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CHRONIC KIDNEY DISEASE: PREVALENCE AND RISK FACTORS (LITERATURE REVIEW)

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Chronic kidney disease (CKD) is a complex of syndromes that occurs as an outcome of various kidney diseases or as a complication caused by diseases of other organs; it often exerts maximum influence on prognosis for a primary disease. It seems an urgent task to improve early CKD diagnostics and reveal risk factors that can cause unfavorable clinical course and development of the pathology. Finding solution to this task will allow reducing terms and improving organization of specialized medical aid provided for patients. The issue related to detection of health risk factors is especially pressing in countries with low and middle incomes. National and international efforts aimed at preventing, detecting, and treating chronic kidney diseases are necessary for decreasing worldwide mortality and morbidity.

The article presents a review of literature data accumulated in PubMed, Elsevier, and Google Scholar databases on epidemiologic issues concerning chronic kidney diseases. We managed to find more than 150 materials; more than 40 articles out of them were analyzed and they turned out to dwell on different aspects of the issue. Special attention is paid to CKD prevalence among population depending on a country, ethnic group, age, and sex as well as to examining risk factors occurring in a specific region or a country.

Literature analysis allowed concluding that CKD prevalence has grown substantially over the last 10 years. Among risk factors there are medical parameters (prevalence of chronic cardiovascular diseases and endocrine system diseases) and social and demographic conditions. It is shown that CKD tends to occur more frequently among people from black race than those from other races. But black people have higher survivability after dialysis than their white counterparts from the same age groups. Awareness about CKD risk factors among population and doctors providing primary medical assistance predetermines efficiency of early diagnostic and further treatment of the disease in low income countries.

Key words: *chronic kidney disease, glomerular filtration rate, terminal kidney failure, prevalence, risk factors, epidemiology.*

Non-communicable diseases are among leading death causes all over the world. Chronic kidney disease (CKD) is among those pathologies that cause mortality including untimely deaths. Over the last decade CKD prevalence has been growing steadily simultaneously with a rapid growth in number of people suffering from cardiovascular diseases and pancreatic diabetes. In 2016 CKD resulted in 1.19 million death cases all over

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the world that was by 28.8 % higher than in 2006. It allowed CKD to take the 11th rank place among death causes in 2016 against the 13th and 27th rank place in 2013 and 1990 accordingly. The WHO predicts that in 2030 CKD will hold the 13th rank place among death cases [1].

Apart from effects produced on mortality growth, CKD also exerts significant influence on population life quality and economic results achieved in a country or a region. Hence, fighting against global CKD epidemic is a vital and complicated task that requires, among other things, early detection of people with arterial hypertension, pancreatic diabetes, and other risk factors. In this case screening as a procedure aimed at detecting potential patients with CKD is important and economically efficient [2]. Experts revealed differentiated inverse dependence between cardiovascular risks and glomerular filtration rate (GFR) that was not dependent from age, sex, and other risk factors [3]. Kidney functional reduction is a predictor of hospitalization, cognitive dysfunction, and low life quality [4–8]. Low awareness about CKD in many countries can crate obstacles for early intervention and some researchers recommend raising this awareness about the disease among people [2].

CKD doesn't only result in deaths but also leads to a significant decrease in life quality and disability. Cross-questioning performed in the USA allowed revealing that difficulties in everyday life were much more frequently mentioned by patients with CKD than by those who didn't suffer from it [9]. Besides, CKD frequently aggravates other chronic diseases such as pancreatic diabetes, hypertension, and cardiovascular diseases and it can impose additional limitations on people's functional abilities. The latest WHO report on global diseases burdens stated that over the last 10 years overall number of lost healthy years due to CKD grew significantly from 29.2 thousand to 35.0 thousand. This calculated amount is higher than one calculated for many neurological disorders including dementia, Parkinson disease and chronic renal failure as well [10].

