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EFFECT OF MALNUTRITION, HORMONES DISTURBANCE AND MALONDIALDEHYDE ON HAIR LOSS IN WOMEN : PATIENTS AT AL-SADER EDUCATIONAL HOSPITAL, BASRAH GOVERNORATE, IRAQ - A CASE STUDY

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ABSTRACT : Hair loss in women has been considered one of the most common problems faced the dermatologists. It is also considered a haunting problem for women because of the association of hair with femininity, beauty and personal strength, and thus can cause psychological problems for them. In Iraq, there was a little attention was advocated to determine the most type and prevalence of hair loss accurately and the associated causes. The aim of the study is to highlight the main physiological causes of hair loss for women in Basra Governorate, Southern Iraq. Given the important role that some hormones and nutrients play in addition to oxidative stress in influencing the appearance of hair loss disease in women. The study was conducted on volunteer patients that visiting the dermatology consultation unit in hospitals affiliated to the Basra Health Administration during the period from September 2019 to the beginning of January 2020. The study was applied on a random sample consisting of 67 women suffering from hair loss and another sample of 21 women as control volunteers sound for the purpose of comparison. The results of the current study have revealed a significant decrease in blood parameters (MCH -MCV-Hb) and a decrease in the level of iron in the patients group compared with the control group indicating the association of anemia with hair loss in women. The results showed a significant decrease in the concentration of zinc and vitamin D in the patients group compared with the control group. The results also showed a significant increase in the concentration of testosterone and a significant decrease in the level of estrogen and thyroid hormone T_3 in the group of patients compared to the control group. Furthermore, the results presented a high level of (MDA) among the patients group compared to the control group, indicating that increased oxidative stress may cause hair loss in women.

Key words : Hair loss, nutrients, hormones, MDA

INTRODUCTION

Hair loss is deemed a common skin disease that affects both females and males alike, of all ages. For many centuries, hair was and remains the most significant sign of beauty for a female, so healthy hair is a sign of well-being, beauty and personal strength for women. Therefore, it is certainly that hair loss in women can cause psychological problems more than men (Brough and Torgerson, 2017). Hair loss affects more than 25% of women in developed countries, but its prevalence among Iraqi women is unspecified (Naif, 2016).

In general, hair loss is driven by many reasons, including; hormonal disturbance, genetic, nutrition and infection. Also, there are many other factors that affect hair growth, such as exposure to stress, pollution, the nature of lifestyle and chronic diseases, consuming some medications,diseases related to metabolism, in addition to some behavioral habits such as smoking and alcohol consumption. Collectively, these reasons affect the hair cycle development directly and also make the hair roots more sensitive to the effect of androgens (Rajendrasingh, 2017).

Thus, there are many types of hair loss in women that due to the driver type. The most common female pattern hair loss (FPHL) is androgenetic alopecia (AGA) that results from a disorder in the secretion of steroid hormones (Herskovitz and Tosti, 2013). The term (AGA) refers to the physiology of the disease, as androgen hormones, particularly testosterone, induce hair loss in people with a genetic predisposition (Likhitkar *et al*, 2018). AGAis characterized by diffuse, non-scarred hair and non-scarring diffuse. Symptoms of hair fall begin through the gradual weakness and smallness of hair follicles

leading to a decrease in the number of hairs, especially in the hair of the central and frontal scalp areas while maintaining the front hairline of the head (Ramos and Miot, 2015).

The other type of hair loss is Telogen effluvium (TE) is the second common type of hair loss (Ozlu and Karadag, 2017). A wide range of potential factors that lead to TE, such as pregnancy, chronic diseases, severe bleeding and lack of nutrition and to undergo surgeries or severe nervous pressure (Harrison and Sinclair, 2002).

There is also a third type of hair loss that is less common than the previous two types, *Alopecia areata*, which is an autoimmune disease that targets hair follicles, causing hair loss without damage to it. The prevalence of the disease is about 1 in 1,000 people worldwide (Engin *et al*, 2017).

