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Effects of aging on the function of the urinary system: longitudinal changes with age in selected urine parameters in a hospitalized population of older adults

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Abstract: Although normal aging does not have a pernicious effect on the homeostasis of fluids, renal reserve in elderly people can be depleted. The purpose of the present study was to assess the relationship between longitudinal changes with age in basic urine parameters (specific gravity and pH) in older men and women, depending on their body height and relative body weight. Longitudinal data on these two quantitative traits of the urine were available for 142 physically healthy individuals, including 68 men and 74 women. All subjects were 45 years of age at the beginning and 70 at the end of the period under investigation. All measurements were taken in accordance with internationally accepted requirements. Specific gravity was assessed using a hydrometer, and pH was measured using a pH meter. ANOVA, *t*-test, and regression analysis were performed. No significant sex differences in specific gravity or urine pH were observed. In both sexes, urine specific gravity decreased with age according to exponential model of regression. In men, there was a gradual increase in the pH of the urine until age 65, and the best fitting regression model was polynomial. In women, on the other hand, there was an exiguous decrease in urine pH throughout the period under study, and the best fitting regression model proved to be exponential. As the process of renal aging commences relatively early in ontogeny and manifests itself in many structural and functional changes, urinalysis and other more sophisticated methods of diagnosis of renal diseases are essential for proper assessment of health status of adults and older individuals. The rate of age-related changes in the analyzed traits of the urine was commensurate in both sexes, thereby revealing no evidence of significant sex differences in terms of renal aging in the period between 45 and 70 years of age.

Key words: aging, changes with age, kidney, longitudinal study, specific gravity, senescence, urinalysis, urine pH, the urinary system

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Introduction

Few studies of aging have focused on longitudinal changes with age in basic urine parameters as crude indicators of progressive deterioration in renal function. The initial stages of age-related changes in the structure and function of the urinary system begin at the age of 20 and become easily detectable within the next 20 years (Seeley et al. 2008). After age 40, average blood flow through the kidneys decreases by 10% per decade, dropping from 600 ml/min/1.73 m^2 at age 40 to around 300 ml/min/1.73 m^2 at age 80 (Macías-Núñez et al. 2008; Halter et al. 2009; Sinclair et al. 2012).

Although normal aging does not have a pernicious effect on the homeostasis of fluids and electrolytes, renal reserve in elderly people can be severely depleted. With aging, a slow but steady reduction in the number and size of nephrons can be observed. Notwithstanding the tremendous reserve capacity of the kidneys, by age 85 roughly half of the glomeruli are not functioning properly, mainly due to glomerular obsolescence (Macías-Núñez et al. 2008; Seeley et al. 2008; Halter et al. 2009). The afferent and efferent arterioles become irregular and twisted. It should be stressed that aging-associated changes are not limited to intrinsic glomerulosclerosis, tubulointerstitial fibrosis, and atrophy of renal vessels. Senescence reduces the renal capacity to secrete and absorb. Thus, the ability to eliminate urea, uric acid, creatine, and toxins from the blood, as well as to concentrate urine gradually decreases with age. These changes heighten the risk of dehydration (Seeley et al. 2008; Sinclair et al. 2012). Older people are also at higher risk of progression from IgA nephropathy to end-stage renal disease (Duan et al. 2013).

Moreover, certain age-related diseases, such as chronic inflammatory state, diabetes, dyslipidemia, hypertension, and other cardiovascular diseases (CVDs), can aggravate renal structural and functional damage, thereby jeopardizing renal perfusion and adding extrinsic risk factors (Weinstein and Anderson 2010). Consequently, the glomerular filtration rate (GFR), which is considered to be an overall index of renal function in health and disease, as well as the effective renal plasma flow (ERPF), tend to diminish throughout consecutive decades of life. The GFR declines from 120 ml/min at age 40 to about 65 ml/min at age 85 (Halter et al. 2009; Sinclair et al. 2012; Weinstein and Anderson 2010). The filtration fraction (FF), which is the ratio of GFR/ERPF, usually increases in elderly people because the denominator decreases with age more than the numerator does. The aging-associated decline in creatinine clearance averages 0.75 ml/min/year. However, there is usually a small proportion of elderly people who show a significant increase in creatinine clearance with age, and there are no age-related changes in approximately 30% of older adults (Lindeman et al. 1985). Nevertheless, we know of no studies that have examined longitudinal changes with age in urine parameters in both sexes, depending on body size, i.e. body height (shorter and taller individuals) and relative body weight (slimmer and stouter individuals). Presumably the lack of such studies results from the fact that longitudinal data on changes with age in urine parameters in the Polish population remain scarce. We have overcome these difficulties by collecting longitudinal data on anthropometric and urine parameters from the Polish Longitudinal Study of Aging (PLSA), carried out in the years 1960–2000 (Borysławski et al. 2015; Chmielewski et al. 2015a; 2015b; 2016). The present study aimed to evaluate the relationship between longitudinal changes with age in basic urine parameters (i.e. specific gravity and urine pH) in aging men and women, depending on their body height and relative body weight. Thus, our study was also aimed at analyzing and assessing the rate and direction of aging-associated changes in urine specific gravity and pH in hospitalized older adults who differed in body height and relative body weight.

