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Laboratory blood test results beyond normal ranges could not be attributed to healthy aging

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Abstract

Aging is related to a decline in the function of many organs. The results of blood tests are essential for clinical management and could change over a lifespan reflecting aging. The aim of this study was to examine serum levels of liver, kidney, and bone marrow function and to study their dynamics as a function of age and sex.

The cross-sectional study conducted in Poland included 180 healthy individuals (20–90 years) divided into subgroups by sex and decade. These included subgroups of ≥65 or <65 years (men and women). We investigated serum levels of creatinine, estimated glomerular filtration rate, estimated effective renal blood/plasma flow, urine pH, urine neutrophil gelatinase-associated lipocalin (NGAL) as well as serum levels of transaminases, bilirubin, total cholesterol (TC), international normalized ratio (INR), and blood morphology.

All parameters were within normal range in all groups. Urine NGAL was higher in men aged ≥65 years than women (25.67 ± 53.65 vs 16.49 ± 34.66, $P = .001$); serum levels of TC and platelet (PLT) count were higher in women than men aged ≥65 years (221.0 ± 41.7 vs 188.4 ± 48.2 and 250.3 ± 47.8 vs 202.5 ± 57.9, $P = .003$ and $P = .038$, respectively). The INR was lower in women (0.97 ± .06 vs 1.19 ± 0.48, $P = .03$).

These blood tests were normal in healthy people aged ≥65 years. Higher PLT and TC and lower INR in women might indicate a higher risk of cardiovascular diseases. These changes in blood tests were not attributed to aging itself.

Abbreviations: ALT = alanine transaminase, ANOVA = analysis of variance, AST = aspartate transaminase, BMI = body mass index, CKD = chronic kidney disease, CVD = cardiovascular disease, eERBF = estimated effective renal blood flow, eERPF = estimated effective renal plasma flow, eGFR = estimated glomerular filtration rate, INR = international normalized ratio, NGAL = neutrophil gelatinase-associated lipocalin, PLT = platelet, RBC = red blood cells, TC = total cholesterol, WBC = white blood cells.

Keywords: aging, cardiovascular risk, laboratory reference values

1. Introduction

Aging is a process of time-dependent deterioration causing gradual decline in the function and the structural changes of many organs. It is important yet difficult to distinguish between senescence—the natural reduction in homeostatic capability—and disease—an abnormal condition that deteriorates the capacity of any organ to maintain its function.[1] Multimorbidity is common in the elderly and complicates healthy aging. According to Rocca et al,[2] 38.9% of the total population of Olmsted County, Minnesota had 1 or more condition, 22.6% had 2 or more conditions, and 4.9% had 5 or more conditions. The prevalence of multimorbidity increases with age, and 2 or more conditions were diagnosed in 77.3% at 65 years and older. Elderly women are slightly more likely than men to have chronic illness.[3] Age-related diseases can significantly alter the functional decline and exhaust the functional reserve of a particular organ when superimposed on normal senescence. On the contrary, it is critical to avoid unnecessary medications that can result from misinterpretation of laboratory tests.

In the aging kidney, some glomeruli are replaced by fibrous tissue. This can affect up to 25% of the glomerular units by the age of 70 years. The mesangium increases and the process of glomerular obliteration leads to the formation of a direct channel between afferent and efferent arterioles. This decreases the glomerular filtration rate (GFR) and effective renal plasma/blood flow (ERPF/ERBF). Other changes include thickening of the intima, fibrosis, and atrophy of some tubules. Podocyte injury is also observed along with apoptosis, changes in tubular reabsorption and secretory capacities, urinary concentration ability, and production of kidney-derived hormones and molecules.[4]

Liver function also deteriorates with age. Cieslak et al[5] reported that the liver ^{99m}Tc-mebrofenin uptake rate is negatively correlated with age. Animal studies showed impaired liver regeneration due to aging. This was expressed by decreased cell cycle and increased autophagy and apoptosis.[6]

The elderly have changes in their blood cell counts. The fall in red cell count is related to a decline in renal function. The changes in neutrophils and platelets (PLTs) are related to background inflammation. Changes in lymphocytes are due to immunosenescence. This can be a result of reduced hematopoietic stem cell reserves.[7,8]

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The aim of the study was to trace the dynamics of changes with age and sex in serum concentrations of selected liver, kidney, and bone marrow parameters in healthy people aged 20 to 90 years to show physiological differences between women and men upon the wide lifespan and to compare the obtained results to widely used laboratory ranges.

