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Review

Association between Glomerular Filtration Rate and Thalassemia: A Systematic Review and Meta-Analysis

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Abstract: Thalassemia is one of the most prevalent genetic disorders worldwide which has been previously found to have an association with several physiological and organ complications. Several studies found both its positive and inverse correlation with glomerular filtration rate (GFR). Therefore, in this meta-analysis, we tried to assess the accurate correlation of thalassemia with GFR. We searched in Google Scholar, PubMed, and ScienceDirect, and from the initial 96 articles we finally could include 15 studies. The quality and publication bias assessment confirmed that all the studies were of high to moderate quality with no publication bias. The main outcome of the mean difference (MD) was -6.45, 95%CI: -18.50, 5.60 (P<0.00001), which indicated a negative correlation of GFR with thalassemia. The sensitivity analyses found one study as a slight outlier and reanalyzing the data excluding that study MD was achieved as -13.90, 95%CI: -24.22, -3.59 (P<0.00001) which even strongly supports our main outcome. Our result determined that the GFR is generally higher in healthy people as compared to thalassemia patients.

Keywords: glomerular; GFR; kidney; thalassemia; anemia; hemoglobin; hereditary diseases

1. Introduction

There are several inherited disorders that are correlated to hemoglobin. Thalassemia is one of the major disorders of hemoglobin related to unusual hemoglobin formation [1]. Thalassemia can be of different types such as α-thalassemia, β-thalassemia, Sickle thalassemia, etc [2,3]. Among them, β-thalassemia is one of the most prominent types of thalassemia caused by single gene alteration. Approximately, throughout the world, 7% of the population bears hemoglobinopathies as carriers of which 1.5% (~80-90 million) are carriers or heterozygotes of β-thalassemia [4,5]. The highest frequencies of β-thalassemia were observed in the Mediterranean and European regions, especially in countries such as Cyprus (15%), Sardinia (10-12%), Greece (8%), Italy (4-5%), Spain (1-2%), UK (0.4%) as well as in eastern and central Europe (0.2-5%) among other continents such as Africa, America, and Asia. In North Africa, the frequency of β-thalassemia was higher in Egypt (2-9%) followed by Morocco (6-7%), Tunisia (5%), and Libya (4-5%). The Maldives displayed the highest rate (18%) of this genetic disease followed by Indonesia (3-10%), India (1-10%), Thailand (3-9%), Pakistan (1-8%), and China-Hong Kong (3-6%) in the South-East region of Asia whereas Iran, Syria, and Oman showed similar rate (4-5%) which was the highest among the other countries of Middle-East and West region of Asia [4]. This prevalence rate clearly presents the current global burden of thalassemia.

As mentioned earlier, thalassemia can be mainly of two different types- α-thalassemia and β-thalassemia, based on the globin chain that is affected. β-thalassemia occurs when the β-globin gene is mutated whereas α-thalassemia occurs due to α-globin gene mutation. Sickle cell anemia on the other hand results due to the heterozygosity of the β-thalassemia and sickle cell genes [2,3]. Again,

thalassemia major (TM) refers to the severity of the clinical condition or phenotype which implies the red blood cell (RBC) transfusion more than eight times in a year, and thalassemia intermedia (TI) refers to the condition where infrequent or absolutely no transfusion is required. Thalassemia minor refers to the condition of being an asymptomatic carrier who might have mild anemia [2,6]. The clinical symptoms such as diarrhea, fever, irritability, abdominal distention, nutritional complications, and enlargement of the liver and spleen are usually expressed within 6-24 months of birth in thalassemia major. In thalassemia intermedia, symptoms might appear between 2-6 years of age with milder anemia where irregular blood transfusions may require depending on the physical condition [6].

Glomerular filtration is a physiological process by which impure blood carrying nitrogenous and other waste materials converts to ultrafiltrate blood by flowing through the glomerular capillaries of the kidney [7]. Estimating the glomerular filtration rate (GFR) is a crucial practice for diagnosis, prognosis, monitoring, and drug dose management especially for kidney diseases [7,8]. Theoretically, the GFR is the outcome of the total number of nephrons times the average single-nephron GFR [7]. Although GFR is a primary index of kidney disease, the changes of GFR were also found to be associated with other diseases such as coronary heart disease (CHD), cardiovascular disease (CVD), fatty liver, UTI and so on [9–12]. Interestingly, GFR was also found to have a correlation with thalassemia, however, in several investigations, a positive correlation between GFR and thalassemia was identified and in some other cases GFR was detected to have an inverse relation with thalassemia [13,14]. Therefore, in this meta-analysis, we tried to evaluate the exact association between GFR and thalassemia.

