

RESEARCH ARTICLE

Open Access



Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in Chinese Han population from Chaoshan region in South China

Lishan Wu[†], Shan Zou[†], Cantian Wang, Xuerui Tan and Min Yu^{*†} 

Abstract

Background: Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are assumed to be prognostic factors in many diseases such as inflammatory diseases, cardiovascular diseases and cancer. However, NLR and PLR are race specific, it is important to determine the reference values of NLR and PLR in different races. The study aimed to investigate the reference range of NLR and PLR in Chinese Han population from Chaoshan region in South China.

Methods: A retrospective study was conducted in the First Affiliated Hospital of Shantou University Medical College in South China. Five thousand healthy adults aged 20–69 years were included. NLR and PLR were determined.

Results: Of 5000 healthy adults, 2500 men and 2500 women were included. The mean NLR and PLR across all ages for men and women were 1.59 ± 0.59 , 92.88 ± 28.70 , 1.62 ± 0.64 and 108.02 ± 32.99 , respectively. The 95% reference range of NLR in normal male and female are 0.43~2.75 and 0.37~2.87, PLR are 36.63~149.13 and 43.36~172.68, respectively. The female had a higher NLR at age 30~49 than the male while the NLR at age 60~69 was higher in male than in female. The PLR was higher in female than in male.

Conclusion: The study provides reference data on NLR and PLR from different age and sex groups in South China. NLR and PLR varied with age and sex.

Keywords: Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio, Reference range

Background

Complete blood count (CBC) test is a simple economic and extensively used basic hematological test which mainly included white blood cell (WBC) count, red blood cell (RBC) count and platelet count. The most abundant white blood cells in healthy humans are neutrophils, which play important roles during acute and chronic inflammation and may be potential therapeutic targets in cardiovascular diseases [1]. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are the proportions of absolute neutrophil to lymphocyte and platelet to lymphocyte counts retrieved

from the CBC test. As markers of inflammation, various studies have demonstrated the correlation between NLR, PLR and many diseases such as inflammatory diseases [2], cardiovascular diseases [3], cancer [4] and long-term type 2 diabetes remission after metabolic surgery [5]. NLR and PLR are assumed to be prognostic factors. Although there have been extensive investigations on NLR and PLR, the normal ranges of NLR and PLR were less investigated. It was reported that the average NLR is 2.15 in the US population [6] and 1.65 in South Korea [7], which suggested that NLR is race specific. Therefore it is important to investigate the ranges of NLR and PLR for evaluating the prognostic role of NLR and PLR in different races. The aim of this study is to explore the reference values of NLR and PLR among the Han populations in Chaoshan District of Guangdong Province in South China.

* Correspondence: 717146@sina.com

Lishan Wu and Shan Zou are equally to the work
Department of Cardiology, the First Affiliated Hospital, Shantou University
Medical College, Shantou 515041, Guangdong, China



Table 1 Main characteristics of the overall cohort based on sex

	Male	Female	P Value
Number	2500	2500	
Age (years, mean ± SD)	44.42 ± 14.02	44.45 ± 14.02	0.924
Mean WBC (×10 ⁹ /L)	6.55 ± 1.28	6.04 ± 1.25	0.059
Mean NE (×10 ⁹ /L)	3.54 ± 0.93	3.34 ± 0.96	0.328
Mean LY (×10 ⁹ /L)	2.35 ± 0.60	2.18 ± 0.56	0.001
Mean NE/LY	1.59 ± 0.59	1.62 ± 0.64	0.002
95% reference range	0.43~2.75	0.37~2.87	
Mean RBC (×10 ⁹ /L)	4.96 ± 0.41	4.50 ± 0.40	0.186
Mean HGB g/L	152.88 ± 11.59	134.45 ± 12.76	0.013
Mean PLT (×10 ⁹ /L)	206.30 ± 40.81	222.22 ± 44.47	0.000
Mean PLT/LY	92.88 ± 28.70	108.02 ± 32.99	0.000
95% reference range	36.63~149.13	43.36~172.68	