2. Materials and methods

The study included 180 healthy individuals between 20 and 90 years of age (mean age, 49 ± 18 years; 94 women and 86 men). They were recruited in Poland in nursing homes and neighborhood in years 2012 to 2014. None had any chronic diseases in their medical history, and none of the participants took any medications. All participants showed normal blood pressure and body mass index (BMI) values. This group was described in more detail previously.[9]

Every subject gave written and informed consent to participate, and the study was approved by the Bioethics Committee of the Medical University of Warsaw (No. KB/10/2010). Whole fasting blood (2 mL) was drawn in polypropylene tubes and allowed to clot for 30 minutes before centrifugation. Serum was obtained by centrifugation for 10 minutes at 1000 *g*. The samples were stored at −80°C before analysis.

To estimate kidney function, we investigated serum level of creatinine, estimated glomerular filtration rate—according to chronic kidney disease epidemiology collaboration formula, ERBF, ERPF, pH of urine, and urine neutrophil gelatinase-associated lipocalin (NGAL).

To estimate liver function, we measured serum aspartate transaminase (AST), alanine transaminase (ALT), bilirubin, total cholesterol (TC), and international normalized ratio (INR).

To estimate bone marrow function, we investigated red blood cells (RBC), hematocrit, hemoglobin, white blood cells (WBC), neutrophils, lymphocytes, monocytes, eosinophils, basophiles, and PLT counts.

The biochemical analysis of serum was performed using Dimension EXL 200 (Siemens, Munich, Germany). Bilirubin concentrations were estimated by the dichromatic endpoint method, creatinine concentration was estimated by Jaffe method; ALT and AST levels were estimated by dichromatic ratio method; and TC was estimated by the polychromatic endpoint method.

Urine pH was measured via the dry-reagent strip tests using iChem Velocity Urine Chemistry System (Beckman Coulter, Brea, CA).

NGAL urine concentrations were estimated via a chemiluminescent method (chemiluminescent microparticle immunoassay [CMIA]) with an ARCHITECT Urine NGAL assay (Abbott Laboratories, Abbott Park, IL) using the ARCHITECT i1000 Abbott (Abbott Laboratories, Abbott Park, IL). The cell morphology was studied with fluorescent flow cytometry using an XT-2000i instrument (Sysmex, Kobe, Hyōgo, Japan).

3. Statistical analysis

Statistical analysis used R (version 3.3 R Development Core team 2016). The results are provided as the mean values and standard deviations. Differences between the groups were analyzed using either Student *t* test (for normally distributed data) or a *U* Mann-Whitney test (otherwise). The correlations between pairs of numerical parameters were studied using Pearson coefficient. Where significant correlations occurred, multivariate linear regression analysis was conducted.

Differences between the groups for both, age (by decades) and sex were analyzed using 2-way analysis of variance (ANOVA), followed by Tukey post-hoc test.

In all analyses results were considered significant if P value was $<.05$.

4. Results

To trace the dynamics of changes with age and sex, participants were divided into subgroups based on sex and decade of life. To detect differences between young and elderly women or men, participants were alternatively divided into those younger than 65 years (young) and those aged at least 65 years (elderly).