2. Materials and Methods

2.1. Search Strategy

Primarily, three different databases such as Google Scholar, PubMed, and ScienceDirect were searched respectively with specific keywords which include "glomerular", "GFR", "thalassemia", "randomized control trial", "RCT", "case-control" and "healthy". "Advanced" search mood was used to search articles in PubMed and ScienceDirect. "Title and abstract" and "Title, abstract, keywords" were used in the "advanced" mood for PubMed and ScienceDirect respectively. However, "allintitle" was used during the search in Google Scholar. The search was adjusted with Boolean operators where necessary. The detailed search strategy has been illuminated in the supplementary Table 1.

2.2. Eligibility Criteria

Narrative or Systematic reviews, Documents, correspondences, book chapters, letter to editor, editorials, or articles that do not focus on Thalassemia and GFR were not considered eligible. Duplicate articles assessed from different databases were removed carefully. Only English-language written articles were considered for this study. However, no year restriction was applied.

2.3. Quality Assessment

To investigate the quality of all the included studies, a number of questions were acquired from the Study Quality Assessment Tools, NIH, and Systematic Reviews: Step 6: Assess Quality of Included Studies, UNC [15,16]. The score was given as a percentage depending on different answers (i.e. Yes= 1, No=0, Unclear=0, NR=no score, NA=no score) with specific scores. The total score ≤50, 60-70, and ≥80 was classified as low-scored study (high risk of bias), moderate-scored study (moderate risk of bias), and high-scored study (low risk of bias) respectively.

2.4. Data Extraction and Analyses

Based on the eligibility criteria data extraction was done carefully from the included studies. Several data regarding the general characteristics of the included studies were extracted along with

the data of mean ± standard deviation (SD) of the GFR and the number of total participants of case and control for meta-analysis. Endnote (version X8) software was operated for data extraction.

A random-effects model of mean difference (MD) with 95% confidence intervals (CIs) was preferred to analyze the difference of GFR level between case and control among the included study. Heterogeneity of the included studies was determined using I^2 statistics ($I^2>75\%$ implies substantial heterogeneity). RevMan (version-5.4) software was used for the Meta-analysis.

2.5. Publication Bias and Sensitivity Analyses

Publication bias and sensitivity analyses were done using different methods of analysis to investigate the strength of the result following previous study with slight modifications [17,18]. Primarily, funnel plot was created to identify the publication bias. Followed by Galbraith's plot was constructed to visualize any outlier studies. Further, forest plot was constructed using the random effect model considering the non-outlier homogenous studies. Again, forest plot was constructed using fixed effect model with all the included studies to reconfirm the main outcome. To construct the funnel and Galbraith's plots RStudio software (version 4.3.0), and the 'metafor' package (version 4.2-0) of R was used.

