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Original Research Paper

Dermatology

CUTANEOUS MANIFESTATIONS OF CHRONIC LIVER DIEASE IN PATIENTS ATTENDING DERMATOLOGY OPD IN KARAIKAL

Sivakumar Sivasubramaniam Professor Department of Dermatology venereology & leprosy, Vinayaka Missions Medical College & Hospitals, Karaikal- 609609

Tony Kuncheria* Post Graduate Department of Dermatology venereology & leprosy, Vinayaka Missions Medical College & Hospitals, Karaikal- 609609 *Corresponding Author

ABSTRACT

Background: The present study was conducted to assess the spectrum of cutaneous changes in chronic liver diseases and to assess any correlation between the skin findings and the type of the liver disease.

Methods: A total of 100 patients above 18 years of age suffering from chronic liver disease with cutaneous manifestations and attending the Dermatology and Venereology department of Vinayaka Missions Medical College and Hospital, Karaikal, Puducherry, India during the period from June 2019 to May 2020 were included in the study.

Results: Out of 100 cases, there were 84 males (84%) and 16 females (16%) with the male to female ratio of 5.25:1. Alcoholic liver disease comprised 62% of the patients in the study, other causes being cryptogenic liver disease (14%), chronic hepatitis infection (12%), Wilson's disease (2%), autoimmune hepatitis (2%), hepatocellular carcinoma (2%), methotrexate induced liver disease (1%) and non-alcoholic steatohepatitis (1%). The most commonest skin finding associated with liver diseases was xerosis (62%). Other skin findings included nail changes (60%), pigmentary changes (55%), hair changes (50%), jaundice (40%), cutaneous infections (31%) and pruritus (27%).

Conclusions: Patients with chronic liver disease can have a wide spectrum of cutaneous manifestations the most important being xerosis, nail changes, pigmentary changes, hair changes, jaundice, infections, pruritus and spider angioma. These changes can give a clue to the presence of the underlying liver disease and its severity. Hence, identifying these signs earlier can lead to prompt diagnosis and effective management of the underlying condition, thereby preventing its complications.

KEYWORDS : Skin manifestations, Chronic liver disease

INTRODUCTION

Chronic liver diseases are one of the leading causes of major health problems worldwide and present as one of the most important cause of morbidity and mortality in India. An association between the skin and the liver disease has been recognized since ancient times. The term *spider* originated in the New York underworld, where barmaids noted "spiders" as evidence of advanced liver disease in their customers[1]. Chronic liver diseases can give rise to numerous extrahepatic disorders among which dermatological lesions occupy a central place and at times point to the etiology of the disease[2]. Often skin manifestations can be the first sign of liver disease[3]. Jaundice, pigmentation, spider telangiectasias, striae distensae, leukonychia, palmar erythema, xerosis and loss of pubic and axillary hair are recognized sequelae of chronic liver diseases[4-6].There are certain dermatoses frequently associated with hepatobiliary disorders which includes lichen planus, urticaria, porphyria cutanea tarda, Vitiligo, malakoplakia, behcet's disease, erythema multiforme and nodosum[7,8].

Other manifestations which are seen with hepatitis B virus and hepatitis C virus infection include rashes, papular acrodermatitis, thrombocytopenic purpura, lichen planus, mooren's ulcer, porphyria cutanea tarda, necrotising cutaneous vasculitis. Liver diseases can also result in various forms of secondary dyslipoproteinemias like hypertrigl yceridemia and low levels of high-density lipoproteins, which manifest in the form of xanthelasmas in the skin, presenting as soft, yellowish asymptomatic plaques especially over the eyelids[9].

Patients with chronic liver disease may develop thinning of hair and hair loss. Nail changes in cirrhosis includes clubbing, thickening of nails, longitudinal ridging, white bands (Muehrke's bands), and brittle nails[10,11]. Those with advanced cirrhosis can present with Terry's nails characterized by a ground glass opacity of nail plate which turns powdery white at its proximal end[12].Bluish discoloration of lunulae may be found in patients with Wilson's disease known as *Azure lunulae*. Splinter hemorrhages and hypertrophic osteopathy also occur in cirrhosis[13].A number of patients with chronic liver disease have nutritional deficiencies predominantly of vitamin B-complex and folic acid. Deficiency of these vitamins leads to changes in skin, nails, hair, and mucosa. Deficiency of iron and zinc also commonly present in patients with chronic liver disease and may lead to certain skin changes.

