Clinical and Experimental Hypertension

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/iceh20

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To cite this article: Silvana Nader Nagib, Saeed Abdelwahab, Ghada Essam El-Din Amin & Mohamed Farouk Allam (2023) What is the prevalence of chronic kidney disease among hypertensive non-diabetic Egyptian patients attending primary healthcare?, Clinical and Experimental Hypertension, 45:1, 2203411, DOI: 10.1080/10641963.2023.2203411

To link to this article: https://doi.org/10.1080/10641963.2023.2203411

Published online: 23 Apr 2023.

CLINICAL AND EXPERIMENTAL HYPERTENSION
2023, VOL. 45, NO. 01, 2203411
https://doi.org/10.1080/10641963.2023.2203411

What is the prevalence of chronic kidney disease among hypertensive non-diabetic Egyptian patients attending primary healthcare?

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ABSTRACT

Background: Although chronic kidney disease (CKD) is considered the major cause of morbidity and mortality in hypertension, the recognition and prevention of CKD remain deficient. CKD is one of the major health challenges in Egypt. CKD affects approximately 13% of the adult population, resulting in significant morbidity, mortality, and health care costs. Patients with more progressive stage 3 or stage 4 CKD experience a high rate of cardiovascular events and death compared to earlier stages of CKD.

Aim: This study was performed to determine the prevalence and risk factors of CKD among hypertensive non-diabetic patients attending primary health care (PHC) centers in Cairo.

Methodology: The study type is a cross-sectional study. Study setting: Two PHC centers: Saraya El-kobba and El-Sharabya. Sampling method: Recruitment of participants was done in one day weekly. Any known essential hypertensive patients aged 18 or more registered in the two PHC centers in Cairo.

Results: The prevalence of CKD was 33% among the hypertensive non-diabetic patients. Among CKD participants, the prevalence is more common in females (59.7%) than males (40.3%), in those who completed primary education and in the illiterates and low socioeconomic class. Surprisingly, it is more common in patients with positive family history of CKD and patients with ischemic heart disease and the antihypertensive drugs use.

Conclusion: CKD has a high prevalence among hypertensive non-diabetic patients, and it has a significant morbidity and mortality among those patients.

ARTICLE HISTORY
Received 13 June 2022
Revised 6 October 2022
Accepted 11 April 2023

KEYWORDS
Prevalence; chronic kidney disease; hypertension; primary health care centers

Introduction

Chronic kidney disease (CKD) is one of the most important health challenges in Egypt. Approximately 13% of the adult Egyptian population is affected by CKD, resulting in significant morbidity, mortality, and health care costs. Patients with stage 3 or stage 4 CKD experience a high rate of cardiovascular events and death compared to earlier stages of CKD (1).

Hypertension is both a cause and a clinical presentation of CKD. The kidney plays an important role in the control of blood pressure; likewise hypertension may predict underlying kidney disease. Poorly controlled hypertension leads to rapid deterioration in kidney function culminating in end-stage kidney disease (ESKD). Hypertension was found to be the third most common cause of CKD in a single-center study in Ghana (2).

KDIGO 2012 defined CKD as abnormalities of kidney structure or function, present for more than 3 months, with consequences on health, and the classification system has been revised to encompass cause and severity. Identifying cause is important in predicting outcomes and guiding the choice of cause-specific treatments. Severity is expressed by the level of glomerular filtration rate (GFR) and albuminuria. Severity is linked to risks for adverse outcomes, including death and kidney outcomes (3).

The stages of CKD are classified as follows: Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m^2); Stage 2: Mild reduction in GFR (60–89 mL/min/1.73 m^2); Stage 3a: Moderate reduction in GFR (45–59 mL/min/1.73 m^2); Stage 3b: Moderate reduction in GFR (30–44 mL/min/1.73 m^2); Stage 4: Severe reduction in GFR (15–29 mL/min/1.73 m^2); and Stage 5: Kidney failure (GFR<15 mL/min/1.73 m^2 or dialysis) (4,5).

In China, the incidence of CKD coexisting with hypertension is 6%–18%, and the prevalence of hypertension in CKD reaches 60%–80% (6). In the United States, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) reported that 1 in 10 American adults have some level of CKD. Kidney disease is the ninth leading cause of death in the United States (7).

