

## COMPLETE BLOOD COUNT AS A DIAGNOSTIC MARKER IN ORAL LESIONS

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### **ABSTRACT**

*Complete Blood Count (CBC) is defined as a blood test requested by a doctor or other medical professional which gives an information regarding the cells in the human blood such as red blood cells, platelets and white blood cells*

**KEYWORDS:** *Complete Blood Count (CBC)*

### **INTRODUCTION**

Complete Blood Count (CBC) is defined as a blood test requested by a doctor or other medical professional which gives an information regarding the cells in the human blood such as red blood cells, platelets and white blood cells. <sup>(1)</sup> It is one of the most common diagnostic tests performed in healthcare. <sup>(3)</sup> It is sometimes referred to as a full blood count (FBC) or a full blood exam (FBE). <sup>(2)</sup> It's a highly automated, low-cost test that looks at the cellular components of a patient's peripheral blood to see if they're anemic or infected. <sup>(3)</sup>

The parameters include Hemoglobin (Hb), indices about red blood cells like Red Blood Cell Count (RBC), Mean Cell Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red cell Distribution Width (RDW), white blood cell parameters like total White Blood Cell Count (WBC) and differential count of neutrophils, basophils, eosinophils, monocytes, and lymphocyte. <sup>(2)</sup> Physicians who fully comprehend the cbc's effectiveness and restrictions, indications, on the other hand, will find it to be a useful tool for establishing challenging diagnoses, monitoring treatment programs, and eliminating more expensive or unneeded testing. <sup>(3)</sup> Anaemia which is the reduced number of RBC's and haemoglobin, is a sign of an underlying condition that must be examined, not a diagnosis. The increase in white blood cell count was thought to be mostly reliant on the body's resistance to infection. <sup>(5)</sup> Infections and WBC malignancies, such as leukaemia, are the most prevalent causes of an elevated number of WBCs. The failure of the bone marrow to manufacture WBCs or an enhanced clearance of WBCs from the blood by a dysfunctional liver or an overactive spleen causes a reduction in WBCs. Toxins or the replacement of normal bone marrow cells by malignant cells can induce bone marrow failure. The majority of the rise in WBCs in the early stages of an infection is due to an increase in neutrophils and the percentage of neutrophils was thought to represent the degree of infection or toxin absorption. Neutropenia can develop as a result of long-term infections that deplete bone marrow reserves, causing output to fall short of need. <sup>(5)(6)(9)</sup> Lymphocytes proliferate as the illness progresses and T lymphocytes, are especially adept at combating viral infections, and their depletion increases vulnerability to viral infections.

Macrophages are very efficient at ingesting bacteria, and a lack of them causes recurring bacterial infections. Eosinophils are triggered by worm infections, whereas basophils are triggered by allergic diseases. <sup>(6)</sup> Thrombocytopenia can be caused by both bacterial and viral illnesses. <sup>(7)</sup> Thrombocytosis is a typical warning sign for a variety of cancers. <sup>(8)</sup> There

was a variation in the complete cell count of individuals with premalignant disorders like Oral submucous fibrosis, oral lichen planus, leukoplakia etc. <sup>(4)</sup> Our review aims to determine variations in complete blood count levels in different oral lesions.

