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Androgenetic Alopecia: A Chronic or Pubertal Onset Disease Retarded by Blood Donation

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Abstract

Background: Androgenetic alopecia is the main cause of hair loss and common baldness that affects psychological more than physiological aspects of people's lives. Studies have shown that this multi factorial disorder is initiated by androgens secretion in pubertal period, minerals limitations, autoimmunity, mental stress, genetic predisposition and some alterations in hematological factors.
Objectives: The aim of this study was to evaluate the involvement of hematologic parameters in this disease using a case control study design.
Methods: In this case-controlled study, two groups each of 80 individuals with androgenetic alopecia were voluntarily included in the study based on their medical histories and clinical examinations and subjected to blood tests for routine hematological parameters. The results were then compared and analyzed using SPSS version 16.0.
Results: Our findings indicated that all the parameters for both groups fall in normal ranges (Mean $\pm$ SD) but the values for RBC, HGB, MCH, MCHC, WBC, LYM and TIBC were significantly higher in patients than in normal group. The average counts of PLT was significantly lower in patients compared with the normal group. Otherwise, Person's tests for statistical correlations between two groups indicated that the pattern of correlations were abnormal in patients.
Conclusions: Our findings indicated the presence of a chronic, immunologic and slowly progressing disorder that causes hair loss, the disease which is in turn triggered in pubertal period upon androgen secretion. We suggest, therefore, that the conditions may be ameliorated by prescription of iron tablet, platelet transfusion and anti-inflammation therapy.

Keywords: Alopecia, Platelet Transfusion, Iron, Inflammation

1. Background

Androgenetic alopecia (AGA), male pattern baldness, common baldness or androgen-dependent alopecia, is the most common form of hair loss in males and females which is associated with psychological discomfort and depression [1, 2].The incidence of AGA is estimated to be 50 percent in both sexes above 50 years of ages [3]. This kind of baldness is described as progressive loss in pigmented terminal hair on the scalp concurrent with predominant onset in puberty upon increase in sexual hormones [4-6]. Histological investigations indicated that elevated androgenic hormones cause marked decrease in hair follicles sizes, probably by decreasing hair progenitor cells [7]. Despite the uncertainty regarding the involvement of androgens in AGA especially in women, no progression of baldness was seen in pre-puberty period. Furthermore, the alopecia could be triggered by androgen injection [8-10].

In men, testosterone is metabolized by 5-α reductase to 5α-dihydrotestosterone, the major circulating metabolite that initiates AGA [8]. It is believed that hair follicles response to androgens is not a dose dependent event; instead, it needs the presence of functional receptors and 5-α reductase in target cells and pubertal concentrations of androgens [6, 9-11].

High rates of cell proliferation in normal hair require sufficient blood and nutrient supply. Iron is one of essential elements required for hair growth and maintenance, i.e. iron deficiency leads to certain kinds of hair loss e.g. female pattern hair loss, telogen effluvium, alopecia areata, alopecia universal [12-17], however some researchers denied such claims [18-22]. Clinically iron deficiency is defined either as an increase in total iron binding capacity (TIBC) over 370 μg/dL or as a decrease in plasma concentra-

tion of ferritin under 40 ng/mL [23-25].

In order to understand the mechanisms underlying AGA, attempts were done to establish statistical correlations between the counts of blood cells with their precursors in bone marrow in AGA patients. The significant correlations were seen between these two populations abnormally. These abnormal correlations can leads to abnormalities like AGA [26-28].

A positive correlation between decreased platelet count and severity of hair loss is a good example in this context. It is well documented that platelet rich plasma preparations (PRP) ignites hair cycle and hair canal formation by secreting various proteins like platelet derived growth factor and cytokines as well as through enhancing cells proliferation. Anti-apoptice effects of PRP also increase survival and anagen phase of hair cycle [29-33].

Given this information, we decided to determine hematological parameters of AGA patients in comparison with those of normal individuals in a bid to construct structural correlations between these parameters. We hoped to lay down some practically useful guidelines for AGA management and treatment.

