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EVALUATION THROMBOCYTOSIS IN CKD STAGE V PATIENT ON HEMODIALYSIS TREATMENT: CASE REPORT

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Abstract

Chronic kidney disease (CKD), also known as renal failure, primarily affects people with a history of hypertension and diabetes. In this medical condition, the rate of filtration or kidney function can decrease over the course of a month or a year. Several studies have found an increase in pro-inflammatory cytokines in patients with CKD. Platelet dysfunction and hyperreactivity have been linked to chronic inflammation. When the platelet count exceeds 450,000/µl thrombocytosis occurs. It is also referred to as thrombocythemia. Reactive thrombocytosis accounts for 80-90% of all thrombocytosis events, with inflammation being one of the most common causes. We report a 67-year-old man presenting to the hospital with fever and weakness. The patient had a history of CKD stage V and currently was rceiving hemodialysis treatment. Laboratory finding showed patient had thrombocytosis. Further examination is required to determine the cause of thrombocytosis in CKD patient.

Keywords: Thrombocytosis, Chronic kidney disease, CKD, Hemodialysis, Treatment

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Introduction

Kidney Disease Improving Global Outcomes (KDIGO) criteria define chronic kidney disease (CKD) as an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m2 for ≥3 months [1]. Diabetes, hypertension, chronic pyelonephritis, chronic glomerulonephritis, autoimmune diseases, polycystic kidney disease, congenital malformations, chronic use of anti-inflammatory medication, and prolonged acute renal disease are the leading causes of CKD [2]. CKD has emerged as a major cause of morbidity and mortality. Every year, the prevalence is expected to rise significantly. It has been identified as a significant risk factor for the development of cardiovascular diseases and premature death [3, 4].

The global prevalence of CKD has been estimated to be 11-13% [5]. In 2017, it was estimated that nearly 700 million people worldwide had CKD, and 1.2 million died from CKD-related disorders [6]. According to the National Basic Health Research (Riset Kesehatan Dasar, Riskesdas), the prevalence of CKD (eGFR60 ml/min/1.73 m2) was 3.8 permil (‰) in 2018, up from 2.0 permil (‰) in 2013 [7]. Furthermore, the burden of CKD is expected to rise in the future, owing to global aging and the rising prevalence of hypertension, obesity, and type 2 diabetes mellitus (T2DM) [8,9].

Thrombocytosis occurs when the platelet count exceeds 450,000/µl. It is also known as thrombocythemia. Thrombocytosis is classified into two types: primary and secondary (or reactive) thrombocytosis. Secondary thrombocytosis, also known as reactive thrombocytosis, is defined as an abnormally high platelet count caused by underlying events such as chronic disease, medication use, or inflammation [10]. In addition to the main trigger mechanism, the pathogenesis of CKD is indicated by progressive glomerulus fibrosis and/or capillary injury due to hypoxia, and nephron function loss caused by tubular atrophy and glomerulus sclerosis. Additionally, an increase in inflammation is thought to be significant throughout this pathophysiological process [11].

Platelet reactivity is important in the development of thrombosis and thromboembolic events, particularly in atherosclerotic cardiovascular disease, which is the leading cause of death in CKD and CVD patients. Here is a case of a 67-year-old man diagnosed with CKD stage V on hemodialysis that was subsequently diagnosed with thrombocytosis.

Case Report

A 67-year-old man in stable condition on hemodialysis was admitted to the hospital with fever and weakness. He had a

medical history of CKD stage V on hemodialysis, hypertension, low back pain, and knee osteoarthritis. The patient also complained loss of appetite since 2 days ago, pain in the waist and knees. Complaints of tightness, coughing, and urinary syndrome are denied. Urinary complaints denied. He had 2 hemodialysis sessions per week using double lumen catheter access. Outpatient medications were folic acid, calcium carbonate, bisoprolol, candesartan, amlodipine, clonidine, spironolactone, and acetylsalicylic acid. Vital signs were stable with heart rate of 100 beats/min, respiratory rate of 20 breaths/min, blood pressure was 140/80 mmHg and oxygen saturation of 97% on temperature air, and body temperature was 37℃. At admission his platelet count was 1,066,000/mm3 (Reference value - RV: 150,000 - 450,000/mm3). Thrombocytosis was confirmed by manual counting, excluding the presence of clots and no signs of thrombotic microangiopathy. The patient was diagnosed with CKD stage 5 on hemodialysis, thrombocytosis, hypertension, low back pain, and knee osteoarthritis. Upon admission to emergency room, patient was given intravenous NaCL 0,9%, ceftriaxone, paracetamol, and omeprazole. The patient was prepared for hemodialysis and was treated with bicarbonate dialysate via double lumen catheter. The patient was started on subcutaneous heparin for deep venous thrombosis prophylaxis.

