NEPHROLOGY - ORIGINAL PAPER

Socioeconomic status and mortality among dialysis patients: a systematic review and meta-analysis

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Abstract

Background The reported association between individual indicators of socioeconomic status (SES) and mortality in dialysis patients was inconsistent in previous studies. We performed a meta-analysis to identify the association between SES and mortality of dialysis population.

Methods The meta-analysis was conducted in accordance with MOOSE guidelines. Cohorts evaluating the association between SES indicators (income, education and occupation) and mortality in dialysis patients were included. Random-effects models were used to pool the adjusted relative risk (RR) from individual studies. Heterogeneity was assessed by Cochrane's Q and the I^2 statistic. Subgroup analyses and sensitivity analyses were performed to identify sources of heterogeneity and to evaluate the robustness of findings.

Results Fourteen studies were finally included. In hemodialysis patients, increased mortality was associated with lower level of income (RR = 1.08, 95%CI [1.01–1.16], $P = 0.035$; $I^2 = 87.9\%$, $P < 0.001$) and occupation (RR = 1.63, 95%CI [1.11–2.38], $P = 0.013$; $I^2 = 0.0\%$, $P = 0.601$). However, no significant association was identified for education (RR = 1.43, 95%CI [0.92–2.25]; $P = 0.112$; $I^2 = 68.3\%, P = 0.001$). In patients receiving peritoneal dialysis, lower level of income (RR = 1.80, 95%CI [1.12–2.88], $P = 0.015$; $I^2 = 75.9\%$, $P = 0.042$), education (RR = 1.27, 95%CI [1.13–1.43], $P < 0.001$; $I^2 = 0.0\%$, $P = 0.684$), and occupation (RR = 3.42, 95% CI [1.35–8.70], $P = 0.010$) were risk factors for increased mortality. Subgroup analysis showed the association between SES indicators and mortality in hemodialysis differed according to geographic locations and study designs.

Conclusion Lower SES (measured by income, education, and occupation) tends to be associated with higher mortality in patients receiving maintenance dialysis. But the magnitude of the associations varied for different individual indicators of SES.

Keywords Socioeconomic status · End-stage renal disease · Dialysis · Mortality · Meta-analysis

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Introduction

End stage renal disease (ESRD), the final stage of chronic kidney disease (CKD), has become one of the major public health concerns due to its association with adverse outcomes, requirement of enormous medical resources, and high prevalence of CKD [1–3]. Renal replacement therapy (RRT), including hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation, could provide maintenance treatment for ESRD patients [4]. Dialysis is still the main RRT modality for ESRD patients. More than 80% of ESRD patients maintain dialysis to sustain life; however, 25% of them die within 1 year while 65% die within 5 years [5]. Socioeconomic status (SES), regarded as a potential risk factor for incidence and progression of CKD [6, 7], could

be determined by income, educational level, occupation, etc. [8, 9]. Although numerous studies have reported the associations between SES and mortality among dialysis population measured by different SES indicators, the results are under controversy in magnitude and direction due to SES disunity. A comprehensive assessment of the total evidence stratified with dialysis modalities is lacking. Thus, we performed a meta-analysis to identify the association between SES and mortality of dialysis population.

Methods

This meta-analysis was performed based on the proposal for Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [10] (Additional file 1). As the included articles were officially published and no human participation was involved, ethical approval was not necessary.

Information source and search strategy

We searched PubMed and Embase databases for articles published from 1974 to August 2018, using keywords relevant to socioeconomic determinants including "socioeconomic status," "socioeconomic position," "socioeconomic disparities," "socioeconomic factors," "social status," "social class," "income," "educational level," "educational status," "employment status" or "occupation" versus "dialysis," "peritoneal dialysis," "hemodialysis," "end-stage renal disease" combined with outcomes defined as "mortality" and "risk of death." There was no restriction on the language or countries of publication in the search process. The detail of our search strategy was shown in Additional file 2. Additionally, we checked the references cited in the identified articles for potential inclusion.

Selection criteria

Studies were independently screened by two reviewers (ST and JL) using the following criteria:

Inclusion criteria: (1) prospective or retrospective cohort studies; (2) patients (≥ 18 years old) diagnosed with ESRD undergoing maintenance HD or PD; (3) reporting the association between at least one measure of SES (income, education, or/and occupation) and mortality in HD or PD patients; (4) providing hazard ratio (HR) or relative risk (RR) with 95% confidence interval (CI), or enough data to calculate them.