Anagen effluvium is also one of hair loss type in women, which distinguished by sudden hair loss in the growth phase (anagen) due to weakness in mitotic division or metabolic activity of hair follicle cells as a result of radiotherapy or chemotherapy that destructs the anagen phase. As a consequent, a sudden hair loss is occurred (Kanwar and Narang, 2013).

Iron deficiency anemia is one of the most common factors causing hair loss and the dermatologist often uses a measure of the level of two serum periods to make sure hair loss is linked to the condition of anemia (Karadag *et al*, 2011). Hodeib *et al* (2017) asserted the relationship between blood parameters and TE hair loss. Their findings revealed a significant decrease in hemoglobin concentration, MCV, MCH and iron in the blood samples of the patients group in comparison with the healthy women.

Likewise, nutrients have important functions in hair growth cycle. Zinc plays a role in speeding up hair follicle recovery and is a strong inhibitor of hair follicle decline in addition to its important role in maintaining the sebaceous glands associated with hair follicles (Dhaher *et al*, 2018; Rahman and Akhter, 2019). Khudhair *et al* (2013) indicated that there was a clear relationship between zinc deficiency and hair loss (TE) in adult women.

Vitamin (D3) is vital nutrient for the health of the body and hair. The main source of this D3 in the body is the internal composition of the skin (Ross and Del Valle, 2011) when exposed to ultraviolet light with a wavelength of 320-290 nm, where the dehydrocholesterol 7-present in the skin turns into vit D3 (de la Puente *et al*, 2020). The function of vitamin D on hair is activation of the differentiation of hair follicles without affecting on increasing the number of their cells, and it has been shown that patients with a hereditary vitamin D receptor deficiency VDR have a high probability of developing hair loss (Zlotogorski *et al*, 2003). Rasheed *et al* (2013) found that the low level of vitamin D in women's serum is associated with telogenic hair loss and androgenic hair loss (AGA).

Endocrine system is counted the main controlling factor of human hair growth, as many hormones such as sex hormones, thyroid hormones, adrenal corticosteroids and prolactin activate or deactivate the production of hair from the hair follicle. However, androgens are the main organizing hormones for hair growth (Alwaleedi, 2015).

Earlier findings indicated the responsibility oftestosterone on hair loss in women, for instance, Nagui *et al* (2013) showed that the high testosterone level caused hair loss type (AGA), in 20 Egyptian women suffering from hair loss. Kurtoðlu *et al* (2019) explained the mechanism of testosterone level increasing in women and highlightedthe activity of 5-alpha reductase enzyme which transforms the estradiol to Dihydrotestosterone.

Conversely, estrogen hormoneis most likely controlling the skin physiology and hair growth. Ohnemus *et al* (2006) stated that the role of the estrogen hormone in hair growth and hair loss is not precisely defined, although the effect of estraidol is evident on all stages of hair growth (anagen, catagen, and telogen). It is noted that the high levels of estrogen during pregnancy lead to the prolongation of the anagenstage, while the low levels of estrogen after childbirth cause transformation of a large number of hair follicles to telogen stage at one time, which leads to an increase in the number of falling hair and causing telogen effluvium (Verdier Sévrain *et al*, 2006).

Thyroid hormones also play crucial roles in growth, differentiation and metabolism, which are important in regulating skin cell regeneration and hair growth. The thyroid gland secretes two biologically active hormones, thyroid hormone T4 and T3 (Dev *et al*, 2016). Studies showed that thyroid disorders are associated with a change in the human skin, the composition and function of hair (Messenger, 2000).

Oxidative stress process one of the factors that contribute to graying of hair and hair loss (Rajendrasingh, 2017). This process mechanism cause metabolic changes that can lead to hair loss under the effect of reactive oxygyn species (ROS)(Rajput, 2018a and Prie *et al*, 2016).

Despite the multiplicity of physiological factors that cause hair loss in women, the studies that discuss these factors comprehensively are very few, and the studies

that dealt with the case of hair loss in Iraqi women are very scarce with rising number of hair loss cases. The current study directed tohighlight the physiological factors that operate asinfluential source of hair loss in women in Basra Governorate.

