Mean Corpuscular Hemoglobin Predicts Length of Hospital Stay Independent of Severity Classification in Acute Pancreatitis Patients: a Retrospective Study

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Research Article

Keywords: mean corpuscular hemoglobin, length of hospital stay, acute pancreatitis, patient management

Posted Date: August 3rd, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-757394/v1>

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Abstract

Background/Objectives: The aim of this study is to explore the relationship between length of hospital stay and mean corpuscular hemoglobin (MCH) in acute pancreatitis (AP) patients.

Methods: The study included 273 AP patients without coronary heart disease, diabetes, hypertension, tumor, psychosis and anemia. The clinical data was collected from electronic medical records.

Results: We separated all data into three groups according to length of hospital stay. We observed that gender ($P=0.017$) and severity classification ($P=0.000$) were significantly correlated with length of hospital stay among three groups. Notably, MCH level was significantly increased among three groups (30.02 ± 1.91 , 30.21 ± 1.81 , 30.92 ± 2.47 pg, $P=0.009$). Thus, we separated all data into two groups according to MCH level, and observed significant increases of length of hospital stay between two groups (11.95 ± 7.03 , 13.96 ± 8.18 days, $P=0.030$). A positive correlation between length of hospital stay and MCH was observed in these individuals ($r=0.172$, $P=0.004$). Multiple linear regression analysis showed that MCH was independently correlated with length of hospital stay, no matter whether severity classification of AP was included ($\beta=0.248$, $P=0.000$; $\beta=0.212$, $P=0.000$).

Conclusions: We concluded that length of hospital stay is correlated with MCH level in AP patients, and the MCH level may predict length of hospital stay independent of severity classification in this disease. Our results may provide a potential evaluation basis for the management of patients with AP.

Introduction

Acute pancreatitis (AP) is an acute inflammatory disease of the pancreas which can result in a systemic inflammatory response syndrome with significant morbidity and mortality, and the incidence rate of AP has increased in recent years¹. AP is one of the most common gastrointestinal causes of hospitalization and results in family financial burden². There is a lack of simple indicators to predict the length of hospital stay of AP. Therefore, the prediction of hospitalization time of patients with acute pancreatitis is conducive to the management of patients and the optimization of clinical diagnosis and treatment efficiency.

Severity classification is correlated with length of hospital stay in AP patients. Previous data showed that both Revised Atlanta Criteria (RAC) and Determinant Based Criteria (DBC), which stratify AP by severity, strongly predict length of hospital stay³. But these indexes cannot predict length of hospital stay at the beginning of hospitalization. A recent work carried out among children demonstrated that certain demographic and clinical factor, such as gender and ethnicity, were independently associated with length of hospital stay for pediatric AP⁴. However, few laboratory parameters are available to evaluate hospitalization in patients with AP.

Blood routine test is the most common clinical test at the beginning of hospitalization. White blood cell count (WBC) could predict severity of AP⁵, but it hasn't been tested in predicting length of hospital stay.

Mean corpuscular hemoglobin (MCH) is the average amount of hemoglobin per red blood cell and is calculated by dividing hemoglobin (HGB) by red blood cell count (RBC). Mean corpuscular volume (MCV) is the average size of a red blood cell, and the Mean corpuscular hemoglobin concentration (MCHC) is the average concentration of hemoglobin. per unit volume of red blood cells. The disease status of AP has a significant impact on blood routine test, and often abnormal hematological parameters predict adverse clinical events in patients with AP. For example, red cell distribution width (RDW) predicts the severity of AP patients in pregnancy⁶. C-reactive protein (CRP) predicts systemic inflammatory response syndrome and death in AP⁷. Total cholesterol concentration predicts the effect of plasmapheresis on hypertriglyceridemic AP⁸. Increased circulating total bile acid levels were associated with organ failure in patients with AP⁹. There are no studies investigating efficacy of MCH, MCV, MCHC, HGB or RBC in predicting length of hospital stay of AP.

Here, the purpose of our study was to evaluate the relationship between hematological parameters and length of hospital stay in patients with AP.

