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# Serum Endocan and Carotid Intima-Media Thickness Evaluation in Male Androgenetic Alopecia Patients

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**Abstract**

**Background and aim of the work:** Patients with androgenetic alopecia (AGA) was correlated with higher prevalence of insulin resistance, hypertension, coronary artery disease, obesity, atherosclerosis and aberrant serum lipid profile. Endocan is a possible immunoinflammatory indicator associated with cardiovascular disease. Patients with AGA appear to be at an increased risk of developing CAD, therefore, clinical evaluation of cases with AGA of grade II is recommended The carotid intima-media thickness (CIMT) is a powerful indicator of future cerebrovascular and cardiovascular disorders. This research intended to examine serum level of endocan and CIMT in male AGA patients. **Patients and Methods:** that research conducted in Dermatology Department, Benha University Hospital, on sixty AGA participants with 20Y old age and gender-matched individuals during the period from January 2021 to August 2021. **Results:** endocan level was considerably lower in control compared to AGA group, but no critical change was seen among groups concerning CIMT. **Conclusion:** Serum endocan was considerably lower in control compared to AGA group, but concerning CIMT, a non-critical change was seen among groups.

**Key words:** CIMT, Serum Endocan, Male Androgenetic Alopecia

## 1. Introduction

Male androgenetic alopecia (AGA) is considered most common types of baldness characterized by progressive hair loss. Generally, male pattern AGA appears as regression of the frontal hairline or hair loss beginning at the vertex and progressing steadily inwards**.** Pathophysiology of AGA is not clearly recognized and androgen and its receptor are considered to be related to this condition**.** Various studies have demonstrated that AGA patients have a marked predisposition to premature atherosclerosis and cardiovascular diseases (1).

CAD risk has been observed to be related to AGA. The well-known risk factors are family history of CAD, hypertension, increased body mass index (BMI), central obesity, hyperglycemia, and dyslipidemia. AGA individuals tend to have a higher chance of having CAD, Consequently, clinical assessment of AGA cases of grade II is recommended (2).

Endothelial dysfunction is considered as an early change in atherogenesis. Cardiovascular illness is related to elevated levels of markers of systemic inflammations. Endocan (previously known as endothelial cell specific molecule-1, ESM-1), is a potential immunoinflammatory marker that may be linked to cardiovascular disease. Multiple organs' vascular endothelial cells secrete endocan. Endocan may play a crucial function in cell adhesion regulation, and elevated plasma levels may indicate endothelial dysfunction. Serum endocan is raised in chronic kidney disease, renal transplant rejection, tumour development, and hypertension, among other diseases (3). CIMT is a widely used surrogate marker for atherosclerosis worldwide. B-mode carotid ultrasound can simply, noninvasively, and reproducibly measure CIMT. CIMT is also a reliable indicator of cerebral and cardiovascular disorders in the future. In addition, regressions of raised CIMT by lipid-lowering and antihypertensive drugs have been reported. Despite the strong association between increased CIMT and cardiovascular disease, it remains unclear whether routine CIMT measurement is useful for the detection of subclinical atherosclerosis in clinical practice (4).

That work purposed to assess endocan level and CIMT in male androgenic alopecia participants in comparison to healthy control sex and age matched individuals.

## 2. Patients and Methods

That research was done on 60 AGA individuals and 20 healthy volunteers who were matched for age and sexe and acted as controls. From January to August 2021, they were chosen from Benha University's outpatient dermatology, venereology, and andrology clinics.

**Inclusion criteria**

Male individuals over 18 years old and were willing to be a part of the study.

**Exclusion criteria**

Exclusion criteria were as following: Recognized septic focus, existence of associated chronic disorder such as cardiovascular disease, diabetes mellitus, and hypertension, history of immunosuppressive therapy, history of active

malignancy, dermatological disorders history, and participants under AGA systemic treatment during least three months prior to study.

