Systematic Review

How does health literacy associated to bio-behavioral and psycho-social outcomes among hemodialysis patients? A systematic review

Leila Zhianfar[1] , Haidar Nadrian[2*] , Zeinab Javadivala[3], Sarisa Najafi[4], Shayesteh Shirzadi[5], Kamyar Pirehbabi[3], Ozra Honarpazhouh[3], Somayeh Azimi[3], Tahyebeh Shirvani[3], Sakineh Haj Ebrahimi[6], Devender Bhalla[7,8,9]

[1]Faculty of Nursing and Midwifery, Mazandaran University of Medical Sciences, Sari, Iran
[2]Social Determinants of Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[3]Department of Health Education & Promotion, Tabriz University of Medical Sciences, Tabriz, Iran
[4]Graduate student in Psychology, Islamic Azad University-Sanandaj Branch, Sanandaj, Iran
[5]Department of Public Health, Neyshabur University of Medical Sciences, Neyshabur, Iran
[6]Faculty of Medicine, Department of Urology, Tabriz University of Medical Sciences, Tabriz, Iran
[7]Nepal Interest Group of Epilepsy and Neurology (NiGEN), Kathmandu, Nepal
[8]Sudan League of Epilepsy and Neurology (SLeN)®, Khartoum, Sudan
[9]Pôle Universitaire Euclide Intergovernmental UN Treaty 49006/49007, Bangui, Central African Republic

***Corresponding Author:** Haidar Nadrian, Email: haidarnadrian@gmail.com

Abstract
Introduction: Although the life expectancy of kidney patients has increased due to hemodialysis (HD), the disease affects their lives in various ways. In this study, we systematically reviewed the relationships between health literacy (HL) and bio-behavioral and psycho-social outcomes in HD patients, to determine the necessary information needed for both micro- and macro-level health decision-making.
Methods: We performed a comprehensive search for globally eligible studies (from 2000 to 2020) on PubMed, EMBASE, ProQuest, CINAHL Nursing, Cochrane Library and Google scholar. The quality assessment of the studies was performed using the standardized tool of the Joanna Briggs Institute (JBI).
Results: Among 29 included studies, 23 and 6 articles were of medium and low quality, respectively, and no article was of high quality. In general, 7210 participants were included in these studies. In total, the lowest, highest and the average level of HL in all researches were reported to be 16%, 76.9% and 31.25% respectively. The findings showed a moderate level of evidence for the relationship of HL with self-care-associated outcomes, disease-related biomarkers, QOL, and perceived social support.
Conclusion: Despite study heterogeneity and low quality, HL was found to be positively contributed to self-care behaviors, perceived social support and QOL of HD patients. HL seems to play an underpinning role in promoting HD patients' QOL and its bio-behavioral and psychosocial determinants.
Keywords: Hemodialysis, Health literacy, Quality of life, Self-care, Social support, Systematic review

Introduction

As a chronic, progressive and irreversible disease, end stage renal disease (ESRD) is a worldwide public health concern.[1] The most common method of treatment worldwide is hemodialysis (HD).[2] According to the Global Burden of Disease (GBD) report, in 2017, Chronic kidney disease (CKD) resulted in 1.2 million deaths and 35.8 million disability-adjusted life years (DALYs), worldwide.[2] Furthermore, the 2019 GBD report found that CKD was the 18th leading cause of DALYs among the 369 diseases analyzed, compared to 29th leading cause in 1990.[3]

In a recent study on the outcomes of HD in the patients, the prevalence of fatigue was 72%, and about 66% had a high level of stress (level B or C). In 25% of the patients, recovery time was more than 6 hours after an HD session. [4] In patients receiving dialysis, higher health literacy (HL) is found to be associated with better mental health and quality of life. So, identifying the characteristics of HL may inform specific interventions to improve patient education and support.[5]

According to WHO, HL is an important skill that patients need to make appropriate health decisions in difficult situations ahead.[6] Low level of HL has significant effects on patients' behavior and has unpleasant consequences,[7] including increased risk of hospitalization,[8] and death.[9] On the other hand, it reduces preventive care and less use of health services.[10] In addition, problems caused by

inadequate HL in HD patients are also seen in the need for self-care,[11] social support,[12] and quality of life.[13]

In HD patients, self-care plays an important role in patients' adaptation to the disease process, improving quality of life,[6] reducing the frequency and duration of hospitalization, reducing treatment costs and patient mortality.[14] Improving perceived social support can prevent adverse physiological complications of the disease, increase the level of self-care among the patients, and have a positive effect on a person's physical, mental and social status, and ultimately lead to increased performance.[15] The results of numerous studies have shown that HL affects the general health status of individuals and quality of life related to health.[16,17]

