



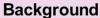
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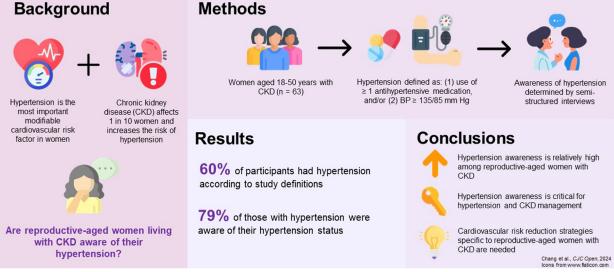
**Original Article** 

# Awareness of Hypertension in Reproductive-Aged Women Living With Chronic Kidney Disease

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# ABSTRACT

Background: Hypertension is the most important modifiable cardiovascular risk factor among women. Chronic kidney disease (CKD), which affects 1 in 10 reproductive-aged women, increases the risk of hypertension: however, awareness of hypertension in this population is unknown. This study aimed to determine hypertension awareness among reproductive-aged women living with chronic kidney disease.

Methods: Women aged 18 to 50 years with CKD were recruited from nephrology clinics in Calgary, Alberta, Canada. Participants completed a semistructured interview and focused chart review, serum and urine laboratory assessment, and a physical examination that included anthropomorphic measurements and 2 automated office blood

# RÉSUMÉ

Contexte : L'hypertension est le principal facteur de risque cardiovasculaire modifiable chez les femmes. La néphropathie chronique, qui touche une femme en âge de procréer sur 10, augmente le risque d'hypertension, mais le niveau de sensibilisation de cette population à ce sujet est inconnu. La présente étude visait à déterminer le niveau de sensibilisation à l'hypertension chez les femmes en âge de procréer atteintes de néphropathie chronique.

Méthodologie : Des femmes âgées de 18 à 50 ans atteintes de néphropathie chronique ont été recrutées dans les cliniques de néphrologie de Calgary, en Alberta (Canada). Les participantes ont été soumises à des entrevues semi-structurées, un examen ciblé du

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pressure readings. Hypertension was defined according to the use of  $\geq$  1 antihypertensive medications and/or an automated office blood pressure reading of  $\geq$  135/85 mm Hg. Data were stratified by hypertension status, as well as by awareness, and descriptively presented as mean  $\pm$  standard deviation, numerical values, and percentages.

**Results:** Sixty-three participants with CKD were included. Thirty-eight (60%) participants had hypertension according to study definitions. Of those with hypertension, 30 participants (79%) were aware of their hypertension status.

**Conclusions:** Hypertension awareness is relatively high in reproductive-aged women living with CKD. However, hypertension awareness is the critical component for hypertension management, and further work is necessary to optimize reduction of cardiovascular risk in this important population.

# Lay Summary

Hypertension, or high blood pressure, is the most important modifiable risk factor for heart disease in women. One in 10 reproductive-aged women have chronic kidney disease (CKD), increasing their risk of hypertension, but their awareness of hypertension is unknown. This study demonstrated that many women with CKD had hypertension, although only 79% were aware of it. Hypertension awareness is a critical component of hypertension management and further work is necessary to improve awareness in this population.

Cardiovascular disease (CVD) is the leading cause of death in women<sup>1</sup> and women in Canada experience high rates of CVD underdiagnosis, along with substandard prevention and treatment of CVD.<sup>2</sup> Hypertension is the most important modifiable risk factor for CVD,<sup>3</sup> and elevated blood pressure may be especially critical in women, in whom increased CVD mortality risk is demonstrated at lower blood pressures compared with men.<sup>4</sup> Further, hypertension occurs earlier in life and progresses more rapidly in women compared with men.<sup>5</sup> Despite this, hypertension remains poorly understood and addressed among the one-third of women who live with hypertension worldwide.<sup>6-8</sup>

Chronic kidney disease (CKD) is strongly and independently linked with hypertension in a bidirectional relationship; not only is hypertension an important cause of CKD, but CKD is equally a risk factor for hypertension.<sup>9</sup> More than one-quarter of individuals with hypertension have concurrent CKD,<sup>10</sup> and the prevalence of hypertension in the CKD dossier médical, des analyses de laboratoire du sérum et de l'urine et un examen physique incluant des mesures anthropométriques et deux lectures automatisées de la pression artérielle réalisées en cabinet. L'hypertension a été définie de la façon suivante : (1) l'utilisation de  $\geq$ 1 agent antihypertenseur, et/ou (2) une lecture automatisée de la pression artérielle en cabinet  $\geq$  135/85 mmHg. Les données ont été stratifiées selon le statut d'hypertension et le niveau de sensibilisation, et elles sont présentées de façon descriptive par la moyenne  $\pm$  l'écarttype, les valeurs numériques et les pourcentages.