Exclusion criteria: (1) undergoing kidney transplantation during the follow-ups; (2) not elaborating specific dialysis modality (HD or PD).

Disagreement was solved by discussion with another reviewer (XZ).

Data extraction

For each qualified publication, the following information was extracted by two independent reviewers (ST and JL): the first author's name, year of publication, country where the study was conducted, ethnicity of participants, study design and settings, number of participants, mean age of participants at enrollment, gender, mean dialysis vintage at baseline, proportion of participants with diabetes, median/mean length of follow-up, main socioeconomic status indicators (income, education, or/and occupation), most-adjusted multivariable HR or RR with 95% CIs and adjusted variables. If SES measures were stratified into more than two ranks, we extracted the HR or RR comparing the most disadvantaged to the most advantaged. Meanwhile, we back-calculated the point estimates and 95% CIs if the risk estimates were in a reverse order.

Quality assessment

We used the Newcastle-Ottawa Scale (NOS) for cohort study [11] to assess quality of the included studies, based on three independent parts: Selection (a maximum of 4 stars), comparability (a maximum of 2 stars), and outcomes (a maximum of 3 stars). No unified standards are well established; thus, we defined: studies with ≥ 7 stars as "good," studies with 4–6 stars as "fair," studies with 0–3 stars as "poor" [12].

Statistical analysis

Statistical analyses were conducted using Stata V.13 software (Stata Corporation, College Station, Texas, USA). P value < 0.05 was considered statistically significant, unless otherwise specified. We used adjusted HRs as effect size, and the HRs were directly counted as RRs, as this approach has been applied widely [13–16]. We pooled adjusted HRs using the DerSimonian and Liard [17] random effect model, which takes into account within-study and between-study variations [18]. To evaluate the between-study heterogeneity on a statistical level, we used Cochrane's Q and the I^2 statistic. For Q-statistic, $P < 0.1$ was considered as statistically significant heterogeneity. Meanwhile, I^2 below 25% is defined as no, 25–50% as low, 50–75% as moderate and over 75% as high heterogeneity [19]. Publication bias was assessed by using funnel plots and Egger's test when the number of combined studies was over two. Revman statistical software, version 5.3, provided by the Cochrane Collaboration, was used to calculate the 95% CIs when necessary.

In addition, subgroup analyses were performed to further evaluate the association between income/educational level and risk of mortality among various HD/PD populations.

Subgroup analyses were planned to be performed according to countries' income level (high-income vs. middle/low-income countries [20]) or geographic locations, and study designs (prospective vs. retrospective studies). The main aim of performing subgroup analyses is to confirm the generalizability of the results and to explore the possible explanation of heterogeneity in pooled analyses.

To assess the robustness of our meta-analysis results, sensitivity analysis was conducted: (i) good-quality studies versus fair-quality studies, (ii) studies with small sample size ($n < 200$) versus studies with larger sample size ($n > 200$).

Results

Search results

A total of 1402 records were identified from electronic databases. After removing duplicates and exclusions, a total of 14 studies (8 for HD, 6 for PD) were included (Fig. 1). We contacted authors through e-mails for missing information before study exclusion, but received no response.

Study characteristics

The 14 included studies [21–34] enrolled 798,303 HD and 20,167 PD patients, with mean/median follow-up durations ranging from 13 months [21] to 41 months [28], and sample sizes ranging from 162 [33] to 589,036 [29] (Table 1). All the studies were multi-center cohort studies except Kim [28]. Five were prospective cohorts [21, 23, 26, 27, 30] and 9 were retrospective [22, 24, 25, 28, 29, 31–34](Table 1). Majority of studies reached "good" NOS ratings ($n = 10$) [22–24, 27–31, 33, 34] and the rest [21, 25, 26, 32] ranked as "fair" (Additional file 3). The funnel plots of each outcome (Additional file 4) and the Egger's test (income and HD mortality: $P = 0.897$, education and HD mortality: $P = 0.246$, education and PD mortality: $P = 0.872$) showed no evidence of

publication bias. (Numbers of included studies were limited for association between income and PD mortality, association of occupation with HD and PD mortality.)

