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SKIN DISEASES, OBESITY AND DIABETES

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Abstract:
The project was conducted to explore the prevalence of skin diseases among diabetes and/or obesity patients. Only a little attention has been paid to its prevalence. obesity alters the barrier of the skin and induces manifestation. The commonest cutaneous manifestations associated with obesity are acanthosis nigricans, acrochordon, striae distensae, plantar hyperkeratosis, and intertrigo. Obesity also associated with hyperandrogenism in women, which promoting skin diseases like hirsutism, acne or androgenic alopecia. Insulin plays an important role in the physiology of the skin. IR induced in patients with chronic inflammation, lead to cutaneous manifestations like psoriasis. Acanthosis nigricans consider an early skin sign of diabetes mellitus. Poor control of diabetes mellitus increases the capability of skin infections. The commonest skin manifestations in diabetes patients are bacterial and fungal infection, skin tags, xeroderma, and brown spots. Weight loss is an important method for humans to decrease metabolic diseases, increase self-confidence, and improve patient lifestyle. Weight loss interventions are different, liraglutide considered one of these interventions as it's showing it's effectively to decrease body weight that leads to improvement or treat skin disease too.

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1. INTRODUCTION:

1.1. Skin disease prevalence and the association with obesity and diabetes

Skin diseases are the fourth common cause of human illness, the one-third approximate expectation of the world population is affected or complain from at least one type of skin disease that can affect their life quality (Tizek et al., 2019). Worldwide, skin diseases can affect humans at any age with high expectations to affect men and elderly people at least one time during their lifetime (Tizek et al., 2019). Squamous cell carcinoma, and basal cell carcinoma, are the most common skin malignancy, 2-3 million new keratinocytes carcinoma globally arises each year (Tizek et al., 2019).

All age groups can be affected by eczema. Acne vulgaris causes a cumulative burden, especially in the first three decades of life and, in the later decades, keratinocytes carcinoma and psoriasis are common. About 70% of patients with skin diseases are not treated or consult dermatologists or physicians. The outside workers are highly exposed to UV light, therefore a high risk for skin diseases will result (Tizek et al., 2019).
Skin diseases in patients with diabetes and obesity are common and continue to increase worldwide, however, this subject has received limited attention (Yosipovich, 2007).

People with diabetes represent a significant proportion of patients that experience skin diseases, ranging from 30% to 92% (Demirseren et al., 2014). These skin diseases include cutaneous infections, psoriasis, and vascular disorders with risk to develop outcomes as ulceration, cutaneous infection, or diabetic foot (de Macedo at al., 2016). The highest prevalence of skin diseases in diabetic patients includes xerosis and cutaneous infection (de Macedo et al., 2016). Follow-up and careful dermatological examination of diabetic patients is required to reduce skin complications and morbidity. Awareness about early detection or diagnosis of skin diseases in diabetic patients is limited, and the failure to start early treatment can lead to severe skin complications, especially if it associated with poorly controlled diabetes mellitus.

Most diabetes patients, with skin complications are related to hyperinsulinemia and hyperglycemia (de Macedo et al., 2016). Patient education, skin hydration, and controlled hyperglycemia can prevent skin disease complications (de Macedo et al., 2016). Insulin resistance causes skin manifestations as it plays an important role in homeostasis, and the physiology of the skin. Insulin resistance is impaired sensitivity to the normal or elevated insulin level and results in hyperinsulinemia, type 2 diabetes mellitus, compensated type 1 diabetes, obesity, and diabetic ketoacidosis. Insulin resistance can be estimated by measuring fasting blood glucose and insulin level (Barbato, 2012; Maaran, 2020). This relationship between insulin resistance and skin diseases is important but has received less attention (Napolitano et al., 2015).

Obesity is a major public health problem in many countries that has high economic consequences (Yosipovich, 2007). The prevalence of obesity (BMI >30 kg/m^2) has significantly increased in the global population leading to increased type 2 diabetes (Demirseren et al., 2014), but the impact of obesity on the skin has received less attention. A study of 750 patients with diabetes mellitus showed that 79.2% had complained of skin diseases (Demirseren et al., 2014). Weight loss is an important option for patients with obesity, not only to treat many types of diseases but also to improve the quality of life (Rosen, 2019). A large proportion of patients with obesity like to improve their skin symptoms, as obesity is responsible to change the skin structure, changing at the skin barrier function, the structure, and the function of skin collagen, sebum production, wound healing, and other dermatological diseases caused by obesity (Yosipovich,2007).

Obesity has been shown to be associated with dermatoses including cutaneous infection, psoriasis, xerosis, inflammatory skin diseases, acanthosis nigricans, keratitis pilaris, acrochordons, striae distensae, lymphedema, and hidradenitis suppurativa. Dermatoses associated with diabetes and obesity include acanthosis nigricans, acne, fibroepithelial polyps, or keloidalis nuchae (Shipman and Millington, 2011).

1.2. Aims of the dissertation

Skin diseases are widely spread especially in obese patients and covers a large number of people around the world that need to be known as minimal research done to discover the prevalence of skin diseases and the effect of the weight loss to decrease or heal the skin diseases. The aim of this research is to describe the prevalence of skin diseases in obesity and/or diabetes in different countries and to compare the prevalence with the normal weight, non-diabetic population. This will be achieved by completing a comprehensive search of the literature.

1.3. Objectives

Obesity is known to be a risk to develop many diseases including diabetes and cutaneous manifestations. The aim of this literature review is to determine and investigate the prevalence of skin diseases in obesity and/or diabetes people in different countries.

2. METHODOLOGY:

2.1. Objectives and PICO

A literature review was conducted following the principles and methods of a systematic review as far as possible. The focused literature search was on studies that investigated the association between skin manifestations in patients with obesity and/or diabetes and in normal population countries. The PECO for this literature review is presented in table 1.

Table 1. (PECO: Skin diseases prevalence and the association in obesity and diabetes)

Population	Adults aged >18 years old
Exposure	Overweight/obesity and/or type 1 or type 2 diabetes mellitus
Control	Normal weight individuals without type 1 or type 2 diabetes mellitus.
Outcome(s)	Prevalence and/or incidence estimates of skin disease

2.2. Eligibility criteria

To be included, studies had to be published between year 2005 and year 2020 and, in the English language. Studies also had to report either the prevalence or incidence of skin diseases and a measure of weight status or obesity (e.g. BMI, waist circumference or % body fat) and/or diabetes.

2.3. Information sources

An extensive literature search was performed using the Google Scholar, PubMed and, Wiley bibliographical databases that were accessed through the University of South Wales library. Other additional studies and reference lists were identified using the "related articles" button in Google Scholar and the reference lists of the studies.

2.4. Search strategy for databases

The selection and search of the literature was conducted using combinations of different keywords, including 'skin diseases', 'skin manifestations', 'skin infection', 'obesity', 'overweight', 'prevalence', 'diabetes' or 'diabetic'.

2.5. Study selection

Only studies with skin or cutaneous manifestations that follow the inclusion criteria were selected.

2.6. Data extraction

The articles were assessed by reading the full article or the abstract to decide its relevance and if it met the inclusion and exclusion criteria.

2.7. Summary measures

The selected informations that included at the summary table was author(s) name with the published year, the type of study design, the country, number of participants (included males and females number with obesity and/or diabetes), age and ethnicity, obesity and diabetes (available data of BMI , type of diabetes and investigations), frequency of skin conditions (the detected skin diseases and its prevalence among participant) and conclusion.

2.8. Risk of bias/ critical appraisal

The selected studies were critically assessed for methodology quality and, bias. Appraising systematic reviews, not trials and NRSI's, and the quality of randomized control trials studies methodology, by using Assessing the Methodological Quality of Systematic Reviews (AMSTAR) checklist.

Searched randomized controlled trials (RCT's) and non-randomized studies of interventions (NRSI's) with fair or good quality were included. Studies included adults, aged >18 years with obesity and/or diabetes who complained from skin diseases. Studies that include males and females from different

countries and ethnicity will be included. Studies included children or patients <18 years old and not report skin conditions or prevalence were excluded. Studies or articles that submitted for more than 20 years of published were excluded. The present articles in more than one database were once included. Not available articles were excluded. Tutor consulted for selected and disagreement articles. References were followed Harvard style, scrutinized the reference lists in the selected articles to resemble other relevant studies that had been overlooked during the database search.

3. RESULTS:

3.1. Study selection

Twelve studies were included in this literature review. Almost all included studies involved participants with skin diseases with diabetes and/or obesity.

3.2. Study characteristics

The extracted data from each study included the author(s) name(s), the study design, country, the number of patients/participants, age and ethnicity, obesity and/or diabetes, the frequency of skin conditions and conclusion.

3.3. Risk of bias within studies

All studies show the correlation between skin manifestations among diabetes and/or obesity patients. No blind or random selection of the participants or to the included physicians, increase the risk of bias.

3.4. Results of individual studies

(Ozlu et al., 2018) determined the skin manifestations in diabetic obese and non diabetic obese patients through a prospective controlled study at Istanbul, Turkey. Included participants were (n= 600) adults. 450 obese patients were divided into two groups, 138 (30%) diabetic obese patients and 312 (70%) non-diabetic obese patients. 370 were females and 80 were males. 150 healthy volunteers were involved, 114 females and 36 males. Mean age ±SD were (37.25 ±11.37) in study group and (35.67 ±11.24) in control group. For the obese patients and healthy controls, the main waist circumferences were (119.72±12.98) and (82.37±9.21cm), mean BMI ±SD in obese and controls were (37.22±6.07) kg/m^2 and (22.23±2.19) kg/m^2. Dermatological examination was performed to all participants by a dermatologist. Criteria to diagnose DM were (HbA1c) ≥6.5% or random glucose value ≥200 mg/dL fasting glucose level ≥126 mg/dL or 2-h postprandial glucose of ≥200 mg/dL. The commonest skin lesions in diabetic obese patients were acanthosis nigricans (47.8%), acrochordon (54.3%), striae distensae (62.3%), planter hyperkeratosis (45.7%). Hirsutism (19.6%) in diabetic obese patients, found to be higher in non-diabetic obese patients (33.1%) compared to striae distensae that found to be lower in diabetic obese patients (62.3%) than non-diabetic obese patients (65.6%). The prevalence of skin conditions found to be higher in obese patients than healthy control patients in different types of skin dermatosis. The results show no significant statistical difference between diabetic obese and non-diabetic obese patients. The main cause of most skin conditions is obesity even if it's associated with diabetes or not.