**Résultats :** Soixante-trois participantes atteintes de néphropathie chronique ont été incluses dans l'étude. Trente-huit (60 %) participantes étaient atteintes d'hypertension selon la définition utilisée dans l'étude. Parmi les participantes hypertendues, 30 (79 %) étaient conscientes de leur statut d'hypertension.

**Conclusions :** Le niveau de sensibilisation à l'hypertension est relativement élevé parmi les femmes en âge de procréer atteintes de néphropathie chronique. Toutefois, la sensibilisation à l'hypertension est un élément clé pour sa prise en charge, et d'autres travaux sont nécessaires pour optimiser la réduction du risque cardiovasculaire dans cette population importante.

population is estimated at between 60% and 90%.<sup>11</sup> Among women living with CKD, the prevalence of hypertension has been estimated at 84%,<sup>12</sup> and elevated blood pressure contributes to the extensive burden of CVD in this population.<sup>13,14</sup> Women living with CKD have an increased relative risk of CVD mortality, and this risk is demonstrated at an earlier stage of CKD compared with men,<sup>15</sup> with the effect amplified in younger women.<sup>13</sup> CKD affects 1 in 10 reproductive-aged women,<sup>16</sup> highlighting the critical importance of hypertension prevention, treatment, and control in this high-risk population.

However, hypertension, colloquially known as a "silent killer" because of its asymptomatic nature, often remains underrecognized.<sup>17</sup> Despite the high prevalence of hypertension, hypertension awareness varies widely and is estimated between 40% and 80%, with reduced awareness in younger populations.<sup>18</sup> The prevalence of hypertension awareness appears to be higher in the setting of CKD: estimated at between 80% and 99%, <sup>12,19,20</sup> although it remains unclear whether this applies specifically to the high-risk population of reproductive-aged women with CKD. Therefore, this exploratory cross-sectional study aimed to determine the awareness of hypertension among reproductive-aged women living with CKD.

# **Materials and Methods**

Adult individuals < 51 years with diagnoses of CKD (ie, markers of kidney damage or estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 m<sup>2</sup> for > 3 months)<sup>21</sup> of any cause and classification who self-identified as women were invited to participate in this study. Participants were recruited via convenience sampling from Alberta Kidney Care South nephrology clinics in Calgary, Alberta, Canada. Convenience sampling methods used recruitment posters, placed in each nephrology clinic and, in addition, all women presenting to the clinics were invited to participate via study invitation cards distributed upon presentation. Participation was voluntary, and confirmation of CKD diagnosis was obtained by

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See page 298 for disclosure information.

participants' primary kidney care providers before beginning the study. Exclusion criteria included use of medications with secondary blood pressure-lowering effects (eg, magnesium supplementation, dopamine agonists for Parkinson disease or hyperprolactinemia, selective  $\alpha$ -1 blockers for benign prostatic hyperplasia) and inability to provide informed consent.

Ethics approval was obtained from the University of Calgary Conjoint Health Research Ethics Board (REB18-0642), and the study was conducted in accordance with institutional policy. Participants received reimbursement for parking costs at the study visit and a \$50 honorarium for participating. Before the study appointment, participants fasted for 12 hours and abstained from alcohol, smoking, and caffeine for 4 hours, although prescribed medications were still taken with sips of water. Those receiving hemodialysis participants 4 l day after a scheduled hemodialysis session. Participants who menstruated were studied during the follicular phase of their menstrual cycles (between day 1 and day 14).