## VARIATIONS IN THE COMPLETE BLOOD COUNT IN ORAL LESIONS

Table 1

Condition	RBC	Hb	MCV	MCH	MCHC	PCV	WBC	Neutro-phil	Baso-phil	Eosino-phil	Mono-cyte	Lympho-cyte	Platelet
<b>ULCERATIVE, VESICULAR AND BULLOUS LESIONS</b>													
Herpes Labialis							↑	↓				↑	
Varicella Zoster Infection		↑					↑				↑		↑
Cytomegal Ovirus	↓	↓						↓			↑	↑	↓
Coxsackie Virus (Hand Foot Mouth Disease)							↑						
Erythema Multiforme	↓	↓					↑	↓					
Steven Johnson Syndrome	↓	↓						↓		↑		↑	
Recurrent Aphthous Stomatitis							↑	↑					
Behcet's Disease							↑	↑					
Pemphigus Vulgaris	↓	↓					↑			↑	↑	↓	
Bullous Pemphi- Goid	↓	↓					↑	↑		↑			
<b>RED AND WHITE LESIONS</b>													
Oral Candidiasis		↓					↑						
Oral Leuko- Plakia							↑			↑		↑	
Oral Erythro- Plakia							↑					↑	
Oral Submucous Fibrosis		↓					↑					↑	
Oral Lichen Planus		↓					↑					↑	
Lichenoid Reaction										↑			
<b>INFECTIOUS DISEASES</b>													
<b>Bacterial Infections</b>													
Syphilis	↓	↓		↓	↓	↓	↓	↓			↑	↑	
Actino- Mycosis							↑	↑					
Tuberculosis	↓	↓					↑						↓
<b>Fungal Infections</b>													
Blasto- Mycosis							↑	↑				↓	
Paracocci Odo- Mycosis							↑			↑			
Mucor- Mycosis							↑	↑					
<b>Viral Infection</b>													
Viral Hepatitis		↓					↑	↑			↑	↑	↓
Acquired Immuno- Deficiencysyndrome	↓	↓					↑	↑				↓	↓
<b>CARCINOMA OF THE ORAL CAVITY</b>													
Oral Squamous Cell Carcinoma	↓	↓					↑					↓	
<b>PIGMENTED LESIONS</b>													
Malignant Melanoma							↑	↑			↑	↓	

## DISCUSSION

From the above study it is seen that most of the oral lesions show an increase in the white blood cell count. In 2014, Shishodiya et al. stated that WBC count is highly variable since it responds to a variety of chronic triggers, and it can even vary with infections, stress, and smoking. <sup>(43)</sup> WBC counts vary widely in the general population and can be impacted by a variety of variables such as age, gender, race or ethnicity, smoking history, and chronic inflammation (Nieto et al., 1992; Cheng et al., 2004). <sup>(10)</sup> According to recent study findings, white blood cells (WBC) have been identified as a biomarker of inflammation and the incidence of any early age-related macular degeneration in the complete blood count (CBC) inquiry (AMD). <sup>(48)(19)</sup> The severity of the infection may be reflected in WBC counts. <sup>(15)</sup> Because of their non-specificity, WBCs have the ability to detect the risk of malignancy. <sup>(4)</sup> Tumour stromal tissue has a large number of WBCs and inflammatory cells, and their cytokine generation appears to be related to tumour severity. <sup>(49)</sup> Tsai et al found that the peripheral total white blood cell (WBC) count, monocyte and neutrophil counts, and neutrophil lymphocyte ratio increased with stage T4 and poor tumour differentiation in their study on squamous cell carcinoma. <sup>(50)</sup> WBC counts might potentially be utilised to determine a patient's prognosis. WBC levels that were abnormally high frequently suggested a bad prognosis. <sup>(15)</sup>

Neutrophils play a role in the inflammatory cascade disease pathophysiology. Patients with higher neutrophil to leukocyte ratios show that this condition has an underlying inflammatory mechanism. <sup>(19)</sup> Increased neutrophil counts and/or decreased lymphocyte counts may inhibit lymphokine- activated killer cells. These are some of the proposed mechanisms underlying cancer patients' shorter survival. <sup>(53)</sup>

Recent research suggests that the eosinophil is a parasite killer cell that can phagocytize antigen- antibody complexes. <sup>(44)</sup> Eosinophils have been shown in vitro to kill parasitic organisms by binding to target membranes via Fc or C3 receptors. <sup>(45)(46)</sup> Eosinophils are IgG-sensitized normal human tissues' killer cells. <sup>(48)</sup> Eosinophilia is most likely connected with pruritus and scratching, both of which transfer the patient's own plasma proteins into his/her skin. <sup>(21)</sup>

Monocytosis is most likely a result of the monocyte's job as a scavenger of particulate matter and pathogens. <sup>(21)</sup> Cytokine that acts as a monocyte growth factor seems to be released resulting in peripheral monocytosis. <sup>(12)(13)</sup> The positive relationship seen in the lymphocyte count in these studies might simply be attributable to the greater neutropenia associated with specific diseases. <sup>(10)</sup> The increased lymphocytes cause a spike in the production of cytokines, which affects the therapy course. Cytokines can have an impact on both the pathophysiology and the prognosis of a therapy. <sup>(31)</sup> Lymphocytopenia may signify a widespread immunological deficit. <sup>(28)</sup>