Boza et al (2012) compared skin manifestations in patients with obesity and a normal weight control group. They included 76 patients (20 males and 56 females) with obesity (BMI ≥30 kg/m^2) and, 73 (20 male and 56 female) controls with BMI (18.5–24.9) kg/m^2. The mean age (SD) of patients was (49.66 ± 15.61) years and (49.11 ± 14.50) years in controls. Obesity was classified as class I (BMI 30–34.9 kg/m^2), class II (BMI 35-39.9 kg/m^2), and class III (BMI ≥40 g⁄m2). All patients were evaluated initially by a review of medical records, medical history, and dermatological examination by a dermatologist. The laboratory assessment consisted of Fasting blood glucose and other investigations. (23.7%) of patients are diabetic with obesity and (9.6%) were controlled. Striae was present in (68.4%) of patients with obesity and (30.1%) of controls; plantar hyperkeratosis (46.7%) in obesity and (9.6%) in controls; Achrochordons (47.94%) in obesity and (15.1%) in controls; Intertrigo (44.7%) in obesity and (6.8%) in controls; Pseudoacanthosis nigricans (27.6%) in obesity and (0%) in controls. From this comparison, Striae is the most common dermatosis in patients with obesity. The BMI classes showed that the Striae in BMI degree I patients is (52%), II (70.4%), and III (83.3%). The prevalence of pseudoacanthosis nigricans increased with BMI: class I (4%), class II (37%), and class III (41.7%). Bacterial infection also increased with BMI: class I(4%), class II (7.4%), and class III (25%). Psoriasis, onychomycosis, androgenic alopecia, hidradenitis, hirsutism, seborrhoeic keratosis, chronic venous insufficiency and rubi nevus were not associated with obesity. There's a clear correlation between skin diseases, obesity, and increased BMI.

Al-Mutairi, (2011) This cross-sectional study found the association between obesity and skin diseases in obese adults. Included overweight or obese patients were 437 (200 male and 237 female) aged 18-74 years. (43.7%) were overweight, 51.7% obese and 4.65% severely obese. The author divided the obesity patients into three groups were grade 1 overweight patients with BMI 25–30 kg/m^2 , grade 2 obese with BMI >30-40 kg/m^2, and grade 3 severely/morbidity obese with BMI >40 kg/m^2. The grades were divided according to age groups (20-29; 30-39; 40-49; 50-59 and ≥60). The collected data from patients were included medical history, diabetic personal and family history, hypertension. Dermatological and systematic examination for all included patients by the same dermatologist. The ordered investigation was fasting and postprandial blood sugar, complete blood count, thyroid function, liver, kidney, and serum lipid profile. For females patients, 69 (15%) with acanthosis nigricans and/or acne, serum FH, LSH, prolactin level, and ultrasound for pelvis were performed. Diabetic patients were 87, detected patients to be diabetic were 49, and 38 were diagnosed already. Acanthosis nigricans and skin tags detected in 39 patients, 15 skin tags, 33 intertrigo, and 12 with acanthosis nigricans and acne. 74 female patients had polycystic ovarian syndrome, hirsutism found in 35, hirsutism and acanthosis nigricans in 22, severe acne, hirsutism, and acanthosis nigricans in 12 female patients. Skin conditions were found to be high among the age group 30-39 (31.8%) years and 40-49 (23.3%) years. The commonest skin diseases in obesity: planter hyperkeratosis 45.1% ; acanthosis nigricans 33.0% ; acrochordon 30.0% ; striae cutis distensae 23.3% ; intertrigo 22.2% and acne vulgaris 21.5%. This study showed that planter hyperkeratosis is the commonest skin disease among obesity patients. The results showed that many skin diseases are more prevalent in obesity.

Svensson et al (2017) determined common skin diseases and their prevalence in European countries. Included participants (n= 12,377) had a median age of 43 years (range 18-74 years) and were from five general European populations (Italy, Germany, the Netherlands, Sweden, and Portugal). A standardized face-to-face questionnaire assessed the occurrence of the most common skin diseases during the past month, past year, or during a lifetime that lasted for more than 3 days in duration. Self-reported results showed the most common skin diseases were warts (41.3%), acne (19.2%), and contact dermatitis (15.0%). The skin diseases diagnosed by a physician were warts (27.5%), acne (11.8), and eczema (11.8). Skin diseases were more common in women to be affected by atopic dermatitis, contact dermatitis, and urticaria compared to men but only skin cancer showed higher prevalence in men (0.6%) than women (0.4%). Age group investigation showed that atopic dermatitis and acne higher with age group 18-34 years old were warts, psoriasis, leg ulcer, and skin cancer increases with age (51-85) years. No age-associated in urticaria, vitiligo, and eczema. (30-50) years age group showed a peak of contact dermatitis. The prevalence of skin diseases were higher in the Netherlands and Germany compared to Italy and Portugal. For physician-diagnosed skin diseases, Germany had the highest prevalence of contact dermatitis (12.7%), atopic dermatitis (9.4%), psoriasis (6.9%), and acne(17.7%). At Netherlands, the highest prevalence of skin diseases were: eczema(24.5%), warts (53.1%), urticaria (9.0%), skin cancer (4.0%), leg ulcer (1.5%) and vitiligo (2.2%).

Shahazad et al (2010) determined skin manifestations in diabetic patients, for >5 years in duration at the Qassim region, Saudi Arabia. Participants (n=196, females 98 and males 98) had a mean age ± SD of 62.9±12.8 years (range 21-103 years). This cross-sectional study used the American Diabetes Association criteria to define the diagnosis including diabetes symptoms with a random blood glucose of ≥11.1 mmol/l (200 mg/dl) or 2-hour plasma glucose of ≥11.1 mmol/l (200 mg/dl) or fasting plasma glucose ≥7.0 mmol/l (126 mg/dl). Of the 196 patients, 192 (98%) had skin manifestations. The most frequent skin manifestations were cutaneous infection (26.9%), skin tags (24.7%), xerosis (23.1%), alopecia legs (21.6%), fungal infection (19.7%), tinea pedis (14.7%), hyperkeratosis feet (12.8%), seborrheic keratosis (7.5%), dry palms (7.5%), candidal infection (4.1%), bacterial infection (3.1%), diabetic dermopathy (3.8%), intertrigo (2.2%), chronic eczema (2.2%) and warts (0.6%). The prevalence of skin manifestations increased with the duration of diabetes.

Tseng et al (2014) showed the prevalence of cutaneous manifestations in elderly diabetic patients through a cross-sectional study in Taiwan. Included male participants (n= 313) had a mean age 85 years, SD 5.5, with range 65-99 years. Mean BMI 22.3, SD 3.34, range 14.1-34.4. 70 patients with type 2 DM. A dermatological examination was performed by a single dermatologist. Diabetes diagnosis followed the guidelines of the International Diabetes Federation: HbA1c ≥6.5%/48 mmol/mol), fasting plasma glucose ≥126 mg⁄dL. The reported skin diseases in diabetic patients were fungal (81.4%), brown spots (74.3%), purpura (32.9%), scabies (31.4%), pruritus (25.7%), skin tags (22.9%), bacterial infection (17.1%) and chronic ulcer (14.3%). The skin diseases in non-

diabetic patients were fungal infection (75.7%), brown spots (28.0%), purpura (24.3%), scabies (21.0%), pruritus (2.1%), skin tags (14.0%), bacterial infection (6.6%) and chronic ulcer (3.7%). In both diabetic and non-diabetic patients, the fungal infection was high. The prevalence of brown spots, chronic ulcer, pruritus, and bacterial infection was higher significantly in diabetic patients compared to non-diabetic patients.

Foss et al (2005) studied the skin lesions in relation to controlled and uncontrolled diabetes mellitus in Brazil. Included participants (n= 403) had a mean age of 19.9±2.3 and 63.1±3.4 years. Type 1 DM patients were 31% and type 2 diabetes patients were 69%, 65.3% were female. All participants were examined by an endocrinologist for metabolic evaluation and dermatologist. 136 diabetic patients were metabolic controlled diagnosed by glycated hemoglobin measures, using ion-exchange chromatography. Adequate control was diagnosed by glycated hemoglobin below 8% and inadequate control above 8%. Skin lesions in diabetes mellitus patients were dermatophytosis (82.6%), actinic degeneration (62.0%), benign skin tumors (23.5%), xerosis (20.8%), candidiasis (12.9%), scars (12.6%), hyperkeratosis (8.6%), atopic dermatitis (6.6%), eczema (5.9%) and acanthosis nigricans (5.9%). Skin diseases among diabetes patients with adequate metabolic control were xerosis (25%), solar elastosis (20.8%), seborrheic keratosis (20.8%), seborrheic dermatitis (12.5%), dermatophytosis (12.5%), candidiasis (4.2%), acanthosis nigricans (4.2%) and juvenile acne were not reported. DM of skin lesions among inadequate metabolic control were dermatophytosis (55.3%), candidiasis (12.5%), juvenile acne (7.2%), seborrheic keratosis (6.2%), acanthosis nigricans (5.4%), solar elastosis (5.4%), seborrheic dermatosis (4.4%) and xerosis (3.6%). The prevalence of skin diseases was high in diabetic patients and poor control of diabetes mellitus increase the capability to have a skin infection.

