

Anemia In Children With Chronic Kidney Disease: Literature Review

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ABSTRACT

The World Health Organization (WHO) defines anemia as a condition in which the hemoglobin level in the blood decreases to less than 12 g/dL in women and less than 13 g/dL in men. The Literature Review study provides an overview of children with anemia, the causes, impacts, and management was given to improve anemia in children with Chronic Kidney Disease (CKD). literature review through database searches: Google Scholar, Proquest, EBSCO, and Science Direct database from 2017 to 2022. Selected studies with anemia criteria, evaluation, and management of anemia in children with CKD. There were six studies in the review which described CKD children as having anemia, anemia caused by multifactor, the impact is an increased risk of hospitalization and death as well as the emergence and development of cardiovascular disease. Anemia that occurs in CKD children gives a picture of low quality of life, high morbidity, and mortality. That comprehensive care is needed between children, parents, nurses, doctors, and nutritionists to reduce the impact of anemia so that quality of life increases

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1. INTRODUCTION

Chronic Kidney Disease (CKD) increases every year in several countries such as the United States, CKD cases in children continue to increase from 2015 to 2017, and there has been a seven-fold increase, from 1,399 to 9,800 children with CKD (CDC, 2017). The incidence in Europe is around 11-12 cases per year per 1 million children with a prevalence of around 50-60 cases per 1 million children. WHO estimates that there will be an increase in the prevalence of kidney disease patients by 41.4% in Indonesia between 1995-2025 (Pandiangan, 2021). Non-communicable diseases such as Chronic Kidney Disease (CKD) continue to be a concern of the Indonesian government to be able to control its increasing every year by launching policies and strategies in the form of the Healthy Living Community Movement (GERMAS) based on INPRES No.1/2017 and improving healthy lifestyles by CERDIK and PATUH behavior and the AMIR Movement, namely the Let's Drink Water Movement. Non-communicable diseases in Indonesia, especially CKD, provide a fluctuating budget burden every year, it was recorded in 2016 that the Social Security Administration Agency (BPJS Kesehatan) for Health amounted to 2.5 trillion rupiahs (Ministry of Health RI, 2018). A sizable budget is issued by the state to reduce the burden on CKD patients. The health budget for children with chronic kidney disorders is 7.6 times higher than that for children without chronic kidney disorders (Hidayati, 2018). CKD in children in Indonesia according to Riskesdas (2018) reaches 1.33 per mil in the age range of 15 to 24 years. CRF has many effects on children's health including cardiovascular disease, nutritional disorders, anemia, growth disorders, bone disease, and neurocognitive deficits and increases the risk of early death in children (Kalantar-Zadeh et al., 2021).

The kidney is an organ that functions to produce erythropoietin where erythropoietin regulates the production of erythrocytes in the bone marrow. In some patients with chronic renal failure, anemia is common. Anemia is a condition in which the level of hemoglobin in the blood decreases (Yuniarti, 2021). Anemia is defined as a hemoglobin (Hb) level of less than 12 g/dL in women and less than 13 g/dL in men, according to World Health Organization criteria (WHO) (Schechter et al., 2019). Anemia in Indonesia uses a limit of 10 gr/dL to receive supporting therapy (Indonesian Renal Registrasi, et al.,

2018). Anemia is a complication and occurs in 80-90% of CRF patients (Aisyafitri et al., 2018). The main cause of anemia in chronic kidney failure is due to reduced red blood cells due to decreased levels of the hormone erythropoietin (EPO) (Garini, 2019).