Planning for modification of physical stressors, improving the level of support for the patients, enhancing the quality of care services provided by the treatment team, upgrading the facilities and equipment and the adoption of an interdisciplinary approach are all believed to improve the care services among in-patients receiving HD treatment.[18] In another review study, the relationships between HL and quality of life among patients receiving HD therapy were highlighted.[19] However, there is a scarcity in the studies on how HL may be associated to social support, self-care behaviors and QOL among HD patients. Healthcare providers of HD patients should be able to identify the effective causes, the benefits of and the barriers to self-care behaviors, social support and quality of life of the HD patients so that they can reduce costs, disability and mortality rates of these patients through developing proper health promotion programs. Therefore, in this study, the relationships between HL and social support, self-care behaviors and quality of life in patients undergoing HD was systematically reviewed to determine the necessary information needed for both micro- and macro-level health decision-making.

Materials and Methods
Study design and search strategy
The current review was conducted based on JBI Data Extraction Form for Systematic Reviews.[20] Studies were searched in the following databases: PubMed, EMBASE, PsycInfo, SID, and Magiran. For additional studies, we also used the Google Scholar and CINAHL search engines, conference papers, and grey literature. Citation and reference searches were conducted for eligible articles, and associated authors were checked for further relevant research. Also, we attempted to contact the authors for missing data or compute it using the stated pre/post-intervention values.

This phase of the study screening yielded a total of 1,336 articles. The selected articles were managed by ENDNOTE X9 software Figure 1. A conclusive combination of keywords related to five main headings of HD, HL, self-care behaviors, social support, and quality of life (as listed in Table S1 of Supplementary file 1) was utilized to retrieve the publications.

Study selection and eligibility criteria
The eligibility and exclusion criteria for the study were formulated, a priori, utilizing the PICO (population, intervention, comparisons, and outcomes) framework. The validity of the content was examined and approved by two members of the research team.
Populations referred to HD patients.
Type of study: were delimited to quantitative observational studies including cohort, case-control and cross-sectional studies.
Outcomes were any reported relationship between HL and perceived social support, self-care behaviors and quality of life.
Setting. There was no limitation based on the type of settings.
Time. All articles published from January 2000 to April 2020 were considered.

Systematic reviews were not included but used to identify additional eligible studies.

Screening the full-text and synthesis
Two members of the research team, SA and OH, independently conducted the screened studies for inclusion. Disagreements about inclusion were resolved in an iterative process via discussion with a third member of the team (HN), and refinement of the inclusion/exclusion criteria until 100% agreement was achieved. Next, both SA and OH reviewed the full texts of the articles and cross-validated the eligibility based on the inclusion as mentioned above criteria. Subsequently, 29 articles were extracted. Reasons for exclusion are listed in Figure 1.

Data extraction (Encoding results)
We categorized the studies according to authors' names, year of publication, setting, sample size, mean age of samples, type and aim of study, scales, characteristics of participants (in terms of language and race), research outcomes, and the HL measures (Table 1).

Quality assessment (risk of bias)
Study quality was scored independently by SA and OH guided by a review of tools for assessing the quality of observational studies (JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies).[22,47] Studies were assigned scores for inclusion, subjects and setting, exposure measured, objective, confounding factors and strategies to deal with, outcomes measured and appropriate statistical analysis.

Scores were combined to indicate study quality and used to inform grading of studies as low, moderate, and high quality. High quality articles met all criteria.
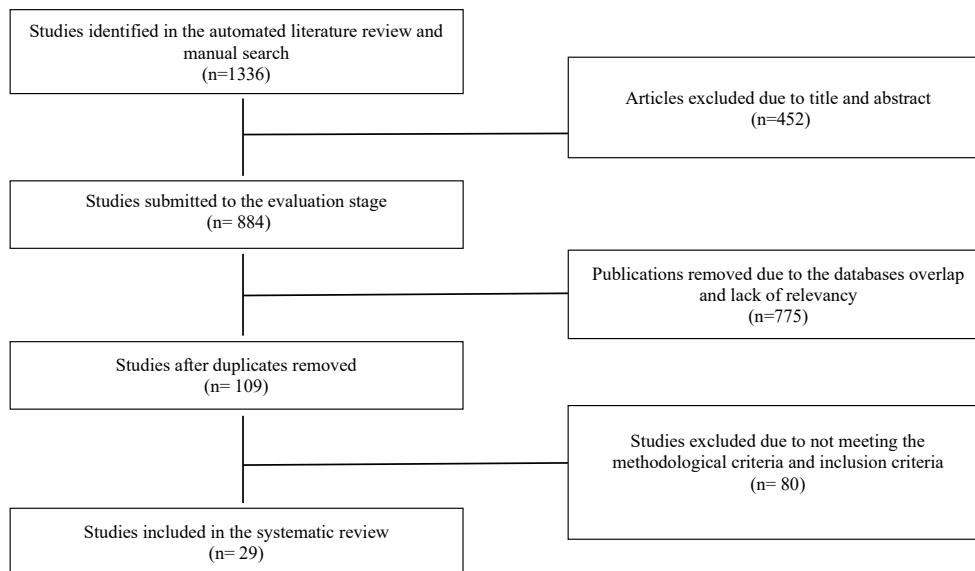
Figure 1. The PRISMA flow diagram of the publications screening