3. Results

3.1. Inclusion of the Study

After the initial search, a total of 96 articles were identified from three online databases (*i.e.* PubMed, ScienceDirect and Google Scholar). From those articles, 36 articles were immediately excluded due to the ineligibility as they were case reports, review articles, correspondence, letter, editorial or original articles worked with animal model, *in vitro*, *in silico* experiments only other than full length research article worked with human case-control model. From the rest 60 articles 24 articles were excluded due to study duplication. From the remaining 36 articles 21 articles were eliminated for not matching with our focus and study criteria (*i.e.* including different types of control, had lack of data, assessed other diseases etc.). Finally, 15 articles were included for this meta-analysis (Figure 1).
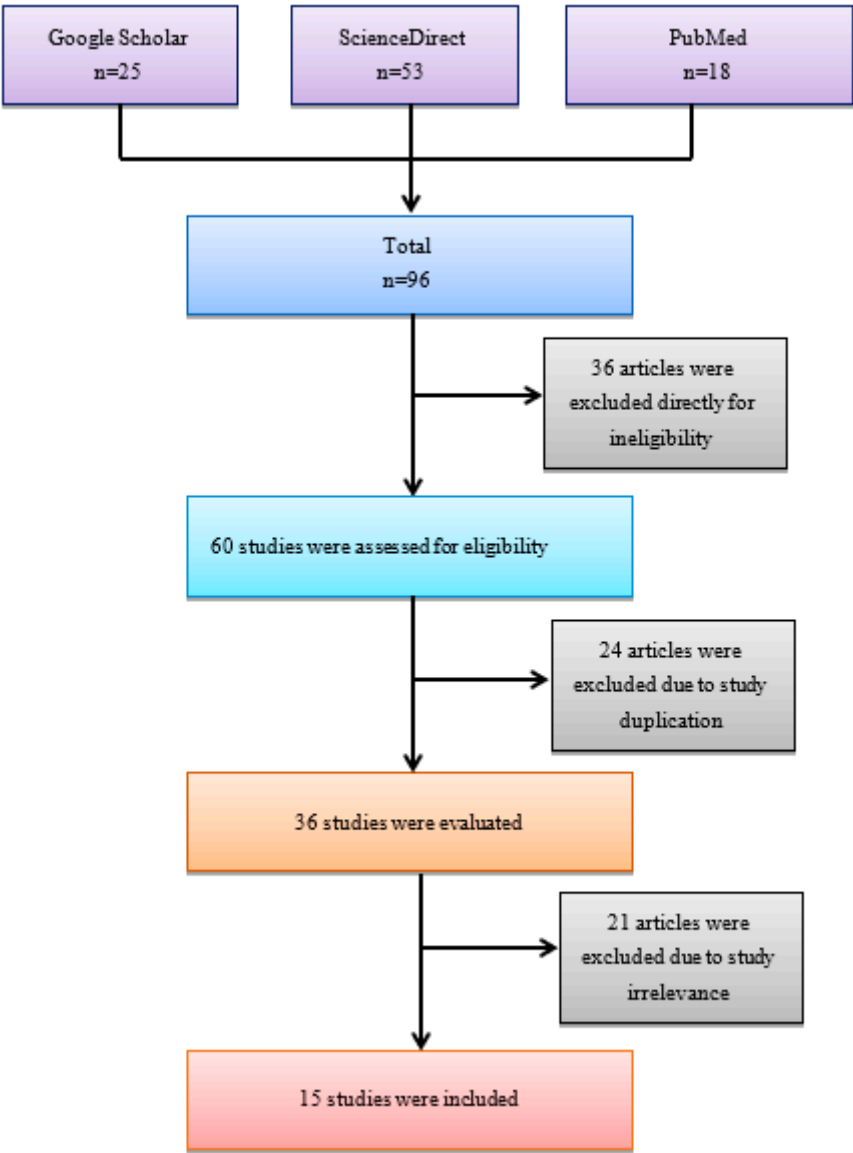
Figure 1. A simplified flow diagram of methodology.

3.2. Assessment of Quality

The quality assessment of the study determined that all the included studies were of moderate (moderate risk of bias) or high quality (low risk of bias) (Table 1). No study had a score of ≤50 with high risk of bias.

Table 1. Quality assessment of the included studies.

Study ID	1	2	3	4	5	6	7	8	9	Overall score (%)
Ahmed 2022	Y	Y	Y	Y	Y	N	U	Y	Y	77.7
Ali 2013	Y	Y	Y	Y	Y	N	NA	Y	Y	87.5
Bilir 2020	Y	Y	Y	Y	Y	N	U	Y	Y	77.7
Behairy 2017	Y	Y	Y	Y	Y	N	U	Y	Y	77.7
Bekhit 2017	Y	Y	Y	Y	Y	N	U	Y	Y	77.7
Capolongo 2020	Y	Y	Y	Y	Y	N	U	Y	Y	77.7
Cetinkaya 2020	Y	Y	Y	Y	Y	N	U	Y	Y	77.7
Ghobrial 2015	Y	Y	Y	Y	Y	N	U	Y	Y	77.7
Hamed 2010	Y	Y	Y	Y	Y	N	Y	Y	Y	88.8

Katopodis 1997	Y	Y	Y	NR	NR	N	U	Y	Y	71.4
Mahmoud 2012	Y	Y	Y	Y	Y	N	NA	Y	Y	87.5
Mahmoud 2021	Y	Y	Y	Y	Y	N	NA	Y	Y	87.5
Saghir 2020	Y	Y	Y	Y	Y	N	NA	Y	Y	87.5
Sen 2015	Y	Y	Y	U	Y	N	U	Y	Y	66.6
Uzun 2015	Y	Y	Y	Y	Y	N	U	Y	Y	77.7

1. Was the research question appropriate? 2. Was the study population clearly defined? 3.Were controls selected from the same or similar population including the same timeframe? 4. Did the author follow proper inclusion and exclusion criteria regarding case-control selection? 5. Were the cases clearly defined and differentiated from controls? 6. Were the assessors of exposure/risk blinded to the case or control status of participants? 7. If less than 100 participants of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible? 8. Did authors use statistical analyses? 9. Were the GFR measurement equation valid to conduct the study?   Y=Yes, N=No, NR=Not reported, U=Unclear, NA=Not applicable   .