Based on research Garini, (2019) it was found that the average hemoglobin level of CKD adolescents undergoing hemodialysis was 6,150 gr/dl. Anemia can also be caused by several other things such as a lack of vitamins, folic acid, iron, bleeding, inflammation, and metabolic toxins that inhibit the formation of erythropoietin. In patients with CKD, iron deficiency can cause anemia, and anemia can also cause abnormal blood iron (Jeng, 2022). Anemia is one of the features of malnutrition in CRF based on the results of biochemical examinations (Purnamawati, 2021). Anemia in CKD has an impact on quality of life (QoL) and increases the risk of morbidity and mortality due to left ventricular hypertrophy (Yu et al., 2021). Management of anemia in patients needs to pay attention to a holistic approach starting from the causes and therapeutic options used to reduce morbidity and mortality and improve the patient's quality of life (Putra & Rahman, 2022). Based on the description above, the problem of anemia in CKD children requires comprehensive treatment from all parties. This literature review study aims to look at the description of anemia in CKD children, the impact and management given to improve anemia in children.

2. METHOD

Literature Search: Google Scholar, Proquest, EBSCO, and Science Direct databases were searched from 2017 to 2022. Articles identified in this search end with 5.114 articles were excluded after reading title and abstract. Found 459 articles selected and included in this review, 32 studies excluded after reading in full, as they did not meet inclusion criteria, and 6 articles were selected and included in this review.

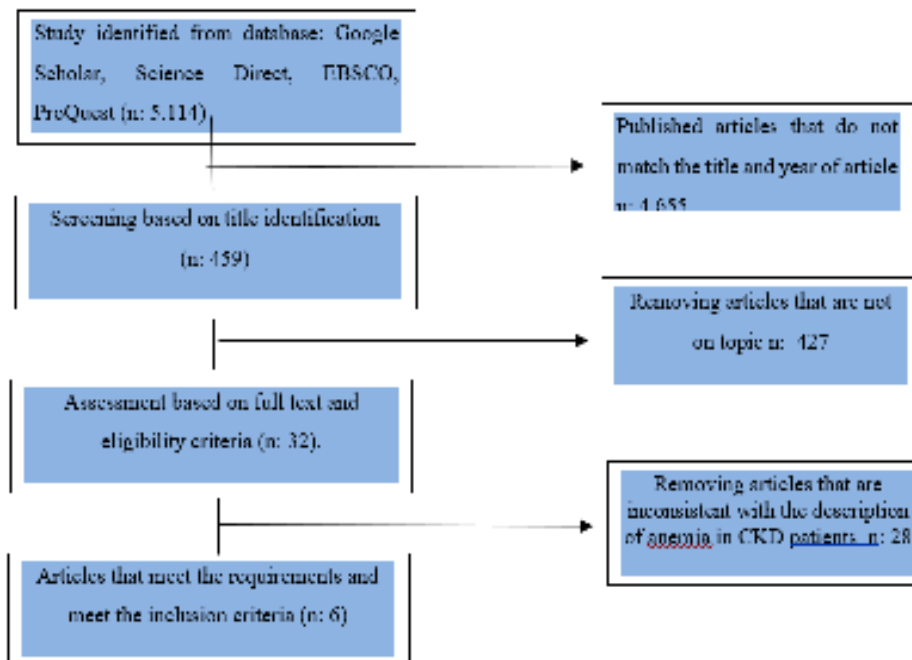


Figure 1. Literature review flowchart

3. RESULTS AND DISCUSSION

The search results on the four databases the researcher found six articles that met the inclusion criteria, the researcher will present the results of the review in the table below:

Table 1. Characterization of publications by reference.