Medium quality articles did not have at least one and at most 4 evaluation criteria .However, this scoring acted as a guide only and grading of studies was decided by discussion between the two researchers, and based on the standard quality evaluation form. The condition of Meta-analysis was not possible due to the heterogeneity of the indicators used to measure the consequences in different studies.

Results

The literature search resulted in a total of 1336 publications. Of these, 452 were excluded due to duplication, and 884 references were based on their titles and abstracts. The remaining 109 studies were retrieved for a detailed evaluation. After the assessment of the full text, a total of 29 studies met our inclusion criteria. Finally, 29 articles satisfied all the review criteria (Figure 1).

Characteristics of the studies

The essential characteristics of the studies are shown in Table 1. The studies were published between 2000 and 2020. In total, 7210 patients were studied. Of 29 studies, 26 were cross-sectional surveys. Except for 6 articles from developing countries [Singapore (2), Iran (2), Brazil (1), Malaysia (1)], 21 articles were from developed countries. Eleven studies were conducted in the United States. Ethnicity data were unavailable for 12 studies (total of 1565 patients),[35-45,48] and age data were unavailable for three studies (total of 757 patients).[30,41,45]

Methodological quality

The quality of studies was assessed by two authors with JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies. It was graded as low for 6 studies and moderate for 23 studies. The details of the methodological

quality information of the studies were presented in Table S2 of Supplementary file 1.

Health literacy rate

In total of 29 studies, the lowest and the highest HL rates were 16% among HD patients with African American ethnicity and 76.9% among White Americans. Among all patients, the average of total HL was calculated to be 31.25%. The highest percentage of HL was reported in two studies from the United States, which were 76.9%[31] and 68%,[25] and were performed on HD patients with a mean age of 52 and 62 years. From the remaining data, in African-American descent[49-51] the average HL was 27.25%, in Americans[13,23,25-28,31,33,52,53] 32.5% and in other races[11,29,30,32,54] were 27.3%. In an Iranian study in 2015, the level of insufficient-borderline and sufficient HL was reported as 34.8% and 65.2%, respectively,[24] and in another study in 2021,[55] the mean score of patients' health literacy was 77.40±12.94. In the studies conducted in Portugal, Brazil, Norway, Malaysia and Sweden, the rate of insufficient HL was reported to be 61.8%, 80.9%, 14%, 28.5%, and 20%, respectively.[36,39-41,43] The mean age of participants was 57.3 years old (only 8 studies over 60). Table 2 defines low health literacy and its relationship to self-care behaviors, perceived social support, quality of life and etc. in hemodialysis patients.

Health literacy and self-care associated outcomes

Six studies[11,25,31,51-53] investigated the relationship between HL and self-care management and their related cognitive factors in HD patients. HL was significantly associated to the promotion of perceived self-efficacy and self-care behaviors,[52] knowledge related to kidney,[26] and self-efficacy and self-management skills,[41] knowledge related to the next stage of kidney transplantation[13,31] and self-

Table 1. List of the retrieved articles according to authors' names, year of publication, setting, sample size, mean age of samples, type and aim of study, scales, characteristics of participants, research outcomes, and the health literacy measures among HD patients

