

Unmasking the Dangers of Fairness Creams: A Review of Heavy Metal Content and Its Nephrotoxic Effects

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ABSTRACT: The skin-whitening creams have been a huge part of society for a fair skin complexion. The benchmark of beauty in many parts of the world today has been entrenched in cultural and historical settings for centuries. These creams may pose serious health risks since many contain heavy metals beyond approved levels. Glomerular diseases, acute renal failure due to ATI and ESKD can be manifestations of kidney damage. When a skin-lightening agent causes heavy metal poisoning in the kidneys, the offending product should be discontinued, management of airway and circulation, chelation therapy and excess of the contaminated material removed. In managing glomerular diseases, glucocorticoids and immuno-suppressive agents should be added together with appropriate drug that is rarely needed at the right moment.

KEYWORDS: Fairness cream, Mercury, Nephrotic syndrome, Kidney Health, Chelation therapy.

I. INTRODUCTION:

The concept of fair skin which was strongly ingrained in ethnic and ancient contexts have been continued through the ages. Today, in numerous locations across the globe, the obsession for the fair skin is an authoritative aesthetic norm. Skin lightening cream use was found to be 27–77% common in population samples from the four corners of the world.

Despite the fact that these skin whitening creams are used as cosmetic enhancers, these may carry substantial health hazards. There is a recommended limit for heavy metal in each cosmetic product. But many of these products contain heavy metals beyond these recommended limits. Kidney is primarily impacted due to these

toxic metals. This impairment can be manifested as glomerulonephritis, acute renal failure brought up from acute renal insufficiency and CKD.

Even though the renal toxic effects of heavy metals are expertly recorded in the literatures, recent investigations show how the use of skin whitening creams are linked to the renal diseases such as membranous nephropathy and minimal change disease^[1]. NELL-1 is an autoantigen correlated with idiopathic membranous nephropathy which is characterized by maliciousness and autoimmune diseases. The studies conducted in the beginning of 2023 show that four successive cases of membranous nephropathy were detected as NELL-1 positive. Each of these cases used skin-whitening products prior to developing symptoms. The application of skin whitening creams is extensive in India and its marketing is intensified by the societal enthusiasm with fair skin.^[2]

The purpose of this systematic review is to assess the evidence on the association of fairness creams and related nephrotoxic effects.

FAIRNESS CREAMS

The epidermal layer is composed of melanin that produces colour and protects the skin from UV radiation. Phenylalanine hydroxylase and tyrosinase are the enzymes that produce melanin. When these reactions produce brown-black pigment called eumelanin, colour to skin and hair, or red pigment called pheomelanin, which gives colour to lips and hair^{[4] [16]}. The skin whitening agents, including hydroquinone, arbutin, azelaic acid, and kojic acid, certainly target the melanin-producing enzymes. Skin whitening creams lighten the skin and reduce the melanin

^[17]. Waxes, moisturisers, antioxidants, and preservatives are commonly used in creams but also contain unknown herbal products, steroids, and hydroquinone^[18]. Many of the heavy metals, like mercury, nickel, cobalt, cadmium, arsenic, and lead, are included^[1]. In South Asia, fairness cream companies develop a strong, dominant desire for fair skin. In colonial circumstances, the term "white" skin implied superiority and power. The promotion of a universal beauty standard has increased as a result of the appearance of a "paler" global entertainment industry. Winners in Indian beauty pageants tend to be tall, slender, and have pale, honey-coloured skin, which promotes Western ideals of beauty. Women in South Asian society are often objectified. The impact of a young woman's skin tone on her marketability to prospective spouses is demonstrated by matrimonial sections and websites. Lotions, face washes, deodorants, and whitening and skin-lightening creams are products for fair skin^[19]. After first focusing on women, companies have recently expanded their offerings to include items designed specifically for men. While the employment of well-known models and actors implies that the items will increase cultural capital and confidence, advertisements and packaging suggest that the products will improve consumers' skin tone and beauty^[20]. Numerous corporations are making money of colourism by associating prosperity, empowerment, and attractiveness with light-colored skin (Nadeem, 2014). While products which are lighten the skin a classified like beauty products in the EU, they are non-prescription medications in the US and quasi-drugs in Japan^{[5][21]}. A strong liking for herbal remedies, but as technology spread, people started using lotions and steroids to be fair. Later, other businesses introduced fairness creams with the unique quality of being equitable.

