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RESEARCH ARTICLE

SKIN PIGMENTATION AND ASSOCIATED DISEASES IN KSA.

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Abstract

The purpose of this study is to determine the relationship between different chronic conditions and exposures, specifically saying: Vitamin D deficiency, Diabetes mellitus, Thyroid disorders, chronic stress, using psychotropic drugs, Chronic kidney disease, and using sun protective creams, and the prevalence of skin dyspigmentation among Saudi population. A significant relationship was found between skin pigmentations and DM, Hyperthyroidism, chronic stress and using sun creams. The results are concordant, in most parts of this study, with the previous studies in different times and regions, done for the same purpose.

Introduction:-

Skin color can range from the darkest to the lightest color. Variation in color of the skin is determined mainly by genetics, exposure to sun, or both. Although the actual color of the skin is affected by many substances, the main substance that determines the color of the skin and its darkness is melanin. Melanin is a skin pigment that is synthesized in specialized cells called melanocytes. Melanocytes is a type of cells derived from neural crest cells, and it's scattered among keratocytes, the main cell type in the epidermis of the skin. Each melanocyte produces a specific amount of melanin, that's eventually transported to the surrounding keratocytes, resulting in pigmenting the skin.

Skin color is not essentially uniform across the whole body. For example, the color of soles and palms is lighter than that of other parts of the body, this is markedly noticed in dark colored people.

The relationship tends to be clear between the geographical area (which points to Ultraviolet rays exposure) and the degree of skin pigmentation among populations. People living near the Equator tend to have darker skin than those living away from it, reasonably because of the difference in exposure to UV light.

"Tanning" of skin can occur with chronic exposure to sunlight containing UV lights. The suggested reason is that tanning makes the skin darker, thus more protective against UV light, which is a hazard that can cause damage and eventually mutations to DNA.

Hyperpigmentation and depigmentation, in another aspect, usually occurs due to disorders in melanin synthesis and distribution among skin cells. These "dyspigmentations" can be either even, or uneven in the form of patchy lesions and discolorations of scattered areas of skin.

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Literature Review:-

Skin pigmentation disorders is divided into two main branches:

1- Skin hypopigmentation:

Albinism:

Albinism is a genetic disorder caused by a mutation in one of the pathways responsible of either synthesis, or transport of melanin across the skin. It's an inherited autosomal recessive disease that affects skin, hair, and in some instances, eyes. A common type of albinism is what called Oculocutaneous albinism (OCA), which affects the three, skin, hair, and eyes. Albinos, the term pointing to patients with albinism, are at risk of developing skin cancer, and severe eye damage.

Vitiligo:

Vitiligo is an autoimmune disorder affecting the melanocytes, and thus preventing the synthesis and transport of melanin across the skin. Vitiligo depigmentation is uneven, irregular, scattered in different sites of the body, varies in severity among patients. Triggers of vitiligo are different too, among which is the stress, the most recalled trigger by patients. The exact cause of this autoimmune process is still unknown.

2- Skin hyperpigmentation:

Melasma:

Areas of darkened skin caused by many factors, like genetic predisposition, hormonal causes, and skin irritation. Melasma can present in pregnancy, Addison's disease, and thyroid diseases.

Chloasma:

Dyspigmentations due to some altered hormonal input, such as pregnancy, combined oral contraceptives, and estrogen replacement therapy.

Solar lentigo:

Skin dyspigmentations due to sun exposure. They can present also in the old.

Association between sex and skin dyspigmentation:

Study	Year	Result
Skin Responses to Ultraviolet Radiation: Effects of Constitutive Pigmentation, Sex, and Ancestry	2002	Males is more affected in skin pigmentations than females, with a statistical significance in Hispanic and European ethnicities. Measurement is done by Erythemal-dose index (EDI).
Sex and MC1R variants in human pigmentation: differences in tanning ability and sensitivity to sunlight between sexes	2016	Females have less tanning ability, and therefore lower phototypes, than males in most populations, as males show greater pigmentation contrast between exposed and unexposed skin regions.

Association between different chronic diseases and skin pigmentation:

Study	Year	Result
Low-Pigment Skin Type and Predisposition for Development of Type I Diabetes	1989	A low-pigment skin type may predispose for the development of type I diabetes.
A Case–Sibling Assessment of the Association Between Skin Pigmentation and Other Vitamin D-related Factors and Type 1 Diabetes Mellitus	2009	light skin pigmentation in unexposed skin sites was associated with higher T1DM risk.
Skin disorders and thyroid diseases, a review article	2001	Hypothyroidism decreases the erythematous appearance of the skin. Hypothyroidism increase the chance of developing friction-induced intraepidermal bullae as well as purpura and ecchymosis. It also increases the skin yellowish discoloration due dysfunctional metabolism of carotene, which eventually deposits in skin.