Remarkably, CKD is also related to substantial expenses on medical services. In the state register in Sweden annual expenses on medical aid rendered to patients suffering from CKD (without dialysis) were 4 times higher than those rendered to an average patient; in case hemodialysis was applied, the difference grew to 45 times [11].

According to KDOQI (Kidney Disease Outcomes Quality Initiative), CKD can be classified into five stages [12] using CKD parameters and data on structural changes in the kidneys (for example, proteinuria). Other recommendation as per NICE allows dividing the stage 3 into 3a and 3b that reflect a growth in cardiovascular risks [13]. As per data obtained via a retrospective study performed in Great Britain, the highest CKD stage is stage 3 determined in more than 90 % cases. 84 % out of them are stage 3a (glomerular filtration rate (GFR) varies from 45 to 59 ml / min/ 1 · 73 m ^{2}) and 16 % are stage 3b (GFR is from 30 to 44 ml / min / 1 · 73 m^2) [14].

CKD reasons vary depending on a country, ethnic group, and age.

Changes in CKD prevalence over time are rather controversial. Data obtained via the Third National Health and Nutrition Examination Survey revealed that over a period from 1999 to 2004 CKD stage 1–4 prevalence grew considerably in comparison with a period from 1988 to 1994 (13.1 % against 10.0 %) [15–17]. Although this high prevalence is partially due to population becoming older, it is also related to growth in hypertension and pancreatic diabetes prevalence [3]. However, results obtained via representative cross-studies performed in Great Britain allowed revealing that prevalence decreased over time within national borders [18].

Diabetic nephropathy is the most widely spread kidney disease that results in renal replacement therapy (RRT) in the USA (44 %) and Great Britain (27.5 %) [19, 20]. On the contrary, primary glomerulonephritis is a basic reason for kidney failure or end-stage renal disease (ESRD) in China [21]. However, approximately 10–15 % patients who had ESRD didn't have any specific renal diagnosis [19, 22].

N.R. Hill et al., researchers at Oxford Universality, performed a systematic review and meta-analysis on the subject; they revealed that average CKD prevalence was higher from stage 1 to 5 (13.4 % against 11.0 %). CKD cases distribution as per stages performed with the use of all the available data was as follows: stage 1 (GFR> 90) 3.5 % (2.8–4.2 %); stage 2 (GFR 60–89) 3.9 % (2,7–5.3 %); stage 3 (GFR 30–59) 7.6 % (6.4–8.9 %); stage 4 (GFR 29–15) 0.4 % (0.3–0.5 %), and stage 5 (GFR<15) 0.1 % (0–0.1 %). It was impossible to analyze specific data on stages 3a/3b due to absence of reports on them. Besides, the same research revealed that a growth in person's age made a significant contribution into CKD prevalence. A growth in CKD frequency with age can be due to peculiarities of applied formulas where an age is usually inversely proportionate to CKD value [3].

K.T. Mills et al. performed a systematic review on CKD prevalence in the world over a period from 2006 to 2013. The results are given in Table 1 [23].

Table 1

Research performed by K.T. Mills; CKD stages depending on sex, age and country income, %

№	CKD stages	Men	Women
1	*CKD stages 1–5 among adults aged ≥20*	10.4 (9.3–11.9)	11.8 (11.2–12.6)
1.1	High income countries	8.6 (7.3–9.8)	9.6 (7.7–11.1)
1.2	Low and middle income countries	10.6 (9.4–13.1)	12.5 (11.8–14.0)
2	*CKD stages 3–5 among adults aged ≥20*	4.7 (3.4–6.7)	5.8 (4.4–8.1)
2.1	High income countries	4.3 (3.5–5.2)	5.7 (4.4–7.6)
2.2	Low and middle income countries	4.6 (3.1–7.7)	5.6 (3.9–9.2)

When performing their meta-analysis, the authors noted that 51 works out of 100 examined one contained data on CKD prevalence varying depending on sex. Average CKD prevalence among men (95 % confidence interval for research in which 5 CKD stages were determined) amounted to 12.8 % (10.8–11.9 %), and the parameter amounted to 8.1 % (6.3–10.2 %) for research in which stages 3–5 were determined. CKD prevalence among women at stage 1–5 amounted to 14.6 % (12.7–16.7 %), and to 12.1 % for research in which stages 3–5 were determined. N.R. Hill, S.T. Fatoba, and J.L. Oke noted that CKD was more widely spread among women than among men [3].