Results of kidney studies are shown in Table 1. Serum creatinine, urine pH, and urine NGAL were within reference values for all subgroups despite differences between them. Correlations between serum creatinine and age and sex were statistically significant ($P=.01$ and $P<.001$, respectively; 2-way ANOVA, $P=.001$ and $P<.001$, respectively). Regression analysis showed serum creatinine to increase annually by 0.0028 mg/dL. Serum creatinine level is also higher in men than women when matched by age and BMI by 0.2382 mg/dL. Among men, in those aged at least 70 years, serum creatinine was significantly higher than that in other groups. A significant difference was observed only between men in their 60s and those aged at least 70 years ($P=.002$). Among women, age-based differences in serum creatinine were not found. Urine NGAL correlated with age ($P=.05$), and among those aged at least 65 years, was significantly greater in men than in women ($P=.01$). Urine pH did not differ with age or sex. Age was correlated with eGFR (2-way ANOVA, $P<.001$), which was lower in elderly people than in young people. No differences were found between women and men. Age-based differences in eGFR were significant only between men in their 60s and those aged at least 70 years ($P<.001$). Sex, age, and the interaction between sex and age were significantly correlated with ERBF (2-way ANOVA, $P<.001$, $P<.001$, and $P=.01$, respectively); only the first 2 were significantly correlated with ERPF (2-way ANOVA, $P<.001$ for both). The ERBFs and ERPFs were lower in women than in men, but only in individuals <65 years of age and in elderly relative to young people. Based on decade of age, significant differences in ERBF and in ERPF were found only between men in their 60s compared with those aged at least 70 years ($P<.001$ for both). These 2 parameters were estimated, and age was considered in all equations. Results of liver function studies are shown in Table 2. Serum bilirubin, AST, ALT, and INR were within reference values in all subgroups despite differences between them. Total serum cholesterol was slightly above the reference range in young people and elderly women. Age was correlated with serum bilirubin ($P=.01$). Men in their 30s had higher (but not significant) bilirubin levels than other groups, but no other significant differences were found between age groups, either among the men or the women. A weak correlation was found between ALT and age ($P=.01$); however, it was impossible to build a regression model describing this relationship. Sex was correlated with both ALT and AST (2-way ANOVA, $P<.001$ for both). Compared to same-aged women, ALT was significantly higher in men aged 20 to 49 years, and AST was significantly higher in men aged 20 to 69 years. No relationships were found between age or sex and INR. Both sex and age were correlated with total serum cholesterol (2-way ANOVA, $P=.04$ and $P<.001$, respectively). Among those aged at least 60 years, serum cholesterol was significantly higher in women compared to

Table 1

Parameters describing renal function stratified by age and sex.

	20–29 Years of age (n = 30)		30–39 Years of age (n = 30)		40–49 Years of age (n = 30)		50–59 Years of age (n = 30)		60–69 Years of age (n = 30)		≥70 Years of age (n = 30)		<65 Years of age (n = 138)			≥65 Years of age (n = 42)		
Parameter	**F (n = 16)**	**M (n = 14)**	**F (n = 15)**	**M (n = 15)**	**F (n = 18)**	**M (n = 12)**	**F (n = 15)**	**M (n = 15)**	**F (n = 15)**	**M (n = 15)**	**F (n = 15)**	**M (n = 15)**	**F (n = 72)**	**M (n = 66)**	***P***	**F (n = 22)**	**M (n = 20)**	***P***
Creatinine, mg/dL	0.81 ± 0.10	1.07 ± 0.14	0.8 ± 0.13	1.05 ± 0.13	0.81 ± 0.12	1.00 ± 0.13	0.85 ± 0.13	0.96 ± 0.09	0.86 ± 0.13	1.02 ± 0.23	0.89 ± 0.14	1.25 ± 0.32	0.82 ± 0.12	1.02 ± 0.15	<.001	0.89 ± 0.13	1.19 ± 0.31	.00
eGFR (CKD-EPI)	102.0 ± 15.4	97.4 ± 15.7	98.2 ± 16.7	93.5 ± 13.6	89.4 ± 14.2	92.3 ± 13.5	78.3 ± 13.5	89.1 ± 9.6	73.3 ± 12.7	78.6 ± 16.6	65.3 ± 13.2	59.3 ± 16.6	90.2 ± 17.5	91.0 ± 14.7	.53	67.1 ± 12.8	63.6 ± 17.5	.48
ERBF, mL/min	779.2 ± 118.7	1228 ± 253.1	846.9 ± 161.8	1109.0 ± 268.5	769.3 ± 160.1	1089.0 ± 131.4	768.8 ± 322.8	946.7 ± 215.3	611.7 ± 123.3	874.0 ± 324.9	499.6 ± 151.7	524.5 ± 164.1	769.4 ± 203.5	1069.0 ± 269.5	<.001	537.3 ± 144.8	575.6 ± 173.4	.36
ERPF, mL/min	464 ± 71.7	651.6 ± 126.0	498.0 ± 97.1	615.5 ± 137.2	464.7 ± 91.4	599.1 ± 78.0	442.3 ± 170.4	523.5 ± 113.6	361.3 ± 52.9	479.9 ± 170.1	290.0 ± 82.2	296.8 ± 92.2	456.6 ± 111.0	585.1 ± 137.8	<.001	309.8 ± 77.7	321.5 ± 93.3	.6
pH	5.84 ± 0.6	6.0 ± 0.65	5.9 ± 0.66	5.7 ± 0.37	5.8 ± 0.62	5.9 ± 0.76	5.7 ± 0.59	5.7 ± 0.65	5.7 ± 0.53	6.1 ± 0.91	5.8 ± 0.49	5.9 ± 0.88	5.81 ± 0.59	5.86 ± 0.7	.1	5.8 ± 0.53	5.88 ± 0.84	.96
Urine NGAL, ng/mL	12.76 ± 11.35	7.89 ± 8.05	8.6 ± 3.32	8.25 ± 6.62	10.99 ± 16.33	13.06 ± 17.06	5.78 ± 4.55	10.36 ± 10.5	9.35 ± 19.76	12.95 ± 7.13	17.05 ± 38.72	30.74 ± 62.93	8.88 ± 10.2	10.15 ± 10.33	.58	16.49 ± 34.66	25.67 ± 53.65	.01

