

Diagnostic usefulness of hair analysis – A review

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ABSTRACT

For laboratory diagnosis, as of date mostly invasive procedures are used to collect biological samples such as blood and other body fluids. Recent research studies have established urine, sweat and saliva based laboratory diagnosis. However, hair analysis based clinical diagnosis is in the infancy. Recently researchers have shown much interest to establish hair as a non-invasive laboratory diagnostic material. Many studies have linked the contents of hair, such as minerals, metabolites, hormones, amino acids and vitamins to the blood levels thereby establishing hair analysis based laboratory diagnosis. This field has expanded during the last two decades and the outcome of such researches have brought out informations on hair based clinical diagnosis for various common diseases such as DM, CVD, reproductive, metabolic, menopause, thyroid and adrenals. The contents of this review article will through some light for future research to firmly establish human hair as the best non invasive biological sample for the diagnosis of various common disorders.

Keywords: Hair, DM, OS, Thyroid, CAD, Menopause.

1. INTRODUCTION

Human hair, a noninvasive biological material could serve as the best sample for the diagnosis of various disorders. Hair contain some 18-20 essential as well as non-essential trace metals, amino acids, proteins, hormones, vitamins and other useful metabolities. Studies have linked the associations of all the above parameters to the blood levels and hence the objective of this review article is to bring out the findings done on hair analysis during the last two decades to make awareness among research scholars to explore various methods to firmly establish hair as a diagnostic material.

1.1. Hair and Diabetes mellitus

The glycation index done on humans hairs in normo- and hyperglycemia, is a reliable

indicator and could be diagnostically useful.^[1]The level of glycosylation of hair is independent of duration of the disease, age, sex and race of the patient as well as colour of the hair, thus providing a universal index of hyperglycaemia in the control of diabetic state. Glycosylation of hair is perhaps the most non-invasive technique readily acceptable to the patients and yet provides a fairly accurate and reliable information regarding hyperglycaemia in the preceding duration in which the hair has been grown.^[2] The level of glycosylated keratin in healthy hairs along the entire length varied within 0.094-0.124 μmol of fructosamine per 100 mg of hair. In about 60% of Type 1 Diabetes Mellitus (T1DM) patients, glycosylated keratin levels along the entire hair length were elevated.^[3]

Hair glycation may serve as a valuable indicator both long-term blood glucose trends and to monitor the relationship between diabetic complications and blood glucose.^[4] The addition of an aldose reductase inhibitor provided inconclusive results in both hair cell determination and neuroganglion cell density; however, generally the inhibitor partially prevented the damage produced by galactose. A high-galactose diet can induce diabetic-like changes in the cochlea.^[5] Obese women have elevated hair K, Hg, Pb and decreased Ca, Mg, Zn and I and in T2DM patients elevated hair K, Na, Hg and decreased Ca, Mg, Zn and Co were observed demonstrating the very similar changes in hair elemental content in both obese and diabetic women, thus suggesting the general pathophysiological mechanisms of metabolic mineral disturbances.^[6]

In male diabetics at the age of 50 years or more, greying of the eyebrows seems to be inhibited or delayed. The presence of dark eyebrows with greying scalp hair in males might be a clinical sign for patients at risk of T2 DM.^[7] The nonessential amino acids Glycine and Glutamate, and the essential amino acid Isoleucine were more abundant in the scalp hair of diabetic patients compared to the hair of control subjects. The associations between the abundance of amino acids of human hair and health status may have clinical applications in providing diagnostic indicator or predicting other chronic or acute diseases.^[8] Some metabolites found in the hair metabolome were significantly correlated with age and Body Mass Index (BMI) and may provides justification for the matching of case and control groups by these two potential confounding factors in future studies. Despite these relationships occurring as statistically significant in the control groups, an assessment of the 95 % confidence intervals show an overlap between the groups, indicating that despite a varied significance, there is little evidence of discordant correlation between the groups. Currently, hair metabolome analysis is in its infancy. It is important to develop a method for LC-MS analysis so that a comprehensive profile of the metabolites in hair can be elucidated using a range of analytical platforms.^[9]

Studies indicate that hair samples are superior to urine samples, and it can provide more valuable information for prevention, diagnostics, treatment and research of diabetes by simultaneously analyzing the hair and urine samples.^[10] Hair analysis is used for estimation of the nutritional status of individuals. The profile of hair mineral imbalance might be useful as a diagnostic tool for the early diagnosis of many

diseases. However, it seems that there is a need to standardize sample preparation procedures, in particular washing and mineralization methods.^[11]