SES and risk of mortality among HD patients

Three prospective [26, 27, 30] and 5 retrospective [24, 29, 31–33] studies were performed in HD patients. Of the 8 studies, 4 reported association between mortality with income [24, 29, 31, 33], 5 with education [26, 27, 30, 32, 33], and 2 with occupation [27, 32]. These studies were conducted in USA ($n = 3$) [24, 29, 30], Asia ($n = 3$) [26, 32] and South America ($n = 2$) [31, 33], with mean/median follow-ups varied from 22.5 months [29] to 31.13 months [33]. Several potential confounders (such as age, gender, years of dialysis, body mass index (BMI), smoking, comorbidities, laboratory results) were adjusted. The pooled RR for mortality in HD patients was 1.08 (95%CI [1.01–1.16], $P = 0.035$; $I^2 = 87.9\%$, $P < 0.001$) for the lowest versus highest level of income, and 1.63 (95%CI [1.11–2.38], $P = 0.013$; $I^2 = 0.0\%$, $P = 0.601$) for lowest versus highest level of occupation. However, lower education was not significantly associated with mortality (RR = 1.43, 95%CI [0.92–2.25], $P = 0.112$; $I^2 = 68.3\%$, $P = 0.001$) (Fig. 2).

SES and risk of mortality among PD patients

Two prospective [21, 23] and 4 retrospective [22, 25, 28, 34] cohorts performed in PD patients were included for analysis. They were conducted in South America ($n = 2$) [21, 23], Asia ($n = 2$) [28, 34], Canada ($n = 1$) [22], and Turkey ($n = 1$) [25], with mean/median follow-ups ranging from 13 months [21] to 41 months [28]. Adjusted confounders included age, gender, modality, time of pre-dialysis care, comorbidities, year of treatment, BMI, laboratory results. Increased mortality among PD patients was significantly associated with lower income (RR = 1.80, 95%CI [1.12–2.88], $P = 0.015$; $I^2 = 75.9\%$, $P = 0.042$) and education attainment (RR = 1.27, 95%CI [1.13–1.43], $P < 0.001$; $I^2 = 0.0\%$, $P = 0.684$) (Fig. 3). Only 1 study [25] evaluated the impact of occupation on mortality in PD patients and showed inverse association (RR = 3.42, 95% CI [1.35–8.70], $P = 0.010$). Except for all-cause death, Xu et al. [34] also reported cardiovascular mortality was significantly associated with lower income (RR = 2.13, 95%CI [1.32–3.45], $P = 0.002$) and education level (RR = 1.85, 95% CI [1.10–3.13], $P = 0.020$).

Subgroup analysis

Based on available data, subgroup analyses were performed to investigate whether the relations between mortality of dialysis patients and SES indicators would change in different circumstances.
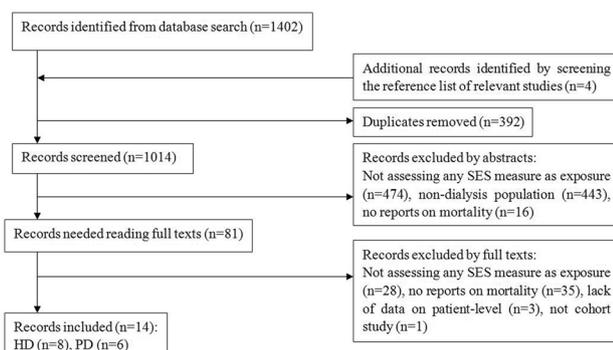

Fig. 1 Flow diagram of included studies. *SES* socioeconomic status, *HD* hemodialysis, *PD* peritoneal dialysis