eGFR CKD-EPI = estimated glomerular filtration rate—according to CKD-EPI formula, ERBF = effective renal blood flow, ERPF = effective renal plasma flow, NGAL = neutrophil gelatinase–associated lipocalin.

Table 2

Parameters describing liver function stratified by age and sex.

	20–29 Years of age (n = 30)		30–39 Years of age (n = 30)		40–49 Years of age (n = 30)		50–59 Years of age (n = 30)		60–69 Years of age (n = 30)		≥ 70 Years of age (n = 30)		< 65 Years of age (n = 138)			≥ 65 Years of age (n = 42)		
Parameter	**F (n = 16)**	**M (n = 14)**	**F (n = 15)**	**M (n = 15)**	**F (n = 18)**	**M (n = 12)**	**F (n = 15)**	**M (n = 15)**	**F (n = 15)**	**M (n = 15)**	**F (n = 15)**	**M (n = 15)**	**F (n = 72)**	**M (n = 66)**	***P***	**F (n = 22)**	**M (n = 20)**	***P***
INR	1.01 ± 0.06	0.99 ± 0.08	0.99 ± 0.07	1.01 ± 0.07	1.01 ± 0.06	0.95 ± 0.07	0.96 ± 0.05	0.97 ± 0.05	0.97 ± 0.08	1.13 ± 0.47	0.97 ± 0.33	1.11 ± 0.33	0.99 ± 0.07	0.98 ± 0.07	.52	0.97 ± 0.06	1.19 ± 0.48	.03
ALT, U/l	22.5 ± 6.7	45.3 ± 35.4	17.6 ± 4.5	35.7 ± 17.5	17.5 ± 5.7	42.4 ± 19.9	22.9 ± 12.8	31.5 ± 11.3	26.5 ± 7.7	28.5 ± 10.3	19.9 ± 6.4	20.1 ± 6.2	20.3 ± 8.1	37.1 ± 21.6	<.001	22.1 ± 8.8	21.6 ± 6.4	.91
AST, U/l	20.1 ± 4.7	25.2 ± 13.5	16.1 ± 4.3	22.6 ± 6.4	17.7 ± 4.6	22.6 ± 5.2	17.7 ± 6.4	24.7 ± 5.5	21.1 ± 6.2	27.6 ± 11.6	20.3 ± 3.9	22.9 ± 5.9	18.2 ± 5.1	24.6 ± 9.3	<.001	21.1 ± 5.3	23.4 ± 5.9	.13
Total cholesterol, mg/dL	187.1 ± 37.3	197.0 ± 28.8	207.3 ± 30.2	191.4 ± 26.2	210.7 ± 45.1	222.3 ± 48.6	246.7 ± 57.9	233.8 ± 34.1	246.1 ± 33.7	206.9 ± 45.6	215.5 ± 45.5	184.5 ± 53.9	218.4 ± 48.3	211.2 ± 40.7	.51	221.0 ± 41.7	188.4 ± 48.2	.002
Bilirubin, mg/dL	0.63 ± 0.28	0.8 ± 0.35	0.84 ± 0.62	0.87 ± 0.38	0.64 ± 0.24	0.53 ± 0.19	0.54 ± 0.1	0.6 ± 0.33	0.62 ± 0.27	0.73 ± 0.17	0.62 ± 0.21	0.68 ± 0.2	0.65 ± 0.35	0.71 ± 0.32	.06	0.65 ± 0.24	0.68 ± 0.18	.38

ALT = alanine transaminase, AST = aspartate transaminase, INR = international normalized ratio.

men, but at other ages, no differences were found between groups.

