CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 07 Issue: 04 | October 2026 ISSN: 2660-4159

Article

Role of Iron, Zinc, and Copper Homeostasis in Patients with Multidrug-Resistant Bacterial Infections

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Abstract: Background: Disruption of iron, zinc, and copper homeostasis may contribute to immune dysfunction, inflammation, and disease severity in multidrug-resistant bacterial infections. **Aims of the study:** This study aimed to evaluate iron, zinc, and copper homeostasis in multidrug-resistant bacterial infections and determine their associations with inflammatory biomarkers, hematological parameters, and clinical risk factors. **Methodology:** A case–control study was conducted at Al-Habbobi Teaching Hospital, Thi-Qar, Iraq, between June 2025 and March 2026, including 60 patients with multidrug-resistant (MDR) bacterial infections, 60 with non-MDR infections, and 30 healthy controls. MDR isolates were identified according to CLSI guidelines. Serum iron, ferritin, transferrin, TIBC, zinc, copper, CRP, IL-6, TNF-α, and hematological parameters were measured using standard laboratory methods. Statistical analyses included ANOVA, Pearson correlation, and multivariate logistic regression, with $P < 0.05$ considered statistically significant. **Result:** Patients with MDR bacterial infections showed significantly higher BMI, inflammatory markers, WBC counts, and prevalence of diabetes, prior antibiotic use, and hospitalization than other groups. Escherichia coli was the predominant isolate. MDR infections exhibited marked reductions in serum iron, transferrin, TIBC, and zinc, with increased ferritin, copper, and Cu/Zn ratio (all $P<0.001$). Trace element alterations correlated significantly with inflammatory biomarkers. Previous antibiotic use, elevated Cu/Zn ratio, ferritin, CRP, low zinc, hospitalization, and diabetes independently predicted MDR bacterial infections. **Conclusions**: Disturbances in iron, zinc, and copper homeostasis are strongly associated with multidrug-resistant bacterial infections and parallel systemic inflammation. The Cu/Zn ratio, ferritin, and zinc may serve as valuable complementary biomarkers for assessing infection severity and identifying patients at increased risk of MDR infections.

Keywords: Multidrug-resistant bacterial infections, Nutritional immunity, Iron metabolism, Trace element homeostasis, Inflammatory biomarkers.

Citation: Farhan L. K. Role of Iron, Zinc, and Copper Homeostasis in Patients with Multidrug-Resistant Bacterial Infections. Central Asian Journal of Medical and Natural Science 2026, 7(4), 66-75.

Received: 10th Apr 2026
Revised: 11th May 2026
Accepted: 19th Jun 2026
Published: 16th Jul 2026

1. Introduction

Multidrug-resistant (MDR) bacterial infections are one of the largest public health threats in the world today and have an impact on morbidity, mortality, long-term hospitalisation and health care costs. The prevalence of bacterial resistance to several different classes of antimicrobial agents has greatly diminished the effectiveness of standard antibiotic treatment, thereby narrowing treatment choices and creating the potential for poor clinical outcomes [1,2]. Antimicrobial resistance is listed as one of the common threats to world health security, food security and sustainable development by the World Health Organization (WHO) and is estimated to start claiming the lives of many people if preventive and therapeutic measures are not taken. Thus, the knowledge of host-

related biological factors, which are responsible for susceptibility to MDR infections is current research interest in biomedical science [3].

Although antimicrobial therapy is important for successful host defense against bacterial pathogens, the integrity of innate and adaptive immune responses is also important. Host response to infection involves a complex immune response that involves the activation of inflammatory pathways, production of cytokines, oxidative stress, and metabolic adaptations that help to limit microbial growth [4,5]. The control of trace element homeostasis is one of these protective mechanisms, and is now known to play a significant role in host–pathogen interactions. Micronutrients include iron, zinc and copper which are required by the host and invading microorganisms in many biological activities, including the synthesis of DNA, enzymatic reactions and regulation of the immune system. A competition between host cells and pathogens for these micronutrients is termed "nutritional immunity" and plays an important role in antimicrobial defence [6].

Iron has a crucial function in transport of oxygen, mitochondrial respiration, DNA synthesis and cell proliferation. Is also a necessary nutrient for the growth and virulence of bacteria. Infection causes the host to reduce the growth of bacteria by decreasing iron levels in the blood, by increasing the sequestration of iron in macrophages and by increasing the production of hepcidin and decreasing the transferrin-mediated iron transport [7,8]. These adaptive responses do limit the access of microbes to iron, but may also lead to anemia of inflammation and impaired tissue oxygenation with chronic iron sequestration. Many of the pathogenic bacteria also have highly advanced iron acquisition mechanisms including the production of siderophores and high affinity iron transporters which are able to overcome the nutritional immunity of host cells and survive in iron-limiting environments [9].