Table 1 Characteristics of 14 included studies

Author (year)	Country	Design	Dialysis modality	Sample size	Mean age (years)	Gender (% male)	Mean dialysis vintage at baseline (years)	Proportion of participants with diabetes (%)	Mean/median follow-up	SES indicators	RR (95% CI)	Adjustments	Study quality
Eisenstein (2009) [24]	USA	Retrospective cohort	HD	186,039	64.0	52.4	nr	42.2	nr	Income	1.018 (0.984–1.054)	Age, gender, baseline facility and clinical characteristics	Good
Kimmel (2013) [29]	USA	Retrospective cohort	HD	589,036	64.0	54.9	nr	55.2	22.5 months	Income	1.07 (1.05–1.09)	Age, sex, dialysis initiation year, BMI, smoking, comorbid conditions	Good
Lockridge (2012) [30]	USA	Prospective cohort	HD	191	54.7	60.2	2.4	22.6	2.4 years	Education	2.60 (1.08–6.78)	Unadjusted	Good
Marinovich (2012) [31]	Argentina	Retrospective cohort	HD	13,466	60.4	57.2	nr	39.1	nr	Income	1.24 (1.15–1.33)	Age, sex, diabetes, comorbidities, initial laboratory results and first vascular access	Good
Shabankhani (2016) [32]	Iran	Retrospective cohort	HD	500	55.94	53.6	nr	46.2	nr	Education	0.62 (0.42–1.21)	Age, sex, body weight, history of cardiovascular disease	Fair
										Occupation	2.16 (0.70–6.66)	Age, sex, body weight, history of cardiovascular disease	
Teixeira (2015) [33]	Brazil	Retrospective cohort	HD	162	48.09	55.6	2.59	33.3	31.13 months	Education	2.32 (0.98–5.52)	Age, hemoglobin, serum albumin	Good
										Income	0.85 (0.60–1.18)	Unadjusted	
Huang (2013) [26]	Taiwan	Prospective cohort	HD	935	56.11	50.6	6.73	22.0	nr	Education	1.70 (1.02–2.86)	Age, gender, HD duration, initial laboratory results	Fair
Imanishi (2017) [27]	Japan	Prospective cohort	HD	7974	61.7	62.0	7.5	31.0	24.9 months	Occupation	1.57 (1.05–2.36)	Age, gender, vintage, comorbidities	Good
										Education	1.41 (1.04–1.92)	Age, gender, vintage, comorbidities	

Table 1 (continued)

Author (year)	Country	Design	Dialysis modality	Sample size	Mean age (years)	Gender (% male)	Mean dialysis vintage at baseline (years)	Proportion of participants with diabetes (%)	Mean/median follow-up	SES indicators	RR (95% CI)	Adjustments	Study quality
Bastos (2011) [21]	Brazil	Prospective cohort	PD	1952	59.0	46.4	nr	41.0	13 months	Income	1.40 (0.99–1.99)	Age, gender, PD modality, time of first RRT, predialysis monitoring, comorbidities	Fair
Chidambaram (2011) [22]	Canada	Retrospective cohort	PD	5162	61.5	56.16	nr	47.54	2.2 years	Education	1.090 (0.709–1.675)	Age, gender, year of treatment	Good
de Moraes (2014) [23]	Brazil	Prospective cohort	PD	9905	58.9	47.0	2.4	41.0	nr	Education	1.26 (1.10–1.45)	Age, race, distance from the dialysis center, PD modality, previous HD	Good
Xu (2012) [34]	China	Retrospective cohort	PD	2171	58.0	49.5	nr	37.6	27.7 months	Income	2.27 (1.64–3.03)	Demographic and bioclinical data, educational level	Good
										Education	1.47 (1.08–2.00)	Demographic and bioclinical data, individual income	
Gulcan (2017) [25]	Turkey	Retrospective cohort	PD	322	47.0	48.4	nr	nr	nr	Occupation	3.42 (1.35–8.70)	Age, gender, albumin levels	Fair
Kim (2017) [28]	Korea	Retrospective cohort	PD	655	48.4	60.9	nr	35.6	41 months	Education	1.11 (0.53–2.33)	Age, gender, BMI, health insurance, comorbidities, laboratory results	Good

SES socioeconomic status, *RR* relative risk, *CI* confidence interval, *HD* hemodialysis, *PD* peritoneal dialysis, *nr* not reported

