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Serum biotin and zinc in male androgenetic alopecia

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Summary

Background: Male androgenetic alopecia (MAGA) is caused by the conversion of the terminal to vellus hair. Zinc is one of the most studied trace elements in hair disorders and biotin is one of the most prescribed supplement for its treatment.

Objectives: The study aimed to evaluate serum zinc and biotin levels in MAGA patients to answer the question if there is a value to add zinc or biotin as a supplements in the MAGA treatment.

Patients and Methods: Sixty MAGA patients and 60 age, sex, and body mass index-matched healthy volunteers were included. We measured serum biotin and zinc in all participants.

Results: Zinc ($\mu\text{g/dL}$) was lower significantly in patients compared to controls ($P = 0.01$), suboptimal biotin (ng/L) levels were in patients, and within normal values in controls ($P = 0.01$). A positive significant correlation was found between serum zinc and serum biotin ($r = 0.489$, $P = 0.001$). Serum zinc and biotin showed a nonsignificant correlation with age and disease duration. A non-significant relation was obtained between the MAGA grades, and zinc ($P = 0.485$) and biotin levels ($P = 0.367$).

Conclusions: Serum zinc showed subnormal value and adding zinc supplement in MAGA treatment is recommended. Serum biotin showed a suboptimal level in MAGA patients that is not correlated with patients' age or disease severity. Biotin supplement in MAGA treatment may add value to hair quality and texture. We recommend future biotin evaluation in serum combined with its metabolites in MAGA patients' urine.

KEYWORDS

androgenetic alopecia, biotin, serum, zinc

1 | INTRODUCTION

Male androgenetic alopecia (MAGA) is a noncicatricial patterned hair loss with the conversion of terminal to vellus hair.¹ The hair integrity depends on an adequate and balanced nutritional intake, and unbalanced diet may result in excessive hair shedding.² The relations of nutritional deficiency with chronic telogen effluvium, female pattern hair loss, MAGA, and alopecia areata were studied.^{3,4}

Zinc has a functional role in hair follicle cycling (animal model),⁵ a critical component in its morphogenesis,⁶ potent dose-dependent

immune-modulator of hair follicles,⁷ regulate hair growth through hedgehog signaling as it is a catagen inhibitor.⁸ Dermatological symptoms of zinc deficiency include nail dystrophy, acral and periorificial dermatitis, cheilitis, brittle hair, delayed wound healing, and skin superinfection.^{4,9} The zinc deficiency effects may appear before serum levels decrease below normal.¹⁰

Biotin is an essential water-soluble vitamin required as a cofactor for carboxylase enzymes.³ Biotin deficiency can be either congenital or acquired secondary to increased raw egg consumption,¹¹ alcoholism, pregnancy, or other medications such as isotretinoin and

valproic acid.¹² Typical dermatological symptoms of biotin deficiency include alopecia, eczematous skin rashes, and seborrheic dermatitis.¹³ Biotin's function in protein synthesis and keratin production, explains its contribution to healthy nail and hair growth.¹⁴

The present study aimed to evaluate serum zinc and biotin levels in MAGA patients. We wanted to answer the question if there is a value to add zinc or biotin as a supplement in the MAGA treatment.

2 | PATIENTS AND METHODS

This case-control study was conducted on 60 MAGA patients and 60 age, sex, and body mass index (BMI) matched healthy volunteers. This study was approved by the Research Ethics Committee in our institute according to the Declaration of Helsinki principles. Any patient with any of the following conditions was excluded from this study: a history of active malignancy, any systemic or autoimmune disease, and any neurological disorder. Patients were excluded if they received topical medications for 1 month or systemic therapy for 3 months before the study. Any participants received zinc or biotin supplementations for 3 months prior to the study were also excluded. All participants gave the informed consent before being subjected to full history taking, BMI estimation, complete general and dermatologic examination. The grading of MAGA was done according to Hamilton-Norwood classification of male balding.^{15,16}

2.1 | Biotin and zinc measurement

After 12 fasting hours, 5 mL of venous blood were collected in a plain tube without anticoagulant from all participants. Samples were left at room temperature for 30 minutes till coagulation, centrifuged at 250 g for 15 minutes, and the resultant serum stored at -20°C until analysis. Serum zinc levels were measured by the colorimetric method using ZINC Fluid Monoreagent provided by Centronic GmbH Company, Wartenberg, Germany (<http://www.centronic-gmbh.de>). The normal reference range for serum zinc is 70-150 $\mu\text{g}/\text{dL}$.¹⁷ Serum Biotin was measured using "Human Vitamin H (Biotin) ELISA kit" provided by Shanghai Korain Biotech Co., Ltd, Shanghai, China. Cat. No.: E3932Hu. (<http://www.korainbio.com>). The normal biotin plasma concentration ranges from 400 to 1200 ng/L, and <200 ng/L is considered deficiency.¹⁸

TABLE 1 The collective data of the MAGA patients and controls

	MAGA group		Control group		Student t test	
	Range	Mean \pm SD	Range	Mean \pm SD	t	P
Age (Y)	20-55	36.13 \pm 8.14	25-44	33.9 \pm 6.21	1.690	0.094
BMI kg/m^2	22-28.9	24.51 \pm 1.55	22.4-25.4	24.15 \pm 1.01	1.509	0.134
Zinc ($\mu\text{g}/\text{dL}$)	40-91	60.27 \pm 10.82	72-93	80.8 \pm 6.47	-12.62	0.01 ^a
Biotin (ng/L)	317-361.2	339.4 \pm 12.13	436.2-583.7	532.82 \pm 35.22	-40.22	0.01 ^a

^a $P < 0.05$ is significant.