2. Methods

2.1. Patients

Our case-controlled study was carried out on 80 AGA patients and 80 healthy controls (voluntary). Participants were recruited from the outpatient of Atieh clinic No: 122, 9th Bustan, Pasdaran, Tehran, Iran. Disease diagnosis and patients enrolment in this study was made based on their medical histories and physical examinations in our clinic. Other kinds of baldness and abnormalities such as thyroid dysfunction and infectious diseases and those taking iron medications were excluded. The same exclusion criteria were used for the controls group in addition to the presence of AGA.

2.2. Hematological Determinations

Ten milliliters of venous blood samples were taken from 12 hours fasted AGA patients and control individuals. Two milliliters of blood were transferred to EDTA contain test tubes to measure hematological parameters of CBC, HGB, HCT, MCV, MCH, and MCHC using automated Sysmex system (Japan). The remaining bloods was left to coagulate and used for serum isolation. Serum iron and total iron binding capacity (TIBC) were measured using biochemical methods. Ferritin concentration was determined using ELISA kit.

2.3. Statistical Tests

Kolmogorov-Smirnov test was used to check the normality of our data. Difference between determined parameters in two groups of AGA and normal individuals were analyzed by independent T-test and the correlation between independent variables assessed by Pearson's test. P value lower than 0.05 was considered as statistically significant for all tests.

2.4. Ethical Approval

All experimental procedures involving human were conducted with due attention to the guidelines approved by the research ethical committee of Shahid Chamran University (Ahvaz, Iran).

3. Results

Our data in Table 1 indicate that cell blood counts in control as well as in AGA patient group fall in normal range when contrasted to reference values, however, both AGA and control groups showed different patterns. As in Table 1, the first hematological parameter is the count of red blood cells (RBC) in two groups as Mean $\pm$ SD. As shown, there is significant increase in RBC counts from 4.57 ± 0.58 in control group to 5.13 ± 0.59 (P value ≤ 0.001) in AGA patients. This increase in RBC count may serve as indication on oxygenation problem in these patients due to a failure in heart-pulmonary circulation, smoking, hypoxia, pulmonary fibrosis or more likely bone marrow disorder which is not sever enough to manifest as polycythemia vera [34].

The results of Person's tests (Table 2) show that there was a negative correlation between RBC counts and WBC count (r = -0.253, P value = 0.016) in control group. This correlation was not seen in AGA patient (r = 0.19, P value = 0.065). This finding can confirm the presence of bone marrow problems. Hematocrit (HCT) was expectedly higher in AGA group. This was directly related to RBC count (Table 1).

However, the mean corpuscular volume (MCV), which represents the average volume of RBC cells, did not change significantly in AGA patient (P value of 0.059). This indicated the normal structure of RBC cells in these patients.

In its nature, RDW-SD, is a standard deviation of the relative distribution of RBC by volume. This parameter increased significantly from 40.48 ± 4.39 fL in normal control to 43.36 ± 3.06fL (P value = 0.006). This parameter may increase, decrease or remain unchanged at different levels of iron, folic acid and/or B12 vitamin deficiency respectively. Thence, higher RDW-SD in AGA patients can be attributed to iron deficiency in these patients caused by

Table 1. Summary Statistics of Independent T-Tests of Blood Parameters of AGA and Control Groups Presented As Mean ±SD

Variables	Reference Range[a]	Control	AGA	P Value
RBC, $\times 10^{12}$ cells/L	4.17 - 7.07	4.57 ± 0.58	5.13 ± 0.59	≤ 0.001
HCT, %	36.4 - 56.8	38.20 ± 5.43	43.97 ± 5.85	≤ 0.001
MCV, fL	80 - 100	83.35 ± 9.47	85.83 ± 8.17	0.059
RDW - SD, fL	39 - 46	40.48 ± 4.39	43.36 ± 3.06	0.006
HGB, g/dL	14.1 - 17.1	13.46 ± 1.12	14.94 ± 1.04	≤ 0.001
MCH, pg	27 - 33	27.28 ± 2.96	28.66 ± 2.51	≤ 0.001
MCHC, g/dL	28.9 - 38.7	32.53 ± 1.02	33.23 ± 1.35	≤ 0.001
TIBC, μg/dL	250 - 400	343.72 ± 86.01	355.72 ± 60.51	0.048
FERI, ng/mL	10 - 250	85.07 ± 8.51	62.98 ± 6.91	0.035
IRON, μg/dL	50 - 175	84 ± 7.40	64.92 ± 5.42	0.05
WBC, $\times 10^9$ cells/L	4.3 - 11.2	5.88 ± 1.72	8.15 ± 3.11	0.005
LYM, %	30 - 49	27.97 ± 12.32	36.68 ± 9.01	≤ 0.001
GRAN, %	45 - 62	66.39 ± 12.67	59.49 ± 10.68	0.001
PLT, $\times 10^3$ platelet/μL	151 - 322	267.79 ± 68.23	238.16 ± 59.70	0.002