Results of bone marrow function studies are shown in Table 3. All parameters were within reference ranges in all subgroups despite differences between them. However, RBC, HT, Hb, monocyte count, and eosinophil count were lower in women than in men younger than 65 years ($P < .001$ in each case). Above that age, this difference disappeared. No statistically significant correlations were found between age and WBC, neutrophils, lymphocytes, monocytes, eosinophils, or basophiles. A weak correlation was found between age and RBC ($P = .05$), Hb ($P = .05$), and PLT ($P = .05$; 2-way ANOVA, $P = .01$). Sex and the interaction between sex and age were correlated with RBC, Hb, and HT (2-way ANOVA, $P < .001$ in each case), and sex was correlated with PLT (2-way ANOVA, $P < .001$). Regression analysis showed that PLT decreases annually by 0.7214 g/L and is lower in men than in women by 45.7983 g/L when matched by age and BMI. No differences were observed based on age.

Significant differences were found in TC, INR, and PLT between women and men aged at least 65 years even though values were within reference ranges. Total serum cholesterol and PLT were higher in women than in men ($P = .003$ and $P = .04$, respectively), and INR was lower in women than men ($P = .03$). Compared to same-aged men, PLT was higher in women younger than 65 years ($P < .001$) and at each decade of life.

5. Discussion

We investigated selected parameters indicating kidney, liver, and bone marrow function in healthy people. Despite the well-known age-related changes, all parameters were within normal reference ranges. We first analyzed serum levels of these parameters separately in men and women aged 20 to 90 years in every consecutive decade of life. We then placed men and women into subgroups: younger than 65 years of age and older than 65 years of age. Despite the changes in parameters denoting age-related decline in function, the organs' functional reserve was sufficiently high to balance this decline. The comparison between men and women, however, revealed some interesting differences.

In the group aged ≥65 years, TC and PLT were significantly higher in women than in men, and the INR was lower. These 3 variables are linked to a higher risk of cardiovascular diseases (CVD). The PLTs are a key player in atherothrombosis.[10] There is a U-shaped association between PLT and all cause and cause-specific mortality; this is independent of other risk factors. A high PLT count is related to an increased risk of cardiovascular mortality due to thrombotic events.[11] Mild PLT elevation is also a risk factor for venous thrombosis.[12] Andrawes et al[13] showed that an INR between 2 to 3 prevents ischemic stroke with acceptable hemorrhagic risk. Anti-PLT drugs and statins are indicated in the elderly to prevent CVD. Our results could indicate that sex is more important in aging than previously believed; however, these results need further research.

There are many similarities between aging kidney and chronic kidney disease (CKD). One of them is reduced GFR. In healthy aging, the decline in GFR is moderate and not inevitable; it is more pronounced in CKD. Normal values of eGFR in the elderly have important implications for the diagnosis of CKD. Patients with CKD are easily confused with those suffering from renal aging when renal function assessment solely by eGFR.[14]

Serum creatinine levels are another useful indicator of renal function. In healthy aging, levels remain within range, but they are always elevated in CKD. ERBF/ERPF was higher in men than

Table 3

Parameters describing bone marrow function stratified by age and sex.