3.3. Study Characteristics

The major characteristics such as study location, study type, demographics of the study participants (i.e. male, female ratio in study, BMI, age, case and control type etc.) and the GFR measuring method were extracted from each of the included study (Table 2). Not reported (NR) was mentioned if any information was not provided in any of the study. Among the studies only the data of participant's BMI were not reported in Ahmed 2022, Ali 2013, Bekhit 2017, Centinkaya 2020, Katopodis 1997, Mahmoud 2021, Saghir 2020, Sen 2015, Uzun 2015 [19–27]. Percentages of male and female participants were missing in Capolongo 2020 [28]. Every single data was reported in Bilir 2020, Behairy 2017, Ghobrial 2015, Hamed 2010, Mahmoud 2012 [13,14,29–31].

Table 2. Characteristics of the included studies.

Study ID	Location	Study type	Participants demographics						Control type	GFR measurement method	References
			Male (%)	Female (%)	BMI	Age	Case type				
Ahmed 2022	**Egypt**	**Case-control**	**64**	36	NR	9.35 ± 6.14	β-TM[a]	Healthy control	Simple height-independent formula	[19]
Ali 2013	Egypt	Cross-sectional	63.2*	36.8*	NR	9.80 ± 1.70*	β-TM	Healthy control	Schwartz formula	[20]
Bilir 2020	Turkey	Cross-sectional	58.23	41.77	18.57 ± 2.32	12.03 ± 4.47	β-TM	Healthy control	Schwartz formula	[13]
Behairy 2017	Egypt	Case-control	64.5	35.5	21.9 ± 5.35	9.5 ± 3.66	β-TM	Healthy control	Schwartz formula	[14]
Bekhit 2017	Egypt	Case-control	46.66*	53.34*	NR	8.30 ± 3.50*	β-TM	Healthy control	Schwartz formula	[21]
Capolongo 2020	Italy	Case-control	NR	NR	23.35 ± 2.35	33.5 ± 13	β-TM	Healthy control	Schwartz formula	[28]
Cetinkaya 2020	Turkey	Case-control	60	40	NR	21.5 ± 23	β-TM	Healthy control	Schwartz formula	[22]
Ghobrial 2015	Egypt	Cross-sectional	61.11	38.89	16.36 ± 0.7	7.96 ± 4.38	Sickle thalassemia	Control	Schwartz formula	[29]
Hamed 2010	Egypt	Case-control	66.67	33.33	16.69 ± 2.75	8.56 ± 3.9	TDβ-TM	Healthy control	Schwartz formula	[30]
Katopodis 1997	Greece	Case-control	47*	53*	NR	37.5*	S-βT	Healthy control	99mTC DPTA	[23]
Mahmoud 2012	Egypt	Cross-sectional	61.33	38.67	17.75 ± 2.6	9.7 ± 1.4	β-TM	Healthy control	Schwartz formula	[31]

Mahmoud 2021	Egypt	Case-control	59	41	NR	9 ± 9.75	β-TM	Healthy control	Schwartz formula	[24]
Saghir 2020	Pakistan	Cross-sectional	100	0	NR	8 ± 3	Thalassemia	Healthy control	99mTC DPTA & 25I labeled iothalamate	[25]
Sen 2015	Turkey	Cross-sectional	55.55	44.45	NR	8.95 ± 4.2	β-TM	Healthy control	Schwartz formula	[26]
Uzun 2015	Turkey	Case-control	52	48	NR	9.95 ± 4.1	β-TM	Healthy control	Schwartz formula	[27]

Here, [a] with and without CKD, *Only case group, β-TM= Beta-thalassemia major, TDβ-TM= Transfusion dependant beta-thalassemia major, TC-DTPA= Technetium diethylenetriaminepentaacetic acid, NR=Not reported .