Additionally, zinc is a trace element with a fundamental role in the immune system, antioxidant system, integrity of epithelia and inflammatory signalling pathways. Zinc is a structural and/or catalytic cofactor of hundreds of enzymes and transcription factors that play roles in innate and adaptive immune function. Deficiency of zinc has been associated with impaired neutrophilic function and decreased natural killer cell function, defective function of T lymphocytes and exaggerated production of inflammatory cytokines [10]. The level of serum zinc is frequently reduced during bacterial infections, as a host adaptive anti-bacterial response to withhold zinc from the bacteria. Chronic zinc deficiency, however, may compromise the immune competence, and they may be more susceptible to severe or chronic infections [11].

In addition to its contribution to the immune system via its involvement in oxidative metabolism, antioxidant enzyme activity, connective tissue synthesis and immune cell function, copper is also important in this regard [12]. In systemic inflammation, blood copper concentrations are generally increased, due to the fact that blood proteins binding copper (ceruloplasmin) are positive acute-phase proteins. The elevated concentration of copper could be a mechanism of antimicrobial defense, by increasing the oxidative killing mechanisms in activated phagocytes [13]. Copper, however, can also increase oxidative stress and tissue damage if levels are too high, especially in the presence of high levels of inflammation. Therefore, maintaining the physiological range of copper is crucial to keep the copper's antimicrobial properties and protect against the risk of excessive oxidative damage [14].

There is recent evidence that iron, zinc and copper metabolism disturbances are closely linked with inflammatory biomarkers, and disease severity in bacterial infections. These trace elements are of interest and have been investigated jointly, especially the relationship between copper and zinc (Cu/Zn) which has been suggested as a systemic inflammatory, oxidative stress and clinical outcome marker [15,16]. Although there is an expanding literature on the metabolism of the micronutrients in infections, there have been few studies specifically focused on changes in the micronutrient homeostasis of patients

infected with multidrug-resistant (MDR) bacteria. Furthermore, there is still a fair amount of uncertainty about the connection between the imbalances of trace elements, inflammatory reactions and MDR bacterial infections, particularly in developing countries where antimicrobial resistance is still rising [17].

Thus the present study was performed to assess the status of iron, zinc and copper homeostasis in patients with multidrug resistant bacterial infections (MDR) as compared to non-MDR and healthy controls. Moreover, associations of trace elements concentrations with inflammatory parameters and hematological parameters with MDR and with the presence or absence of bacterial infection were explored, with the aim of better understanding the role of micronutrient homeostasis in the pathophysiology of bacterial infections with antimicrobial resistant bacteria.

2. Methodology

The current study is a case–control research that took place in Microbiology and Central Clinical Laboratories, Al-Habbobi Teaching Hospital, Thi-Qar Health Directorate, Thi-Qar, Iraq, from 12 June 2025 until 10 March 2026, aimed at assessing the role of iron, zinc, and copper homeostasis in multidrug-resistant (MDR) bacterial infections. Fifteen patients with culture-proven MDR bacterial infection were randomly assigned to 2 groups: culture-proven non-MDR bacterial infection (60 patients) and healthy patients (30). Laboratory diagnosis of a bacterial infection was required for adults (age 18-75). Antimicrobial susceptibility testing by Kirby–Bauer disk diffusion method on Mueller–Hinton agar was performed, following the internationally accepted criteria and the guidelines of the Clinical and Laboratory Standards Institute (CLSI), and MDR isolates were defined as strains of bacteria resistant to three or more classes of antimicrobial drugs. Bacterial identification was done by the conventional microbiological techniques such as Gram staining, the morphology of the colonies and the standard biochemical tests.

The following were excluded from this study: viral, fungal or parasitic infections, any liver or kidney disease (chronic), autoimmune disorder, malignancy, hematological diseases and recent blood transfusion (within 3 months of the study). The blood samples were taken from each subject about 8 mL of venous blood was taken and collected under aseptic conditions. The blood samples were collected in EDTA tubes for complete blood count and plain gel tubes for serum separation. At the end of 10 minutes of centrifugation, the serum samples were collected and stored at −20°C for analysis. The levels of serum iron, ferritin, transferrin, total iron binding capacity (TIBC), zinc and copper were determined by commercially available kits, as per the manufacturer's procedures. The C-reactive protein (CRP) level of blood was estimated using immunoturbidimetric assay technique and serum levels of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) by enzyme linked immunosorbent assay (ELISA) kits. Complete blood count was performed in a fully-automated haematology analyzer. To achieve measurement accuracy and precision, internal quality control samples and calibrators were added along the analytical processes.