Materials and methods

The material used in the present study was collected at the Regional Psychiatric Hospital for Mentally Challenged People in Cibórz, Lubuskie Province, Poland. The data were obtained from a computerized registry at the archives of case history at the hospital. In the years 1960–2000, the asylum provided care for impoverished people from the lower socio-economic strata, and functioned as long-term sheltered accommodation for people with social recommendations. The reason for keeping these people there for many years was to separate them from the rest of the socialistic society, which was a socially and politically motivated decision (Borysławski et al. 2015; Chmielewski et al. 2015a; 2015b; 2016) Medical data on health profiles, which were stored at the archive of case history, concerned a population of 3500 patients. Longitudinal data were available from 142 physically healthy individuals, including 68 men and 74 women, who were 45 years old at the commencement and 70 years old at the end of the period under study. Thus, the chosen group of inmates stayed continuously at the hospital for at least 25 years. The subjects were categorized into six age categories, i.e.: 45, 50, 55, 60, 65, and 70 years. All the patients underwent regular physicals during their lengthy stay at the hospital. The leading causes of death were predominantly aging-associated diseases, i.e. cardiovascular disease and cancer (Chmielewski et al. 2015a), and there were no significant differences between the studied population and the general Polish population in respect of main causes of deaths (Chmielewski and Borysławski 2015). During their stay at the hospital, the patients took powerful psychoactive drugs. Therefore, we carefully selected patients who were hardly ever treated with very strong medicines, or who had been treated so every once in a while. It is noteworthy that the patients lived for many years under very similar environmental conditions and maintained virtually the same daily schedule, lifestyle, and diet (Chmielewski et al. 2015b; 2016). This fact undoubtedly boosts the value of the study sample and makes it quite unique.

The standard procedure for collecting the urine specimens was conducted in accordance with the internationally accepted recommendations (Borysławski et al. 2015; Chmielewski et al. 2015b). The patients were required to give a sample of urine mid-stream in a sterile and disposable container once a month. The samples were collected in the morning. Urine assessment involved color, clarity, presence of bacterial cultures, blood cells, glucose, protein, pH, specific gravity, etc. For the purpose of the study, we selected only data on two basic quantitative parameters: pH was measured using a pH meter, and specific gravity was assessed using a hydrometer. The normality of the data distribution was tested with the K-S test. One-way analysis of variance (ANOVA), Student's *t*-test, and regression analysis were employed to scrutinize the rates and directions of the age-related changes in the analyzed urine parameters.

To test changes with age in the selected urine parameters, as well as to reveal possible differences between individuals who differed in body size, two anthropometric measures were used, and two dichotomous divisions of the study sample were made. The medians of body height (169.5 cm for men, 155.8 cm for women) at the age of 45 were used to divide the sample into shorter and taller subjects. The medians of body mass index, BMI (22.9 kg/m^2 for men, 24.0 kg/m^2 for women) at the age of 45 were used to divide the sample into slimmer and stouter subjects, $N=34$ for each subgroup of men and $N=37$ for each subgroup of women.

To determine the rate and patterns of changes with age in the analyzed characteristics, regression analysis with the method of least squares was run. The goodness of fit of a given regression model was confirmed only when a coefficient of determination (R^2) reached the highest value, and an unknown parameter (β_0) as well as a coefficient of regression (β_1) were statistically significant ($p<0.05$). For the purpose of our study, five types of functions were tested: (I) linear function, $y = \beta_1$ age $+ \beta_0$, (II) logarithmic, $y = \beta_1 \ln$ age $+ \beta_0$, (III) polynomial, $y = \beta_1$ age$^2 + \beta_2$ age $+ \beta_0$, (IV) exponential type I, $y = \beta_1$ age^a, and (V) exponential type II, $y= \beta_1 e^{a(\text{age})}$, where ($y$) represents a value of an analyzed characteristic changing through aging, (β_2) denotes the second coefficient of regression, (a) stands for the exponent, and (e) is the base of the natural logarithm.

Results

The baseline characteristics of the study population are presented in Tables 1–5. The specific gravity of urine in men decreased with age, in accordance with the matched exponential function ($y = 1027.009x^{-0.002}$, $R^2 = 0.241$) for which the estimated regression value was close to statistical significance. Similarly in women, the specific gravity of urine decreased with age in line with the exponential model ($y = 1032.678x^{-0.004}$, $R^2 = 0.700$), but these changes were statistically significant ($p<0.05$). No differences in the specific gravity of urine between men and women in the six age categories were found (*t*-test, $p>0.05$). Thus, the regression curve illustrating changes in the specific gravity of urine in subsequent age categories for men and women was U-shaped (Fig. 1A). For both sexes the polynomial function had the highest goodness-of-fit value, but the values of estimates were not statistically significant. The lowest specific gravity of urine was recorded for men aged 65–72.5 years and women aged 57.5–65 years.