Author/ year	Setting/ year	Sample size	Age Mean (SD)	Study design	Goal of study	Instrument	Target group/ race	Study outcome	Mean of HL (%)
Green 2013[21]	USA 2009-2011	260	62	Cohort	Prevalence and demographic and clinical population of HL in patients undergoing continuous HD	REALM	African-American	Adherence to dialysis program, emergency visits and ESRD-related hospitalizations	16%
Lai 2013[11]	Singapore 2013	63	57/7 (10/1)	Cross-sectional	Relationship between self-management behaviors and HL in diabetic ESRD patients	FCCHL	Chinese, Indian and Malay	Diabetes self-management behaviors	51%
Umeukeje 2016[12]	USA 2012-2015	377	55 (15/3)	Cross-sectional	Healthcare providers support patient independence	s-TOFHLA / BHLS	American	Adherence to medication, Serum phosphorus levels, age and racial differences	56%
Grubbs 2009[23]	USA 2007-2008	62	52/4 (12/2)	Cross-sectional	Relationship between HL and access to kidney transplantation	s-TOFHLA	American	Risk of kidney transplant rejection	Mean 25.6 Inadequate 32.3%
Jones 2016[13]	Canada 2015	106	50/07 (12/87)	Cross-sectional	HL and knowledge and patient satisfaction before kidney transplantation	s-TOFHLA	Canadian, Filipino, South Asian, Black, White and others	Knowledge of kidney transplantation, and understanding of the need for anti-transplant rejection pills, self-confidence in taking drugs after transplantation	Mean 32.6 (4.5)
Qobadi 2014[24]	Iran 2014	204	50/9 10/9	Cross-sectional	HL, negative emotions and self-care	s-TOFHLA	Iranian	Self-care behaviors, depression, anxiety, stress	inadequate 25%, marginal 9.8%, adequate 65.2%
Cavanaugh 2010[25]	USA 2005-2008	480	62	Cohort	Relationship between low HL and increased mortality in ESRD patients	REALM	American	Possibility of death due to disease	32% of patients had limited, 68% had adequate HL
Cavanaugh 2015[26]	USA 2009-2012	150	52/2 (13/9)	Cross-sectional	HL in HD patients	REALM, s-TOFHLA, BHLS	African-American	Knowledge of HD, knowledge related to kidney disease	23%
Green 2011[27]	USA 2009-2010	260	64	Cross-sectional	Demographic characteristics and HL	REALM	African-American	Serological indicators, burden of symptoms, quality of life, mental health and depression	34%
Flythe 2017[28]	USA 2014-2016	154	59 (15)	Cross-sectional	Relationship between psychosocial factors with 30-day readmission in hospital	REALM	Blacks (North Carolina)	Depression, social support, HL and 30-day readmission to hospital	49%
Adeseun 2012[29]	USA 2008-2010	72	51/6	Cross-sectional	Relationship between HL and hypertension and other risk factors for cardiovascular disease	s-TOFHLA	African-American	High blood pressure; Systolic and diastolic blood pressure, lipoprotein (HDL and LDL), BMI, waist to hip ratio and smoking	21% had limited HL
Brice 2014[30]	USA 2014	227	-	Cross-sectional	Correlation of HL questionnaires in HD patients	s-TOFHLA, SILS, TILS	African-American, white	-	129 (55%) adequate, 70 (30%) inadequate, 37 (16%) marginal HL
Dageforde 2015[31]	USA 2012-2013	104	54 (12)	Cross-sectional	Identify patient barriers in evaluating kidney transplantation	BHLS	46 percent white	Perceived knowledge and concern about HL related to kidney transplantation	Limited (23.1%) Adequate (76.9%)
Foster 2011[32]	USA 2009	311	58 (15)	Cross-sectional	Evaluation of personal distress preparedness in HD patients	s-TOFHLA	African-American, Latin	Preparing for public and personal disasters related to dialysis and HL	inadequate 30.3, marginal 19.3, adequate 50.4 mean 23.1

Table 1. Continued.