Ahmed et al (2009) evaluated the prevalence of skin manifestations in diabetes mellitus patients through a descriptive study in Battagram, Pakistan. Among 350participants, 30 (8.4%) patients had type 1 and 320 (91.4%) patients had type 2 diabetes, there were 193 (55.1%) females and 157 (44.9%) males. The mean age was 54.0±8.5 years. Twenty-three (6.6%) had adequate glycaemic control and 327 (93.4%) were uncontrolled. The duration of DM ranged between 1-12 years, 140 (40%) patients had 5-10 years, 137 (39.1%) 10 years, and 73 (20.9%) up to 5 years. All patients were examined for skin lesions. Random or fasting blood glucose and two or more previous blood sugar readings were recorded. HbA1c was not available. Of 350 patients, 268 (76.6%) had skin manifestations. Detected skin manifestations included skin infection (30.9%), ulcer and gangrene foot (12.9%), pruritus (7.1%), vitiligo (5.7%), skin tags (3.7%), diabetic dermopathy (4.2%), acanthosis nigricans (2.9%), eruptive xanthomas (2.6%) and diabetic bullae (0.6%). Cutaneous manifestations in IDDM patients were skin infections (0.9%), diabetic dermopathy (0.9%) , vitiligo (2%), ulcers and foot gangrene (0.3%), skin tags (0.6%) and eruptive xanthomas (0.6%). Cutaneous manifestations in type 2 diabetes were skin infections (30%), ulcers and foot gangrene (12.6%), pruritus (5.7%), vitiligo (3.7%), diabetic dermopathy (3.4%), skin tags (3.1%), acanthosis nigricans (2.9%), eruptive xanthomas (2%) and diabetic bullae (0.6%). In DM patients, the commonest skin disease was skin infection, foot ulcers, and gangrene.

Ragunatha et al (2011) studied the effect of diabetes control on cutaneous disorders through a cross-sectional descriptive study in Pakistan. Included participants (n=500, 286 males and 214 female), had a mean age of 58.2±11.9, and 53.3±10.8 years respectively. Mean duration of diabetes 5.5±5.8 years. Eight-two percent had diabetes <10 years duration, 98.8% of patients had type 2 diabetes. All patients were screened for skin diseases, fasting, and postprandial plasma sugar test. Histological and microbiological investigations were done to diagnose skin diseases. The mean fasting plasma glucose was 129.97±48.65 mg/dI. FPG <130 mg/dI was present in 60% of the patients and in 12% of the patients FPG was 130–140 mg/dI. Of 500 patients, 257 had cutaneous manifestations specific to diabetes. Skin manifestations were fungal infections (13.8%), bacterial infections (6.8%), candidiasis (3.6%), acanthosis nigricans (5.0%), acrochordon (26.2%), bullous diabeticorum (0.4%), vitiligo (1.6%), lichen planus (1.8%), psoriasis (0.6%), erythema (6.2%), eczemas (7.8%), pruritus (5.2%), xerosis (4.4%), idiopathic guttate hypomelanosis (14.4%), seborrheic keratosis (15.8%), dermatosis papulosa nigra (27.6%), melasma (4.0%), nail dystrophy (4.0%), eruptive xanthoma (0.6%), and melanonychia (2.6%). Skin manifestations of insulin resistance like acanthosis nigricans and acrochordon were common, followed by bacterial and fungal infections. The prevalence of skin manifestation in well-controlled diabetic patients is low. The prevalence of cutaneous infection was high in diabetic patients.

Khalil et al (2011) studied obesity and skin diseases with a 2-year retrospective cohort study. Participants were, selected randomly from a dermatology clinic at

Qassim, Saudi Arabia. Patients were divided by BMI into exposed and non-exposed. Included (n= 177), male cohorts (61 obese and 48 nonobese). Females cohorts (32 obese and 36 non-obese). The mean age of males was 41.2±12.1 years in patients with obesity and 36.3±16.8 in patients without obesity. The mean BMI in males with obesity was 31.9±5.41 kg/m^2 and 23.0±1.37 kg/m^2 in non-obese. Frequency of skin diseases in obese males was 77% and 33.3% in non-obese. The mean age of females was 29.1±9.6 years in patients with obesity and 25.6±4.3 years in non-obese. The mean BMI of females was 31.23±4. 97 kg/m^2 in obese and 22.06±2.43 kg/m^2 in non-obese. The frequency of skin diseases in females with obesity was 96.8% and 16.6% in non-obese. In males with obesity, the skin diseases were acanthosis nigricans (42.6%), stria distensae (34.4%), cellulite (13.1%), skin tags (11.4%), planter keratosis (8.10%), xerosis (6.5%), pruritus (3.2%), tinea pedis (18.0%), intertrigo (14.7%), bacterial folliculitis (13.1%), tinea cruris (6.5%), tinea versicolor (3.2%) and candida infection (1.6%). In non-obese males, skin xerosis was 16.6%, tinea pedis 8.3%, and there were no other skin diseases. In females with obesity, the prevalence of skin diseases was skin distensae (72.2%), acanthosis nigricans (52.7%), cellulite (41.6%), xerosis (27.7%), skin tags (22.2%), pruritus (22.2%), planter keratosis (22.2%) hirsutism (19.4%), bacterial folliculitis (36.1%), tinea pedis (8.3%) and intertrigo (19.4%). In non-obese females, skin diseases were stria distensae (12.5%), cellulite (12.5%), xerosis (6.26%), pruritus (6.25%), skin tags (6.2%), planter keratosis (3.12%), acanthosis nigricans (3.1%), bacterial folliculitis (28.1%) and hirsutism (0%). These results showed a strong correlation between skin diseases and obesity, as the incidence of skin diseases was high among obese patients compared to non-obese. The prevalence of acanthosis nigricans and striae distensae were high among exposed females and males.

Nizar et al (2016) determined the frequency of skin diseases in type 2 diabetes mellitus through a descriptive cross-sectional study in Karachi, Pakistan. Included participants (n= 203 59% female and 41% male), had a mean age of 50±11 years respectively. Mean duration of diabetes 8.5±7 years. Patients with glycemic satisfactory control was (33%) and unsatisfactory control was (68%). Dermatological and general examination was performed. Glycemic control was assessed by fasting blood sugar, HbA1c and random blood sugar. HbA1c >7 was defined as unsatisfactory glycemic control. The mean fasting plasma glucose was 156±50 mg/dI, RBS mean ±SD was 213±79 and the mean HbA1C ±SD was 8.6±1.5. Skin manifestations were bacterial infection (26%), fungal infection (22%), acanthosis nigricans (20%), diabetic foot (16%), nail change (16%), diabetic dermopathy (9%), acrochordons (10%), pruritus (8%) and diabetic bullae (2%). Unsatisfactory glycemic control skin diseases were bacterial infection (30%), fungal infection (28%), acanthosis nigricans (18%), diabetic foot (18%) and acrochordons (10%). Satisfactory glycemic control skin diseases were bacterial infection (18%), fungal infection (10%), acanthosis nigricans (26%), diabetic foot (12%) and acrochordons (11%). Patients with type 2 diabetes mellitus had a higher incidence of bacterial and fungal infections. Diabetic foot and acanthosis nigricans are less common in satisfactory patients.

Galdeano et al (2010) studied the prevalence of skin diseases in diabetic patients through a protocoled, transversal, descriptive and observable study in Argentina. Included participants (n= 125) were diabetic, 57% females. 15 patients with type 1 DM and 110 patients with type 2 DM. The mean age was 58.9 ±15.43 years. All patients was hospitalized and 50.4% was diabetic for >10 years in duration and 60% of the patients was obese. The skin diseases were xeroderma (69%), dermatophytosis (52.8%), onychomycosis (49%), tinea pedis (39%), diabetic dermopathy (35%), diabetic foot (24%), candidiasis (17%), intertrigo (10%) and seborrheic keratoses (8%). In comparison between patients with DD and patients without DD, the male patients >50 years were highly significantly affected with diabetic foot and tinea pedis, with no significant difference in the type of DM. The incidence of skin lesions was high in diabetic patients.

3.5. Synthesis of results and summary table

Table 1. Frequency of Skin Conditions in Different Population in Relation to the Presence of Obesity and-or Diabetes.

Reference	**Study Design**	**Country**	**Number of Participants**	**Age & Ethnicity**	**Obesity and Diabetes**	**Frequency of Skin Conditions**	**Conclusion**
(Ozlu at el., 2008)	Prospective controlled study	Turkey	600 in total, 450 patients with obesity (138 with diabetes, 370 female) and 150 controls without obesity or diabetes (114 females)	Kurdish Turks. 37.25±11.37 and 35.67±11.24 years is the mean ages of obese patients and controls.	BMI values are mean ± Standard Deviation for cases and controls (37.22±6.07 and 22.23±2.19) kg/m2. (119.72±12.98 and 82.37±9.21) is the mean waist circumstance in obese and control patients. diabetes was defined as HBA1c level ≥6.5% or FBG level ≥126 mg/dL or postprandial glucose ≥200 mg/dL 2h or random glucose value ≥200 mg/dL was done to the patients with DM classical symptoms considered as main criteria to diagnose DM.	Acanthosis nigricans: 47.3% in obesity, 47.8% in diabetic obese, 3.3% in controls. Acrochordon: 52.4% in obesity, 54.3% in diabetic obese, 3.3% in controls. Striae distensae: 64.7% in obesity,62.3% in diabetic obese, 3.3% in controls. Planter hyperkeratosis: 46.4% in obesity, 45.7% in diabetic obese, 3.3% in controls. Hirsutism 29.1% in obesity, 19.6% in diabetic obese 1.3% in controls.	The prevalence of skin diseases is higher in patients with obesity than controls and no significant statistical difference between diabetic obese and non-diabetic obese patients.

(Boza at el., 2012)	Comparative study	Brazil	149, 76 obese (20 male, 56 females) and 73 controls (20 males, 53 females)	Mixed-race. The mean age ±SD in obease patients is (49.66 ± 15.61) and (49.11 ± 14.50) in controls.	People and including parameters were 76 Obese patients with BMI (≥30 kg⁄m2) and 73 controls with BMI (18.5–24.9 kg⁄m2), obese group were divided into 3 classes, class I (BMI 30–34.9 kg⁄m2), class II (BMI 35- 39.9 kg⁄m2), and class III (BMI ≥40 g⁄m2). weight (kg) ± SD in obese (105.3 ± 26.13 Kg) and (58.58 ± 8.12 kg) in controls, Diabetes in obese people (23.7%), and controls (9.6%), hight, waist circumstance, and blood pressure.Lab evaluation(fasting glucose, cholesterol, HDL, and triglycerides.	Striae: 68.4% in obese, 30.1% in controls. Plantar hyperkeratosis: 46.7% in obese, 9.6% in controls. Acrochordons: 47.94% in obese, 15.06% in controls. Intertrigo: 44.7% in obese, 6.8% in controls. Pseudoacanthosis nigricans: 27.6% in obese, 0% in controls. Distribution of BMI shows that striae in degree I (52%), II (70.4%), III(83.3%). Pseudoacanthosis nigricans: degree I (4%), II (37%), III (41.7%). Bacterial infection: degree I (4%), II (7.4%) and III (25%).	This study concludes a clear correlation between obesity, increasing BMI, and skin diseases.