Methods

The study was conducted retrospectively in the First Affiliated Hospital of Shantou University Medical College in South China. CBC tests between February 2018 and July 2018 were reviewed and collected consecutively from healthy persons aged 20–69 years without diagnosed diseases including acute or chronic infection, heart failure, renal failure, autoimmune or hematopoietic diseases. The healthy adults were divided into groups according to gender and age. A total of 5000 healthy adults were included. Neutrophil, lymphocyte and platelet counts were determined by the Coulter method. NLR and PLR were calculated as the ratio of neutrophil cell and platelet count to lymphocyte cell count, respectively. The samples were excluded with WBC less than 3.5 × 10⁹/L or more than 9.5 × 10⁹/L and platelet less than 125 × 10⁹/L or more than 350 × 10⁹/L. The study was approved by the ethics committee of Shantou University Medical College.

Data are presented as mean ± SD. Differences between group means were assessed by an unpaired Student’s *t*-test for single comparisons or by ANOVA

for multiple comparisons using SPSS 16.0. *P* value < 0.05 was considered significant.

Results

In present study, there are 5000 CBC tests. Two thousand five hundred men and 2500 women were included. As shown in the Table 1, the differences of age, WBC counts, neutrophils (NE) counts and RBC counts between the male and female were not significant. The male had a higher lymphocyte (LY) counts and hemoglobin (HGB) than the female while the female had a higher platelet (PLT) counts, NLR and PLR. The mean NLR and PLR across all ages for men and women were 1.59 ± 0.59, 92.88 ± 28.70, 1.62 ± 0.64 and 108.02 ± 32.99, respectively. The 95% reference range of NLR in normal male and female are 0.43~2.75 and 0.37~2.87, PLR are 36.63~149.13 and 43.36~172.68, respectively. NLR and PLR were analyzed based on sex and age (500 cases in each group), which were showed in Figs. 1 and 2 and Tables 2 and 3. The female had a higher NLR at age 30~49 than the male while the NLR at age 60~69 was higher in male than in female. The NLR was affected by age. In female the NLR increased with aging at age 20–49 while decreased in age groups of > 50 years. There is a sex difference in PLR at age 30~59, with higher in female than in male. The PLR decreased in women older than 50 years.

Discussion

In present study we measured the NLR and PLR in 5000 Chinese healthy adults. We found that the 95% reference range of NLR in normal male and female are 0.43~2.75 and 0.37~2.87, PLR are 36.63~149.13 and 43.36~172.68, respectively. The NLR and PLR vary by sex and age.

CBC, an economic and extensively used basic hematological test, included a hemogram and differential WBC count. Though the CBC test was usually used to the diagnosis of anemia, certain cancers, infection and immunodeficiencies, it has been recently found that some parameter of CBC such as NLR and PLR are associated with activity, morbidity and mortality in different diseases.

