ORIGINAL ARTICLE

PREDICTORS OF HAIR ZINC DEFICIENCY AND ITS ASSOCIATION WITH THE SEVERITY OF COMMUNITY-ACQUIRED PNEUMONIA IN DR. CIPTO MANGUNKUSUMO NATIONAL GENERAL HOSPITAL

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ABSTRACT

Background: Zinc deficiency can cause immune disorders that can increase the severity of community-acquired pneumonia (CAP). One of the potential biomarkers of zinc deficiency is hair zinc levels because they are more stable. However, because zinc levels are not routinely tested, clinical predictors are needed to determine the profile of patients at risk of zinc deficiency, especially in CAP patients.
Methods: This study is a cross-sectional study using primary data. Ninety-three adult patients who were hospitalized with CAP at Cipto Mangunkusomo National General Hospital in July-August 2023 were included in this study. Sampling used the consecutive sampling method. Hair zinc levels were analyzed using spectrophotometry. Zinc intake during the last month was assessed using a semiquantitative food frequency questionnaire (FFQ). Medical history was obtained from hospital medical records and laboratory examinations. Bivariate tests using chi-square tests were performed on age, sex, nutritional status, diabetes mellitus, malabsorption, chronic kidney disease, liver cirrhosis, HIV/AIDS, and malignancies with hair zinc deficiency. Identification of predictors for hair zinc deficiency was carried out using a multivariate logistic regression test. A bivariate test was also performed using chi-square to assess the association between hair zinc deficiency and the severity of CAP, and then a multivariate analysis was performed on confounding variables.
Results: 10.75% of patients experienced hair zinc deficiency. Predictors for hair zinc deficiency in community-acquired pneumonia patients were diabetes mellitus (PR 4.800; 95% CI 1.339 – 17.199) and HIV/AIDS status (PR 6.000; 95% CI 1.356 – 26.544). There was no significant relationship between hair zinc deficiency and the severity of CAP.
Conclusion: The prevalence of hair zinc deficiency in this study population was 10.75%. Predictors for hair zinc deficiency in community-acquired pneumonia patients are diabetes mellitus and HIV/AIDS. However, there was no association between hair zinc deficiency and the severity of CAP in this study population.
Keywords: predictors, hair zinc deficiency, community-acquired pneumonia

ABSTRAK

Latar Belakang : Defisiensi seng dapat menyebabkan gangguan imunitas yang memperberat manifestasi klinis dari pneumonia komunitas. Seng pada rambut merupakan biomarker yang potensial karena kadarnya lebih stabil. Namun, karena pemeriksaan kadar seng tidak rutin dilakukan, dibutuhkan prediktor klinis terkait profil pasien yang berisiko mengalami defisiensi seng, secara khusus pada pasien pneumonia komunitas.
Tujuan : Mengetahui prediktor defisiensi seng rambut pada subjek pneumonia komunitas dan mengetahui hubungan antara defisiensi seng rambut dengan derajat beratnya klinis pneumonia komunitas.
Metode : Penelitian ini merupakan penelitian potong lintang dengan menggunakan data primer. Sembilan puluh tiga pasien dewasa yang menjalani rawat inap di RSCM pada bulan Juli-Agustus 2023 disertakan dalam studi. Pengambilan sampel menggunakan metode consecutive sampling. Kadar seng rambut dianalisis dengan metode spektrofotometri. Asupan seng selama sebulan terakhir dinilai dengan menggunakan food frequency questionnaire semikuantitatif. Riwayat medis diperoleh dari rekam medis RS dan pemeriksaan laboratorium. Dilakukan uji bivariat menggunakan Chi-Square terhadap usia, jenis kelamin, status gizi, asupan seng, diabetes melitus, malabsorpsi, penyakit ginjal kronik, sirosis hepatis, HIV/AIDS, dan keganasan dengan defisiensi seng rambut. Identifikasi faktor prediktor defisiensi seng rambut dilakukan dengan uji multivariat regresi logistik. Selain itu juga dilakukan uji bivariat menggunakan Chi-square untuk menilai hubungan antara defisiensi seng rambut dan derajat beratnya pneumonia komunitas, kemudian dilakukan analisis multivariat terhadap variabel perancu.
Hasil: Sepuluh koma tujuh lima persen (10,75%) pasien mengalami defisiensi seng rambut. Faktor prediktor defisiensi seng rambut pasien pneumonia komunitas yaitu diabetes melitus (PR 4,800; IK 95% 1,339 – 17,199) dan status HIV/AIDS (PR 6,000; IK 95% 1,356 – 26,544). Tidak didapatkan hubungan bermakna antara defisiensi seng rambut dan derajat beratnya klinis pneumonia komunitas.
Kesimpulan: Prevalensi defisiensi seng rambut pada populasi studi ini yaitu 10,75%. Faktor prediktor defisiensi seng rambut pada pasien pneumonia komunitas antara lain diabetes melitus dan HIV/AIDS. Namun tidak didapatkan hubungan antara defisiensi seng rambut dengan derajat beratnya klinis pneumonia komunitas pada populasi studi ini.
Kata kunci: prediktor, defisiensi seng, seng rambut, pneumonia komunitas

