

Medication-related health literacy in patients on hemodialysis assessed with the RALPH interview guide

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ABSTRACT

Objectives: To study medication-related health literacy (HL) among patients on hemodialysis using phosphate-binding medication (PBM) and explore its association with medication adherence.

Methods: This planned sub-study was part of a prospective intervention study in patients on hemodialysis with a high serum phosphate concentration and high PBM burden. Functional, communicative, and critical medication-related HL were assessed using the Recognizing and Addressing Limited Pharmaceutical Literacy interview guide, and self-reported PBM adherence was evaluated using the MARS-5 (Medication Adherence Report Scale-5) questionnaire. Primary outcome was the proportion of patients who perceived difficulties in ≥ 1 HL domain, secondary outcome was the prevalence of perceived difficulties within the HL domains. Exploratory outcome was the association between medication-related HL and self-reported adherence to PBM. Data analysis was performed using descriptive statistics and univariable and multivariable logistic regression. Covariates for logistic regression were age, gender, number of medications, and PBM and total pill burden.

Results: Of the 75 patients, 81 % perceived difficulties, mainly in the critical domain. Around 65 % of the patients experienced difficulties assessing the applicability and reliability of information. 26.7 % of the patients had a MARS-5 score ≤ 22 and were classified as non-adherent. No association was found between medication-related HL in general and medication adherence (OR 1.13, 95 %CI 0.31–4.10). However, age was significantly associated with adherence (OR 1.05, 95 %CI 1.02–1.09).

Conclusions: Over 80 % of patients on hemodialysis using PBM experience difficulties in using and applying medication and treatment information. These results suggest that patients on hemodialysis need more support to effectively use this information.

Practice implications: Healthcare professionals should guide patients in the adequate use and application of treatment information, to improve the effective use of PBM. Universal use of HL-sensitive communication strategies in patients on dialysis, including the teach-back method, could enhance patient understanding and engagement, potentially improving self-management and medication adherence.

1. Introduction

The impact of hemodialysis on patients' lives is substantial due to the high treatment and symptom burden. Treatment burden consists of the work associated with navigating healthcare and self-management of health and disease, such as adapting lifestyle, medication management,

medical visits, and laboratory tests [1,2]. An important aspect of treatment burden is pill burden [3,4]. The mean total pill burden for patients on hemodialysis is 15.6 [3,5], and phosphate-binding medication (PBM) pill burden generally comprises 30–50 % of the total pill burden [6,7].

The burden of treatment adds to the burden of symptoms [2]. Symptom burden is high in patients with CKD and in those on

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hemodialysis [8–10] and exerts a negative influence on the quality of life [8]. Symptom burden is also associated with non-adherence to medication [9]. With the progression of chronic kidney disease to renal failure and hemodialysis, the burden of disease, including its self-management, increases, while at the same time, the capacity of patients to cope may diminish because of increasing symptoms, such as fatigue, and lower functional status [11].

The high disease and treatment burden entails the complexity of self-management in dialysis treatment. For patients on dialysis, medication self-management is challenging due to the high number of different medications, high pill burden, side effects, and complex medication regimens with multiple administration times [12,13]. Treatment with PBM is especially complex, as it has a high pill burden and has to be taken during all protein-rich and phosphate-rich meals and drinks. Furthermore, a correct timing of the intake of PBM is paramount for its effectiveness, as intake before or after meals diminishes the effect.

To promote the correct use of PBM, patients on dialysis receive extensive information and instructions from multiple healthcare professionals (HCPs), such as prescribers, (dialysis) nurses, dieticians, and pharmacists. However, to effectively handle these instructions, adequate health literacy skills are required.

Health literacy skills comprise the cognitive and social skills needed to gain access to, understand, and use the information to manage health conditions [14]. Limited HL occurs in 16–53 % of the patients on hemodialysis [15–22]. A higher prevalence of limited HL is seen in patients with high levels of comorbidity and those with low socioeconomic status [18,20,23]. The wide range in the reported prevalence of limited HL is at least partially caused by differences in instruments. Older studies reported a prevalence of 27 % of limited HL in patients on hemodialysis but investigated only functional literacy [18]. More recent studies used instruments investigating functional, communicative, and critical health literacy and reported a prevalence of low HL in 20.3–31.7 % and moderate HL in 54.1–59.4 % of the patients on hemodialysis, resulting in suboptimal (low or moderate) HL in 77–83 % of the patients [20,24,25].