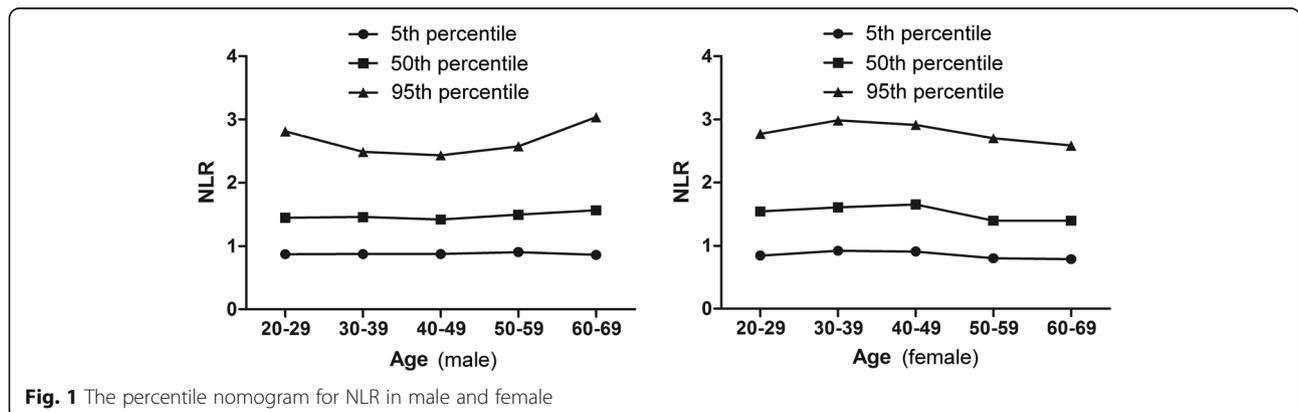


Fig. 1 The percentile nomogram for NLR in male and female

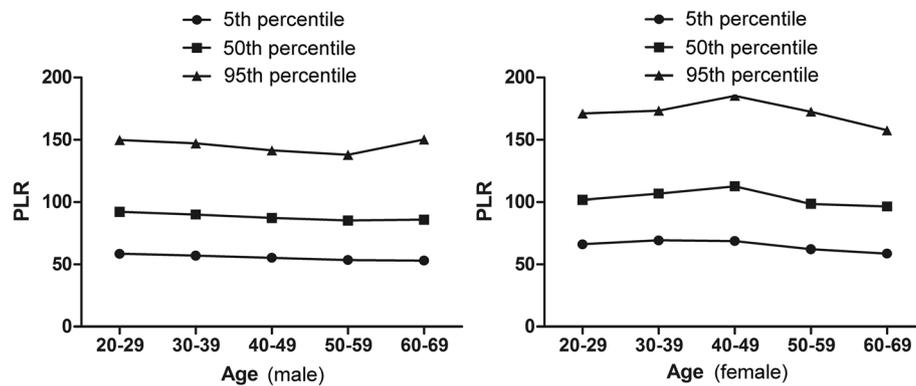


Fig. 2 The percentile nomogram for PLR in male and female

In active rheumatoid arthritis [8], systemic lupus erythematosus [9] and Takayasu’s arteritis [10], NLR and PLR were significantly increased than that in the control and can be used to evaluate disease activity. In patients with hepatocellular carcinoma after hepatectomy, postoperative NLR and PLR were associated with recurrence [11]. Additionally, admission NLR can be used to predict worse outcomes and hospital mortality in patients with acute type A aortic dissection [12–15].

Though NLR was used widely in many diseases, the cut off points for risk stratification were arbitrary used in these studies, which did not consider the factors affecting the NLR such as the disease category, age, and race of patients. In the studies from western countries a higher cutoff value was suggested than that in Asian or African. In fact the NLR in the United States population was generally higher than Asian races. It was reported that NLR is 2.24 in Whites and 1.76 in Blacks in the United States [6] while 1.65 in South Korea [7] and 1.72 in central China [16]. The effects of sex on NLR varied with race. There was no significant difference with NLR between in men and women in the United States population [6] while significant in Asian [7, 16]. In present study, we found that the mean NLR across all ages was higher in female than in male, which is consistent with studies in other Asian countries [7]. The mechanisms

for sex-related differences in NLR are not well known. Sex hormones such as estrogen level may be attributed to the difference. The female had higher estrogen level than the male. It had been found that estrogen can delay neutrophil apoptosis [17], which led to higher NLR in female. Though NLR was different between sexes, a study from central China showed that it is higher in male than in female [16] while it is the reverse in present study, suggesting there is regional variations in NLR.

NLR can be also affected by age, especially in female. Estrogen decreased dramatically after menopause [18]. Thus, it was not surprising that the NLR in women is higher in age groups of < 50 years than > 50 years [7, 19], which was also verified in present study.

