

Comorbid Diseases in Patients on Dialysis: The Impact on Anemia

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Low hemoglobin (Hb) levels and Hb variability have been the focus of a number of recent reports in the medical literature (Fishbane & Berns, 2005). A wide variety of causative factors for this phenomenon have been cited, including acute or chronic comorbid medical conditions and intercurrent events, anemia management practices, and patient characteristics. This article examines the prevalence of comorbid medical conditions and related intercurrent events in patients on dialysis, and the potential impact of these conditions on anemia. A case study is used to illustrate the nurse's role in assessing and managing anemia when Hb levels are affected by comorbid conditions.

Comorbid Conditions: Prevalence in Patients on Dialysis

Comorbid medical conditions are common in patients on dialysis, and are an important contributing factor to clinical outcomes and quality of life. The most straightforward approach to assessing the burden of comorbid diseases in patients on dialysis is to document the presence or absence of such diseases. In a representative assessment, the Dialysis Outcomes and Practice Patterns Study (DOPPS) documented the

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Patients on dialysis frequently present with a multitude of comorbid diseases. Many of these conditions can either directly aggravate preexisting anemia, or lead to acute or chronic inflammatory or infectious conditions that can lower hemoglobin levels. Awareness of these conditions and their compounding effect on anemia can help nurses when interpreting the results of longitudinal trends in hemoglobin and enable them to intervene proactively to minimize the effect of these conditions on hematological parameters.

prevalence of comorbid diseases in 3,856 patients who were new to dialysis (see Table 1). The results revealed a high comorbidity burden in many patients on dialysis, with the most common disorders including cardiovascular diseases, hypertension, and diabetes. In an international comparison of comorbidity burden, the authors also found that the United States dialysis population has a significantly higher incidence of these comorbidities than patients in Europe, with many patients affected by multiple disease processes (Goodkin et al., 2003).

While an assessment of the absence or presence of comorbidities

offers valuable insights regarding the confounding factors affecting patients on dialysis, it may not take into account either the severity of a comorbid condition, or the cumulative effects of multiple coexisting comorbid conditions. To evaluate these factors, several researchers have used a case-mix model that incorporates an evaluation of disease burden and a patient's functional ability to assign a disease severity score. One commonly used assessment instrument is the Index of Coexistent Diseases (ICED). The ICED score is derived from the peak scores of two assessments of disease and health: (a) the Index of Disease Severity (IDS),

Table 1
Prevalence of Comorbid Diseases Among Patients Incident to Dialysis in the United States

Comorbid Condition	Percent of Patients
Hypertension	83.2%
Coronary artery disease	49.8%
Congestive heart failure	45.8%
Diabetes mellitus	45.7%
Other cardiac diseases	36.3%
Cardiomegaly	34.9%
Left ventricular hypertrophy	34.4%
Peripheral vascular disease	26.1%
Peptic ulcer disease	16.2%
Cellulitis or gangrene	11.3%
Gastrointestinal bleed	9.9%
Cancer	9.6%

Note: Adapted from Goodkin et al. (2003).

Table 2
Comorbidities in Patients with Hb Less Than 11 g/dL Versus 11 g/dL or Higher

Comorbidity	Hb Less Than 11 g/dL	Hb 11 g/dL or Higher
CHF	42.5%	28.8%
AIDS	3.1%	1.0%
Hypertension	77.5%	68.6%
ASHD	37.3%	32.4%
CVA	12.7%	10.5%
PVD	28.6%	22.8%
Other cardiac	44.8%	30.7%
Cancer	10.6%	6.4%
COPD	14.2%	10.8%
Liver disease	11.8%	8.9%
Gastrointestinal	12.9%	5.9%

All $p < 0.05$

Note: Adapted from: Kausz, Solid, Pereira, Collins, & St. Peter (2005)

which categorizes diseases into 19 specific categories, and (b) the Index of Physical Impairment (IPI), which is an observer-based assessment of 11 functional domains that helps measure the impact of diseases on functional ability. In combination, these indices are used to assign a comorbidity severity score that ranges from level 0 (no comorbidity) to level 3 (severe comorbidity) (Miskulin, et al., 2003).

In a representative analysis, the Choices for Healthy Outcomes in Caring for End-Stage Renal Diseases (CHOICE) Cohort study used the ICED to assess the prevalence and severity of comorbid conditions in a group of 1,441 patients who were starting hemodialysis or peritoneal dialysis. The results showed that 64% of patients had a moderate or severe comorbidity index score, indicating a high burden of disease. (Miskulin, et al., 2003). Further, it appears that the comorbidity burden in patients on dialysis increases over time. In the CHOICE study, for example, ICED measurements in a subgroup of 222 patients who were assessed at baseline, 12, and 24 months found that the prevalence of comorbid diseases and

the severity of disease increased progressively over time. Overall, the mean number of disease categories affecting each patient increased during follow-up: from 5.7 ± 2.6 diseases at baseline, to 7.1 ± 2.7 diseases at 12 months, and 7.8 ± 2.8 diseases at 24 months. Similarly, physical impairment worsened with time, with the number of IPI categories present in each patient increasing from 2.6 ± 1.8 at baseline, to 3.0 ± 2.3 after 24 months. These data highlight the fact that patients on dialysis typically are affected by multiple, often severe, comorbidities that can compromise functional ability and negatively affect quality of life (Miskulin, et al., 2003).