[a] Reference values were obtained from references [35, 36].

increased hemoglobin and RBS syntheses. Significant increase in HGB, MCH and MCHC in AGA patients (Table 1) in contrast to control group are in good agreement with our hypothesis.

On the other hand, reasonable increase in TIBC from 343.72 ± 86.01 to 355.72 ± 60.51 μg/dL (P value < 0.05) in AGA patients, decrease in ferritin from 85.07 ± 8.51 to 62.98 ± 6.91 ng/mL (P value < 0.05) and decrease in iron concentration from 84 ± 7.40 to 64.92 ± 5.42 μg/dL (P value < 0.05) all provide evidences for iron deficiency in AGA patients [37].

Table 1 also indicates that white blood cell (WBC) count increased reasonably from 5.88±1.72 in control group to 8.15 ± 3.11 × 10^9 cells/L (P value < 0.001) in AGA patients. Increase in WBC may be induced by different factors as anemia, corticosteroids medications, smoking, infections, rheumatoid arthritis, allergy, leukemia, mental or physical stress and tissue damage [37]. Although, WBC discrepancy in AGA patients falls within the normal range but this factor may play role in the disorder. Moreover, as stated before, the lake of a negative correlation between WBC and RBC may herald a bone marrow complication.

Lymphocytes and granulocytes are the two major types of WBC and expressed as percent of total WBC in blood. According to data presented in Table 1, there were increased percent of lymphocytes and decreased percent of granulocytes in AGA that confirmed the suspected presence of chronic infectious or allergic reactions. The mechanism which disturbed bone marrow hematopoiesis and led to abnormal correlations seen between RBC, WBC, platelets and some other hematological parameters depicted in Table 2 [38].

Platelets are cell fragments produced by megakaryocytes in bone marrow and released to bloodstream with different roles as in blood coagulation. Normal count of platelets is 150 - 400 × 10^3 platelets/μL. Sever decrease in platelet count to a level lower than 50 × 10^3 platelets/μL leads to thrombocytopenia. This condition may be caused a consequence of chemotherapy, irradiation, autoimmune background and some medications use. Thrombocytopenia manifested clinically as internal or external bleeding such as in nosebleeds, prolonged bleeding from minor cuts, and blood in the urine or stool [39, 40].

As mentioned earlier, platelets are absolutely essential for hair growth and platelet rich plasma preparations are potentially useful in prevention of hair loss [3-11]. Despite the facts that the platelets count in AGA patients was at normal range with 238.16 ± 59.70 × 10^3 platelet/μL, but it was lower than that in control group with 267.79 ± 68.23 × 10^3 platelet/μL (P value < 0.01). This may exacerbate the hairs loss.

Tables 2 - 3 summarizes the Person's correlations for hematological parameters in patients and control groups. It is obvious from Table 3 that in control group there are positive but weak and not significant correlations between platelet with each of WBC and RBC count (with P value >

Table 2. Results of Pearson's Tests of Hematological Parameters Except of PLT; b, Pearson's Tests of PLT in AGA and Control Groups