In Egypt a cross-sectional study was conducted on the relatives of patients with CKD from a community-based screening program to detect the prevalence and risk factors for microalbuminuria (MA). The prevalence of MA was more than 10% in the population screened and higher in the subjects with diabetes, hypertension, obesity, or cardiovascular disease (CVD) (8).

Unfortunately, the number of patients developing ESRD as a complication of hypertension is increasing in Egypt. However, the diagnosis of hypertensive ESRD is one of

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exclusion and no pathologic data corroborate this classification. These patients suffer from a diversity of diseases, including accelerated hypertension and atherosclerotic disease of the large arteries and undiagnosed chronic renal disease. It is also identified that mild-to-moderate hypertension can lead to ESRD. Therefore, additional studies are essential to determine the frequency with which essential hypertension leads to ESRD in Egypt (9).

Multiple guidelines recommend that patients with diabetes or hypertension be screened annually for CKD. Furthermore, patients with other risk factors, including CVD, older age (more than 60), racial or ethnic minorities, history of low birth weight, obesity, exposure to known nephrotoxins, low income or education level, autoimmune diseases, systemic infections, urinary tract infections, nephrolithiasis, neoplasia, recovery from acute renal failure, reduction in kidney mass, and a family history of CKD, warrant consideration for screening. The American College of Physicians and the American Academy of Family Physicians recommend against screening for CKD in asymptomatic adults without risk factors (10).

However, more than 90% of patients who have CKD remain unidentified. Hypertension and diabetes are the main risk factors of CKD. Therefore, early screening and avoidance of progression of CKD having a very high cardiovascular risk are extremely essential challenges and goals for primary health care (PHC) physicians (11).

Our study aimed to determine the prevalence and risk factors of CKD among hypertensive non-diabetic patients attending PHC centers in Cairo, Egypt.

Methodology

Participants

The study participants comprised 200 hypertensive non-diabetic patients of both sexes registered for two PHC centers in Cairo: Saraya El-kobba and El-Sharabya. They were recruited, from the internal medicine clinics of both PHC centers, in one day weekly. All the hypertensive patients were enrolled in the study till completion of the sample size.

Sample size was calculated according to the previous study of da Silva and collaborators (2016) that was conducted in Brazil and showed that 39% of hypertensive non-diabetic patients had CKD. Setting total hypertensive non-diabetic patients in both PHC centers 400, with confidence level (1α) 95%, precision 5%, and proportion 39%, the sample size was found to be 191 patients (approximated to 200). Sample size was calculated using the EpiDat 4.2 program.

Participants with the following criteria were excluded:

(1) Any cases suffering from diabetes mellitus.
(2) Pregnant females.
(3) Any cases suffering from secondary hypertension
(4) Any cases suffering from CKD due to polycystic kidney disease, primary glomerulonephritis, obstructive uropathy or autoimmune diseases-like systemic lupus erythematosus and rheumatoid arthritis.
(5) Individuals with a history of drug addiction/NSAIDs abuse.

An agreement to informed consent was obtained from all subjects, fulfilling the study criteria, before taking part in the study. The protocol of this study was approved by the Institutional Review Board (IRB) of Ain Shams University Graduate School of Medicine.

Study tools

All study participants were subjected to

An interview questionnaire: The questionnaire was divided into four parts

First part inquired about the sociodemographic data about the age, sex, level of education, occupation, smoking habit, having exercise regularly, gravidity, parity, and past history of preeclampsia (in females).

Second part inquired about information about hypertension duration, control, medication compliance, and drugs taken.

Third part inquired about the past history of CVDs, ischemic heart diseases, cerebrovascular strokes, surgical operations done, and contrast dye exposure.

Fourth part inquired about family history of hypertension, diabetes mellitus, and CKD.