Unlike NLR, the PLR is less investigated. There is also a sex difference in PLR, with higher in women than in men [7]. The difference may be associated with the higher platelet counts in women. Many studies have found that females have higher platelet count than males [20–23]. The mechanisms of sex-related difference in platelet count are also not well known. One explanation is that there is lower serum iron in menstruating and elder women, which stimulates platelet production [24–26]. Additionally, sex hormonal difference such as estrogen

Table 2 Neutrophil-to-lymphocyte ratio at different groups

Subgroup (age)	Neutrophil-to-lymphocyteratio (male)	Neutrophil-to-lymphocyteratio (female)	P value
20~29	1.57 ± 0.61	1.64 ± 0.59	0.675
30~39	1.55 ± 0.56	1.72 ± 0.68 [#]	0.004
40~49	1.53 ± 0.52	1.74 ± 0.61 [#]	0.000
50~59	1.60 ± 0.55	1.52 ± 0.62 ^{##}	0.223
60~69	1.71 ± 0.68 [△]	1.51 ± 0.64 ^{##}	0.005

[△]compared with group age 20~59 (P < 0.01) [#]compared with group age 20~29 (P < 0.05)

^{##}compared with group age 20~49 (P < 0.01)

Table 3 Platelet-to-lymphocyte ratio at different groups

Subgroup (age)	Platelet-to-lymphocyte ratio (male)	Platelet-to-lymphocyte ratio (female)	P value
20~29	96.16 ± 28.48	107.46 ± 31.15	0.176
30~39	94.91 ± 30.49	111.91 ± 32.93 [#]	0.017
40~49	91.84 ± 26.84	116.41 ± 34.49 ^{##} *	0.000
50~59	89.82 ± 26.72 [△]	103.80 ± 32.83 ^{△△}	0.001
60~69	91.67 ± 30.38	100.53 ± 31.11 ^{△△}	0.922

[△]compared with group age 20~39 (P < 0.01) [#]compared with group age 20~29 (P < 0.05)

^{△△}compared with group age 30~49 (P < 0.01) ^{##}compared with group age 30~39 (P < 0.05)

^{*}compared with group age 20~29 (P < 0.05)

level may be also play a role. It was reported that estrogens favour platelets formation in mouse [27]. Apart from sex, platelet count varies by age, being higher in youth than in old age [28, 29], which may be associated with hematopoietic stem cell. In elderly people a reduction in hematopoietic stem cell reserve would lead to reduction of the platelets formation.

Though the female has a higher PLR than the male, another study from central China showed no difference between gender groups in PLR [16], suggesting regional variation of PLR in China.

A few limitations were apparent in present study. First, the study is a retrospective study and routine blood analyses were collected from healthy populations in the checkup center of hospital, the effects of chronic concealed inflammation and smoking [30] on NLR and PLR can not be excluded. Secondly, owing to the geographic difference of platelet counts [21, 31], the reference range of PLR in healthy population in Chaoshan region may be different from other regions in China.

Conclusion

In summary, we found that the reference range of NLR and PLR in male was different from in female from Chaoshan region in South China. The NLR and PLR varied with age and sex.

Abbreviations

CBC: Complete blood count; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; WBC: White blood cell

Acknowledgements

Not applicable.

Authors' contributions

LSW and SZ drafted the manuscript. CTW and XRT were involved in data collection. MY conceived of the study. All authors read and approved the final manuscript.

Funding

None.

Availability of data and materials

Raw data supporting the obtained results are available at the corresponding author.

Ethics approval and consent to participate

The study was approved by the ethics committee of Shantou University Medical College. The need for consent was waived because of the retrospective data. Dr. Min Yu granted administrative permissions to access the raw data.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 3 November 2018 Accepted: 20 May 2019