Study data were collected during 1 study session by a consistent research nurse and were comprised of a semistructured interview and focused chart review, physical examination, as well as serum and urine laboratory assessment. The interview and chart review guides were developed by reviewing literature and consulting with experts in hypertension and nephrology to capture baseline demographic and medical history, including cardiovascular risk factors and medication use. The physical examination included anthropomorphic measurements (ie, body mass index [BMI], abdominal circumference) in addition to 2 blood pressure measurements, collected according to Hypertension Canada guidelines<sup>22</sup> from the right arm with a Dinamap ProCare (model 100X, GE HealthCare, Chicago, Illinois, USA) automated office blood pressure (AOBP) machine. Blood pressure measurements were taken after 10 minutes of rest without speaking in a quiet, private, temperature-controlled room. The first blood pressure reading was discarded, and the mean of 2 systolic and diastolic blood pressures was calculated for each participant. In the event of an abnormal blood pressure result, meeting criterion for hypertension (> 135/85), there was no immediate intervention, although participants were informed of the result by the study nurse and advised to discuss it with their primary or nephrology care provider. Participants were also provided with an option for assistance from the study team in alerting their nephrology care provider of the abnormal result. Laboratory assessments analyzed by Alberta Precision Laboratories, included an estimated glomerular filtration rate (eGFR) and urine albumin-tocreatinine ratio.

Hypertension was defined according to the use of  $\geq 1$ antihypertensive medication, captured from the semistructured interview or focused chart review, and/or an AOBP reading of  $\geq 135/85$  mm Hg.<sup>22</sup> The criteria chosen to define hypertension were adapted from the Hypertension Canada clinical guidelines<sup>22</sup> for this cross-sectional study and were intended to be pragmatic in recognition of the high prevalence of hypertension in CKD and that many participants may already be treated for hypertension. Awareness of hypertension was defined by an answer of "yes" to the interview question "Do you have hypertension or high blood pressure?"

Baseline characteristics were pooled as well as stratified by hypertension and awareness status and represented as mean  $\pm$  standard deviation (SD) as well as numerical values and

percentages, when appropriate. Any differences among strata were assessed using Mann-Whitney U and Fisher's exact tests for continuous and categorical variables, respectively. The prevalence and awareness of hypertension was reported as numerical values and percentages. A sensitivity analysis assessed the robustness of the results by excluding participants with CKD treated with dialysis. Data were organized and analyzed descriptively using Microsoft Excel (version 16.74, Microsoft Corporation, Redmond, California, USA). Full statistical analyses were performed using STATA (version 18.0 BE; StataCorp, College Station, Texas, USA) and were 2-tailed with a significance of 0.05.

# Results

### Participant characteristics

Participant characteristics are outlined in Table 1. In total, 63 participants were included. There were no significant differences between the hypertensive and normotensive groups. The mean age of all participants was 37 years, ranging from 19 to 50, and most participants self-identified as White (68%). The most common medical comorbidities reported included hypertensive disorders of pregnancy (in those who experienced pregnancy), dyslipidemia, and diabetes. Although the most common risk factor for hypertension was alcohol use, the prevalence of nonsteroidal anti-inflammatory drug (NSAID) use, and smoking was also high. BMI and abdominal circumference were similar between the hypertensive and normotensive groups, with pooled mean values of 27 kg/m<sup>2</sup> and 86 cm, respectively. The most common cause of CKD was glomerular disease, and the majority of participants had G1- and G2-classified CKD. A total of 9 (15%) participants had stage G5 CKD treated with dialysis. The mean urine albumin-to-creatinine ratio was 38 mg/mmol, indicating severely increased albuminuria.

# Prevalence of hypertension

In total, 38 (60%) participants had hypertension according to study definitions (Table 2). Among the 38 participants who met either criterion of hypertension, 33 (87%) met the definition of hypertension through the use of  $\geq 1$  antihypertensive medication, whereas 19 (50%) had mean blood pressure readings of  $\geq 135/85$  mm Hg. More than one-third of participants with hypertension (n = 14; 37%) met the definition through both criteria, highlighting that 74% of individuals with elevated blood pressure at the study visit were already treated with antihypertensive medications. Interestingly, of the 25 participants who were classified as normotensive, 3 selfreported hypertension or high blood pressure without meeting the definition of hypertension in our study. Reasons for this finding is unknown, although we speculate that this may represent individuals with previous or resolved acute diagnoses of hypertension or individuals with masked hypertension.