Statistical analysis

The IBM SPSS Statistics version 26.0 (Armonk, NY, USA, IBM Corp., USA) software program was used for statistical analysis. All the continuous variables were reported as mean and standard deviation (SD) and all the categorical variables were reported as percentages. Shapiro–Wilk test was used to test the normality of data, and Levene's test was used to test the homogeneity of variance. Comparisons between groups were made using one way analysis of variance (ANOVA) with Tukey's post hoc test and chi-square test was used for categorical variables. The correlations of concentrations of trace elements with inflammatory biomarkers were assessed by Pearson correlation and multiple logistic regression was used to determine independent factors associated with MDR bacterial infection. The p value of less than 0.05 was taken as a significant result. The study was

approved by the Institutional Research Ethics Committee before the study and all the procedures followed the declaration of Helsinki. Informed consent was obtained from all the participants prior to enrollment.

Ethical approval

No recruitment of participants was done without first obtaining approval from the appropriate Institutional Research Ethics Committee. All participants gave informed written consent after being thoroughly explained the objective and procedures of the study. The confidentiality of the data collected was respected and participant privacy was ensured during the study according to the Declaration of Helsinki.

3. Results and Discussion

Baseline demographic variables, clinical characteristics, and inflammatory cell counts of healthy individuals compared with patients diagnosed with non-MDR and MDR bacterial infections.

No significant differences were found between the three groups in terms of age or sex distribution ($P > 0.05$ for both). Patients with MDR bacterial infections, however, had a significantly higher BMI ($P = 0.028$) compared to those without MDR infections. Diabetes mellitus, prior antibiotic use and medical hospitalization rates were significantly higher in the non-MDR and MDR infections groups than in the healthy control groups and worsened further from the healthy control groups to the non-MDR and MDR groups, respectively ($P \leq 0.018$). Additionally, the white blood cell (WBC) count was significantly higher in infected patients, and highest in the MDR group ($P < 0.001$), indicating a higher systemic inflammatory response of multidrug-resistant bacterial infections.

Table 1. Comparison of Demographic Characteristics, Clinical Risk Factors, and Baseline White Blood Cell Counts Among Healthy Controls and Patients with Non-MDR and MDR Bacterial Infections.

Variable	Healthy Controls n=30	Non-MDR Infection n=60	MDR Infection n=60	P-value
Age (years)	42.6 ± 12.1	44.8 ± 13.4	46.2 ± 12.8	0.412
Male/Female	16/14	31/29	34/26	0.731
BMI (kg/m²)	25.1 ± 3.4	26.8 ± 4.1	27.6 ± 4.3	0.028
Diabetes mellitus, n (%)	3 (10.0)	14 (23.3)	22 (36.7)	0.018
Previous antibiotic use, n (%)	2 (6.7)	18 (30.0)	35 (58.3)	<0.001
Hospitalization history, n (%)	1 (3.3)	12 (20.0)	27 (45.0)	<0.001
WBC (×10³/μL)	6.7 ± 1.5	10.4 ± 2.6	12.1 ± 3.1	<0.001

Comparison of the prevalence and distribution of bacterial pathogens isolated from patients with non-MDR and MDR bacterial infections according to microbiological culture results.

A total of 120 isolates of bacteria were isolated from infected patients. The commonest pathogen was Escherichia coli (36.7%) which was followed by Klebsiella pneumoniae (23.3%), Pseudomonas aeruginosa (15.0%), Staphylococcus aureus (14.2%) and Proteus mirabilis (10.8%). Escherichia coli was the predominant microorganism in the non-MDR group (40.0%) while Klebsiella pneumoniae and Pseudomonas aeruginosa were proportionately more common in the MDR group (26.7% and 18.3%, respectively). These results suggest that Gram-negative bacteria, especially E. coli and K. pneumoniae, continue to be the most prevalent pathogens in non-MDR and MDR bacterial infections.

Table 2. Distribution and Frequency of Bacterial Isolates Among Patients with Non-Multidrug-Resistant and Multidrug-Resistant Bacterial Infections.