Fig. 2 SES and HD mortality. *SES* socioeconomic status, *HD* hemodialysis, *RR* relative risk, *CI* confidence interval
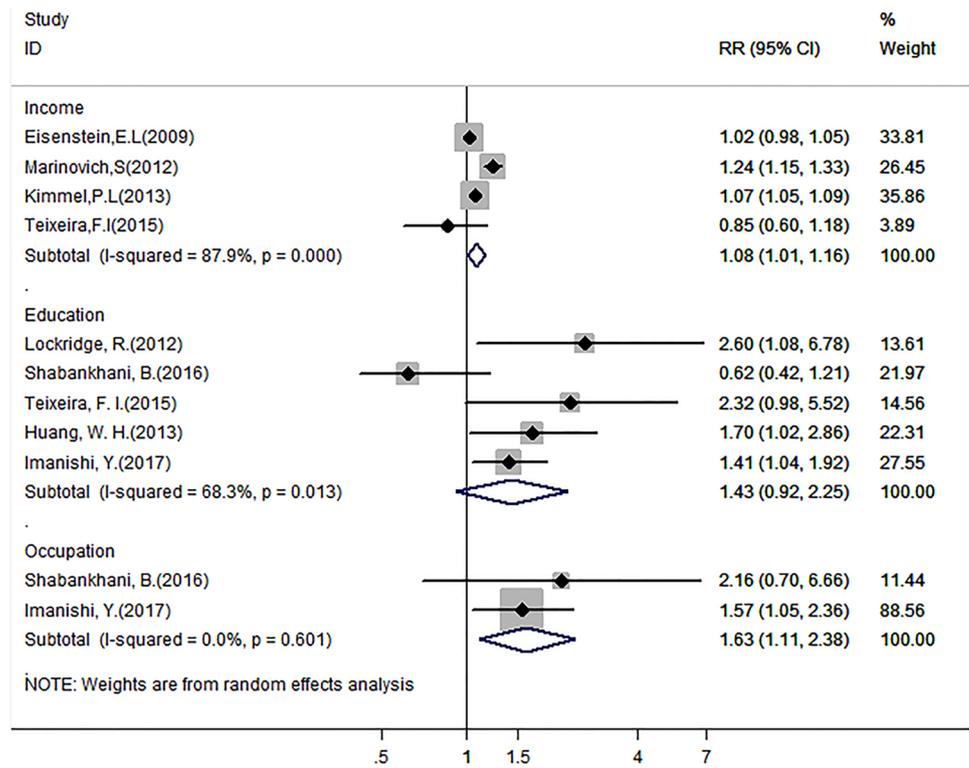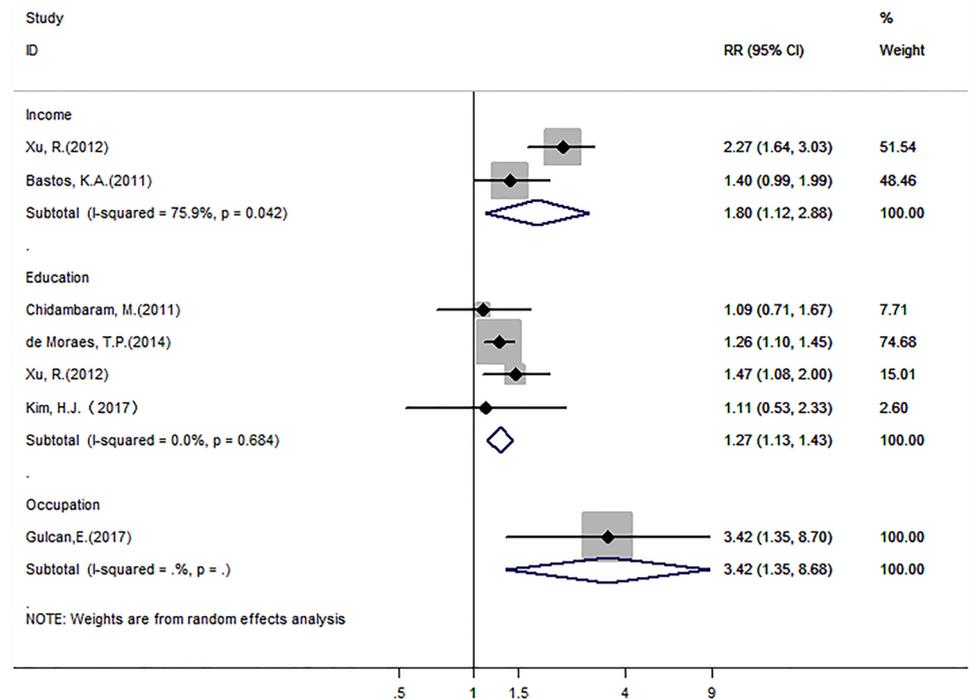

Fig. 3 SES and PD mortality. *SES* socioeconomic status, *PD* peritoneal dialysis, *RR* relative risk, *CI* confidence interval

In HD patients, for the association with income, 2 studies [24, 29] were conducted in the USA, a high-income country. The pooled RR was (RR = 1.05, 95%CI [1.00–1.10], $P = 0.040$; $I^2 = 82.5\%$, $P = 0.017$). Nonetheless, the association was not significant in two middle/low income countries [31, 33] (RR = 1.07, 95%CI [0.74–1.53], $P = 0.719$; $I^2 = 78.2\%$, $P = 0.032$). All those 4 studies were retrospective [24, 29, 31, 33], so the pooled RR (RR = 1.08, 95%CI [1.01–1.16], $P = 0.035$; $I^2 = 87.9\%$, $P < 0.001$) was significant (Fig. 4).

