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Original Article

Clinical analysis of hospital-acquired infections in patients with multiple myeloma: a study of 200 cases

Hece Cai, Fugui Sun, Weihua Shen, Xianghai Bian

Department of Hematological Oncology, Haiyan County People's Hospital, Jiaxing 314300, Zhejiang, China

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Abstract: Objective: To investigate the clinical characteristics of hospital-acquired infections (HAIs) in patients undergoing treatment for multiple myeloma. Methods: A retrospective analysis was conducted on 200 patients with multiple myeloma treated at Haiyan County People's Hospital in Jiaxing. The incidence rate, sites of infection, and causative pathogens of HAIs were recorded. Patients were divided into an infection group (n=37) and a non-infection group (n=163) based on the presence of HAIs. According to follow-up outcomes, they were further classified into a recurrence group (n=76) and a non-recurrence group (n=124). Risk factors associated with HAIs in patients with multiple myeloma were analyzed, and the predictive value of serum immunoglobulin A (IgA) and immunoglobulin G (IgG) levels for the recurrence of multiple myeloma was assessed. Results: Among the 200 patients with multiple myeloma, the incidence of HAIs was 18.5%. The respiratory tract was the most commonly affected site, with Gram-negative bacilli being the predominant pathogens. Multivariate logistic regression analysis identified neutropenia, age ≥60 years, chemotherapy, low serum albumin levels, high Revised International Staging System (R-ISS) stage, elevated body mass index (BMI), and comorbid diabetes mellitus as significant risk factors for infection following multiple myeloma treatment (all $P<0.05$). In addition, receiver operating characteristic (ROC) analysis revealed that serum IgA and IgG levels were strong predictors for recurrence in patients with multiple myeloma, with area under the curve (AUC) values of 0.936 and 0.914, respectively. IgA showed a sensitivity of 97.8% and specificity of 93.5%, while IgG demonstrated a sensitivity of 83.3% and specificity of 80.0%. Conclusion: Patients with multiple myeloma are at increased risk of developing HAIs after treatment, particularly respiratory infections caused by Gram-negative bacilli. Moreover, serum IgA and IgG levels may serve as reliable biomarkers for predicting disease recurrence.

Keywords: Multiple myeloma, chemotherapy, hospital-acquired infection, risk factors, recurrence prediction

Introduction

Multiple myeloma (MM) is a malignant hematologic disease characterized by the proliferation of abnormal plasma cells within the bone marrow. These aberrant cells disrupt normal hematopoiesis and impair immune function, rendering patients highly susceptible to a wide range of infections [1, 2]. The global incidence of MM varies considerably and is influenced by multiple factors, including geographic location, ethnicity, sex, and age [3, 4]. Epidemiological studies indicate that the prevalence of MM is relatively higher in North America and Europe, with advanced age (particularly individuals over 60 years), racial background, and male sex recognized as significant risk factors [5, 6].

Current treatment modalities for MM include chemotherapy, targeted therapies, immunotherapy, and stem cell transplantation [7]. While these interventions have significantly improved survival, they are often associated with profound immunosuppression. The use of glucocorticoids and chemotherapeutic drugs further exacerbates the risk of infection. Infections in MM patients can result in prolonged hospitalization, increased healthcare burden, and, in severe cases, mortality [8]. Although infections are a well-recognized complication in MM, most studies have focused primarily on hospital-acquired infections (HAIs), with limited exploration of factors predictive of recurrence or long-term prognosis [9]. Given the regional variability in MM incidence and outcomes, it is crucial to

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identify population-specific risk factors for HAIs to improve the overall prognosis of affected patients in specific regions.

General data and methods

General data

A retrospective analysis was conducted on 200 patients with MM who were admitted to the Hematology Department of Haiyan County People's Hospital in Jiaxing, China, between January 2018 and December 2023. Inclusion criteria were as follows: (1) Age >18 years; (2) Diagnosis confirmed according to the established clinical guidelines for the diagnosis and treatment of MM [10]; (3) Availability of complete clinical data; (4) Good treatment compliance and cooperation; (5) Newly diagnosed cases of MM without prior treatment. Exclusion criteria included: (1) Age >70 years; (2) Presence of other concurrent malignancies; (3) History of prior treatment for other hematologic disorders; (4) Severe cardiac or renal dysfunction. Patients were divided into an infection group (n=37) and a non-infection group (n=163) based on the presence of HAIs. This study was approved by the Ethics Committee of Haiyan County People's Hospital.