Platelets may play an essential role in inflammatory processes, according to some research. <sup>(19)</sup> Dissemination by intravascular coagulopathies, impairment of thrombocytopaenia by virus-induced amegakaryocyte mutation, direct interaction between the virus and platelets in blood circulation (e.g., phagocytosis or platelet aggregation, release, and thrombocytosis), an antigen-antibody complex that impairs platelet function, and antiplatelet antibodies that directly antagonise platelet- specific antibodies are some of the hypothesised mechanisms in thrombocytopenia. <sup>(39)</sup>

As anaemia is typically connected with the inflammatory process of chronic conditions such as cancer, the anaemia reported here may have been attributable to the disease itself. <sup>(51)(52)</sup> The existence of additional chronic comorbidities is most likely to be responsible for this finding of disease-related anaemia. <sup>(29)</sup> Excessive production of pro-inflammatory cytokines, such as IL-6, TNF- $\alpha$  and IFN- $\gamma$ , contributes to anaemia through reduced production of erythropoietin, suppressed response of bone marrow to erythropoietin, and altered iron metabolism, which may in turn impair erythropoiesis. <sup>(54)</sup> Anaemia is related with a worse prognosis and higher mortality in patients with head and neck cancer, and it is frequently overlooked before to and throughout cancer therapy. As a result, the presence of anaemia at the time of oral cancer diagnosis may put these individuals at a higher risk of poor response to antineoplastic therapy. <sup>(29)</sup>

The combined reduction of few haematological parameters in certain conditions may be due to immune-mediated death of infected cells or stromal dysfunction in the bone marrow. <sup>(14)</sup> Suppressive effect on the bone marrow and may result in pancytopenia. <sup>(31)</sup>

## **HERPES LABIALIS**

Differences in the most abundant types of WBC might be related to susceptibility to a common viral infection. The observed association of higher lymphocytes and occurrence of herpes labialis in the present study stands in apparent contrast to the accepted role of adaptive immunity in controlling HSV-1 infection. Elevated lymphocytes could be a marker for another factor associated with herpes labialis risk, or may indicate a long-term increase that results from an earlier infection. The positive association with lymphocyte count observed in these analyses could also simply be due to the relative neutropenia associated with herpes labialis; however, no apparent confounding or effect modification between lymphocyte and granulocytes was observed. Finally, these findings may indicate a need for an intact or activated lymphocyte population in the symptomatic expression of HSV-1 infection, even within the normal range of WBC counts. <sup>(10)</sup>

## **VARICELLA ZOSTER INFECTION**

A certain cytokine, acting as a monocyte growth factor, would thus appear to be secreted from VZV- reactivated monocytes, consequently giving rise to peripheral monocytosis in VZV infected individuals. (12) VZV infection had a beneficial effect on bone marrow function particularly platelet production. (13)

## **CYTOMEGALO VIRUS**

The various theories of CMV infection-induced thrombocytopenia were described by Crapnell et al., as CMV-induced direct cytotoxicity to hematopoietic cells with immune-mediated destruction of infected cells or impairment of bone marrow stromal function (14).

## **COXSACKIE VIRUS (HAND FOOT MOUTH DISEASE)**

WBC counts increased with the severity of the illness. (15)

## **BECHE'T'S DISEASE**

studies shows that the Neutrophils are higher in patients with active BD compared to controls and BD patients in remission, these high levels suggests that neutrophils play a role in the inflammatory cascade of BD and disease pathophysiology, Wbc increase accounts for a infection present in the body. (20)

## **TUBERCULOSIS:**

The mean serum haemoglobin level in was found to be less thus reflecting anaemia, this is largely be due to chronic inflammation. Godwin et al. (2010) mention that the alterations in the red blood cell function especially in the immune-compromised state of the patients. WBC count in patients was increased because WBCs increase during infection, due to the increased polymorphonuclear leukocytes and macrophages as a part of the body's immune defence mechanism to combat the invading bacterial population. (34)

## **SYPHILIS**

The study shows alteration in WBC, neutrophil, RBC, haemoglobin, PCV, MCH, and MCHC and elevation in lymphocyte and monocyte of the syphilis subject compared to the control. It could be as result of suppressed bone marrow activity. (32)

## **HIV**

Haematological abnormalities found in the current study were anaemia, leukopenia, neutropenia, lymphopenia, and thrombocytopenia. In the present study, prevalence of anaemia and thrombocytopenia decreased and the prevalence of Leukopenia, Neutropenia, and Lymphopenia was an increase after initiation of HAART. (41)

## **CONCLUSION**

A complete blood cell count with differential ispart of routine clinical practice. These haematological parameters are easy to monitor and are cost efficient. It also determines disease prognosis and hence can be used as a cheap biomarker of inflammation.

