

Clinical Characteristics, Foot-Associated Risk Factors, Offloading Practices and Radiological Assessment in Patients with Type 2 Diabetes Mellitus and Chronic Charcot's Neuroarthropathy: A Case-Control Study from India

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Abstract

Background: The Charcot foot syndrome is a serious and potentially limb-threatening lower-extremity complication of diabetes. However, data regarding the clinical characteristics and risk factors associated with chronic Charcot's neuroarthropathy in Indian patients with Type 2 Diabetes mellitus remains sparse. Our study was aimed at elucidating the clinical and radiological characteristics, associated risk factors and treatment modalities employed in patients with chronic Charcot's Neuroarthropathy in a cohort of Indian Type 2 Diabetes Mellitus patients.

Methods: During the period of January 2012 to January 2016, a total of 1811 patients with Type 2 diabetes mellitus attending the Integrated Diabetes Foot Clinic at a Tertiary care referral hospital of South India were screened and 90 patients with chronic Charcot's arthropathy were identified based on clinical and radiological features. Out of the remaining patients with non-Charcot foot related conditions, an age and duration of diabetes-matched group of 326 patients who consented for the study were selected as controls

Results: Our study revealed a 4.9% prevalence of chronic Charcot's Neuroarthropathy, with midfoot being the commonest site involved. While dermopathy, fissures, clawing and callosities were the predominant foot-associated disorders ($p=0.001$), major risk factors included poor glycaemic control, previous ulcerations and previous amputations ($p=0.001$). Further, a Meary's angle greater than 15° and calcaneal pitch of less than 17° can be novel radiological adjuncts to the evaluation of chronic Charcot's in these patients.

Conclusions: Our study presents valuable insight into the clinical and radiological characteristics of the largest cohort of Asian Indian diabetics with chronic Charcot's neuroarthropathy till date.

Introduction

Charcot neuropathic osteoarthropathy (CN), commonly referred to as the Charcot foot, is a condition affecting the bones, joints, and soft tissues of the foot and ankle, characterized by inflammation in the earliest phase and subsequently leading to the "rocker-bottom" deformity in its classical presentation. The pathogenetic mechanisms involve an interplay of diabetes, sensory-motor neuropathy, autonomic neuropathy, trauma, and metabolic abnormalities of bone. Though first described in 1883, this condition remains an enigmatic and challenging problem for the clinician.

Given the paucity of data on the clinical aspects and risk factors for Charcot's arthropathy from India, we aimed to study the clinical and radiological features, risk factors and treatment modalities in a cohort of patients with Charcot's foot attending a tertiary care referral centre of India.

Materials and Methods

A comparative, case-control study was carried out amongst patients attending the Integrated Diabetes Foot Clinic in the Department of Endocrinology, Diabetes & Metabolism at CMC Vellore in Tamil Nadu, India. As well as treating the local population, this centre serves as a national referral centre for patients from throughout India. The multidisciplinary diabetic foot clinic involves endocrinologists, physical medicine

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rehabilitation and orthotics experts and vascular surgeons. It provides specialized care to a wide diversity of foot problems in diabetes. Patients with a known diagnosis of type 2 diabetes, as defined by the criteria of the American Diabetes Association (ADA) and attending the foot clinic were invited to participate in the study. A diagnosis of chronic Charcot's foot was made on the basis of X-ray findings, clinical symptoms and signs consistent with Charcot neuroarthropathy. Age matched people with diabetes attending the Foot Clinic for non-Charcot complications were invited to participate as controls. Demographic data and medical histories were taken from participants, including age, sex, weight, height, duration of diabetes, antidiabetic regimen, occupation, smoking habit and employment status. Biochemical investigations included the most recent HbA1c, fasting plasma glucose, lipid profile and creatinine levels. Clinical (presence of pain, purulent discharge, swelling, increased temperature, erythema) or biochemical (total and differential leucocyte count, ESR and CRP) evidence of infection were documented in all. Radiological evidence of Charcot foot was based on findings of plain x-ray film, verified by two radiology consultants. Radiological findings were categorised according to the Sanders and Mrdjencovic classification system (Table 1). Meary's angle (Figure 1) was also calculated by measuring the angle between the line originating from the centre of the body of the talus, bisecting the taller neck and head, and the line through the longitudinal axis of 1st metatarsal. Meary's angle is generally close to zero degrees. In addition, the Calcaneal pitch (Figure 2) was calculated by measuring the angle created by a line drawn from the calcaneal tuberosity to the plantar aspect of the distal