Table 1 Laboratory results at hospital admission

White Blood Count (x109/L)	33,34
Hemoglobin (g/L)	8,3
Hematocrit (%)	28,2
Platelet (x103/mm3)	1,066
SGPT (U/L)	21
SGOT (U/L)	26
Random Blood Sugar (mg/dL)	111
Ureum (mg/dL)	180
Creatinine(U/L)	14.8
Natrium (mmol/L)	128
Kalium (mmol/L)	5.8
Chloride (mmol/L)	104
Antigen SARS-CoV-2	Negative

Discussion

Present case report showing that the patient having history of long standing hypertension that lead to Chronic Kidney Disease. CKD might have correlation with the increase of platelet, due to chronic inflammation. The patient was treated with drug therapy, and hemodialysis. Chronic kidney disease (CKD) is associated with accelerated atherosclerosis from early stages [12], as well as with an increased risk of venous thromboembolism [13,14]. Premature mortality is increased by CKD, primarily due to adverse cardiovascular (CV) events such as stroke, myocardial infarction, heart failure, or sudden death. Furthermore, CKD patients are more likely to die from fatal cardiovascular events rather than progress to end-stage kidney disease. 'Traditional' cardiovascular risk factors include diabetes, arterial hypertension, and hyperlipidemia [15].

Platelets are blood components produced in the bone marrow that play an important role in the clotting process. Thrombocytosis occurs when the platelet count exceeds 450,000/l. It is also known as thrombocythemia. Thrombocytosis is classified into two types: primary and secondary (or reactive) thrombocytosis. Primary thrombocytosis results from an uncontrolled abnormality in platelet production by bone marrow progenitor cells. They are usually classified as myeloproliferative neoplasms. Secondary thrombocytosis, also known as reactive thrombocytosis, is defined as an abnormally high platelet count as a result of underlying events, disease, or medication use. The more common type is secondary thrombocytosis, which is usually detected in routine laboratory results. Secondary thrombocytosis affects 80% to 90% of people who have thrombocytosis [16]. Because thrombocytosis can have a variety of causes, evaluating a patient with thrombocytosis demands careful examination of patient history, comorbid conditions, other hematologic variables, and past platelet counts [17].

CKD is associated with an increase in abnormal platelets that causes both hemorrhagic and thrombotic pathology. Some of its systemic complications include deep vein thrombosis, pulmonary emboli, myocardial infarcts, and renal vessel thrombosis. Therefore, further treatment regarding thrombocytosis should take place [18]. This patient received 80 milligrams of acetylsalicylic acid. Due to an increased thromboembolic risk, patients with thrombocytosis should take acetylsalicylic acid (aspirin). Acetylation is accomplished by acetylsalicylic acid. As a result, aspirin inactivates cyclooxygenase (COX)-1 and inhibits the production of prostaglandin H2 (a precursor of thromboxane A2). Aspirin achieves this effect via its acetyl group, which becomes covalently attached to Ser529 of the COX-1 enzyme's active site. Aspirin's mechanism of action includes acetylation of fibrinogen. Acetylation increases the porosity of the fibrin network, which speeds up fibrinolysis [19].

Proinflammatory cytokines such as IL-6 and IL-11 promote megakaryocyte maturation, which may lead to thrombocytosis and predispose to thromboembolic events and death [20]. Because of the complexities of altered platelet function in advanced CKD, diagnosis remains difficult. For the analysis of platelet dysfunction, a variety of global hemostasis screening tests and particular platelet function assays are available. After a peripheral blood smear review confirms the diagnosis of thrombocytosis, the diagnostic evaluation shifts to deciding if the process is reactive or clonal in nature. Understanding the fundamental causes of reactive thrombocytosis is an important first step in this procedure. In adults, the most common causes of reactive thrombocytosis are infection (usually acute), tissue damage, chronic inflammatory disorders, and malignancy, with one or more of these processes present in more than 75% of cases [21].