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Predictors of Hair Zinc Deficiency and Its Association with the Severity of Community-Acquired Pneumonia in Dr. Cipto Mangunkusumo National General Hospital

BACKGROUND

Community-acquired pneumonia is a major cause of hospitalization, mortality, and significant healthcare costs. The multiplication of pathogens at the alveolar level and the host's reaction to it result in pneumonia. Pneumonia may present in more severe clinical manifestations if the activity of pathogens invading the alveoli exceeds the ability of macrophages to remove them.[1]

Zinc deficiency is associated with impaired innate and adaptive immunity, thereby increasing the frequency and duration of infections, especially community-acquired pneumonia.[2] Zinc deficiency can be caused by insufficient intake, impaired absorption, increased need for or loss of zinc, and impaired utilization of zinc.[3] Conditions that can increase the risk of zinc deficiency are older age, malabsorption syndrome, diabetes, HIV/AIDS (acquired immune deficiency syndrome), chronic kidney disease, liver cirrhosis, and malignancy.[4,5] Data regarding the epidemiology of zinc deficiency are still limited and varied. Sandjaja et al.[6] reported serum zinc deficiency in 19.7% of healthy adult men and 29.2% of women. While Satyani et al.[7] reported hair zinc deficiency of 41.5% in head and neck cancer patients on radiation therapy.

Research on the relationship between zinc deficiency and community-acquired pneumonia is still limited and generally uses blood zinc samples. Bhat et al.[8] reported that serum zinc levels in community-acquired pneumonia subjects were lower than those in controls. Meydani et al.[9] reported that serum zinc levels are strongly associated with the incidence and duration of pneumonia as well as the use and duration of antibiotics. Although it is more commonly used, serum zinc levels are only found to be 0.1% in circulation and are highly dependent on food intake, time of sample collection, technique of sample collection and storage. Hair zinc samples are potential examination because they have higher levels than blood and are more stable.[2,10] A systematic review by Lowe et al.[11] reported that examination of hair zinc samples was effective with homogeneous studies (I2= 0%) and good effect size (weighted mean difference 13.24; CI 95% 11.91-14.56), while serum/plasma zinc studies were highly heterogeneous (I2= 93.6%). To the best of our knowledge, this study is by far the first to assess the relationship between hair zinc deficiency and the clinical severity of community-acquired pneumonia.

METHODS

Study design and participants

This cross-sectional study recruited adult patients (18 years old or older) admitted to the emergency department and inpatient wards with CAP at Cipto Mangunkusomo National General Hospital in July-August 2023. Hair samples (200 mg) were taken for zinc level examination in patients who agreed to participate. Meanwhile, patients with decreased consciousness or cognitive impairment and unaccompanied by a caregiver who could be asked about a semiquantitative food frequency questionnaire (FFQ); who had received zinc supplementation; and who had a history of consumption of proton pump inhibitors, H2 receptor antagonists, diuretics, sodium valproate, penicillamine, quinolone antibiotics, tetracycline, and iron supplementation for at least 8 weeks in at least 4 weeks before treatment were not recruited. Diagnostic predictor factors for hair zinc levels assessed in this research are age, sex, nutritional status, and comorbidities (diabetes mellitus, chronic kidney disease, HIV/AIDS, malabsorption, malignancy).

