

Cutaneous manifestations in patients with chronic kidney disease of unknown aetiology treated at the General Hospital, Polonnaruwa

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Abstract

Chronic kidney disease of unknown aetiology (CKD-U) is a significant medical problem affecting the residents of the North Central Province. Cutaneous manifestations are seen in 50-100% of patients with chronic kidney disease.

We have conducted a study to describe the prevalence of cutaneous manifestations in patients with chronic kidney disease of unknown aetiology presenting to the General Hospital, Polonnaruwa.

63 consecutive patients with a diagnosis of chronic kidney disease (based on biochemical and/ or radiological evidence) without any underlying aetiology were enrolled in the study. All patients were examined for the presence of cutaneous manifestations attributable to kidney disease. An interviewer administered questionnaire was used.

The average age of the study population was 60.16 years with a male preponderance (78%). The average duration of CKD-U was 3.92 years. The majority (77%) comprised of farmers and the average duration of residence within the district was 43.42 years. Well water was the major source of water and 85.71% gave a history of use of pesticides in farming.

All participants except one (98.38%) had at least one skin manifestation. The commonest manifestations were xerosis (64.51%), pruritus (35.48%), hyperpigmentation (27.41%), glossitis (25.81%) and palmar pigmentation (22.58%). There were no specific cutaneous manifestations attributable to arsenic or other heavy metal poisoning but callosities of the palms and soles were seen in 29.03% of the participants.

Cutaneous manifestations commonly occur in patients with CKD-U and need to be addressed in their management.

Introduction

Chronic kidney disease of unknown aetiology (CKD-U) is a significant medical problem affecting the residents of the North Central Province¹. Residents of some areas like Medirigiriya in the Polonnaruwa district and Medawachchiya and Padaviya in the

Anuradhapura district are particularly prone to the kidney dysfunction.

Cutaneous manifestations are commonly seen in patients with chronic kidney disease. Studies have shown that 50-100% of patients with CKD have at least one cutaneous manifestation². Some features are specific to chronic kidney disease while some manifestations are non specific. Xerosis, pigmentary changes and pruritus are the commonly seen non-specific manifestations in the skin. Changes in the hair, nails and the mucosae have also been reported in CKD.

Significance of the research

Chronic kidney disease of unknown aetiology affects a significant proportion of the residents of the Polonnaruwa district. Approximately 800 patients are being followed up in the Renal Clinics at the General Hospital, Polonnaruwa. Even though some patients with symptomatic cutaneous manifestations are referred to the Skin Clinic, the prevalence of skin manifestations in CKD in the Polonnaruwa district has not been studied.

An estimation of the prevalence of cutaneous manifestations will help the clinicians in tailoring the management plan to address these problems as well. In case of a high incidence of problems like xerosis emollients may be included in the routine management plan of the renal clinic instead of referring the patients to the Skin Clinic, which is inconvenient to the patient.

There are several hypotheses regarding the causative factors of CKD-U. None of these hypotheses have been universally accepted by the scientific community. The presence of high amounts of arsenic in the drinking water and/ or contamination of rice

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due to pesticides containing arsenic and other heavy metals has been recently proposed as a cause for CKD affecting the North Central Province. Chronic arsenic poisoning is an entity with a multitude of cutaneous manifestations. Cutaneous features may be the first indication of chronic arsenic poisoning. With the current interest in arsenic as a cause for CKD-U it is of utmost importance that patients with CKD be examined for features of chronic arsenic exposure.

Objectives

Primary objective

To describe the prevalence of cutaneous manifestations in patients with chronic kidney disease of unknown aetiology.

Secondary objectives

To determine the common cutaneous manifestations in the study population. To determine whether cutaneous manifestations attributable to chronic arsenic poisoning are present in patients with chronic kidney disease.

Methodology

A descriptive study was carried out at the Renal and Dermatology Clinics at the General Hospital, Polonnaruwa.

63 consecutive patients with a diagnosis of chronic kidney disease (based on biochemical and/or radiological evidence) fulfilling the following criteria were enrolled in the study.

- Over 30 years of age.
- Residing within the North Central Province for more than 10 years.

Patients with a secondary cause for the renal disease like diabetes mellitus, polycystic kidney disease, connective tissue disorders or renal calculi and those who did not consent were excluded.

As the participants were not subjected to any invasive procedures or investigations, informed verbal consent was obtained from the participants before the questionnaire was completed.

An interviewer administered questionnaire, with details on demographic characteristics and clinical features was completed for each patient. All the patients were initially examined by one of the medical

officers in Dermatology. Doubtful clinical features were verified by the Consultant Dermatologist. All patients needing treatment or follow up were provided with treatment and/or given an appointment to attend the Dermatology Clinic.