It is estimated that the Indian market for fairness creams is worth 800 crores, and the market for fairness creams for the men's is around 200 crores. "Hindustan Lever Ltd.'s", "Fair & Lovely", "CavinKare's", "Fairever", "Godrej's Fairglow", "Emami's", "Fair and Handsome", "Ponds", "Dream fairness" are the top contenders. "Fair & Lovely" was the first fairness cream that "Hindustan Lever Limited" introduced in 1975, and it controlled the market until 1998. In 1998, "CavinKare" introduced a cream for fairness under the "Fairever" brand, which quickly gained 15% of the market. Other businesses gradually entered the industry, including Godrej, Ponds,

Himalaya, and Emami, as well as the fairness cream market^[6]. "The global value of the skin-lightening market is anticipated to reach \$12 billion USD by 2027". It currently accounts for half of the skincare market in India. "It is reported that 40% of African women, including 77% of Nigerian women, bleach their skin, but data are hard to come by". "169 women, primarily of South Asian descent, participated in the Garne survey; Daily, one hundred and twenty two of them applied skin-lightening creams"^[7].

HEAVY METAL CONTENT IN FAIRNESS CREAMS

Various products used for whitening of skin ranges from homemade concoctions to scented creams manufactured by multinational companies^[7]. Various organic and inorganic substances are contained in the skin whitening creams such as mercury, steroids, hydroquinone, tretinoin, p-arbutin, 5-Hydroxy-2(hydroxymethyl)-4-pyrone, Lepargylic acid, GSH, AHA and niacinamide. Amongst mercury and hydroquinone cause the most adverse effects^{[3][15]}.

In case of herbal fairness creams, even most of the advertisements claim to have no added chemicals, all these products have chemical base to provide them texture, consistency and preserving ability^[8]. Mercury is a heavy metal used in skin whitening creams. It is generally a nerve toxin. Mercury was restated by other namely "mercurous chloride, calomel, mercuric, mercurio". The prolonged use of mercury carrying skin whitening creams might provoke swelling of excretory organs. Compounds containing mercury gets easily absorbed through skin and tend to accumulate in the body when applied topically^[9]. It is added in these products as it competitively inhibits tyrosinase enzyme. It competes with copper and attacks cysteine in substrate site of tyrosinase thus causing deactivation of enzyme^[4]. It was stipulated on the minimata convention that manufacturing, import and export of cosmetics (excluding eyelashes) which contain more than 1ppm of mercury will not be permitted after the year 2020^[10].

As compared to the average values reported in other WHO regions, the products made in the Levant region was found to contain ten times higher content of mercury. The mercury content in products from the Levant and the Far-East regions was found to be higher than the products picked up from particular geographic area. It was reported that 0.4% of cream contain ammoniated mercury.

Among one hundred and eighty three skin-elucidative product consumers in "Japan, Indonesia, Tanzania, and Iran", total mercury levels range between 0 and 900 g^[11].

Cadmium and Arsenic may be incorporated into cosmetics along with colour additives or with other raw materials^{[8][22]}. Hexavalent Chromium (Cr+6) is a compound that is caustic and sensitive to the epidermal layer. "The International Agency for Research on Cancer (IARC)" has take on Cr+6 compounds as carcinogen. It may cause adverse effects like skin ulceration,eczema,and hypersensitive reactions. If inbreathed,Cr+6 compounds cause sore and perforation of the mucosal membranes of septum nasi, asthmatic bronchitis, bronchospasms, exasperation of the throat and fluid retention^[9]. Nickel may cause allergic reactions if comes in contact with the skin. The studies on animals proved that if consumed in high amounts, it will affect kidney, stomach and liver^[9].