**Administrative design**

The Research Ethical Committee of Benha Faculty of Medicine authorized that research in accordance with the Helsinki declaration's requirements.

**Ethical consideration**

Prior to collecting blood samples, every member provided written informed consent, data protection and privacy of persons were recognized at total study stages, participants had the complete freedom to give up from study with no repercussions, and data gathered were not abused.

**All participants will be split to two groups**

- Group A: 60 AGA male patients.
- Group B: Twenty Volunteers matched on age and gender serve as the control group.

**Methods**

**Every individual was required to endure**

**Comprehensive history**

- Personal history: name, age, employment, residence, and smoking or other medically significant habits.
- The patient's medical history, involving the start, course, and longevity of AGA.
- Past history: drug history (kind and duration), concomitant systemic illnesses, endocrine disorders, and past surgery.
- History of previous AGA therapy (type, dose and duration).
- AGA family history.

**General examination**

- It was done to exclude systemic disease.
- The body height and weight were measured to assess BMI.

**Local examination**

- AGA severity and grade were evaluated using the Hamilton and Norwood classifications, The Hamilton-Norwood scale Fig (1) was a useful classification tool for male pattern hair loss. Scale categorized clinical features to 7 phases and provided balding progression visual representation (5).

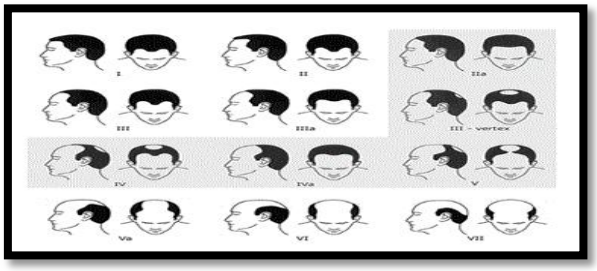

**Fig (1)** Hamilton–Norwood classification of male balding (5).

**Laboratory investigations**

All individuals' serum endocan levels were determined**.**

**Blood Sampling**

- Under strict aseptic conditions, 5 cc of whole venous blood was extracted and left for 20 minutes until coagulation.
- The blood has been spunat 2000-3000 round per min. and serum was isolated and kept at -40º c until use.

**Measurement of endocan blood level**

- The quantitative serum endocan was performed by the available commercial kits according to manufacturers' instructions.

**Assessment of CIMT**

CIMT is the distance between the lumen–intima interface and the media–adventitia interface of the artery wall, as assessed on carotid ultrasonographic pictures**.** CIMT was assessed in the supine position using high-resolution, bright-mode ultrasonography (B-mode).

Ultrasonographic pictures of the left and right common carotid arteries were used to quantify CIMT. The transducer was adjusted such that the walls of the common carotid artery were aligned to the footprint of the transducer, and the lumen diameter was maximised in the longitudinal plane**.** An area 1 cm proximal to the carotid bifurcation was located, and CIMT of the distal wall was calculated as the length between the lumen–intima and media–adventitia interfaces.

At 1-mm increments, intima–media thickness was measured at four contiguous locations, and the mean of these four parameters was utilized for analysis. After taking parameters of the right and left common carotid arteries, the mean of the two readings was computed**.**

**Statistical Methods**

Version 25 of SPSS was used for data administration and statistical analysis (IBM, Armonk, NY, US). Kolmogorov–Smirnov test (for cases), the Shapiro–Wilk test (for controls), and direct data visualisation approaches were used to determine the regularity of quantitative data (for both). The numerical data were reported as means and standard deviations or medians and ranges based on normality tests. As numbers and percentages, categorical data were summed up. For normally and non-normally distributed numerical variables, the independent t-test or Mann-Whitney U test was used to analyze quantitative data across study groups. Utilizing Chi-square test, categorical data were compared.

