

A CLINICAL STUDY OF CUTANEOUS MANIFESTATIONS IN LIVER DISEASES

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HOW TO CITE THIS ARTICLE:

Jai Gavli, Anand Kumar Dubey, Anna Alex, RK Jain. "A clinical study of cutaneous manifestations in liver diseases". Journal of Evolution of Medical and Dental Sciences 2013; Vol2, Issue 39, September 30; Page: 7523-7529.

ABSTRACT: BACKGROUND: Liver dysfunction is associated with protean manifestations in skin, nails and hairs. **OBJECTIVE:** To study cutaneous manifestations in liver diseases. **METHODS & MATERIALS:** The patients of liver disease of any etiology and either sex, from January 2010 to December 2010, presenting in the Department of Medicine, Department of Gastroenterology, Department of Dermatology and Venereal Diseases, Gandhi Medical College and associated Hamidia Hospital Bhopal, were enrolled in study. A comprehensive proforma was completed for every case which included careful history, cutaneous and systemic examination. **RESULTS:** Out of 100 patients, 66 were male and 34 were female. The most common cause of liver disease was hepatitis B virus infection (32% cases) followed by alcoholic liver disease (26% cases). Hepatitis C related liver disease (14 % cases), cholestatic disease (8% cases), and hepatocellular carcinoma (6% cases). Wilson's disease (4% cases), 2% cases of autoimmune etiology and in 8% cases the etiology could not be identified. The most common skin manifestation observed was xerosis(78% cases) followed by pigmentary changes (70% cases) with guttate hypopigmentation being more common (48% cases) while hyperpigmentation (40% cases), oral lesions (46% cases), yellowish discoloration of skin and eyes (40% cases), pruritis (45% cases), striae distensae (36% cases), Taenia infection (29% cases), Petechiae, ecchymosis and bruise (19% cases), urticaria (18% cases), Xanthelasma (8% cases), dermatitis(7% cases) and vitiligo, dupuytren's contracture and spider naevi (3% each). **CONCLUSION:** We conclude that there is a strong correlation between skin and liver disease and further studies could be undertaken to identify the patients where skin manifestations could be the first sign of liver disease

INTRODUCTION: Chronic Liver Diseases are a leading cause of major health problems in developing countries and present as one of the most important cause of morbidity and mortality in India. Liver is the one of the most vital and second largest organ of the body, any dysfunction in the liver leads to pathological changes in the largest organ of the body- the skin. There is a association between liver disease and skin which can be as - Hepatobiliary disease causing skin manifestation in many ways^{1,9}, Liver diseases may cause skin changes, Liver and skin may be involved by the same pathological process, Skin disease may cause liver abnormalities, Liver may get damaged by drugs used to treat skin diseases.

Often skin manifestations can be the first sign of liver disease¹. Chronic Liver Disease can give rise to numerous extrahepatic disorders among which skin disease occupy a central place Jaundice, xerosis, pruritis, pigmentary changes, loss of pubic and axillary hairs, leuconychia, spider naevi, telangiectasias, striae distensae with dilated veins on abdomen, palmar erythema all are recognized sequelae of liver disease^{12, 14}.

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There are certain dermatoses frequently associated with hepatobiliary disorders including lichen planus, urticaria, porphyria cutanea tarda, Vitiligo, malakoplakia, behcet's disease, erythema multiforme and nodosum. 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. The pathogenesis although not clear but autoimmune phenomenon has been incriminated in these diseases.

Early detection by recognizing skin manifestation may help to initiate early treatment and reduce serious complications, sequelae, morbidity and mortality.

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

MATERIALS AND METHODS: The present study was a cross section based observational study which included 100 patients of liver disease from January 2010 to December 2010, presenting in the Department of Medicine, Department of Gastroenterology, Department of Dermatology and Venereal Diseases, Gandhi Medical College and associated Hamidia Hospital Bhopal, were enrolled in study.

A comprehensive proforma was completed for every case which included careful history, cutaneous and systemic examination. During history taking emphasis was on presenting complaints age of onset, progress and duration of disease and treatment taken – drugs and any medical procedure done. Personal particulars like intake of alcohol, tattoo marks, history of blood transfusion, needle pricks and physical relations and number of partners.