**REFERENCES**

1. National Cancer Institute. NCI Dictionary of cancer terms [Internet]. Available from <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/completeblood-count>. [Retrieved: 21 Jun2018]
2. Agrawal D, Sarode R. Complete Blood Count or Complete Blood Count with Differential: What's the Difference? *Am J Med*. 2017 Aug 1;130(8):915-6.
3. Dixon LR. The complete blood count: physiologic basis and clinical usage. *The Journal of Perinatal & Neonatal Nursing*. 1997 Dec;11(3):1-18. DOI: 10.1097/00005237-199712000-00003. PMID:9451188.
4. Indra G, Maragathavalli G, Deepika Rajendran. Complete Blood Count as a Diagnostic Marker in Oral Lichen Planus. *International Journal of Research in Pharmaceutical Sciences*. 2020;11(SPL3):1766-1771.
5. Agrawal D, Sarode R, Complete Blood Count or Complete Blood Count with differential: What's the difference?, *The American Journal of Medicine* (2017), doi: 10.1016/j.amjmed.2017.03.049.
6. Dean L. *Blood Groups and Red Cell Antigens* [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2005. Chapter 1, Blood and the cells it contains.
7. Bertschi L. CE: Back to Basics: The Complete Blood Count. *AJN, American Journal of Nursing*. 2021;121(1):38-45.
8. Wojtukiewicz MZ, et al. Platelets and cancer angiogenesis nexus. *Cancer Metastasis Rev* 2017;36(2):249-62.
9. George-Gay B, Parker K. Understanding the complete blood count with differential. *Journal of PeriAnesthesia Nursing*.2003;18(2):96-117.
10. Parks C, Andrew M, Blanciforti L, Luster M. Variation in the WBC differential count and other factors associated with reporting of herpes labialis: A population-based study of adults. *FEMS Immunology & Medical Microbiology*.2007;51(2):336-343.
11. Asaduzzaman, Mohammad & Akram, Md & Mrida, Hossen & Hasan, Md & Faruq, Omar & Juliana, Farha & Islam, Mohammad & Kabir, Mohammad. (2018). The Effect of Herpes Simplex .Virus Infection on Different Blood Parameters: A Transverse Study. 81-89. 10.9790/0853-1709078189.
12. Tsukahara T, Yaguchi A, Horiuchi Y. Significance of Monocytosis in Varicella and Herpes Zoster. *The Journal of Dermatology*.1992;19(2):94-98.
13. Al-Anazi K, Al-Jasser A, Evans D. Effect of varicella zoster virus infection on bone marrow function. *European Journal of Haematology*.2005;75(3):234-240.
14. Flores-Chang BS, Arias-Morales CE, Wadskier FG, Gupta S and Stoicea N (2015) Immune thrombocytopenic purpura secondary to cytomegalovirus infection: a case report.
15. Li Y, Zhu R, Qian Y, Deng J (2012) The Characteristics of Blood Glucose and WBC Counts in Peripheral Blood of Cases of Hand Foot and Mouth Disease in China: A Systematic Review. *PLoS ONE* 7(1): e29003.