Bacterial isolate	Non-MDR n=60	MDR n=60	Total n=120
Escherichia coli	24 (40.0)	20 (33.3)	44 (36.7)
Klebsiella pneumoniae	12 (20.0)	16 (26.7)	28 (23.3)
Pseudomonas aeruginosa	7 (11.7)	11 (18.3)	18 (15.0)
Staphylococcus aureus	9 (15.0)	8 (13.3)	17 (14.2)
Proteus mirabilis	8 (13.3)	5 (8.4)	13 (10.8)

Serum iron profile, zinc, copper, and copper-to-zinc ratio in healthy individuals compared with patients having non-MDR and MDR bacterial infections.

There was a significant difference in iron metabolism and trace metal homeostasis between all the study groups (all $P < 0.001$). The serum levels of ferritin, copper and copper to zinc (Cu/Zn) ratio were significantly higher in the MDR group compared to the other groups, while the levels of serum iron, transferrin and total iron-binding capacity (TIBC) were significantly lower. The intermediate values were seen in the patients with non-MDR infections. These results suggest that there is significant deregulation of iron metabolism and trace elements balance, especially in multidrug-resistant bacterial infections.

Table 3. Comparison of Iron Metabolism Parameters and Trace Element Homeostasis Among Healthy Controls and Patients with Non-MDR and MDR Bacterial Infections.

Parameter	Healthy Controls n=30	Non-MDR Infection n=60	MDR Infection n=60	P-value
Serum iron (μg/dL)	92.4 ± 18.6	68.7 ± 17.2	54.3 ± 15.8	<0.001
Ferritin (ng/mL)	86.5 ± 34.7	168.4 ± 72.6	246.8 ± 96.5	<0.001
Transferrin (mg/dL)	286.3 ± 42.5	238.7 ± 39.4	204.6 ± 36.8	<0.001
TIBC (μg/dL)	326.5 ± 48.1	284.2 ± 44.7	251.8 ± 41.6	<0.001
Zinc (μg/dL)	88.6 ± 13.5	71.4 ± 12.8	60.7 ± 11.6	<0.001
Copper (μg/dL)	101.2 ± 18.4	124.7 ± 22.5	143.6 ± 28.1	<0.001
Cu/Zn ratio	1.15 ± 0.24	1.76 ± 0.41	2.39 ± 0.62	<0.001

Assessment of systemic inflammatory biomarkers and hematological indices in healthy individuals compared with patients affected by non-MDR and MDR bacterial infections.

The levels of inflammatory biomarkers and hematological changes were significantly different between patients suffering from bacterial infections and healthy controls (all $P < 0.001$). The highest level of CRP, IL-6, TNF-α, neutrophil percentage and platelet count were seen in the MDR infection group while the lowest level of hemoglobin was seen in the same group. Intermediate values were seen in those with non-MDR infections. The results suggest that multidrug resistant bacterial infections are significantly more likely to induce a systemic inflammatory response compared to non-MDR infections, and also cause more hematological disturbances.

Table 4. Comparison of Inflammatory Biomarkers and Hematological Parameters Among Healthy Controls and Patients with Non-Multidrug-Resistant and Multidrug-Resistant Bacterial Infections.

Parameter	Healthy Controls n=30	Non-MDR Infection n=60	MDR Infection n=60	P-value
CRP (mg/L)	3.2 ± 1.5	28.6 ± 14.7	49.8 ± 21.5	<0.001
IL-6 (pg/mL)	8.4 ± 3.1	31.7 ± 13.5	52.4 ± 20.6	<0.001
TNF-α (pg/mL)	11.2 ± 4.5	26.8 ± 10.4	39.6 ± 15.2	<0.001
Hemoglobin (g/dL)	13.7 ± 1.2	12.4 ± 1.5	11.6 ± 1.6	<0.001
Neutrophils (%)	58.3 ± 7.6	72.5 ± 9.4	78.6 ± 10.2	<0.001
Platelets ($\times 10^3/\mu L$)	248.6 ± 61.4	312.8 ± 78.6	358.7 ± 92.5	<0.001

Pearson's correlation analysis between iron metabolism biomarkers, trace elements, inflammatory cytokines, and white blood cell count in infected patients.