Treatment methods

All patients included in this study received chemotherapy in accordance with established clinical guidelines for the diagnosis and treatment of MM. The primary treatment regimens administered were VAD (vincristine, pirarubicin, and dexamethasone) and VMP (bortezomib, melphalan, and prednisone). Drug dosages were determined based on the guidelines and were adjusted according to each patient's body surface area [11].

Data collection

Routine clinical data were collected for all patients in both groups. Hematologic parameters included hemoglobin levels, white blood cell (WBC) count, and platelet count, while coagulation status was assessed using prothrombin time (PT). Biochemical indicators of liver and renal function - including serum albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, blood urea nitrogen (BUN), and total bilirubin - were measured using a fully automated biochemical analyzer (Roche, Switzerland). Additionally, serum levels of protein induced by vitamin K absence or antagonist-II (PIVKA-II) and alpha-fetoprotein (AFP) were assessed using a microparticle chemiluminescent immunoassay.

Venous blood samples (5 mL) were collected from fasting patients in the early morning. Samples were centrifuged at 3,500 rpm for 5 minutes with a centrifuge radius of 10 cm. Serum C-reactive protein (CRP) levels were measured using an automated immunoassay analyzer (Centaur XP, Siemens, Germany). Serum levels of interleukin-6 (IL-6), immunoglobulin A (IgA), and immunoglobulin G (IgG) were determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits, following the manufacturer's protocols.

Follow-up after discharge

Post-discharge follow-up was conducted through a review of medical records and telephone interviews. The follow-up period concluded on December 31, 2024. According to the latest edition of the Chinese Guidelines for the Diagnosis and Treatment of Multiple Myeloma, patients were evaluated at 3-month intervals to assess disease status, including achievement of complete remission or occurrence of relapse.

Statistical analysis

Statistical analyses were performed using SPSS version 26.0. Continuous variables were expressed as mean ± standard error of the mean (SEM). Group comparisons for normally distributed continuous data were conducted using independent samples t-tests. Categorical data were presented as frequencies (percentages) and compared using the chi-square (χ^2) test. Receiver operating characteristic (ROC) curve analysis was used to assess the predictive performance of serum IgG and IgA levels for disease relapse in patients with multiple myeloma. A *p*-value of <0.05 was considered statistically significant.

Results

General characteristics of the study population

A total of 200 hospitalized patients diagnosed with MM were included in this study, compris-

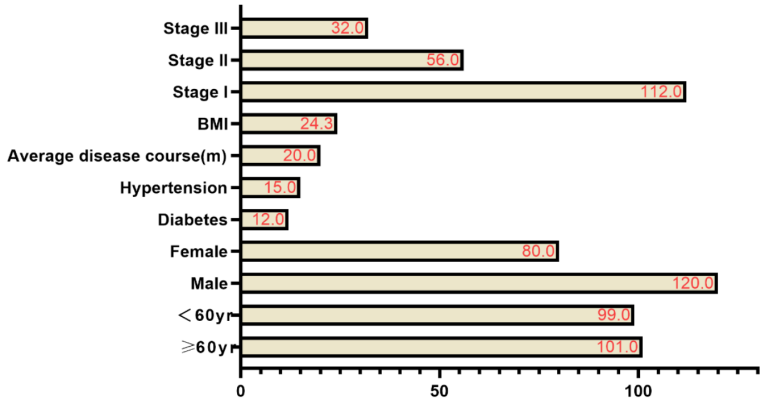

Figure 1. General information of the patient cohort. Note: BMI, body mass index.