2.2 | Statistical analysis

Data were collected, revised, coded and entered into the Statistical Package for Social Science (IBM SPSS, IBM, Armonk, NY, USA) version 20. Qualitative data were presented as number and percentages while quantitative data with parametric distribution was presented as mean, standard deviations (SD) and ranges. Student *t* test (*t* test) was used for numerical variables of normally distributed samples. Pearson's correlation coefficient was used to detect the relationship between two continuous variables. The nonparametric test (Spearman's correlation coefficient) was used to measure the strength of association between two variables. Fisher's exact test (*F* test) was used to know whether the proportions for one variable are different among values of the other variable. *P* values <0.05 was considered statistically significant.

3 | RESULTS

Table 1 shows that there was a nonsignificant difference between MAGA and controls as regards age (mean \pm SD = 36.13 \pm 8.14, 33.9 \pm 6.21, respectively; $P = 0.094$) and BMI (mean \pm SD = 24.51 \pm 1.55, 24.15 \pm 1.01, respectively; $P = 0.134$). The serum zinc level ($\mu\text{g}/\text{dL}$) was lower significantly in patients compared to controls (mean \pm SD = 60.267 \pm 10.817, 80.8 \pm 6.47 respectively; $P = 0.01$), suboptimal biotin levels ($\mu\text{g}/\text{dL}$) were in patients while it was within normal values in controls (Mean \pm SD = 339.4 \pm 12.125, 532.82 \pm 35.224, respectively; $P = 0.01$).

Table 2 shows the correlations between the measured variable in patients' group. There was a positive significant correlation between serum zinc and serum biotin ($r = 0.489$, $P = 0.001$). Serum zinc showed

TABLE 2 The correlations of serum zinc, biotin, and other variables in the MAGA group

Pearson correlation	Serum zinc ($\mu\text{g}/\text{dL}$)		Serum biotin (ng/L)	
	r	P	r	P
Serum biotin	0.489	0.001 ^a	—	—
Age (y)	-0.226	0.082	-0.114	0.387
BMI (kg/m^2)	0.322	0.012 ^a	0.087	0.508
Disease duration (y)	-0.231	0.075	-0.022	0.868

^a $P < 0.05$.

TABLE 3 The relation between MAGA grades and serum zinc and biotin levels

	G III n = 22	G IV n = 20	G V n = 18	F test	
	Mean ± SD	Mean ± SD	Mean ± SD	F ^a	P
Serum zinc (µg/dL)	62.364 ± 7.108	59.750 ± 9.904	58.278 ± 14.962	0.734	0.485
Serum biotin (ng/L)	342.309 ± 6.935	338.075 ± 13.434	337.317 ± 15.216	1.019	0.367

^aF: Fisher's Exact test, $P < 0.05$ is significant.

TABLE 4 Serum zinc and biotin ROC curve

	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy (%)
Serum zinc (µg/dL)	≤71	86.67	100	100	71.4	95
Serum biotin (ng/L)	≤361.2	100	100	100	100	100

NPV: negative predictive value; PPV: positive predictive value.

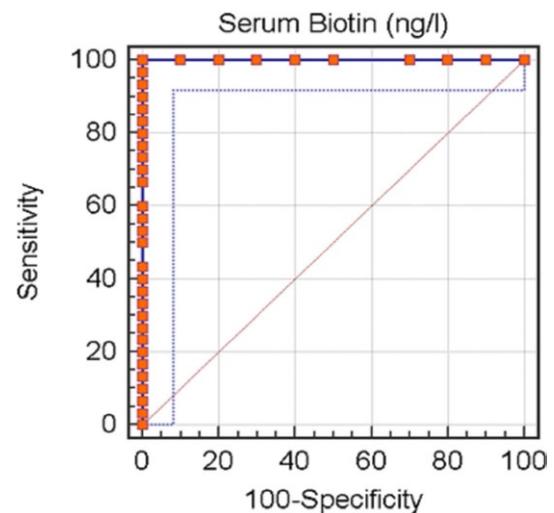
a negative nonsignificant correlation with age ($r = -0.226$, $P = 0.082$) and disease duration ($r = -0.231$, $P = 0.075$), while it showed a positive significant correlation with BMI ($r = 0.322$, $P = 0.012$). Serum biotin showed a negative nonsignificant correlation with patients' age ($r = -0.114$, $P = 0.387$), BMI ($r = -0.087$, $P = 0.508$) and disease duration ($r = -0.022$, $P = 0.868$).