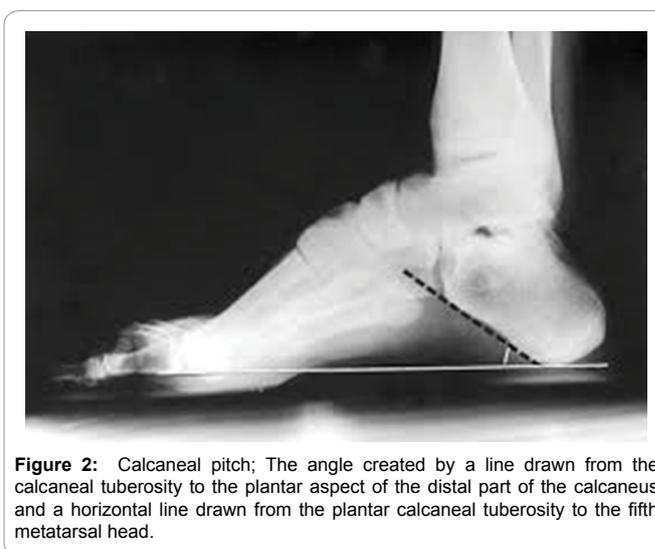


Figure 2: Calcaneal pitch; The angle created by a line drawn from the calcaneal tuberosity to the plantar aspect of the distal part of the calcaneus and a horizontal line drawn from the plantar calcaneal tuberosity to the fifth metatarsal head.

Sander's and Frykberg's classification	Pattern of involvement
Type I	Metatarsophalangeal (MTP) and Interphalangeal (IP) joints
Type II	Tarso-metatarsal (TMT) joints
Type III	Naviculocuneiform, Talonavicular, and Calcaneocuboid joints
Type IV	Ankle and subtalar joints
Type V	Calcaneum

Table 1: Sander's and Frykberg's anatomical classification of chronic Charcot's Neuroarthropathy.

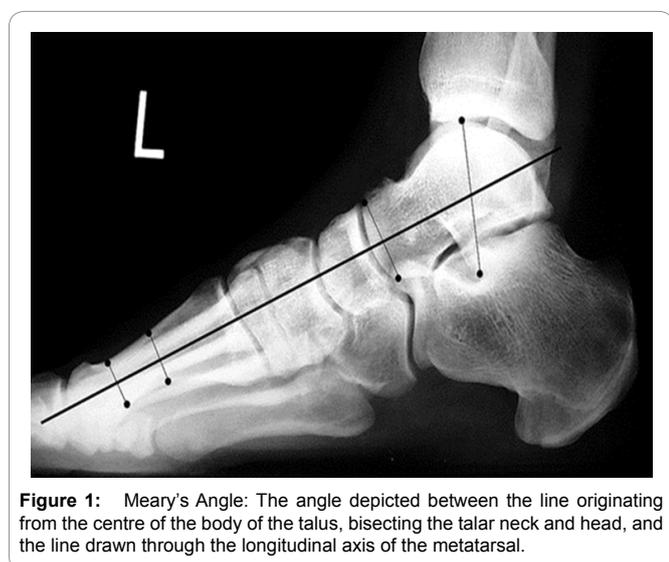


Figure 1: Meary's Angle: The angle depicted between the line originating from the centre of the body of the talus, bisecting the talar neck and head, and the line drawn through the longitudinal axis of the metatarsal.

part of the calcaneus and a horizontal line drawn from the plantar calcaneal tuberosity to the fifth metatarsal head. A smaller angle indicates arch lowering. The affected joints were also assessed for instability. Radiological evidence of osteomyelitis was also documented. A diagnosis of nephropathy was made in the presence of proteinuria of greater than 150mg/24hrs) or microalbuminuria of greater than 30mg in 24 hours. Retinopathy was considered to be present if any typical diabetes related changes were seen on fundoscopy. Peripheral vascular disease was diagnosed if peripheral pulses (dorsalis pedis and posterior tibial) were absent and ankle brachial pressure index was less than 0.9. Disease specific data including foot ulceration, location of ulcers and recommended off-loading treatment were also documented. Neurological assessment of the feet was sought to detect the loss of protective sensation (10 g monofilament) and vibratory sensation (128 hz tuning fork and more than 25 V on biothesiometry). The presence of painful neuropathy was determined by an interview. Clinical assessment was conducted to detect the presence of callus, anhidrosis (dry skin), fissures, tinea pedis, active ulceration, corns, dermopathy, cellulites, oedema or amputation at enrolment. Treatment options included different forms of orthoses, non-weight bearing aids and custom made insoles for footwear.