Table 1. Distribution of infection sites (%)

Infection site	Number of cases	Composition ratio (%)
Lower respiratory tract	11	29.74
Upper respiratory tract	7	18.92
Oral cavity, gums	6	16.22
Urinary and reproductive tract	4	10.81
Stomach, intestine	3	8.11
Skin, anus	2	5.41
Blood	2	5.41
Venous intubation site	1	2.7
Bile duct	1	2.7
Total	37	100

ing 120 males and 80 females. The age of the patients ranged from 49 to 92 years, with a median age of 66 years. Among them, 101 patients were younger than 60 years, while 99 patients were 60 years or older. Additional baseline characteristics are presented in **Figure 1**.

Infection status in multiple myeloma patients

Of the 200 patients, 37 developed HAIs. The most frequently involved site was the respiratory tract, followed by the oral cavity and urinary tract. The distribution of infection sites is detailed in **Table 1**.

Pathogenic microorganisms in multiple myeloma patients with infection

A total of 37 pathogenic strains were isolated from clinical specimens, including throat swabs, sputum, blood, urine, secretions, and indwelling catheters. The detailed distribution of these pathogens is shown in **Table 2**.

Comparison of baseline characteristics between infected and non-infected multiple myeloma patients

Compared with non-infected patients, those who developed infections were significantly older and had more advanced disease stages, more complex chemotherapy regimens, higher body mass index (BMI), and a greater prevalence of diabetes. No statistically significant differences were observed in other baseline characteristics. Details are presented in **Table 3**.

Comparison of serum granulocyte parameters between infected and non-infected multiple myeloma patients

Significant differences were observed in granulocyte and lymphocyte counts between infected and non-infected patients. In contrast, total white blood cell (WBC) counts and hemoglobin levels did not differ significantly between the two groups. Details are shown in **Table 4**.

Comparison of serum liver and kidney function indicators and albumin levels between infected and non-infected multiple myeloma patients

Serum albumin levels were significantly lower in infected patients compared with those without infection. However, there were no significant differences between the two groups in liver function, kidney function, or total serum protein levels. Details are shown in **Figure 2**.

Logistic regression analysis of factors associated with hospital-acquired infection in multiple myeloma patients

Multivariate logistic regression analysis identified the following variables as independent

Table 2. Distribution of the pathogenic microorganisms (%)

Pathogen	Number of cases	Composition ratio (%)
Gram-negative bacillus (G-)	15	40.54
Klebsiella pneumoniae	6	12.24
E. coli	3	8.16
Acinetobacter baumannii	2	8.16
Enterobacter cloacae	1	6.14
Pseudomonas aeruginosa	1	6.14
Aeromonas hydrophila	1	2.04
Maltooligomonas maltogenes	1	2.04
Gram-positive cocci (G+)	12	32.43
Staphylococcus aureus	6	12.24
Staphylococcus epidermidis	3	6.14
Streptococcus pyoacid	1	2.04
Enterococcus faecium	1	2.04
Enterococcus faecalis	1	2.04
Fungus	10	27.03
Candida albicans	7	18.93
Candida tropicalis	1	2.7
Candida Kerou	1	2.7
Candida glabrata	1	2.7
Total	37	100

Table 3. Comparison of general information between infected and non-infected individuals

Variable	Infection group (n=37)	No-infection group (n=163)	Statistical value	P
Age			4.522	0.0335
≥60 years old	17	20		
<60 years old	56	107		
BMI	22.5±2.0	26.0±1.9	-10.018	<0.001
Chemotherapy regimen			12.088	<0.001
VAD	15	93		
VMP	22	60		
Diabetes	6	6	21.737	<0.001
Hypertension	3	12	0.063	0.802
Disease course	20.1±2.2	20.2±2.2	-0.25	0.803
R-ISS staging			26.478	<0.001
I	12	100		
II/III	25	63		

Note: BMI, body mass index; VAD, vincristine, adriamycin, dexamethasone; VMP, velcade, melphalan, prednisone.

risk factors for HAIs in patients undergoing treatment for MM: neutropenia, age ≥60 years, chemotherapy, low serum albumin level, advanced R-ISS staging, elevated BMI, and presence of comorbid diabetes. Details are presented in **Table 5**.