#### Awareness of hypertension

Among the 38 participants with hypertension, 30 (79%) reported awareness of their hypertension status, whereas 8 (21%) were unaware (Fig. 1). A sensitivity analysis determined that hypertension awareness was unchanged when

#### Table 1. Participant characteristics

Characteristics	Pooled $(n = 63)$	Hypertensive $(n = 38)$	Normotensive $(n = 25)$
Age (years)	37 ± 8	38 ± 8	35 ± 7
Female sex n (%)	63 (100)	38 (100)	25 (100)
Race/ethnicity n (%)*			
Asian	16 (25)	8 (21)	8 (32)
Black	2 (3)	1 (3)	1 (4)
Indigenous	3 (5)	0 (0)	3 (12)
Latinx	3 (5)	2 (5)	1 (4)
White	43 (68)	30 (79)	14 (56)
Medical history n (%)			
CAD	1 (2)	1 (3)	0 (0)
CVD	3 (5)	2 (5)	1 (4)
DM	10 (16)	8 (21)	2 (8)
Dyslipidemia	12 (19)	9 (24)	3 (12)
HDP	$14 (42)^{\dagger}$	$11(55)^{\ddagger}$	$3(23)^{\$}$
MI	2(3)	2 (5)	0 (0)
Stroke	3 (5)	1 (3)	2(8)
Hypertension risk factors n (%)	5 (5)	1 (5)	2 (0)
Alcohol use	39 (62)	25 (66)	14 (56)
Combined OCP use	8 (13)	5 (13)	3 (12)
NSAID use	21 (33)	14 (37)	7 (28)
Recreational drug use	15 (24)	8 (21)	7 (28)
Smoking	20 (32)	14 (37)	6 (24)
Menstruation n (%)	40 (63)	22 (58)	18 (72)
BMI (kg/m <sup>2</sup> )	$27 \pm 8$	22(93) 27 ± 6	$28 \pm 10$
Abdominal circumference (cm)	$\frac{27 \pm 8}{86 \pm 20}$	$\frac{27 \pm 6}{87 \pm 20}$	$\frac{28 \pm 10}{86 \pm 20}$
Cause of CKD n (%)*	80 ± 20	07 ± 20	$80 \pm 20$
DM	4 (6)	4 (11)	0 (0)
Drug-induced CKD	$\frac{4}{2}(3)$	$\frac{4}{11}$ (11) 1 (3)	$     \begin{array}{c}       0 & (0) \\       1 & (4)     \end{array} $
Glomerular disease	28 (44)	16 (42)	$1 (4) \\ 12 (48)$
Hypertension		3 (8)	$ \begin{array}{c} 12 (48) \\ 0 (0) \end{array} $
Medullary sponge kidney $\pm$	3 (5) 7 (11)	. ,	. ,
nephrolithiasis	/ (11)	6 (16)	1 (4)
PKD	8 (13)	5 (13)	3 (12)
Reflux nephropathy $\pm$ obstructive	2 (3)	1 (3)	1 (4)
nephropathy Other/unknown	10 (10)	2 (0)	7 (20)
	10 (16)	3 (8)	7 (28)
CKD classification n (%)	26 (12)	15 ((0)	11 (10)
G1 (eGFR $\geq$ 90)	26 (42)	15 (40)	11 (46)
G2 (eGFR 60-89)	15 (24)	10 (26)	5 (21)
G3 (eGFR 30-59)	9 (15)	5 (13)	4 (17)
G4 (eGFR 15-29)	2 (3)	2 (5)	0 (0)
G5 (eGFR < 15)		1 (3)	$0 (0)^{\parallel}$
G5 treated with dialysis	9 (15)	5 (13)	4 (17) <sup>  </sup>
ACR (mg/mmol)**	$38 \pm 112^{**}$	$49 \pm 139$	$21\pm34^{\dagger\dagger}$

Data are mean  $\pm$  SD, unless otherwise indicated. P < 0.05 indicates statistically significant difference vs hypertensive group.