B. Bowe, Y. Xie, T. Li, and A.H. Mokdad examined morbidity with CKD stage 3–5 detected when patients were rendered primary medical-sanitary aid; over the examined period (2010–2014) it amounted to 71.9 per 1,000 people with huge difference as per geography (urban/rural settlements), socio-demographic factors (age, deprivation), and clinical factors (number and type of concomitant diseases).

Overall CKD prevalence was inversely proportionate to its gravity (3a stage, 31.8 per 1,000; 3b stage, 25.3 per 1,000; stage 4, 11.7 per 1,000; and stage 5, 3.3 per 1,000 thousand). There were no substantial differences in prevalence as per patients' sex.

Graver CKD stages were widely spread among elderly people (≥ 65 years old), especially among people aged from 75 to 80 (345.1 per 1,000) and people older than 80 (397.6 per 1,000).

There was great CKD prevalence among people with 3 or more concomitant diseases; overall, it was equal to 281.7 per 1,000 people, most of them having stages 3a and 3b (98.9 and 109.6 per 1,000 people). CKD prevalence was high among people with comorbid dementia (303.3 per 1,000), pancreatic diabetes and arterial hypertension combined (267.4 per 1,000 people), Parkinson disease (223.7 per 1,000 people), and chronic obstructive lung disease (221.3 per 1,000 people) [24].

In Kazakhstan comorbidity was examined by O.J. Narmanova in 2008. The author revealed high prevalence of factors making for CKD growing progressively worse in patients with glomerular diseases: 23.37 exam-

ined patients had arterial hypertension; 31.73 %, diagnostically significant proteinuria; 56.03 % suffered from anemia; 35.49 % patients had hypoproteinemia. A direct correlation was detected between prevalence of the revealed factors and CKD and an inverse one between CKD and comorbidity. Analysis of CKD prevalence among dispensary patients suffering from AH, pancreatic diabetes, and primary and secondary nephropathy revealed that 71.5 % examined patients had CKD stages 1–2; 17.7 %, stage 3; 1.3 % stages 4–5 that is, functional disorders in the kidneys were irreversible[1].

As regards geography, higher CKD prevalence was detected in rural areas (86.2 per 1,000 people) than in urban ones (68.4 per 1,000 people). Literature contains a lot of data on factors that determine inequality regarding health preservation in remote urban and rural settlements; the most widely spread ones are remoteness from public healthcare organizations, geographical isolation, limited number of medical aid suppliers, and socioeconomic factors [24].

When analyzing chronic diseases burden in the USA, researchers revealed that over a period from 2002 to 2016 CKD burden was growing in the USA and was ahead of other non-communicable diseases. Over the last 15 years in the USA certain changes have occurred in demographic, social, and epidemiologic trends. Those changes probably made for changes in chronic kidney disease (CKD) epidemiology.

In the USA an increase in CKD DALY was related to an increase in susceptibility to risk (40.3 %), ageing (32.3 %), and population growth (27.4 %). CKD parameters standardized as per age increased by 18.6 % with a growth in metabolic risk factors and, to a lesser extent, in diet-related ones that amounted to 93.8 % and 5.3 % accordingly [24].

CKD in the South Asia has the same widely variable prevalence as in developed countries. Reasons that cause CKD are different, and in some regions there is high prevalence of CKD caused by glomerulnephritis and obstructive nephropathy as well as CKD with unknown etiology [25].

When analyzing these collaborators in studies on global diseases burden in the USA over a period from 2002 to 2016, researchers revealed a 52.6 % growth in CKD DALY. CKD burden grew in all the states but rates of change (2002–2016) and burden in 2016 varied depending on a particular state. States on the south (including Mississippi and Louisiana) had burden that was more than 2 times higher than in other states (for example, CKD DALY standardized as per age amounted to 321 per 1,000 in Vermont whereas in Mississippi it amounted to 697 per 1,000 people).