Limited health literacy (HL) is associated with poor self-management in chronic diseases [26,27]. Suboptimal adherence, as part of poor self-management, occurs in approximately 50 % of the patients with CKD [28] and is associated with disease progression and increased mortality [29,30]. Adherence to PBM is particularly challenging due to the high pill burden and complex medication regimen [6,31–34].

In patients with chronic diseases, including chronic kidney disease, some studies show an association between limited HL and medication non-adherence, though the results vary and the association is weak [20, 27,35–42]. Correlations between HL skills and self-management behavior, including medication adherence, may be stronger for communicative and critical HL skills than for functional HL skills [39,40, 43]. Besides HL, various other factors influence medication adherence, such as patient beliefs, disease knowledge, patient-provider relationships, and the ability to understand and use mathematics in daily life [41]. HL itself influences many of these factors, which further increases the complexity of the association between HL and medication adherence [38].

As far as we know, no studies have been published regarding medication-related HL in hemodialysis patients. Patients on dialysis use approximately 10–15 different medications [5,44] and medication is an important aspect of medical treatment in hemodialysis. Furthermore, HL varies with the content of a disease and its treatment [14]: in this case, the content of a high SPC and its treatment with PBM, in the context of hemodialysis treatment. This content, as well as this context, is very complex and demanding, which hampers the effective use of PBM and often leads to suboptimal medication adherence and treatment outcomes. To fill the knowledge gap regarding this topic, this study investigated medication-related HL in patients on hemodialysis using PBM and explored its association with medication adherence to PBM.

2. Methods

2.1. Study design and setting

This study was a planned sub-study of a prospective intervention study (PIDO-P study) conducted in Franciscus Gasthuis and Vlietland, a teaching hospital with a hemodialysis facility for 250 patients in the area of Rotterdam, The Netherlands. This study investigated a complex, combined adherence-improving pharmacist intervention in patients on hemodialysis. All patients from the PIDO-P study participated in this sub-study.

2.2. Study population

The study population consisted of adult patients on hemodialysis with a high serum phosphate concentration (SPC) and a pill burden of ≥ 6 sevelamer equivalent units of PBM. This patient group was selected as we expected these patients to have a higher risk of suboptimal adherence due to the high SPC notwithstanding treatment with 6 or more sevelamer tablet equivalents. Patients with insufficient language proficiency were excluded because of the difficulty of acquiring informed consent and performing consultations. Mild cognitive impairment was not an exclusion criterion per se. However, cognitive impairment resulting in failure to understand study procedures was an exclusion criterion. Patients had to be on dialysis for at least three months as we needed three months of retrospective data for the primary outcome measure of the main study. Medication had to be dispensed by the hospital's outpatient pharmacy, to minimize the risk of discrepancies in PBM between the hospital's medical records and pharmacy dispensing. Patients in a nursing home were excluded to further minimize the risk of PBM discrepancies.

Screening process Every month, patient data, including the last phosphate concentration, average phosphate concentration over 90 days, and PBM dose, were extracted automatically from the hospital's general electronic medical records. After extraction, patients were screened manually applying the inclusion and exclusion criteria.

2.3. Study procedures and data collection

If patients were considered eligible for the study, they were approached on the hemodialysis ward and were provided information, in writing and verbal, about the study. If patients agreed to participate, they provided written informed consent. Data on medication-related HL, using the RALPH (Recognizing and Addressing Pharmaceutical Literacy) interview guide and self-reported medication adherence to PBM using MARS-5 (Medication Adherence Report Scale 5) were collected as part of the baseline assessments of the main study (PIDO-P). Both the RALPH interview guide and MARS-5 were administered verbally, on the hemodialysis ward, by one of the investigators (FJvdO) or a trained pharmaceutical sciences student. The time to complete both questionnaires was 8–10 minutes.