Impact of Comorbidities on Anemia

Data indicate that the presence of comorbidities can have a profound effect on Hb. Ebben, Gilbertson, and Collins (2005), conducted an analysis of 152,846 patients on dialysis. Patients whose Hb remained consistently below 11 g/dL, fluctuated below 11 g/dL, or fluctuated from above to below Hb during a 6-month

period typically had a higher comorbidity burden than patients who never experienced Hb below 11 g/dL. Patients with chronic or periodic anemia had a higher incidence of arteriosclerotic heart disease, congestive heart failure, peripheral vascular disease, cancer, and gastrointestinal bleeding. The authors concluded that Hb levels that remain below 11 g/dL or periodically fluctuate to below 11 g/dL appear to be highly confounded by medical complications. Note that the National Kidney Foundation's Kidney Disease Outcomes Initiative recommends that the lower limit for Hb should be g/dL, with insufficient evidence to recommend routinely maintaining Hb levels 13 g/dL in patents receiving erythropoiesis stimulating agents (National Kidney Foundation, 2006).

The association between the presence of comorbidities and an increased risk for anemia was confirmed in a study of 130,544 patients new to hemodialysis who were followed for up to 9 months. In this analysis, the 19,096 (14.6%) patients who did not achieve a Hb of 11 g/dL or higher within 4 to 9 months of starting dialysis were studied to determine the characteristics that were associated with low Hb. The results showed that, compared with those who did achieve a Hb of 11 g/dL or higher, those with lower Hb levels were more likely to be younger, minorities, have more comorbidities, be hospitalized more frequently, have longer hospital stays, and dialyze using a catheter (Kausz, Solid, Pereira, Collins, & St. Peter, 2005).

This analysis also found an association between a high comorbidity burden and Hb levels below 11 g/dL (see Table 2). For those with low Hb levels, about 50% had evidence of a chronic diagnosis that could explain the anemia, with common causative conditions including pancytopenia, aplastic anemia, inflammatory disease, cancer/cancer therapies, hemolysis, chronic blood loss, and AIDS. Another 35% had acute or chronic infectious disorders that explained the decrease in Hb. Overall, more than

Table 3
Common Infectious and Inflammatory Conditions in Patients on Dialysis

Inflammatory Conditions	Infections
Pericarditis	Access site infection
Diabetic skin ulcer	Urinary tract infection
Surgery	Pneumonia
Rheumatoid arthritis	Tooth abscess
Gout	Hepatitis B/C
Lupus	HIV/TB
Inflammatory bowel disease	Peritonitis
Malignancy	Respiratory infection
Gangrene	Perinephric abscess
Fracture	Soft tissue infection
Soft tissue trauma	CMV infection
Osteoarthritis	Wound infection
Transplant rejection	Gum disease
Phlebitis	Osteomyelitis

Note: Adapted from: Breiterman-White (2006).

80% had an identifiable reason for a low Hb level, with many of these causes being correctable. The data also suggested that patients with a high comorbidity burden are more susceptible to inflammatory diseases or infections that could exacerbate anemia (Kausz, et al., 2005).

Comorbidities or the medications used to treat them, contribute to anemia through a wide variety of mechanisms. Some conditions, such as secondary hyperparathyroidism, malignancies, gastrointestinal bleeding, and human immunodeficiency virus, can directly cause anemia, leading to acute or chronic decreases in Hb and an increase in Epoetin alfa dose requirements (Goicoechea, Vazquez, Ruiz, Gomez-Campdera, Perez-Garcia, & Valderrabano, 1998; United States Renal Data System, 2003). More commonly, comorbidities such as diabetes, cardiovascular disease, and arthritis are associated with acute or chronic infectious or inflammatory disorders that can contribute to anemia. Several studies have shown that patients on dialysis

are acutely susceptible to infectious and/or inflammatory conditions (see Table 3). In a recent study of 1,761 patients on hemodialysis, for example, the potential presence of an acute or chronic inflammatory disorder was assessed through serial measurement of C-reactive protein (CRP) (Bradbury, Krishnan, & Critchlow, 2006). This study demonstrated that elevated CRP levels signifying the presence of acute or chronic infectious or inflammatory disorders are common in patients on dialysis, with 39% having CRP levels over 15 and under 30 mg/L, and 29% having CRP levels of 30 mg/L or higher. Overall, 68% of patients on dialysis in this study had CRP levels of 15 mg/L or higher (Bradbury et al., 2006). (Note: In comparison, the author's facility defines normal CRP as 3 mg/L or less, based on an analysis of normal versus abnormal CRP values compiled from the literature and laboratory reference texts.)