**3.Results:**

The mean disease onset was 22 ±4 years. Median illness period was 4 years and extended between 1 and 15 years. Grade IV (35.0%) was the greatest repeated grade **(Table 1).**

**Table (1)** Disease characteristics in the patients group

| **Disease characteristics** | | |
|---|---|---|
| **Age of disease onset (years)** | Mean ±SD | 22 ±4 |
| **Disease duration (years)** | Median (range) | 4 (1 - 15) |
| **AGA grade** | Grade III n (%) | 19 (31.7%) |
| | Garde IV n (%) | 21 (35%) |
| | Grade VI n (%) | 20 (33.3%) |

The serum endocan was measured in sera of all patient and control. Endocan level was considerably lower control compared to patient group. The CMIT was measured in patient and control group and there was no critical change among both groups

**4. Discussion**

Present study revealed that mean disease onset was 22 ±4 years. Median illness period was 4 years and extended from 1 to 15 years. The most frequent AGA grade was grade IV (35.0%), followed by grade VI (33.3%), then grade III (31.7%).

(6), found that The most prevalent form of alopecia was grade II (27.27 percent), trailed by grade I (22.12 percent) and grade III (3.5 percent) (21.78 percent ) (7), explained that according to the Hamilton-Norwood classification, 24 (32.4%) of 74 AGA participants were in stage II, 26 (35.1%) were in stage III, 17 (23 percent) were in stage VIII, 1 (1.4 percent) were in stage V, and 6 (8.1 percent) were in stage VII. Also, (8), 12 percent of 100 male participants with early onset AGA had type I alopecia, 25 percent had type II alopecia, 29 percent had type III alopecia, and 12 percent had type IV baldness. 7 percent of patients had type V, 9 percent had type VI, and only 6 percent had the most severe type VII alopecia regarding the Hamilton and Norwood categories. The mean number of months from the beginning of alopecia was 40.55±27.67. (9), a mean age of onset of 29.750±7.736 years was reported. Approximately 77percent of patients analyzed related to intensity 1 (normal-to-mild AGA), while 23percent of the cases related to sensitivity 2 (severe AGA) (moderate or severe AGA).

However, Endocan (formerly referred to as endothelial cell specific molecule-1, ESM-1) is a possible immunoinflammatory indicator which may be associated with cardiovascular disease, chronic kidney disease, renal transplant rejection, tumour development, and hypertension (3).

However previous studies had investigated endocan in different diseases like hypertension (10), cardiovascular diseases, (11), chronic kidney disease (12).

Hypertensive patients had higher circulating endocan levels, as (10), reported that the median endocan level in hypertensive patients (2.03 ng/mL) was considerably higher than in the control group.

Among the first and most prominent alterations associated with hypertension is endothelial dysfunction. It has a crucial function in cerebrovascular and cardiovascular pathophysiological disorders, as well as harm to target organs induced by essential hypertension. The primary component in diastolic purpose depending on endothelium is NO. Whenever activity of endothelium is compromised, NO production is dramatically reduced and vascular ROS production is elevated, resulting hypertension and in arterial vasoconstriction (13).

Endocan stayed irrespective and strongly linked with hypertension, according to clinical evidence. Increases in endocan by 1 pg/mL raised hypertension occurrence by 32,2 percent (14). In the initial hypertensive stages, serum endocan is dramatically elevated and favorably linked with renal enzyme, norepinephrine (10), CIMT (15) and hsCRP (3)**.**

Consequently, serum endocan may serves as a novel indicator of essential hypertension. Hypertension is a key risk factor for coronary heart disease. Endocan levels in hypertensive individuals were substantially linked with prevalence and intensity of coronary heart disease. (16).

Patients with coronary artery disease (CAD) had greater serum endocan than individuals without, as (17) Hypertensive individuals with CAD exhibited considerably greater serum endocan than those without.

And (11)**,** In there meta-analysis, demonstrated that serum endocan levels were considerably elevated in those with cardiovascular disease. High blood endocan levels may be a risk factor for CVD.