(Al-Mutairi, 2011)	Prospective Study	Kuwait	overweight or obese 437 patients (200 males and 237 females)	Kuwaiti, Arabs. Age: 18-74 years divided into 5 groups.	437 patients were included (200 male, 237 females) categorized into 3 grades: grade 1, 43.7% were overweight with (BMI >25–30), grade 2, 51.7% were obese (BMI >30–40), and grade 3 4.65% were severly obese (BMI > 40). according to age groups divisison, the highest incidence in 30-39 and 40-49 years old patients. Diabetic patients were 78, 38 diagnosed already. During the study, 49 cases of diabetes mellitus were detected. medical history including data: age, sex, occupation, family and personal history of diabetes, obesity and hypertension. fasting, postprandial blood sugar levels, kidney, liver and thyroid function test. female patients with hirsutism and-or acanthosis nigricans and-or acne 69(15%) investigated for FH, LSH, prolactin and pelvic ultrasound. 74 female patients were diagnosed with polycystic ovarian syndrome-hyperandrogenism, hirsutism in 35, acanthosis nigricans and hirsutism in 22, severe acne, hirsutism and acanthosis nigricans in 12.	87 diabetic patients, acanthosis nigricans and skin tags were in 39 patients, skin tags: 15, intertrigo: 33, acne and acanthosis nigricans:12 commonest skin diseases in obesity patients, plantar hyperkeratosis: 45.1%, acanthosis nigricans: 33.0%, skin tags(acrochorda): 30.0%, striae cutis distensae: 23.3%, intertrigo: 22.2%, acne vulgaris: 21.5% and hirsutism: 15.8%.	this study showed that skin diseases are prevalent more with obesity.

(Svensson at al., 2017)	Cross-sectional study	5 countries were included (Germany, Italy, the Netherlands, Portugal and Sweden)	12,370 participants (53.9%) females in total.	Mixed European ethnicity. Age 14-47 years, median age 43 years. Investigation for skin diseases divides patients into 3 age groups: 18-34; 35-50 and 51-85 years.	Not reported	Skin diseases diagnosed by physician: contact dermatitis 8.3%, atopic dermatitis 7.1%, other eczema 11.8%, psoriasis 4.6%, warts 27.5%, acne 11.8%, skin cancer 2.6%, leg ulcer 0.5%, vitiligo 1.1% and urticaria 6.6%. Skin cancer 0.6% higher than women 0.4%. Atopic dermatitis and acne peak at age group 18-34 years, contact dermatitis peak in 30-50 years, and warts, psoriasis leg ulcer, and skin cancer peak with age 51-85 years. In Germany, contact dermatitis 12.7%, atopic dermatitis 9.4%, psoriasis 6.9% and acne 17.7% were higher compared to other European countries. Netherlands, eczema 24.5%, warts 53.1%, urticaria 9.0%, skin cancer 4.0%, leg ulcer 1.5% and vitiligo 2.2%.	Skin diseases diagnosed by physicians across European countries were higher in Germany, Sweden and the Netherlands compared to Italy and Portugal.
(Shahzad at al., 2011)	Prospective observational study	Saudi Arabia	196 participants with DM, 98 males and 98 females, >5 years duration	Age range 21-103 years, Mean ± SD 62.86±12.81, age of onset range 10-80 years and mean SD 48.46±11.44 with DM. Saudis, Arabs. Reporting between 2008-2009.	196 patients with diabetes for more than 5 years. American Diabetes Association criteria used to define the diagnosis including diabetes symptoms plus: fasting plasma glucose ≥7.0 mmol/l (126 mg/dl); randome blood glucose concentration ≥11.11 mmol/l (200 mg/dl); 2-hour plasma glucose of ≥11.1 mmol/l (200 mg/dl) during orally glucose tolerance test. 130 patients had a positive family history and 192 with skin manifestations.	Skin manifestations in DM patients: diabetic dermopathy 3.8%, skin tags 24.7%, xerosis 23.1%, alopecia legs 21.6%, spots 20.0%, feet hyperkeratosis 12.8%, seborrheic keratosis 7.5%, dry palms 7.5%, acanthosis nigricans 0.9%, intertrigo 2.2%, cutaneous infection 26.9%, fungal infections 19.7%, tinea pedis 14.7%, candidal infections 4.1%, warts 0.6% and bacterial infections 3.1%.	The prevalence of skin manifestations is high in diabetic patients and increasing as the duration of diabetes increased.

(Tseng et al., 2014)	Cross-sectional study	Taiwan	313 male participants, 70 with DM type 2 patients.	Mean age 85 years, SD 5.5, range 65-99. BMI mean 22.3, SD 3.34, range 14.1-34.4. 70 were type 2 Diabetes Mellitus. This study done in Taiwan, Chinese. Conducted in 2012.	Diabetes diagnosis followed the global guidelines of the International Diabetes Federation: HbA1c ≥6.5%/48 mmol/mol, fasting plasma glucose ≥126 mg/dL.	Skin manifestations in diabetic patients: fungal 81.4%, brown spots 74.3%, purpura 32.9%, scabies 31.4%, pruritus 25.7%, skin tags 22.9%, bacterial infections 17.1%, chronic ulcer 14.3%. Skin manifestations in non-diabetic patients: fungal infection 75.7%, brown spots 28.0%, purpura 24.3%, scabies 21.0%, pruritus 2.1%, skin tags 14.0%, bacterial infection 6.6% and chronic ulcer 3.7%.	The prevalence of skin diseases were significantly higher in patients with DM compared to non-diabetic patients.
(Foss et al., 2005)	Cross-series study	Brazil	403 patients, 31% were type 1 DM and 69% type 2 DM. 65.3% were females.	Mean age 19.9±2.3 and 63.1±3.4. This study done in Brazil, mixed-race. Conducted in 2005.	Glycated hemoglobin using ion-exchange chromatography measured for 136 patients, 28 were type1 DM, 4(14%) had adequate metabolic control, 24(86%) inadequate control and 108 type 2 DM, 20(17.6%) had adequate control, 88(82.4%) inadequate control.	Skin manifestations in diabetes mellitus patients: dermatophytosis 82.6%, actinic degeneration 62.0%, benign skin tumors 23.5%, xerosis 20.8%, candidiasis 12.9%, scars 12.6%, hyperkeratosis 8.6%, atopic dermatitis 6.6%, eczema 5.9% and acanthosis nigricans 5.9%. DM skin lesions among adequate metabolic control: xerosis 25%, solar elastosis 20.8%, seborrheic keratosis 20.8%, seborrheic dermatitis 12.5%, dermatophytosis 12.5%, candidiasis 4.2%, acanthosis nigricans 4.2% and juvenile acne not detected. DM skin lesions among inadequate metabolic control: dermatophytosis 55.3%, candidiasis 12.5%, juvenile acne 7.2%, seborrheic keratosis 6.2%, acanthosis nigricans 5.4%, solar elastosis 5.4%, seborrheic dermatitis 4.4% and xerosis 3.6%.	The prevalence of skin diseases were high in diabetic patients and poor control of DM increases the capability to skin infection.

(Ahmed et al., 2009)	Descriptive study	Pakistan	350 patients, 30 were type 1 and 320 were type 2 DM. 193 females and 157 males.	Mean age 54±8.53 years. Type 1 and type 2 DM. 23 adequate glycaemic control and 327 were uncontrolled. This study done in Pakistan, Battagram, multi-ethnic. Conducted in 2008.	Patients diabetes duration between 1-2 years. 140 patients had 5-10 years DM, 137 up to 10 years and 73 up to 5 years. Random or fasting blood glucose and reading of two or more previous blood sugar were recorded. HbA1c were not available.	Detedcted skin manifestations: skin infection (30.9%), ulcer and gangrene foot (12.9%), pruritus (7.1%), vitiligo (5.7%), skin tags (3.7%), diabetic dermopathy (4.2%), acanthosis nigricans (2.9%), eruptive xanthomas (2.6%) and diabetic bullae (0.6%). Cutaneous manifestations in IDDM patients: skin infections (0.9%), diabetic dermopathy (0.9%), vitiligo (2%), ulcers and foot gangrene (0.3%), skin tags (0.6%) and eruptive xanthomas (0.6%). Cutaneous manifestation in NIDDM: skin infections (30%), ulcers and foot gangrene (12.6%), pruritus (5.7%), vitiligo (3.7%), diabetic dermopathy (3.4%), skin tags (3.1%), acanthosis nigricans (2.9%), eruptive xanthomas (2%) and diabetic bullae (0.6%).	The prevalence of skin diseases were high in diabetes patients.

(Ragunatha et al., 2011)	Cross-sectional study	Pakistan	500 patients, 98.8% were type 2 DM. 286 males and 214 females.	Mean age 58.2±11.96 and 53.3±10.78 years.type 1 and type 2 DM. This study done in Pakistan. Conducted in 2011.	Mean diabetes duration were 5.5±5.8 years. Fasting and postprandial plasma sugar test were screened. 82% of patients were diabetic <10 years. Mean FPG was 129.97±48.65 mg/dI. FPG were <130 mg/dI in 60% of patients and 12% were 130-140 mg/dI.	Skin manifestations in diabetic patients: fungal infections (13.8%), bacterial infections (6.8%), candidiasis (3.6%), acanthosis nigricans (5.0%), acrochordon (26.2%), bullous diabeticorum (0.4%), vitiligo (1.6%), lichen planus (1.8%), psoriasis (0.6%), erythema (6.2%), eczemas (7.8%), pruritus (5.2%), xerosis (4.4%), idiopathic guttate hypomelanosis (14.4%), seborrheic keratosis (15.8%), dermatosis papulosa nigra (27.6%), melasma (4.0%), nail dystrophy (4.0%), eruptive xanthoma (0.6%) and melanonychia (2.6%).	The prevalence of skin manifestations in well-controlled diabetic patients is low. The prevalence of cutaneous infection was high in diabetic patients.