MATERIALS AND METHODS

Sample collection

Eighty eight volunteer women participated in this study. Twenty one of 88 womenwere healthy and 71 were suffering from hair loss. All volunteer were observed and diagnosed by dermatological consultant in Dermatology Department at Al-Sader Educational Hospital.Volunteers' age range was between 20-40 years old.

Blood samples were withdrawn by the laboratory of dermatology Department staff. Approximately (5 mL) of the ulnar venous blood antecubital vein. Twomilliliters of blood were put in EDTA tube to perform a complete blood picture test (CBP). The remaining blood were keptin Gel tube and left for a period of 10 - 5 minutes.After that serum were prepared by centrifuging the blood at 3500 rpm for 15 minutes. Serum was divided and placed in Eppendorf tubesand kept at -20°C until the tests were performed.

Some blood parameters were measured, including Red blood cell (RBC) and White blood cells(WBC), Hemoglobin (Hb), Mean corpuscular volume(MCV), Hematocrit (HCT) and Mean Corpuscular Hemoglobin. Using the Hematology analyzer (sysmex XP – 300, Japan).

Determination of iron concentration

The serum iron level was determined by using BIOLABO-FRANCEIron Metering Test Kit. Where the iron level was estimated according to the colorimetric method approved by Tietz (1999). This method relies on the iron -transferrin unlinking in an acid medium then Fe^{+3} reduced to F^{+2} by ascorbic acid that given a color complex called Fe renemeasured at 600nm wavelength. The reading represents the amount of iron in the sample.

Determination of zinc concentration

The serum zinc level was determined using the (LTA-ITALY) zinc tester. The zinc level was estimated according to the Colorimetric method approved by (Maringoni, 1991). The zinc interacts with the chromogen in the reagent, forming a colored compound.The color intensity is proportional to the concentration of zinc present in the sample. Reading were obtained at a wave length of 600 nm (620 - 580 nm).

Determination of vitamin D

Morris method (2005) was used to measure the level of vitamin D. This method depends on the competitive interaction between the hormone of the sample and the hormone-enzyme conjugate using the kits supplied by Accu bind, USA.

Determination of hormones concentration

Serum concentration of testosterone, estrogen and thyroid hormones were evaluated using Enzyme-Linked Immunoassay (ELISA) type (Biotek-USA) and the specific kits of each hormone specified in the study and prepared by the American company (Accu bind USA).Testosterone concentration was determined ccording to (Dorfman and Shipley, 1956), while estrogen hormone was evaluated in according to Gautray *et al* (1981) and Chopra *et al* (1971) was used as reference to determine the thyroid hormone concentration.

Determination of Malondialdehyde (MDA)

The Competitive-ELISA was used to estimate the level of MDA using a kits supplied by the American company (Elabascince). The method relies on the competitive reaction between MDA in the solid phase with MDA in the sample based on the association with Biotinylated Detection Ab specific to MDA.

Statistical analysis

Statistical Package for Social Sciences (SPSS, V. 23) was used to analyze data. Data normality was tested to determine the type of statistical tests. T-test and Analysis of Variance (ANOVA) were used to compare the mean of control samples and patient samples at the probability level ($P \leq 0.05$) for both blood and nutrients measurements. While Kruskal-Wallis Test and Mann Whitny U test were used for analyzing hormones and MDA data.

RESULTS

Blood parameters

Table 1 showed the differences in blood parameters between patients and control group. A significant decrease in blood parameters in women who are suffering from hair loss. Hemoglobin concentration decreased significantly ($p \leq 0.001$) in patient women (Hb 11.3545 ± 1.03436 g/dL) in comparison with the control group (12.3762±1.00195 g/dL). A significant decrease ($p \leq 0.001$) was counted also in the MCV in women with hair loss, it was 83.3818 ±7.40567 μm^3, whereas, it was 88.104 ± 3.700 μm^3 recorded in control group. Mean cell hemoglobin showed the similar trend. It was 28.8619 ± 3.06912 g / dL in control group, while in patient, this gauge decline markedly ($p \leq 0.001$) to reach 25.7136 ± 4.11548 g/dL. On another hand, the RBC, WBC and HCT did not vary significantly.