		Hypercholesterolemia, resulting from hypothyroid state, is also manifested in the skin of hypothyroid patients; both tuberous and eruptive xanthomas. Hyperthyroidism increases the erythematous appearance of the skin. Thyroid neoplasia associated with MEN2B syndrome is associated with café-au-lait Spots and diffuse lentigos.
Effects of psychological stress on skin and hair pigmentation in Polish adolescents	2012	the level of perceived stress was negatively correlated with skin pigmentation levels.
Drug-Induced Skin Pigmentation Epidemiology, Diagnosis and Treatment	2001	With psychotropic drugs, violet or purple-gray metallic pigmentation may occur only on sun-exposed areas, mainly the face and the extremities, with a striking sparing of the facial wrinkles. The mucous membranes are spared but the pigmentation may affect nail beds and the exposed parts of the eye (sclera, cornea and lens) as well. These pigmentary changes appear progressively after a long period of time in patients receiving high cumulative doses of the triggering drug.
Skin changes in patients with chronic renal failure	2011	Generalized hyper-pigmentation has been re-ported in patients with Chronic Renal Failure.

Methodology:-

Study design:
This is an analytical cross-sectional study.

Study Setting and period:
This is an analytical cross-sectional study conducted in the Kingdom of Saudi Arabia (General population) from 21/6/2020 till 21/10/2020

Study population and sampling:
Study participants:
Inclusion criteria; General population and patients with color change of skin.
Exclusion criteria; none.

Sampling method and size:
The study is carried out by questionnaire. Sample size is 520 cases, calculated using OpenEpi for sample size calculation for cross sectional studies, hypothesizing the true answers accordingly.

Measurements:-

Explanatory variables:
1. Sociodemographic characteristics: Region, gender.
2. Disease-related information: skin pigmentation, hypopigmentation or hyperpigmentation, site in skin of color change, vitamin D deficiency, use of creams to maintain the color of the skin, awareness of skin color change.

Outcome measures:
The outcome measure is by counting the ratio of the number of patients have a skin pigmentation and associated disease this will be measured: By determining the extent of the diseases that occurred with skin pigmentation.

Prevalence study:
was carried out to test the questionnaire if easily understood and the response of the participants. Data from the cross-sectional study was used to calculate the sample size.

Data Management and Analysis plan:
Data is entered and analyzed using SPSS version 25.0. Descriptive statistics are performed and categorical data are displayed as frequencies and percentages, while measures of central tendencies and measures and dispersion are used to summarize continuous variables. Univariate and multivariate analysis are performed to investigate association between skin pigmentation and associated disease. Statistical significance is set at a P value of 0.05 or less.

Ethical considerations:
Administrative approval is sought from the unit of biomedical ethics research committee. Ethical approval is sought from the ethical committee of the faculty of medicine, King Abdulaziz University. An informed consent is sought from the participants.