Although there was a slow increase in urine pH that lasted until the age of 65 in men, and an exiguous but steady decrease in pH in women, no significant sex differences were observed in any of the six age categories (*t*-test, $p>0.05$). Interestingly, the changes with age in the tested urine parameter followed different patterns in both sexes. The model of regression proved to be polynomial in men ($y = -0.0006x^2 + 0.0657x + 4.0\ 19$, $R^2 = 0.389$) but exponential type I in women ($y = 6.613x^{-0.031}$, $R^2 = 0.597$). The pH value reached a peak at the age of 65 years in men and at the age of 45 years in women. The troughs, however, occurred in the last age categories in both

Table 1. Baseline characteristics of two tested urine parameters (specific gravity and pH) in both sexes in six consecutive age categories. The differences between arithmetic means were assessed using *t*-test

Age	Analyte	Men ($N=68$)		Women ($N=74$)		*t*-test	*p*-value
		Mean	SD	Mean	SD		
45	Specific gravity (g/l)	1018.8	5.3	1019.1	4.9	0.36	0.721
	pH	5.9	0.6	5.9	0.6	0.31	0.757
50	Specific gravity	1019.4	4.7	1018.7	5.0	0.85	0.395
	pH	5.9	0.5	5.9	0.5	0.51	0.611
55	Specific gravity	1018.3	4.7	1017.5	3.8	1.17	0.245
	pH	5.9	0.5	5.8	0.4	0.97	0.332
60	Specific gravity	1018.3	4.5	1017.9	4.1	0.54	0.588
	pH	5.9	0.5	5.9	0.4	1.15	0.250
65	Specific gravity	1017.3	4.5	1017.4	4.4	0.04	0.965
	pH	6.0	0.5	5.8	0.4	1.95	0.053
70	Specific gravity	1018.8	5.8	1017.7	4.3	1.32	0.189
	pH	5.8	0.6	5.8	0.5	0.36	0.717

sexes. Thus, with aging, the pH of urine in men increased steadily up to age 65 years and then decreased at the age of 70 years. The polynomial regression model had the highest goodness-of-fit value, but changes were not statistically significant. In women, unlike in men, the pH of urine decreased with age, in accordance with the matched exponential function, for which the estimated regression value was close to statistical significance. However, no differences were found in the pH of urine in men compared with women in any of the six subsequent analyzed age categories (*t*-test, $p>0.05$). The curve representing changes in the pH of urine in men and women in consecutive age categories was U-shaped, with the lowest values for age 65–72.5 years (Fig. 1B). The highest goodness-of-fit value for both sexes was found for the polynomial regression model, but changes proved to be statistically nonsignificant, although in men they were close to statistically significant values.

As for subjects who differed in body size, taller men had higher values of the specific gravity of urine compared with shorter men only at the age of 45 (Fig. 2A), whereas taller women had higher

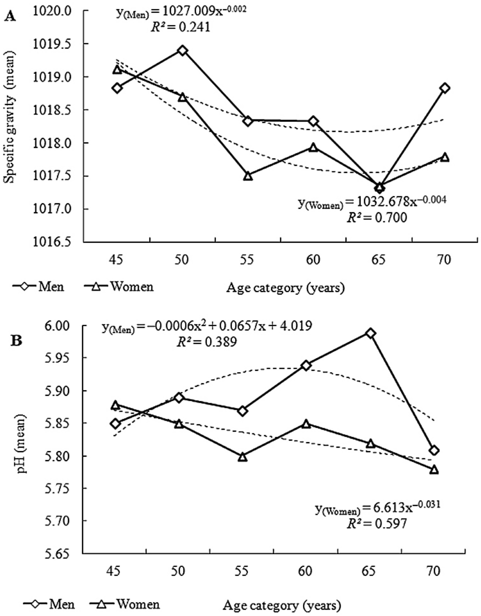

Fig. 1. Changes with age in specific gravity (A) and pH of urine (B) in men ($N=68$) and women ($N=74$) throughout the period under study (longitudinal data): arithmetic means and curves of regression with best fitting functions and coefficients of determination are shown

Table 2. Baseline characteristics of two tested urine parameters (specific gravity and pH) in taller and shorter men in six consecutive age categories. The differences between arithmetic means were assessed using *t*-test