ACR, albumin-creatinine ratio; BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HDP, hypertensive disorders of pregnancy; MI, myocardial infarction; NSAID, nonsteroidal anti-inflammatory drug; OCP, oral contraceptive pill; PKD, polycystic kidney disease; SD, standard deviation.

\* Proportions/percentages do not add up to 100%, as participants were able to self-identify as multiple races/ethnicities.

<sup>†</sup>33 participants included, as only these participants have experienced pregnancy.

<sup>‡</sup>20 participants included, as only these participants have experienced pregnancy.

<sup>§</sup>13 participants included, as only these participants have experienced pregnancy.

<sup>¶</sup>62 participants included, as data from 1 participant were unavailable.

<sup>1</sup>24 participants included, as data from 1 participant were unavailable,

\*\* 56 participants included, as data from 1 participant were unavailable.

<sup>††</sup>21 participants included, as data from 1 participant were unavailable.

participants with CKD treated with dialysis were excluded from the analysis. Further, the hypertensive participants were stratified by awareness to assess for any differences in demographic, medical, and risk-factor characteristics (Table 3). No significant differences were noted between the 2 groups, other than an increased proportion of unawareness in participants with medullary sponge kidney +/- nephrolithiasis, within the context of the small sample. When stratified by age (18 to 28 years, n = 6; 29 to 39 years, n = 14; 40 to 50 years, n = 18), no significant difference in hypertension awareness was demonstrated among strata (Fig. 2). Further, no significant difference in hypertension awareness was demonstrated between those with or without a history of hypertensive disorders of pregnancy (P = 0.29). Interestingly, individuals with hypertension treated with antihypertensive medication(s) did not have higher awareness compared with individuals with

 Table 2. Prevalence of hypertension

Prevalence of hypertension $(n = 63)$	n (%)
Hypertensive	38 (60)*
Defined by use of $\geq 1$	33 (87)
antihypertensive medications	
Defined by BP $\geq$ 135/85 mm Hg	19 (50)
Defined by both criteria	14 (37)
Normotensive	25 (40)

Proportions/percentages do not add up to 100%, as participants may be classified as hypertensive according to multiple definitions.

BP, blood pressure.

\* Defined by either criterion.

hypertension not treated with antihypertensive medication(s) (P = 0.95). Individuals classified as hypertensive by study visit AOBP readings of  $\geq 135/85$  mm Hg, however, were more likely to be aware of their hypertension compared with hypertensive individuals with well-controlled blood pressure on antihypertensive medications (P = 0.04).

#### Discussion

To our knowledge, this is the first study to examine the awareness of hypertension among reproductive-aged women living with CKD. Key findings of this study demonstrated that, in reproductive-aged women living with CKD, there was a high prevalence of hypertension (60%) (defined by the use of  $\geq 1$  antihypertensive medications and/or an AOBP of  $\geq 135/85$  mm Hg<sup>22</sup>), and of the reproductive-aged women with hypertension, 79% were aware of their hypertension. These results suggest that although hypertension awareness is relatively high, there is a need to improve hypertension awareness further in this important population in which hypertension is common and the risk of cardiovascular mortality is high.

In the general population, awareness of hypertension is variably low.<sup>23-30</sup> A global systematic analysis reported that although one-third of the global adult population has hypertension, only 46.5% of people with hypertension were aware of their condition.<sup>31</sup> Further, results of a systematic review suggested that hypertension awareness varies by region, and, for example, although 58% of Canadians were aware of their

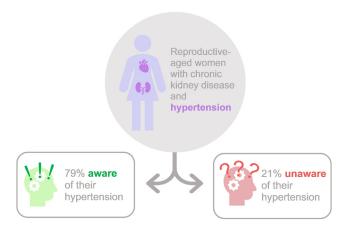


Figure 1. Awareness of hypertension among participants with chronic kidney disease and hypertension.