RISK AND DISEASES ASSOCIATED WITH FAIRNESS CREAMS

Hazardous materials such as "white lightning," "white lead mixtures", "moonshine" fine particle such as used since ancient Rome to achieve a light complexion.Melanocytes found at dermal-epidermal junctions generate melanin, which is then transferred to the skin's keratinocytes and causes skin pigmentation. "Tyrosinase", "copper-containing enzyme" that acts like chemical that slows down the formation of "melanin".Many skin-lightening medications, such as hydroquinone, arbutin, azelaic acid, Kojic acid, etc., may target this enzyme^[23]. The majority of skin-lightening lotions promise to lighten the skin by lowering the amount of melanin. A variety of cosmetic goods also contain "heavy metals" such as "lead", "cadmium", "arsenic", "nickel", "cobalt", and "Urine kidney injury molecule-1" and "tissue inhibitor matrix metalloproteinase 1" are two indicators of kidney damage that exhibited a substantial and powerful favorable connection at the amount of "arsenic" and "cadmium biomarkers". Customers of all demographics are at risk from the latent danger posed by the fact that products contain these harmful substances^[1].

According to Chinese traditional medicine, skin whitening creams containing hg are the source of metal exposure. "In general populations the urinary concentrations of mercury in patients were 4 to 55 times higher than the reference value". Mercury has been in metallic

organic inorganic forms, though it is a heavy metal, leading to nephrotoxicity. The body is absorbing mercury in the form of inhalation, ingestion, skin, and injection. The overuse and incorrect administrationof mercury-containing skin-lightening cream and improper use of Chinese traditional medicines may lead to the accumulation of mercury in the body. As mercury exists in several forms, it may damage the several systems, specifically the "kidneys", "nervous system", "gastrointestinal tract". Mercury-associated glomerulonephritis is "regularly misperceived as primarily a glomerular disorder and the lack of clinical symptoms^[12]".

Adult nephrotic syndrome is often due to MN^[24]. Autoantibodies opposed "phospholipase A2 receptor antigen", "thrombospondin type 1 domain-containing 7A", and neural epidermal growth factor-like 1 protein due to primary MN and immune-mediated disease. Melanocytes found at dermal-epidermal junctions create melanin, which is then transferred to the skin's keratinocytes and causes skin pigmentation. "Tyrosinase", "copper-containing enzyme" that serves as the "melanin restriction enzyme" production, uses enzymatic processes to convert L-tyrosine into melanin. Many skin-lightening medications, such as hydroquinone, arbutin, azelaic acid, Kojic acid, etc., may target this enzyme. The majority of skin-lightening lotions promise to lighten the skin by lowering the amount of melanin. Mercury exposure is very low in the general population and arises as a result of increased duration of work exposure. The various existences of mercurial compounds, the amount taken, duration of contact overall impact led to mercury's toxicity profile. The application in "Chinese treatment," skin whitening cream is linked to MN secondary to mercury intake. Natural and elemental mercury can pass across the "blood-brain barrier" and cause brain damage, whereas "inorganic mercury salts" are harmful to the "kidney or gut". Short-term susceptibility causes dose-related acute tubular injury, which is most common among the parsrecta, during a period for "low-grade chronic tubulointerstitial" or "glomerular illness".^{[13][25]}

Mercury is a usual heavy metal that has able dangerous effects either human and environmental health^[26]. A high level of "mercury compounds" is another way that poisoning might occur. In beauty products, that is unlawfully used to eliminate face debris "and lighten the appearanceand defeat the synthesis of melanin. After entering the blood, mercury compounds that

have been absorbed through the skin, digestive tract, and respiratory tract cleave to produce mercury ions, then build up in the kidney and the brain, causing harm to the musculoskeletal, nervous, cardiovascular, and renal systems. The renal system is among the organs common in danger of "mercury poisoning" because of metals high affinity for kidney tissue. A certain level of mercury buildup in the body causes kidney disease, which manifests as toxic encephalopathy and proteinuria. Apart from the typical symptoms of "mercury poisoning", which include "tremor", "gingivitis", the activity individuals with renal damage due to mercury poisoning often exhibit oedema, change in "urine volume", "proteinuria", and "nephrotic syndrome", for some situations, an average "asymptomatic" mercury poisoning occurs^[14].