Baseline data

The research data were collected by documenting basic demographic, clinical, and other supporting data. Zinc intake was assessed with a semiquantitative FFQ. The clinical severity of pneumonia was determined using 2019 ATS/IDSA CAP guidelines for severe CAP criteria. Spectrophotometry was used to measure hair zinc levels at Jakarta Regional Health Laboratory.

Statistical analysis

Research data analysis was carried out using SPSS version 24.0 and STATA. A bivariate analysis was conducted followed by a multivariate logistic regression to identify predictors for hair zinc deficiency and the association between hair zinc deficiency and the clinical severity of community-acquired pneumonia. This research received ethical approval and research location from the Health Research Ethics Committee, Faculty of Medicine, University of Indonesia.

RESULTS

Out of 109 community-acquired pneumonia subjects, 16 were excluded (four subjects with decreased consciousness and no caregiver, 1 subject consumed zinc supplements, 1 subject consumed PPIs, 3 subjects consumed diuretics, and 7 subjects refused to participate). As a result, 93 subjects were included in this study. The characteristics of the subjects involved in this study can be seen in Table 1. Hair zinc deficiency in community-acquired pneumonia subjects was 10.75%. The mean age of the research subjects was 53.15 (SD 16.40) years. The majority of the subjects were female (73.12%). The most common comorbidity was malignancy (35.48%). The majority of nutritional status in this study was normal (36.56%). The study subjects consisted of 33 subjects (35.48%) with severe community-acquired pneumonia and 60 subjects (64.52%) with nonsevere community-acquired pneumonia. There were 10 subjects (10.75%) with hair zinc deficiency and 83 subjects (89.25%) without hair zinc deficiency.

Table 1. Baseline Characteristics of the Subjects

Characteristics	Subjects (n = 93)
Age, mean (SD)	53.15 (16.40)
Age group (n,%)	
≥ 60 years old	34 (36.56)
18 - 59 years old	59 (63.44)
Sex, n (%)	
Male	25 (26.88)
Female	68 (73.12)
Education, n (%)	
Low education level	16 (17.20)
Middle education level	50 (53.76)
High education level	27 (29.03)
Comorbidity, n (%)	
Diabetes Mellitus	15 (16.13)
Chronic Kidney Disease	28 (30.11)
Liver cirrhosis	5 (5.38)
Malignancy	33 (35.48)
Malabsorption	1 (1.08)
HIV/AIDS	6 (6.45)
Anthropometry	
Body weight (mean, SD)	52.42 (11.39)
Height (median, IQR)	157 (154-160)
Body mass index (mean, SD)	21.22 (4.32)
Nutritional status (n, %)	
Underweight	27 (29.03)
Normal	34 (36.56)
Overweight	20 (21.51)
Obese	12 (12.90)
Severity of CAP (n, %)	
Severe	33 (35.48)
Nonsevere	60 (64.52)
Zinc intake (median, IQR)	6.10 (3.70-9)
Zinc intake (n, %)	
Insufficient	54 (58.06)
Adequate	39 (41.94)
Hair zinc level (median, IQR)	142.39 (98.12 – 208.15)
Hair zinc deficiency category (n, %)	
Deficiency	10 (10.75)
Without hair zinc deficiency	83 (89.25)

The association between hair zinc deficiency and the independent variables analyzed using the chi-square test showed that diabetes mellitus was found to be a significant predictor of hair zinc deficiency, as listed in Table 2. Diabetes mellitus, chronic kidney disease, and HIV/AIDS were included in the multivariate analysis to identify predictors for hair zinc deficiency among these variables.