hypertension, less than 45% of individuals from China and Latin American countries were aware of their hypertension.<sup>32</sup> In keeping with the previously published literature, our study suggests that hypertension awareness among those with CKD may be higher compared with the general population, although research in this population is limited.<sup>12,19,20,33</sup> In our study, hypertension awareness in reproductive-aged women living with CKD was found to be 79%, similar to previous studies conducted in CKD populations in which hypertension awareness has been reported as low as 72%<sup>33</sup> to as high as 99%.<sup>12</sup> Further, in 1 study, hypertension awareness was highest in those with stage 3 to 4 CKD (67%) compared with stage 1 to 2 CKD (55%) among individuals without histories of CVD; however, a history of CVD increased awareness 3-fold.<sup>20</sup> People living with chronic illnesses have great interest in learning about their health and using various sources of health information,<sup>34</sup> which may explain why hypertension awareness appears to be higher in the CKD population and even more so in the CKD population with history of CVD. However, 21% of participants in our study were unaware of their hypertension. Limited health literacy, which is associated with poor health outcomes, is common in CKD<sup>35</sup> and may contribute to this result.

Hypertension awareness appears to vary by gender, with higher awareness in women.<sup>23,25,32</sup> A large global study reported that 53% of women were aware of their hypertension compared with 40% of men.<sup>31</sup> This is mirrored by Canadian data, which also suggest a greater awareness of hypertension among women (65% compared with 53% of men).<sup>28</sup> Previous studies have demonstrated that women tend to have greater health literacy than men,<sup>36,37</sup> which may contribute to the higher prevalence of hypertension awareness among women. Particularly in recent years, heart health campaigns directed specifically at women may have contributed to this increased awareness.<sup>38</sup> Hypertension awareness is an integral component of management of hypertension and has the potential to influence adoption of risk-reduction lifestyle changes and adherence to management strategies.

Despite evidence for increased awareness of hypertension in women,<sup>23,25,32</sup> literature suggests that hypertension management may be suboptimal in Canadian women.<sup>28,39</sup> An analysis of the Canadian Heart Health Surveys reported that 29% of women treated for hypertension did not achieve blood pressure targets compared with 19% of men.<sup>28</sup> To our knowledge, this gender difference has not been studied in individuals with CKD, but within our study population, there was a concerning signal for suboptimal control of hypertension in reproductive-aged women with CKD. Specifically, in this study, nearly three-quarters of participants with elevated blood pressure at the time of the study visit were already treated with antihypertensive management, highlighting that although they had received treatment for their hypertension, the treatment may be suboptimal. This finding is especially important within the context of sex-related differences and gender-related biases in hypertension management overall.<sup>39</sup>

Hypertension management may be especially important in women.<sup>4</sup> It has become evident that important sex- and gender-related differences exist in hypertension, and women experience a steeper increase in cardiovascular risk with incremental blood pressure increases compared with men.<sup>40-42</sup> Further, increased cardiovascular mortality is demonstrated

Table 3. Characteristics of participants with hypertension, by awareness of hypertension

Characteristics	Aware $(n = 30)$	Unaware $(n = 8)$
Age (years)	$38 \pm 8$	$39 \pm 10$
Female sex n (%)	30 (100)	8 (100)
Race/ethnicity n (%)*		
Asian	7 (23)	1 (13)
Black	1 (3)	0 (0)
Indigenous	0 (0)	0 (0)
Latinx	1 (3)	1 (13)
White	23 (77)	7 (88)
Medical history n (%)	. ,	
CAD	0 (0)	1 (13)
CVD	2 (7)	0 (0)
DM	8 (27)	0 (0)
Dyslipidemia	8 (27)	1 (13)
HDP	$10(63)^{\dagger}$	$1(25)^{\ddagger}$
MI	1 (3)	1 (13)
Stroke	1 (3)	0 (0)
Hypertension risk factors n (%)	- (0)	• (•)
Alcohol use	18 (60)	7 (88)
Combined OCP use	2 (7)	3 (38)
NSAID use	11 (37)	3 (38)
Recreational drug use	7 (23)	1 (13)
Smoking	10 (33)	4 (50)
Menstruation n (%)	17 (57)	5 (63)
BMI (kg/m <sup>2</sup> )	$27 \pm 6$	$25 \pm 5$
Abdominal circumference (cm)	$89 \pm 21$	$81 \pm 12$
Cause of CKD n (%)*	•7 =	
DM	4 (13)	0 (0)
Drug-induced CKD	1 (3)	0 (0)
Glomerular disease	13 (43)	3 (38)
Hypertension	3 (10)	0 (0)
Medullary sponge kidney $\pm$	2 (7)	4 (50) <sup>§</sup>
nephrolithiasis	2 (/)	1 (30)
PKD	5 (17)	0 (0)
Reflux nephropathy $\pm$ obstructive	0 (0)	1 (13)
nephropathy	0 (0)	1 (15)
Other/unknown	3 (10)	0 (0)
CKD classification n (%)	5 (10)	0 (0)
G1 (eGFR $\geq$ 90)	10 (33)	5 (63)
G2 (eGFR 60-89)	8 (27)	2 (25)
G3 (eGFR 30-59)	5 (17)	$     \begin{array}{c}       2 \\       0 \\       0     \end{array}     $
G4 (eGFR 15-29)	2 (7)	0 (0)
$G_{5} (eGFR < 15)$	1(3)	0 (0)
G5 treated with dialysis	4 (13)	1(13)
ACR (mg/mmol)	$62 \pm 156^{\circ}$	$5 \pm 10$
	02 ± 170	) ± 10