(18) identified 340 individuals suffering ACS, comprising ST-elevation MI (STEMI), non-STEMI, and unstable AP. According to clinical evidence, endocan performance are significantly and independently connected to MACE and myocardial infarction thrombolysis risk score. Additionally, endocan level is uniquely associated with STEMI incidence (19).

Endocan and hsCRP concentrations were observed to be considerably raised in acute myocardial infarction individuals, however no association was present among concentrations of hsCRP and endocan (20).

Cardiovascular illness culminates in heart failure. Throughout clinical follow-up, average endocan concentration in CHF participants was 3.38 ng/mL (normal concentration is 1 ng/mL). A relation was observed among concentration of chronic heart failure and HF incidence. (21).

(22) reported that microvascular angina (MVA) patients had greater elevated endocan than controls. Endocan concentrations were similar across obstructive CAD and MVA individuals. Linkage between concentrations of endocan and CAD degree and intensity was irrespective to influencing variables. Therefore, they hypothesized that concentrations of endocan may be used to detect endothelium-dependent inflammatory reactions.

Also, (12) observed that chronic kidney disease (CKD) with identical CVD individuals have higher concentration of endocan than CKD without CVD individuals. In CKD with CVD individuals, endocan concentration favorably connect with other inflammatory predictors, involving soluble vascular adhesion molecule-1 and soluble intercellular adhesion molecule-1.

In our study regarding CIMT, non-critical change was reported among AGA and control groups. Similarly, (23) said that no considerable association among AGA and CIMT was found. In contrast to (24) who observed that the CIMT has increased statistically significantly in the AGA group, than controls, that change may be a result to study sample size and age change.

(25) 126 male AGA patients aged 18 to 55 without a history of chronic illness were recruited in the study. Based on Hamilton baldness scale as adjusted by Norwood, cases were categorized into three groups (mild, moderate, and severe). Severe group had considerably higher CIMT values than mild and moderate groups. While there was no critical change in the frequency of abnormal CIMT between mild and moderate groups, both mild and moderate groups had less frequency of aberrant CIMT compared to severe group.

However, (26) conducted that serum endocan positively related to mean CIMT , and body mass index in the psoriatic patients. In addition, (27) reported that non-parametric Spearman's correlation study found a positive association between endocan and BMI.

This contradicted earlier studies of an inverse relationship between serum endocan and BMI, as (28) who reported that serum endocan was inversely connected with BMI and CRP concentration, and favorably associated to HDL concentration. and (10) who reported that endocan concentration was correlated negatively with body mass index.

Potential disparities in such findings may be attributed to changes in age, gender, and ethnicity accounted for in earlier research. In addition, the degree of obesity and phenotypes of adiposity differ wildly across people, which may possibly clarify this debate. BMI is the most often used metric for assessing obesity in the general population. Nevertheless, it has certain limitations, since it cannot provide data on body shape and fat mass, nor can it differentiate between fat depots and muscle mass (29)**.**

(30) and (15) showed a substantial rise in endocan levels in hypertensive individuals. Furthermore, they observed a correlation among higher concentrations of endocan levels and CIMT. In a study of systemic lupus erythematosus patients, a substantial positive connection was discovered between serum endocan and CIMT.(31)**.**

However, in the study by (32) 159 participants were involved in the research, group I (grade I&II) with mean age of 40±7 years consisting of 49 individual, the group II (grade II&IV) with mean age of 40±7 years involved 71 participants, and the group III (grade V&VI)with mean age of 40±5 years had 39 individual. They found that CIMT values increased significantly according to grades as it was 0.61±0.17 in grade I&II, 0.76±0.15 in grade III&IV, and 0.98±0.14 in grade V & VI. In addition, CIMT was well correlated to BMI, and patients' age.

## 5. Conclusion:

Endocan level was considerably lower in control compared to AGA group, but non-critical change was seen among groups concerning CIMT.

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