The use of whole hair samples and on-line solid phase extraction resulted in a significant reduction in sample throughput times, increasing the applicability of this method for research questions where a larger number of samples needs to be processed.^[12] There is also increasing concern in the lay community about this risk. These results indicate the need for additional research, and the opportunity to benefit from strategic partnerships in community-collaborative approaches in order to better understand the potential "cost of beauty."^[13]

1.2. Hair and Reproduction

Hair Ethyl Glucuronide (hEtG) testing demonstrated an association between Gamma Glutamyl Transferase (GGT) and Phosphatidylethanol (PEth). Validity of hEtG improved in patients with less frequent shampooing and those who did not use hair dyes/chemical treatments.^[14] Multiparous cows that became pregnant by 100d postpartum had lower concentrations of hair cortisol at d 42 and 84 in milk. Other biomarkers associated with metabolic status and acute inflammation, such as glucose, β -hydroxybutyrate, haptoglobin, and ceruloplasmin, were not strongly correlated with measurements of cortisol in hair. Hair cortisol measurements appear to be associated with clinical disorders and have a direct association with pregnancy status; however, concentrations of hair cortisol may not be suited to differentiate situations of stress with lower magnitudes, such as the development of subclinical disease.^[15] Short-term fluctuations of $\delta(15) N$ values may be the result of changes in an individual's metabolic balance, and that metabolic imbalance poses a confounding factor to ancient dietary studies when using rapidly growing tissues such as hair.^[16]

Generalized linear mixed models with random intercepts accounting for within-woman correlations across treatment cycles were used to evaluate the association of hair Hg with In Vitro Fertilization (IVF) outcomes adjusted for age, BMI, race, smoking status, infertility diagnosis, and protocol type. Hair Hg levels were not related to ovarian stimulation outcomes (peak estradiol levels, total and mature oocyte yields) or to fertilization rate, embryo quality, clinical pregnancy rate or live birth rate.^[17] In a mutually adjusted model, all but education, multiple jobholding, hair characteristics and premature delivery remained statistically significant.

Maternal hair cortisol in the last trimester of pregnancy is determined by many factors. Delivery mode, BMI and season of delivery should be considered when investigating the association between Hepatocellular Carcinoma (HCC) and further outcomes in mothers shortly after delivery.^[18]

Hair hormone levels differed regionally for wild lynx, indicating that spatial variability should be a consideration in wildlife hormone studies spanning large spatial scales. The use of hair hormone analysis by enzyme immunoassay may hold promise for differentiating sex in felids, but the technique will require further refinement and validation before it could be applied broadly and reliably.^[19] The diagnosis by the hair mineral analysis protocol is very essential and quite detailed in providing a unique insight into nutritional biochemistry. It is much more accurate from the serum analysis for all these trace elements because for the low cost and the accuracy of the storage levels that hair analysis provide, while serum just inform us about the temporary levels of minerals because they are transported to different tissues of the body, and not being stable. So, serum analysis can bring confusion to the evaluation of a patient. The other major advantage of the report in hair analysis is the regulation of the Phyco-Neuro-Endocrine-Axis (PNEA) and targeted detoxification, which can bring the balance of the human body, without the need of dietary supplements most of the time.^[20] Hair mineral analysis has its limitations, considering the reliability of inter and intra laboratory analysis comparing with blood analysis. As such, clinicians should be cautious when applying hair mineral analysis as an ancillary tool. Each laboratory requires continuous refinement from now on for inducing standardized normal reference levels.^[21]

It was shown that calcium and iron daily intake by the women was below the recommended value. Only few women had low concentrations (below reference values) of magnesium, copper and zinc in hair. Statistically significant differences were shown between age groups. Generally, the concentrations of minerals in hair in the younger (19–30 years) and the older women (41–50 years) were higher than in hair of middle-aged women (31–40 years). The content of calcium, magnesium, iron and zinc in daily diets of women correlated inversely with copper level in their hair. Food products with good bioavailability of iron and calcium should be recommended for women of child bearing age in all age groups.^[22]