Medication-related HL was investigated using the RALPH interview guide. The RALPH interview guide has recently been developed in the Netherlands as the first specific instrument to investigate and assess medication-related HL in clinical pharmacy practice [45,46]. The RALPH is a practice-based, validated interview guide consisting of three open and eight multiple-choice questions, in which the functional, communicative, and critical HL domains are investigated (see Box 1 for the questions) [45]. By design, the RALPH interview guide was not developed to score or quantify HL [45,46]. It mainly has an alerting function identifying difficulties with medication-related HL in general and in the three domains. Furthermore, it explores the different aspects of medication-related HL more qualitatively. For questions on activities such as the search for information or the participation in shared decision-making, patients were asked to motivate their answers in case they responded not to engage in these activities.

Box 1

RALPH questions (from Vervloet et al RSAP 2018).

Medicine being discussed:

Does the patient **ask you** to **read** the text on the medication label **out loud**?

- ☐ Yes
☐ No

1. Can you tell me **what** you use this medicine for?

Answer:

Answer correct?

- ☐ Yes
☐ No
☐ Patient does not know

2. Can you tell me **how** you should use this medicine (according to the medication label)?*If necessary, ask about the frequency and the timing of the intake*

Answer:

Answer correct?

- ☐ Yes
☐ No
☐ Patient does not know

3. *If there is a special precaution/warning on the medication label.*Can you tell me **in your own words** what the precaution/warning means?

Answer:

Answer correct?

- ☐ Yes
☐ No
☐ Patient does not know

4. What do you do if the information about this medication given by the pharmacist is **different** from the information you are given by the physician, for example, on how often you should take the medicine?

- ☐ Patient searches for the correct information in or asks for clarification from **reliable sources**
☐ Patient searches for the correct information or asks for clarification, but **not necessarily in/from reliable sources**
☐ Patient **does not search** for the correct information **nor asks for clarification**

5. Imagine you have **a question** about this medicine, for example, about how you should take it, how easy or difficult is it for you to ask one of your healthcare providers (*e.g. physician, pharmacist, pharmacy technician*) this question?

- ☐ Very easy
☐ Quite easy
☐ Quite difficult
☐ Very difficult

6. Imagine you have **concerns** about this medicine, for example about possible side effects, how easy or difficult is it for you to discuss these concerns with one of your healthcare providers (*e.g. physician, pharmacist, pharmacy technician*)?

- ☐ Very easy
☐ Quite easy
☐ Quite difficult
☐ Very difficult

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(continued)

7. How easy or difficult is it for you to find information about this medicine in words you understand ? For example, if you want to find out whether you can take another medicine without a prescription from the drugstore (paracetamol or a cough syrup) alongside this medicine.	
☐ Very easy ☐ Quite easy ☐ Quite difficult ☐ Very difficult	☐ Patient does not look for information. Reason:
8. If you come across information about your illness or this medicine in the newspaper or the Internet, how easy or difficult is it for you to judge whether this information is relevant to you ?	
☐ Very easy ☐ Quite easy ☐ Quite difficult ☐ Very difficult	☐ Patient does not come across any information. Reason:
9. If you come across information about your illness or this medicine in the newspaper or the Internet, how easy or difficult is it for you to judge whether this information is reliable ?	
☐ Very easy ☐ Quite easy ☐ Quite difficult ☐ Very difficult	☐ Patient does not encounter any information. Reason:
10. How easy or difficult is it for you to decide together with your healthcare provider about the treatment of your illness, for example, whether you might want to try another medicine?	
☐ Very easy ☐ Quite easy ☐ Quite difficult ☐ Very difficult	☐ Patient does not want to participate in the decision making. Reason:

Answers to the RALPH interview guide questions in the functional domain were scored as “correct”, “incorrect”, or “patient does not know”. For quantitative data analysis, answers were dichotomized into correct or incorrect; the latter included the option “patient does not know”. Answers to questions in the communicative domain were scored on a four-point Likert scale ranging from “very easy” to “very difficult”. These responses were also dichotomized for analysis into easy (Likert scale scores “very easy” and “easy”) or difficult (Likert scale scores “difficult” and “very difficult”). The option “not searching for information” was classified as perceiving difficulties with this specific skill. Answers to the questions in the critical domain were scored in the same way, except for the answer to the one question about using reliable sources, which was dichotomized into “correct” or “incorrect”. This dichotomization was performed in analogy with the study in which the RALPH was validated [45]. Explanations to multiple-choice questions 7–10 from the RALPH interview guide were qualitatively explored. Afterwards, the answers were classified into themes.

Self-reported medication adherence was assessed using MARS-5, see Box 2 [47]. The MARS-5 questionnaire has been validated in several chronic diseases with good validity and high test-retest reliability [47].

The MARS-5 instrument does not mention a specific period, so we did not mention a period to patients. MARS-5 total scores may range from 5 to 25, with higher scores indicating better medication adherence. MARS-5 was reported as a continuous outcome variable but was also dichotomized into adherent (MARS score ≥ 23) or non-adherent (MARS score < 23) in analogy with prior studies [48,49].

2.4. Data sources and measurements

Laboratory parameters, age, sex, country of birth, and medication data were extracted from the electronic medical records of the hospital (Hix version 6.2, Chipsoft, Amsterdam, the Netherlands). Country of birth was registered to determine if the study population was representative of the total dialysis population of our hospital. Renal diagnosis was extracted from dialysis medical records (Diamant version 3.17.3, Diasoft, Leusden, the Netherlands). Other medication data (medication dispensing mode) were extracted from pharmacy records (CGM Pharmacy, version 82, CompuGroupMedical the Netherlands, Echt, the Netherlands). Study data were registered in Castor EDC (Electronic Data Capture) version 2023.3.0.0 (Castor, Amsterdam, The Netherlands).

Box 2 MARS-5.

Item	Always	Often	Sometimes	Rarely	Never
I forget to take my medicines	1	2	3	4	5
I alter the dose of my medicines	1	2	3	4	5
I stop taking my medicines for a while	1	2	3	4	5
I decide to skip a dose	1	2	3	4	5
I take less than instructed	1	2	3	4	5

Table 1
Baseline patient characteristics (n = 75).

Characteristic	
Age; years; mean $\pm$ SD	65 $\pm$ 15.6
Male sex; n (%)	49 (65.3)
Country of birth; n (%)	
The Netherlands	46 (61.3)
Suriname	14 (18.7)
Turkey	4 (5.3)
Cabo Verde	4 (5.3)
Nigeria	3 (4.0)
Other	4 (5.3)
Renal diagnosis; n (%)	
Hypertension	23 (30.7)
Diabetes mellitus	15 (20.0)
Other	32 (42.7)
Unknown	5 (6.7)
Phosphate concentration; mmol/L, mean $\pm$ SD	2.04 $\pm$ 0.45
Medication dispensing; n (%)	
Automated weekly medication dispensing system;	56 (74.7)
Dispensing on patient's request	19 (25.3)
Number of medications; mean $\pm$ SD	12.7 $\pm$ 5.0
Total pill burden*; mean $\pm$ SD	22.3 $\pm$ 7.7
PBM pill burden; mean $\pm$ SD	8.5 $\pm$ 2.9
Adherent patients (MARS-5 $\geq$ 23); n (%)	56 (74.7)

* Pill burden was defined as the number of daily units (e.g. tablets) patients had to take. One sevelamer sachet of 2.4 g counted as 3 daily units. Medication administered during hemodialysis was not included. Topical products, such as creams, were counted by the frequency of administration. Medication used when necessary was counted as 1 time daily. PBM= phosphate-binding medication; MARS-5: Medication Adherence Report Scale

Pill burden was defined as the number of daily units (e.g. tablets, sachets) patients had to take. Medication administered during hemodialysis was not included. Topical products, such as creams, were counted by the frequency of administration. Medication prescribed as needed was counted as one time daily.