Table 2. Bivariate Analysis for Predictor Factors of Hair Zinc Deficiency

Variables	Hair Zinc Levels		PR (CI 95%)	p value
	Deficiency (n=10)	Without deficiency (n=83)		
Age group (n,%)				
Elderly	5 (14.71)	29 (85.29)	1.735 (0.537 – 5.601)	0.357
Non elderly	5 (8.47)	54 (91.53)		
Sex, n (%)				
Male	4 (16.00)	21 (84.00)	1.813 (0.554 – 5.934)	0.325
Female	6 (8.82)	62 (91.18)		
Nutritional status (n, %)				
Underweight	3 (11.11)	24 (88.89)	0.944 (0.229 – 3.893)	0.937
Overweight	0 (0.0)	20 (100.0)	-	-
Obese	3 (25.0)	9 (75.0)	2.125 (0.550 – 8.209)	0.274
Normal	4 (11.76)	30 (88.24)	Ref	
Comorbidity, n (%)				
Diabetes Mellitus				
Yes	4 (26.67)	11 (73.33)	3.467 (1.104 – 10.886)	**0.033**
No	6 (7.69)	72 (92.31)		
Chronic Kidney Disease				
Yes	5 (17.86)	23 (82.14)	2.321 (0.725 – 7.435)	0.156
No	5 (7.69)	60 (92.31)		
Liver cirrhosis				
Yes	1 (20.0)	4 (80.0)	1.955 (0.302 – 12.678)	0.482
No	9 (10,23)	79 (89,77)		
Malignancy				
Yes	5 (15.15)	28 (84.85)	1.819 (0.564 – 5.863)	0.317
No	5 (8.22)	55 (91.67)		
Malabsorption				
Yes	0 (0.0)	1 (100.0)	-	-
No	10 (10.87)	82 (89.13)		
HIV/AIDS				
Yes	2 (33.3)	4 (66.7)	3.625 (0.971 – 13.533)	0.124
No	8 (9.2)	79 (90.8)		
Zinc Intake				
Insufficient	4 (7.41)	50 (92.59)	0.481 (0.145 – 1.603)	0.234
Adequate	6 (15.38)	33 (84,62)		

A multivariate logistic regression test using the backward method showed that diabetes mellitus and HIV/AIDS had a significant effect on hair zinc deficiency ($p<0.05$), with the prevalence ratio shown in Table 3.

Table 3. Multivariate Analysis for Predictor Factors of Hair Zinc Deficiency

Variables	PR (CI 95%)	p value
Step 1		
Diabetes Mellitus	4.217 (1.095 – 16.259)	0.037
Chronic Kidney Disease	1.828 (0.563 – 5.934)	0.315
HIV/AIDS	5.729 (1.316 – 24.935)	0.020

Step 2		
Diabetes Mellitus	4.800 (1.339 – 17.199)	0.016
HIV/AIDS	6.000 (1.356 – 26.544)	0.018

Hair zinc deficiency was not associated with the severity of CAP (p>0.05), as shown in Table 4.

Table 4. Bivariate Analysis of the Association of Hair Zinc Deficiency and Severity of CAP

Variables	Severity of CAP		PR (CI 95%)	p value
	Severe (n = 33)	Non severe (n = 60)		
Hair zinc deficiency				
Deficiency	4 (40.0)	6 (60.0)	1.145 (0.505 – 2.595)	0.746
Without hair zinc deficiency	29 (34.94)	54 (65.07)		

To determine the association between confounding variables and severity of CAP, the bivariate test was conducted and showed a significant association between HIV/AIDS and severity of CAP, with a crude PR of 2.589 (1.614 – 4,154) and p<0.0001, as shown in Table 5.

A multivariate logistical regression test of independent variables showed that HIV/AIDS, nutritional status, and CKD were confounding variables with PR delta >10%. A fully adjusted PR of 0.698 (0.326 – 1.491) with a p value of 0.354 was obtained, as shown in Table 6.

Table 5. Bivariate Analysis of the Association of Confounding Variables and the Severity of CAP

Variables	CAP Clinical Severity		PR (CI 95%)	p value
	Severe (n=33)	Non severe (n=60)		
Age group (n,%)				
Elderly	12 (35.29)	22 (64.71)	0.991 (0.559 – 1.759)	0.977
Non elderly	21 (25.59)	38 (64.41)		
Nutritional status, n (%)				
Underweight	14 (51.85)	13 (48.15)	1.603 (0.871 – 2.950)	0.130
Overweight	3 (15.0)	17 (85.0)	0.464 (0.146 – 1.475)	0.193
Obese	5 (41.67)	7 (58.33)	1.288 (0.560 – 2.959)	0.551
Normal	11 (32.35)	23 (67.65)	Ref	
Comorbidity, n (%)				
Diabetes Mellitus				
Yes	4 (26.67)	11 (73.33)	0.717 (0.294 – 1.750)	0.465
No	29 (37.18)	49 (62.82)		
Chronic Kidney Disease				
Yes	12 (42.86)	16 (57.14)	1.326 (0.760 – 2.315)	0.320
No	21 (32.31)	44 (67.69)		
Liver cirrhosis				