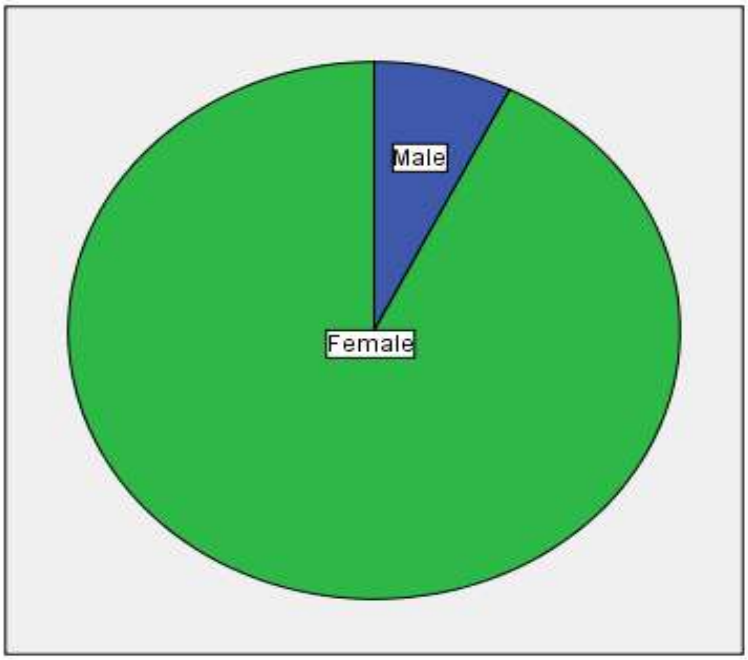
Results:-

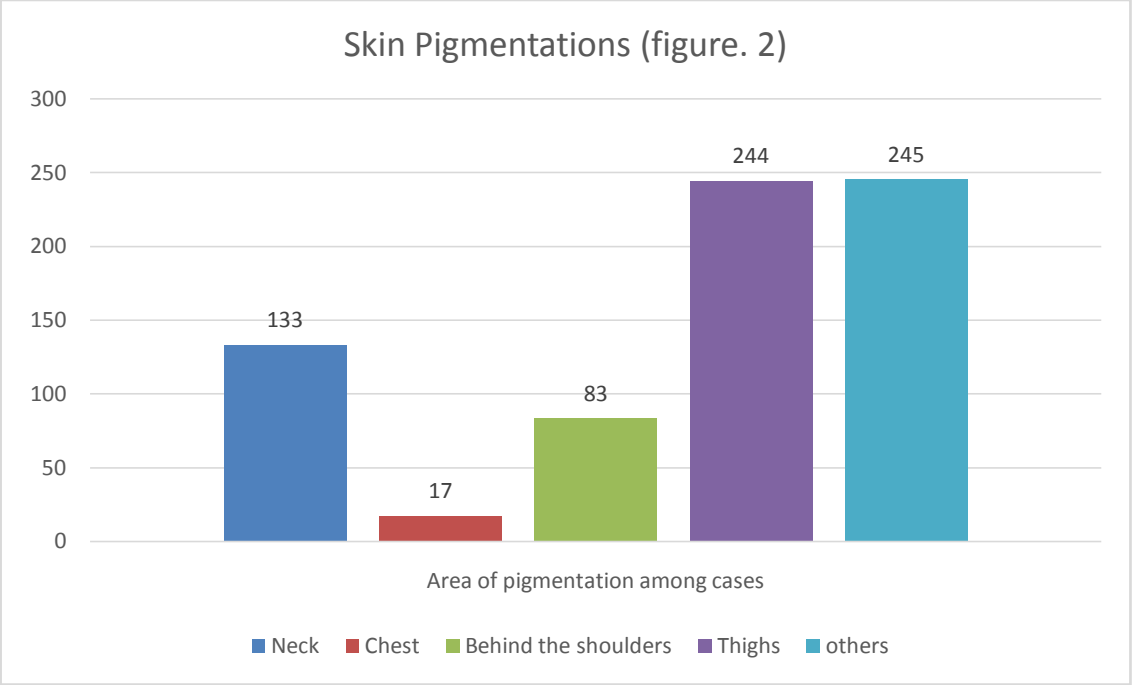
Descriptive Data:
Sample size is 520 cases. Sex distribution is as follows: 38 (7.3%) males, and 482 (92.7%) females.
Geographical region distribution is as follows: Northern area 20 (3.8%), southern area 9 (1.7%), central area 294 (56.5%), Eastern area 43 (8.3%), and Western area 154 (29.6%).

Skin pigmentation:
419 cases (80.6%) stated they have skin pigmentations while 101 cases (19.4%) don't have. These are distributed according to figure 2.

As for the type of skin pigmentations, 24 (4.6%) have hyperpigmentation, while 393 (75.6%) have hypopigmentations. The rest (103, 19.8%) have no pigmentations.

Distribution of pigmentation according to type is as follows: 138 (26.5%) are due to infections, 157 (30.2%) are due to sunlight, while 118 (22.7%) are melasma, mostly due to pregnancy. The rest have no pigmentations.





Association of skin pigmentations with different variables:

Variable	**Present** skin pigmentation (n)	**Absent** skin pigmentation (n)	p-value
Vitamin D deficiency	268	151	0.394
Diabetes mellitus	9	410	0.041
Hypothyroidism	31	388	0.402
Hyperthyroidism	0	419	0.004
Chronic stress	55	364	0.044
Psychotropic drugs	16	403	0.151
Chronic Kidney disease	3	416	0.394
Using sun creams	229	190	0.045

Association between Vit D deficiency, hypothyroidism, using psychotropic drugs, and chronic disease, and skin pigmentation was statistically insignificant, while association with Diabetes mellitus, hyperthyroidism, chronic stress, and using sun creams was significant.

Discussion:-

The results of this study are concordant, in some parts, with the results of previous different studies discussing the same association, between skin pigmentations and different chronic diseases and exposures to drugs and psychological stress. In other parts of study, there is insignificant statistical relationship, this could be due to inequal distribution of cases, sampling errors and bias, especially those including large number of female cases against male cases, which probably affects the prevalence of some risk factors and disease among the study population.

There was a significant association between diabetes mellitus and the presence of skin pigmentations in this the study. This is concordant with the results of another studies, taking the study of AC Ziegler, et all. as an example. In this study, Skin pigmentation was found to be associated with the risk of developing Type 1 DM.

Also in this study, there is a significant relationship between hyperthyroidism and skin pigmentation. This is true when compared with a review study done by H Niepomniszcze, et all. in that article, hyperthyroid state was associated with significant increase in prevalence of skin pigmentations and nail changes.

Chronic stress also plays an important rule in raising the chances of developing skin pigmentations. This is concordant with a Polish study conducted on Polish adolescents, who are naturally at high risk of stress, and was found that stress increases the chances of skin dyspigmentation, specifically saying: hypopigmentations.

Conclusion:-

Skin pigmentation has an obvious relationship with different chronic dieases and exposures among Saudi populations, significantly with DM, Chronic stress, Hyperthyroidism, and Using sun creams.

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