Comparison of serum immunoglobulin IgA and IgG levels between infected and non-infected multiple myeloma patients

At admission, no statistically significant differences were observed in serum immunoglobulin IgA and IgG levels between infected and non-infected patients (both P> 0.05). However, the infected group showed lower serum IgA and IgG levels compared to the non-infected group after infection (both P <0.05). Details are provided in **Table 6**.

Predictive performance of serum immunoglobulins IgA and IgG for disease relapse in multiple myeloma patients

During follow-up, 76 of the 200 patients experienced disease relapse. Univariate analysis revealed differences in serum IgA and IgG levels, age, R-ISS stage, and prevalence of diabetes between the relapsed and non-relapsed groups, as shown in **Tables 7** and **8**. Meanwhile, multivariate analysis confirmed that serum IgA and IgG levels, along with the R-ISS stage, were independent predictors of relapse in MM. Moreover, statistical analysis revealed that IgA and IgG had strong predictive value for relapse, with areas under the curve (AUCs) of 0.949 and 0.914, respectively. Further details are provided in **Table 9** and **Figure 3**.

Discussion

Multiple myeloma is a common hematologic malignancy primarily affecting plasma cells within the bone marrow [12, 13]. Under physiological conditions, plasma cells function as ter-

Table 4. Comparison of serum inflammatory indicators between the two groups of patients

Parameter	Infection group (n=37)	No-infection group (n=163)	Statistical value	P
Neutrophil value				
≥0.5	17	50	8.167	0.004
<0.5	20	113		
Lymphocyte value				
≥0.5	15	100	12.211	0.001
<0.5	22	63		
Total white blood cell count (10×9)	4.45±0.64	4.52±0.65	-0.593	0.554
Hemoglobin level (g/L)	11.8±0.56	12.0±0.60	-1.852	0.065

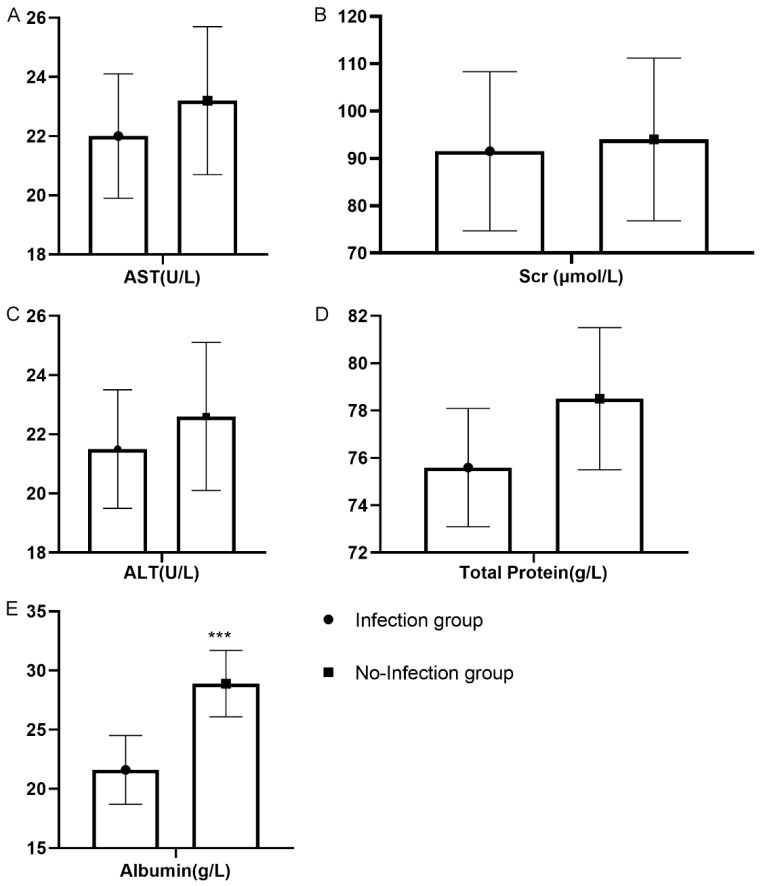

Figure 2. Comparison of serum liver and kidney functions and albumin contents between infected and non-infected groups. A: Serum ALT levels; B: Serum creatinine levels; C: Serum AST levels; D: Serum total protein concentrations; E: Serum albumin levels. Compared with the infected group, ***P<0.001. Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