Results

1. The clinical and laboratory features

Table 1 included the characteristics of all participants. Because the average length of hospital stay for AP patients was 14 days in Zhongda Hospital, and the average length of hospital stay in three-A class hospitals of Nanjing city was 8 days., we separated all data into three groups according to 8 and 14 days of length of hospital stay. Significant difference in the value distribution of gander (P = 0.017) and severity classification (P = 0.000) was found. We observed significant increases of MCH among three groups (30.02 ± 1.91 , 30.21 ± 1.81 , 30.92 ± 2.47 pg, P = 0.009). We also noticed significant difference of RBC among three groups (4.75 ± 0.45 , 4.77 ± 0.56 , $4.54 \pm 0.62 \times 10^{12}/L$, P = 0.007). There were no significant differences for other variables, including age, smoke, alcohol, cholecystectomy, WBC, HGB, MCV and MCHC.

Table 1. The clinical and laboratory data in whole population according to length of hospital stay

length of hospital stay (day)	≤ 8 N = 83	9–14 N = 95	≥ 15 N = 95	P-value
Gender (male, %)	52, 62.7%	66, 69.5%	47, 49.5%	0.017*
Age (year)	44.0 ± 16.5	44.7 ± 16.1	46.7 ± 16.9	0.518
Smoke (n,%)	13, 15.7%	18, 18.9%	17, 17.9%	0.844
Alcohol (n,%)	11, 13.3%	16, 16.8%	13, 13.7%	0.754
Cholecystectomy (n,%)	3, 3.6%	6, 6.3%	6, 6.3%	0.666
Severity classification				0.000***
Mild (n, %)	78, 28.6%	87, 31.9%	80, 29.3%	
Moderately (n, %)	1, 0.4%	1, 0.4%	0, 0%	
Severely (n, %)	4, 1.5%	7, 2.6%	15, 5.5%	
WBC (10 ⁹ /L)	10.49 ± 5.36	11.01 ± 4.64	11.27 ± 4.58	0.559
RBC (10 ¹² /L)	4.75 ± 0.45	4.77 ± 0.56	4.54 ± 0.62	0.007**
HGB (g/L)	142.49 ± 14.44	143.85 ± 15.97	139.34 ± 17.38	0.141
MCV (fL)	88.89 ± 5.25	89.16 ± 4.93	90.18 ± 5.06	0.197
MCH (pg)	30.02 ± 1.91	30.21 ± 1.81	30.92 ± 2.47	0.009**
MCHC (g/L)	337.41 ± 10.86	338.93 ± 12.28	342.97 ± 21.84	0.054
The demographic characteristics and laboratory parameters of study participants (n = 273) according to tertiles of length of hospital stay (day). WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin content.				

Due to the above interesting results between length of hospital stay and MCH, we separated all data into two groups according to the median number of MCH (Table 2). We observed significant increases of length of hospital stay between two groups (11.95 ± 7.03 , 13.96 ± 8.18 days, $P = 0.030$). We also noticed significant difference of gender ($P = 0.029$), RBC ($P = 0.000$), MCV ($P = 0.000$), MCHC ($P = 0.000$) between two groups. There were no significant differences for other variables, including age, smoke, alcohol, cholecystectomy, WBC, HGB and severity classification.

Table 2. The clinical and laboratory data in whole population grouped according to MCH

MCH (pg)	≤ 30.3 N = 142	> 30.3 N = 131	P-value
Gender (male, %)	77, 54.2%	88, 67.2%	0.029*
Age (year)	44.3 ± 17.2	46.1 ± 15.7	0.363
Smoke (n,%)	21, 14.8%	27, 20.6%	0.207
Alcohol (n,%)	18, 12.7%	22, 16.8%	0.336
Cholecystectomy (n,%)	10, 7.0%	5, 3.8%	0.243
Severity classification			0.067
Mild (n, %)	132, 48.4%	113, 41.4%	
Moderately (n, %)	1, 0.4%	1, 0.4%	
Severely (n, %)	9, 3.3%	17, 6.2%	
WBC (10 ⁹ /L)	10.65 ± 4.90	11.26 ± 4.78	0.294
RBC (10 ¹² /L)	4.83 ± 0.57	4.53 ± 0.50	0.000***
HGB (g/L)	140.20 ± 16.57	143.68 ± 15.43	0.074
MCV (fL)	86.60 ± 4.10	92.51 ± 4.19	0.000***
MCH (pg)	29.04 ± 1.38	31.88 ± 1.76	0.000***
MCHC (g/L)	335.36 ± 10.84	344.76 ± 19.14	0.000***
length of hospital stay (day)	11.95 ± 7.03	13.96 ± 8.18	0.030*
The demographic characteristics and laboratory parameters of study participants (n = 273) according to the median number of MCH. WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin content.			