2.5. Outcome parameters

The primary outcome was the proportion of patients who perceived difficulties in one or more HL domains.

The secondary outcome was the prevalence of the most frequently perceived difficulties within the HL domains.

Exploratory outcomes were self-reported medication adherence to PBM as measured with MARS-5 and the association between the presence of perceived difficulties in one or more HL domains and self-reported medication adherence at baseline.

2.6. Data analysis

2.6.1. Sample size and study power

The sample size of this sub-study was based on a sample size calculation for the primary outcome of the main (PIDO-P) study. As this sub-

study's primary and secondary outcome parameters consisted of descriptive statistics, no additional sample size calculation was performed. Because of the small sample size, there was limited power to detect associations with a high degree of certainty. Therefore, the analysis of the association between medication-related HL and PBM adherence was only exploratory.

Quantitative data were analyzed using descriptive statistics. Associations between one or more perceived difficulties in the domains of the RALPH and dichotomized medication adherence (MARS-5 <23: non-adherent, $\geq$ 23: adherent) were explored using univariable logistic regression. Using multivariable logistic regression association, the results were adjusted for the following covariates: age, sex, number of medications, PBM pill burden, and total pill burden. The results of the logistic regression analysis were described as odds ratios (OR) with a 95 % confidence interval (95 % CI). The Hosmer-Lemeshow test and Nagelkerke R square were used to assess goodness-of-fit. All statistical analyses were performed with IBM SPSS Statistics version 29.0.2 (IBM Corp, Armonk, NY, USA).

2.7. Ethics

This study was evaluated by the Medical Ethical Committee Utrecht (MEC-U) and was considered not to be subject to the Dutch Medical Research Act (registration number W21.142). The MEC-U approved the patient information and the informed consent form. The executive board of Franciscus Gasthuis and Vlietland Hospital approved the study. Handling of patient data was under the General Data Protection Regulation.

3. Results

A total of 75 patients participated in the study (Table 1). Approximately two-thirds of the patients were male, with a mean age of 65; 39 % of patients had a country of birth other than the Netherlands. The main renal diagnoses were hypertensive and diabetic nephropathy, with a prevalence of 30.7 % and 20.0 %, respectively. Patients used a mean of 12.7 different medications with a mean total pill burden of 22.3 and a mean PBM burden of 8.5.

In Fig. 1, the study flow chart is visualized.

3.1. Health literacy: percentage of patients perceiving difficulties

Sixty-one (81 %) patients perceived at least one difficulty within one or more HL domains, and fifty-nine (79 %) of the patients perceived difficulties within the critical domain (Fig. 2). Fifty patients (67 %) perceived difficulties in more than one domain: twenty-six (35 %) in two domains and twenty-four (32 %) in all three domains. Eleven (15 %) patients perceived difficulties in only one domain, which was mainly the critical domain.

3.2. Specific difficulties in the three health literacy domains

The most frequently perceived difficulties were a lack of adequate assessment of both the applicability and reliability of information (62.7 and 66.7 %, respectively), finding understandable information (52.0 %), and a lack of knowledge of the indication (38.7 %). Almost half of the patients did not search for understandable information. Furthermore, 33.3 % of patients did not engage in shared-decision making or found this difficult to do (Table 2).

The motivations for not seeing or looking for information, as mentioned in patients' responses to questions 7–9 of the RALPH interview guide, could be grouped into six main themes: 1) trust in the nephrologist, 2) a caregiver, such as a child, or partner, sees or looks for information, 3) the patient does not use the internet or has difficulties using the internet, 4) the patient has no need for information, 5) the patient does not encounter information, 6) when the patient needs

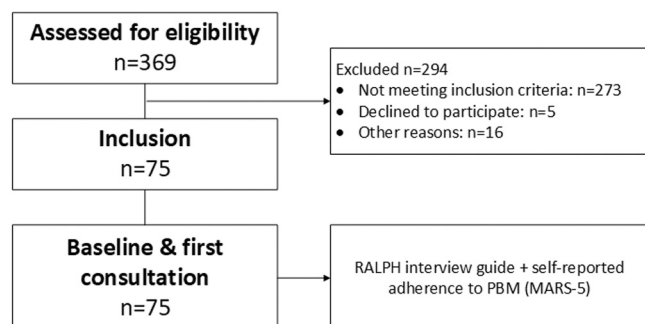


Fig. 1. Study flow chart.