Similar heterogeneity was detected in European countries. For example, prevalence of CKD stages from 1 to 5 varied from 3.31 % in Norway to 17.3 % in the northwest Germany; prevalence of CKD stages from 3 to 5 varied from 1.0 % in the central Italy to 5.9 % in the northwest Germany. Similarly, in Asian countries, for example, in China, prevalence of CKD stages from 1 to 5 varied greatly, from 6.7 % in the southern China to 18.3 % in the southwest China [25].

O.Yu. Gerasimova and L.N. Semchenko noted in their works that in Russia there were no available authentic data on a number of patients who suffered from kidney diseases and chronic renal failure. From 2003 to 2013 a number of urogenital system diseases grew by 31.6 %. In 2013 a number of patients suffering from renal failure on average amounted to 44.6 per 100 thousand people and it was 2.2 times higher than in 2003 [26].

B.T. Bikbov and N.A. Tomilina noted in the first part of the report issued basing on data provided by the Russian register of substitute kidney therapy that annual growth in number of people suffering from CKD was well in line with world trends [27]. O.I Apolikhin et al. stated that a number of patients with CKD on average grew by 9.9 % every year [28].

[1] O.J. Narmanova. Epidemiologic and medical-organizational aspects of improving specialized medical aid rendered to patients with chronic renal failure: abstract of the thesis ... Doctor of Medical Sciences. Astana, 2008, 140 p. (in Russian).

CKD prevalence as per geographical regions was also examined by British researchers. The results revealed that CKD prevalence was higher in developed regions such as Europe, USA, Canada, and Australia, than in regions with developing economies such as African countries located south from Sahara and India, excluding Iran where similar parameters were high. Research results are given in Table 2 [3]. CKD prevalence is probably predetermined with nutritional disorders, high body mass index (BMI), high systolic blood pressure, and concomitant diseases that are spread in a specific country [19].

Table 2

CKD prevalence as per geographic regions

Regions	CKD stages 1–5 % (95 % CI)	CKD stages 3–5 % (95 % CI)
South Africa, Senegal, Congo	8.66 (1.31–16.01)	7.60 (6.10–9.10)
India, Bangladesh	13.10 (11.01–15.19)	6.76 (3.68–9.85)
Iran	17.95 (7.37–28.53)	11.68 (4.51–18.84)
China, Taiwan, Mongolia	13.18 (12.07–14.30)	10.06 (6.63–13.49)
Japan, South Korea, Oceania	13.74 (10.75–16.72)	11.73 (5.36–18.10)
Australia	14.71 (11.71–17.71)	8.14 (4.48–11.79)
The USA, Canada	15.45 (11.71–19.20)	14.44 (8.52–20.36)
Europe	18.38 (11.57–25.20)	11.86 (9.93–13.79)

K.T. Mills et al. reported in their research work that overall CKD prevalence depending on stage 1 to 5 varied from 4.5 to 25.7 % in South Korea; from 4.1 % among men in Salvador and Saudi Arabia to 16.0 % among women in Singapore; CKD stage from 3 to 5 varied from 1.3 % among men in China to 15.4 % among men in Nepal, and from 1.7 % among women In Singapore to 21.3 % among women in Nepal [23]. 12.5 % adults aged 40 and older suffered from CKD in Pakistan [29].

CKD prevalence depending on an ethnic group was examined by Pakistan researchers. In Pakistan CKD prevalence was estimated as per different communities in several research works. T.H. Jafar et al. (2003) estimated proteinuria prevalence as a CKD marker in four ethnic groups. They detected the highest prevalence among Sindhi (9.5 % among men and 10.3 % among women) and Muhajir (8.2 % among men and 4.7 % among women); the lowest prevalence was detected among Baluchi (2.4 % among men and 4.2 % among women) and Pashtun (2.5 % among men and 1.2 % among women) [25].