Infection, inflammation, tissue injury, iron deficiency, haemolysis, malignancy, and other causes of an acute phase response are the most common secondary (or reactive) causes of thrombocytosis. These are typically characterized by elevated C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), but not always. Platelets are mostly small, with a normal platelet volume. Other features of the blood film may indicate an underlying cause, such as acute infective or inflammatory processes [17].

Pro-thrombotic conditions in patients with advanced CKD appear to be associated with an abnormal ratio of coagulation factors and coagulation inhibitors, decreased fibrinolytic activity, endothelial dysfunction, and platelet hyperactivity [22–24]. In advanced CKD, the incidence of bleeding and thrombosis increases, making these significant causes of morbidity and mortality in affected patients [25–27]. Advanced CKD is linked to higher levels of C-reactive protein, interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α, all of which are linked to platelet hyperreactivity [28]. Many acute phase reaction markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), have been found to be significantly elevated in patients with reactive thrombocytosis [21].

Since CRP is associated with inflammation, a method for predicting CRP is useful for forecasting inflammation. CRP short pentraxin is a well-established inflammatory biomarker in kidney disease. CRP is a protein found in the acute phase. Because inflammation persists in CKD, it promotes glomerulosclerosis. This process is aided by the existence of inflammatory cytokines such as IL-6, IL-1, and TGF-. There is an influx of monocytes and macrophages, which eventually produce type 1 and 2 collagen, resulting in glomerulosclerosis. As a result, CRP levels rise in CKD [29].

The erythrocyte sedimentation rate (ESR) test is one of the most commonly used laboratory tests for determining infection, acute phase of inflammation, autoimmune disease, or cancer [30]. Another study involves 45 HD patients. They concluded that ESR levels in HD patients were mildly elevated, as they were in the general population. They also discovered a linear relationship between platelet count and ESR [31].

TNF-α is significantly elevated in CKD patients. According to a study by Lee et al, circulating TNF-α levels are significantly higher in CKD patients compared to controls, and TNF-α levels are independently associated with the severity of CKD. These results are consistent with previous large epidemiological studies [32]. The longitudinal study by Shankar et al. also suggested that TNF-α receptor 2 levels was positively associated with the risk of developing CKD [33]. It is possible, however, that albuminuria selectively activates cytokines and increases TNF-α. Furthermore, patients with CKD may have decreased clearance of these cytokines [34].

Elevated plasma IL-6 levels are common in CKD patients [35], and this is largely due to increased production caused by oxidative stress, chronic inflammation, and fluid overload. Meanwhile, decreased IL-6 clearance due to impaired renal function adds to its accumulation. Therapeutic hemodialysis and peritoneal dialysis stimulate inflammatory responses and increase IL-6 production in patients with end-stage renal disease (ESRD) [36]. Furthermore, patients with a faster rate of renal failure development had higher circulating levels of IL-6 soluble receptor [35].

IL-1 is a master regulator of inflammation, controlling a variety of innate immune processes. Chronic inflammation caused in part by high circulating levels of IL-1. Because circulating levels of both the pro-inflammatory cytokine IL-1 and its naturally occurring receptor antagonist (IL-1Ra) are elevated in CKD, it is an additional distinguishing feature of the disease [37].

Although flow cytometry analysis of platelets is limited to specialized laboratories, it is a sophisticated method for quantifying platelet receptors, distinct platelet functions in response to various platelet agonists, and platelet interactions with other blood cells. Flow cytometry has been used successfully to analyze platelet activation and dysfunction in CKD patients [38]. Platelet aggregation assays can be used to determine the hyperaggregability and hypoaggregability of platelets. Platelet aggregation in hemodialysis patients can be measured using a whole-blood aggregometer and screen filtration pressure [39].