minally differentiated B lymphocytes responsible for the production of immunoglobulins, playing a key role in humoral immunity. However, mutations in these cells can lead to abnormal proliferation, resulting in tumor formation. The progression of MM disrupts normal bone marrow function and impacts the skeletal system, immune system, and other vital organs. Epidemiological data from the International Agency for Research on Cancer indicate a rising global incidence of MM, with a higher prevalence among middle-aged and elderly populations [14].

Previous studies have reported an infection incidence of approximately 20% among MM patients, primarily attributed to chemotherapy and corticosteroid use, which compromise host immunity and increase susceptibility to infections. In our cohort, the incidence of hospital-acquired infections was 18.5%, slightly lower than previously reported rates [15]. This discrepancy may be explained by our hospital's location in a coastal region with relatively greater economic resources, advanced medical infrastructure, and higher clinical expertise, alongside a strong emphasis on infection prevention during treatment. However, both our findings and existing domestic and international studies consistently highlight a notably high prevalence of HAIs in MM patients [16]. Previous studies have reported that lung infections are among the most common infections in multiple myeloma patients. Consistent with these findings, the present study also identifies respiratory

Table 5. Multivariate analysis of nosocomial infections in patients with multiple myeloma

Factor	β	OR	95% CI	P
Agranulocytosis	0.884	2.450	1.011-5.228	0.028
Age ≥60 years old	0.663	2.055	1.629-5.433	0.031
Chemotherapy regimen	1.650	5.706	1.853-16.162	0.001
Albumin level	0.866	2.545	1.077-5.803	0.016
High R-ISS stage	0.863	2.456	1.005-5.308	0.035
BMI	1.053	2.788	1.179-5.453	0.022
Diabetes	0.953	2.330	1.326-4.772	0.024
IgA (g/L)	1.327	3.772	1.280-8.043	0.011
IgG (g/L)	1.348	3.850	1.468-7.993	0.010

Note: BMI, body mass index; R-ISS, Revised International Staging System.

Table 6. Comparison of serum immunoglobulins between the two groups of patients

Variable	Infection group (n=37)	No-infection group (n=163)	Statistical value	P
IgA (g/L)				
At admission	58.5±4.9	59.0±4.7	0.709	0.479
During infection	40.3±3.5	45.5±3.6	9.811	<0.001
IgG (g/L)				
At admission	39.2±3.4	40.0±3.9	1.431	0.154
During infection	30.0±3.2	37.1±3.3	14.624	<0.001

Note: IgA, immunoglobulin A; IgG, immunoglobulin G.

Table 7. Univariate analysis of risk factors for recurrence in multiple myeloma patients

Variable	Recurrent patients (n=76)	Non-recurrent patients (n=124)	Statistical value	P
Age (years)	68.9±5.0	64.0±5.1	6.644	<0.001
IgA (g/L)	35.2±3.2	41.2±3.4	12.350	<0.001
IgG (g/L)	38.1±3.1	41.4±3.8	6.379	<0.001
R-ISS staging (II+III)	42	46	6.311	0.012
Diabetes	6	6	0.780	0.377
Chemotherapy regimen			0.845	0.358
VAD	30	83		
VMP	46	41		
BMI	25.6±3.2	26.0±3.0	0.892	0.373
Agranulocytosis	55	78	2.839	0.092

Note: IgA, immunoglobulin A; IgG, immunoglobulin G; BMI, body mass index; R-ISS, Revised International Staging System; VAD, vincristine, adriamycin, dexamethasone; VMP, velcade, melphalan, prednisone.

tract infections as the predominant type of infection in this population [17]. The increased susceptibility to respiratory infections in MM patients is multifactorial. The hospital environment inherently poses a high risk for infections, partly due to factors such as inadequate air circulation and increased exposure to airborne pathogens. Additionally, chemotherapy-induced mucosal injury and impairment of the ciliary clearance mechanism compromise the respiratory tract's innate defenses, thereby facilitating bacterial colonization and infection. Pulmonary infections in MM patients are often persistent and difficult to fully resolve, resulting in residual lung damage. Consequently, these patients are at significantly heightened risk for recurrent respiratory infections during subsequent hospitalizations [17, 18].