Yes	1 (20.0)	4 (80.0)	0.550 (0.092 – 3.275)	0.511
No	32 (36.36)	56 (63.64)		
Malignancy				
Yes	11 (33.33)	22 (66.67)	0.909 (0.504 – 1.639)	0.751
No	22 (36.67)	38 (63.18)		
HIV/AIDS				
Yes	5 (83.33)	1 (16.67)	2.589 (1.614 – 4.154)	**<0.0001**
No	28 (32.18)	59 (67.82)		

Table 6. Multivariate Analysis of Confounding Variables

Variables	PR (CI 95%)	p value	Delta PR
Crude PR :			
Hair zinc deficiency	1.145 (0.505 – 2.595)	0.746	
Adjusted PR *:*			
+ HIV/AIDS	0.931 (0.394 – 2.196)	0.870	**22.98**
+ Nutritional status	0.780 (0.342 – 1.779)	0.555	**19.35**
+ Chronic kidney disease	0.699 (0.309 – 1.580)	0.390	**11.58**
+ Diabetes mellitus	0.714 (0.318 – 1.601)	0.413	2.10
+ Hepatic cirrhosis	0.726 (0.323 – 1.629)	0.438	1.65
+ Malignancy	0.725 (0.327 – 1.607)	0.429	0.13
+ Age	0.698 (0.326 – 1.491)	0.354	3.86

We also carried out an analysis of differences in hair zinc levels in the independent variables based on age group, diabetes mellitus, HIV status, and glucose control. There was a significant difference between the median hair zinc levels of the elderly group and the non elderly group, as shown in Table 7.

Table 7. Differences in Hair Zinc Levels in Elderly and Non Elderly Subjects

Variables	Elderly (n=34)	Non-elderly (n=59)	p value
	Median (IQR)	Median (IQR)	
Hair zinc level (µg/g)	116.37 (87.30-167.31)	149.54 (115.90 – 245.91)	0.027

There was also a significant difference in the hair zinc levels of the diabetic and nondiabetic groups, as shown in Table 8.

Table 8. Differences in Hair Zinc Levels of Diabetic and Non Diabetic Subjects

Variables	Diabetic (n=15)	Non Diabetic (n=78)	p value
	Median (IQR)	Median (IQR)	
Hair zinc level (µg/g)	92.54 (72.99-127.69)	146.82 (111.54-227.05)	0.006

There was also a significant difference in hair zinc levels between the HIV/AIDS group and the non-HIV/AIDS group (median 86.01 [RIK 67.98 – 114.61] vs median 144.78 [IQR 101.61 – 220.17], respectively), as shown in Table 9.

Table 9. Differences in Hair Zinc Level of HIV status

Variables	HIV/AIDS (n=6)	Non HIV/AIDS (n=87)	p value
	Median (IQR)	Median (IQR)	
Hair zinc level (µg/g)	86.01 (67.98 – 114.61)	144.78 (101.61 – 220.17)	0.045

A one-way ANOVA test on the subjects with diabetes was carried out to determine the difference in mean hair zinc levels between each glucose control group, as shown in Table 10. There were no significant differences between the glucose control groups.

Table 10. Differences in Hair Zinc Level based on Glucose Control

Variables	n (%)	Hair zinc level (µg/g)	p value
Diet	7 (46.7)	93.16 ± 63.57	0.444
Anti-diabetic drugs	3 (20)	164,95 ± 119.32	
Insulin	5 (33.3)	112,5 ± 74.1	

DISCUSSION

The prevalence of hair zinc deficiency in community-acquired pneumonia subjects was found to be 10.75% in this study, while previous studies by Bhat et al.[8], Devrajani et al.[12], Meydani et al.[9], and Saleh et al.[13] reported that the prevalence of plasma/serum zinc deficiency in community-acquired pneumonia was 30-65%. The differences may be due to the different types of zinc samples used and differences in the characteristics of the research subjects. Although serum zinc levels were more frequently measured, hair zinc levels are considered a potential biomarker reflecting circulating zinc levels at the time of hair synthesis and are not affected by exogenous zinc exposure. At normal hair growth rates (1 cm per month), hair zinc levels reflect zinc uptake by hair follicles 4-8 weeks before sampling.[2] In this cross-sectional study, hair growth rate was not measured, and heterogeneous population characteristics in this study may affect the rate of hair growth, which may influence hair zinc levels in this study.