(Khalil et al., 2011)	Retrospective cohort study	Saudi Arabia	Included cohorts (n=177). 61 obese, 48 nonobese males and 32 obese and 36 nonobese females.	Male obese mean age ±SD 41.23±12.09 and 36.33±16.83 in non-obese with BMI ±SD 31.9±5.41 in obese and 23.0±1.37 in non-obese. Female obese mean age ±SD 29.11±9.56 and 25.61±4.27 in non-obese with BMI ±SD 31.23±4.97 in obese and 22.06±2.43 in non-obese. This study done in Saudi Arabia, Qasim, Arabs.	Present of diabetes or hypertention in male obese (34.4%) and (16.6%) in non-obese. Present of diabetes or hypertention in obese female (12.5%) and (0%) in non-obese. Fasting blood glucose, BMI, waisr-hip ratio and blood pressure were measured.	Skin diseases in male obese: acanthosis nigricans (42.6%), stria distensae (34.4%), cellulite (13.1%), skin tags (11.4%), planter keratosis (8.10%), xerosis (6.5%), pruritus (3.2%), tinea pedis (18.0%), intertrigo (14.7%), bacterial folliculitis (13.1%), tinea cruris (6.5%), tinea versicolor (3.2%) and candida infrction (1.6%). In non-obese males, only skin xerosis were (16.6%), tinea pedis (8.3%) and other skin diseases were (0%). In obese females, the skin diseases were skin distensae (72.2%), acanthosis nigricans (52.7%), cellulite (41.6%), xerosis (27.7%), skin tags (22.2%), puritus (22.2%), planter keratosis (22.2%) hirsutism (19.4%), bacterial folliculitis (36.1%), tinea pedis (8.3%) and intertrigo (19.4%). In non-obese females, skin diseases were stria distensae (12.5%), cellulite (12.5%), xerosis (6.26%), pruritus (6.25%), skin tags (6.2%), planter keratosis (3.12%), acanthosis nigricans (3.1%), bacterial folliculitis (28.1%) and hirsutism (0%).	The prevalence of skin diseases were significantly increased among obese patients.
(Nizar et al., 2016)	Descriptive cross-sectional study	Pakistan	203 patients, 59% females and 41% males with type2 diabetes mellitus, mean duration 8.5±7 years.	Mean age 50±11 years. 33% were satisfactory control and 68% unsatisfactory patients. This study done in Karachi, Pakistan. Conducted in 2014.	Patients with type 2 DM. Mean FBS ±SD 156±50, RBS mean ±SD 213±79 and HbA1C mean ±SD 8.6±1.5. Unsatisfactory glycemic control defined as HbA1C >7.	Skin manifestations were bacterial infection (26%), fungal infection (22%), acanthosis nigricans (20%), diabetic foot (16%), nail change (16%), diabetic dermopathy (9%), acrochordons (10%), pruritus (8%) and diabetic bullae (2%). Unsatisfactory glycemic control skin diseases were bacterial infection (30%), fungal infection (28%), acanthosis nigricans (18%), diabetic foot (18%) and acrochordons (10%). Satisfactory glycemic control skin diseases were bacterial infection (18%), fungal infection (10%), acanthosis nigricans (26%), diabetic foot (12%) and	Type 2 DM patients have high incidence of bacterial and fungal infections.

						acrochordons (11%).	
(Galdeano et al., 2010)	Protocoled, transversal, descriptive and observable study	Argentina	Included participants were (n= 203), 59% female and 41% male.	Mean age were 50±11 years with mean diabetes duration 8.5±7 years. glycemic satisfactory control were (33%) and unsatisfactory control were (68%). This study done in Argentina. Conducted in 2009.	15 patients were type 1 DM and 110 patients were type 2 DM. All patients were admitted to the hospital.	The skin diseases were xeroderma (69%), dermatophytosis (52.8%), onychomycosis (49%), tinea pedis (39%), diabetic dermopathy (35%), diabetic foot (24%), candidiasis (17%), intertrigo (10%) and seborrheic keratoses (8%).	The incidence of skin lesions was high in diabetic patients.

BMI= body mass index
DM= diabetes mellitus
IDDM= insulin-dependent diabetes mellitus
NIDDM= non-insulin-dependent diabetes mellitus
FBG= fasting blood glucose
SD= standard deviation

3.6 Results summary

In four studies, the main criterion to diagnose DM was HBA1C levels and in eight studies, it was fasting blood glucose. Two studies compared skin diseases in patients with adequate DM and non-adequate DM, other study compared the skin diseases in type 1 DM and type 2 DM, four studies found the skin diseases in obese participants and two studies found the skin diseases in obesity participants by measuring the BMI. Three of the studies were conducted in Pakistan, two in Brazil, another two in Saudi Arabia, one study in Turkey, one in Argentina, one in Kuwait and another one in Europe. There are four cross-sectional studies, the remaining were prospective controlled, comparative, prospective, observational, cross-series, descriptive and cohort study. The sample size greatly varied, ranging from 149 to 12,370 participants. The samples age varied from 18 to more than 100 years. Almost all of included participants in the studies were examined by a dermatologist with full medical history for any diseases. Some of the studies were conducted at the endocrinology clinic, dermatology clinic or to the admitted hospital patients. The summary table will list all the articles (see Table 1). All the studies were included adult males and females whom considered diabetic and/or obese with skin manifestations.

4. DISCUSSION:

This systematic review identified 12 studies (n= 15,901 patients) assessing the prevalence of skin diseases in relation to obesity and/or diabetes in adults aged ≥18 years. Previous reviews are extremely limited. In comparison between the studies, the results of this review confirmed that skin manifestations are common and high among adults with obesity and diabetes, and less common in adults without obesity and/or diabetes. The review has also known that the prevalence of skin diseases varies geographically and probably reflects the fact that skin diseases are complex influenced by both diabetes or obesity.

4.1. Skin and Insulin Resistance

Insulin is a hormone that is produced by beta cells of islets of Langerhans in the pancreas, plays an important role in control blood glucose levels. Insulin has an important role in the physiology and homeostasis of the skin, but the exact function remains controversial. In control healthy people, insulin regulates the equilibrium between differentiation and proliferation of keratinocytes, that is important for the formation of the epidermal structure (Napolitano et al., 2015). In patients with chronic inflammation like psoriasis or acne, pro-inflammatory cytokines will be produced in high levels to activate p38MAPK, which induces insulin resistance by serine phosphorylation of IRS, that blockade the differentiation and increased the proliferation of basal keratinocytes at the same time (Napolitano et al., 2015). Insulin resistance (IR) is clinically defined as the inability of a known quantity of endogenous or exogenous insulin to elevate glucose uptake and exploitation in an individual as much as it does in normal people. The IR causes insufficiency in insulin-stimulated glucose transport in fat tissues, skeletal muscle, and suppression of the production of glucose in the liver (Napolitano et al., 2015). As a result of IR, the pancreas will produce more insulin than normal, leading to a hyperinsulinemia condition (Napolitano et al., 2015). IR will accelerate lipogenesis and increase fatty acid production, levels reduce of sex hormone-binding globulin (SHBG), increases follicle-stimulating hormone (FSH) and luteinizing hormone (LH), leading to an increase in the production of ovarian androgens and in their biologically active portion that potentially leading to hyperandrogenism (Napolitano et al., 2015). Hyperandrogenism is a common endocrine disorder that affects women of productive age (Napolitano et al., 2015). Polycystic ovarian syndrome (PCOS) is the commonest and most frequent hyperandrogenic linked disorder, for the dermatologist, the most important skin conditions linked to (PCOS) include psoriasis, acne, hirsutism, alopecia, and acanthosis nigricans (Napolitano et al., 2015).

4.2. Skin and Diabetes Mellitus

Diabetes is a life-threatening disease, in 2015 the death of 5 million people was accounted for worldwide. The prevalence of diabetes mellitus is increasing (Bustan et al., 2017). According to a new estimation, 415 million adults currently suffer from

diabetes, and it is expected to raise this number to 642 million by 2040 (Makrantonaki et al., 2016). Elevated glucose blood levels affect the skin among systemic organs, and the onset of these metabolic conditions can also be predicted by skin disorders (Makrantonaki et al., 2016).

Skin signs are seen and observed among people with diabetes with variable durations and in prediabetic patients (Bustan et al., 2017). Patients can develop acanthosis nigricans as an early sign of diabetes, especially when the patient has additional risk factors to develop DM, including obesity (Bustan et al., 2017). The majority of included studies use HbA1c or fasting blood glucose measurements to assess DM. Regardless of the methods applied, there is overall agreement that acanthosis nigricans is significantly increased in patients with diabetes (Ahmed et al.,2009; Raguantha et al., 2011; Nizar et al., 2016; Shahzad at el, 2011). Foss et al (2005) showed that 5.0% of patients with diabetes had acanthosis nigricans, 4.2% in patients with adequate metabolic control, and 5.9% among patients with inadequate metabolic control.

The main studies findings have shown a high prevalence of skin diseases among diabetes patients compared with healthy controls and shown no statistically significant difference between diabetic obese ana non-diabetic obese (Ozlu at el., 2008). While Boza at al (2012) showed a clear correlation between obesity and increasing BMI with skin diseases. These statements also align with the published findings of Al-Mutairi (2011) and Khalil et al (2011), as they showed that the prevalence of skin diseases was significantly increased among patients with obesity.

The prevalence of cutaneous manifestations is high in diabetic patients (Ahmed et al.,2009; Galdeano et al., 2010) and increase as the duration of diabetes increase (Shahzad et al., 2011). Patients with diabetes had significantly higher prevalence of skin diseases compared to non-diabetic patients (Tseng et al., 2014). Poor control of diabetes mellitus patients, increase the capability of skin diseases especially skin infection (Foss et al., 2005; Ragunatha et al., 2011). The prevalence of skin manifestations among well-controlled diabetes mellitus patients is low. Type 2 diabetic patients have a high incidence to develop bacterial and fungal infections (Nizar et al.m 2016).