During the period of January 2012 to January 2016, a total of 1811 patients with type 2 diabetes mellitus attending the foot clinic were screened and 90 patients with chronic Charcot's arthropathy were identified. Out of the remaining patients with non-Charcot foot related conditions, an age and duration of diabetes-matched group of 326 patients who consented for the study were selected as controls. The study was approved by the Institutional Ethics Committee (IRB No: 8378) of Christian Medical College, Vellore. Appropriate informed consent was obtained from all study participants and confidentiality of data was maintained throughout the study.

Statistical analysis was carried out using SPSS (version 16; SPSS, Chicago, IL). The data was examined for data entry errors and outlier values. Bivariate analysis was carried out using the paired *t*-test for continuous variables and Chi-squared tests for categorical variables. A *p*-value of less than 0.05 was considered statistically significant.

Results and Analysis

Baseline characteristics

Our study identified 90 patients (112 feet) diagnosed with chronic Charcot's neuroarthropathy. These patients represented 4.9% of the total cohort of the diabetic foot clinic (1811 patients) over the study duration. The baseline characteristics of these patients are summarized in (Table 2).

The cases and controls were matched for their age and diabetes duration (in years). There were no significant differences in the sex, hypertension, lipid profiles, employment or smoking status distribution between the cases and controls. Body mass index (BMI) was significantly greater among cases (mean 29.3 kg/m²) than controls (mean 26.2 kg/m²; p= 0.02) while glycaemic control as reflected by the Hba1c (9.6% vs 8.1%) or fasting plasma glucose (198 mg/dl versus 166 mg/dl) was significantly better amongst the controls than cases (p<0.05). While participants with Charcot's were significantly more likely to have a concurrent diagnosis of diabetic peripheral neuropathy (p=0.01), there were no significant differences in the incidence of nephropathy and retinopathy between the two groups.

Foot-associated pathologies

Foot-associated pathologies were compared between the two groups. The findings are outlined in (Table 3).

Participants with Charcot's foot had a significantly greater evidence of peripheral neuropathy in the form of loss of vibration sense and 10g-monofilament sensation (p=0.001) indicating a loss of protective sensation. Those with Charcot's arthropathy had a significantly larger number of callosities, skin fissures, drying of skin and clawing of the toes (p=0.001), while there were no differences in the frequencies of fungal infestation, cellulites and peripheral arterial or venous involvement. Previous trauma (p=0.001), ulcerations (p=0.001) and amputations (p=0.01) were significantly greater in those with Charcot's foot.

Characteristics	Cases(n=90)	Controls(n=326)	p-value
Male (%)	62.2%	60.5%	0.18
Mean (SD) age	59.2 (10)	60.3 (10)	0.18
Mean (SD) BMI (kg/m ²)	29.3 (5.0)	26.2 (3.8)	0.02
Mean (SD) duration of diabetes (years)	15.1 (7.5)	15.6 (7.4)	0.31
Mean (SD) HbA1c (%)	9.6 (2.1)	8.1 (2.8)	0.01
Mean (SD) fasting plasma glucose(mg/dl)	198(42.1)	166(39.6)	0.03
Mean(SD) LDL-cholesterol(mg/dl)	112(28.1)	109(32.2)	0.16
Mean(SD) Triglyceride (mg/dl)	166(52.2)	184 (59.4)	0.25
Mean (SD) creatinine (mg/dl)	1.3 (0.9)	1.1 (0.6)	0.12
% smokers	37	41	0.22
% employed	44	46	0.11
% hypertension	66	71	0.45
% OAD only	31	30	0.51
% insulin only	13	16	0.29
% OAD with Insulin	56	54	0.18
% retinopathy	42	44	0.69
% nephropathy	37	39	0.25
% neuropathy	94	62	0.01

Table 2: Baseline characteristics.