Early detection by recognizing skin manifestations may help to initiate early treatment and reduce serious complications, sequelae, morbidity and mortality of chronic liver diseases.

Aim Of The Study:

The present study is aimed to study the cutaneous manifestations and particular pattern linked to etiology of liver disease.

MATERIALS AND METHODS:

Study type: Hospital based cross-sectional study
Study design: Open label, descriptive clinical study.
Study period: June 2019 to May 2020
Study sample: 100 patients suffering from chronic liver disease with cutaneous manifestations
Study place: Department of Dermatology and Venereology at the Vinayaka Missions Hospital, karaikal, Puducherry

Inclusion criteria

- Patients suffering from chronic liver disease with cutaneous manifestations who didn't have established skin disease prior to the onset of chronic liver disease
- Participants who were more than 18 years old, and who had written informed consent

Exclusion criteria

- Participants, who were less than 18 years old
- Patients who had established skin diagnosis prior to onset of chronic liver disease

- Those who had refused to sign an informed consent

Methodology

Detailed history taking and complete clinical examination was done and the clinical data was recorded as per the proforma. Routine and relevant investigations were recorded for all patients. Dermatological investigations including nail clippings and skin scrapings with 10% potassium hydroxide mount, skin biopsy for histopathology, pus for culture and sensitivity whenever required were done.

Statistical Analysis

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 17. Significance was tested using chi-square test; a p value of less than 0.05 was considered to be significant. Anova test and independent t-test were also done wherever required.

RESULTS

Out of 100 cases, there were 84 males (84%) and 16 females (16%) with the male to female ratio of 5.25:1. In this study, most of the patients had more than one cutaneous manifestation.

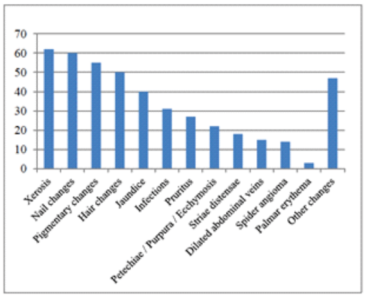

Figure 1: Cutaneous features in chronic liver disease.

Xerosis was the commonest skin manifestation seen in 62% of the patients. 66.7% of the patients with chronic viral hepatitis and 64.5% of patients with alcoholic liver disease had xerosis. However, the association was not statistically significant ($p>0.05$). Pigmentary changes were seen in 55% cases which manifested in two forms, as guttate hypopigmentation (40% cases) and hyperpigmentation (24% cases). Out of which, 9 patients had both guttate hypopigmentation and hyperpigmentation. Other important changes seen were jaundice (40%), skin infections (31%), pruritus (27%), ecchymosis (22%), striae distensae (18%), dilated veins over the abdomen (15%), spider angiomas (14%) and palmar erythema (3%) . Thinning of hairs seen in 50% cases, followed by loss of axillary and pubic hair in 12% cases. .

Other less common cutaneous manifestations include eczema in 10%, urticaria in 9%, ichthyosis in 5%, fissuring of the soles and excoriations over extremities in 4%, atrophic glossitis in 3%, angular cheilitis in 2% patients. Fissured tongue, gynaecomastia, Dupuytren's contracture, vitiligo, pellagra, follicular hyperkeratosis and oral lichen planus were seen in one patient each. Dermatitis artefacta was seen in 3 patients. These patients had superficial burns due to skin branding which was used for treatment of jaundice.

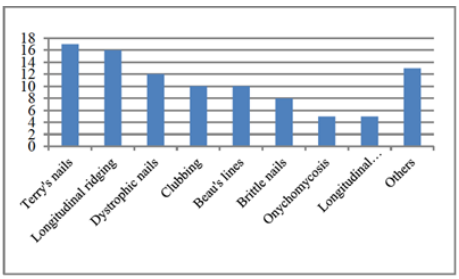

Figure 2: Nail changes in chronic liver disease patients.