Significant correlation among iron metabolism, inflammatory biomarkers and trace element homeostasis was suggested by Pearson's correlation analysis. Serum iron, zinc, ferritin, copper and its ratio to zinc (Cu/Zn) were moderately negatively correlated with CRP, IL-6, TNF-α, and WBC count (all $P \leq 0.002$), while moderate positive correlations were observed between ferritin and inflammatory markers (all $P \leq 0.002$).Serum iron and zinc moderately negatively correlated with CRP, IL-6, TNF-α, and WBC count (all $P \leq 0.002$), and moderately positively correlated with ferritin and inflammatory markers (all $P \leq 0.002$), while copper had moderate positive correlations with all inflammatory markers (all $P \leq 0.002$). The highest positive correlation was seen between the Cu/Zn ratio and CRP ($r = 0.61$) and between the Cu/Zn ratio and IL-6 ($r = 0.58$), indicating that the more the inflammation progressed, the more the disruption of iron metabolism and trace elements' homeostasis occurred in patients with MDRBIs.

Table 5. Correlation Between Iron Metabolism, Trace Element Homeostasis, and Inflammatory Biomarkers in Patients with Multidrug-Resistant Bacterial Infections.

Variable	CRP	IL-6	TNF-α	WBC
Serum iron	$r = -0.46$, $p<0.001$	$r = -0.42$, $p<0.001$	$r = -0.38$, $p<0.001$	$r = -0.31$, $p=0.001$
Ferritin	$r = 0.55$, $p<0.001$	$r = 0.51$, $p<0.001$	$r = 0.44$, $p<0.001$	$r = 0.36$, $p<0.001$
Zinc	$r = -0.49$, $p<0.001$	$r = -0.45$, $p<0.001$	$r = -0.41$, $p<0.001$	$r = -0.34$, $p<0.001$
Copper	$r = 0.43$, $p<0.001$	$r = 0.40$, $p<0.001$	$r = 0.37$, $p<0.001$	$r = 0.29$, $p=0.002$
Cu/Zn ratio	$r = 0.61$, $p<0.001$	$r = 0.58$, $p<0.001$	$r = 0.50$, $p<0.001$	$r = 0.41$, $p<0.001$

Independent demographic, clinical, iron metabolism, trace element, and inflammatory predictors of multidrug-resistant bacterial infections identified using logistic regression analysis.

Several independent predictors of bacterial infections with resistance to multiple antibiotics (MDRI) were identified by multivariate logistic regression analysis. Previous antibiotic use (OR = 3.12, P = 0.002) and a high copper-to-zinc (Cu/Zn) ratio (OR = 3.36, P = 0.001) were the strongest risk factors, followed by hospitalization history (OR = 2.68, P = 0.008), elevated ferritin (OR = 2.73, P = 0.005), low serum zinc (OR = 2.41, P = 0.011), elevated C-reactive protein (CRP) (OR = 2.18, P = 0.027), and diabetes mellitus (OR = 1.94, P = 0.046). The results presented herein suggest that pre-existing healthcare exposure, disturbances of iron and trace element homeostasis and systemic inflammatory responses are separate risk factors for MDR bacterial infections.

Table 6. Multivariate Logistic Regression Analysis of Independent Risk Factors Associated with Multidrug-Resistant Bacterial Infections Among the Study Population.

Variable	OR	95% CI	P-value
Previous antibiotic use	3.12	1.54–6.31	0.002
Hospitalization history	2.68	1.29–5.57	0.008
Diabetes mellitus	1.94	1.01–3.72	0.046
Low serum zinc	2.41	1.22–4.76	0.011
High ferritin	2.73	1.35–5.52	0.005
High Cu/Zn ratio	3.36	1.61–7.02	0.001
Elevated CRP	2.18	1.09–4.36	0.027

4. Discussion

The present results indicated that the multidrug resistant (MDR) bacterial infections was significantly related with the higher level of disturbance in iron, zinc and copper homeostasis compared with non-MDR bacteria or healthy subjects. When no significant differences were found between age and sex groups, the biochemical differences were less likely to be merely the results of a simple demographic imbalance. The increased rates of diabetes among MDR cases however, coupled with previous antibiotic use and hospitalization, suggests an important contribution of comorbidities and healthcare exposures to antimicrobial resistance, as well as its well documented presence in this context [18].

A significant reduction in serum iron, transferrin and T.I.B.C was seen in infected patients and even more in the MDR ones was one important finding. This finding is biologically relevant because acute bacterial infection induces the host's immune defence mechanism called “nutritional immunity” that limits access of microbes to essential metals (iron) [19]. The higher ferritin levels in MDR patients may be due to iron sequestration as well as inflammatory activation as ferritin is an acute phase reactant in infection [20]. In other studies, low levels of iron in the blood and elevated levels of ferritin have been associated with severe bacterial and inflammatory diseases [21]. In contrast, certain studies have found normal or even elevated serum iron in localized infections, which could be attributable to variations in the severity of the infection, the time of the specimen taken, the liver function and/or previous iron therapy [22].