Results

There were 63 participants with 49 (78%) males and 14 females. The ages ranged from 36 to 88 years with an average of 60.16 years. The majority 47 (74.6%) were within 51 to 70 years of age (figure 1).

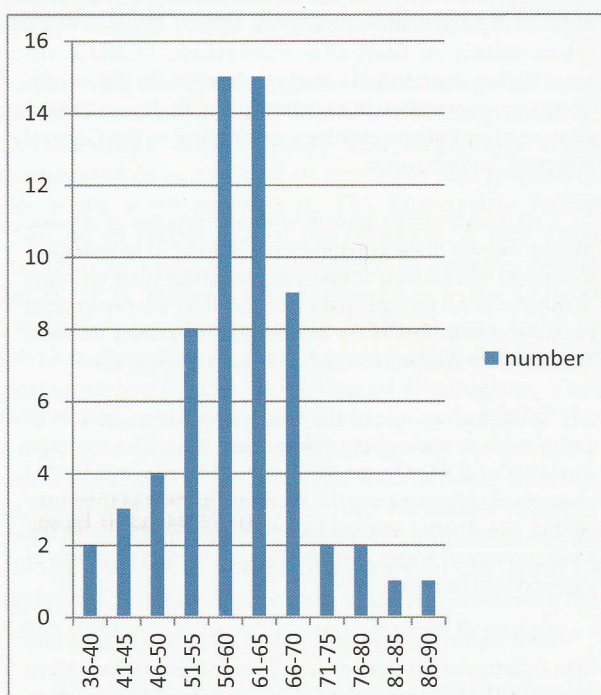


Figure 1. Age distribution of the sample.

Thirty seven (58.73%) participants were from Thamankaduwa, Dimbulagala and Hingurakgoda medical officer of health (MOH) areas (figure 2). The number of patients from Medirigiriya MOH area was less as most of the patients from that area were followed up at Base Hospital, Medirigiriya. The average duration of residence within the area was 43.42 years (range 15 - 70 years).

Paddy cultivation was the occupation of 77% of the sample (figure 3). All except one participant (98.38%) used well water as the source of drinking water. Fifty four (85.71%) participants admitted to using pesticides in cultivation.

The mean duration of CKD-U in the sample was 3.92 (0.25 - 22) years. Sixty two (98.38%) participants

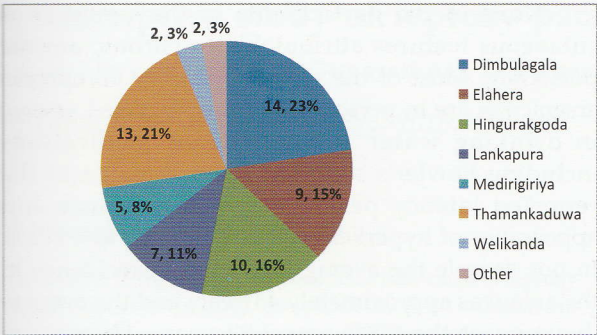


Figure 2. Distribution among MOH areas.

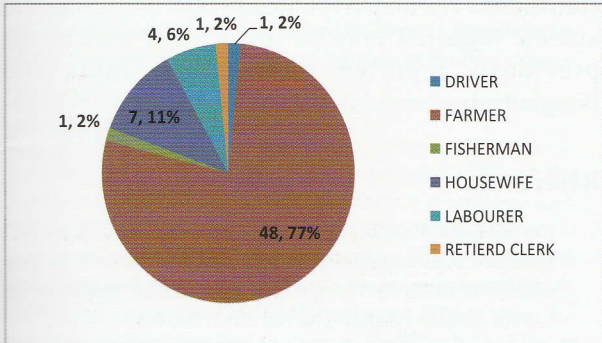


Figure 3. Occupation of the participants.

had at least one cutaneous feature attributable to chronic kidney disease. More than 3 manifestations were seen in 25 (39.68%) patients (table). Xerosis (64.51%), pruritus (35.48%), generalized pigmentation (27.41%), glossitis (25.81%) and palmar pigmentation (22.58) were the commonest cutaneous features of chronic kidney disease. The frequency of occurrence of all cutaneous manifestations is given in table.

Table. Features and frequency attributable to CKD

Number of features	frequency
0	1
1	8
2	13
3	16
>3	25

It was interesting to note that 18/63 patients (29.03%) had callosities of the palms and soles which could be attributed to their occupation and habit of walking barefoot. No cutaneous features specific to chronic arsenic poisoning were seen in this sample.