"MCD" is an additional often-documented reason for "nephrotic" disorder connected in application to "fairness creams". The creams are refused as part of the treatment, and D-penicillamine chelation therapy was given. In the comparison of MGN and MCD, MGN had lower remission rates and shorter exposure time to mercury. Moreover, compared to MGN patients, MCD patients had noticeably high urine amounts. Compared to MGN and MCD, which are based only on case reports and case series, the evidence linking IgA nephropathy to cosmetics and heavy metals is somewhat weak^[1]

TREATMENT AND MANAGEMENT

Treatment for nephrotoxicity and neurotoxicity caused by heavy metal contents in skin whitening creams are done by the removal of product (stop using the skin lightening cream), supportive treatment (maintain airway, circulation, etc.), chelation therapy, and decontamination. Basically, management of glomerular diseases are treated with therapies like glucocorticoids and immunosuppressive agents; steroids may also be used rarely^[1]

The Management and prognosis are multifaceted. Physicians initially advised patients to discontinue the cosmetic product. Not only do cosmetics cause toxicities, but also several allied factors including occupational, dietary, self-medication with NSAIDs. Some underlying diseases like diabetes, hypertension, etc., contribute to heavy metal toxicities and lead to the occurrence of glomerular diseases. ^[1] Chelation therapy is given to patients with severe exposure to metal intoxication like hydrargyria, plumbism,

arsenicosis, nickel allergy, itai-itai disease, etc. and having organ toxicity symptoms. Adjuvant therapy can be done with steroids^[13]. An association of chelation therapy with corticosteroids or immunosuppressors is effective. Immunosuppressive agents are rarely used. Mainly the persistence of severity after chelation therapy is treated by corticosteroids. ^[1]Mercury toxicity by using fairness cream results in severe renal glomerular disease namely membranous glomerulopathy, MCD, acute tubular necrosis causing acute renal failure, CKD or chronic kidney diseases, FSGS or focal segmental glomerular sclerosis, etc. All these diseases are analysed by using histopathological examinations. For management, discontinuation of products is advised and if severity exists, treatment with D-penicillamine along with adjuvant steroid is assigned. In a study with D-penicillamine (chelation therapy), normal blood mercury levels were reached within 7 months but approximately 16 months were required for normalizing the urine mercury levels.

Due to secondary exposure to membranous neuropathy (MN), which will cause significant morbidity, the discontinuation of the product is done. Severely exposed patients were treated with the chelator sodium dimercaptopropane sulfonate or a combination with glucocorticoids. Some with ototoxicity, which is not cured by chelation therapy, are treated with steroids complementarily. Optimal treatment is ambiguous. Subordinate levels of mercury are cautiously supervised. Immunosuppressive drugs elicit remission by reduced proffering of autoantibody. Multimodality for 2.5 months versus chelation therapy for 4.5 months is recommended. ^[13]All sorts of mercury bring about tubular or glomerular damage; inorganic mercury is more nephrotoxic ^[32]. Plasmodium malaria initiates immune complex nephrotic syndrome in African countries; however, edema of the face and periphery is brought about by "Butone extra strong night cream," which holds amino mercuric chloride, so the cream stopped. Furosemide was employed to manage edema following a six-month period. of nephrotic syndrome set aside^[33]

For the removal of organic mercury, methyl or dimethyl mercury is used. For chelation therapy, chelating agents like DMSA and DMPS are used which pull out mercury from the body. DMPS is administered intravenously while intravenous regulation of DMSA is unattainable. ^[34]

II. CONCLUSION

This review draws attention to the increasing risk of nephrotoxicity that skin-whitening creams represent, especially given the presence of hazardous “metals like mercury” within it. Usually, it is a neurotoxin. Long-term use of skin-whitening creams with “mercury may cause diseases in the kidneys, liver, and urinary system”. “According to the International Agency for Research on Cancer (IARC), Cr+6 compounds are carcinogenic”. Adverse symptoms include dermatitis, skin ulcers, and allergic responses could result from it. “Asthmatic bronchitis”, “bronchospasms”, “irritation of the pharynx and larynx”, “edema”, “ulceration” and “perforation of the nasal septum”. If nickel gets on your skin, it might trigger allergic responses. Excessive consumption will impact the kidney, stomach, and liver, according to animal research. “MGN” showed shorter exposure times to mercury and poorer remission rates as compared to “MCD”. Also, MCD patients showed much higher urine levels than MGN patients. At first, doctors told patients to stop using the product and after significant exposure, steroids can be used as adjuvant therapy and chelation therapy. Chelation therapy works well when combined with immunosuppressive drugs or glucocorticoids. Corticosteroids are primarily used to treat the severity that persists following chelation therapy.

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