3.4. Main outcome

The forest plot including all the studies (n=15) (Figure 2) investigated that the mean difference (MD) of GFR level was -6.45, 95%CI: -18.50, 5.60 (P<0.00001) favoring the healthy control as compared to the Thalassemia patient. The determined I2>97% for the analysis implied that the heterogeneity of the included studies was significantly high.
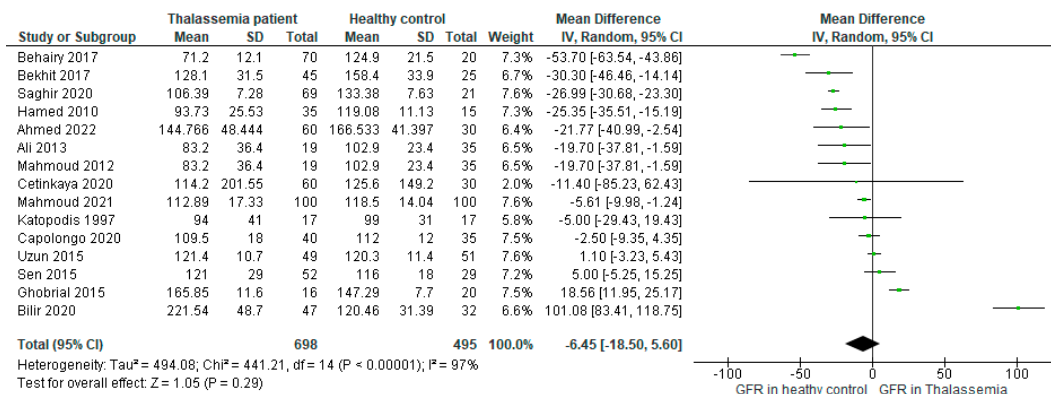
Figure 2. Forest plot showing the mean difference (MD) of GFR in patients with Thalassemia as compared to healthy controls in the random effect model.

3.5. Assessment of Publication Bias and Sensitivity Analysis

Funnel plot was constructed based on all the included studies confirmed to be no high asymmetry in the plot (Figure 3).
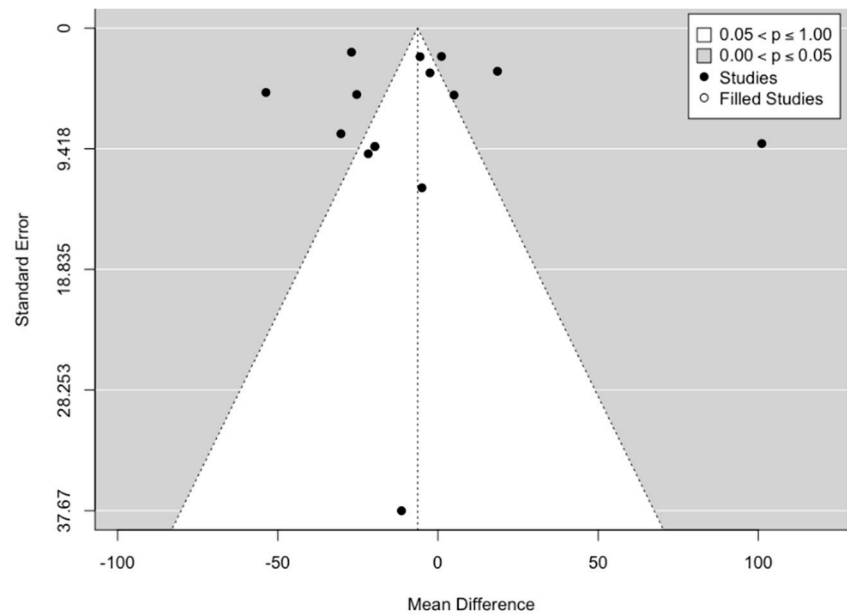
Figure 3. Funnel plot investigating the publication bias reporting GFR in Thalassemia patients in comparison to healthy controls.