Overall, hair cortisol measurements appear to be associated with clinical disorders and have a direct association with pregnancy status;

however, concentrations of hair cortisol may not be suited to differentiate situations of stress with lower magnitudes, such as the development of subclinical disease.^[23] The menstrual estradiol and progesterone rhythm of female hair is similar to that of female serum. The ratio of hair estradiol to serum estradiol in the female is 41.2% and that of hair progesterone to serum progesterone is 59.0%; the ratio of hair testosterone to serum testosterone in male is 116%. There are significant correlations between hair and serum steroid hormones of healthy human adult such as γ -estradiol, γ -progesterone and γ -testosterone.^[24] Primiparity influences both chronic maternal hormonal profiles and infant development and these effects may, in part, reflect differential reproductive and maternal effort in mothers with varied care taking experience. In addition, infant exposure to relatively higher levels of maternal cortisol during the late fetal and early postnatal periods is predictive of poorer developmental outcomes.^[25]

A longer duration of obesity was associated with facial hair. Another analysis found that teenage obesity was greater for never-pregnant married women than for previously pregnant married women and for women having ovarian surgery for polycystic ovaries than for women having ovarian surgery for other reasons. This also supports an association of obesity with anovulatory cycles. These findings showing evidence of abnormal ovulation, menstrual abnormalities and excess hair growth in obese women may be explained by the recent studies of others demonstrating an association between obesity and hormonal imbalances.^[26]

1.3. Hair and Thyroid diseases

Hair appears to be a valuable and robust biological indicator tissue for assessing long-term iodine status. An adequate iodine status corresponds with hair iodine uptake saturation of 0.565–0.739 $\mu\text{g/g}$ (55–65%).^[27] All patients with alopecia, irrespective of the pattern of alopecia should be screened for Thyroid Stimulating Hormone (TSH) and Thyroid Peroxidase Antibodies (TPOAb) as they are good screening tools and cost effective.^[28] Thyroid hormone signaling is an important determinant of the mobilization of stem cells out of their niche in the hair bulge, and they correlate with skin defects observed in mice and alterations found in human thyroid disorders.^[29] Premenopausal Female Pattern Hair Loss (FPHL) patients turned out to show much lower serum ferritin concentration (FC) than age/sex-matched controls. Among MPHL patients, 22.7% of them showed serum FC lower than 70 $\mu\text{g/L}$, while no one had serum FC lower 70 $\mu\text{g/L}$ in healthy age matched males

which suggest that iron may play a certain role especially in premenopausal FPHL patients. The initial screening of iron status could be of help for hair loss patients.^[30]

Low iodine levels are consistent with previous reports of abnormal thyroid function, which likely affected development of speech and cognitive skills. Low lithium in the mothers may cause low levels of lithium in the young children, which could have affected their neurological and immunological development and investigations of iodine, lithium, and other elements are warranted.^[31] Moderate elevation in prolactin (PRL) levels in association with diffuse or androgenetic hair loss can be neglected as causative for the hair loss, because there is no evidence that they have an influence to the pattern, the extent or the duration of the hair loss. These results are supported by investigations of other authors who described only in high doses of PRL an inhibiting effect on human hair follicles in vitro. Nevertheless, moderate constantly elevated PRL levels should induce further diagnostics to exclude a PRL-producing tumor of the pituitary gland.^[32]

The autoradiographic studies of human hair demonstrated that iodine is rapidly incorporated into external layers of the hair root and can be removed easily during washing. These data were confirmed after iodine exposure using the human hair/nude mouse model. Hair does not provide satisfactory information about exposure due to unstable incorporation of iodine. The most useful medium for biological monitoring of astronauts exposed to high doses of iodine in drinking water is urine, when adjusted for creatinine, and saliva, if quantitative evaluation of flow rate is provided.^[33] The levels of hair T3 and T4 were significantly lower in patients with depression in disease episode than that in pre-disease episode or in healthy controls. Moreover, patients with depression in pre-disease episode had a higher hair T4 level than healthy controls. No significant correlation was observed between hair T3 or T4 levels and the Hamilton depression rating scale and Hamilton anxiety rating scale scores and that hair thyroid hormones levels change with the episodes of depressions, which may be helpful for pathological studies of depression.^[34]

1.4. Hair and adrenal function

Hair cortisol concentrations appeared to vary in accordance with the clinical course. Based on these data, Hair cortisol measurement is a novel method for assessing dynamic systemic cortisol exposure and provides unique historical information on variation in cortisol, and that more

research is required to fully understand the utility and limits of this technique.^[35]