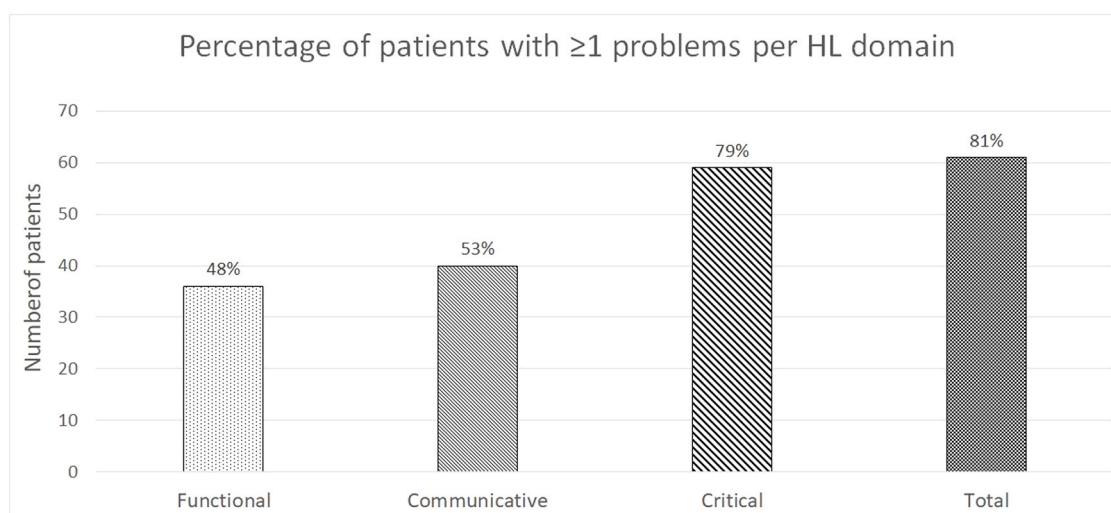


Fig. 2. Percentage of patients with perceived problems per HL domain (n = 75).

Table 2

Medication-related health literacy in patients on hemodialysis using PBM (n = 75).

Health literacy domain		n (%)
Functional	Being able to read*	71 (94.7)
	– Yes	46 (61.3)
	Indication for use	67 (92.0)
	– Correct	65 (86.7)
	User instructions	
Communicative	– Correct	
	Understanding of precautions or warnings	
	– Correct	
	Asking questions #	69 (93.2)
	– Easy	70 (94.6)
Critical	Expressing concerns#	36 (48.0)
	– Easy	
	Finding understandable information	
	– Easy	
	Assessing information applicability	28 (37.3)
	– Easy	25 (33.3)
	Assessing information reliability	50 (66.7)
	– Easy	53 (70.7)
	Shared decision-making	
	– Easy	
	Contradictory information	
	– Correct	

* If patients were unable to read the label due to vision problems, they were asked if they were able to read using visual aids. If this was the case, we scored them as able to read. # One patient did not provide an answer. PBM: phosphate-binding medication

information, he asks the nephrologist. Putting high trust in the nephrologist was the main motivation for not seeing or looking for information in 35–45 % of the cases. The second motivation, a caregiver looking for information, was provided by 19–29 % of the cases. Motivations three to five were mentioned by 13–18 % of the cases. Around 10 % of the patients did not look for information but asked the nephrologist. Variation in these percentages was caused by differences in patient responses to the three questions. For 91 % of the patients who did not participate in shared decision-making, the motivation was a high trust in the nephrologist.