Data are mean  $\pm$  SD, unless otherwise indicated.

ACR, albumin-creatinine ratio; BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HDP, hypertensive disorders of pregnancy; MI, myocardial infarction; NSAID, nonsteroidal anti-inflammatory drug; OCP, oral contraceptive pill; PKD, polycystic kidney disease; SD, standard deviation.

\* Proportions/percentages do not add up to 100%, as participants were able to self-identify as multiple races/ethnicities.

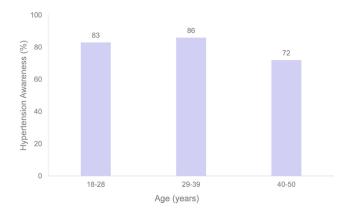
 $^{\rm T}16$  participants included, as only these participants have experienced pregnancy.

<sup>‡</sup>4 participants included, as only these participants have experienced pregnancy.

 ${}^{\$}P < 0.05$  indicates statistically significant difference vs aware group.

<sup>¶</sup>27 participants included, as data from 3 participants were unavailable.

at lower systolic blood pressures in women compared with men.<sup>4</sup> Finally, reducing hypertension may have a larger impact on cardiovascular mortality in women,<sup>25,43</sup> solidifying hypertension awareness as the first step for hypertension-related cardiovascular risk reduction. Interestingly, in our



**Figure 2.** Awareness of hypertension among participants with hypertension, stratified by age (n = 38). \*P < 0.05 indicates statistical significance between groups.

study, in contrast to our expectations, hypertension awareness was not significantly higher in women treated with antihypertensive medication compared with those with elevated blood pressure alone. This finding raises questions about not only health literacy but also the quality of health education related to antihypertensive medication use in this population. Educational interventions are effective strategies to improve health literacy and adherence to medication in hypertension,<sup>4</sup> likely in part through improvement in awareness, and may be underused in this medically complex population. Furthermore, in our study, whether or not they were treated with antihypertensive medications, participants with elevated blood pressure at their study visits were significantly more likely to be aware of their hypertension than participants with wellcontrolled blood pressure on antihypertensive medications. This finding may be explained in part by patient-related factors such as mistrust or denial, highly prevalent in hypertension, which contribute to medication nonadherence and disengagement with health care providers.<sup>4</sup>

The importance of hypertension awareness in this population is further highlighted by the fact that 1 in 3 women have hypertension, <sup>6-8,31</sup> and the prevalence of hypertension is much higher in women with CKD,<sup>12</sup> similar to our reported prevalence in this study (60%). Specific to women with CKD, hypertension also accelerates the progression of CKD,<sup>46-48</sup> possibly even more in women compared with men.<sup>49</sup> Therefore, hypertension awareness is also important to prevent progression of CKD in this already high-risk population.