Author/ year	Setting/ year	Sample size	Age Mean (SD)	Study design	Goal of study	Instrument	Target group/ race	Study outcome	Mean of HL (%)
Taylor 2016[33]	UK 2011-2013	2621	58 (47-67)	Cross- sectional	Determining the frequency and extent of limited HL in ESRD	SILS	British	Waiting for a transplant, preparing for a transplant, comorbidity, socioeconomic status and language skills	16%
Vourakis 2012[34]	-	122	54	Cross- sectional	Relationship between HL with phosphate and albumin levels	-	22% black	Phosphate and albumin levels	-
Bahadori 2018[35]	Iran	130	50% over 60	Case study	Relationship between HL and general health	HELIA	47.7% illiterate	General health	53.8% inadequate HL
Martins 2016[36]	Portugal	68	66/7	Cross- sectional	Relationship between demographic factors and HL	HLS- EU-Q	Majority of elderly	Family relationships, time required for treatment	61.8% inadequate HL
Indino 2019[37]	South Australia	42	54/4 (13/5)	Cross- sectional	Relationship between HL and adherence to treatment (Self-reporting)	FCCHL	-	Adherence to diet, fluids and medication	High HL (percentage not reported)
Indino[38] 2017	South Australia	42	54/4 (13/5)	Cross- sectional	Relationship between HL with adherence to treatment (Self-reporting) and quality of life	FCCHL	-	Adherence and quality of life	High HL (percentage not reported)
Bezzera 2019[39]	Brazil	42	59.5% over 41	Cross- sectional	Relationship between demographic factors and HL	STOFHLA	-	-	80.9% inadequate HL
Stomer 2019[40]	Norway	30	67 (13)	Cross- sectional	Relationship between demographic factors and HL	HLQ	187 CKD (30 HD)	Depression, loneliness, comorbidity	14% low HL
Lim 2019[41]	Malaysia	84	-	Cross- sectional	Relationship between HL with nutritional knowledge, health beliefs, self-management skills and diet adherence	HLS- EU-Q	-	Nutritional knowledge, health beliefs, self-management skills and diet adherence	28.5% inadequate HL
Skoumalova 2019[42]	Slovakia	452	63/6	Cross- sectional	Relationship between HL and diet and fluid intake	HLQ	-	Serum phosphate, serum potassium, IDWG	-
Stomer 2019[40]	Norway	30	67 (13)	Cross- sectional	Relationship between HL with quality of life and adherence to long-term treatment	HLQ	187 CKD (30 HD)	Quality of life and adherence to long-term treatment	14% low HL
Lennerling 2020[43]	Sweden	50	52	Cross- sectional	HL status	NVS	-	-	Low HL (20%)
Griva 2020[44]	Singapore	221	59	Cross- sectional	Relationship between HL with depression, annual service use and mortality	HLQ	Diabetic HD patients, 58% Chinese	Depression, annual service use and mortality	-
Shayan 2018[45]	Iran	446	-	Cross- sectional	Relationship between HL and quality of life in diabetic and non-diabetic HD patients	TOFHLA	223 diabetic and 223 non-diabetic HD patients	Quality of life	Adequate HL in 5.4% diabetic and 17.5% non-diabetic patients
Zavacka 2020[46]	Slovakia	542	63.6 (14.1)	Cross- sectional	Relationship between HL and the decision-making process regarding VA type selection	HLQ	542 HD patients	Higher HL in HD patients is associated with a higher chance of having AVF	-

STOFHLA, Short Test of Functional Health Literacy in Adults; REALM, Rapid Evaluation of Adult Literacy in Medicine; REALM-T, transplant-specific version of the Rapid Estimate of Adult Literacy in Medicine; BHLS, Brief Health Literacy Screener; NVS, Newest Vital Sign; SILS, Single-Item Literacy Screener; TILS, Two-Item Literacy Screener; HLS- EU-Q, European Health Literacy Questionnaire; FCCHL, Functional, Communicative and Critical Health Literacy; HELIA, Health Literacy Instrument for Adults (Persian version); HLQ, Health Literacy Questionnaire; HD, hemodialysis; HL, health literacy; ESRD, End Stage Renal Disease; AVF, arteriovenous fistula; VA, vascular access

Table 2. Health literacy and its relationship to bio-behavioral and psycho-social outcomes among hemodialysis patients in the retrieved articles

Author / Year	Self-care behaviors	Adherence to treatment	social support	Use of health services	Disease-related outcomes and biomarkers	Quality of life
Green 2013,[21]		Increased incidence of incomplete dialysis treatment; missed (0.6% vs 0.3%; adjusted IRR, 2.14; 95% CI, 1.10-4.17)		Increase emergency visits (annual visits, 1.7 vs 1.0; adjusted IRR, 1.37; 95% CI, 1.01-1.86)Increased hospitalization due to ESRD (annual hospitalizations, 0.9 vs 0.5; adjusted IRR, 1.55; 95% CI, 1.03-2.34)		
Lai 2013,[11]	Communication, critical and overall HL was associated with diabetes self-management (r = 0.40; P = 0.001, r = 0.32; P = 0.011 and r = 0.35; P = 0.005, respectively)					
Umeukeje 2016,[22]		Lack of connection with adherence to treatment		Lack of connection with the use of health care	Lack of correlation with serum phosphorus levels	
Grubbs 2009,[23]					Increased risk of transplant rejection (adjusted hazard ratio [AHR] 0.22; 95% CI 0.08, 0.60; P = 0.003	
Jones 2016,[13]	Relationship between higher HL and knowledge about kidney transplantation (r = 0.52; P = 0 .05)	Relationship between HL and understanding the need to take anti-transplant rejection pills (r = 0.38; P = 0.05) and self-confidence in taking drugs after transplantation (r = 0.32; P = 0 .05)				
Qobadi 2015,[24]	Relationship between inadequate HL and poor self-care behaviors (b = 0.043; P < 0.001)					Relationship between HL and depression (b = -0.15; P < 0.001), anxiety (b = -0.11; P < 0.001) and stress level (b = -0.10; P < 0.001)
Cavanaugh 2010,[25]					Increased risk of death from disease due to limited HL (HR 1.54; 95% CI 1.01 to 2.36)	
Cavanaugh 2015,[26]	Relationship between HL and knowledge of HD (0.43; 95% CI: 0.28–0.55); P < 0.001) and knowledge of kidney disease (0.41; 95% CI: 0.27–0.54)					
Green 2011,[27]					Lack of relationship between limited HL and serological indicators and burden of disease symptoms	Lack of connection between limited HL and quality of life, mental health and depression
Flythe 2017,[28]			Increased chances of 30-day readmission in hospital and poor social support by controlling confounding variables 2.57 (1.10–5.91)	Increased chances of 30-day readmission in hospital and limited HL by controlling confounding variables 2.20 (0.99–4.97)		Increased chance of 30-day readmission in hospital and depressive symptoms by controlling confounding variables 2.33 (1.02–5.15)