Published online: 27 May 2019

References

- Bonaventura A, Montecucco F, Dallegri F, Carbone F, Lüscher TF, Camici GG, et al. Novel findings in neutrophil biology and their impact on cardiovascular disease. *Cardiovasc Res*. 2019. <https://doi.org/10.1093/cvr/cvz084> [Epub ahead of print].
- Alan S, Tuna S, Türkoğlu EB. The relation of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume with the presence and severity of Behçet's syndrome. *Kaohsiung J Med Sci*. 2015;31(12):626–31. <https://doi.org/10.1016/j.kjms.2015.10.010>.
- Wang X, Zhang G, Jiang X, Zhu H, Lu Z, Xu L. Neutrophil to lymphocyte ratio in relation to risk of all-cause mortality and cardiovascular events among patients undergoing angiography or cardiac revascularization: a meta-analysis of observational studies. *Atherosclerosis*. 2014;234(1):206–13. <https://doi.org/10.1016/j.atherosclerosis.2014.03.003>.
- Bowen RC, Little NAB, Harmer JR, Ma J, Mirabelli LG, Roller KD, et al. Neutrophil-to-lymphocyte ratio as prognostic indicator in gastrointestinal cancers: a systematic review and meta-analysis. *Oncotarget*. 2017;8(19):32171–89. <https://doi.org/10.18632/oncotarget.16291>.
- Bonaventura A, Liberale L, Carbone F, Vecchié A, Bonomi A, Scopinaro N, et al. Baseline neutrophil-to-lymphocyte ratio is associated with long-term T2D remission after metabolic surgery. *Acta Diabetol*. 2019. <https://doi.org/10.1007/s00592-019-01345-2> Epub ahead of print.
- Azab B, Camacho-Rivera M, Taioli E. Average values and racial differences of neutrophil lymphocyte ratio among a nationally representative sample of United States subjects. *PLoS One*. 2014;9(11):e112361. <https://doi.org/10.1371/journal.pone.0112361>.
- Lee JS, Kim NY, Na SH, Youn YH, Shin CS. Reference values of neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. *Medicine (Baltimore)*. 2018;97(26):e11138. <https://doi.org/10.1097/MD.00000000000011138>.
- Fu H, Qin B, Hu Z, Ma N, Yang M, Wei T, et al. Neutrophil- and platelet-to-lymphocyte ratios are correlated with disease activity in rheumatoid arthritis. *Clin Lab*. 2015;61(3–4):269–73.
- Qin B, Ma N, Tang Q, Wei T, Yang M, Fu H, et al. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. *Mod Rheumatol*. 2016;26(3):372–6. <https://doi.org/10.3109/14397595.2015.1091136>.
- Pan L, Du J, Li T, Liao H. Platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio associated with disease activity in patients with Takayasu's arteritis: a case-control study. *BMJ Open*. 2017;7(4):e014451. <https://doi.org/10.1136/bmjopen-2016-014451>.
- Li C, Wen TF, Yan LN, Li B, Wang WT, Yang JY, et al. Postoperative neutrophil-to-lymphocyte ratio plus platelet-to-lymphocyte ratio predicts the outcomes of hepatocellular carcinoma. *J Surg Res*. 2015;198(1):73–9. <https://doi.org/10.1016/j.jss.2015.05.003>.
- Lafçi G, Çiçek ÖF, Uzun HA, Yalçinkaya A, Diken AI, Turak O, et al. Relationship of admission neutrophil-to-lymphocyte ratio with in-hospital mortality in patients with acute type I aortic dissection. *Turk J Med Sci*. 2014;44(2):186–92.
- Karakoyun S, Gürsoy MO, Akgün T, Öcal L, Kalçık M, Yesin M, et al. Neutrophil-lymphocyte ratio may predict in-hospital mortality in patients with acute type a aortic dissection. *Herz*. 2015;40(4):716–21. <https://doi.org/10.1007/s00059-014-4121-2>.
- Sbarouni E, Georgiadou P, Analitis A, Voudris V. High neutrophil to lymphocyte ratio in type a acute aortic dissection facilitates diagnosis and predicts worse outcome. *Expert Rev Mol Diagn*. 2015;15(7):965–70. <https://doi.org/10.1586/14737159.2015.1042367>.
- Kalkan ME, Kalkan AK, Gündeş A, Yanartaş M, Öztürk S, Gurbuz AS, et al. Neutrophil to lymphocyte ratio: a novel marker for predicting hospital mortality of patients with acute type a aortic dissection. *Perfusion*. 2017;32(4):321–7. <https://doi.org/10.1177/0267659115590625>.
- Meng X, Chang Q, Liu Y, Chen L, Wei G, Yang J, et al. Determinant roles of gender and age on SII, PLR, NLR, LMR and MLR and their reference intervals defining in Henan, China: a posteriori and big-data-based. *J Clin Lab Anal*. 2018;32(2). <https://doi.org/10.1002/jcla.22228>.