Based on the bivariate test, it was found that diabetes mellitus, CKD and HIV/AIDS had a p value <0.2, which then proceeded to multivariate analysis. Based on the multivariate logistic regression test, the predictors for hair zinc deficiency in community-acquired pneumonia patients were diabetes mellitus (PR 4.800; 95% CI 1.339 – 17.199) and HIV/AIDS (PR 6.000; 95% CI 1.356 – 26,544).

The mean age of the research subjects was 53.15 (SB 16.40) years. There were 34 subjects (36.56%) who were elderly, which was similar to the average age of subjects in the study by Bhat et al.[8] The elderly population, apart from being at risk of community-acquired pneumonia infection, is also reported to have a low intake of zinc, which is associated with an increased risk of infection. The relationship between age group and hair zinc deficiency in this study was not significant, but hair zinc levels in the elderly group (median 116.37; IQR 87.3-167.31) were significantly lower than those in the non elderly group (median 149.54; IQR 115.9-245.91) (p = 0.027).

In contrast to the study by Bhat et al.[8], the subjects in this study were predominantly female (73,12%). This may be because male subjects often have shorter hair (200 mg of hair samples were needed for hair zinc examination), so they did not meet the inclusion criteria. Because of the increased need for zinc during pregnancy, lactation, and extra excretion during menstruation, zinc insufficiency is more common in women.[14] However, there was no significant relationship between sex and zinc deficiency in this study. The median hair zinc levels in males and females in this study were 133.52 (IQR 92,07 – 151,48) and 146.78 (IQR 101.18 – 262.49),

respectively, which did not differ significantly (p = 0.089).

Similar findings were reported by Bertazzo et al.[15] who found that there was no difference in the mean hair zinc levels in males compared to females (200.97 ± 9.68 µg/g compared to 209.81 ± 9.49 µg/g). The uneven proportion of subjects between genders is thought to have caused insignificant differences in hair zinc levels in this study.

Malnutrition can cause changes in the zinc absorption capacity of the small intestinal mucosa; on the other hand, obesity can lead to oxidative stress and chronic inflammation, both of which increase the utility of zinc.[16,17] In this study, no significant difference was found between nutritional status and hair zinc deficiency. A similar finding by Hong et al.[18] which showed no significant association between hair zinc levels and BMI. This study did not assess nutritional status using parameters other than BMI, so further research can be carried out to determine the relationship between hair zinc levels and other surrogate markers of nutritional status.

Zinc intake can cause zinc deficiency in hair if it occurs over a long period of time. Theoretically, lack of intake is one of the causes of zinc deficiency in humans. Suliburska et al.[19] did not find a significant relationship between zinc intake and zinc levels in hair. In this study, there was also no significant relationship between hair zinc levels and zinc intake, where the median hair zinc levels in the group with insufficient zinc intake was 145.08 µg/g (IQR 98.12 – 213.29) and in the sufficient zinc intake group was 133.71 µg/g (IQR 95.89 – 133.71). Meanwhile, from the bivariate analysis in this study, a protective relationship was found between insufficient zinc intake and hair zinc deficiency, with a PR of 0.481 (0.145 – 1.603) and a p value = 0.234. This variable was not included into multivariate analysis because the protective relationship was not in accordance with theory and the p value cutoff for multivariate analysis was 0.20. The discordance was thought to occur because zinc intake patterns can only be traced retrospectively for the last one month, while zinc levels in hair represent circulating zinc in the last 4-8 weeks. In this study, the median zinc intake was 6.1 mg/day (IQR 3.7 – 9), where it was found that 54% of subjects had insufficient zinc intake.