Previous studies have established that infections in MM patients are primarily bacterial, with Gram-negative bacilli identified as the predominant causative pathogens. The bacterial origin of infections in this patient population aligns with findings from prior research [19]. Fungal infections were identified as secondary pathogens in these patients. The increased risk of fungal infections is attributed to chemotherapy-induced immunosuppression, prolonged use of broad-spectrum antibiotics, and corticosteroid therapy administered to some patients [20].

Multiple factors have been shown to influence the susceptibility to infection in MM patients [21]. Our analysis identified neutropenia, age ≥60 years, chemotherapy, low albumin level, high R-ISS stage, elevated BMI, and comorbid diabetes as significant risk factors for infection. The underlying mechanisms are as follows: Neutropenia, a common compli-

Table 8. Multivariate analysis of risk factors for recurrence in multiple myeloma patients

Variable	β	OR	95% CI	P
IgA (g/L)	0.695	2.331	1.578-7.112	0.017
IgG (g/L)	0.702	2.409	1.328-6.509	0.021
R-ISS staging	1.449	5.615	1.742-8.253	0.001

Note: IgA, immunoglobulin A; IgG, immunoglobulin G; R-ISS, Revised International Staging System.

Table 9. Analysis of the efficacy of serum IgA and IgG levels in predicting disease recurrence

Detection index	Sensitivity	Specificity	AUC (95% CI)
IgA	97.8%	83.3%	0.949 (0.898-0.991)
IgG	93.5%	80.0%	0.914 (0.851-0.977)

Note: IgA, immunoglobulin A; IgG, immunoglobulin G.

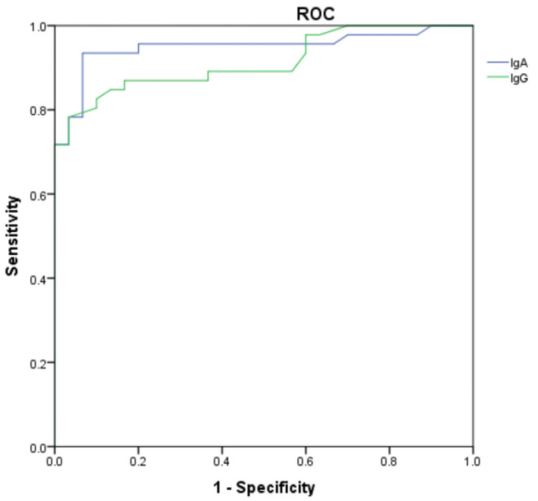

Figure 3. ROC curves of serum IgA and IgG levels for predicting disease recurrence in multiple myeloma patients. Note: ROC, Receiver operating characteristic; IgA, immunoglobulin A; IgG, immunoglobulin G.