Parameter	20–29 Years of age (n = 30)		30–39 Years of age (n = 30)		40–49 Years of age (n = 30)		50–59 Years of age (n = 30)		60–69 Years of age (n = 30)		≥70 Years of age (n = 30)		<65 Years of age (n = 138)		P	≥ 65 Years of age (n = 42)		P
	F (n = 16)	M (n = 14)	F (n = 15)	M (n = 15)	F (n = 18)	M (n = 12)	F (n = 15)	M (n = 15)	F (n = 15)	M (n = 15)	F (n = 15)	M (n = 15)	F (n = 72)	M (n = 66)		F (n = 22)	M (n = 20)	
RBC, T/L	4.531 ± 0.324	5.3 ± 0.257	4.645 ± 0.344	5.108 ± 0.285	4.563 ± 0.248	5.169 ± 0.188	4.649 ± 0.349	4.19 ± 0.349	4.671 ± 0.202	4.907 ± 0.384	4.695 ± 0.385	4.717 ± 0.45	4.589 ± 0.301	5.077 ± 0.332	<.001	4.730 ± 0.326	4.796 ± 0.448	.88
HCT, %	0.4 ± 0.02	0.47 ± 0.03	0.41 ± 0.02	0.44 ± 0.02	0.39 ± 0.03	0.45 ± 0.01	0.42 ± 0.02	0.45 ± 0.03	0.42 ± 0.02	0.45 ± 0.03	0.42 ± 0.03	0.43 ± 0.03	0.407 ± 0.024	0.45 ± 0.026	<.001	0.42 ± 0.03	0.437 ± 0.04	.15
HGB, g/L	134.1 ± 6.0	159.1 ± 9.2	136.7 ± 9.0	151.1 ± 7.0	130.2 ± 9.8	153.0 ± 5.4	138.0 ± 7.9	150.5 ± 11.9	139.9 ± 7.6	150.5 ± 11.2	135.5 ± 11.3	143.1 ± 1.0	134.7 ± 8.5	152.9 ± 9.5	<.001	138.1 ± 10.8	145.1 ± 13.3	.13
WBC, G/L	6.102 ± 1.43	6.367 ± 1.305	6.43 ± 1.697	5.89 ± 1.159	5.628 ± 1.304	6.192 ± 1.348	6.317 ± 1.348	7.0 ± 2.042	5.751 ± 0.959	6.223 ± 1.388	6.419 ± 1.593	6.599 ± 1.263	6.025 ± 1.426	6.311 ± 1.466	.27	6.328 ± 1.469	6.628 ± 1.420	.62
Neutrophils, G/L	3.508 ± 1.207	3.428 ± 1.155	3.548 ± 1.485	3.133 ± 0.755	3.267 ± 1.023	3.472 ± 1.101	3.681 ± 1.035	3.891 ± 1.557	3.014 ± 0.641	3.537 ± 1.024	3.747 ± 1.222	3.971 ± 1.106	3.417 ± 1.148	3.462 ± 1.118	.79	3.599 ± 1.082	3.957 ± 1.183	.31
Lymphocytes, G/L	1.942 ± 0.502	2.124 ± 0.45	2.17 ± 0.444	1.817 ± 0.519	1.685 ± 0.358	1.986 ± 0.535	1.958 ± 0.481	2.153 ± 0.609	2.058 ± 0548	1.937 ± 0.556	1.867 ± 0.519	1.875 ± 0.462	1.934 ± 0.472	2.004 ± 0.539	.36	1.945 ± 0.546	1.902 ± 0.479	.87
Monocytes, G/L	0.486 ± 0.13	0.601 ± 0.142	0.558 ± 0.141	0.622 ± 0.156	0.444 ± 0.12	0.532 ± 0.163	0.513 ± 0.165	0.674 ± 0.235	0.482 ± 0.127	0.575 ± 0.21	0.548 ± 0.115	0.571 ± 0.146	0.49 ± 0.138	0.604 ± 0.192	<.001	0.546 ± 0.124	0.576 ± 0.133	.68
Eosinophils, G/L	0.141 ± 0.124	0.191 ± 0.177	0.133 ± 0.095	0.288 ± 0.119	0.212 ± 0.138	0.183 ± 0.077	0.139 ± 0.08	0.258 ± 0.104	0.172 ± 0.121	0.146 ± 0.113	0.223 ± 0.188	0.161 ± 0.067	0.16 ± 0.121	0.216 ± 0.131	.003	0.206 ± 0.157	0.172 ± 0.088	.94
Basophiles, G/L	0.0199 ± 0.017	0.023 ± 0.013	0.025 ± 0.012	0.028 ± 0.023	0.020 ± 0.01	0.02 ± 0.01	0.025 ± 0.014	0.024 ± 0.012	0.025 ± 0.016	0.029 ± 0.013	0.035 ± 0.022	0.028 ± 0.023	0.022 ± 0.014	0.025 ± 0.015	.29	0.032 ± 0.02	0.027 ± 0.02	.25
PLT, G/L	281.5 ± 44.6	249.2 ± 38.7	250.8 ± 48.1	219.4 ± 76.3	284.3 ± 71.4	230.8 ± 39.6	284.3 ± 48.1	245.0 ± 45.9	233.4 ± 43.9	222.3 ± 53.4	259.0 ± 44.9	203.0 ± 53.4	271.8 ± 55.1	235.7 ± 51.0	<.001	250.3 ± 47.8	202.5 ± 57.9	.004