Ahmed et al (2009) compared skin diseases in insulin-dependent diabetes mellitus patients with non-insulin-dependent diabetes mellitus patients and the results showed a high prevalence of skin diseases in NIDDM, and the commonest skin diseases were skin infection, foot ulcers, and foot gangrene. The unsatisfactory glycemic control in type 2 diabetes mellitus patients shows a high incidence of skin manifestations include bacterial infection, fungal infection, acanthosis nigricans, and diabetic foot compared to skin manifestations in satisfactory glycemic control patients (Nizar et al., 2016) in another study, (Foss et al., 2005) shows that the prevalence of skin diseases among diabetic patients are high, also, poor control of DM patients, increases the capability to a skin infection. Skin diseases among inadequate metabolic control are dermatophytosis and candidiasis with high incidence compared to metabolic control diabetes mellitus (Foss et al., 2005).

Skin diseases appear to be high in the control European population, a study reporting the incidence of age-specific rates showed a dual peak of atopic dermatitis and acne around 18-34 years of age, another peak of contact dermatitis around 30-50 years, and a peak of skin cancer around 51-85 years old (Svensson et al., 2017). According to the age group division of obesity patients, the highest incidence in 30-39 years and 40-49 years old patients (Al-Mutairi, 2011).

4.3. Skin and Obesity

Obesity is a major public health problem worldwide, with an increase in its prevalence over the past two decades (Hirt et al., 2019). The effect of obesity on the skin is still underestimated. Obesity and increased body mass index affect skin barrier, skin physiology, collagen structure, and healing of the wound. It also affects the sweat glands, sebaceous glands, and causes lymphatic and circulatory changes (Hirt et al., 2019). Obesity is associated with skin barrier function changes, also obesity significantly increased erythema and transepidermal water loss. There is frequently elevated androgens, growth hormones, insulin, and insulin-like growth factors in obese patients, and have been demonstrated to elevate sebaceous gland activity and the effect on the severity of acne (Yosipovich et al., 2007). Patients with obesity have larger skin folds and more sweat with overheated, because of the thickness of subcutaneous fat layers, cause friction and moisture that lead to many skin manifestations. Obese diabetic women patients with a BMI greater than 25 kg/m^2, have a higher pH skin surface than women with a BMI less than 25 kg/m^2. (Yosipovich et al., 2007). Obesity also can cause lymphedema, a collection of protein-rich

lymphatic fluid in subcutaneous tissues. Ozlu et al (2008) reported skin diseases in the obese patients: acanthosis nigricans 47.3%, acrochordon 52.4%, striae distensae 64.7%, and plantar hyperkeratosis. (Boza at al., 2012) shows a clear collaboration between skin diseases, increasing BMI, and obesity, the most frequent skin diseases among obesity was striae distensae 68.4%, planter hyperkeratosis 46.7%, acrochordon 47.94%, and intertrigo 44.7%. (Al-Mutairi, 2011) shown that acanthosis nigricans among the obesity group was 33.0%, planter hyperkeratosis 45.1%, skin tags 30.0%, and intertrigo 22.2%. (Khalil et al., 2011) compared skin manifestations in obese female and obese male, the most frequent skin manifestations among obese females: striae distensae 72.2%, acanthosis nigricans 52.7%, cellulitis 41.6%, xerosis 27.7%, skin tags, plantar hyperkeratosis, and pruritus were 22.2%, in obese males the most frequent skin manifestations were acanthosis nigricans 42.6%, striae distensae 34.4%, tinea pedis 18.0% and intertrigo 14.7%.

According to our studies, most of the studies showed that the most frequent skin diseases among obese patients are acanthosis nigricans, acrochordon, striae distensae, skin tags, intertrigo, and plantar hyperkeratosis. The most frequent skin diseases among diabetes obesity patients were acanthosis nigricans 47.8%, acrochordon 54.3%, striae distensae 62.3% and planter hyperkeratosis 45.7% (Ozlu at el., 2008). Obesity has a metabolic effect, as it may cause gout and hyperandrogenism, which in turn are associated with skin diseases, such as bacterial infection, candida skin infection, inflammatory skin diseases, onychomycosis or, it lead to cause a chronic dermatosis such as psoriasis, rosacea and hidradenitis suppurativa (Hirt et al., 2019). The relation between obesity and increased risk of skin cancer still debatable. Obesity is related to premature hair graying and rare skin conditions. The physicians need to understand these clinical signs and underlying systematic disorders to facilitate the diagnosis early for better management and treatment.

The most common cutaneous manifestation in obesity patients was acanthosis nigrican, which appear to patients as velvety, symmetrical, hypertrophic, hyperpigmented plaque that many appear in many locations in the body, commonly in the groin, perioral, elbows, face, axilla, flexor, umbilicus and posterior neck (Yosipovich et al., 2007). The skin changes in acanthosis nigricans are associated frequently with insulin resistance and hyperinsulinemia (Yosipovich et al., 2007; Hirt et al., 2019). Patients might completely regress after weight loss. The lesion also might appear as a sign of internal malignancy like aggressive adenocarcinoma of the gastrointestinal tract (Hirt et al., 2019).

Acrochordon is a pedunculated soft brown papule, localized commonly at the friction sites: axilla, neck, inframammary folds, and inguinal regions. Acrochordons symptoms: pain, itching, and rubbing against clothes. Pathologically, it's associated with insulin resistance, growth factors, mast cells, inflammatory medications, androgens, estrogens and might caused by human papilloma virus infection (Hirt et al., 2019). Stria distensae is hypopigmented linear striations that are localized in the breasts, hips, abdomen, upper arms, lower back, thighs, and buttocks (Hirt et al., 2019). Planter hyperkeratosis is associated with obesity, affects the foot, heels, and great toe. Its results as a compensatory mechanism due to subcutaneous thickening. Overweight alters the anatomy of the foot and transfers elevated pressure over bony prominences of the sole and weight-bearing areas, leads to injury and mechanical trauma. Obesity in general increases the risk to develop infectious diseases, including skin infections. The mechanisms possibly associate obesity with decreased cell mediated immune responses, pro-inflammatory state, and decrease pharmacologic interactions with antimicrobial agents. Although, the inability or difficult mobility to maintain adequate levels of hygiene will increase and exacerbate the problem. Patients with higher BMI will increase the incidence of erythrasma, cellulitis, candida folliculitis, candidiasis, intertrigo, tinea cruris, necrotising fasciitis and methicillin resistant staphyloccus aureus infection are more commonly found in obese patients (Hint et al., 2019). Intertrigo is an inflammatort, of two opposed close skin surfaces, with common sites within skin folds like axillary area, abdomin and inframammary areas. Its appear like a macerated erythematous plaques. In obese patients, the skin folds is larger with more sweat, which increases moisture and friction leading to inflammation and macerations. Cellulitis in obese patients has a higher incidence and more arises on the legs in coexisting lymphedema patients. Candidia albicans found to me more frequent in obese patients, and it might cause intertrigo, folliculitis and hand or feet paronychia (Hint et al., 2019).

The prevalence of obesity is increasing, also cause an increase in skin manifestations and other diseases (Rosen et al., 2019). Weight loss in obese patients is associated with a decrease in morbidity and mortality and improves quality of life (Rosen et al., 2019). Treating obesity and other obesity-associated problems has a significant economic impact on health care systems (Mancini and de Melo, 2017) Long-term, unsatisfactory outcomes can be seen in obesity treatment, as its physiology is complex and there are inherent difficulties related to the preservation of lifestyle improvements. Obesity is determined by environmental and genetic factors. Anti-obesity drugs have become legitimate medications as obesity is a chronic disease, growing worldwide, and requires long term treatment (Mancini and de Melo, 2017). A large proportion of people living with obesity have a desire to decrease their weight, by taking weight loss medications or by other weight loss procedures. To treat obesity, patients should begin with lifestyle interventions like diet or exercise and then, can progress to medical treatment. If treatment fails the with medications or nonsurgical interventions, then other procedural techniques need to be considered. Bariatric surgery is generally decided for patients with morbid overweight (BMI≥ 40 kg/m2) (Rosen et al., 019). These interventions are important, as they help patients to reduce their weight and obesity-related comorbidities. The effect of weight-loss interventions on skin conditions has not been reviewed in depth. A variety of dermatological changes may appear, depending on the weight loss intervention.

4.4. Skin and Oral Weight Loss Medications

Weight loss medications have increased over the past decade as obesity increased worldwide. Synthetic amines for short term use, are the most common anti-obesity medication, working by increasing satiety and decreasing food intake and cause 5%weight loss. On the skin, it's associated with scleroderma, urticaria, and xerosis. Metformin treated obesity, with benefits in many skin conditions including acne, hirsutism, acanthosis nigricans, hidradenitis supportive, psoriasis skin cancer, and eruptive xanthomas (Rosen et al., 2019). The reported side effects of using Metformin, include lichen plans, psoriasiform drug eruption, leukocytoclastic vasculitis, acute alopecia, and bullous pemphigoid (Rosen et al., 2019). Topiramate was approved initially to treat convulsant patients, but it was also discovered to have properties to decrease weight (Rosen et al., 2019). The drug effect corticotrophin-releasing hormone, neuropeptide Y, and type II glucocorticoid receptors, causing weight loss. Phentermine in combination with topiramate is approved for weight loss. Palmar erythema, pruritus, and hypohidrosis have been reported (Rosen et al., 2019). Blocking of B-endorphin action at the u-opioid receptor is the action of naltrexone medication (Rosen et al., 2019). Bupropion is an antidepressant drug that acts by inhibiting noradrenaline and dopamine reuptake and can affect the skin by inducing pityriasis, pustular psoriasis, subacute cutaneous lupus erythematosus, acute generalized exanthematous and, aquagenic pruritus (Rosen et al., 2019). Other diseases that can cause by those medications include Stevens-Johnson syndrome, hypersensitivity reactions, and erythema multiforme (Rosen et al., 2019). Weight loss is associated with improved blood pressure, triglycerides, fasting glucose, and HDL cholesterol levels (Mancini and de Melo, 2017). Patients lost 5-10% of body weight, increased odds of achieving 0.5% in HbA1c,systolic BP decrease 5-mmHg, Diastolic BP decrease 5-mmHg, triglycerides decrease 40 mg/dl and HDL cholesterol increase 5mg/dL. More weight loss than range 10-15% shows better odds improvements (Mancini and de Melo, 2017).