17. Ober C, Loisel DA, Gilad Y. Sex-specific genetic architecture of human disease. *Nat Rev Genet.* 2008;9(12):911–22. <https://doi.org/10.1038/nrg2415>.
18. Molloy EJ, O'Neill AJ, Grantham JJ, Sheridan-Pereira M, Fitzpatrick JM, Webb DW, et al. Sex-specific alterations in neutrophil apoptosis: the role of estradiol and progesterone. *Blood.* 2003;102(7):2653–9.
19. Chen Y, Zhang Y, Zhao G, Chen C, Yang P, Ye S, et al. Difference in leukocyte composition between women before and after menopausal age, and distinct sexual dimorphism. *PLoS One.* 2016;11(9):e0162953. <https://doi.org/10.1371/journal.pone.0162953>.
20. Bain BJ. Ethnic and sex differences in the total and differential white cell count and platelet count. *J Clin Pathol.* 1996;49(8):664–6.
21. Wu X, Zhao M, Pan B, Zhang J, Peng M, Wang L, et al. Complete blood count reference intervals for healthy Han Chinese adults. *PLoS One.* 2015;10(3):e0119669. <https://doi.org/10.1371/journal.pone.0119669>. eCollection2015.
22. Kibaya RS, Bautista CT, Sawe FK, Shaffer DN, Sateron WB, Scott PT, et al. Reference ranges for the clinical laboratory derived from a rural population in Kericho, Kenya. *PLoS One.* 2008;3(10):e3327. <https://doi.org/10.1371/journal.pone.0003327>.
23. McIlhagger R, Gow AJ, Brett CE, Corley J, Taylor M, Deary IJ, et al. Differences in the haematological profile of healthy 70 year old men and women: normal ranges with confirmatory factor analysis. *BMC Blood Disord.* 2010;10:4. <https://doi.org/10.1186/1471-2326-10-4>.
24. Beguin Y. Erythropoietin and platelet production. *Haematologica.* 1999; 84(6):541–7.
25. Kadikoylu G, Yavasoglu I, Bolaman Z, Senturk T. Platelet parameters in women with iron deficiency anemia. *J Natl Med Assoc.* 2006;98(3):398–402.
26. Pirrie R. The influence of age upon serum iron in normal subjects. *J Clin Pathol.* 1952;5(1):10–5.
27. Nagata Y, Yoshikawa J, Hashimoto A, Yamamoto M, Payne AH, Todokoro K. Proplatelet formation of megakaryocytes is triggered by autocrine-synthesized estradiol. *Genes Dev.* 2003;17(23):2864–9. <https://doi.org/10.1101/gad.1128003>.
28. Biino G, Santimone I, Minelli C, Sorice R, Frongia B, Traglia M, et al. Age- and sex-related variations in platelet count in Italy: a proposal of reference ranges based on 40987 subjects' data. *PLoS One.* 2013;8(1):e54289. <https://doi.org/10.1371/journal.pone.0054289>.
29. Biino G, Gasparini P, D'Adamo P, Ciullo M, Nutile T, Toniolo D, et al. Influence of age, sex and ethnicity on platelet count in five Italian geographic isolates: mild thrombocytopenia may be physiological. *Br J Haematol.* 2012;157(3):384–7. <https://doi.org/10.1111/j.1365-2141.2011.08981.x>.
30. Gumus F, Solak I, Eryilmaz MA. The effects of smoking on neutrophil/lymphocyte, platelet/lymphocyte ratios. *Bratisl Lek Listy.* 2018;119(2):116–9. https://doi.org/10.4149/BLL_2018_023.
31. Hong J, Min Z, Bai-shen P, Jie Z, Ming-ting P, Xian-zhang H, et al. Investigation on reference intervals and regional differences of platelet indices in healthy Chinese Han adults. *J Clin Lab Anal.* 2015;29(1):21–7. <https://doi.org/10.1002/jcla.21721>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