In the case of thrombocytosis, it is critical to monitor the patient's complete blood count (CBC) over time. CBC can be used to monitor patients who have previously been diagnosed with blood cell disorders to see how their condition has reacted to treatment and may be utilized to monitor for side effects of some medications. Consider myeloproliferative neoplasm in the case of prolonged thrombocytosis. It's important to know which genetic mutation a patient has, whether it's JAK2, CALR, or MPL, because each of these mutations affects the clinical characteristics, complications, and survival of myeloproliferative neoplasm [40, 41]. Platelet reactivity is critical in the development of thrombosis, particularly in the presence of known atherosclerotic cardiovascular disease (as is frequently present in CKD patients). Anti-platelet therapy is used to reduce the occurrence of thrombotic events [42].

Conclusion

We presented a case of 67-year old patient with CKD stage V on hemodialysis treatment with the presence of thrombocytosis. Thrombocytosis is associated with chronic inflammation in CKD. High platelet count was present in this patient. Further examinations can be utilized to differentiate the cause of thrombocytosis, such as acute inflammatory markers (CRP, ESR, TNF-α, IL-1, and IL-6). Platelet reactivity and dysfunction in CKD patients may be detected using flow cytometry and platelet aggregation assays. In cases of prolonged thrombocytosis, a genetic mutation exam should be considered to rule out myeloproliferative neoplasm. Antiplatelet therapy is essential for thrombocytosis patients in order to reduce the occurrence of thrombotic events.

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None

Conflict of Interest

All authors declare there is no conflict of interest in this study.

Statement of Ethics

The patient provided written informed consent for his case to be published.

Author Contribution

PNAN, IWS designed the study. PNAN retrieved the data. PNAN, IWS analyzed the data descriptively. PNAN, IWS wrote the manuscript. All authors approved the final version of the manuscript.