16. Lo S, Huang Y, Huang C, Tsao K, Li W, Hsieh Y et al. Clinical and epidemiologic features of Coxsackie virus A6 infection in children in northern Taiwan between 2004 and 2009. *Journal of Microbiology, Immunology and Infection*. 2011;44(4):252-257.
17. Hafsi W, Badri T. Erythema Multiforme. 2021 Aug 7. In: *Stat Pearls [Internet]*. Treasure Island (FL): Stat Pearls Publishing; 2021 Jan–. PMID:29261983.
18. Oakley AM, Krishnamurthy K. Stevens Johnson Syndrome. [Updated 2021 Apr 19]. In: *Stat Pearls [Internet]*. Treasure Island (FL): Stat Pearls Publishing; 2021Jan
19. Terzi, Suatetal. "Status of Neutrophils, Lymphocytes and Plateletsin Patients with Recurrent Aphthous Stomatitis: A Retrospective Study." *Iranian journal of otorhinolaryngology* vol.28,89 (2016):421-424.
20. Rifaioglu E N, BülbülŞen B, EkizÖ, Cigdem Dogramaci A. Neutrophiltolymphocyteratioin Behçet's disease as a marker of disease activity. *Acta Dermatovenerol Alp Pannonica Adriat*. 2014;23(4):65-7. PMID:25527038.
21. Grace A W. Pemphigus Vulgaris: A Study of the Blood Picture. *Arch Derm Syphilol*. 1947;55(6):772–782.doi:10.1001/archderm.1947.01520060034004
22. Bushkell L L, Jordon R E. Bullouspemphigoid: acause of peripheral blood eosinophilia. *JAmAcad Dermatol*. 1983 May;8(5):648-51. doi: 10.1016/s0190-9622(83)70073-3. PMID:6345605.
23. Ding S, Deng Q, Xiang Y, Chen J, Huang J, Lu J. Bullous pemphigoid associated with milia, increasedserumIg E, autoantibodiesagainstdesmogleins, and refractory treatmentinayoung patient. *An Bras Dermatol*. 2017;92(5 Suppl 1):34-36.doi:10.1590/abd1806-4841.20176124
24. Lu, S.-Y. Oral Candidosis: Pathophysiology and Best Practice for Diagnosis, Classification, and Successful Management. *J. Fungi* 2021, 7, 555. <https://doi.org/10.3390/jof7070555>
25. Kim H, Park B, Lee M. Effects of bacteria and yeast on WBC counting in three automated hematology counters. *Annals of Hematology*.2008;87(7):557-562.
26. Singh S, Singh J, Samadi F, Chandra S, Ganguly R, Suhail S. Evaluation of hematological parameters in oral cancer and oral pre-cancer.2022.
27. Suryana K. Lichenoid Reaction Caused by Antihistamines and Corticosteroids. *JAsthma Allergy*. 2020;13:205-211. Published 2020 Jun 30.doi:10.2147/JAA.S251046
28. Phulari R G S, Rathore R S, Shah A K, Agnani S S. Neutrophil: Lymphocyteratioandoralsquamous cell carcinoma: A preliminary study. *J Oral Maxillofac Pathol*. 2019 Jan-Apr;23(1):78-81. doi: 10.4103/jomfp.JOMFP\_160\_17. PMID: 31110421; PMCID:PMC6503793.
29. Sganzerla J, Krueger G, Oliveira M, Gassen H, Santos M, Celeste R et al. Relationship between anemia and oral cancer: a case-control study. *Brazilian Oral Research*.2021;35.
30. Gandini, Sara & Ferrucci, Pier & Botteri, Edoardo & Tosti, Giulio & Barberis, Massimo & Pala, Laura & Battaglia, Angelo & Clerici, Alessandra & Spadola, Giuseppe & Cocorocchio, Emilia & Martinoli, Chiara. (2016). Prognostic significance of hematological profiles in melanoma patients. *International journal of cancer*. 139.10.1002/ijc.30215.