Age	Analyte	Taller men (N=34)		Shorter men (N=34)		*t*-test	*p*-value
		Mean	SD	Mean	SD		
45	Specific gravity (g/l)	1020.3	5.5	1017.3	4.7	2.42	0.018
	pH	5.9	0.5	5.8	0.6	0.23	0.821
50	Specific gravity	1020.3	4.6	1018.5	4.7	1.58	0.119
	pH	5.9	0.5	5.9	0.6	0.26	0.794
55	Specific gravity	1018.9	4.5	1017.7	4.9	1.06	0.295
	pH	5.8	0.5	5.9	0.5	1.07	0.290
60	Specific gravity	1018.7	4.3	1018.0	4.7	0.57	0.566
	pH	5.9	0.6	6.0	0.5	0.67	0.504
65	Specific gravity	1017.2	4.0	1017.5	5.0	0.26	0.795
	pH	6.0	0.7	6.0	0.5	0.11	0.915
70	Specific gravity	1018.8	5.0	1018.9	6.5	0.06	0.950
	pH	5.8	0.6	5.8	0.7	0.40	0.693

values of this parameter compared with shorter women at the age of 55 (Fig. 3A). The goodness of fit of regression curves (exponential type I function, for taller men: $y = 1042.473x^{-0.006}$, $R^2 = 0.647$; for shorter men: $y = 1011.759x^{0.002}$, $R^2 = 0.178$; for taller women: $y = 1030.947x^{-0.003}$, $R^2 = 0.593$; for shorter women: $y = 1034.413x^{-0.004}$, $R^2 = 0.342$) illustrating the aging-associated changes in the specific gravity of urine of both groups of men and women was not statistically significant.

There were no statistically significant changes with age in the specific gravity of urine in stouter men (y =

Table 3. Baseline characteristics of two tested urine parameters (specific gravity and pH) in stouter and slimmer men in six consecutive age categories. The differences between arithmetic means were assessed using *t*-test

Age	Analyte	Stouter men (N=34)		Slimmer men (N=34)		*t*-test	*p*-value
		Mean	SD	Mean	SD		
45	Specific gravity (g/l)	1018.3	5.1	1019.4	5.5	0.86	0.393
	pH	5.9	0.5	5.8	0.7	0.44	0.659
50	Specific gravity	1019.3	5.3	1019.5	4.1	0.13	0.895
	pH	5.9	0.5	5.9	0.5	0.12	0.905
55	Specific gravity	1019.0	4.3	1017.7	5.0	1.23	0.222
	pH	5.8	0.4	5.9	0.5	0.47	0.637
60	Specific gravity	1018.1	4.3	1018.6	4.7	0.40	0.688
	pH	6.0	0.6	5.9	0.4	1.17	0.244
65	Specific gravity	1018.2	5.0	1016.4	3.7	1.72	0.090
	pH	6.0	0.5	6.0	0.7	0.55	0.584
70	Specific gravity	1019.5	5.7	1018.2	5.8	0.92	0.359
	pH	5.7	0.7	5.9	0.6	1.21	0.231

Table 4. Baseline characteristics of two tested urine parameters (specific gravity and pH) in taller and shorter women in six consecutive age categories. The differences between arithmetic means were assessed using t-test

Age	Analyte	Taller women (N=37)		Shorter women (N=37)		t-test	p-value
		Mean	SD	Mean	SD		
45	Specific gravity (g/l)	1018.5	4.8	1019.8	5.0	1.13	0.262
	pH	5.9	0.5	5.9	0.6	0.23	0.821
50	Specific gravity	1018.7	4.8	1018.8	5.3	0.07	0.943
	pH	5.8	0.5	5.9	0.6	0.26	0.794
55	Specific gravity	1018.6	4.0	1016.4	3.4	2.61	0.011
	pH	5.8	0.5	5.8	0.4	1.07	0.290
60	Specific gravity	1017.9	4.0	1018.0	4.3	0.20	0.843
	pH	5.9	0.5	5.8	0.4	0.67	0.504
65	Specific gravity	1016.9	4.9	1017.8	4.0	0.82	0.416
	pH	5.9	0.4	5.8	0.4	0.10	0.915
70	Specific gravity	1017.7	4.2	1017.7	4.5	0.01	0.996
	pH	5.8	0.5	5.7	0.6	0.40	0.693

$1016.491x^{0.0005}$, $R^2 = 0.023$), slimmer men ($y = 1037.641x^{-0.005}$, $R^2 = 0.460$), and slimmer women ($y = 1024.32x^{-0.002}$, $R^2 = 0.376$; see Figures 2B and 3B). In stouter women ($y = 1041.096x^{-0.005}$, $R^2 = 0.796$), however, the regression curve illustrating the aging-associated changes in this parameter assumed the shape of exponential type I function (Fig. 3B) and only this model of regression with age was statistically significant.