Cutaneous examination including inspection of oral cavity, examination of hairs and nails, genitals, mucosa and skin. All the patients underwent complete investigations including Haematological and biochemical test, ultrasonography, viral markers and antibody profile. In most patients etiology was known and patients had prior admissions in past.

RESULTS: Out of 100 patients, 66 were male and 34 were females. Patients between age of 20-70 years. Among the etiology the study showed that most common cause was hepatitis B related liver disease (32% cases) followed by alcoholic liver disease (26% cases) as second most common cause. Hepatitis C related liver disease was seen in 14 % cases, cholestatic liver disease was seen in 8% cases, hepatocellular carcinoma was seen in 6% cases. Wilson's disease in 4% cases, 2% cases of autoimmune etiology and in 8% cases the etiology could not be identified.

The most common skin manifestation observed in our study was xerosis, which was seen in 78% cases. The second common manifestation observed was pigmentary changes seen in 70% cases, in which guttate hypopigmentation was more common seen in 48% cases while hyperpigmentation was seen in 40% cases.

Other changes seen were oral lesions seen in 46% cases, yellowish discoloration of skin seen in 40% cases, pruritis seen in 45% cases, striae distensae seen in 36% cases, Taenia infection was seen in 29% cases, Petechiae, ecchymosis and bruising were seen in 19% cases, urticaria was seen in 18% cases, Xanthelasma was seen in 8% cases, dermatitis was seen in 7% cases and vitiligo, dupuytren's contracture and spider naevi were seen in 3% cases each.

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S. No.	Etiology of liver disease	Number of Cases	Percentage of Cases
1	HBV Related Liver Disease	32	32%
2	Alcoholic Liver Disease	26	26%
3.	HCV Related Liver disease	14	14%
4.	Hepatocellular Carcinoma	6	6%
5.	Cholestatic Liver disease	8	8%
6.	Wilson's Disease	4	4%
7.	Unknown Etiology	8	8%
8.	Autoimmune Liver Disease	2	2%

TABLE 1: ETIOLOGY AND TYPE OF DISORDER / DISEASE (N=100)

S. No.	Manifestations	No. of Cases	Percentage
1	Xerosis	78	78%
2.	Pigmentary changes:	70	70%
	- Guttate Hypopigmentation	48	48%
	- Hyperpigmentation	40	40%
3.	Oral cavity lesions	46	46%
4.	Pruritis	45	45%
5.	Yellowish discoloration of skin	40	40%
6.	Distensae Striae with Dilated Abdominal veins.	36	36%
7.	Taenia Versicolor	29	29%
8.	Petechiae, Ecchymosis, Bruise	19	19%
9.	Urticaria	18	18%
10.	Xanthelasma	8	08%
11.	Dermatitis	07	07%
12.	Spider Naevi	03	03%
13.	Dupuytren's Contracture	03	03%
14.	Ichthyosis	03	03%
15.	Vitiligo	03	03%

TABLE 2: TYPES OF SKIN MANIFESTATIONS (N=100)

“Majority of patients had more than one manifestation”

DISCUSSION: In this study, out of 100 patients, 66 were male and 34 were females. The male to female ratio was 1.8:1, showing male preponderance. A similar study by Niaz A et al 2010 showed out of 164 cases 53.7% were males and 46.3% females. The greater ratio of male patients was attributed to greater access of males to health services and alcoholic liver disease which is found in males one of the common type of liver disease in males. Among the etiology the study showed that most common cause was hepatitis B related liver disease (32% cases) followed by alcoholic liver disease with 26 % patients as second most common cause. In a similar study done by Atul M et al 2003, showed that hepatitis C was more common than hepatitis B. In other study done by Niaz A

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Shaikh et al 2010, Hepatitis C related liver disease was seen in 52.4% cases and hepatitis B related liver disease in 40.9% cases.

The higher incidence of hepatitis B related liver disease was attributed to- increased availability of serological test, screening for viral markers in hepatic involvement and in transfusion of blood and its related products and for both minor and major surgical procedures. This was an important reason for incidental diagnosis of viral hepatitis (hepatitis B and hepatitis C), which were previously left undiagnosed in general population. Hepatitis C related liver disease was seen in 14 % cases, cholestatic liver disease was seen in 8% cases, hepatocellular carcinoma was seen in 6% cases. Wilson's disease in 4% cases, 2% cases of autoimmune etiology and in 8% cases the etiology could not be identified.