Correlation (P Value)		Control Group	AGA Group
RBC	HGB	0.73 (0.001)	0.68 (0.001)
RBC	HCT	0.65 (0.001)	0.72 (0.001)
RBC	MCV	-0.27 (0.010)	-0.21 (0.049)
RBC	MCH	-0.21 (0.039)	-0.19 (0.068)
RBC	MCHC	0.14 (0.165)	0.11 (0.282)
RBC	RDW-SD	-0.28 (0.238)	-0.31 (0.003)
HGB	HCT	0.79 (0.001)	0.98 (0.001)
HGB	MCV	0.34 (0.001)	0.43 (0.001)
HGB	MCH	0.49 (0.001)	0.58 (0.001)
HGB	MCHC	0.56 (0.001)	0.52 (0.001)
HGB	RDW-SD	-0.08731	0.085638
HCT	MCV	0.30 (0.004)	0.40 (0.001)
HCT	MCH	0.28 (0.006)	0.51 (0.001)
HCT	MCHC	0.17 (0.102)	0.36 (0.001)
HCT	RDW-SD	0.09 (0.704)	0.13 (0.210)
MCV	MCH	0.84 (0.001)	0.81 (0.001)
MCV	MCHC	0.21 (0.041)	0.29 (0.005)
MCV	RDW-SD	0.77 (0.001)	0.46 (0.001)
MCH	MCHC	0.64 (0.001)	0.57 (0.001)
MCH	RDW-SD	0.40 (0.078)	0.46 (0.001)
MCHC	RDW-SD	-0.42 (0.068)	-0.21 (0.048)

0.05) respectively. In AGA patients, the weak correlations are replaced with significant ones with P value < 0.05. These strong correlations may exert more regulatory effects on platelet count. The abnormal regulations again decrease platelet count in AGA patient and therefore baldness progression. Like RBC, hematological parameters of HGB, HCT and RDW also increased in AGA patients and correlated negatively with platelets, so that by decreasing platelet count worsened hair loss.

Table 3.

Correlation (P Value)		Control Group	AGA Group
PLT	WBC	0.039 (0.71)	0.23 (0.004)
PLT	RBC	0.005 (0.95)	-0.26 (0.012)
PLT	HGB	-0.19 (0.06)	-0.33 (0.001)
PLT	HCT	-0.22 (0.03)	-0.24 (0.017)
PLT	RDW	-0.23 (0.03)	-0.45 (0.045)

4. Discussion

Our findings indicated that, in AGA patient, the parameters of RBC, HCT, HGB, MCV, MCH, MCHC and RDW fell within normal ranges, but they were still significantly higher than those in control group, except for MCV that was similar in both groups. The elevated parameters may contribute to chronic and mild increase of erythropoiesis that provides RBC of normal morphology and constant MCV. Pearson's tests indicated that overall correlations between blood parameters in AGA patient were evidently irregular in contrast to control group. This may confirm the presence of a suspected background disorder. Our data also showed that in AGA patients iron reservoirs were slightly diminished as evidenced by elevated TIBC. Our data in parallel with others' reports indicated that such a hidden iron deficiency could threaten normal hair growth and maintenance and lead to accelerated hair loss and baldness [18-22].

Another factor suggested to mediate hair fall is an increased autoimmune reaction against hair follicles [41]. This hypothetical mechanism was confirmed by a significant increase in WBC count and lymphocyte percent in contrast to other WBC cells (Table 2). This allergic reaction could be mediated by proinflammatory effects of prostaglandin D2 released by WBC cells like lymphocytes with inhibitory effects on hair growth in AGA patients [42].

This immunological susceptibility could potentiate hair loss in AGA patients that is known to be triggered by androgens in pubertal period. Finally, the most important finding of this work with potential usage in AGA management was the significant decrease of platelet count in patient group. Since it is well accepted that platelets are necessary for normal hair growth and differentiation, the decrease in platelet count can be incriminated as an important factor causing or worsening AGA baldness. In this direction, platelet negative correlation with other hematological parameters (Table 3) again may leads to more decrease in platelet count.

4.1. Conclusion

Given our findings and others' previous reports, we may come up with some practical hint of possible usage in AGA treatment. We may suggest prescription of supplementary iron medications as micronutrient for hair follicle growth, regulation of RBC count by blood donation, platelets pheresis autotransfusion and reduction of immunological reactions via medications use as new treatment protocols subject to further investigations.

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Footnotes

Authors' Contribution: Daryush Daer visited patients in his clinic, ordered diagnostic test and added them to this study, Mohammad Reza Dayer analyzed and developed the concept and designed experiments. Fatemeh Dehghani participated in data manipulation and preliminary analysis. Mohammad Reza Dayer finalized data analysis, developed the main idea of manuscript and writes whole the text. Sayed Mohammad Reza Alavi rechecked and discussed the statistical part of manuscript. Mohammad Saaid Dayer participated to the improvement of the output and discussion of manuscript.

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