argue could be present that the subjects analyzed in this study were not representative of an healthy elderly population, authors tried to reduce the deviation by excluding those with present illness and of strong suspicion of disease from their laboratory data mentioned above. Thus there is a need to establish certain criteria to define "healthy elderly population" before conducting a future research by increasing the number of object groups in liaison with a number of laboratories.

In this study, compared with young adults, elderly people had significant increases in AST, ALT, ALP, GGT, LD, BUN, total cholesterol, triglyceride, and glucose. However, the values of most of the parameters in elderly people were similar to the common reference intervals currently used. Yet, the limitation of this study is that the 12-hour fast of the subjects was not identified in the case of triglyceride.

For most liver enzymes, the significant increases were observed in the elderly people. This finding agrees with those reported by several investigators [8,10,11]. Tietz et al. [8], however, reported higher values in 60- to 90-year-old population than younger people and then decrease after 90 years old. Fulop et al. [12] found no changes of AST. In spite of some variations, their results obtained in elderly population were
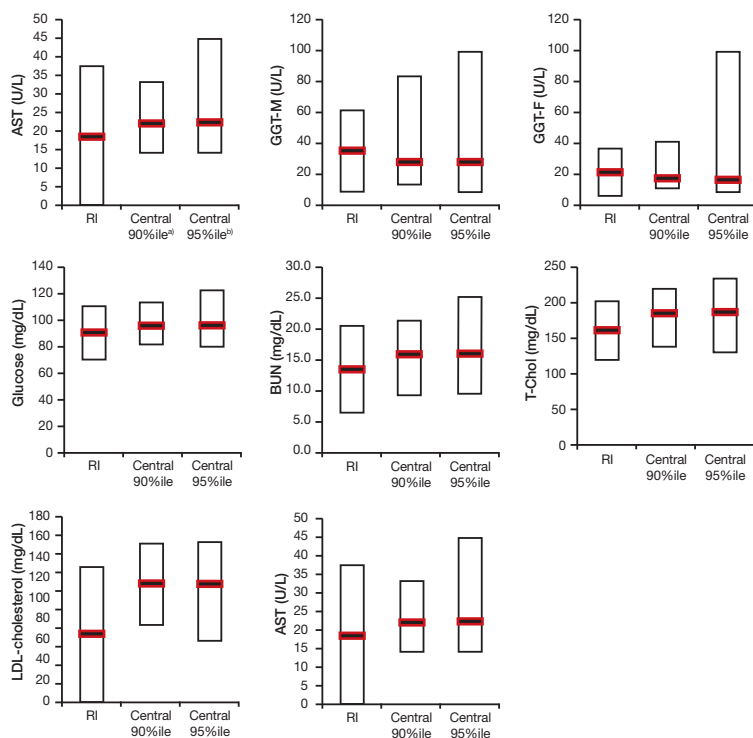
elderly people is difficult, because first, the exact definition of age for "elderly" is not clear, second, their characteristics are very heterogenous in terms of nutrition, physical activity, and medication, and third, the morbidity rates increase with age as the prevalence of cardiovascular disease, stroke, or malignancy is too high [3,6-9]. In general, "elderly" is taken to mean over 65 years of age, thus, the inclusion criterium of

Figure 2. Central 90th percentile, central 95th percentile of clinical chemistry values in elderly people. AST, aspartate transaminase; RI, common reference interval; GGT, gamma-glutamyl transpeptidase; BUN, blood urea nitrogen; T-Chol, total cholesterol; LDL, low-density lipoprotein; ALT, alanine transaminase. a) 5.0 to 95.0 percentile in the age group I (65 years or above) of the research subjects. The upper and lower limits of the box are the 95.0 and 5.0 percentile and the horizontal bar is the median value. b) 2.5 to 97.5 percentile in the age group I (65 years or above) of the research subjects. The upper and lower limits of the box are the 97.5 and 2.5 percentile and the horizontal bar is the median value (n=1,215).

in good agreement with their reference values [8,10-13]. GGT values in this study showed modest increase by age in both men and women, and were needed to be compromised.

We found an increase in glucose values with age, and this finding was also observed in other reports [8,10,14]. Although the distribution patterns of glucose values for elderly people were much higher than the usual reference intervals, the value of 97.5 percentile in elderly population was still lower than the cutoff value for a diagnosis of diabetes. As we know the high prevalence of diabetes in elderly population, a careful

monitoring will be needed.

There was an increase of urea nitrogen with age. This finding agreed with most studies [6,8,14] from the aspect of decreased renal function with age. On the other hand, creatinine values showed no remarkable changes in this study, and were also very variable according to researchers [8,14]. The reason was thought that decrease in renal creatinine excretion was compensated with the low production by decreased renal mass in elderly person.