Clinical examination

(a) Arterial blood pressure was measured twice using a sphygmomanometer.
(b) Anthropometric measurements:

(i) Weight was measured by a digital scale. The participant stands with minimal movement with hands by their side. Shoes and excess clothing were removed. Weight was approximated to the nearest 0.5 kg.
(ii) Standing height was measured using a stadiometer.
(iii) Body mass index (BMI, weight/height "m^2") was calculated.
(iv) Waist and hip circumference are measured using non-stretch flexible fiberglass tapes.
(v) The waist hip ratio is calculated as waist measurement divided by hip measurement (W ÷ H).

Laboratory investigations

(1) A 2.5 mL of blood sample was drawn from the participants and was sent to the Central Laboratories of El-Demerdash Hospital, Ain Shams University to determine the serum creatinine level.
(2) A spot urine sample was collected in a transparent plastic container and was sent to the Central Laboratories of El-Demerdash Hospital, Ain Shams University to measure the Protein Creatinine Ratio (PCR).

Then, the GFR was calculated using the Modification Diet in Renal Disease formula (MDRD) Equation. This calculator uses the four-variable equation from Levey 2006 (sex, age, race, and serum creatinine). The CKD stages were estimated using the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines.

Table 1. CKD stages according to e-GFR among the study participants.

	All participants (*N* = 200), 100%	
CKD Stages	N	%
Stage 1(GFR≥90 mL/min/1.73 m^2)	59	29.5%
Stage 2(GFR = 60–89 mL/min/1.73 m^2)	74	37%
Stage 3a(GFR = 45–59 mL/min/1.73 m^2)	29	14.5%
Stage 3b(GFR = 30–44 mL/min/1.73 m^2)	24	12%
Stage 4(GFR = 15–29 mL/min/1.73 m^2)	13	6.5%
Stage 5(GFR<15 mL/min/1.73 m^2)	1	0.5%
Total	200	100%

The following criteria were applied in order to classify stages of CKD:

Stage 1: GFR ≥ 90 mL/min/1.73 m^2

Stage 2: GFR between 60 and 89 mL/min/1.73 m^2

Stage 3A: GFR between 45 and 59 mL/min/1.73 m^2

Stage 3B: GFR between 30 and 44 mL/min/1.73 m^2

Stage 4: GFR between 15 and 29 mL/min/1.73 m^2

Stage 5: GFR<15 mL/min/1.73 m^2.

Individuals with a GFR<60 mL/min/1.73 m^2 (i.e., stages 3A, 3B, 4, and 5) were considered to be affected by CKD.

Statistical analysis and package

First, the following descriptive analysis was done: frequency, percentages, and mean and standard deviation (SD). Thereafter, a comparison was done using Student *t*-test for quantitative variables and Fisher exact test for qualitative variables. The level of significance was set at a *p* value equals to or less than 0.05. Data entry and statistical analysis were done using Statistical Package for Social Science (SPSS) version 23.0.

Results

The study shows that the prevalence of CKD (i.e. GFR<60 mL/min/1.73 m^2) among hypertensive non-diabetic patients (i.e. Stages 3a, 3b, 4 and 5) was found to be 33%.

Table 1 shows the distribution of individuals according to the classification stages of GFR following the recommendation of KDIGO 2013. The majority of patients lie is stage 2.

Table 2 compares sociodemographic data of CKD and non-CKD patients; age and less physical exercise were important risk factors for CKD.

Table 3 compares CKD and non-CKD patients regarding information about hypertension; long duration of hypertension and non-adherence to treatment were a predictive risk factor for CKD.

Table 2. Sociodemographic data among CKD and non-CKD patients.

		CKD GFR < 60; N = 67		No CKD GFR ≥ 60; N = 133		
Sociodemographic data *		Mean		Mean		P-value**
Age		58.45		50.54		0.002
		N	%	N	%	
Gender	Female	40	59.7	79	59.6	0.823
	Male	26	40.3	55	41.4	
Education	Illiterate	14	20.9	20	15	0.765
	Primary education	18	26.9	41	30.8	
	Preparatory education	15	22.4	38	28.6	
	Secondary education	14	20.9	26	19.5	
	University	5	7.5	9	6.8	
Occupation	Not working/housewife	14	20.9	82	61.7	0.006
	Retired	19	28.4	27	20.3	
	Legislators, senior officials, and managers	1	1.5	2	1.5	
	Professionals	1	1.5	4	3	
	Technicians and associate professionals	4	6	6	4.5	
	Clerks	1	1.5	2	1.5	
	Service workers and shop and market sales workers	3	4.5	1	0.8	
	Skilled agricultural and fishery workers	2	3	3	2.3	
	Craft and related workers	3	4.5	3	2.3	
	Plant and machine operators and assemblers	7	10.4	3	2.3	
	Elementary occupations	9	13.4	6	4.5	
	Armed forces	0	0	2	1.5	
Smoking Status	Never smoke	43	64.2	96	72.2	0.6
	Ex-smoker	13	19.4	20	15	
	Currently smoker	10	14.9	18	13.5	
Physical Activity	Yes	1	3	4	2.2	0.005
	No	65	97	130	97.8	