ALT = alanine transaminase, AST = aspartate transaminase, HCT = hematocrit, HGB = hemoglobin, PLT = platelets, RBC = red blood cells, WBC = white blood cells.

in women in all decades of life; however, this difference disappeared when men and women aged ≥65 years was considered. These differences usually result from differences in body size and blood volume.

NGAL increased from the seventh decade of life regardless of sex; however, we observed higher urine secretion of NGAL in men than in women starting from the fifth decade of life. The difference reached statistical significance in both groups at age ≥65 years. NGAL is filtered by the glomerulus and is reabsorbed by megalin-dependent mechanisms in proximal tubules. It is also produced locally by injured tubules. Thus, urinary NGAL is increased in proximal tubule injuries.[15,16] We speculate that age-dependent tubule deterioration is more pronounced in men than in women. The ability to acidify urine is preserved both in men and women despite the aging process; however, it is usually altered in patients with CKD.[4]

The consequences of aging on liver function are largely unknown. We investigated parameters such as bilirubin and transaminases—products of metabolic processes performed by the liver and not due to liver function per se; however, they are widely used as "liver function tests."[6] The serum bilirubin levels were constant at all ages with no sex differences. Higher levels of AST and ALT were observed in men than in women in the group aged <65 years. This might result from dietary habits and lifestyle.[17] The highest levels of ALT occurred in men aged 20 to 49 years, and this age-dependent variation was not observed in women. Our results concur with Danielsson et al[18] findings that also reported a positive correlation between age and ALT in men.

PLT levels were higher in women than in men at all ages. They were in the group aged ≥65 years than the younger cohort. These results agree with the literature.[12] Lower PLT results from diminished hematopoietic stem cell reserves in the bone marrow. Alternatively, lower PLT could be a survival advantage so that participants older than 65 years had lifelong lower PLT than the average population, which allows them to reach the eighth or ninth decade of life.[12]

PLTs have many functions, and the differences in PLT levels between women and men and older versus younger are important. Despite their role in maintenance, hemostasis, and CVD, PLTs are also involved in inflammation and immunity regulation. PLTs play a crucial role in promoting liver regeneration and stopping liver fibrosis. They are also involved in cancer development at each stage of metastasis—from separation of cancer cells from the primary tumor to proliferation at the metastatic site.[17,19] PLT counts are not the only indicator of PLTs function. They also depend on PLT distribution, mean PLT volume, and PLT size.[10]

Other blood cell counts were within the normal value range despite age and sex differences. The RBC, Ht, Hb, monocyte, and eosinophil counts had sex differences in the younger population. Starr et al,[8] showed similar results, but they showed persistently higher RBC and monocyte counts in men. This could be because they studied elderly people (79 and 87).[9]

This study has limitations. First, the number of participants was small, and this was exemplified when divided into groups based on decade of life. Most adults, especially those who are elderly, have at least 1 medical condition, and it was very difficult to identify an adequate number of participants without medical histories. Second, using self-reporting for medical histories was a primary enrolment condition, rendering those histories subject to inaccuracies. To minimize this confounding factor, 2 independent statistical analyses were applied, yielding comparable results. Participants were, however, aged 20 to 90 years, imparting a strength in that normal ranges of investigated parameters were established based on age. In addition, the group aged at least 65 years was smaller than those younger than that, but this reflects the actual distribution of people in society. Also, 1 ethnic group was used, so these results might not be generalizable to other populations. A further potential limitation is incomplete adjustments for covariates that influenced the data, such as dietary habits, as mentioned in the Discussion.

In conclusion, the functional reserve in the healthy aging public is sufficiently high to balance age-dependent structural and functional deteriorations of the kidney, liver, and bone marrow. Blood test results showed normal values and indicated that disease, rather than physiological factors or healthy aging, cause outliers. Cardiovascular prevention should be considered, particularly in women aged at least 65 years even when blood pressure is normal and other diseases are not present.

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