The importance of obtaining histories of possible food and non-food environmental sources of contamination, the suitability of hair sampling to identify the origin of the contamination, and the opportunity to warn parents about hazards related not only to oral contraceptives, but also custom-compounded topical hormone preparations.^[36] A low incidence of chromosomal abnormalities and thus question routine chromosomal analysis at the baseline evaluation of transsexualism, suggest that it be considered only in cases of abnormal history or hormonal examination.^[37] Scalp hair has a fairly predictable growth rate of approximately 1 cm/month, and the most 1 cm segment approximates the last month's cortisol production as the mean value. The analysis of cortisol in hair is a highly promising technique for the retrospective assessment of chronic stress.^[38]

Elevated hair cortisol levels found among regular exercisers are not necessarily pathological. Thus, one should practice caution when associating athletes' elevated hair cortisol with poor mental health or disease. Hair cortisol analysis can contribute to a more complete understanding of how long-term cortisol elevation mediates stress-related effects on the health and performance of recreational exercisers and elite athletes. Nevertheless, it is crucial for exercise and sport scientists to consider whether their research questions can be adequately addressed, given that regular intense exercise results in substantially augmented hair cortisol levels. One should practice caution when associating athletes' elevated hair cortisol with poor mental health or disease. Hair cortisol analysis can contribute to a more complete understanding of how long-term cortisol elevation mediates stress-related effects on the health and performance of recreational exercisers and elite athletes. Nevertheless, it is crucial for exercise and sport scientists to consider whether their research questions can be adequately addressed, given that regular intense exercise results in substantially augmented hair cortisol levels.^[39]

Hair cortisol is a proxy measure to the total retrospective activity of the HPA axis over the preceding months, much like hemoglobin A1c is a proxy measure of glucose control over the past 3 months.^[40] Physical activity, adiposity, and substance abuse may be correlates with hair cortisol concentrations. In contrast to measures of short-term cortisol release (saliva, blood, and urine), cigarette smoking and use of oral contraceptives appear not to be associated with hair cortisol concentrations. Studies of pregnant

women indicate increased hair cortisol concentrations across successive trimesters. The study of hair cortisol presents a unique opportunity to assess chronic alterations in cortisol concentrations in epidemiologic studies.^[41]

The concentrations of cortisol, cortisone, and dehydroepiandrosterone in hair were significantly correlated to mental and physical stress as well as to subjective stress perception. Steroid concentrations in hair are decisive predictors for an increase in the long-term-Hypothalamic Pituitary Axis (HPA) axis activity. Moreover, this biomarker is suitable for capturing the stress level after burdening events and physical activity.^[42] Since the advent of this methodological advance, hair cortisol has already been used as an index of chronic HPA activity and stress in human clinical and nonclinical populations, in a variety of laboratory-housed and wild-living animal species, and in archival specimens that are many decades or even centuries old. Moreover, because human hair is known to grow at an average rate of about 1 cm/month, several studies suggest that cortisol levels in hair segments that differ in proximity to the scalp can, under certain conditions, be used as a retrospective calendar of HPA activity during specific time periods preceding sample collection.^[43]

Hair cortisol analysis advances the science of aging by better characterizing chronic stress as a risk factor for chronic illness progression and as a biomarker of the effectiveness of stress reduction interventions.^[44] In patients with an unconfirmed diagnosis who have already started glucocorticoid treatment, it may provide information on cortisol levels before the treatment began. Patients need to be able to provide samples of scalp hair that are at least 1 cm in length, and use of glucocorticoids and hydrocortisone cream must be determined. Hair analysis of historical cortisol levels is a promising tool for use in clinical practice but requires further study.^[45]

1.5. Hair and cardiac diseases

The degree of gray/white hairs is related to extent of Coronary Artery Disease (CAD). Hair graying is a risk marker for CAD independent of age and other traditional risk factors. Biological age may be important in determining total risk of patients. During assessment of cumulative Cardiovascular risk factors (CVRF) effects on human body, presence of biological aging signs may be useful in identifying individuals with increased risk of CVD.^[46] The presence of premature graying of hair was associated with 3.24 times the risk of

CAD on multiple logistic regression analysis. The presence of premature graying of hair was associated with an increased risk of CAD in young smokers. Premature graying of hair can be used as preliminary evidence by clinicians for classifying patients at risk for premature CAD especially in smokers.^[47] The association with Coronary Heart Disease (CHD) depends on the severity of vertex baldness and also exists among younger men. Thus, vertex baldness might be more closely related to atherosclerosis than frontal baldness, but the association between male pattern baldness and CHD deserves further investigation.^[48] A statistically highly significant direct association was observed between the hair lithium and cobalt concentrations, which suggests a role of lithium in the transport and distribution of vitamin B12.^[49]