*Quantitative data are expressed as mean ± SD; the number in parentheses adjacent to the actual number indicates percentage of cases.

**Student's *t*-test for continuous variables and Pearson's Chi square test for categorical variables.

Table 3. Comparison between CKD and non-CKD patients as regards information about hypertension.

		CKD GFR < 60; N = 67		No CKD GFR ≥ 60; N = 133		
Hypertension		N	%	N	%	P value*
Duration	<5 years	20	30.3	92	69.2	0.005
	5–10 years	16	24.2	31	23.3	
	>10 years	30	45.5	12	7.5	
Monitoring of blood pressure	Yes	23	34.3	47	35.3	0.975
	No	44	65.7	86	64.7	
Drug adherence	Yes	54	80.6	114	85.7	0.009
	No	13	19.4	19	14.3	

*Pearson's Chi square test for categorical variables.

Table 4. The antihypertensive dugs used among CKD and non-CKD patients.

	CKD GFR < 60; N = 67		No CKD GFR ≥ 60; N = 133		
Medication used	N	%	N	%	P value*
Beta blockers	28	41.79	47	35.34	0.000
Calcium channel blockers	12	17.91	2	1.5	
Angiotensin converting enzyme inhibitors+ thiazides	13	19.4	66	49.62	
Angiotensin receptors blockers + thiazides	5	7.46	8	6.01	
Beta blockers + loop diuretics (Lasix)	4	5.97	1	0.75	
Beta blockers + K sparing diuretics (Aldactone)	3	4.48	4	3	
Calcium channel blockers + Thiazides	2	2.99	5	3.76	

*Pearson's Chi square test for categorical variables.

Table 5. Past medical history and family history among between CKD and non-CKD patients.

		CKD GFR < 60; N = 67		No CKD GFR ≥ 60; N = 133		
Variable		N	%	N	%	P value*
Past medical history of	Congestive heart failure	20	29.9	27	20.3	0.111
	Ischemic heart disease	11	16.4	16	12	0.003
	Renal surgical operations	3	4.5	7	5.3	0.257
	Dye exposure	10	14.9	5	3.8	0.006
Family history of	Hypertension	45	67.2	25	18.8	0.425
	Diabetes mellitus	59	88.1	36	27.1	0.349
	Chronic kidney disease	12	17.9	19	14.3	0.006

*Pearson's Chi square test for categorical variables.

Table 4 compares CKD and non-CKD patients regarding antihypertensive drugs; angiotensin converting enzyme inhibitors with thiazides were found to protect against CKD.

Table 5 shows that past medical histories of ischemic heart disease and dye exposure, together with family history of CKD, are risk factors for CKD.

Table 6 shows that high BMI and waist/hip ratios are important risk factors for CKD.

Discussion

The findings of the present study demonstrate an alarming prevalence of CKD among the hypertensive non-diabetic patients attending the PHC centers El-Sharabya and Saraya El-kobba assessed: 33% (95% CI: 33.0e44.2). Longitudinal studies in the 1980s, such as Hypertension, Detection and Follow-up Program and Intervention Study of Multiple Risk Factors, demonstrated a significant prevalence and incidence of CKD among systolic arterial hypertension (SAH) patients, which has continued up till date (11,12).

In Spain, an observational study of SAH patients reported that 40% of those assessed exhibited reduced GFR, which is similar to the results of the current study. It is notable that

Table 6. Clinical examination and anthropometric measures among CKD and non-CKD patients.