cation in MM patients, plays a crucial role in predisposing patients to infections. Neutrophils are a vital component of innate immunity, responsible for the clearance of invading pathogens including bacteria and viruses. A reduction in neutrophil count compromises this first line of defense, markedly increasing the risk of infection. Clinical studies indicate that neutropenia is especially prevalent among MM patients, particularly those undergoing chemotherapy, as chemotherapy drugs not only target malignant plasma cells but also suppress normal bone marrow function, impairing neutrophil production. Consequently, when designing chemotherapy regimens, clinicians must carefully evaluate patient's neutrophil counts and implement strategies to minimize infection risk. With advancing age, the immune system undergoes progressive decline, markedly diminishing the body's ability to resist infections. Moreover, elderly patients frequently present with comorbid chronic diseases - such as cardiovascular diseases and hypertension - that further compromise immune function and overall health. Consequently, age constitutes a critical determinant of infection risk in patients with MM. The choice of chemotherapy regimen also influences the incidence of infections. Different chemotherapy drugs and protocols vary in their immunosuppressive effects; some induce profound neutropenia, while others exhibit a relatively milder impact. Therefore, treatment planning must involve careful evaluation of the patient's baseline health and treatment tolerance to optimize therapeutic outcomes while minimizing infection risk. Serum albumin levels represent another key factor influencing infection susceptibility. Albumin, a major plasma protein, plays essential roles in maintaining colloid osmotic pressure and supporting various physiological processes. Hypoalbuminemia not only reflects poor nutritional status but is also associated with impaired immune competence. Previous studies have shown that MM patients with reduced albumin levels exhibit a significantly higher incidence of infection compared to those with normal levels. Additionally, an advanced R-ISS stage indicates more severe disease and is often associated with an increased risk of infection. The R-ISS incorporates serum β2-microglobulin, albumin levels, and chromosomal abnormalities to stratify disease severity. Patients at higher R-ISS stages generally have more complex diseases and greater immunosuppression. BMI is also implicated as a contributing factor; elevated BMI is often linked to metabolic disorders that adversely affect immune function. Research has found a certain correlation between BMI and infection prevalence. Lastly, comorbid dia-

betes significantly elevates infection risk due to inherent immune dysfunction and impaired host defenses. This susceptibility is further exacerbated in patients undergoing treatment for major diseases such as MM. Accordingly, effective management of diabetes and maintenance of stable glycemic control are essential components of infection prevention strategies. These observations align with findings reported in previous studies [22-25].

Despite advances in therapeutic strategies that have improved clinical outcomes for MM patients, the disease remains incurable, and relapse risk remains high even after achieving complete remission. Therefore, establishing an effective prevention and monitoring system is crucial for improving patient prognosis. In MM, malignant plasma cells - responsible for the synthesis and secretion of immunoglobulins - undergo abnormal proliferation, leading to significant alterations in serum immunoglobulin levels. These changes reflect the degree of plasma cell differentiation and activation, rendering immunoglobulin concentrations as valuable biomarkers for assessing disease status and tumor burden. Our study demonstrated significant changes in serum IgA and IgG levels during episodes of infections in MM patients. ROC curve analysis confirmed the robust predictive value of both IgA and IgG for disease relapse. The biological basis for these findings lies in the pivotal roles of IgA and IgG in immune defense. IgA is predominantly distributed on mucosal surfaces and in body fluids, serving as a first line of defense against pathogen invasion. IgG, the most abundant immunoglobulin in serum, exhibits a potent toxin-neutralizing capacity and mediates various immune functions. Prior studies have similarly reported that fluctuations in IgA and IgG levels correlate strongly with relapse in MM. Specifically, abnormal variations in these immunoglobulin levels during treatment often indicate an increased risk of disease relapse, supporting our findings and those of previous research [26, 27].

In summary, HAIs occur following treatment of multiple myeloma, with respiratory tract infections being particularly prevalent and are influenced by multiple risk factors. Identification of these high-risk factors enables the implementation of targeted preventive and management strategies in clinical practice. However, this study has several limitations. The relatively small sample size from a single center and the heterogeneity in disease severity among nested cases may limit the generalizability of the findings. Therefore, large-scale multicenter studies are needed to further validate and extend these findings. Additionally, this study did not assess the combined predictive performance of the two serum immunoglobulin markers for MM relapse, given that each marker individually demonstrated strong diagnostic efficacy. Evaluating their joint predictive value would be a valuable extension of the robustness of the conclusions. Finally, the follow-up duration was relatively short, and longer-term longitudinal studies are required to fully establish the prognostic utility of serum biomarkers in predicting relapse in MM patients.

Disclosure of conflict of interest

None.

Address correspondence to: Fugui Sun, Department of Hematological Oncology, Haiyan County People's Hospital, No. 699, Jianfeng Road, Wuyuan Sub-District, Haiyan County, Jiaxing 314300, Zhejiang, China. Tel: +86-15257390585; E-mail: Sunguifu@126.com

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