Among the various types of skin manifestations, study revealed xerosis as the most common skin lesion (n=78% cases). Xerosis was a protean manifestation of liver dysfunction due to prolonged and decompensated nature of disease and complemented by malnutrition and catabolic state. It was present in all types of liver diseases, among these commonest with cholestatic disease (100% cases) followed by hepatitis B infection (87.5% cases). Other causes were Wilson's disease (75% cases), Hepatocellular carcinoma (75% cases), 71.43% cases of hepatitis C infection, 50% cases of alcoholic liver disease and chronic liver disease of unknown etiology each. The findings are similar with study done by Miraj² et al 2005 where Xerosis was seen in 72% cases.

Pigmentary changes were seen in 70% cases which manifested in two forms, as hyperpigmentation (40% cases) and Guttate hypopigmentation (48% 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. It was attributed to hormonal imbalance between MSH, ACTH and effects of estrogen. Hyperpigmentation was seen in 100% cases of Wilson's disease and liver disease with unknown etiology, hepatocellular carcinoma (75% cases), hepatitis C infection (42.86% cases), hepatitis B infection (25% cases) and in 25% cases of alcoholic liver disease. It was not seen in autoimmune and cholestatic liver disease.

Guttate hypopigmentation was seen in all cases of hepatocellular carcinoma and autoimmune liver disease (100%), and 75% cases of unknown etiology. 50% patients of alcoholic liver disease and hepatitis B infection had guttate hypopigmentation with absence of the same in Wilson's and cholestatic disease. Miraj et al 2005 showed pigmentation as commonest finding observed. Oral cavity lesions were seen in 46% cases as cheilitis, stomatitis and bald tongue attributed to malnutrition, catabolic state and low socioeconomic status. It was most common in alcoholic patients both with alcoholic liver (76.9%) or other forms of liver disease.

Pruritis was seen in 45% cases. It was multifactorial⁸ and impaired liver function leads to accumulation of toxins and bile salts in body and deposition in skin, causes irritation and itching. Pruritis was observed in all cases of Cholestatic disease (100%) followed by hepatitis B infection (50% cases). Other causes were alcoholic disease (42.3%), hepatitis C infection (37.5%) hepatocellular carcinoma (33.33% cases) and 25% cases of unknown etiology and Wilson's disease each. Atul M Kochhar¹¹ et al 2003 showed pruritis in 92% % cases as commonest symptom. Sarkany I⁹ et al 1988 showed 40% patients of alcoholic liver disease had generalized pruritis. Sayal and

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Gupta et al³ 1997 showed pruritis in 10.8% patients. In another study Sayal et al⁴ 1997 showed pruritis in 8.2% patients.

Yellowish discoloration of skin and eyes (icterus) was seen in 33% of cases. It was due to accumulation of bilirubin under the skin and becomes clinically apparent when level more than 2.5 mg% (manifestation of jaundice)⁴². It was seen in 100% cases with cholestatic and autoimmune disease. A similar study done by Sayal and Gupta et al³ 1997, showed icterus in 26% cases. Another study done by Sayal et al⁴ 1997 observed icterus in 20% patients. The study of Niaz A et al¹⁰ 2010 showed jaundice in 35.4% cases.

Striae distensae with dilated abdominal veins was seen in 36% cases. It was seen in decompensated liver disease with ascites and was due to hormonal imbalance and increased level of estrogen. In a similar study done by Sayal et al⁴ 1997 prominent dilated veins on abdomen as the most common cutaneous manifestation was seen in 28.6 % patients. Another study done by Sayal and Gupta et al³ 1997, showed Striae distensae in 2.2% and prominent dilated veins on abdomen in 30.4% cases.

Taenia Versicolor was seen in 29% cases, more commonly with patients with decompensation. It is associated with low socioeconomic status and poor personal hygiene. In a similar study by Gatha S Rao⁶ 2004 Tinea Versicolor was observed in 14% cases.