There were no significant differences in the pH urine values between taller and shorter subjects of both sexes (Figs 4A and 5A). In taller men ($y = -0.0003x^2$ $0.037x + 4.839$, $R^2 = 0.09$) and in short-

Table 5. Baseline characteristics of two tested urine parameters (specific gravity and pH) in stouter and slimmer women in six consecutive age categories. The differences between arithmetic means were assessed using t-test

Age	Analyte	Stouter women (N=37)		Slimmer women (N=37)		t-test	p-value
		Mean	SD	Mean	SD		
45	Specific gravity (g/l)	1019.9	4.7	1018.3	5.1	1.39	0.169
	pH	6.0	0.6	5.8	0.5	1.74	0.085
50	Specific gravity	1019.7	5.7	1017.8	4.0	1.68	0.098
	pH	5.9	0.6	5.9	0.5	0.01	0.993
55	Specific gravity	1017.9	4.3	1017.1	3.3	0.95	0.245
	pH	5.8	0.5	5.8	0.4	0.52	0.605
60	Specific gravity	1018.3	4.5	1017.6	3.7	0.83	0.411
	pH	5.8	0.4	5.9	0.5	0.85	0.400
65	Specific gravity	1017.5	4.7	1017.2	4.3	0.29	0.770
	pH	5.8	0.4	5.9	0.4	1.49	0.139
70	Specific gravity	1017.8	4.0	1017.6	4.7	0.16	0.871
	pH	5.7	0.5	5.8	0.6	0.63	0.529

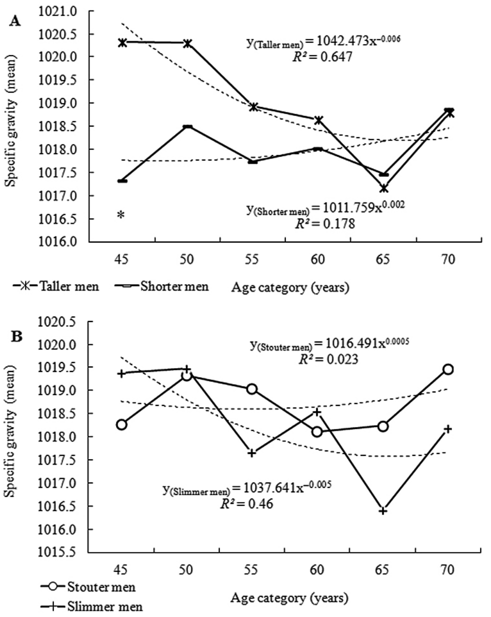

Fig. 2. Changes with age in specific gravity in taller and shorter men (A) and in stouter and slimmer men (B) throughout the period under study (longitudinal data): arithmetic means and curves of regression with best fitting functions and coefficients of determination are shown

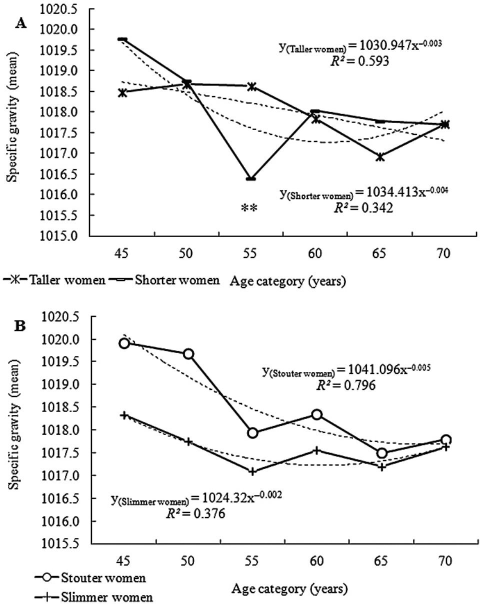

Fig. 3. Changes with age in specific gravity in taller and shorter women (A) and in stouter and slimmer women (B) throughout the period under study (longitudinal data): arithmetic means and curves of regression with best fitting functions and coefficients of determination are shown

er men ($y = -0.0008x^2 + 0.094x + 3.198$, $R^2 = 0.779$), the regression models were polynomial, but they were statistically nonsignificant (Fig. 4A). In taller women ($y = -6.174x^{-0.013}$, $R^2 = 0.077$), like in both groups of men, the curve of regression had low goodness-of-fit value and, therefore, this model of regression was statistically nonsignificant. In shorter women, however, the model of regression was exponential type I and had high goodness-of-fit value, thus the curve of regression for shorter women (exponential function) was statistically significant ($y = 7.087x^{-0.05}$, $R^2 = 0.862$; Fig. 5A).

Likewise, no statistically significant differences in urine pH between stouter and slimmer subjects were observed (Figs 4B and 5B). There were also no significant changes with age in this parameter in stouter men ($y = -0.0009x^2 + 0.099x + 3.182$, $R^2 = 0.444$), slimmer men ($y = -0.0002x^2 + 0.032x + 4.855^{-0.031}$, $R^2 = 0.435$), and slimmer women ($y = 5.182x^{0.029}$, $R^2 = 0.252$). In stouter women, however, the model of regression was exponential type I ($y = 8.448x^{-0.092}$, $R^2 = 0.876$) and the curve of regression illustrating these changes with age had high goodness-of-fit value and thus was statistically significant (see Fig. 5B).