Data also indicate that comorbidities or intercurrent events frequently lead to hospitalization, which is also

associated with a significant and prolonged decrease in Hb. A representative analysis of 71,360 patients on hemodialysis conducted by Solid, Gilbertson, and Collins (2005), for example, found that Hb levels typically begin to decrease 1 or 2 months prior to hospitalization, and remain depressed for 2 or more months following hospitalization. The largest decreases in Hb were associated with infectious and bleeding events, which led to a post-hospitalization decrease in Hb of 0.55 g/dL and 0.73 g/dL, respectively. An analysis of the study results also showed that Epoetin alfa dose requirements remained elevated above pre-hospitalization levels for more than 6 months post-hospitalization. These results suggest the continued presence of an underlying condition (e.g., inflammation) that affects red blood cell production and Hb outcomes for a prolonged period following hospitalization.

Nursing Implications – Case Study

The high prevalence of comorbid conditions in patients on dialysis, and the direct or indirect effect of these diseases on anemia, represent a management challenge for nephrology nurses and other members of the nephrology team. The fact that patients typically present with multiple comorbid conditions means that there may be several factors that are simultaneously affecting anemia. The nursing implications for managing anemia in patients with multiple comorbid conditions are explored in the following case example.

BT is a 65-year-old patient with end stage renal disease secondary to diabetes mellitus who has been on hemodialysis for 8 years. Comorbid conditions include congestive heart failure, hypertension (controlled with antihypertensives), rheumatoid arthritis, and left ventricular hypertrophy. The patient also has a history of diabetes-related foot infections and has had three gangrenous toes removed over the past 4 years. The patient has been dialyzing using an arteriovenous

graft, and is scheduled for conversion to an arteriovenous (AV) fistula.

BT's Hb had been stable for several months at 11.7 g/dL, when longitudinal trends in Hb revealed a gradual decrease over 3 weeks to a Hb of 11.2 g/dL. Simultaneously, iron levels had changed slightly, with ferritin increasing from 245 ng/mL to 365 ng/mL and transferrin saturation decreasing from 30% to 25%. Physical examination of the extremities and vascular access site was negative and no intervention was prescribed at this time. The patient was admitted to the hospital for conversion of the arterialized upper arm outflow vein of her forearm graft to a direct upper arm AV fistula.

Upon return to the dialysis facility, the Hb had decreased to 10.9 g/dL. A concomitant increase in ferritin to 565 ng/mL and a decrease in transferrin saturation to 22% were attributed to inflammation resulting from the access placement. The Epoetin alfa dose was consequently increased by 25% from baseline levels.

Six weeks later, the patient's Hb level had still not responded. A subsequent head-to-toe assessment and discussion with the patient revealed that she had noticed a dull tooth ache for the past few months. She had not mentioned the tooth-ache because she was afraid of dentists, and had not had a dental appointment for several years. Intervention by the nurse and social worker resulted in a dentist visit, which revealed an infected and abscessed tooth. Antibiotics were prescribed, the area around the tooth was drained, and a cavity was filled.

Two weeks later, the Hb level began to increase. After 5 more weeks, longitudinal trends revealed that the Hb was rising and approaching 12.0 g/dL. The dose of Epoetin alfa was proactively decreased by 25% to reduce the rate of rise and avoid exceeding a Hb of 12.0 g/dL.

Discussion

Vascular access procedures and hospitalization are obvious sources of infection and inflammation that can lead to a fall in Hb levels. However, comorbidities such as diabetes can negatively affect the immune system and

make patients susceptible to a wide range of infectious and inflammatory disorders. In this case, the most obvious locations for a diabetes-induced infection—the extremities—were negative. Further, the need for an access revision and hospitalization seemed to explain the drop in Hb. It was not until the Hb continued to be depressed, despite an increase in the dose of Epoetin alfa, that further assessment revealed the abscessed tooth.

Nurses should recognize that patients with multiple comorbidities often are affected by many factors that can simultaneously affect Hb levels. Longitudinal trends in Hb levels can be invaluable in detecting the potential presence of these conditions, and prompting the need for further assessment. In such cases, the decrease in Hb can often be muted by interventions to correct the underlying disorder, and proactively increasing the dose of Epoetin alfa, when appropriate, to decrease the impact on Hb.

Nurses should also be aware that the need to track longitudinal changes in Hb is vital during the period when a comorbidity-induced intercurrent event is being corrected. As the underlying condition resolves and Hb levels begin to rise, it is important to assess the longitudinal trends in Hb. If Epoetin alfa doses were increased in response to an intercurrent event and the Hb is rising and approaching 12.0 g/dL, a proactive decrease in the dose is appropriate to ensure that the Hb does not exceed recommended limits.

Conclusion

Patients on dialysis are frequently affected by multiple comorbidities that can directly or indirectly contribute to anemia. The systemic and chronic nature of these diseases leads to frequent intercurrent events that can depress Hb levels. Management of these patients necessitates an individualized approach to assess for the presence of multiple conditions that may be simultaneously affecting Hb levels, and adjustment of therapies, as appropriate, to minimize the impact on anemia-related outcomes.

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Note: *The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government.*