Fig. 4 Subgroup analysis for income and HD mortality. *HD* hemodialysis, *RR* relative risk, *CI* confidence interval
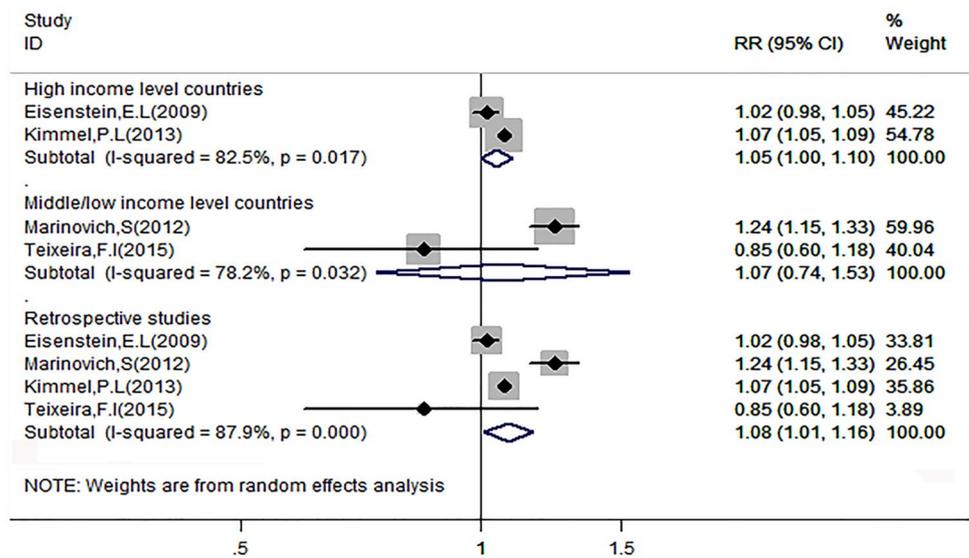
For education, the results differed between studies performed in Asian and non-Asian regions, and between prospective and retrospective cohorts. The association between mortality and education was only significant in non-Asian counties [30, 33] (RR = 2.45, 95%CI [1.30–4.59], P = 0.006; I^2 = 0.0%, P = 0.859) and in prospective studies [26, 27, 30] (RR = 1.55, 95%CI [1.20–1.99], P = 0.001; I^2 = 0.0%, P = 0.426) (Fig. 5).

Additionally, we performed subgroup analyses to investigate whether the relations between PD mortality and educational level would change by geographic areas (Asia vs. others) and study design (prospective or retrospective) (Fig. 6). The direction and magnitude of association in subgroup analyses did not markedly differ from the overall pooled results listed above (Fig. 3). Subgroup analysis was not conducted for income and occupation since only a small number of studies were included.