Lower albumin values in elderly people reported by other authors [8,10,12,15] suggested that it was attributed to either aging process alone or decreased state of health of these individuals. Serum iron values were also lower than those in young adults and confirmed by most [8,16,17] but not all studies.

Fraser et al. [18] brought up a question that biological variabilities should increase with age because of the compromised homeostasis, however, they confirmed that within-subject variations in elderly people were similar to those in younger subjects. Biological variations in elderly people were not investigated in this study. It was thought to be important aspect in geriatrics laboratory and needed further evaluation.

Conclusion

For routine clinical chemistry tests these results

suggest that the common reference values in general are applicable to elderly people, even though some parameters showed wider distributions in elderly. However, when interpreting chemistry test results in elderly people, one should take the agerelated alterations into deep consideration. For further attempts to define the reference values for various laboratory tests in the elderly population, this study will provide a meaningful information.

Acknowledgements

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요약

　노인의 경우 질병에 이환되어도 임상증상이 없거나 비전형적일 수 있으므로 진단의학검사결과의 올바른 해석은 질병의 진단과 경과관찰에 매우 중요하다. 진단의학검사는 종목에 따라 연령에 영향을 받는 것이 있으며 젊은 성인에 대한 참고 구간을 기준으로 노인에서 검사결과의 해석을 하는 것은 적합하지 않을 수 있다. 저자들은 통상적으로 사용하고 있는 참고 구간이 노인에게도 그대로 적용할 수 있는지 알기 위해 노인인구를 대상으로 임상 화학 검사결과의 분포 양상을 조사하였다. 경북대학교병원 건강증진센터를 방문한 65세 이상의 노인 2,604명 가운데 설문조사, 검사결과, 진료기록 등을 기준으로 건강한 노인 1,215명을 선정하였고(그룹 I), 65세 미만의 건강한 성인 1,827명을 대조군으로(그룹 II) 비교하였다. 하룻밤 공복상태후의 혈액 샘플을 채취하여 임상화학검사를 시행하였다. PASW 프로그램을 이용, Kol-mogorov-Smirnova test로 결과 값의 분포양상을 보고 Mann-Whitney test와 Kruskal-Wallis test로 그룹별 결과를 비교 평가하였다. 노인의 중앙 95 백분위 수를 계산하면, 총 단백질, 알부민, alkaline phosphatase, lactate dehydrogenase, 크레아티닌, 요산, 트리글리세라이드, high-density lipoprotein-콜레스테롤, 그리고 전해질은 통상 사용하는 참고구간 내에 있었다. Aspartate transaminas와 alanine transaminase의 경우는, 노인에서 중앙 95 백분위 수 값은 참고구간을 벗어났으나, 중앙 90 백분위 수 값은 일반적인 참고구간과 호환되었다. 반면에 gamma-glutamyl transpeptidase, blood urea nitrogen, 총 콜레스테롤, low-density lipoprotein-콜레스테롤, 그리고 포도당의 중앙 90 백분위 수 값의 하한은 참고구간의 하한을 벗어나지 않았으나 상한의 경우 상한보다 높은 값을 보여 주었다. 통상적인 임상화학검사의 경우, 비록 일부 감사종목의 값이 노인에서 더 넓은 분포양상을 보였으나, 일반적으로 사용되는 참고범위는 노인에게 적용될 수가 있을 것으로 보인다.

핵심용어: 임상화학검사; 참고범위; 노인

Peer Reviewers　Commentary

우리나라 혈액화학검사 결과의 참고구간은 주로 정상 성인을 기준으로 작성된 것이고 흔히 교과서나 제조사가 제시한 참고구간을 소수의 자료로 검증하여 사용하는 경우가 많은데 본 연구는 65세 이상 1,215명의 건강인과 65세 미만 1,827명의 비교적 다수의 수검자를 대상으로 비교 분석하여 유용한 자료가 될 것이다. 아직 표준화되지 않은 종목이 많아 타 검사 기관과의 검사종목 결과의 절대값 비교는 힘들지만 65세 미만의 결과와 65세 이상의 결과와의 상대적 비교는 가능하여 검사 결과의 해석에 도움이 된다. 즉, 대부분의 종목이 두 군간의 차이가 없었으나 일부 종목은 65세 이상에서 더 넓은 분포를 보여 비정상 결과로 오인될 수 있는데 비해 본 연구의 결과를 참고하여 불필요한 추가 진료를 막을 수 있을 것이다.

[정리: 편집위원회]