Table 1 : Blood parameters variations between women with hair loss and the control group (n=67, 21).

Investigations	Mean ± SD		P-value
	Patients group	Control group	
White blood cells WBC (x10^3/µL)	7.382± 1.842	6.985± 1.918	0.3
Red blood cells RBC (x10^6/ µL)	4.5971± 0.611	4.662 ± 0.438	0.6
Hemoglobin concentration Hb(g/dL)	11.354 ± 1.034	12.376 ± 1.001	0.001
Hematocrit HCT%	37.565 ± 3.046	39.376 ± 2.430	0.15
Meancell average MCV –(µm^3)	83.381 ± 7.405	88.104 ± 3.700	0.001
MeanCell hemoglobin MCH –(g/dL)	25.713 ± 4.115	28.861 ± 3.069	0.001

Table 2 : The differences in some nutrients (Iron - Zinc - Vit D) between the Women with hair loss and the control group (n = 67, 21).

Investigations	Mean ± Standard deviation		P-value
	Patients group	Control group	
Iron (mg/dl)	62.040±50.60	87.818±50.035	0.05
Zinc (mg/dl)	67.085± 50.475	140.158±60.597	0.001
Vit D (ng/ml)	12.613±9.261	42.414±13.479	0.001

Table 3 : Hormones (testosterone, estradiol and T3) and MDA concentration in women with hair loss and control group (n = 67, 21).

Investigations	Median (min – max)		P-value
	Patients group	Control group	
Testosterone ng / dl	0.9 (0.63 - 2.625)	0.387(0.2-0.6)	0.001
Estradiol pg/ml	61.4 (14-141.7)	95 (15-189)	0.001
T3 ng/ml	0.54(0.2 - 2.2)	0.685(0.4-1.6)	0.045
MDA ng/mL	985(713.3 -10181	250(138 - 1001)	0.001

Iron concentration in serum

The concentration of iron in the serum of women with hair loss decreased significantly ($p \leq 0.05$), it was (62.0400 ± 50.60394 mg/dl), in comparing with the control group (87.8181 ± 50.03536 mg/dl) (Table 2).

Zinc concentration in serum

A significant decline ($p \leq 0.001$) was detected in the concentration of zinc in women with hair loss (67.0855 ± 50.47555 mg/dl) in comparison with the control group (60.59783 ±140.1585 mg/dl) (Table 2).

Vitamin D concentration in serum

Vitamin D concentration in women with hair loss showed a similar trend as other nutrientswhich was 12.6132 ± 9.26136 ng/ml, this level was significantly (pd" 0.001) less than the vitamin D in control group, which was 42.4145 ± 13.47956 ng/ml ($p \leq 0.001$) (Table 2).

Testosterone concentration in serum

Table 3 showed the level of hormones in collected samples. Testosterone in patients was higher significantly ($p \leq 0.001$) than in healthy women. 0.9 (0.63-2.625) ng/dl that and 0.387 (0.2-0.6) ng/dl, respectively.

Estradiol concentration in serum

Estridol concentration in patient women with hair loss showed a lower significant level ($p \leq 0.001$) than in women at control group. As in Table 3, it is clear that the concentration of estradiol in patients was 61.4 (14 -141.7) pg/ml, while in the control group was 95 (15-189)pg/ml.

Triiodothyronine (T3) concentration in serum

Similarly, triiodothyronine (T3) hormone showed a significant low concentration ($p \geq 0.045$) in the women with hair loss syndrome when it is compared with the women in control group. As shown in Table 3, the concentration of T3 was 0.54 (0.2-2.2) in hair loss women, while it was 0.685 (0.4-1.6) ng/ml in control group.

Malondialdehyde MDA concentration in serum

Table 3 exhibited the concentration of MDA in patient and healthy women. A significant higher level ($p \leq 0.001$) of MDA was detected in women with hair loss which reached up to 985 (713.3 -10181) ng/mL than in control group, which was 250 (138-1001)ng/mL.