Discussion

The kidney is a paired organ located on both sides of the spine at the rear of the abdominal cavity, behind the stomach and under the liver, and is also the largest

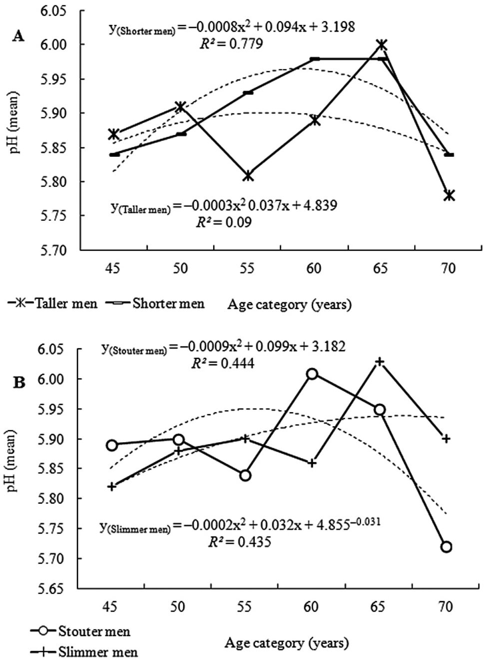

Fig. 4. Changes with age in urine pH in taller and shorter men (A) and in stouter and slimmer men (B) throughout the period under study (longitudinal data): arithmetic means and curves of regression with best fitting functions and coefficients of determination are shown

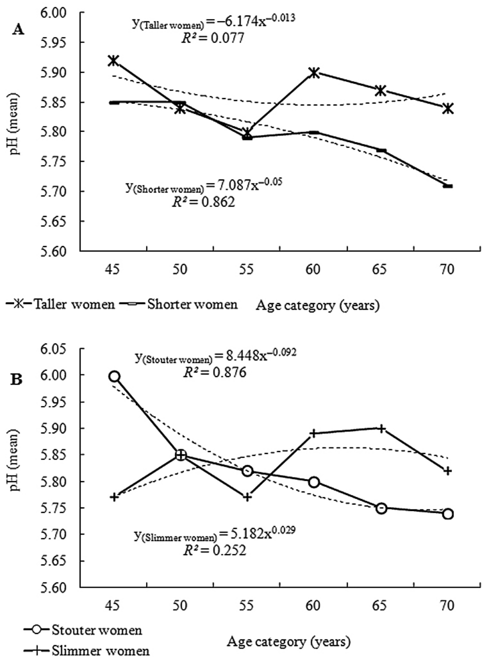

Fig. 5. Changes with age in urine pH in taller and shorter women (A) and in stouter and slimmer women (B) throughout the period under study (longitudinal data): arithmetic means and curves of regression with best fitting functions and coefficients of determination are shown

organ in the retroperitoneal space. Each kidney has an outer renal cortex and an inner renal medulla and the former is a continuous band of pale tissue that completely surrounds the latter (Drake et al. 2015). It serves many essential physiological roles, such as an excretory function (urine production), a regulatory function, by maintaining homeostasis, and an important endocrine function, by direct involvement in the synthesis and degradation of hormones (Lote 2012; Alpern et al. 2013; Kurts et al. 2013). Renal failure manifested by anuria leads to death within a week.

Urine is produced only in functional nephrons. The filtration of a protein-free fluid containing dissolved substances in plasma takes place in the renal corpuscules via glomerular capillary walls and the inner parts of their capsules. In the proximal convoluted tubule, the active reabsorption of sodium and passive absorption of water (about 80%) take place. This process is called obligatory water absorption as it does not depend on the fluid intake volume. Further stages of water reabsorption are facultative and take place mainly in the distal convoluted tubules (Lote 2012; Alpern et al. 2013; Mescher 2013). It is well known that reabsorption rates depend on the intake of fluids and current physiological demand. Potassium, amino acids, glucose, and vitamins are absorbed in the proximal tubule. The urine in Henle's loop becomes hypertonic. In the distal convoluted tubule, calcium, magnesium, sodium, and carbonate ions are reabsorbed and potassium secreted. In the collecting duct system, sodium and urea are reabsorbed, and ammonia secreted in its wall, which then binds with a hydrogen cation and a chloride anion and is excreted during micturition in the form of ammonium chloride (Lote 2012; Alpern et al. 2013).

It has been well established that the aging kidney undergoes numerous age-related changes in its structure and function (Macías-Núñez et al. 2008; Seeley et al. 2008; Halter et al. 2009). The first signs of deterioration usually occur as early as age 20 and become easily detectable by age 50. The regressive changes take place particularly in the renal cortex as a result of alterations in afferent and efferent vessels, which in turn can jeopardize renal filtration and mechanisms of urine concentration. Consequently, the renal ability to eliminate urea, uric acid, creatine, and toxins from the blood decreases with age. Likewise, the capacity to secrete and reabsorb diminishes and eventually many nephrons are impaired. The process of renal senescence consists in glomerulosclerosis, glomerular obsolescence, and tubulointerstitial fibrosis (Macías-Núñez et al. 2008; Seeley et al. 2008; Halter et al. 2009; Sinclair et al. 2012; Alpern et al. 2013; Mescher 2013).