This confirmed the absence of any publication bias. Again, due to high heterogeneity, we further considered the data for sensitivity analysis. For sensitivity analyses we initially constructed Galbraith's plot. From Galbraith's plot, Bilir 2020 was considered as a single outlier study (Figure 4).
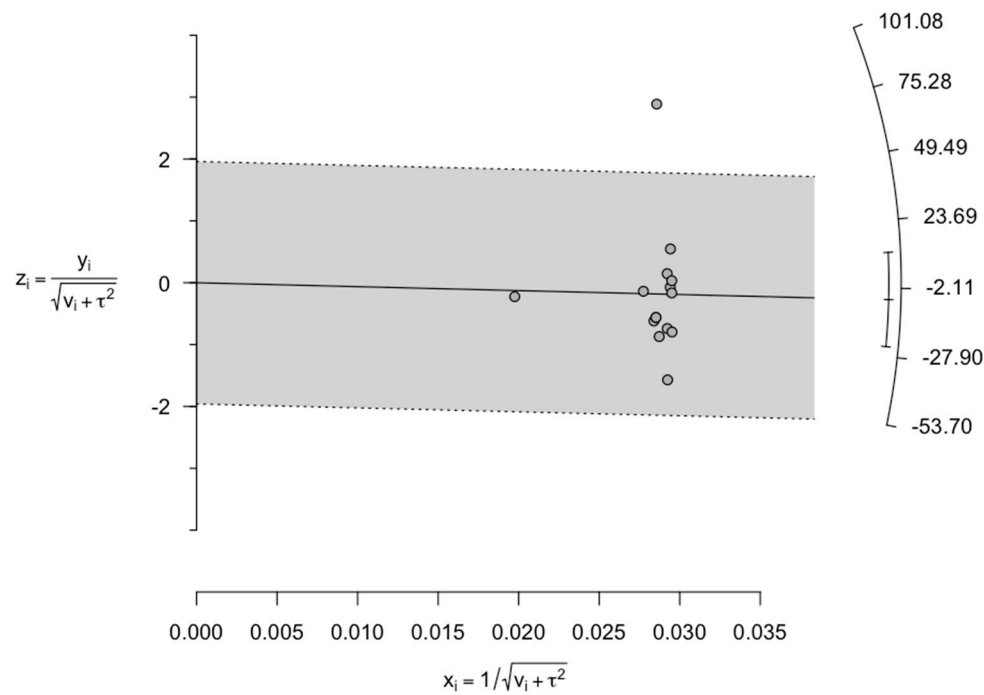
Figure 4. Galbraith plot displaying the plausible sources of heterogeneity. Studies within the limits are interpreted as homogeneous. Studies outside the limits may be outliers. According to the plot, one study (Bilir 2020) was found to be an outlier.

Therefore, excluding Bilir 2020 the forest plot was constructed further using 14 studies (Figure 5), where the mean difference (MD: -13.90, 95%CI: -24.22, -3.59 (P<0.00001)) was found to be two times

higher than the main outcome (-6.45, 95%CI: -18.50, 5.60 (P<0.00001), (Figure 2)) favoring the higher GFR in healthy control. Besides, the heterogeneity reduced (I2=95%) in comparison to the main result as well.

Study or Subgroup	Thalassemia patient Mean	SD	Total	Healthy control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Behairy 2017	71.2	12.1	70	124.9	21.5	20	7.9%	-53.70 [-63.54, -43.86]
Bekhit 2017	128.1	31.5	45	158.4	33.9	25	7.1%	-30.30 [-46.46, -14.14]
Saghir 2020	106.39	7.28	69	133.38	7.63	21	8.5%	-26.99 [-30.68, -23.30]
Hamed 2010	93.73	25.53	35	119.08	11.13	15	7.9%	-25.35 [-35.51, -15.19]
Ahmed 2022	144.766	48.444	60	166.533	41.397	30	6.6%	-21.77 [-40.99, -2.54]
Ali 2013	83.2	36.4	19	102.9	23.4	35	6.8%	-19.70 [-37.81, -1.59]
Mahmoud 2012	83.2	36.4	19	102.9	23.4	35	6.8%	-19.70 [-37.81, -1.59]
Cetinkaya 2020	114.2	201.55	60	125.6	149.2	30	1.6%	-11.40 [-85.23, 62.43]
Mahmoud 2021	112.89	17.33	100	118.5	14.04	100	8.4%	-5.61 [-9.98, -1.24]
Katopodis 1997	94	41	17	99	31	17	5.8%	-5.00 [-29.43, 19.43]
Capolongo 2020	109.5	18	40	112	12	35	8.2%	-2.50 [-9.35, 4.35]
Uzun 2015	121.4	10.7	49	120.3	11.4	51	8.4%	1.10 [-3.23, 5.43]
Sen 2015	121	29	52	116	18	29	7.9%	5.00 [-5.25, 15.25]
Ghobrial 2015	165.85	11.6	16	147.29	7.7	20	8.3%	18.56 [11.95, 25.17]
Total (95% CI)			651			463	100.0%	-13.90 [-24.22, -3.59]

Heterogeneity: Tau² = 324.31; Chi² = 288.80, df = 13 (P < 0.00001); I² = 95%
Test for overall effect: Z = 2.64 (P = 0.008)