In our study population of reproductive-aged women with CKD, nearly one-half of participants who had experienced pregnancy reported hypertensive disorders of pregnancy, although a history of a hypertensive disorder of pregnancy was not associated with increased awareness of hypertension. Hypertension in pregnancy is a high-risk state for both maternal and fetal complications.<sup>50,51</sup> Furthermore, hypertensive disorders of pregnancy are independent predictors of future CVD.<sup>52</sup> In CKD, hypertensive disorders of pregnancy are especially common and may result in devastating maternal complications and pose severe risks to the fetus.<sup>53</sup> Therefore, emphasis on management of hypertension, beginning with

awareness, is imperative for pregnant women with CKD or those aiming to pursue pregnancy.<sup>53,54</sup>

# Strengths and limitations

This study has several strengths. First, this novel study is the first of our knowledge to address a key aspect of hypertension management and cardiovascular risk reduction in the especially high-risk population of reproductive-aged women living with CKD. Second, the study population demonstrated notable diversity in terms of age, as well as both cause and classification of CKD. Finally, all study measurements were standardized and collected by a consistent and experienced registered nurse.

There were also important limitations within our study. First, the definition of hypertension used in this study had the potential to overestimate the prevalence of hypertension through misclassification of individuals with white-coat hypertension, for which we were unable to assess. However, a recent meta-analysis comparing AOBP with out-of-office blood pressure readings, including daytime ambulatory and home blood pressure monitoring, demonstrated no significant difference between measurement techniques and postulated that AOBP may actually reduce the white-coat effect.<sup>55</sup> Second, we were unable to determine if participants were using antihypertensive medications such as reninangiotensin-aldosterone system inhibitors for the purposes of hypertension or for other reasons, such as management of proteinuria, which also had the potential to contribute to overestimation of hypertension prevalence in this study. In addition, despite the diversity of CKD within our study population, there was limited representation of individuals with advanced CKD not treated with dialysis, limiting the generalizability of the findings to advanced CKD. Interestingly, however, hypertension awareness in CKD appears to be higher in advanced stages of CKD.<sup>20</sup> Similarly, although the ethnic identities of our study sample closely mirrored the ethnic makeup of the population (Calgary, Alberta, Canada),<sup>56</sup> greater ethnic diversity within our sample would have been beneficial, especially given the increased risk of hypertension among Black, Indigenous, and South Asian populations in Canada.<sup>57,58</sup> Furthermore, in the context of recruitment methods relying on convenience sampling, there is potential for selection bias in the form of healthyvolunteer bias, which may have affected the results of this study. Finally, the recruitment of participants from a single site and limited sample size of this study may reduce the overall generalizability of our conclusions about hypertension awareness among reproductive-aged women living with CKD; however, this is the only study to our knowledge that examines this important topic.

# Conclusions

This study found that nearly 4 in 5 reproductive-aged women living with CKD and hypertension demonstrated awareness of their hypertension. Although hypertension awareness in this population was higher compared with previously reported hypertension awareness in the general population,<sup>23-32</sup> and similar to hypertension awareness in other CKD populations,<sup>12,19,20,33</sup> 21% of participants remained unaware of their hypertension. Younger women

with CKD are especially at elevated risk for hypertension, <sup>13,14</sup> and hypertension awareness is a critical component of cardiovascular risk reduction. We are hopeful that this exploratory cross-sectional study will provide an initial contribution to this large and significant gap in knowledge and care for reproductive-aged women living with CKD and inform larger and more comprehensive prospective studies that will further evaluate the awareness and control of hypertension in this important population. Further, research powered to identify potential modifiable factors that can predict reduced awareness, as well as interventions to improve awareness and control are urgently warranted. Finally, qualitative assessment of perspectives of reproductive-aged women with CKD will be helpful to understand both barriers and facilitators of effective hypertension care. Overall, hypertension is the most important modifiable cardiovascular risk factor in women,3 and reproductive-aged women living with CKD have up to a 1000-times risk of cardiovascular mortality.<sup>13</sup> Strategies to improve hypertension awareness in this high-risk population have the potential to have a positive impact on management of hypertension and ultimately reduce the high cardiovascular burden for reproductive-aged women with CKD.

#### **Ethics Statement**

Ethics approval was obtained from the University of Calgary Conjoint Health Research Ethics Board (REB18-0642), and the study was conducted in accordance with institutional policy.

# **Patient Consent**

The authors confirm that patient consent forms have been obtained for this article.

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#### **Disclosures**

The authors have no conflicts of interest to disclose.

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