Discussion

There are several studies describing cutaneous manifestations of chronic kidney disease, both from Asia and other parts of the world. Studies from India show that more than 70% of patients with CKD have xerosis of the skin, while changes in pigmentation and pruritus are also seen commonly^{3,4}. The common cutaneous findings from other parts of the world were comparable to those from India^{5,6}, while ecchymoses, a feature seen in patients on haemodialysis, was seen in patients from Iran⁷. Changes in the palms and soles, macular pigmentation and keratotic pits, were reported in a study from Puerto Rico⁸.

Half and half nails and changes in nail colour were the common nail changes^{3,4,6}. Hair loss, both in the scalp and other body areas, has been reported. In most studies there was no clear difference in cutaneous manifestations between patients on maintenance haemodialysis and those being managed conservatively.

Cutaneous manifestations are commonly seen among patients with chronic kidney disease of unknown aetiology (CKD-U). The prevalence reported in other studies ranges between 79 - 100% (4). In our sample 98.38% patients had at least one cutaneous manifestation.

Xerosis of the skin (64.51%) was the commonest cutaneous manifestation in this sample. The incidence of xerosis reported in previous studies varies from 40 - 90%. Atrophy of eccrine sweat glands and pilosebaceous units has been attributed as possible aetiological factors for xerosis. In patients on haemodialysis reduced hydration of the stratum corneum also may contribute to dry skin.

Pruritus was seen in 35.48% of patients. Previous studies have reported incidence of pruritus varying between 12-90%. The incidence of pruritus was more in patients receiving haemodialysis. This may possibly be due to the relatively longer duration of the disease in the group of patients on dialysis, but some researchers have suggested that dialysis may precipitate pruritus in patients with CKD. Xerosis of the skin, secondary hyperparathyroidism, mast cell degranulation, pruritogenic cytokines, derangement of divalent ion metabolism and changes in cutaneous

innervation are thought to be the aetiological factors for the pruritus. The pruritus in our patients was of mild to moderate severity, but some patients may have intractable itch causing considerable distress.

Generalized pigmentation occurred in 27% of the study population. The changes in colour of the skin reported in chronic kidney disease include pallor, yellowing of the skin and hyperpigmentation. The possible causes for the hyperpigmentation are sun exposure, elastosis and hyperchromia after initiation of dialysis. The reported incidence varies from 7.5 - 50%. Palmar pigmentation was seen in 22.8% of the sample.

The commonest mucosal change was glossitis (25.81%). The incidence of glossitis in other studies was lower than that of our sample. The possible reasons for the high incidence of glossitis may be poor oral hygiene and, associated nutritional deficiencies. The effect of betel chewing should also be considered. The other mucosal changes include furred tongue, scrotal tongue, herpes simplex infections, aphthae and angular stomatitis.

The aetiological factors for CKD-U are not determined yet. Being a farmer, drinking water from wells in the fields, use of pesticides in farming, presence of renal dysfunction in the family, use of Ayurvedic medications and snake bites have been reported as risk factors for CKD-U⁹.

Pigmentary changes, in the form of finely freckled hyper and hypo-pigmentation symmetrically distributed in the trunk and limbs (rain drop pigmentation), and arsenical keratoses (raised, focal hyperkeratotic lesions in the palms and soles are diagnostic of chronic arsenicosis. It should be kept in mind that thickening of pressure points in the palms and the diffuse thickening of the soles in manual labourers should be differentiated from the focal hyperkeratosis of chronic arsenicosis. Other cutaneous features of chronic arsenic poisoning include pre-malignant lesions and skin malignancies, exfoliative dermatitis, Mee's lines and arsenic deposits in hair.

It is interesting to note that 29% of participants in our study had callosities in the palms and soles. This is indicative of their occupation as farmers and the habit of walking barefoot. Care should be taken to differentiate callosities from focal keratoses due to chronic arsenic poisoning.

None of the participants in the sample has cutaneous features attributable to chronic arsenic poisoning. Most of the reported studies on chronic arsenicosis are in persons who have ingested arsenic in drinking water and in various medications including Fowler's solution. In such instances the reported latency period between exposure and appearance of hyperkeratosis is 6 months to 3 years. In our sample the average duration of residence in the area was approximately 43 years and the average duration of the CKD was 3.92 years. Hence it is unlikely that these persons may have been exposed to arsenic in the drinking water. One proposed mechanism is the contamination of the water and the rice by arsenic in the pesticides used in paddy cultivation. We may hypothesize that the amount of arsenic ingested may be lower than that in the previously reported studies from India and Bangladesh.

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