3.3. Self-reported medication adherence and the association between medication-related health literacy and adherence

The median MARS-5 score at baseline was 24 (see Table 1); 20 (26.7 %) patients were classified as non-adherent (MARS <23). The

most frequent reason for non-adherence was forgetfulness (in 41.9 % of participants), followed by taking less medication than instructed (in 16.2 % of participants) and deciding to skip a dose (in 10.8 % of participants).

No association could be found between perceived difficulties in one or more health literacy domains and self-reported adherence to PBM (as a dichotomized variable, OR 1.13 95 % CI 0.31–4.10, Nagelkerke R square 0.001). Several factors possibly influencing self-reported adherence to PBM were investigated. There was a significant association between age and self-reported PBM adherence (OR 1.05; 95 % CI 1.02–1.09; Hosmer-Lemeshow p-value=0.864, Nagelkerke R square 0.158); gender, number of medications, PBM pill burden, and total pill burden were not significantly associated with adherence.

4. Discussion and conclusion

4.1. Discussion

More than eighty percent of patients on hemodialysis using PBM perceived at least one difficulty with medication-related HL, mainly in the critical domain, most often with assessing the reliability and applicability of information. No association was found between medication-related HL in general and self-reported adherence.

No other studies in patients with CKD and on dialysis have reported on medication-related HL using the RALPH interview guide or other medication-specific HL instruments. This makes it difficult to compare the results of this study to previous research. However, we do want to place our results in a broader framework.

The prevalence of difficulties with HL found in patients on hemodialysis in this study is substantially higher than previously reported [15–17,21,24,50]. A meta-analysis from 2017 showed that 26.7 % of the patients on hemodialysis had limited HL [18]. It is important to note that the studies included in this meta-analysis used HL instruments that only assessed the functional domain [18,51]. More recently, HL instruments such as the Health Literacy Questionnaire (HLQ) and the RALPH interview guide (investigating medication-related HL) were developed, including the functional, communicative, and critical HL domains. Since 2017, three studies have investigated HL in patients on hemodialysis using the HLQ [20,24,25]. In these studies, 14.2–23.1 % of the patients had high levels of HL. Our findings align with the results from the abovementioned studies as 19 % of the patients in this study did not experience any difficulties with HL which corresponds with a high level of HL.

When focusing on the separate HL domains, difficulties in the

communicative and critical HL domains occurred with approximately the same frequency as in earlier reports [43,52]. Almost eighty percent of the patients experienced difficulties within the critical HL domain, which is comparable with earlier data [43,52]. Furthermore, two-thirds of the patients experienced difficulties assessing the reliability of medication information. This finding is comparable to data from Dutch community pharmacies, where 64.0 % of the patients with chronic diseases experienced difficulties with this skill [45]. In contrast with earlier data, more patients experienced difficulties with finding understandable information (52.0 % versus 39.3 % reported earlier) [45]. This finding can be explained by the high percentage of patients who do not look for information, which may be caused by the very high treatment and symptom burden in dialysis, which leaves patients overburdened and overwhelmed.

No association was found between medication-related HL and adherence in general. This lack of association has been described before in CKD and patients on hemodialysis [20,42].

A remarkable finding of this study was that the majority of patients on hemodialysis could correctly reproduce user instructions for PBM, but that the actual intake of PBM did not correspond with these instructions. The translation of knowledge to actual behavior is challenging for patients with limited HL [12,53]. The current study's findings suggest this may also be the case for patients on hemodialysis.

This study has several strengths. As far as we know, this was the first study in patients on hemodialysis investigating medication-related HL using the RALPH interview guide. The content of PBM in the treatment of a high SPC as well as the context of hemodialysis treatment are among the most complex and demanding in healthcare. At the same time, the patient's ability to deal with the large quantities of medication and treatment information is reduced, due to increased symptoms and lower functional status. This study highlighted the specific difficulties patients encounter in medication-related HL within this content and context. Moreover, the study provided a detailed insight into the difficulties individual patients perceived. These data may be used to support medication management in patients on dialysis and help improve their medication self-management skills.