Due to the decrease in estrogen levels in women of perimenopausal and postmenopausal age, the zona glomerulosa producing aldosterone in the renal cortex undergoes physiological atrophy, manifested by a decreased level of enzymes and number of cells, and a gradually reduced secretion of aldosterone. Aldosterone binding to its receptors in renal tubules induces reabsorption of sodium and secretion of potassium and protons. It is known, for example, that patients with chronic renal disorders present with hypercalcemia and metabolic acidosis. Therefore, it is reasonable to predict that deficiency of aldosterone is associated with reduced reabsorption of sodium and increased excretion of potassium and protons into the tubular lumen. Proton loss leads to a decrease in the pH of urine and an increase in the pH of plasma. This can be a tentative explanation as to why the pH of urine is reduced in aging women but not in men, as we observed in our study. Moreover, estrogens stimulate the synthesis of NO, which dilates blood vessels and stimulates angiogenesis. These factors reduce the risk of myocardial infarction, and thus the incidence of acute coronary syndrome in premenopausal women is lower than in men of the same age. Because of the vasodilating and antiatherogenic activity, these are also factors with a protective effect on the renal artery. Improved renal perfusion improves cell viability. It has been observed that the lower estrogen levels in the blood of postmenopausal women have a significant negative suppressing effect on blood flow in the renal artery, which contributes to a decrease in the pH of urine in older women due to the above-described mechanism.

It should be pointed out that with age renal function due to the continued loss of functional nephrons gradually deteriorates in both sexes (Macías-Núñez et al. 2008; Halter et al. 2009). The loss of functional nephrons leads to a decrease in the number of macula densa, and thus a gradual reduction in the number of juxtaglomerular cells producing renin (angiotensinogenase), which is a hormone and enzyme hydrolyzing angiotensinogen, a substance produced mainly in the liver by hepatocytes, into angiotensin 1.

Then in the lungs, convertase transforms angiotensin 1 into angiotensin 2 (by enzymatic cleavage), which increases the aldosterone level in blood. Reduction in renin levels is associated with decreased levels of aldosterone, which leads to urinary acidification in the above-presented mechanism.

Our observations revealed that the specific gravity of urine in the studied population of patients aged 45 to 70 years decreases with age, and this trend is more pronounced in women than in men. However, there were no significant differences between men and women in the specific gravity of urine in subsequent age categories. It should be noted that the specific gravity of urine is affected by various factors, mainly by urine dilution processes, so hydration level plays an important role, but also by other substances, such as glucose, urea, uric acid, electrolytes, radiographic contrast agents or protein (in cases of severe proteinuria).

Renal function is reflected in the glomerular filtration rate (GFR), which in a healthy adult should be about 100–130 ml/min/1.73 m^2, regardless of sex. After the age of 40 years this rate gradually decreases by about 0.4–1.2 ml/min per year. This process is associated with a decrease in the number of functional nephrons. Some studies on the production and secretion of urea in younger and older women have shown a greater decrease in the excretion of urea with age (up to 56% reduction) than in urea production (only a 27% reduction vs. younger women). This causes an increase in plasma urea concentration and, more importantly, a relative decrease in the excretion of urea – a substance increasing the specific gravity of urine. This partly explains our observation that the specific gravity of urine decreases with age. Interestingly, Musch et al. 2006 demonstrated that whereas plasma creatinine does not increase with age, plasma urea does and such changes are accompanied by a decrease in fractional urea excretion. In general, glomerular filtration decreases with aging, yet this alteration is not related to an increase in plasma creatinine, as a result of a concomitant aging-associated decline in muscle mass and creatinine production. The results of some earlier studies show that there is a natural increase in plasma urea in elderly individuals (Corless et al. 1975; Jansen and Harrill 1977). Fehrman-Ekholm and Skeppholm (2004) established that GFR decreases by approximately 1.05 ml/min/year in very old individuals and, therefore, the best formula for estimation of clearance is that of Levey since the formula of Cockroft-Gault seems to underestimate GFR in elderly people.

We found that the specific gravity of urine in men tends to be higher than in women, regardless of age. This most likely results from the fact that the urine concentration determined by the ratio of creatinine in the urine to plasma creatinine levels is higher in men by 21–39% compared to women (there is a 150 mosm/kgH_2O difference between men and women), without any differences in the relative volume of excreted urine in both sexes. Because of this, men are more predisposed to developing nephrolithiasis, hypertension or chronic kidney disease (CKD) than women. The progression of chronic kidney disease in men is usually more rapid than in women. Furthermore, men have generally greater prevalence and susceptibility to hypertension, urolithiasis, and renal disease (Neugarten et al. 2000; Parks et al. 2003; Sandberg and Ji 2003; Reyes et al. 2005; Perruca et al. 2007; Macías-Núñez et al. 2008; Seeley et al. 2008; Halter et al. 2009; Sinclair et al. 2012; Alpern et al. 2013).