It was found that prevalence of the ear-lobe crease increases with advancing age, and the incidence was much more higher in Sindhis in whom the overall incidence of CAD is also significantly high. Bilateral diagonal ear-lobe crease was found to be significantly associated in patients with documented CAD, and a significant difference was also observed between men with and without CAD in the presence of ear-canal hair with age matched group. The combined presence of ear-lobe crease and ear-canal hair was more definite and more sensitive index of underlying CAD.^[50]

The median HCC was 22.3 pg/mg of hair (23.5 interquartile range). In multivariable linear regression analyses, an association was observed between log-transformed HCC and BMI, respiratory rate, and the physical summary score. Independent predictors of log-transformed HCC change after 12 weeks were mental summary score and diastolic blood pressure. In patients with structural heart disease a positive association exists between HCC and BMI. Mental health status may predict a change in long-term cortisol over time.^[51] Hair Hg was not associated with stroke risk, but among those with hair Hg above the median level, higher serum long-chain n-3 Poly unsaturated fatty acids (PUFA) concentrations were associated with a higher risk of ischaemic stroke. In men, serum n-3 or n-6 PUFA or hair Hg were not associated with stroke risk; however, the interaction between Hg and long-chain n-3 PUFA with regard to ischaemic stroke risk warrants further investigation.^[52] Hair analysis should be based on a diagnostic hypothesis such as cadmium intoxication or copper deficiency rather than on the ease of analysis or attempts to explain vague symptoms because within-person variability is large and

interlaboratory agreement on normal values is poor.^[53]

1.6. Hair and menopause

In a study of pre- and postmenopausal women without alopecia, menopausal status significantly influenced hair parameters, specifically hair growth rate, percentage anagen and hair diameter distributions, most notably in the frontal scalp. Hair density decreased with age, but was not correlated with menopausal status. Analyses of hair amount using a model of hair density and hair diameters suggest that the impact of changing hair parameters is most notable in the mid-forties for women.^[54] Vitamins also have impact on the state of hair: C vitamin, group B and A vitamins. Minerals which influence hair growth are: Zn, Fe, Cu, Se, Si, Mg and Ca. It is worthwhile to pay closer attention to diet in women who besides hormone changes and undertaken pharmacotherapy are additionally exposed to chronic stress and improperly conducted cosmetic's and hairdresser's treatments.^[55] The manganese status of the vegetarians, as indicated by elevated hair manganese levels, was higher, almost certainly as a result of the significantly higher manganese intake of this group.^[56] No patient in this cohort reported scalp hair loss on testosterone therapy. Studies reported some increase in facial hair growth. Subcutaneous testosterone therapy was found to have a beneficial effect on scalp hair growth in female patients treated for symptoms of androgen deficiency. The fact that no subject complained of hair loss as a result of treatment casts doubt on the presumed role of testosterone in driving female scalp hair loss. These results need to be confirmed by formal measurements of hair growth.^[57]

High blood Hg levels were associated with a lower risk of having osteoporosis in postmenopausal women. Studies are necessary to clarify the association of osteoporosis with the level of heavy metals in biomarkers for long-term exposure such as hair or fingernail.^[58] FPHL also known as female androgenetic alopecia is a common condition afflicting millions of women that can be cosmetically disrupting. Prompt diagnosis and treatment are essential for obtaining optimal outcome.^[59]

The menopausal symptom "more clumsy than usual" was influenced by marital status, hypertension and the presence of CVD. Menopausal status and abdominal obesity induce the loss of sexual interest. Obesity could be involved in menopausal symptomatology among Slovak midlife women. Obese women have a higher susceptibility to increase in facial hair and

backache, and women with abdominal obesity to loss of sexual interest.^[60]

1.7. Hair and oxidative stress

It is essential for Malaysian women to obtain a good antioxidant status by consuming a diet rich in vitamins A and E as well as selenium and adopt healthy behaviour to reduce oxidative stress (OS) in order to prevent breast cancer.^[61] High Mn accumulation may contribute to the high OS. The mechanism of its high accumulation was not explained by food materials or drinking water. In order to suppress the high OS, elimination of the high Mn accumulation should be urgently studied.^[62] There are many signaling pathways (PI3K-AKT/PKB, AKT/PKB, Wnt, ERK and Ras) involved in the regulation of apoptosis and proliferation in cochlear hair cells with OS injury and these signaling pathways are linked to each other to form a network. PI3K-AKT/PKB signaling pathway seems to be the most active in cochlear hair cells with OS injury.^[63]