Arabs account for approximately 20 % of population in Israel. In the country socioeconomic position and other difference regarding Arabs can create a situation similar to that of African Americans in the USA [30]. According to the Register on Kidneys maintained by «Israeli Society of Nephrology and Hypertension» and «Israel Center for Disease Control» by the end of 2007 there were 4,800 patients with CKD in Israel including 23 % ethnic Arabs (both Muslim and Arabian Christians). From 1997 to 2007 in Israel the disease frequency grew by 71 % [30].

Approximately 11 % adults in the USA probably have a chronic kidney disease that is progressing into its irreversible form and at present can't be cured. B.B. Newsome et al. reported in several research works that 125 thousand African Americans, being 6.5 % of the overall examined sampling (1.9 million people), accounted for 14.9 % cases of progressing CKD [31].

«Healthy People 2020», a program existing in the USA, has been focusing on the nation health over the last few years. Its goal is to assess and predict changes in public healthcare. Among other things, assessment includes analyzing specific risk factors that cause CKD and end-stage renal disease (ESRD) [32]. As we can see from Table 3, it was revealed within «Healthy People 2020» implementation that CKD prevalence grew both among African Americans and their white counterparts [33, 34].

Table 3

Patients treated due to CKD as per race/ethnic group, data provided by «Healthy People 2020»

Parameters	Black / African Americans		White		Targets approved within «Healthy People 2020»
	2006	2015	2006	2015	
% of patients with CKD c treated by a nephrologist at least 12 months prior to substitute kidney therapy start	23.2 %	32 %	27.9 %	37 %	30.4 %
New ESRD cases per 1 million people	1114	895	294	312.1	352
% of patients who had kidney transplantation within 3 years time since ESRD was diagnosed	9.1 %	7 %	21 %	16.2 %	20.1 %
Number of deaths per 1,000 patient-years for people on dialysis	170.9	135.8	258.1	207.4	187.4

When estimating patients' health within Composite Health Care System (CHCS) procedures, experts obtained the following results: overall, 8,318 patients were examined, 5,849 (70.3 %) of them were whites, 1,344 (16.2 %) were blacks, and 1,125 (13.5 %) belonged to other races that were not identified. CKD stage 3 was diagnosed in 5,459 white patients (93.3 %), and stage 4, in 390 (6.7 %). CKD stage 3 was diagnosed in 1,205 black patients (89.7 %), and stage 4, in 139 (10.3 %). People belonging to unidentified races had CKD stage 3 in 94.7 % cases (1,065 patients), and stage 4 in 5.3 % cases (60 patients) [35].

There was a study on determining ethnic differences in chronic kidney disease progressing among people suffering from pancreatic diabetes in Great Britain performed with the use of data taken from East London database over a period from 2006 to 2016; the study revealed that 6,274 patients out of 120,591 adults with pancreatic diabetes also had CKD; those patients aged 25-84 were whites, South Asian people, and blacks. 81.5 % white people had CKD stage 3a; 15.7 %, stage 3b; and 2.8 %, stage 4. 82.9 % South Asian people had CKD stage 3a; 13.9 %, stage 3b; and 3.2 %, stage 4. 83.6 % black patients had CKD stage 3a; 13.2 %, stage 3b; and 3.2 % stage 4 [36].

Approximately 25 % people with CKD have very poor literacy regarding health and it to a greater extent influences people with low socioeconomic position and obviously results in greater risks of adverse clinical outcomes [37, 38].

Raising awareness and literacy among population is a basic task in fighting CKD; it is also very important to early detect the disease and provide a patient with treatment by a nephrologist already at its early stages [2]. The latter is especially significant due to CKD developing mostly symptomless at early stages (before major renal failure occurs) [39].