Petechiae, ecchymosis, bruise and purpuras were seen in 19 % cases, as a result of liver dysfunction leading to a state of deficient clotting factors and hypersplenism and thrombocytopenia¹. A similar study done by Sayal and Gupta et al³ 1997, showed purpuras in 2.2% cases. Urticaria was seen in 18% of cases, more common in alcoholic liver disease. It was attributed to alcohol induced allergic response. A study done by Atul M Kochhar et al 2003¹¹ showed chronic urticaria in 60% cases.

Xanthelasma was seen in 8% cases. It was a common manifestation of hypercholesterolemia, which was common feature of compromised liver, as in primary biliary cirrhosis and other forms of cholestatic diseases. Liver disease can lead to various forms of dyslipoproteinemia. Studies suggest that total plasma cholesterol level was elevated in as many as 50% of patients with compromised liver function (derangement in lipid metabolism). Dermatitis was seen in 7% cases.

Spider naevi were seen in only 3% cases. These vascular lesions occur with elevated estrogen level, as in cirrhosis, estrogen therapy, severe malnutrition or during pregnancy. In a similar study by Gatha S Rao⁶ 2004 showed spider naevi in 2.5% patients. A similar study done by Sayal, Gupta et al³ 1997 showed spiders in 4.3% cases. The study of Niaz A et al¹⁰ 2010 revealed spiders in 31.1% cases. The study done by Miraj² et al 2005, showed spider naevi and palmar erythema in 36% cases. Ichthyosis was seen in 3% cases. It was associated with xerosis and pruritis.

Vitiligo and Dupuytren's contracture were seen only in 3% cases each. It was due to fibrosis and thickening of palmar fascia. It appears to be associated with excess alcohol consumption.

Nail changes were seen in 72% of patients. Salem et al¹³ 2010 in his study showed that nail changes were present in 68% of patients. The most common being Terry's nail seen in 75 % cases. It was attributed to liver cirrhosis. Findings were consistent with the study done by Miraj et al², having Terry's nail in 80% cases. Sarkany I⁹ 1988 showed similar results with Terry's nail was observed in 80% cases with cirrhosis. Onychomycosis was seen in 50% cases as second common manifestation. Salem et al¹³ in his study showed that among nail changes: onychomycosis was the most common finding seen in 18% cases followed by in descending order, longitudinal striations, brittle nails,

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clubbing of nails, dystrophic nails, leukonychia and longitudinal melanonychia. Leukonychia, brittle nails and clubbing was seen in 12.5% of cases of each. It was seen in hypoalbuminemic states like chronic liver disease. The study done by S K Sayal et al⁴1997; who had less nail findings, clubbing in 16.3% and leukonychia in 4.1% cases. Another study done by Gupta and Sayal et al³ showed clubbing in 19.5% and leukonychia in 4.3% cases. Shiny nails were seen in 37.5% of patients. These were attributed to persistent itching as in cholestatic disease and primary biliary cirrhosis. Horizontal and vertical striae were seen in 8.33% and 5.5% cases respectively. Nail and hair changes were seen in 80.76% of cases as the most common finding in alcoholic liver disease.

All patients had hair changes and some had more than one change. The most common change was thinning of hairs seen in 75% cases and followed by premature graying in 60% cases, loss of axillary hairs in 58% and pubic hairs in 52% cases. Alopecia was seen in 56% cases. Palmoplantar Hyperhidrosis was seen in 50% of cases of alcoholic liver disease. It was attributed to lesion in central sweat control mechanism; G S Rao et al⁶. There was a case of pachyonychia congenita with decompensated liver disease where despite of extensive investigations the etiology of liver disease cannot be identified. There were no patients of drug induced skin changes. In majority of cases the diagnosis of liver disease had been established and they presented late with complications like decompensation and hepatic encephalopathy.

CONCLUSION: We conclude that there is a strong correlation between skin and liver disease and further studies could be undertaken to identify the patients where skin manifestations could be the first sign of liver disease.

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Date of Submission: 16/09/2013.
Date of Peer Review: 17/09/2013.
Date of Acceptance: 23/09/2013.
Date of Publishing: 26/09/2013.