31. Obeagu, Emmanuel & Azuonwu, Obioma & Didia, Blessing & Obeagu, Getrude & Florence, Onyenweaku. (2017). *Determination of Haematological Changes Associated with Syphilis in Subjects in Umudike, Abia State, Nigeria*. 2017. 1-4.10.29011/IDDT-118.
32. Sharma S, Hashmi MF, Valentino III DJ. *Actinomycosis*. [Updated 2021 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021Jan-.
33. Rohini K, Surekha Bhat M, Srikumar PS, Mahesh Kumar A. *Assessment of Hematological Parameters in Pulmonary Tuberculosis Patients*. *Indian J Clin Biochem*. 2016;31(3):332-335. doi:10.1007/s12291-015-0535-8
34. Frost H, Anderson J, Ivacic L, Meece J. *Blastomycosis in Children: An Analysis of Clinical, Epidemiologic, and Genetic Features*. *Journal of the Pediatric Infectious Diseases Society*. 2015;6(1):49-56.
35. Boswell, Elizabeth & Aziz, Hassan. (2004). *Blastomycosis: a case study of a dimorphic fungal disease*. *Clinical laboratory science : journal of the American Society for Medical Technology*. 17.145-8.
36. Pineda Ruiz J, Montoya Bernal A, Correa López H, Cruz Tangarife X, Campiño Martínez M. *Paracoccidioidomycosis aguda-subaguda ganglionar con eosinofilia asociada*. *Acta Médica Colombiana*.2020;46(1).
37. Marques de Macedo P, de Oliveira L, Freitas D, da Rocha J, Freitas A, Nucci M et al. *Acute Paracoccidioidomycosis Due to Paracoccidioides brasiliensis SI Mimicking Hypereosinophilic Syndrome with Massive Splenomegaly: Diagnostic Challenge*. *PLOS Neglected Tropical Diseases*.2016;10(4):e0004487.
38. Ghafur A, Shareek PS, Senthur NP, Vidyalakshmi PR, Ramasubramanian V, Parameswaran A, Thirunarayan MA, Gopalakrishnan R. *Mucormycosis in patients without cancer: a case series from A tertiary care hospital in South India*. *J Assoc Physicians India*. 2013 May;61(5):305-8. PMID:24482941.
39. Tsai MH, Lin KH, Lin KT, et al. *Predictors for Early Identification of Hepatitis C Virus Infection*. *Biomed Res Int*. 2015;2015:429290.doi:10.1155/2015/429290
40. Lin SM, Chu CM, Shih LY, Liaw YF. [Hematological abnormalities in acute viral hepatitis and acute hepatitis in HBsAg carrier]. *Changcheng Yi Xue Za Zhi*. 1991 Dec;14(4):253-8. Chinese. PMID:1797369.
41. Damtie S, Workineh L, Kiros T, Eyayu T, Tiruneh T. *Hematological Abnormalities of Adult HIV-Infected Patients Before and After Initiation of Highly Active Antiretroviral Treatment at Debre Tabor Comprehensive Specialized Hospital, Northcentral Ethiopia: A Cross-Sectional Study*. *HIV/AIDS (Auckl)*.2021;13:477-484
42. Burket, Greenberg M, Glick M. *Burket's oral medicine*. New York: BC Decker Inc;2003.
43. Narang D, Mohan V, Singh P, et al. *White blood cells count as a pathological diagnostic marker for oral precancerous lesions and conditions: A randomized blind trial*. *Eur J Biotechnol Biosci* 2014;2:27-29.
44. Sullivan T J, Kulczycki AJr: *Immediate hypersensitivity responses*, in Parker CW, editor: *Clinical immunology*, ed. 1. Philadelphia, 1980, W. B. Saunders Co., pp.134-142.-142.

45. Metcalfe DD, et al: Human eosinophil adherence to serum treated sepharose. Granule associated enzyme release and requirement for activation of the alternate complement pathway. *J Immunol* 119:1744-1750,1977.
46. David JR, Butter worth AE: Immunity to *Schistosomamansoni*. Antibody-dependent eosinophil-mediated damage to schistosomula. *Fed Proc* 36:2176-2180, 1977.
47. Parillo J E, Fauci A S: Humaneosinophils. Purification and cytotoxiccapability of eosinophils from patients with hypereosinophilic syndrome. *Blood* 81:457-473,1978.
48. Shankar A, Mitchell P, Rohtchina E, et al. Association between circulating white blood cell count and longterm incidence of age-related macular degeneration: The blue mountains eye study. *Am J Epidemiol*2007;165:375-382.
49. Balkwill F. Cancer and the chemokine network. *Nat Rev Cancer*.2004;4:540-50.
50. Tsai YD, Wang CP, Chen CY. Pretreatment circulating monocyte count associated with poor prognosis in patients with oral cavity cancer. *Head Neck*.2014;36(7):947-53.
51. Fraenkel PG. Understanding anemia of chronic disease. *Hematology/Am Soc Hematol Educ Program*.2015;2015(1):14-8.
52. Joosten E, Lioen P. Iron deficiency anemia and anemia of chronic disease in geriatric hospitalized patients: how frequent are comorbidities as an additional explanation for the anemia? *Geriatr Gerontol Int*. 2015Aug;15(8):931-5.
53. Teramukai S, Kitano T, Kishida Y, Kawahara M, Kubota K, Komuta K, et al. Pretreatment neutrophil count as an independent prognostic factor in advanced non small cellung cancer: An analysis of Japan multinational trial organisation LC00□03. *Eur J Cancer*2009;45:1950□8.
54. Weiss G, Goodnough LT. Anemia of chronic disease. *N Engl J Med*.2005;352(10):1011–23.