References

1. Kelly DM, Ademi Z, Doehner W, et al. Chronic Kidney Disease and Cerebrovascular Disease: Consensus and Guidance From a KDIGO Controversies Conference. *Stroke*. 2021;52(7):e328-e346. doi:10.1161/STROKEAHA.120.029680]
2. Braun MM, Khayat M. Kidney Disease: Chronic Kidney Disease. *FP essentials*. 2021;509(Suppl 1):20-25.]
3. Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: Global dimension and perspectives. *The Lancet*. 2013;382(9888):260-272. doi:10.1016/S0140-6736(13)60687-X]
4. Stemer G, Laml-wallner G, Kuegler I, et al. Comprehensive evaluation of clinical pharmacists ' interventions in a large Austrian tertiary care hospital. Published online 2012:529-534. doi:10.1136/ejhpharm-2012-000131]
5. Al-Shdaifat EA, Manaf MRA. The economic burden of hemodialysis in Jordan. *Indian Journal of Medical Sciences*. 2013;67(5):103-116. doi:10.4103/0019-5359.122734]
6. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. *The Lancet*. 2020;395(10219):200-211. doi:10.1016/S0140-6736(19)32989-7]
7. Hustrini NM, Susalit E, Rotmans JI. Prevalence and risk factors for chronic kidney disease in Indonesia: An analysis of the National Basic Health Survey 2018. *Journal of global health*. 2022;12:04071. doi:10.7189/jogh.12.04071]
8. Darlington O, Dickerson C, Evans M, et al. Costs and Healthcare Resource Use Associated with Risk of Cardiovascular Morbidity in Patients with Chronic Kidney Disease: Evidence from a Systematic Literature Review. *Advances in Therapy*. 2021;38(2):994-1010. doi:10.1007/s12325-020-01607-4]
9. Glassock RJ, Warnock DG, Delanaye P. The global burden of chronic kidney disease: Estimates, variability and pitfalls. *Nature Reviews Nephrology*. 2017;13(2):104-114. doi:10.1038/nrneph.2016.163]
10. Schafer AI. Thrombocytosis. 2015;314(11):1171-1172.]
11. Rachmadi D, Rudiansyah M, Bandiara RIA, Lubis L. A Narrative Review: The Inflammation in Chronic Kidney Disease (CKD). *International Journal of Pharmaceutical Research*. 2021;13(02):258-265. doi:10.31838/ijpr/2021.13.02.058]
12. Drüeke TB, Massy ZA. Atherosclerosis in CKD: Differences from the general population. *Nature Reviews Nephrology*. 2010;6(12):723-735. doi:10.1038/nrneph.2010.143]
13. Wattanakit K, Cushman M, Stehman-Breen C, Heckbert SR, Folsom AR. Chronic kidney disease increases risk for venous thromboembolism. *Journal of the American Society of Nephrology*. 2008;19(1):135-140. doi:10.1681/ASN.2007030308]
14. Folsom AR, Lutsey PL, Astor BC, Wattanakit K, Heckbert SR, Cushman M. Chronic kidney disease and venous thromboembolism: A prospective study. *Nephrology Dialysis Transplantation*. 2010;25(10):3296-3301. doi:10.1093/ndt/gfq179]
15. Mathew RO, Bangalore S, Lavelle MP, et al. Diagnosis and management of atherosclerotic cardiovascular disease in chronic kidney disease: a review. *Kidney International*. 2017;91(4):797-807. doi:10.1016/j.kint.2016.09.049]
16. Sałacki AJ, Wysokiński A. Reactive thrombocytosis resulting from frequent blood donations as an extremely rare cause of st segment elevation myocardial infarction in the case of a 19-year-old male. *Annals of Agricultural and Environmental Medicine*. 2018;25(4):602-604. doi:10.26444/aaem/74196]
17. Harrison CN, Bareford D, Butt N, et al. Guideline for investigation and management of adults and children presenting with a thrombocytosis. *British Journal of Haematology*. 2010;149(3):352-375. doi:10.1111/j.1365-2141.2010.08122.x]
18. Toprak SK, Karakuş S, Şahin FI. Esansiyeltrombositeminingençerişkindekiakuttrombotikkomplikasyonu. *Turkish Journal of Hematology*. 2011;28(4):350-351. doi:10.5152/tjh.2011.70]
19. Tóth L, Muszbek L, Komáromi I. Mechanism of the irreversible inhibition of human cyclooxygenase-1 by aspirin as predicted by QM/MM calculations. *Journal of Molecular Graphics and Modelling*. 2013;40:99-109. doi:10.1016/j.jmgm.2012.12.013]
20. Molnar MZ, Streja E, Kovesdy CP, et al. High platelet count as a link between renal cachexia and cardiovascular mortality in end-stage renal disease patients. *American Journal of Clinical Nutrition*. 2011;94(3):945-954. doi:10.3945/ajcn.111.014639]
21. Bleeker JS, Hogan WJ. Thrombocytosis : Diagnostic Evaluation , Thrombotic Risk Stratification , and Risk-Based Management Strategies. 2011;2011. doi:10.1155/2011/536062]
22. Lutz J, Menke J, Sollinger D, Schinzel H, Thürmel K. Haemostasis in chronic kidney disease. *Nephrology Dialysis Transplantation*. 2014;29(1):29-40. doi:10.1093/ndt/gft209]
23. Boccardo P, Remuzzi G, Galbusera M. Platelet dysfunction in renal failure. *Seminars in Thrombosis and Hemostasis*. 2004;30(5):579-589. doi:10.1055/s-2004-835678]
24. Yang K, Du C, Wang X, et al. Indoxyl sulfate induces platelet hyperactivity and contributes to chronic kidney disease-associated thrombosis in mice. *Blood*. 2017;129(19):2667-2679. doi:10.1182/blood-2016-10-744060]
25. Melgaard L, Overvad TF, Skjøth F, Christensen JH, Larsen TB, Lip GYH. Risk of stroke and bleeding in patients with heart failure and chronic kidney disease: a nationwide cohort study. *ESC Heart Failure*. 2018;5(2):319-326. doi:10.1002/ehf2.12256]
26. Molnar AO, Bota SE, McArthur E, et al. Risk and complications of venous thromboembolism in dialysis patients. *Nephrology Dialysis Transplantation*. 2018;33(5):874-880. doi:10.1093/ndt/gfx212]
27. Ocak G, Noordzij M, Rookmaaker MB, et al. Mortality due to bleeding, myocardial infarction and stroke in dialysis patients. *Journal of Thrombosis and Haemostasis*. 2018;16(10):1953-1963. doi:10.1111/jth.14254]
28. Tripepi G, Mallamaci F, Zoccali C. Inflammation markers, adhesion molecules, and all-cause and cardiovascular

mortality in patients with ESRD: Searching for the best risk marker by multivariate modeling. *Journal of the American Society of Nephrology*. 2005;16(3 SUPPL. 1):83-88. doi:10.1681/ASN.2004110972]