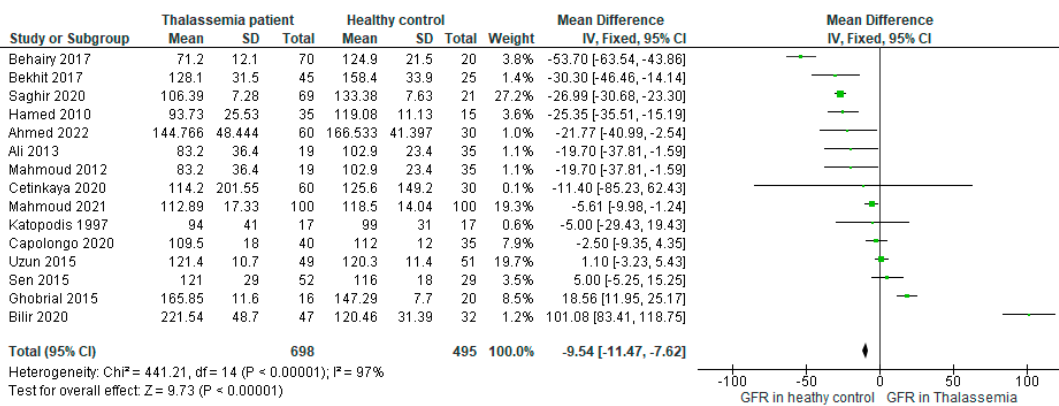**Figure 5.** Forest plot showing the mean difference (MD) of GFR in patients with Thalassemia as compared to healthy controls in the random effect model excluding the outlier study (n=1).

Similarly, reconstruction of the forest plot including all the included studies using fixed effect model was found to be favoring healthy control as compared to Thalassemia patients (MD: -9.54, 95%CI: -11.47, -7.62) (Figure 6) which also supported the main outcome. These sensitivity analyses further supported the strength of our primary result.

Study or Subgroup	Thalassemia patient Mean	SD	Total	Healthy control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Behairy 2017	71.2	12.1	70	124.9	21.5	20	3.8%	-53.70 [-63.54, -43.86]
Bekhit 2017	128.1	31.5	45	158.4	33.9	25	1.4%	-30.30 [-46.46, -14.14]
Saghir 2020	106.39	7.28	69	133.38	7.63	21	27.2%	-26.99 [-30.68, -23.30]
Hamed 2010	93.73	25.53	35	119.08	11.13	15	3.6%	-25.35 [-35.51, -15.19]
Ahmed 2022	144.766	48.444	60	166.533	41.397	30	1.0%	-21.77 [-40.99, -2.54]
Ali 2013	83.2	36.4	19	102.9	23.4	35	1.1%	-19.70 [-37.81, -1.59]
Mahmoud 2012	83.2	36.4	19	102.9	23.4	35	1.1%	-19.70 [-37.81, -1.59]
Cetinkaya 2020	114.2	201.55	60	125.6	149.2	30	0.1%	-11.40 [-85.23, 62.43]
Mahmoud 2021	112.89	17.33	100	118.5	14.04	100	19.3%	-5.61 [-9.98, -1.24]
Katopodis 1997	94	41	17	99	31	17	0.6%	-5.00 [-29.43, 19.43]
Capolongo 2020	109.5	18	40	112	12	35	7.9%	-2.50 [-9.35, 4.35]
Uzun 2015	121.4	10.7	49	120.3	11.4	51	19.7%	1.10 [-3.23, 5.43]
Sen 2015	121	29	52	116	18	29	3.5%	5.00 [-5.25, 15.25]
Ghobrial 2015	165.85	11.6	16	147.29	7.7	20	8.5%	18.56 [11.95, 25.17]
Bilir 2020	221.54	48.7	47	120.46	31.39	32	1.2%	101.08 [83.41, 118.75]
Total (95% CI)			698			495	100.0%	-9.54 [-11.47, -7.62]

Heterogeneity: Chi² = 441.21, df = 14 (P < 0.00001); I² = 97%
Test for overall effect: Z = 9.73 (P < 0.00001)

Figure 6. Forest plot showing the mean difference (MD) of GFR in patients with Thalassemia as compared to healthy controls in the fixed effect model. .

4. Discussion

To the best of our knowledge, this is the single meta-analysis that focused on the association between thalassemia and GFR, compiling the research data from all over the world. Research says thalassemia can alter GFR through mechanisms such as renal hypoxia, iron overload, oxidative stress, and renal tubular dysfunction [25,32].

Thalassemia results in chronic anemia from the decreased synthesis of functional hemoglobin. Anemia lowers the blood's ability to transport oxygen, which causes tissue hypoxia, notably in the kidneys and thus causes renal hypoxia. Renal hypoxia may result in diminished renal performance, including a drop in GFR. Again, to treat their anemia, people with thalassemia frequently need blood transfusions. Iron overload in the body may result from these transfusions. The kidneys, among other organs, can become overloaded with iron, which can cause tissue damage and malfunction. Damaged kidneys brought on by iron excess may lower GFR [25].