Absence of awareness about CKD all over the world can be partially due to CKD diagnostics being based on laboratory blood tests (creatinine contents in blood serum or cystatin C contents necessary for estimating glomerular filtration rate (GFR)) and urine tests (for urine sediments, especially albuminuria); these tests are probably less available than a tonometer or a glucometer that are used in hypertension and diabetes diagnostics. A wide-scale examination performed in Canada revealed alarmingly low awareness about CKD as only 8 % patients suffering from it knew their diagnosis; elderly people and women less frequently knew

about it [40]. Overall awareness about CKD among population in general and even population groups running high cardiovascular risks amounted to less than 10 % in 12 countries with low and middle incomes [41]. Research performed in Hong Kong revealed that less than a half of its citizens knew that hypertension and diabetes, being the major ESRD causes, could damage kidney functions [42].

T.H. Jafar et al. performed a quantitative study and revealed that not only patients were poorly aware about CKD; doctors working in primary healthcare were also rather ignorant. Doctors who took part in the study mentioned limited knowledge and lack of confidence in a possibility to cure CKD at its early stage. Though doctors working in primary healthcare knew such terms as «urea» and «creatinine», they didn't perform preventive CKD screening among their patients and didn't treat those who suffered from it; instead, they sent such patients to specialized medical organizations. Also some doctors noted that cultural beliefs and standards of their patients often contradicted clinical recommendations and it created additional problems in treating CKD [43–45].

Doctors from two towns in Cameroon took part in a study focusing on determining literacy among medical personnel; the study revealed that only 58.8 % questioned doctors were able to determine CKD correctly. Less than a half (44 %) knew that CKD had 5 stages and 73.8 % wrong answers were given by specialists in the field. It was also revealed that more than 90 % doctors knew basic risk factors that caused CKD; more than 80 % knew basis CKD complications; and more than 90 % knew that hemodialysis and transplantation were basic tools used in substitute kidney therapy. But still, peritoneal dialysis that was not used in the country at that moment was poorly known to questioned doctors. As regards detecting CKD, some doctors (12.7 %) still relied solely on creatinine in blood serum when diagnosing the disease. Accordingly, patients in Cameroon were not aware about CKD and its complications and doctors weren't able to properly slow down the disease progressing up to ESRD in such patients [44].

Therefore, our examination of literature sources on chronic kidney disease prevalence has yielded the following results:

– chronic kidney disease occurs in approximately 12 % of the overall world population. CKD prevalence is growing steadily together with other most significant non-communicable diseases;

– CKD risk factors are pancreatic diabetes, arterial hypertension, cardiovascular diseases, high body mass index, as well as social-demographic factors such as population growing older, low incomes, medical aid being poorly available, and low awareness about CKD among patients and doctors working in primary health care;

– most studies on CKD prevalence concluded that the disease was more frequent among women than among men. Average CKD prevalence among men (95 % confidence interval for studies where 5 CKD stages were determined) amounted to 12.8 % (10.8–11.9 %) and to 8.1 % (6.3–10.2 %) for studies where CKD stages 3–5 were determined. CKD prevalence among women for studied where stages 1–5 were determined amounted to 14.6 % (12.7–16.7 %) and to 12.1 % for studied where stages 3–5 were determined;

– studies perform over a period from 2006 to 2013 revealed that CKD prevalence in countries with middle and low incomes was higher than in countries with high incomes. However, British researchers revealed in their works performed prior to 2014 that CKD prevalence was higher in developed regions such as Europe, the USA, Canada, and Australia that in regions with developing economies such as African countries located south from Sahara and India;

– Composite Health Care System (CHCS) database contained data on a number of new ESRD cases being 2.8 times higher among blacks than among whites in the USA; number

of deaths per 1,000 patient-years among people on dialysis was 1.5 times lower among blacks. It indicates that CKD is more frequent among black people but they survive dialysis more often than their white counterparts of the same age;

– regardless of all above mentioned determinants, raising awareness and literacy among doctors working in primary healthcare is the major task in fighting CKD; early detection and timely treatment promotes less frequent transitions of the disease from its 3 and 4 stages into stage 5, a terminal one.

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