	All participants (*N* = 200), 100%		
Variable	CKD GFR < 60; N = 67	No CKD GFR ≥ 60; N = 133	P value*
Age	58.45	50.54	0.002
SBP	135.08	131.31	0.283
DBP	91.67	88.88	0.349
Weight	89.27	85.93	0.321
Height	1.69	1.67	0.541
BMI	31.11	27.68	0.005
Waist circumference	101.64	100.6	0.064
Hip circumference	105.08	103.47	0.224
Waist/hip ratio	0.96	0.67	0.006

*Student's *t*-test for continuous variables.

this was the greatest prevalence found in all published studies (11).

In Brazil, a cross-sectional study conducted by Da Silva and collaborators (2016) revealed that the hidden prevalence of CKD among SAH patients attending PHC centers in the town of Porto Firme in Minas Gerais (Brazil) is 38.3% (13).

In India, Mohanty and collaborators (2020) stated that there is a scarcity of data in the national registry on the incidence and prevalence of CKD. Hence, the accurate burden of CKD is lacking. The approximate prevalence is around 800 per million populations, and the incidence of ESKD cases is about 200 per million populations (14). In our study, in total, 14.3% were diagnosed with CKD and the prevalence of CKD without diabetes or hypertension was 10.8% (12).

Tonner and collaborators (2019) stated the prevalence of CKD among patients with hypertension was 26.3%, which is less than that reported in an earlier single-center study in Ghana showing a prevalence of CKD of 46.9% among hypertensive patients.

The worldwide prevalence of CKD is 11%–13% with age-standardized prevalence among the population aged 20 years and above, occurring in 10.4% of males and 11.8% of females (2).

The prevalence of various stages of CKD in our study was stages I (29.5%), II (37%) IIIa (14.5%), IIIb (12%), IV (6.5%), and V (6.5%).

Our current study revealed that CKD prevalence is more common in females (59.7%) than in males (40.3%). This is not keeping with Mohanty et al.'s study (2020) conducted India, which stated that in developing countries, the prevalence is 10.6% females and 12.5% males, and in developed countries, 8.6% of males and 9.6% of females are living with CKD (14).

With regard to education, in our study the prevalence of CKD is higher among those who completed their primary school (26.9%), illiterate (20.9%), those who completed their preparatory school (22.4%), and secondary school (20.9%) than those who completed their university (7.5%), which is much similar to the cross-sectional study conducted by Ravi Kumar assessing the prevalence of CKD and its determinants in rural Pondicherry (India) showing that prevalence of CKD is higher among the illiterate people (27.2%) than the literate ones (20.6%) (15).

With regard to occupation, the prevalence of CKD is more among the retired patients (28.4%) and the housewives (20.9%), elementary occupations (13.4%), and plant with machine operators (10.4%) than the professionals, associate professionals, and the clerks (7.6%), which is similar to the study conducted by Mohanty and collaborators (2020) that reported that the CKD of unknown origin was found more among members of the lower socioeconomic group (70%) and among farmer and agricultural labor (48%) (14).

Da Silva and collaborators (2016) as well reported that when the prevalence ratio was assessed, it was negatively associated with CKD, without statistical significance. Studies have shown that low socioeconomic level is a risk factor for noncommunicable diseases; it has also been associated with the incidence of CKD. Possible explanations for the association with CKD include the difficulty of access to know that CKD is more in low socioeconomic class, health care systems, and the inadequate control of illnesses such as SAH and diabetes, which affect the understanding of the disease and the adhesion to its treatment. In a study conducted in the state of Rio Grande do Sul using CKD patients in dialysis, patients in hemodialysis exhibited significantly lower levels of education, lower family income, and lower active employment levels than the general population of the region (13).

As for the duration of hypertension, it is known that the CKD prevalence rate is higher in long-standing uncontrolled hypertension. In our study, CKD prevalence varies as follows: 30.3% in those whose duration is less than 5 years, 24.2% for 5–10 years, and 45.5% for more than 10 years. This corresponds with the results conducted by Da Silva and collaborators (2016) that reported CKD prevalence among SAH patients>10 years is 55%, while that among SAH patients<10 years is 45% (13).