Thus, renal function deteriorates with age, which partly results from the slow loss of kidney weight, particularly in the renal cortex (Jones et al. 1998). In addition, sclerotic lesions can form in the walls of renal blood vessels, leading to the degeneration and atrophy of glomeruli, and reduced blood flow through the kidneys per minute. However, in healthy subjects the glomerular permeability does not change significantly with age.

Interestingly, obese subjects with normal renal function have an increased glomerular filtration rate (Salazar and Corcoran 1988). Furthermore, Gryglewska et al. (1998) reported that obesity, particularly its abdominal type (visceral or apple-shaped) is associated with intraperitoneal or intrarenal hypertension. This contributes to increased sodium reabsorption and retention, increases the excretion of protein in urine, strongly promotes nephropathy (e.g. glomerulosclerosis), and stimulates the renin-angiotensin system, which is associated with a general increase in blood pressure (Hall et al. 2003; Bosma et al. 2004; Fox et al. 2004).

Under normal conditions the specific gravity of urine in healthy adults ranges between 1020–1032 g/l, and depends mainly on the amount of fluid intake. However, in many renal diseases it is significantly lower (about 1010 g/l), indicating the decreased ability of the kidneys to concentrate urine. Wieczorowska-Tobis and Talarska (2008) suggest that in elderly people the kidneys are not capable of the maximum concentration, or the maximum dilution of urine, and the osmolarity of urine drops by about 5% per decade of life, despite the compensatory increase in the secretion of vasopressin with age. Impaired urine concentration in elderly subjects was also reported by some other authors (Abrams et al. 1999), a phenomenon which, combined with the reduced flexibility of the bladder, can cause the problematic urinary frequency very characteristic for elderly people. In men, problems with prostatic hypertrophy in older age may further exacerbate the described condition and cause particular discomfort.

These age-associated changes are reflected in our findings on the specific gravity of urine. In both sexes the specific gravity of urine decreases with age: differences in men are close to the level of statistical significance, and significant in women, but there are no significant differences between men and women in individual age categories. In stouter women, the urine specific gravity also decreases significantly with age. In other categories distinguished based on body shape, changes with age are not statistically significant. The specific gravity of urine in taller men is significantly higher than in shorter men only at the age of 45 years (1020.32 vs. 1017.33 g/l), and in taller women compared to shorter women at the age of 55 years (1018.63 vs. 1016.39 g/l). The specific gravity of urine is also significantly higher in heavier women compared with lighter women aged 50 years (1019.99 vs. 1017.42 g/l). However, there were no significant differences between men and women in the specific gravity of urine in subsequent age categories.

In subjects with normal renal function, the pH of urine is about 6.0. Urine pH may, however, change depending on the diet and medical conditions. Diets rich in protein increase the acidity of urine, while diets rich in fruit result in its alkalinity. In certain chronic conditions (e.g. diabetes mellitus) the pH of urine often drops below 6.0. An important role of the kidneys is to maintain the acid-base balance of blood, and thus in subjects with normal renal function more acidic substances than alkaline ones are excreted. However, the analysis of subjects representing both sexes demonstrated no significant changes in the pH of urine associated with aging, and reduction in pH was only found in women who were shorter, heavier, and stouter. Thus, there were no statistically significant differences between men and women in the pH of urine in subsequent age categories. Moreover, no significant differences in urine pH were recorded between subjects from different groups of the study sample. Since there were no significant differences between mean values of specific gravity of the urine and urine pH in subsequent age categories in men and women, as well as between the compared groups of subjects, we believe that the age-related changes in the basic urine parameters tested in the present study are not sufficient and appropriate indicators of renal aging.

Conclusions

The natural process of renal aging commences relatively early in ontogeny and manifests itself in some structural and functional changes in the urinary system in both sexes. Therefore, urinalysis and other more sophisticated methods of diagnosis of renal diseases are essential for proper assessment of health status of adults and older individuals. The rate of age-related changes in the analyzed traits of the urine was commensurate in both sexes, thereby revealing no evidence of significant sex differences in terms of renal aging in the period between 45 and 70 years of age. There were no significant differences between mean values of specific gravity of the urine and urine pH in subsequent age categories in men and women as well as between the compared groups of subjects. Therefore, we conclude that the age-related changes in these basic urine parameters are not good and appropriate indicators of the process of renal aging. More longitudinal and cross-sectional studies of aging of the urinary system in both sexes are needed.

Authors' contributions

PC conceived the study, analyzed the data, interpreted the results, and wrote this article. BS and KB served as principal investigators for the research, supervised the research, analyzed the data, and commented on the final draft. KC, JC, and PD collected the data and performed statistical analysis. All authors participated in the development of the research concepts, assumptions, and methods.

Conflict of interest

The authors declare that they have no conflict of interest.

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