Table 2. Continued.

Author / Year	Self-care behaviors	Adherence to treatment	social support	Use of health services	Disease-related outcomes and biomarkers	Quality of life
Adeseun 2012,[29]	Lack of relationship between HL and smoking				Relationship between adequate HL and low blood pressure (systolic and diastolic blood pressure); No relationship between HL and lipoprotein (HDL and LDL) levels, BMI, waist to hip ratio	
Brice 2014,[30]						
Dageforde 2015,[31]	Relationship between HL and adequate knowledge with the stage after kidney transplantation in comparison with limited HL (90% vs. 34%; $P < 0.001$)					
Foster 2011,[32]	Lack of connection between HL and preparedness for general disasters and disasters related to dialysis					
Taylor 2016,[33]			Relationship between limited HL and socioeconomic status		Relationship between limited HL and comorbidities and poor English language skills	
Vourakis 2012,[34]					Association of limited HL with low phosphate and lack of association with albumin	
Bahadori 2018,[35]						Relationship between HL and general health status
Martins 2016,[36]			Higher HL in patients with better family relationships	Relationship between HL and the time required for treatment		
Indino 2019,[37]		Relationship between higher HL and improved adherence to diet (OR 3.66; 95% CI 1.08-12.43, $P = 0.03$), fluid restriction (OR 4.92; 95% CI 1.13-21.35, $P = 0.03$) and medication (OR 11.88; 95% CI 2.26-62.44, $P = 0.003$)				
Indino 2017,[38]		Relationship between higher HL and improved adherence				Relationship between HL with psychological and environmental domains of quality of life
Bezzera 2019,[39]						
Stomer 2019,[40]		Relationship between some subscales of HL and medication	Relationship between some HL subscales and living alone		Relationship of some HL subscales and comorbidities	Relationship between some HL subscale and depression
Lim 2019,[41]	Relationship between HL and nutritional knowledge ($r = 0.704$), perceived benefits ($r = 0.408$), perceived barriers ($r = -0.435$), self-efficacy ($r = 0.531$) and self-management skills ($r = 0.691$)	Relationship between HL and diet adherence with control of confounders ($b = 0.899$, $P = 0.004$)				

Table 2. Continued.

Author / Year	Self-care behaviors	Adherence to treatment	social support	Use of health services	Disease-related outcomes and biomarkers	Quality of life
Skoumalova 2019,[42]		Relationship between HL with diet and fluid intake			Relationship between low HL and high serum phosphate (OR:0.77; 95% CI: 0.63–0.94), high non-adherence (OR: 0.74; 95% CI: 0.62–0.89) and overhydrated (OR: 0.78; 95% CI: 0.65–0.94)	
Stomer 2019,[40]		Relationship between some subscales of HL and adherence to long-term treatment				Higher quality of life in groups with higher HL
Lennerling 2020,[43]						
Griva 2020 [44]				Relationship between some subscales of HL and the rate of hospitalization	Correlation of some HL subscales with mortality rate	
Shayan 2018,[45]					Less HL in diabetic than non-diabetic patients	Lack of connection between HL and quality of life
Zavacka 2020,[46]	Relationship between some subscales of HL with vascular access					

IRR, incidence rate ratio; HL, health literacy

management of diabetes in HD patients.[11]