As for blood pressure control and antihypertensive, 65% of CKD were not controlled on their treatment regimen, of which 35% of them were in fact compliant – thus a huge proportion of patients were not placed on the correct anti-proteinuric antihypertensive agents [e.g. angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs)]. From the list of antihypertensive agents, we can conclude that 41.79% of CKD take beta blockers (BBs), 17.91% take calcium channel blockers (CCBs), 19.4% take ACEIs and thiazides, 7.46% take ARBs and thiazides, 5.97% take BBs and Lasix, 4.48% take BBs and Aldactone, and 3% take CCBs and thiazides, which means that the CKD prevalence is more common in those who use BBs. There is statistically significant difference between those CKD patients and non-CKD regarding the antihypertensive drug used. However, Tannor and collaborators (2019) stated that the use of ACEI and ARBs was not significantly protective of CKD, which is not similar to our study results (2). Also, Komaroff and collaborators (2018) conducted their first study to the authors' knowledge that estimated changes in relationships between use of antihypertensive medications and stages of CKD for American hypertensive adults with CKD. They stated that their results are consistent with the population-based ecological study in the United Kingdom and suggest that significant increases in advanced stages of CKD can be potentially attributable to the treatment with ARB polytherapy, perhaps, damaging the kidney and increasing albuminuria (16).

As for clinical examination there is a statistically significant relationship between CKD patients and non-CKD patients regarding the age, BMI, and waist hip circumference.

These results were similar to the studies conducted by Da Silva and collaborators (2016) clarifying that the expressive prevalence of CKD in individuals over 60 years of age corroborates the findings of several studies, which stated that advancing age is an established risk factor for this disease (13). The prevalence of CKD among individuals aged between 61 and 70 years was 3.01 times greater than that of adults aged between 25 and 50 years. Similarly, the prevalence of CKD was 5.36 times greater among individuals aged 71 years or more.

Regarding the physical activity, those involved in less physical activity (98.5%) were also at increased risk of developing CKD. Decreased physical activity leads to obesity. Obesity is associated with hypertension and DM. Increased BMI has been

shown to lead to CKD through DM and hypertension and through other pathophysiology such as hyperfiltration leading to focal segmental glomerulosclerosis, which presents with heavy proteinuria (22.5%).

Tonner and collaborators (2019) reported that obesity shares an intimate relation with the development and the progression of CKD. It is a risk factor for hypertension and diabetes, both also established risk factors for CKD. The prevalence of overweight/obesity in our study was high, much higher than rates reported in the general population. Of this, 65.2% had CKD. Other studies also reported high prevalence of obesity in CKD cohorts. Waist circumference rather than BMI is said to be a better measure of obesity and correlates more accurately with CKD risk and CVD outcomes (2).

As for toxemia of pregnancy, the prevalence of CKD among those who had past history of toxemia of pregnancy was 20% compared to 13.9% in those with no history, and there is no statistically significance between them.

In this study, the prevalence of proteinuria accounts for 22.5% of all CKD patients, which is somewhat similar to the results conducted by Da Silva and collaborators (2016) that revealed the prevalence of MA is 22.5%. The prevalence of CKD according to eGFR using MDRD formula is 34%, while the prevalence of CKD according to protein/creatinine ratio is 22.5% (13).

In total, 39 individuals were diagnosed with CKD by estimating the GFR through the CKD-MDRD formula and did not exhibit high proteinuria. In addition, 27 individuals with proteinuria were not classified as CKD patients using the CKD-MDRD formula, which may suggest that these individuals were in the early stages of the disease.

Most of the studies assess the CKD using albuminuria, while this study assesses CKD using proteinuria, which is a barrier for comparison between different studies.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The author(s) reported there is no funding associated with the work featured in this article.

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Ethical considerations

This research was conducted according to the principles of Declaration of Helsinki. The proposal and conduct of the study were ethically cleared by the Research Ethics Committee at the Faculty of Medicine, Ain Shams University (Cairo, Egypt). Written informed consent was taken from selected participants. All information provided by the participants was kept confidential. In addition, any information leading to the identification of study participants was not included in data collection tool.

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