Fig. 5 Subgroup analysis for education and HD mortality. *HD* hemodialysis, *RR* relative risk, *CI* confidence interval
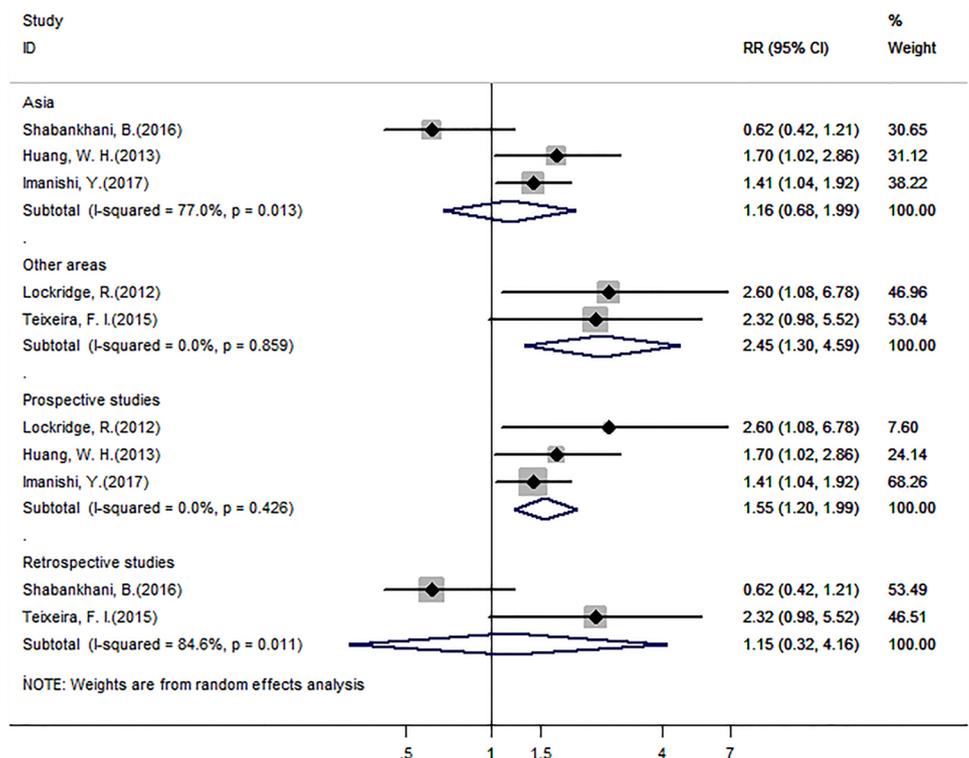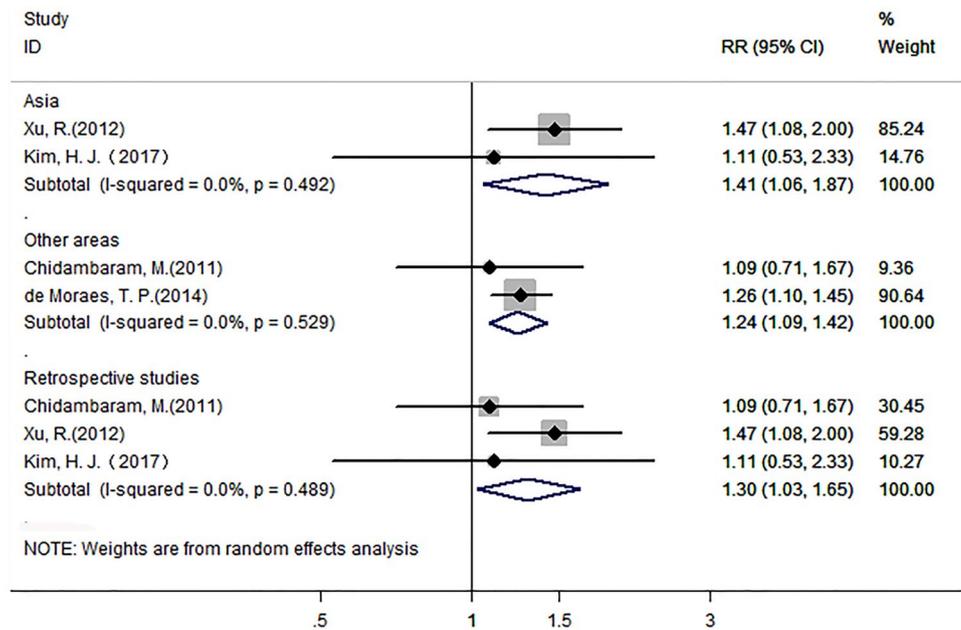
Fig. 6 Subgroup analysis for education and PD mortality. *PD* peritoneal dialysis, *RR* relative risk, *CI* confidence interval

Sensitivity analysis

We performed sensitivity analysis for studies with large sample size and good quality. When eliminating studies with small sample size ($n < 200$) or fair quality, all results were consistent to the meta-analysis results using all 14 studies.

Discussion

The results of our meta-analysis indicated, despite the trend of increased mortality associated with lower SES status, the association between the risk of death in dialysis patients and individual SES indicators varied. For example, in HD patients, education was not a significant risk factor for death, and income level was not associated with increased mortality in middle-/lower-income countries.