Some limitations also need to be mentioned. First, the study sample was relatively small, with 75 patients. Notwithstanding this small sample, this study provided valuable insights into important aspects of medication-related HL in patients on dialysis. Second, selection bias may have occurred, as patients with insufficient language proficiency were excluded. This probably led to an underestimation of the prevalence of perceived problems with medication-related HL, as these patients are very likely to experience difficulties with medication-related HL. However, the percentage of patients on hemodialysis with adequate HL in this study did not differ substantially from data obtained using the Health Literacy Questionnaire in the hemodialysis population [20,24,25]. The third limitation is that the RALPH interview guide has been developed to detect difficulties in the three HL domains and to qualitatively explore these difficulties. The RALPH interview guide was not designed to quantify medication-related HL. This specific design makes it challenging to compare our results with data obtained with other HL instruments. The fourth limitation is that the MARS-5 questionnaire has not been validated in patients with CKD with limited HL. This may have influenced the outcomes. However, the MARS-5 questionnaire has been validated in patients with hypertension [47]. Furthermore, we administered the MARS-5 verbally, and during the interviews, we encountered no other limitations when using MARS-5 besides the known limitations from self-reported outcome measures, such as recall and social desirability bias [54]. Literature data show that self-reported medication adherence as assessed with MARS-5 generally is high, with median values of around 23 [26]. The data from this study (median MARS-5 score of 24, IQR 22–25) thus are consistent with the literature, therefore we have no indication of MARS-5 not being suitable to monitor self-reported adherence in patients with limited HL. The fifth limitation is that this was a small mono-center study, which may limit

generalizability to other hospitals or countries. However, the baseline characteristics of the population were generally comparable with Dutch data and data from the Dialysis Outcomes and Practice Patterns Study (DOPPS), a prospective cohort of patients on hemodialysis from 20 countries [55–58]. Lastly, we were not able to adjust for marital status, number of household members and duration of when performing logistic regression analysis, because these parameters were not collected. However, this regression analysis was only exploratory and should be interpreted with caution.

5. Conclusion

Over eighty percent of patients on hemodialysis using PBM perceived difficulties in one or more medication-related health literacy domains. These findings imply that patients on hemodialysis need more support to effectively use health and medication information to improve self-management and medication management, especially when using PBM. HCPs involved in CKD care should cut the large quantity of complex disease and treatment information into manageable pieces and help and train patients to translate this information. Sometimes patients need to take very small steps to be able to effectively use this information at home. HCPs can help patients in taking these steps and improve their medication management and self-management skills and behavior. This is especially important for patients with limited HL, as for them, the translation of knowledge to actual behavior is particularly challenging [12,53].

Further research regarding medication-related HL in patients on hemodialysis, as well as patients with CKD in general, and its relation with medication adherence, is necessary to corroborate our findings. Preferably, future research should also focus on the relationship between different domains of medication-related HL to medication adherence and include possible determinants such as educational level, marital status, and household members in the data collection.

Practice implications

HCPs involved in care for patients with CKD and on hemodialysis, such as nephrologists, nurse practitioners, dietitians, and pharmacists, should be aware of the high prevalence of suboptimal medication-related HL in this patient group. Patients with CKD and on hemodialysis, seem to need a more step-wise approach to incorporate the large quantity of complex disease and treatment information, for example regarding a high SPC and PBM, into their daily routine to ensure the effective use of medication. HCPs can help them with this task. However, HCPs need to adjust their information and communication strategy. Applying universal precautions can be helpful communication strategies⁵⁹⁶⁰. Applying universal precautions means that HCPs assume that the burdens of the disease, therapy, and healthcare system exceed the HL skills of all patients [61]. These universal precautions consist of improving spoken and written information (e.g. by providing individualized information using infographics and animations) and improving patient self-management and empowerment [59]. Part of improving spoken information is consequently using the teach-back method, which has been proven effective in patients with CKD [60].

CRedit authorship contribution statement

van den Oever Francisca Johanna: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Erwin C. Vastbinder:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Schrama Yvonne C.:** Writing – review & editing, Investigation, Funding acquisition, Conceptualization. **Ellen S. Koster:** Writing – review & editing, Supervision, Methodology, Formal

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