Nail changes were seen in 60% of the patients. The most common change was Terry's nails seen in 17% of the patients, followed by longitudinal ridging which was seen in 16% of the patients. Other major findings included dystrophic nails (12%), Beau's lines (10%) , clubbing (10%), brittle nails (8%), onychomycosis (5%) and longitudinal melanonychia (5%).Leuconychia was seen in 6% of the patients and onycholysis was seen in 3% of the patients. 3% of the patients had subungual hyperkeratosis. Muehrcke's lines was seen in one patient.

Table 1 : Petechia/Purpura/ecchymosis and INR

Petechiae/Purpura/ Ecchymossis	No of Patients	INR(Mean)	Std deviation
Present	22	1.54	0.284
Absent	78	1.22	0.188

There was a positive correlation between increased international normalized ratio (INR) values and presence of petechiae/purpura/ecchymosis ($p<0.05$). The mean INR in patients who had petechiae/purpura/ecchymosis was 1.54 as compared to 1.22 in patients without the findings .

Table 2 : Petechiae/Purpura/ecchymosis and MELD score.

Petechiae/Purpura/ Ecchymossis	No of Patients	Mean MELD Score	Std deviation
Present	22	15.23	5.299
Absent	78	12.76	5.046

The mean model end stage liver disease score in patients with purpura and ecchymosis was 15.23 as compared to 12.76 in those without the finding. The P value was statistically significant (<0.05). 50% of the patients had hair changes. .It was also found that patients with petechiae/purpura/ ecchymosis had more severe liver disease compared to patients who didn't have the lesions.

Table 3 : Cutaneous infections in patients with chronic liver disease.

Cutaneous infections		Alcoholic liver disease (n=62)	Cryptogenic (n=14)	Hep B/C (n=12)	ALD+ Hep B (n=4)	Others (n=8)	Total (n=100)
No infections	No. of patients	40	10	9	2	8	69
	%	64.5%	71.4%	75.0%	50.0%	100%	69%
Oral candidiasis	No. of patients	12	4	1	1	0	18
	%	19.3%	28.6%	8.3%	25.0%	0.0%	18%
Cellulitis	No. of patients	5	0	2	0	0	7
	%	8.1%	0.0%	16.7%	0.0%	0.0%	7%
Folliculitis	No. of patients	2	0	0	0	0	2
	%	3.2%	0.0%	0.0%	0.0%	0.0%	2%
Tinea corporis	No. of patients	6	0	0	1	0	7
	%	9.7%	0.0%	0.0%	25.0%	0.0%	7%
P. versicolor	No. of patients	1	0	0	1	0	2
	%	1.6%	0.0%	0.0%	25%	0.0%	2%

Oral candidiasis was the commonest infection seen in 18% of the patients. Cellulitis and tinea corporis was seen in 7% of the patients, out of which 2 patients had both cellulitis and tinea corporis. Pityriasis versicolor and folliculitis was seen in 2 patients each .

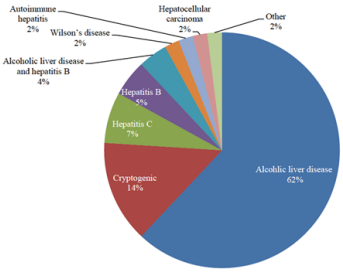

Figure 3 : Causes of chronic liver disease

The most common cause of chronic liver disease was alcoholic liver disease. Alcoholic liver disease comprised 62% of the patients in the study, other causes being cryptogenic liver

disease (14%), chronic hepatitis infection (12%), Wilson's disease (2%), autoimmune hepatitis (2%), hepatocellular carcinoma (2%) methotrexate induced liver disease(1%) and non-alcoholic steatohepatitis (1%). 4% of the patients had both hepatitis B and alcohol induced liver disease .

