



Title	Age as a factor in severe bacterial infection in transfusion-dependent patients with thalassemia major [2] (multiple letters)
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Reply

SIR—We note the comments of Drs. Lee and Li [1] with interest. According to their quotation from the study by Wang et al. [2], the incidence of severe bacterial infections in patients with thalassemia major was 1.6 infections/100 patient-years, with one-half of the isolates being *Klebsiella* species. This was consistent with the incidence of *Klebsiella* infection in our study (0.78 infections/100 patient-years) [3]. We believe that the results from these 2 studies should have impressed on readers the importance of *Klebsiella* infection in patients with thalassemia major in Asia.

In their letter, Lee and Li [1] combined data from the results of our study [3] with data from Wang et al. [2] and from their own hospital and suggested that age is a significant determining factor for *Klebsiella* infection in patients with thalassemia major. There were only 4 cases of severe bacterial infections, with 2 cases of *Klebsiella* infection, in Lee and Li's series [1]. The small number of patients makes it impossible to appreciate the spectrum of infections in their cohort. Furthermore, it is difficult to draw conclusions from studies that have different objectives; ours focused only on *Klebsiella* infection [3], and that of Wang et al. [2] focused on all kinds of severe bacterial infections. In our study,

we had considered age and other factors that Lee and Li [1] had also suggested, including history of splenectomy, deranged liver function, hepatitis C virus seropositivity, and ferritin level, as possible predictors of *Klebsiella* infection. However, none were shown to be significant by multiple logistic regression analysis. The suggestion by Lee and Li [1] that age may be an important risk factor is solely based on observation, with no controlled analysis, and we are of the opinion that this uncontrolled data cannot provide any reliable information about predictors of *Klebsiella* infection in this group of patients.

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Reply

SIR—We thank Lee and Li [1] for comparing their experience with the occurrence of severe bacterial infection in transfusion-dependent patients who have thalassemia major with the recent studies by Chung et al. [2] and our own study [3]. In examining specific risk factors, they suggest that age may be the only significant determining factor in the occurrence of severe bacterial infections in this group of patients.

It is true that, in Taiwan as well as in Hong Kong, the quality of treatment of thalassemia in early childhood differs between the older and the younger cohorts of patients [4, 5]. However, when we assessed risk factors in patients >10 years of age in our cohort of patients with thalassemia ($n = 69$; attack rate, 1.74 infections/100 patient-years), we identified delays in the start of iron-chelating therapy ($P < .001$), history of splenectomy ($P < .001$), and diabetes mellitus ($P = .011$), but not hepatitis C infection ($P = .061$), as risk factors for severe bacterial infections. By logistic regression analysis, history of splenectomy and age at the start of iron-chelating therapy were identified as independent risk factors. As mentioned in our article [3], today nearly all of the younger cohort of our patients with thalassemia major can receive adequate blood transfusions and iron-chelating therapy; time is needed to observe whether the occurrence of severe bacterial infection is reduced under such circumstances.

We are interested in the finding that *Klebsiella* species have been identified as the most important pathogens in this group of patients in Hong Kong, as well as in Taiwan. As Chung et al. [2] noted, the reports they could find of *Klebsiella* infection in patients with thalassemia were all from Asia. It is not clear why there is paucity of reports of *Klebsiella* infection from other places, such as Mediterranean Europe, where thalassemia is prevalent. The influence of environmental and/or genetic factors could play a role in susceptibility to infections [6]. Ko et al. [7] studied the distribution of mutations associated with β -thalassemia in Chinese patients and found that the 4 most common mutations, IVS-II-654 (C→T), codons 41/42 frameshift (-TCTT), and nonsense codons 17 (A→T) and -28 (A→G), are the same in Taiwan and in south China. However, in Taiwan the most common mutation is IVS-II-654, whereas in south China, the most common mutation is the codons 41/42 frameshift. The relation of host genetics and *Klebsiella* infection in

this group of patients is a subject for further study.

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