The upsurge of oxidative stress by creating an imbalance between the antioxidant defense mechanism and the generation of reactive oxygen species (ROS) inside the body may occur because of thalassemia. The renal vasculature and glomeruli may be harmed through the oxidative stress, ultimately impairing the GFR. Thalassemia can also interfere with the renal tubules, which are crucial

for reabsorbing filtered chemicals and preserving fluid and electrolyte balance. Electrolyte imbalances and poor water absorption carried on by renal tubule dysfunction can eventually have an negative impact on GFR [32].

Through the MD value of our main outcome (MD: -6.45, 95%CI: -18.50, 5.60) (Figure 2) we determined that the GFR was higher in healthy population as compared to the people with thalassemia disease. This finding ultimately indicates that the GFR is generally disrupted in thalassemia patients whether an individual may or may not have a current or have previous history of any types of kidney disease which is further supported by previous researches [25,32].

From our analysis we found exceptional results where the MD value of GFR was higher in thalassemia patients in comparison to healthy control (Figure 2). Among the included studies MD value of GFR was found the highest in Thalassemia patients in Bilir 2020 (MD: 101.08, 95%CI: 83.41, 118.75) followed by Ghobrial 2015 (MD: 18.56, 95%CI: 11.95, 25.17), Sen 2015 (MD: 5, 95%CI: -5.25,15.25) and Uzun 2015 (MD: 1.1, 95%CI: -3.23, 5.46).

Billir et al. mentioned that the small sample size of their study could be one of the reasons for such unusual positive correlation between thalassemia and GFR. Besides, age, prolonged anemia and medicinal side effects or toxicity were supposed to have an association with this incident as well [13,33]. Deferoxamine is a popular medicine which is used in thalassemia as a chelating agent. This was used in thalassemia in both the studies Bilir 2020 and Ghobrial 2015 [13,29]. Research observed the effect of subcutaneous deferoxamine on 27 patients with thalassemia major, where interestingly it was identified that after the deferoxamine treatment, 41% of the patients' GFR values were above the normal range [34]. Therefore, the argument that the deferoxamine toxicity plays a role in increasing GFR might be possible but need to be confirmed through further rigorous research. Again, increased proteinuria in thalassemia patients was investigated in both the studies of Bilir 2020 and Ghobrial 2015. Besides, Ghobrial et al. also stated that among the sickle thalassemia patients muscle mass and diet were not maintained accordingly, which lead to increased serum protein which translated into enhanced proteinuria [13,29]. A previous study claimed the high prevalence of microalbuminuria in patients with sickle cell leads to macroproteinuria, and ultimately chronic renal failure, where glomerular hyperfiltration is the early step [35]. Therefore, enhanced proteinuria might be another plausible cause of increased GFR in thalassemia patients.

The disease thalassemia has a wide range of morbidities and affects practically all organ systems. Among thalassemia patients who depend on blood transfusions, renal illness is one of the leading causes of death. Early detection of kidney illness is crucial to avoid impairment since it might arise from progressive renal tubular and glomerular damage [36]. The results indicate a substantial relationship between thalassemia and GFR. The GFR can be helpful for the early detection and prevention of renal failure in thalassemia patients since this study demonstrated a notable difference between GFR in healthy control and thalassemia patients. Hence, it is important for thalassemia patients to periodically monitor their GFR rate. Thus, the above finding can help patients with thalassemia major in identifying renal diseases, lowering the fatality rates.

It is necessary to evaluate GFR using a more precise approach. An approach like this could make it possible to identify GFR decline early in TM patients and stop or slow its progression to acute kidney injury (AKI), chronic kidney disease (CKD), any other kidney related complications and the requirement for renal replacement therapy (RRT) [37]. GFR can be determined through the identification of the clearance rate of different endogenous or exogenous biomarkers such as inulin, creatinine, Cystatin C, iohexol etc. and all are clinically accepted [24,38,39]. However, the measurement methods and biomarkers need to be more specified to get highly accurate results, which is crucial for the proper diagnosis, prognosis, medication, and treatment of patients. The adoption of a highly precise and specified technique could enable the early diagnosis of decreased GFR in TM and delay the steady decline towards kidney dysfunction.

5. Conclusions

In conclusion, thalassemia patients are more susceptible to renal glomerular and tubular damage, which is rarely detected in conventional renal testing. GFR in thalassemia patients is a

reliable indicator for evaluating glomerular thus kidney dysfunction. In thalassemia patients, the GFR can be useful for the early identification or even prevention of renal failure since it varies between healthy controls and cases.

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