4.4.1. Treatment of Obesity with Liraglutide 3.0 mg

Liraglutide is a glucagon-like peptide 1 (GLP-1) receptor agonist, which 97% homology to native GLP-1, the extension of GLP-1 circulating half-life from 1 to 2 minutes to 13 hours. Agonist receptors of GLP-1 have an effective therapy to treat obesity and type 2 diabetes, this effect includes liraglutide. Liraglutide gets attention to be the most studied drug, also to its effect on the limbic system. Clinical weight loss and statical significance were observed in patients using liraglutide 3.0 mg (Mancini and de Melo, 2017). Treatment of type 2 diabetes mellitus the first approved to liraglutide in Europe in 2009, and for its effect on the limbic system, it has become the most studied drug (Davies et al., 2015).

Davies et al (2015) investigated liraglutide safety and effectiveness versus placebo for weight loss in adults with type 2 diabetes, overweight, and/or obesity. In 1361 included participants, 846 were randomized, across 126 sites in 9 different countries. Included patients had a BMI >27.0 kg. The 56 weeks RCT (2:1:1), placebo-controlled (n= 212), double-blind, parallel-group trial, observation for 12 weeks off drug follow up period, investigate subcutaneous liraglutide 3.0 mg treatment, once-daily (n= 423). Participants who completed the treatment period of 56 (76%) weeks was higher with liraglutide 3.0 mg than placebo (66%). Liraglutide 3.0 mg mean body weight of 105.7 kg and for placebo (106.5 kg). Mean weight loss for liraglutide 3.0 mg 6.0- (6.4 kg) and 2.0% (2.2 kg) placebo. There was a clear significant weight loss with liraglutide 3.0 mg compared with placebo. Also, treated participants with liraglutide 3.0 mg were significantly more likely to lose 5% to 10% bodyweight compared with placebo. There was also a significant reduction in BMI and waist circumference with liraglutide 3.0 mg compared to placebo. There is no adverse events of cessation safety of the treatment were noted. Liraglutide 3.0 mg was significantly associated with improved glycemic control (HbA1c levels and achieving targets, fasting plasma glucose levels, prandial plasma glucose, fasting glucagon level, proinsulin to insulin ratio, proinsulin levels, and HOMA IR indices) compared to placebo (Davies et al., 2015). Patients who received liraglutide 3.0 mg for 56 weeks showed reduced use of oral hypoglycemic agents than placebo. Liraglutide 3.0 mg showed that systolic blood pressure was significantly decreased than placebo. Also, liraglutide 3.0 mg showed improvements in HDL-C, VLDL-C, triglycerides, and total cholesterol levels compared to placebo, although there was no effect on free fatty acids or LDL-C. C-reactive protein, urinary albumin - creatinine ratio, and plasmin activator inhibitor 1 were improved with liraglutide 3.0 mg. Urinary albumin-to-creatinine ratio was lower in liraglutide participants by 20% than the placebo. There are significant fibrinogen levels increased with 3.0 my liraglutide. vs placebo. As obesity affects patients mental health and quality of life, liraglutide (3.0 mg) was found to improve the total score of the IWQoL-Lite questionnaire, so it improves the physical function score (Davies et al., 2015). The study was not report or noted any safety after cessation the drug and weight loss was maintained to 56 weeks only. More further studies are required to found if the liraglutide 3.0 mg effects are maintaining with continuing the treatment for the longer-term.

4.4.2. The effect of Liraglutide on Skin Manifestations

(Xu ,et al., 2019) investigated the safety and effectiveness of liraglutide on psoriasis in type 2 diabetes patients, through a prospective cohort study. They found that PASI mean value decreased from 15.7 ±1.8 to 2.2 ±3.0 after 12 weeks of treatment and, there was also a significant improved of HbA1c. BMI and waist circumference were improved and C-peptide levels increased. There was significant reduction in thickness of the epidermal layer after the treatment. They also found that liraglutide improved the skin conditions of psoriasis type 2 diabetes patients effectively, as it may related to anti inflammation effect.

(Lin, et al., 2020) determined the effect of liraglutide on psoriasis treatment throughout a randomized controlled trial. Twinty-five participants with psoriasis and type 2 diabetes were included and randomized for 12 weeks were divided into control group or liraglutide group. After 12 weeks of treatment, the mean DLQI decreased from 22.00 ± 5.85 to 3.82 ± 3.60. In treatment group, there was a significant change compared to the baseline value of DLQI and PASI. Pathological changes of IL-17, IL-23, TNF-a and psoriasis skin as its shows improvement.

One case report for a 19 year old patient with obesity and 8 years history of hidradenitis suppurativa, and other diseases, anemia, high platelet level, leukocytosis, high liver enzymes and hypoalbuminemia. The patient received combination treatment includeding liraglutide. Liver enzymes returned to normal levels after one year, and other metabolic and hematological diseases treated after 3 years of started the treatment. Right axillary lesions were treated completely. The patient gets weight loss, improved her lifestyle and her diseases were treated (Khandalavala, 2017). This is the goal of weight loss.

4.4.3. Liraglutide 3.0 mg, Other Side-Effects

In general, liraglutide can cause withdrawal. The most frequent side effects are gastrointestinal upset like nausea, diarrhea, vomiting, and constipation. Hypoglycemia was observed more than placebo. Increase the mean heart rate of 2.0/min and 2.1/min compared to placebo -1.4/min, and the mean heart rate returned to its baseline after treatment stops (Davies et al., 2015). Heart arrhythmias were higher with liraglutide 3.0 mg than placebo. The most frequent cardiac arrhythmias were sinus tachycardia and tachycardia during the treatment with 3.0 liraglutide (Davies et al., 2015). After cessation of liraglutide, participants regained weight and decreased systolic blood pressure and fasting plasma

glucose, in nondiabetic patients, mild weight gain reported (Davies et al., 2015).

4.4.4. Semaglutide and weight loss

Semaglutide is a glucagon-like peptide-1 receptor agonist, once per week, it is allowing subcutaneous administration. Once per week subcutaneous semaglutide for type 2 diabetes mellitus treatment has been approved by the Food and Drug Administration (FDA) and the European Medicine Agency (EMA). Recently, semaglutide has been evaluated as an antiobesity drug in phase II dose-finding trials (Christou et al., 2019). The mechanism of semaglutide includes insulin stimulation secretion from beta cells in the pancreas and decrease glucagon production from alpha-pancreatic cells, both dependent on glucose, thus decreasing postprandial and fasting plasma glucose. Apart from lowering the glucose levels, semaglutide promotes weight loss. A recent study investigated the semaglutide mechanism in weight loss inducing, showed that twelve weeks, once weekly subcutaneous administered semaglutide (first 4 weeks 0.25 mg, next 4 weeks 0.5 mg and the remaining 4 weeks 1.0 mg) resulted in (-5.0kg) weight loss in a greater way compared with placebo (+1.0 kg) in obesity participants but without type 2 diabetes mellitus (Christou et al., 2019). O'Neil et al (2018) did a double-blind, randomized placebo and active-controlled, dose-ranging, multicenter, phase II trial study, included adults with body mass index of 30 kg/m^2 and more. Participants received treatment once-daily subcutaneous injection for 52 weeks. They received semaglutide at one of 5 doses (0.05 mg, 0.1 mg, 0.2 mg, 0.3 mg or 0.4 mg) injected subcutaneously. As a result, there is a significant great body reduction observed on treatment at weight 52 than placebo. Semaglutide doses for more than 0.1 mg showed significant weight loss. High semaglutide doses of 0.2 mg or more daily, showed that 83% of patients lost 5% or more and 56%-65% lost 10% or more of the baseline weight (O'Neil et al., 2018). In posthoc analyses, 29%-41% of patients lost 15% or more and 11%-27% lost 20% or more of the main baseline weight (O'Neil et al., 2018). Semaglutide is associated with a decrease in libitum energy intake during taking the meals resulting in decreased ad libitum total energy intake, without any effect on the metabolic rate. The decrease of total energy intake appeared to be attributed to suppress the appetite, food aversion, or nausea. Treated with semaglutide can induce less hunger food desire or craving, lead to a lower preference for high-fat food, better-eating control, and meal portion size. Appetite suppression with semaglutide treatment may be mediated caused by relevant central mechanisms that involve the hypothalamus (Christou et al., 2019). Semaglutide 0.5 mg and 1.0 mg, reduced the body weight by 2.5 kg to 5.7 kg. Patients on subcutaneous semaglutide with type 2 diabetes mellitus can observe a reduction in HbA1c and body weight. Using semaglutide subcutaneous once weekly in type 2 diabetes mellitus may not reflect the right potential of semaglutide induced weight loss. All the trials reported only baseline weight loss minus after treatment body weight, a parameter unavoidable influenced by baseline body weight (Christou et al., 2019). Semaglutide in trials decreased bodyweight across all the body mass index. The greater weight loss was observed across the higher baseline body mass index for 0.5 and 0.1 mg. Semaglutide once per week 0.5 mg can decrease the weight of no more than 5 kilograms, with up to 46% of participants at least achieving 5% weight loss after 56 weeks. Semaglutide once per week 1.0 mg can decrease the weight of no more than 7 kilograms with up to 63% of participants achieving at least 5% weight loss also after 56 weeks. Semaglutide to treat obesity showed its effectiveness and appears to be a promising drug in obesity and type 2 diabetes mellitus patients. Lifestyle intervention should combine two main factors which are weight loss and euglycemia. Patients with type 2 DM and obesity respond less to weight management drugs compared to patients without type 2 DM, potentially because of weight-increasing antidiabetic drugs (Christou et al., 2019).