Characteristic	Cases(n=90)	Controls(n=326)	p-value
% Callosities	75	54	0.001
% Anhidrosis	82	55	0.001
% Skin fissures	67	49	0.01
% Corn	11	18	0.44
% Clawing of toes	63	44	0.01
% Hallux valgus	06	08	0.51
% Tinea pedis	43	48	0.14
% Cellulitis	15	11	0.64
% Loss of vibration sensation	89	55	0.001
% Loss of 10g monofilament test	90	58	0.001
% Neuropathic pain	48	40	0.19
% Peripheral vascular disease	26	30	0.10
% Venous insufficiency	14	12	0.36
% History of ulceration	68	47	0.001
% Previous trauma	64	39	0.001
% Previous amputation	36	21	0.01

Table 3: Foot-associated pathologies.

Pattern of involvement(Charcot's)	N=112 (100%)
Right foot (%)	55 (49)
Left foot (%)	30 (27)
Bilateral (%)	22 (20)
Ulcers in Charcot foot (%)	N= 66 (59%)
Forefoot	19(69)
Midfoot	41(62))
Hindfoot	6 (9%)
Pattern of involvement according to Sander's and Frykberg's classification: N=112 (100%)	
Type I (%)	12(11)
Type II (%)	54(48)
Type III (%)	29(26)
Type IV (%)	13(12)
Type V (%)	4(3)
More than 1 type	65(58)
Types of offloading: N=112 (100%)	
Moulded insole (%)	54(48)
Total contact cast (%)	23(21)
Others (Wheelchair, crutches, AFO, PTB, Air cast) (%)	35(31)

Table 4: Pattern of involvement and offloading modalities.

Characteristics of patients with Charcot's Neuroarthropathy

The characteristics of foot involvement in the Charcot's group is outlined in (Table 4). A total of 112 feet in 90 patients were evaluated as part of the study. The right foot was predominantly involved in 49% (55/112) of Charcot's feet, while bilateral disease was seen in 20% (22/112). In accordance with Sander's classification (as described in Table 1), Type II was the commonest variety seen in 54 (out of 112 feet,48%) while Type V the least common seen in only 4 out of 112 Charcot's feet(3%). However, more than half the patients (58%) had combined radiological disease. Overall, ulcerations were detected in 66(59%) of 112 feet, with mid-foot being the commonest ulcer site (62%). Offloading was advised to all patients with Charcot's foot. While moulded insoles were used by nearly half the patients (48%), the total contact cast could be done in a minority (21%) of the 112 affected

feet. Other off-loading techniques like wheelchair, crutches, AFO and pneumatic casts were offered to 31% of the patients.

Meary's angle + Calcaneal pitch

Meary's angle was calculated for 105 out of the 112 affected feet. The reasons for inability to calculate the angle in 5 cases was a complete collapse of the talus and in 2 cases was resorption of the 1st metatarsal. The calcaneal pitch was calculated for 109 feet. It was not possible to calculate the angle for 3 patients due to complete destruction of the fifth metatarsal. The angle at which the Meary's angle was taken to be pathological was above 15 degrees, of which there were 55 cases (52%). The angle at which the calcaneal pitch was taken to be pathological was below 17 degrees, of which there were 61 cases (56%). Further, in those with an elevated Meary's angle, there was a significantly greater prevalence of mid-foot ulcers ($p=0.001$) while in those with a reduced calcaneal pitch, both forefoot ($p=0.001$) and mid-foot ($p=0.001$) ulcers were significantly more. Radiological evidence for instability of the ankle joint was significantly greater in Charcot's feet with abnormalities of either of the Meary's angle or calcaneal pitch $p=0.01$.

Discussion

In our study there was a prevalence of Charcot's arthropathy of 4.9% in Asian Indian diabetic subjects. Though initial studies have reported Charcot's as a rare complication of diabetes occurring in 0.08%-1%, [1] recent data suggests a prevalence of up to 7.5% [2] in some populations. A lack of uniform clinical and radiological markers for Charcot's foot results in delayed or missed diagnosis in up to 25%, [3] thus explaining the apparently lower prevalence rates.

Amongst the baseline characteristics, patients with Charcot's foot had a significantly greater BMI. This has been reported previously by Chisholm and colleagues who suggest that obesity is a predisposing factor for Charcot arthropathy since at least two thirds of Charcot patients are obese [4]. With respect to controls matched for age and duration of diabetes, patients with Charcot's had significantly poorer glycemic control, a finding which agrees with the that of Fabrin and colleagues [5]. While the higher concordance of peripheral neuropathy with chronic Charcot's was in keeping with existent literature, [6,7] our study failed to show a significant difference in other microvascular complications between the cases and controls. The latter could be due to the similar duration of diabetes in the two groups.