Figure 5:Guttate hypopigmentation

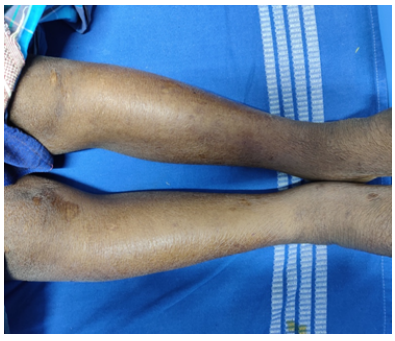

Figure 4: Xerosis

Figure 6:Scleral Icterus

Figure 7:Striae distensae

DISCUSSION

The age of the patients included in the study varied from 19 years to 71 years. The average age of the patients was 45.72 years. There was a male preponderance in our study. Males constituted 84% and females 16%, with the male to female ratio of 5.25:1. A similar study by Niaz et al (2010) also showed that out of 164 cases, 53.7% were males and 46.3% females[14].Study done by Gavli et al also showed a male preponderance with 66% males and 34% females[15].The most common cause of chronic liver disease in our study was alcoholic liver disease (62%) followed by cryptogenic liver disease (14%). Sayal et al and Yoon et al also showed alcohol to be the commonest cause for liver cirrhosis[16,17].

Among the various types of skin manifestations, xerosis was the most common finding seen in our study (62%). It was present in all types of liver diseases, and was most commonly found in patients with chronic viral hepatitis (66.7%) followed by alcoholic liver disease (64.5%). However the association was not found to be statistically significant ($p>0.05$). In the study done by Khan et al and Gavli et al also xerosis was the commonest cutaneous finding (72% and 78% respectively)[15,18]. Pigmentary changes were seen in 55% cases which manifested in two forms, as hyperpigmentation (40% cases) and guttate hypopigmentation (24% cases). Hyperpigmentation was seen in two patterns, one as diffuse pigmentation more prominent on sun exposed areas and extremities. Other as pigmented spots over the skin of abdomen, back and bilaterally over extremities, more over hands and foot and rarely over face. Guttate hypopigmentation was seen more commonly over abdomen, back and lower limbs. However, Khan et al showed pigmentation as the commonest finding observed[18].

Jaundice was seen in 40% of cases in our study. It was seen in 100% cases who had both alcoholic liver disease and hepatitis B infection. 46.8% of the patients with only alcoholic liver disease had jaundice, followed by cryptogenic liver disease (28.6%) and chronic viral hepatitis (25%). This difference in presence of jaundice in various liver diseases was found to be statistically significant (p value <0.05). A similar study done by Sayal et al, showed jaundice in 26% cases[16].The study by Niaz et al showed jaundice in 35.4% cases[14].

Pruritus was seen in 27% of the patients in this study. Sayal et al showed pruritus in 10.8% patients[16]. In another study, Gavli et al noted pruritus in 45% of the patients[15]. Pruritus was seen more in patients who had alcoholic liver disease with hepatitis B infection (50% cases), followed by cryptogenic liver disease (35.7% cases). Even though the severity of the liver disease was more in patients with higher grades of pruritus, the values obtained were not statistically significant. There was a significant association of higher grades of pruritus with higher total bilirubin levels. Petechiae, purpura and echymosis were seen in 22% of the patients. The findings were comparable to the study done by Gavli et al which had 19% patients with the manifestation[15]. In our study there was a significant association between increased INR value and presence of petechiae, purpura and ecchymosis ($p<0.05$). It was also noted that patients who had petechiae, purpura andecchymosis had more severe liver disease, based on MELD score ($p<0.05$).

In our study, spider angioma was seen in 14% of the cases. 14.5% of the alcoholic liver disease patients and 13.2% of the patients with non-alcoholic liver disease had spider angioma. However, the increased frequency of spider angioma in alcoholic liver disease was not statistically significant. In studies done by Khan et al and Niaz et al, spider angioma were seen in 36% and 31.1% of the patients respectively.14,18 Gavli et al observed spider angiomas in only 3% cases[15].