2. The correlation between length of hospital stay and laboratory data in whole population

As shown in Fig. 1, the positive correlation between length of hospital stay and MCH was observed in these individuals ($r = 0.172$, $P = 0.004$). In order to further explore the correlation between length of hospital stay and other laboratory data, we did the correlation between length of hospital stay and other laboratory data in whole population (Table 3). Length of hospital stay correlated with gender ($r = -0.123$, $P = 0.042$), severity classification ($r = 0.182$, $P = 0.003$), WBC ($r = 0.128$, $P = 0.034$), RBC ($r = -0.190$, $P = 0.002$). Length of hospital stay had no correlation with age, smoke, alcohol, cholecystectomy, HGB, MCV, MCHC.

Table 3. The correlation between length of hospital stay and other laboratory data in whole population

	correlation coefficient	P-value
Gender (male, %)	-0.123	0.042*
Age (year)	0.095	0.117
Smoke (n,%)	0.037	0.539
Alcohol (n,%)	0.018	0.763
Cholecystectomy (n,%)	0.044	0.467
Severity classification	0.182	0.003**
WBC ($10^9/L$)	0.128	0.034*
RBC ($10^{12}/L$)	-0.190	0.002**
HGB (g/L)	-0.088	0.146
MCV (fL)	0.101	0.095
MCHC (g/L)	0.101	0.096
MCH (pg)	0.172	0.004**
WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin content.		

3. The correlation analyses in multiple linear regression analysis

The correlation analyses were carried out in all subjects. The basic demographic characteristics, such as gender, age and severity of AP, might influence length of hospital stay⁴. The laboratory parameters of study participants, such as WBC and HGB, might influence length of hospital stay as well. Therefore, gender, age, severity classification, WBC, HGB and MCH were included as independent variables in multiple linear regression analysis. We did two regression models to investigate the correlation between length of hospital stay and laboratory data (Table 4). We did linear regression based on gender, age, WBC, HGB and MCH in model 1, and model2 added severity classification on the basis of model 1. The results found that length of hospital stay was correlated with MCH in both model 1 and model 2 (beta = 0.248, P = 0.000 in model 1; beta = 0.212, P = 0.000 in model 2). Length of hospital stay was correlated with severity classification and gender independently (beta = 0.212, P = 0.000; beta = 0.211, P = 0.001; beta = -0.171, P = 0.015 respectively), as shown in Table 4.

Table 4. The factors related to length of hospital stay in AP patients in multivariable linear regression analysis

Model 1 (linear regression based on gender, age, WBC, HGB and MCH)

	Unstandardized coefficients		Standard	P-value
	B	SE	Beta	
Gender	-3.428	1.087	-0.219	0.002**
Age	0.031	0.028	0.067	0.264
WBC	0.244	0.092	0.155	0.009*
HGB	0.019	0.034	0.039	0.590
MCH	0.897	0.215	0.248	0.000***

Model 2 (linear regression based on gender, age, WBC, severity classification, HGB and MCH)

	Unstandardized coefficients		Standard	P-value
	B	SE	Beta	
Gender	-2.672	1.088	-0.171	0.015*
Age	0.022	0.027	0.048	0.415
WBC	0.155	0.094	0.098	0.101
HGB	-0.002	0.034	-0.005	0.943
Severity classification	2.729	0.796	0.211	0.001**
MCH	0.767	0.214	0.212	0.000***
WBC, white blood cell; HGB, hemoglobin; MCH, mean corpuscular hemoglobin				

Discussion

We found that length of hospital stay had a relationship with MCH level in AP patients, and the multiple linear regression analysis showed that MCH level positively correlated with length of hospital stay independent of severity classification of AP.

The severity classification of AP was a strong risk factor of length of hospital stay in AP patients, and the more serious the patient was, the longer they stayed in hospital (Table 1). We also found that gender was another a risk factor of length of hospital stay. The female patients stayed longer than male ones (Table 1), and this phenomenon consisted with previous report in pediatric AP patients⁴. After adjustment for severity classification and gender, length of hospital stay still positively correlated with MCH (P = 0.000, Table 4).