Nine out of 29 studies examined the relationship between HL and treatment adherence and its related dimensions in the patients. Higher HL was related with improved adherence to diet (OR 3.66; 95% CI 1.08-12.43, $P = 0.03$), and fluids (OR 4.92; 95% CI 1.13-21.35, $P = 0.03$). Higher functional HL was associated with less adherence difficulties (per 1-point higher: -1.79 [95% (CI): -2.59 to -0.99]).[56]

Five studies examined the relationship between HL and the use of healthcare services and its related aspects in patients undergoing HD. Low levels of HL were significantly contributed to increased emergency visits (annual visits, 1.7 vs 1.0; adjusted incidence rate ratio [IRR], 1.37; 95% CI, 1.01-1.86) and hospitalization due to ESRD (annual hospitalizations, 0.9 vs 0.5; adjusted IRR, 1.55; 95% CI, 1.03-2.34).[21] Low HL was also associated to low socioeconomic status of the patients,[33] and increase in the duration of treatment.[44]

Health literacy and perceived social support
Four studies[12,27,33,44] examined the relationship between HL and perceived social support in HD patients. According to the findings, the patients with higher levels of HL missed fewer treatment sessions, less hospitalized, and less dependent on others. There was also a direct relationship between HL and the level of family support.[33] Poor social support during hospitalization may be risk factors for readmission in dialysis patients. Our findings suggest that hospital-based assessments of psychosocial factors may improve readmission risk prediction.[44] Female gender, low education level, more prescribed medications, and depressive symptoms were associated with lower HL. Living alone and the presence of co-

morbidities were more common in people with less HL.[27] Patients with higher monthly income show better HL in all dimensions.[23]

HL and disease-related biomarkers
Twelve studies examined the relationship between HL and at least one of the bio-makers and disease-related outcomes in HD patients. In Grubbs study, in the U.S., low HL was associated with an increased risk of renal transplant rejection (adjusted hazard ratio [AHR] 0.22; 95% confidence interval 0.08, 0.60; $P = 0.003$).[23] In Cavanaugh study, in the U.S., limited HL increased the risk of dying from the disease (HR 1.54; 95% CI 1.01 to 2.36).[25] Limited HL was also associated with co-morbidity, high serum phosphate, and over-hydration.[42]

Health literacy and health-related quality of life
In our review, 8 studies[13,21,23,25,28,30,32,54,57] were found on the relationship between HL and quality of life, health status and their associated factors, such as depression, and stress levels in HD patients. In Qobadi study, in Iran, HL was associated with higher levels of depression (b = -0.15; $P < 0.001$), anxiety (b = -0.11; $P < 0.001$), and stress (b = -0.10; $P < 0.001$).[52] In two other studies, adequate HL was found to be effective in controlling hypertension and increasing life expectancy.[21,30] Patients with good HL levels were found to be with higher quality of life.[58]

Discussion
In this study, we systematically reviewed the studies that investigated the contribution of HL to some bio-behavioral and psychosocial outcomes among patients under HD. Our systematic review on the literature published until 2020 showed the significant expansion of HL research in

HD patients. A total of 29 studies published since 2000 were identified, within which 7188 patients were studied. In terms of geographical variation of studies, only 6 studies were conducted in developing countries and, 21 articles were performed in developed countries. More than one third of the research was conducted in the United States, which represents this country as a pioneer in considering HL as a social determinant of health among HD patients.

The average score for HL in all studies was 31.25%. In a systematic study, Taylor et al[59] reviewed 29 studies that investigated the associations of HL to patient outcomes in chronic kidney disease in the United States. They reported that limited HL affects 25% of people with chronic kidney disease (CKD) and may reduce self-management skills leading to poorer clinical outcomes. By disproportionately affecting people of low socioeconomic status and nonwhite ethnicity, limited HL may increase health disparities. By comparing the findings of this study with HL interventions in chronic conditions[60] it can be concluded that HL optimization interventions appear to be important for improving health outcomes in chronic conditions (with diabetes and heart disease as the most targeted chronic conditions). To ensure the development of cumulative knowledge in this field, we need theory-based interventions, with consistency in methods, and more appropriate and comprehensive measures to understand the complexity of interventions.