DISCUSSION

The current results revealed a significant low concentration of Hb, MCH and MCH in the blood of patients group when compared to the healthy group.

Simultaneously, a significant low concentration of iron was detected. This finding was in consistent with the previous findings of Hodeib *et al* (2017) and Fatani *et al* (2015), that indicated to decline in red blood corpuscular parameters in women who experienced hair loss and this output might elucidate the hair loss in women. In the same trend the decrease of the level of iron supports the occurrence of red blood corpuscles disturbance. Subsequently, iron deficiency anemia is the case of disease that may lead to hair loss in women. However, iron deficiency probably induces the hair loss in another mechanism. This mechanism can be interpreted by the role of iron as a cofactor of the ribonucleotide reductase enzyme (DNA synthesis) in the hair stem cells (Elledge, 1992).

Iron deficiency also causes morphological changes in red blood cells, as they are characterized by a decrease in blood pigmentation and small cell size and this condition is called hypochromic microcytic anemia (Stockholm and Scott, 2002). It is possible that hair loss can be caused by the weakness in the ability of red blood corpuscles in carrying the adequate amount of oxygen as a result of iron deficiency, in turn,that may lead to weakening of the hair follicles to start the anagen phase after the telogen rest stage. Thus, nutrients deficiencyoccurs in the body is regarded as a stress, prevents cell proliferations during growth stage and keep the hair in the resting phase (Rajput, 2018b; Rushton *et al*, 2011).

It is clear from the current results that zinc was in low level in women, who experience hair loss. In fact, Zinc deficiency can occur in patients consuming large amounts of cereal grain (which contains aphytate considered to be chelating agent of zinc), in those with poor meat consumption other causes of zinc deficiency include anorexia nervosa (Almohanna *et al*, 2019).

The exact mechanism of how zinc deficiency affects hair loss has not been accurately understood yet (Kondrakhina *et al*, 2020). Although, some studies indicate that zinc plays an important role in functional activities within hair follicles and it also speeds up the recovery of follicles (Plonka *et al*, 2005). Also, zinc deficiency may trigger hair loss as a result of a defect in zinc regulation of enzymes as zinc works as an enzyme coenzymes for a large number of enzymes, which participate in almost all metabolism processes that occur in the body. Consequently, that may affect hair growth and interrupt cycle of hair follicles (Kil *et al*, 2013).

It also demonstrated that zinc is involved in regulating the growth and death of skin papillary cells in the human hair follicle (HFDPCs), which are specialized cells found in the base of hair follicles and are necessary to stimulate the growth of hair follicles (Kondrakhina *et al*, 2020). In addition to this it mayzinc deficiency leads to hair loss as a result of its effect on the zinc finger function necessary to make many transcription factors that regulate hair growth through the Hedgehog Signaling pathway (Karashima *et al*, 2012).

It is believed that the optimal concentration of vitamin D is necessary to delay the phenomena of aging, including this hair loss and may explain the importance of vitamin D for hair. Moreover, some data clearly show that activation of vitamin D receptors, which were found in two major groups of hair follicle cells: epidermal keratinocytes and mesodermal skin papilla cells dermal papilla cells,play central role in the hair follicle cycle specifically starting anagen phase (Rasheed *et al*, 2013; Malloy and Feldman, 2011; Aksu *et al*, 2014 and Bikle, 2015).

Testosterone increasing in patients' samples are also responsible for hair loss type AGAin women with a genetic predisposition to infection (Price, 2003). Trüeb (2015) mentioned that the increase in the level of the DHT hormone interacts with the increase of the androgen receptors in the skin papilla cells (DPCs) and thus stimulates the secretion of (TGF-beta1) transforming growth factor-beta2 that causes changes in the hair follicles. Some studies have shown an increase of androgen receptor (AR) receptors in skin papilla (DPCs) in the front hair follicles of women, who undergo thinning as a result of reducing hair follicles compared with occipital hair, in addition to increasing activity (α-reductase 5), which is a responsible enzyme to convert testosterone to (DHT) in areas of hair loss of the scalp compared to other areas of the head (Ramos and Miot, 2015; Ustuner, 2013).