At the beginning of data analysis, we also found a correlation between length of hospital stay and MCH without excluding anemic patients (data not show). We suspected that this correlation might due to the

reduction of HGB, so we excluded anemic patients in this study. Surprisingly, after excluding anemia, length of hospital stay and MCH are still correlated statistically (Fig. 1, Table 3), and HGB was not the risk factor of length of hospital stay according to the multiple linear regression analysis (Table 4). At the other hand, we also found that RBC was not a risk factor of length of hospital stay according to multiple linear regression analysis ($P = 0.900$, data not show). Because MCH is calculated by dividing HGB by RBC, these interesting results implied that MCH might affect length of hospital stay through mechanisms other than anemia.

Long hospital stay is associated with high hospital occupancy, increased costs, and adverse patient outcomes, such as persistent organ failure^{10–12}. The previous studies showed that low MCH level is one of the earliest and sensitive indicators of iron deficiency in different populations^{13–15}, suggesting that MCH positively correlated with iron level. Iron is one of the most important metal ions in human body, but it is also a potentially toxic element. So its systemic homeostasis is strictly regulated¹⁶. Iron overload is a risk of pancreatic endocrine diseases, such as diabetes¹⁷, and results in pancreatic β cell failure, impaired glucose tolerance and insulin sensitivity^{18,19}. Iron overload also cause the pancreatic exocrine diseases, such as pancreatitis and pancreatic adenocarcinoma²⁰. In the present study, length of hospital stay positively correlated with MCH probably because of higher iron level in these patients.

The present results had some limitations. First, this was a retrospective study from electronic medical records, serum samples of patients could not be obtained. Thus we could not measure concentration of iron or iron transporter in serum. Second, our sample size was small, and we needed to expand the sample to verify our conclusion in the future. Third, in different hospitals, there might be slight differences among treatment of AP, which might lead to different length of hospital stay data for same patients in different hospitals. Finally, the patients' financial situation and willingness of treatment might be a potential confounding factor that affects our final outcome.

In conclusion, the evaluation of length of hospital stay is conducive to the management of patients by hospital. We demonstrate that length of hospital stay is correlated with MCH level independent of severity classification in AP patients, and the MCH level may have an effect on predicting length of hospital stay in this disease.

Materials And Methods

Data collection

A total of 273 patients with AP from Zhongda Hospital, School of Medicine, Southeast University were included in the retrospective study, and the diagnosis of all patients with AP were defined in accordance with the criteria of IAP/APA evidence-based guidelines²¹. Patients with known coronary heart disease, diabetes, hypertension, tumor and psychosis were excluded. Patients with anemia (HGB < 120 g/L for male and HGB < 110 g/L for female) were also excluded. Demographic and clinical characteristics of subjects were obtained from electronic medical records. Severity classification (mild, moderately,

severely) was performed according to Marshall scoring system²². The study was approved by Ethics Committee for Clinical Research of Zhongda Hospital, Affiliated to Southeast University and was performed according to the Declaration of Helsinki. The informed consent was waived by Ethics Committee for Clinical Research of Zhongda Hospital, Affiliated to Southeast University.

Statistical analysis

SPSS software version 23.0 was used to analyze all data. Continuous variables were shown as the means $\pm$ standard deviation, and categorical variables were presented as percentages. The comparisons among three groups of continuous variables were performed by One-Way ANOVA. The comparisons of ordinal categorical variables were performed by Rank Sum Test, and Chi-Square Test was used to compare unordered categorical variables among three groups. Spearman's correlation analyses were employed to examine the correlations between length of hospital stay and MCH appropriately. The multiple linear regression analysis was performed to analyze the independent effects of length of hospital stay in all subjects. A P-value of < 0.05 was considered to be statistically significant.

Declarations

Acknowledgements

This study was supported by the National Natural Science Foundation of China (NSFC) [grant number 81800571 (Hao Lin)]; the Talent Project of Dual Creative Ph.D. from Jiangsu Province [grant number 1190000047 (Hao Lin)].

Author contributions

H.L. and T.Y. contributed equally. H.L. designed this project. H.L., T.Y. and R.X. collected data. H.L. and T.Y. did the statistical analysis. X.L. support the data of the average length of hospital stay. H.L. and T.Y. wrote the manuscript. All authors reviewed the manuscript.

Conflict of interest

We declare no conflict of interest.

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Figures

Figure 1

The correlation between length of hospital stay (length of hospital stay) and mean corpuscular hemoglobin (MCH) of study participants ($n = 273$). Spearman's correlation analyses were employed to examine the correlations between length of hospital stay and MCH appropriately. Correlation coefficient was 0.172, and P-value was 0.004.