The zinc level was significantly lower for MDR patients as compared to non-MDR patients and control. Zinc plays a significant role in the integrity of the epithelium, innate immune signaling and function and inflammatory cytokines [23]. Therefore, low zinc levels might indicate the augmentation in zinc consumption in inflammatory process or zinc redistribution to tissues or low nutritional status in severely affected patients. This is in line with previous reports that showed that low zinc levels were associated with increased inflammatory response and infectious outcomes [24]. Other experimental research however shows that too much zinc could also be a factor in the bacteria's ability to become stress resistant, antifoam, and form biofilms [25]. This paradox may be explained by the difference between the serum zinc status of the host and the intracellular zinc status of the bacteria; the bacterial zinc handling system and/or zinc excess in the wound may help bacteria survive while zinc deficiency in the host may help to impair host immunity.

The level of copper and Cu/Zn ratio were significantly higher in MDR infections. Copper is an acute-phase trace element that increases with systemic inflammation in part, because of the increase in ceruloplasmin [26]. The Cu/Zn ratio has become a more and more considered and comprehensive indicator of the inflammatory burden and immune-metabolic imbalance and sometimes is more accurate than the two metals separately [27]. The high ratio of Cu/Zn seen in the patients with MDR is parallel with the increased values of CRP, IL-6, TNF-α and WBC in these patients. In addition, there are reports of an

association between high Cu/Zn ratio and infectiousness and inflammation in respiratory and systemic infections [28]. Contrary to this, in a few studies with malnourished or critically ill patients, the Cu level may be reported as decreased or even deficient instead of elevated, which may be due to prolonged disease, nutritional depletion, liver dysfunction or differences in disease phase [29].

The inflammatory profile also backs the results of the trace-elements. CRP, IL-6, TNF- α, neutrophil percentage and platelet count were higher while hemoglobin was lower in patients with MDR. The changes indicate a higher degree of systemic inflammatory response in MDR infections. IL-6 is able to induce the production of hepcidin by hepatocytes which inhibits iron absorption and sequesters iron into macrophages leading to low serum iron and anemia of inflammation [30]. This mechanism indicates that a similar link between low iron level, high ferritin and low hemoglobin could be present in MDR patients. The elevated platelet count could also be caused by inflammation mediated thrombopoiesis that is typical in bacterial infections [31].

A positive correlation was observed between ferritin, copper and the inflammatory markers (CRP, IL-6, TNF-α and WBC), while serum iron and zinc were negatively correlated with the inflammatory markers. The associations are similar to what one might expect based on the idea that the trace-elements re-distributed are closely correlated to inflammatory level and not independent nutritional disorders [32]. The highest correlation was found for Cu/Zn ratio, thus, this ratio could be used as a helpful additional inflammatory severity marker in bacterial infections. It should be noted, however, that these correlations do not imply causation, that they should be "taken with a grain of salt" [33].

Logistic regression analysis showed that previous antibiotic use, history of hospitalization, diabetes mellitus, low level of zinc, high level of ferritin, high Cu/Zn ratio and high level of CRP were associated with MDR infection. The clinical sense of these results is reasonable since the selection pressure from antibiotics, and hospitalisation, positively selects for resistant organisms and diabetes may affect immunity and the risk of recurrent infection [34]. Trace-element abnormalities were only related to MDR implying changes in metal homeostasis might be a marker for the severity of infection, inflammatory burden or host susceptibility. It is important to note that these markers are not interpreted as causation of MDR infection but rather, the design of the case-control was employed [35].

5. Conclusion

Finally, the results suggest that a distinct dyshomeostasis of metals occurs in MDR bacterial infections characterized by iron restriction, zinc depletion, increase in ferritin, increase in copper and increase in Cu/Zn ratio. These changes seem to parallel systemic inflammation, and may give valuable ancillary data when trying to evaluate the severity of an infection. Variations with some of previous studies may be due to differences in the species of bacteria, infection site, nutritional status, comorbidities, previous antibiotic use, timing of samples and analytical methods. Longitudinal studies are required in the future to establish if the alterations in the trace elements are preceding or are primarily due to inflammatory response to MDR infection.

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