Autor, Year and Country	Title	Type of Study	No. Of participants/Age group	Result
(Garini, 2019), Indonesia	Hemoglobin Levels in Patients with Chronic Renal Failure Undergoing Hemodialysis	Cross Sectional	48 CKD patients	The average hemoglobin level with a duration of hemodialysis ≤ 12 months = 7,600 gr/dl, > 12 months = 8,186 gr/dl.
(Lestari et al., 2019), Indonesia	Role of hepcidin to identify the type of anemia in chronic kidney disease in children	Cross Sectional	34 Patients aged 2-18 years.	Hepcidin has positive correlation with ferritin. This study concluded anemia of chronic disease (ACD) is the most type of anemia in CKD besides mixed anemia.
(Aisyafitri et al., 2018), Indonesia	Description of Anemia in Peripheral Blood Examination in Patients with Chronic Kidney Disease with Hemodialysis Therapy at RSU Santo Antonius Pontianak	Cross Sectional	46 patients Ages 14-24 and adults	Based on the degree of anemia experienced by patients, moderate anemia is the most common cause of CKD cases. According to morphology, normochromic normocytic anemia is the most common form in CKD patients.
(Yu et al., 2021), Taiwan	Low serum iron is associated with anemia in CKD stage 1-4 patients with normal transferrin saturations	Observational study	2500 pasien CKD Stage 1-5	CKD stage 1-4 patients with normal Low transferrin saturation (TSAT) but low serum iron are still at risk for anemia
(Lebensburger et al., 2017), America	Evaluating risk factors for chronic kidney disease in pediatric patients with sickle cell anemia	the study cohort reported	94 Participants 10 to 21 years.	In older children and adolescent sickle cell anemia (SCA) patients, nocturnal hypertension and hyperuricemia, two CKD risk factors, were linked to reduced eGFR.
(Singh et al., 2022), America.	A longitudinal analysis of the effect of anemia on health-related quality of life in children with mild-to-moderate chronic kidney disease	Observational cohort study	733 Pediatric Patients	According to children's HRQOL ratings, anemia was found to be substantially related with lower overall HRQOL

Table 2. Specific hemoglobin

Age (years)	Hemoglobin (g/dl)
0.5–5	< 11.0
5–12	< 11.5
12–15	< 12.0
> 15 Male	< 13.0
> 15 Female	< 12.0

Table 2. WHO age- specific hemoglobin thresholds for defining anemia in children (Atkinson & Warady, 2018). Children with chronic kidney disease (CKD) frequently develop anemia, and iron homeostasis dysregulation is a major factor in the etiology of this condition. For anemia to be effectively treated fast and effectively, iron status must be optimized (Hayes, 2019). Low Hb levels are associated with low blood albumin, elevated parathyroid hormone (PTH) levels, high serum ferritin levels, and use of biocompatible dialysates on the International Pediatric Peritoneal Dialysis Network (IPPN) register. Anemia can also be caused by erythropoietin deficiency and/or dysregulation, iron-restricted erythropoiesis, inflammation and hepcidin up-regulation, chronic blood loss, uremia and oxidative stress, hyperparathyroidism and myelofibrosis, nutritional deficiencies, Medications (Atkinson & Warady, 2018). Anemia has a negative impact on HRQOL in children with CKD that lasts throughout time but does not seem to be progressing (Singh et al., 2022). Untreated anemia dramatically increases the risk of developing and dying from CKD. One of the most common and clinically significant effects of CKD in children is anemia, which is associated with a number of negative clinical outcomes, such as an increased risk of hospitalization and death and the emergence and development of cardiovascular disease (CD) risk factors, such as left ventricular hypertrophy (LVH) (Atkinson & Warady, 2018). Common signs of anemia are weakness, fatigue, lethargy, tiredness and inattention. Apart from that, complaints such as lightheadedness and dizziness often appear, the mucous membranes of the eyelids, lips, tongue, skin, and pale palms (Nurrahman et al., 2020).

Base on Barkate et al. (2017) The pathophysiology of anemia is very complicated. Within the vicious circle known as the cardiorenalemic syndrome, congestive heart failure can both cause and result from CKD (Figure 2). Congestive heart failure can harm the kidneys directly or indirectly by inducing inflammation that impairs erythropoiesis and iron metabolism. Decreased cardiac output affects the blood supply to the kidneys, causing renal ischemia, which leads to the development of anemia due to impaired hormonal activity of the kidneys.