On another side, the reduction in (17β-estradiol) hormone in women with hair loss compared to its level in the control group comes to support the increase of DHT. Perhaps the effect of estrogen deficiency on increasing hair loss in women through the absence of estrogen function in regulating the growth of hair follicles. As it is supposed that estrogen works to prolong the anagen stage of the hair follicle cycle, so a decrease in the level of estrogen may shorten the period of the growth phase and move to telogen resting and thus generates telogen hair (Yip *et al*, 2012; Mirmirani, 2016).

Furthermore, the reason for hair loss is due to an imbalance in the protective role that estrogen plays against testosterone, as 17β-estradiol possesses the ability to reduce the level of testosteron by stimulating the

activity of aromatase, which is an enzyme that works to convert testosterone into estrogen inside the hair follicle (Levy and Emer, 2013). The presence of high levels of aromatase in the front hair line in women with androgenic hair loss which remains conservative in its shape without being exposed to hair loss when compared to the areas of the head in which hair loss occurs, so a decrease of 17ß-Estradiol to increase the level of testosterone that converts to DHT, which causes increased hair loss in women (Hammes and Levin, 2019).

Richardson *et al* (2011) also indicated that estrogen has cell protection against the effects of oxidative stress in a number of tissues.As oxidative stress results as a result of exposure to ultraviolet radiation, inflammation and high ROS, causing increased damage to DNA, proteins and fats, which may cause premature skin aging associated with hair aging that is manifested in decreased melanocyte function and graying and reduced hair production and hair loss (Masaki, 2010).

Thyroid hormones plays a crucial role in the erythropoiesis formation process by contributing to the proliferation of erythroid progenitors in the bone marrow. Moreover, thyroid hormones increase the delivery of oxygen to tissues by increasing levels of 2-3 Diphosphoglycerate (Archana and Vijaya, 2019). Therefore, the low level of thyroid hormone T3 may lead to an increased hair loss due to its negative effect on the formation of blood cells and the transportation of oxygen to the hair follicles, especially with a decrease in the level of iron in the blood. Akbaº *et al* (2019) indicated that the low level of thyroid hormone with iron deficiency in women leads to stimulating telogen hair loss due to the effect on the formation of red blood cells, which leads to anemia and thus reduces the oxygen supply to hair follicles. That also support the asserted the occurrence of anemia in patient groupin current output. Also, the lack of thyroid hormone has a direct effect on hair follicles, which causes hair loss, as thyroid disorders affect the hair follicle growth cycle, as it was observed that patients with hypothyroidism have prominent deformities in the hair, so a deficiency is accompanied thyroid gland with telogenic hair loss, along with dry, brittle and dull hair (Kasumagic, 2014).

MDA increasing level in the samples of patient women was spotted in current results. This high level of MDA can attributed to different kinds of exposure to pollution factors and/or the stress psychological situations (Rajput, 2018a). The oxidative stress resulting from increased ROS plays an important role in hair loss Koca *et al* (2005). Itami (2004) showed the mechanism in which androgen prevents hair growth by secreting TGF β1 in (DPCs) after which Hee (2008) analyzes the details of this mechanism, as it showed that the DHT raises the levels of free radicals (ROS) in papilla cells (DPCs), which in turn leads to the secretion of TGF β1, which prevents the proliferation of epithelial cells and stimulates programmed cell death and thus prevents hair growth, and this belief has confirmed this during the use of antioxidants to promote hair growth well without using DHT antioxidants.

CONCLUSION

The study has come up with the fact that the most common types of hair loss in women in Basra Governorate, was telogen effluvium is based on the results of the study that showed the presence of iron anemia in addition to nutrient deficiency in a large group of patients who had caused poor nutrition in the hair follicles and led to hair loss. Also, oxidative stress due to pollution may play an important role in increasing hair loss in Basra Governorate. Consequently, the increasing of hair loss occurrence in Basrah may due to many synchronized physiological reasons that combined together. Further investigation are required to show the effect of water and air pollution on hair loss.

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