In this study, a significant association was found between diabetes mellitus and hair zinc deficiency mellitus (PR 4.800; 95% CI 1.339 – 17.199; p = 0.016). In addition, there were significant differences in hair zinc levels between subjects with diabetes mellitus (median = 92.54 µg/g; IQR 72.99 – 127.69) and those without diabetes mellitus (median = 146.82 µg/g; IQR 111.54 – 227.05). A similar finding was reported by Kazi et al.[21], Hotta et al.[22], Chen et al.[23], and Tadayon et al.[24], who reported that the hair zinc levels of subjects with diabetes mellitus were significantly lower than those of controls. The incidence of hyperzincuria, which could explain the condition of zinc deficiency in subjects with diabetes mellitus, was not examined in this study.

Although tubular damage in CKD can lead to zinc insufficiency, our study found no association between CKD and hair zinc deficiency. Ochi et al.[25] and Dlugaszek et al.[26] found a similar finding; however, their study only involved hemodialysis patients. Urinary zinc levels were not investigated, so the degree of zinc excretion through the kidneys is unknown.

Malabsorption syndrome can change the integrity of gastrointestinal mucosal cells and reduce zinc absorption.[4] Malabsorption was defined as chronic diarrhea for at least 4 weeks or a history of bowel resection with a remaining small bowel length < 200 cm. In this study, there was no association between malabsorption and hair zinc deficiency. There was only 1 subject with symptoms of malabsorption, making it difficult to assess the relationship with hair zinc deficiency.

Liver cirrhosis can cause zinc deficiency due to impaired function of albumin synthesis in the liver, excretion of zinc in the urine, and impaired zinc absorption in the intestine.[27]

However, no significant association was found between liver cirrhosis and hair zinc deficiency in this study, which was assumed to be due to the small number of subjects with liver cirrhosis.

Zinc deficiency in HIV/AIDS can occur through impaired absorption, excessive excretion in chronic diarrhea, and various opportunistic infections that increase zinc requirements.[4] In this study, HIV/AIDS was a significant predictor of hair zinc deficiency (PR 6.000; 95% CI 1.356 – 26.544; p = 0.018). In addition, there were also significant differences in hair zinc levels between HIV/AIDS (median 86.01 µg/g; IQR 67.98 – 114.61) and those without HIV/AIDS (median 144.78 µg/g; IQR 101.61 – 220.17). A similar finding was reported by Malviya et al.[28], but the study was conducted on HIV subjects compared to healthy controls.

Malignancies can cause zinc deficiency through impaired intake due to the course of the cancer, side effects of anticancer therapy, and oxidative stress.[29] In this study, there was no significant relationship between malignancy and hair zinc deficiency, and there was no significant difference in hair zinc levels between subjects with and without malignancy. Similar findings were reported by Golasik et al.[30], who found that hair zinc levels in subjects with laryngeal cancer and healthy controls were not significantly different, which is thought to be due to the wide range of hair zinc levels in both subjects with laryngeal cancer and controls.

From the bivariate analysis test, there was no significant association between hair zinc deficiency and the severity of community-acquired pneumonia. Different results were reported by Devrajani et al.[12], Saleh et al.[13], and Bhat et al[8]. which shows a relationship between serum zinc deficiency and the severity of pneumonia. This difference is thought to be due to differences in the samples used in the research.

This study is the first study in Indonesia and in the world to analyze hair zinc levels to assess zinc deficiency in CAP subjects. Limitations in this study include a cross-sectional study design that only assessed zinc levels at one time so that the rate of hair growth that could influence differences in zinc levels is unknown; determining comorbidities such as liver cirrhosis, malignancy, and HIV/AIDS using only laboratory data or imaging in medical records; possible residual confounding factors such as stage of comorbidities that were not assessed in this study; and the presence of confounders such as nutritional status, HIV/AIDS, and CKD. This study also did not measure zinc in the serum, so the correlation between the levels of zinc in the serum and hair could not be determined.

It is necessary to carry out further prospective studies related to hair zinc deficiency in populations with diabetes mellitus, the elderly and HIV/AIDS to look for the effects of zinc supplementation in these populations while also assessing the stage of comorbidities and their influence on zinc deficiency.

Conclusion

The prevalence of hair zinc deficiency in this study population was 10.75%. Predictors for hair zinc deficiency in community-acquired pneumonia patients are diabetes mellitus and HIV/AIDS. There were also significant differences in hair zinc levels, which were lower in groups with advanced age (> 60 years old), diabetes mellitus, and HIV/AIDS. However, there was no association between hair zinc deficiency and the severity of CAP in this study population.

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