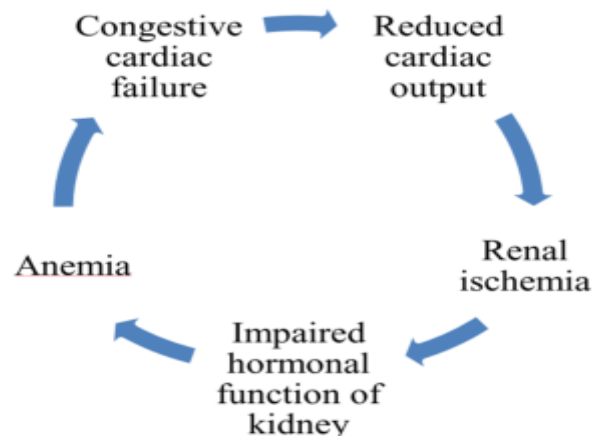


Figure 2. The pathophysiology of anemia (Barkate et al., 2017)

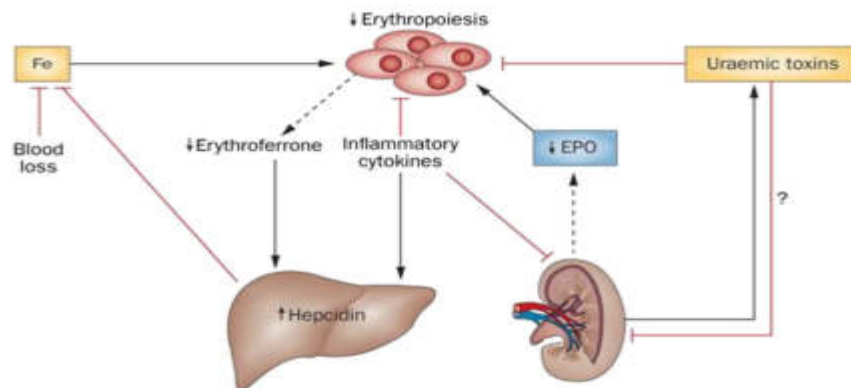


Figure 3. In renal anemia, the kidney's ability to produce EPO is impaired (Atkinson & Warady, 2018)

The picture 3. above provides an overview of the process of anemia in children with CKD. Inflammatory cytokines impair iron intake and mobilization through inhibiting erythropoiesis in the bone marrow, EPO generation in the kidney, and hepcidin production in the liver. Reduced erythropoietin production, which results from a drop in erythroblast numbers as a result of EPO insufficiency, also helps to maintain greater levels of hepcidin. Plasma EPO levels in people with severe CKD are greatly influenced by the liver. Only poorly known is how uremic poisons affect the pathophysiology of renal anemia (Atkinson & Warady, 2018).

Anemia consequences can be lessened by early detection, prompt treatment, and appropriate care. Erythropoiesis-stimulating agents (ESAs) are one of the crucial treatments for anemia in people with CKD. An effective therapeutic option for treating anemia in CKD patients is darbepoetin, an ESA. It has significantly improved the management of anemia. The effectiveness and safety data, as well as the main advantages and functions of darbepoetin alfa in the treatment of anemia in CKD patients, were evaluated in this study. The efficacy and safety of Darbepoetin were examined during a 28-week study in peritoneal dialysis-dependent children (n = 25) in a multicentre study in Japan. Every two weeks, intravenous darbepoetin is given to maintain a hemoglobin level between 11.0 and 13.0 g/dL (Barkate et al., 2017). The creation and widespread application of recombinant human erythropoietin (rHuEPO) in both adults and kids has eliminated the need for RBC transfusions, which was made more difficult by viral infections linked to transfusions, iron excess, and also sensitization. As mentioned above, up to 40% of children with severe CKD exhibit consistently low Hb levels when receiving treatment with an ESA, so treatment with an ESA alone is typically insufficient (Atkinson & Warady, 2018).

4. CONCLUSION

Anemia that occurs in CKD children gives a picture of low quality of life, high morbidity and mortality. Clinical manifestations experienced by children such as weakness, fatigue, lethargy, paleness and lack of attention can be felt by children, so that comprehensive care is needed between children, parents, nurses, doctors and nutritionists to reduce the impact of anemia so that quality of life increases. during chronic disease conditions. Appropriate therapy is very helpful to improve the condition of anemia in children.

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