The Glutathione (GSH) concentrations were significantly greater in the post grafting group than in the group subjected to ischemia. Increasing the GSH concentrations used in food preservation solutions does not reduce the oxidative effects of cold ischemia and reperfusion injury during hair transplantation surgery.^[64]

The body possesses endogenous defence mechanisms, such as antioxidative enzymes and non-enzymatic antioxidative molecules, protecting it from free radicals by reducing and neutralizing them. With age, the production of free radicals increases, while the endogenous defence mechanisms decrease. This imbalance leads to the progressive damage of cellular structures, presumably resulting in the ageing phenotype. Ageing of hair manifests as decrease of melanocyte function or graying, and decrease in hair production or alopecia. There is circumstantial evidence that OS may be a pivotal mechanism contributing to hair graying and hair loss. New insights into the role and prevention of OS could open new strategies for intervention and reversal of the hair graying process and age-dependent alopecia.^[65] Enzyme kinetics, which leads to gradual loss of hair color. Notably under in vitro conditions, Met oxidation can be prevented by L-methionine. Some data feed the long-voiced, but insufficiently proven, concept of H₂O₂-induced oxidative damage in the entire human hair follicle, inclusive of the hair shaft, as a key element in senile hair graying, which does not exclusively affect follicle melanocytes. This new insight could open new strategies for intervention and reversal of the hair graying process.^[66]

The antioxidant treatment reduced the lipid peroxidation, potentiated the endogenous antioxidant defense system at OHC level in both exposures but it failed to ameliorate the oxidative imbalance and cell death of Deiters' cells in the styrene and combined exposures. Current antioxidant therapeutic approaches to preventing sensory loss focus on hair cells alone. It remains to be seen whether targeting supporting cells, in addition to hair cells, might be an effective approach to protecting exposed subjects.^[67] Hair bulb melanocytes are especially susceptible to free radical-induced aging. When human scalp skin anagen hair follicles from graying individuals to macroscopic and immunohistomorphometric analysis and organ culture, it was found evidence of melanocyte apoptosis and increased OS in the pigmentary unit of graying hair follicles. The "common" deletion, a marker mitochondrial DNA-deletion for accumulating OS damage, occurred most prominently in graying hair follicles. Cultured unpigmented hair follicles grew better than pigmented follicles of the same donors, and cultured pigmented hair follicles exposed to exogenous OS (hydroquinone) showed increased melanocyte apoptosis in the hair bulb. OS is high in hair follicle melanocytes and leads to their selective premature aging and apoptosis. The graying hair follicle, therefore, offers a unique model system to study OS and aging and to test antiaging therapeutics in their ability to slow down or even stop this process.^[68]

Procyanidin oligomers strongly bind to keratin in hair and inhibit the breakdown of hair caused by oxidative damage in an analysis of hair using electrophoresis, transmission electron microscope, and fluorescence dye. Such results confirm that procyanidin oligomers can be applicable as a potential candidate to the development of hair care with protective effect on hair damage.^[69] The role of copper in these oxidative processes indicates that its presence in hair and its consequent impact on hair damage via free radical formation. The role of chelants N,N'-ethylene diaminedisuccinic acid (EDDS) and histidine in preventing free radical formation shows to improve hair health.^[70] Regardless of their age, the studied women felt much more stress related to their life situation and were characterized by stronger skin pigmentation than the examined men. No sex differences were identified with regard to hair pigmentation. In the studied period of ontogenesis (18-22 years of age), hair pigmentation levels increased with age, while skin melanization remained stable. Disregarding the effects of age and sex, the level of perceived stress was negatively correlated with skin pigmentation levels; no such relationship was found for hair melanization.^[71]

2. CONCLUSIONS

Among the various non invasive biological material based laboratory diagnosis, hair analysis is now emerging as a new technique. Research done during the last two decades have established its clinical useful in the diagnosis of various human disorders such as DM, cardiac, reproductive, menopause, endocrine disorders, vitamins deficiency, mineral deficiency, alopecia, hirsutism and many other diseases disorders. A direct associations between the circulating parameters associated with each diseases have been established between blood and hair. The contents of this review articles and its results presented are based on publications done during the last two decades will certainly help future research scholars to undertake more studies based on hair analysis and to establish an acceptable procedure to implement this as routine test in clinical laboratories.

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