According to Hamilton-Norwood MAGA grades, the patients' group included patients of grades III (22 patients), IV (20 patients), V (18 patients), and the serum zinc level (mean ± SD = 62.364 ± 7.108, 59.750 ± 9.904, 58.278 ± 14.962, respectively; $P = 0.485$) and biotin (mean ± SD = 342.309 ± 6.935, 338.075 ± 13.434, 337.317 ± 15.216, respectively; $P = 0.367$) showed a nonsignificant relations to MAGA grades (Table 3). Receiver operating characteristic curve shows, accuracy was 95% for serum zinc and 100% for serum biotin, sensitivity was 86.67 for serum zinc and 100 for serum biotin, and specificity was 100 in both serum zinc and serum biotin (Table 4 and Figures 1 and 2).

4 | DISCUSSION

The exact mechanism of how zinc affects hair loss has not fully understood, although zinc-related metalloenzymes may have the potential to regulate hair growth.¹⁹ It is also a potent inhibitor of hair follicle regression and accelerates hair follicle recovery.⁵

In the current study, MAGA patients showed serum zinc levels significantly lower than the control group consistent with previous reports.^{19,20} Kil et al¹⁹ showed significantly lower serum zinc level in MAGA patients compared to control but still within normal value limit. Aiempnakit et al²⁰ found that serum zinc levels were lower in MAGA patients compared to controls, of note, serum zinc in patients and controls were lower than normal value limit. On the other hand, Ozturk et al²¹ who did not detect any significant difference in serum zinc levels between MAGA in Turkish patients and controls

**FIGURE 1** Serum biotin ROC curve

($P = 0.46$), but they found significantly lower zinc level in the hairs of MAGA patients. The difference in nutritional habits and sampling can explain the inconsistent results.

Our study revealed that serum zinc levels showed a nonsignificant correlation as regards the MAGA clinical grades consistent with previous reports.^{19,21} Also, there was a nonsignificant correlation between serum zinc and patients' age consistent with other reports.^{19,20} We found that serum zinc showed a significant correlation with patients' BMI. Ozturk et al²¹ found higher serum zinc in MAGA patients with high BMI than those with low BMI but that difference was nonsignificant ($P = 0.13$).

Biotin deficiency is rare, as intestinal bacteria are typically able to produce adequate levels of biotin. No clinical trials have shown efficacy in treating hair loss with biotin supplementation in the absence of deficiency.⁹ The biotin marketed supplements for hair loss rely on the fact that biotin showed positive effects in the

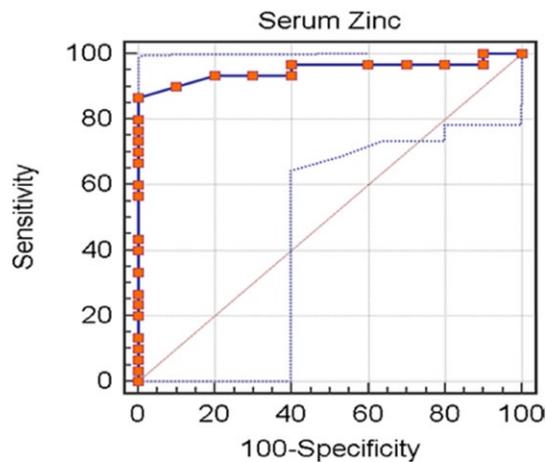


FIGURE 2 Serum zinc ROC curve

brittle fingernails treatment.²² Patel et al¹⁴ analyzed 18 case-reports of biotin relation with hair and nail growth and found clinical improvement after receiving biotin in all cases, and three reported cases of uncombable hair syndrome showed improvement in hair quality after a few months of biotin treatment. Prager et al²³ reported 60% improvement in MAGA patients after treatment with an oral combination containing not only biotin but also niacin, β -sitosterol and saw palmetto extract.

To the best of our knowledge, this is the first study that evaluated biotin serum levels in MAGA patients. We found that serum biotin was at the suboptimal level compared to controls and showed nonsignificant correlations with patients' age, BMI, disease duration, and severity. A previous report suggested that increased urinary excretion of 3-hydroxyisovaleric acid was a more accurate measure of biotin deficiency.¹⁸ We recommend further studies to evaluate biotin deficiency in serum combined with estimation of biotin metabolites in urine of MAGA patients to confirm our finding.

In conclusion, serum zinc showed subnormal value and adding zinc supplement in MAGA treatment is recommended. Serum biotin showed a suboptimal level in MAGA patients that is not correlated with patients' age or disease severity. Biotin supplement in MAGA treatment may add value to hair quality and texture.

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CONFLICTS OF INTEREST

The authors are responsible for all the current study content and have no conflicts of interest.

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