HL was identified to have substantial implications for improving several socio-psychological and bio-behavioral outcomes in HD patients. In the present study, HL was significantly associated with the promotion of perceived self-efficacy, [41] self-care behaviors, [52] knowledge related to kidney and HD,[26] knowledge related to the post-kidney transplant stage, [13, 31] and diabetes self-management[11] in dialysis patients. Also, higher HL was associated to improved adherence to diet, fluids, and medication.[13,41,42,48,56] Results of previously published systematic reviews[61-63] have shown that self-care interventions have been able to greatly reduce the symptoms of the disease in the patients with chronic diseases. Self-efficacy provides a useful framework for understanding and predicting adherence to self-care behaviors and the effectiveness of self-management in the treatment of the chronic diseases, like kidney disease. [64] In other words, HL is reported as an important factor in determining self-care indicators, including adherence to medication, diet and exercise. Inadequate HL is also reported as an important barrier to patients' adherence to treatment instructions.[65]

The findings of our review also revealed remarkable contributions between patients' HL and various aspects of perceived social support,[28,36,40] and the use of health services.[12,21,33,44] HD patients in developing and underdeveloped countries are generally facing added burden to their illness, due to inherent healthcare insufficiencies, financial costs, and inadequacies in social support and health services.[66] We also identified direct associations between the level of HL of the patients and their level of family support.[36] The relations between the patients and their social environment, particularly family and society, provide a fundamental basis for social support, which strengthens the mechanism of coping with the chronic disease.[67] The family members' engagement level and enrichment of their perception, awareness and self-efficiency in providing the expected support to a patient with ESRD has been proven in a recent study.[68] The role of family support of an ill member of the family in embracing health related advantages was also pinpointed in several previous studies.[69-71]

As a social determinant of health, HL is reported to have a significant effect on the quality of life of patients with chronic diseases, including HD patients.[5,72] Sorensen et al. found that low HL was associated to poor quality of life in HD patients, which might be due to reduced accessibility and less use of medical care, and increased stress load, as a results of increased daily life challenges, poor self-management and decreased self-efficacy.[73] Therefore, HL should be considered as an underpinning factor that facilitates the practice of health behaviors, adherence to a healthy lifestyle, and ultimately improvement in the patients' quality of life. In our review, the effect of HL on patients' quality of life was found to be more remarkable than its effect on HD patients' self-care behaviors and perceived social support, which might be due to its synergistic effect on improving self-care and social support in these patients.

Limitations
Due to the weakness of the articles in providing reliable and definite indicators for all studied variables, meta-analysis was not possible. Many articles were identified with poor reporting, due to the lack of clarity in the instruments they used to assess HL, and the process they applied to assess it in practice. A high level of heterogeneity was also identified in the outcome variables in various studies. Therefore, it was not possible for us to provide a definitive and exact answer for the relationships of HL with self-care behaviors, perceived social support and quality of life in HD patients.

Conclusion
According to the results of our systematic review, HL was positively contributed to self-care behaviors, perceived social support and quality of life of the patients undergoing HD. HL seems to play an underpinning role in promoting HD patients' QOL and its bio-behavioral and psychosocial determinants, which represents this health determinant as a core category that should be kept in mind while planning for health promotion programs among HD patients. Health policymakers, health

practitioners and healthcare providers of the HD patients should take into account HL during the development of practical guidelines for patients' health promotion and QOL improvement. In future research, there should be a focus on investigating the contribution of HL to disease-related biomarkers, such as serum phosphate and albumin. It is also recommended to consider HL while designing cohort, case-control and/or longitudinal studies aiming at the provision of stronger evidence for such associations.

Authors' Contribution

Conceptualization: Haidar Nadrian, Zeinab Javadivala, Ozra Honarpazhouh, Sakineh Haj Ebrahimi.
Data curation: Leila Zhianfar, Sarisa Najafi.
Formal analysis: Shayesteh Shirzadi.
Funding acquisition: Haidar Nadrian.
Investigation: Tahyebeh Shirvani, Somayeh Azimi, Ozra Honarpazhouh.
Methodology: Haidar Nadrian, Devender Bhalla.
Project administration: Haidar Nadrian, Kamyar Pirehbabi, Ozra Honarpazhouh.
Resources: Haidar Nadrian, Sarisa Najafi
Software: Zeinab Javadivala, Shayesteh Shirzadi, Leila Zhianfar.
Supervision: Haidar Nadrian, Zeinab Javadivala.
Validation: Sarisa Najafi, Leila Zhianfar.
Visualization: Somayeh Azimi, Tahyebeh Shirvani.
Writing-original draft: Kamyar Pirehbabi, Leila Zhianfar, Ozra Honarpazhouh.
Writing-review & editing: Haidar Nadrian, Leila Zhianfar, Zeinab Javadivala, Devender Bhalla, Sarisa Najafi.

Competing Interests

The authors have no conflicts of interest to declare.

Ethical Approval

This research was ethically approved in Ethics Committee, Tabriz University of Medical Sciences (Ethics Code: IR.TBZMED.VCR. REC.1398.294).

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Supplementary Files

Supplementary file 1 contains Tables S1 and S2.

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