Palmar erythema was seen in only 3% of the patients in our

study. Study done by Sayal et al in Pune had 4.3% patients with palmar erythema[16].Khan et al had 36% of the patients with palmar erythema and spider angioma in his study[18].No cases of palmar erythema were seen in the study conducted by Gavli et al[15].Infections were seen in 31% of the patients with commonest being oral candidiasis, seen in 18% of the total patients. Study done by Kowalczyk et al showed oral candidiasis in 28.6% of the cirrhotic patients[20]. Cellulitis was seen in 7% of the patients in our study. In a study done by Rongey et al, cellulitis was seen in 19.3% of the patients[21]. In our study, dermatophyte infection was observed in 7% of the cases. Pityriasis versicolor and folliculitis were seen in 2% cases each. Rao et al noted dermatophyte infection in 4.5% of the alcoholic patients[22]. Pityriasis versicolor was observed in 14% of the patients by Rao et al, while Gavli et al noted the same in 29% of the patients[15,22].

Nail changes were seen in 60% of patients in our study. Salem et al and Gavli et al in their studies showed nail changes in 68% and 72% of patients respectively[15,19] .The most common finding in our study was Terry's nails, seen in 17% cases, followed by longitudinal ridging which was seen in 16% of the patients. Other major findings included dystrophic nails (12%), Beau's lines (10%), clubbing (10%), brittle nails (8%), onycho-mycosis (5%) and longitudinal melanonychia (5%). Leuconychia was seen in 6% of the patients. Onycholysis and subungual hyperkeratosis were seen in 3% of the patients. Muehrcke's lines were seen in only one patient.Sayal et al found clubbing in 19.5% and leukonychia in 4.3% cases[16]. In a study done by Salem et al, 18% of the patients had onychomycosis, 10% of the patients had brittle nails, 7% cases had clubbing and 6% had dystrophic nails[19].Gavli et al found Terry's nails in 75% cases followed by onychomycosis in 50% cases[15]. Muehrcke's nails were not reported in the studies done by Salem et al, Niaz et al and Gavli et al[14].

50% of the patients in our study had hair changes and some had more than one change. The most common finding was thinning of hairs (50%), followed by loss of axillary and pubic hair in 12% cases. Gavli et al foundthinning of hair in 75% cases, loss of axillary hairs in 58% and loss of pubic hairs in 52% cases[15].According to a study done by Khan et al non-scarring hair loss from axilla and pubic region was present in 64% cases[18].Eczema was seen in 10% of the patients in our study. This finding is comparable to the study done by Gavli et al in which 7% of the patients had eczema[15]. 18% of the patients in our study had abdominal striae while 15% cases had dilated abdominal veins. The study done by Niaz et al noted dilated veins in 6% of the patients[14]. However, Gavli et al reported 36 out of 100 patients with dilated abdominal veins and straiedistensae. 9% of the patients had urticaria in our study. Gavli et al found urticaria in 18% of cases[15]. 5% cases had ichthyosis in our study. Sayal et al found ichthyosis in 15.2% cases[16].In our study fissuring of the soles and excoriations over extremities were noted in 4% of the patients. 3% of the patients had atrophic glossitis, 2% had angular chelitis and 1 patient had fissured tongue. In the study by Gavli et al oral cavity lesions were seen in 46% cases as cheilitis, stomatitis and bald tongue[15]. Oral lichen planus was seen in one patient in our study. Khan et al noted lichen planus in 4% of the patients[18]. However, Gavli et al and Niaz et al didn't observe lichen planus in any of their patients[14,15].Only one patient in our study had gynaecomastia. The patient had alcoholic liver disease. This was low compared to study done by Niaz et al where the incidence was 13.6%[14]. Dupuytren's contracture, vitiligo and pellagra were seen in one patient each. In the study by Gavli et al, vitiligo and Dupuytren's contracture were seen in 3% cases each.Follicular hyperkeratosis was seen in 1 of the patients.

CONCLUSION

Our study was a humble effort to identify the spectrum of cutaneous manifestations in patients with chronic liver diseases. However, larger studies are necessary to establish the precision of our observations that correlate the cutaneous manifestations with chronic liver disease and to identify the patients where skin manifestations could be the first sign of liver disease. Identifying these signs earlier can lead to prompt diagnosis and effective management of the underlying condition, thereby preventing its complications.

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