The effects of lower SES on clinical outcomes have been previously reported [35–37]. Porche et al. [38] once suggested that healthy conditions of individuals with poorer financial status were usually associated with high rates of injury, disability, illness, and premature death. Besides, the correlations between socioeconomic status and health disparities have been extensively reported worldwide [39, 40]. Similar to our results, Sandhu et al. [41] found in their study that dialysis population with higher Social Adaptability Index calculated on education, employment, income, marital status and substance abuse, had lower mortality rates. Additionally, a systematic review [42] reported that lower education was associated with higher dialysis mortality.

The influence of lower SES on mortality might be due to: (1) physical conditions at baseline [34]; (2)

health-related behaviors [43]; (3) complication rates [44] and treatment to complications [45, 46], like cerebrovascular diseases [34, 47], technique failure [30] and peritonitis[34]; (4) social stratification in communities [48]; (5) environmental hazards [49]; (6) distances to dialysis centers [50, 51]; (7) access to sanitation, healthcare and other basic services [42, 52]; (8) insurance and health literacy [53].

In our study, income and occupation, but not education, affected HD mortality significantly. The results are different from Parameswaran et al.'s study [54], in which education was reported to be associated with patients' outcomes. Explanations for the insignificance between education and mortality in HD are as follows: (1) Different grouping standards of educational level exist; (2) studies were conducted in different countries and areas. Further analysis revealed that, in studies conducted in non-Asian countries, lower education was a risk factor for mortality. (3) Some patients underwent dialysis in dialysis centers [26, 27, 32, 33] while others at home [30]. (4) In Shabankhani's [32] study, we extracted the adjusted RR between illiterate versus bachelor's and higher degrees, which suggested illiterate as a protective factor instead. Illiterate was proved to be a harmful factor when compared to diploma and primary school in their study. It is maybe due to the rather faraway ranks or large sample size variations between two ranks. Consequently, we got a significant difference (RR = 1.60, 95% CI [1.25–2.03] $P < 0.001$; $I^2 = 0.0\%$, $P = 0.477$) after removing this study (Fig. 7). This could also be the possible reason why education does not have an effect on mortality in Asian countries. (5) Possibly, there is no significant association between education and HD mortality, as Teixeira study [33] showed.
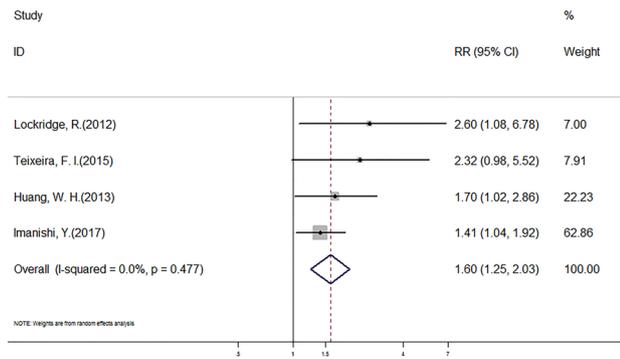
Fig. 7 Education and HD mortality excluded Shabankhani's. *HD* hemodialysis, *RR* relative risk; *CI* confidence interval

Another interesting result of this meta-analysis is that the association between HD mortality and lower income was only significant in studies conducted in USA (a high-income country). The possible explanations are: (1) access to dialysis favored economically advantaged patients in the USA [55]; (2) high heterogeneity existed in studies conducted in middle-/low-income studies, suggesting potential differences in included patients' characteristics, study designs, and different grouping standards of income. This phenomenon merits further investigation.

To the best of our knowledge, this is the first meta-analysis exploring SES and dialysis mortality. The sample size was sufficient to allow a robust result. As mentioned before, our included studies are of high quality, which means the results are convincing. The rigidity of inclusion criteria minimized the potential of bias during selection. Two authors independently assessed studies and resolved disagreements after discussion. However, there are several limitations of our study: (1) Definition and classification of SES across studies were different, which may introduce high heterogeneity. (2) Income or education was evaluated at the beginning of dialysis, which ignored possible changes during the whole process. (3) If participants had lower SES because of their disease, the effects of association could be overestimated. (4) Publication bias could hardly be avoided since we conducted a search among conference databases and relevant society websites. (5) The levels of adjustments for confounders were highly varied across studies. Future subgroup analyses based on degree of adjustments could be done when there are adequate well-designed future studies. Moreover, with adequate future studies, further analyses could consider the association between SES and cause-specific dialysis mortality.

Conclusion

We found that lower SES, measured by income, education, and occupation, tends to be associated with higher dialysis mortality, but the magnitude of association varies in the individual components of SES.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interest.

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