29. Lalramenga PC, Gupta S, P N. Study of C-Reactive Protein Significance in Chronic Kidney Disease. *International Journal of Contemporary Medical Research [IJCMR]*. 2019;6(6):10-13. doi:10.21276/ijcmr.2019.6.6.48]
30. Witarini Dewi MM, Herawati S, Mulyantari NK, Prabawa IPY. The comparison of erythrocyte sedimentation rate (ESR) modify Westergren Caretium Xc-A30 and Westergren Manual in Clinical Pathology Laboratory, Sanglah General Hospital, Denpasar, Bali. *Bali Medical Journal*. 2019;8(2):487-490. doi:10.15562/bmj.v8i2.1401]
31. Alsomaili MI braheem, Yousuf M, Hejaili F, Almotairi W, Al-Sayyari AA. Erythrocyte sedimentation rate in stable patients on chronic hemodiaysis. *Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia*. 2015;26(6):1149-1153. doi:10.4103/1319-2442.168589]
32. Gupta J, Mitra N, Kanetsky PA, et al. Association between albuminuria, kidney function, and inflammatory biomarker profile in CKD in CRIC. *Clinical journal of the American Society of Nephrology : CJASN*. 2012;7(12):1938-1946. doi:10.2215/CJN.03500412]
33. Shankar A, Sun L, Klein BEK, et al. Chronic Kidney Disease : a Population-Based Cohort Study. 2012;80(11):1231-1238. doi:10.1038/ki.2011.283.Markers]
34. Lee BT, Ahmed FA, Lee Hamm L, et al. Association of C-reactive protein, tumor necrosis factor-alpha, and interleukin-6 with chronic kidney disease Epidemiology and Health Outcomes. *BMC Nephrology*. 2015;16(1):1-6. doi:10.1186/s12882-015-0068-7]
35. Pecoits-Filho R, Heimbürger O, Bárány P, et al. Associations between circulating inflammatory markers and residual renal function in CRF patients. *American Journal of Kidney Diseases*. 2003;41(6):1212-1218. doi:10.1016/S0272-6386(03)00353-6]
36. Caglar K, Peng Y, Pupim LB, et al. Inflammatory signals associated with hemodialysis. *Kidney International*. 2002;62(4):1408-1416. doi:10.1046/j.1523-1755.2002.00556.x]
37. Nowak KL, Chonchol M, Ikizler TA, et al. IL-1 Inhibition and Vascular Function in CKD. Published online 2016:1-10. doi:10.1681/ASN.2016040453]
38. Jurk K. Analysis of platelet function and dysfunction. *Hamostaseologie*. 2015;35(1):60-72. doi:10.5482/hamo-14-09-0047]
39. Waki K, Hayashi A, Ikeda S, et al. Measuring Platelet Aggregation in Dialysis Patients With a Whole Blood Aggregometer by the Screen Filtration Pressure Method. *Therapeutic Apheresis and Dialysis*. 2011;15(2):203-206. doi:10.1111/j.1744-9987.2010.00899.x]
40. Doig K, Butina M. FOCUS : IN TERPRETING T HE COMPLETE BLOOD CO UNT A Methodical Approach to Interpreting the Platelet Parameters of the Complete Blood Count.]
41. Falchi L, Kantarjian HM, Verstovsek S. Assessing the Thrombotic Risk of Patients with Essential Thrombocythemia in the Genomic Era. 2018;31(9):1845-1854. doi:10.1038/leu.2017.150.Assessing]
42. Elani Streja, MPH, Csaba P Kovesdy, MD, Sander Greenland, DrPH JDK, MD, Charles J McAllister, MD, Allen R Nissenson, MD, and KamyarKalantar-Zadeh MMP. Erythropoietin, Iron Depletion and Relative Thrombocytosis: A Possible Explanation for Hemoglobin-Survival Paradox in Chronic Kidney Disease. 2017;52(4):727-736. doi:10.1053/j.ajkd.2008.05.029.Erythropoietin]