4.4.5. Semaglutide side effects

Semaglutide can cause common side effects like gastrointestinal tract disorders like vomiting, nausea, constipation, or diarrhea. Those side effects depend on the dose of treatment and occurring primarily during the two weeks of initiation of semaglutide with mild to moderate severity (Christou et al., 2019). There is a low incidence of hypoglycemia, other reported side effects include an increase in pancreatic lipase, headache, influenza infection, nasopharyngitis, and injection site nodule may occur rarely (Christou et al., 2019).

Semaglutide was found to be more effective than other once-weekly GLP-1 RAs, to manage both glycaemic and weight control. Also, semaglutide was found to be less costly compared to achieve the endpoint of HbA1c <7% without hypoglycemia and without gaining weight (Christou et al., 2019).

4.5. Skin Improvement After Weight Loss

4.5.1. Liposuction

Liposuction is the commonest performed method for fat removal (Rosen et al., 2019). This procedure is used to change body contour by subcutaneous fat aspiration, and it is not a weight-loss procedure. Only 1500 ml of fat should be removed, to avoid blood transfusion. Aesthetic problems like regulation contour, increase the complication of large volume liposuction. Other serious complications like infection, deep vein thrombosis (DVT), bleeding, fat embolism, or pulmonary embolism can occur (Rosen et al., 2019). Changes of the skin associated with liposuction include laxity, necrosis of the skin, infection, hyperpigmentation, ecchymosis, and sensory loss. Skin retraction happens naturally after liposuction in 90% of the patients, this retraction rate may depend on some of the factors in each patient like genetics, laxity of the skin, obesity degree, and anatomic location of the procedure, as most skin retraction will be high at the areas with higher fibrous septae in the superficial fat layer (Rosen et al., 2019). Skin retraction in the upper abdomen and medial thigh is poor after liposuction, while in the back, thick septae helps with faster retraction. A new technique like laser assisted liposuction, ultrasound-assisted liposuction, or radiofrequency assisted liposuction was found to increase the tightening of the skin and enhance the efficiency of the liposuction procedure (Rosen et al., 2019).

There is a strong association between obesity and lymphedema. To manage or treat lymphedema, patients involve surgical or conservative therapy, to improve the quality of life. Liposuction is one of the choices that has been used to manage lymphedema by removing the accumulation of subcutaneous adipose and fibrotic tissue. After liposuction, the mechanism to improve the lymphedema by increasing the flow of the blood, decrease lymphatic production because of decrease subcutaneous adipose tissue, and enhance lymph drainage from superficial to the deep lymphatic system (Rosen et al., 2019).

Massive weight loss causes redundant skin, which is a major detriment to life quality. The complication of redundant skin will include infection, frictional discomfort, or different types of rash. The main treatment to improve life quality is body contouring surgery, with around 74% of patients going with it (Rosen et al., 2019).

An effective way to improve psoriasis and hidradenitis suppurativa is bariatric surgery, but the side effect should be considered. The complication of bariatric surgery includes PASH (pyoderma gangrenosum, acne, and hidradenitis suppurativa), redundant of the skin, and vasculitis. Removing of subcutaneous fat by liposuction procedure might cause bleeding, infection, and necrotizing the skin (Rosen et al., 2019).

4.6. Bariatric surgery

Bariatric surgery ia a legitimate choice in combating obesity. Bariatric surgery is associated with decrease comorbidities and metabolic diseases related to obesity (Rosen et al., 2019). Bariatric procedures cause malabsorption or restrictive malabsorption of the food, while sleeve gastrectomy limits the malabsorption and gastric capacity. Gastric bypass is the commonest bariatric surgery but is categorized as restrictive malabsorption (Rosen et al., 2019).

Skin manifestations and bariatric surgery
4.6.1. Hidradenitis Suppurativa

Obesity was reported as being associated with hidradenitis suppurativa. Metabolic diseases like insulin resistance and chronic inflammatory diseases associated with obesity were found to be decreased. After bariatric surgery, chronic inflammatory reduction explained the hidradenitis suppurativa improvements. One case reported hidradenitis suppurativa improvement in months of bariatric surgery (Rosen et al., 2019). A retrospective survey for 35 HS patients who received bariatric surgery, and 69% of patients improved (Rosen et al., 2019).

4.6.2. Psoriasis
Overweight or obese patients who achieve substantial weight loss and complain from psoriasis showed improvement of psoriasis and its severity, incidence, and quality of life after bariatric surgery. The majority of patients reported significant improvement of psoriasis after one year of the surgery. In a retrospective survey, 62% of the patients noted improvement (Rosen et al., 2019). The cause of this improvement in psoriasis by decreased tumor necrosis factor (TNF) or leptin hormone decreased. Psoriasis treatment can not be related to the surgery, but more related to weight loss. Studies reported that psoriasis incidence and reduction after restrictive malabsorptive surgery improved greatly than restrictive surgery, and the reason is unknown, but after bypass surgery, it may be explained by an increase in GLP-1 levels. GPL-1 is a gut-derived hormone used for diabetes treatment like liraglutide as it can cause weight loss to obese patients. Psoriasis enhancing might be related to inflammation decrease, the effect of TNF-a inhibited and T-cell proliferation and preservation regulated (Rosen et al., 2019).

4.6.3. Skin Changes in Diabetic Patients

Dermatological conditions associated with metabolic syndromes will change after bariatric surgery. Acanthosis nigricans is common in diabetic patients, and bariatric surgery show improvement of this condition and also improvement of necrobiosis lipodica. These changes are related directly to improve the control of diabetes mellitus (Rosen et al., 2019).

After bariatric surgeries, there are common insufficient nutrients levels, the most frequent nutrient deficiencies are vitamin C, vitamin A, vitamin B12 vitamin B1, folate, vitamin K, vitamin D, iron, copper, selenium, and zinc. These vitamin and nutrients deficiencies might manifest as skin changes, and it's common, because of the difficulties in maintaining the nutritional supplements (Rosen et al., 2019).

After bariatric surgeries, patients report alopecia range (12% to 93%). After six months of surgery, telogen effluvium in association with deficiency of nutrition like iron or zinc is reported. After taking vitamin supplements, there's an improvement in alopecia reported (Rosen et al., 2019).

Bowel associated dermatosis arthritis syndrome is classically found after gastrointestinal surgeries. It is neutrophilic dermatitis associated with arthralgias, fever, myalgia, pustules or papules, and inflammatory macules. This syndrome can be seen after three months to five years after the surgery. Intestinal bypass and nonbypass gastrointestinal surgeries are also associated with dermatosis arthritis syndrome. Pathophysiology of this syndrome still uncertain. One theory describes these changes in the intestine as overgrowth of the intestinal bacteria induces immunity response, bacterial peptidology can induce antigen-antibody complex deposition and formation (Rosen et al., 2019).

Other reported skin conditions after bariatric surgeries include angiosarcoma, Henoch-Scholein purpura, panniculitis, necrotizing vasculitis, and herpetiformis.

5.1. Limitations and strengths of this review

The finding of the studies cannot be confirmed due to lack of similar research. It is recommended for further studies to focus on the prevalence and incidence of skin diseases over a long period of time. Cutaneous diseases should promote screening for diabetes and prediabetes, as early detection may improve the prognosis of diabetes especially obesity patients. Patients with diabetic dermopathy should examined for other microangiopathies including nephropathy and retinopathy.

Unfortunately, It was not possible to compare skin diseases in different adult age groups in this review, as many of the studies did not include this level of data.

There were a number of studies on skin diseases and research on prevalence was limited. Future studies examining obesity or diabetes patients with skin diseases should be reported routinely by age and gender in standardized way to facilitate the results comparison between different studies.

More studies are important to our understanding of skin diseases in obesity patients and also in diabetic patients, and there is a need for future research by using standardized methodology to complete gaps that still exist on the skin disease incidence and prevalence over time.

To the best of our knowledge, this is a systematic review aiming to investigate the skin diseases in diabetic and/or obesity patients. The literature search presents the available evidence and some issues that require further research and investigation.

A general critique, that applies to most of the studies, is sampling bias. Most of the participants were selected from dermatology clinic or endocrinology clinic. Lack of blinding of participants and physicians consider as a major critique, which may entail further bias.

Liraglutide and semaglutide are effective medications for weight loss and patients needs to have a better lifestyle. Limited studies and research found. Some studies showed the effectiveness of those medications on psoriasis and other skin conditions. It is recommended to investigate for other skin diseases after Liraglutide and semaglutide for more than 52 weeks.

CONCLUSION:

The most recent studies demonstrate a strong association between skin diseases and obesity and/or diabetic patients. Cutaneous manifestations require further investigation to its association to obesity and diabetes. However, early detection of skin manifestation consider as important to prevent metabolic diseases especially insulin resistance.

Dermatologists should be aware of the effect of weight loss medications on the skin. Type 2 diabetes, obesity, or overweight patients, on subcutaneous liraglutide 3.0 mg daily, will decrease their weight over 56 weeks of use. There is significant improvement in psoriasis in patients with type 2 diabetes after liraglutide treatment. Other further studies are needed to investigate liraglutide long-term use effectiveness and its safety. Also further investigations to approve its effective on psoriasis treatment and inflammatory factors depression (IL-17, IL-23 , and TNF-a).
Semaglutide provides clinical meaningful, in body weight and HbA1c levels with low risk of hypoglycemia and minimal injection site reaction. As it offers low glucose, further investigations are needed. Also, no specific studies for the effect of liraglutide and semaglutide on cutaneous manifestations, for the best to all patients, physicians must report any skin condition improved.

Obesity continues to rise in the population, the weight loss procedures and therapies become more prevalent. Weight loss procedures as bariatric surgery and liposuction showed its effectiveness, as it's beneficial to the patients overall. Weight loss can improve skin manifestations as hidradenitis suppurativa or psoriasis. The side effects of bariatric surgery might be massive as it can cause nutritional deficiencies, redundant skin, or vasculitis. Liposuction is helpful to improve lymphedema but also can cause skin redundancy, infection, or skin necrosis.

Different weight loss methods can minimize morbidity and improve cutaneous symptoms. For better management of cutaneous effects on obesity and/or diabetes patients in the future, medical participants should report the cases they faced.

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