Analysis of the foot-related pathologies revealed a significantly greater loss of 10g-monofilament and vibration sense. This is in keeping with the findings [8] of loss of protective sensation as a key pathogenetic event leading to Charcot's arthropathy.

Dermopathy, skin fissures, anhidrosis and callus formation were all significantly associated with Charcot in the present study. Given the significant correlation of these changes with diabetic peripheral polyneuropathy, [9] their predominance in those with Charcot's arthropathy is expected. The significant increase in clawing could be attributed to the underlying motor neuropathy, in turn leading to abnormal loading of the foot and further damage to the arch of the foot. Amongst the predisposing factors, previous trauma was significantly higher in Charcot's arthropathy-related group in our study. Trauma is the most common etiological

factor encountered in the pathogenesis of Charcot arthropathy and was reported to be present in 22–53% of the cases [10,11]. Capillary leakage and subsequent formation of edema is a physiological response to blunt trauma [12] with higher energy trauma causing a disruption of the marrow trabeculae leading to interstitial fluid and haemorrhage accumulation within the marrow spaces. When this condition occurs in the foot of a non-diabetic patient, it is painful and following the cessation of ambulation, local inflammation of the foot subsides. However, in a neuropathic patient, the insensitive foot does not experience pain as the appropriate response. Therefore, a lack of required immobilization flares up the inflammatory cycle [13]. A history of previous ulcerations and amputations were significantly associated with Charcot's arthropathy in the present study - a finding [14] which is consistent with existing research - and confirms the increased risk of ulceration secondary to foot deformities amongst patients with Charcot's arthropathy. There were no positive correlations between Charcot's arthropathy and peripheral vascular insufficiency in our study cohort. Similar findings were reported by Rosenblum, Foltz and Leung and colleagues [6,7,15]. However, the presence of Doppler studies could not be performed in all cases and hence this finding needed more critical analysis. Although previous studies used the same methods as used in the present study for evaluating the vascularity of the foot (palpation of the dorsalis pedis and posterior tibial pulses), these methods maybe considered an insufficient test in the person with Charcot's arthropathy and may be a limitation of our study.

In this case-control study with Charcot's feet, the right foot was predominantly involved in nearly half the patients (49%), while bilateral disease was seen in 20%. The most common pattern of involvement was the Lisfranc's joint (Type II), which is in accordance with the distribution reported worldwide [16]. The commonest site of an ulcer in the Charcot's foot was the mid-foot, probably explained by the occurrence of Charcot's deformities and pressure alterations most commonly in the mid-foot region [17]. While moulded insoles were commonly prescribed footwear for Charcot's foot, the Total Contact cast (TCC) was used by only a minority (21%) of subjects in the study population. Studies by Fife and colleagues [18] have shown only 16% of patients with diabetic foot ulcers end up using a TCC, primarily due to the fear of complications, unwillingness for close long term follow-up and a perceived reduction in activity levels.

Our study is the first of its sort to utilize the radiological markers of Meary's angle and Calcaneal pitch in Chronic Charcot's arthropathy. Radiographs are the primary initial imaging method for evaluation of the foot in patients with diabetes. Their easy availability and relative lack of expense makes it an easy tool to provide information on the structural deformities in Charcot's foot [19]. While subtle fractures and dislocations are common in early stages, the reduction in the calcaneal inclination and disruption of the talo-first metatarsal angle has been well documented [20]. Our study has revealed that a Meary's angle of greater than 15 degrees and a calcaneal pitch of less than 17 degrees to be highly prevalent in Charcot's arthropathy. Further, Charcot's arthropathy was significantly associated with ulcerations in the Charcot foot ($p=0.001$) and joint instability, thereby serving as useful radiological adjuncts.

Conclusions

Our study is one of the largest single-centre experiences in Charcot's foot worldwide and to the best of our knowledge the largest from an Indian tertiary care referral centre. It provides valuable insight into the understanding of the clinical features and risk factors associated with Charcot's arthropathy in the Indian population with diabetes. Poorer glycaemic control, peripheral neuropathy and previous ulcerations are the major risk factors associated with chronic Charcot's. Significant alterations in the Meary's angle and Calcaneal pitch angle can aid as novel radiological adjuncts to prompt diagnosis and therapeutic interventions in chronic Charcot's arthropathy.

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Disclosure

The authors of this article declare no potential conflicts of interest or financial interests relevant to the subject of the manuscript.

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