Interstitial lung disease in Africa – a need for recognition and earlier diagnosis

There is a distinct dearth of epidemiological studies on the burden of interstitial lung disease (ILD) in Africa. A paper published in 2021 on the global prevalence of ILD declared '…there are continents (e.g., South America and Africa) without English language literature on the topic'.[1]

In this issue of the *AJTCCM*, Palalane *et al.*[2] report the clinical, radiological and serological features in 124 patients with connective tissue disease-associated ILD (CTD-ILD) seen over a 1-year period at a tertiary-level hospital in Western Cape Province, South Africa (SA). It would have been interesting to ascertain the proportion of all ILDs made up by CTD-ILD. In Brazil, also an upper-middle-income country, CTD-ILD accounted for 24.8% of 1 000 consecutive ILD patients.[3]

A PubMed search for a series of CTD-ILD patients in Africa for comparison revealed only a single article published from Nigeria in 2021 which documented 31 cases of ILD (9.7%) among 318 CTD patients over a 7-year period.[4] There were some interesting differences between this study and the one reported here. CTD diagnosis occurred at a younger age in the Nigerian study (38.8 years) compared with the local study (45.0 years) The outcome in the Nigerian study was dismal, with 12.9% requiring long-term domiciliary oxygen therapy and 16.1% mortality. Although rheumatoid arthritis (RA) also formed the majority of CTD patients in the Nigerian study, RA subjects were least likely of the CTD patients to develop ILD (2.6%) compared with 29.8% in the SA cohort. None of the patients smoked, whereas 60.5% in the local study were current or ex-smokers. This supports existing evidence that tobacco smoke is a risk factor for ILD. Whereas 31.5% were diagnosed with ILD at the time of diagnosis of CTD in the SA study, this occurred in 74.2% of the Nigerian study, suggesting late presentation and/or delayed diagnosis in that country.

An anomaly in the local study is that usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP) patterns on HRCT scan occurred with similar frequency in RA. This is contrary to findings in most reports of RA-associated ILD (RA-ILD) where UIP is the most common pattern in both caucasian[5] and black patients.[6] Interestingly, a lower incidence of idiopathic pulmonary fibrosis (IPF), also characterised by a UIP pattern, has been noted in black patients.[7,8] This emphasises the influence of genetic and racial differences on phenotypes in different ILDs. The RA patients in the current study comprised 16.2% black patients and 78.4% patients of mixed ancestry. Chris Hani Baragwanath Academic Hospital in Johannesburg, the largest hospital in the southern hemisphere, serves a mainly black population. My personal impression over 25 years at this institution is that the predominant ILD pattern in our RA-ILD patients is UIP. One of my co-consultants is currently analysing the pulmonary manifestations in our cohort of RA patients. We await these results with interest.

Another unusual finding of Palalane *et al.*'s study[2] is that patients with UIP demonstrated better lung function than other ILD subtypes, despite the generally accepted association of UIP with worse outcome than other histological patterns of ILD. This is difficult to explain, except to note that there are many other factors which may affect lung function measurements, including comorbidities. A significant proportion of the study population had gastro-oesophageal reflux disease, previous TB and chronic obstructive pulmonary disease (COPD), all of which may influence lung function parameters. The extent of radiological involvement by UIP is also an important determinant and was not documented. In addition, the number of patients with UIP was relatively small (n=33). Alternatively, the patients with NSIP may have had disproportionately advanced disease. It is noteworthy that worse outcomes in patients with a UIP pattern are not a universal finding. Zamora-Legoff *et al.*[5] found that in 181 RA-ILD patients, 5-year survival did not differ between those with UIP, NSIP or organising pneumonia.

A notable observation reported by Adegunsoye *et al.*[7] was the finding that in a large USA cohort of 1 640 patients with ILD, of whom 222 were African-American, the latter group was found to have decreased all-cause mortality (19% v. 27%, over the 10-year study period) compared with non-African-Americans. African-Americans also had greater odds of having CTD-ILD (odds ratio 6.28) and were younger in age at ILD diagnosis.

Sarcopaenia, characterised by loss of skeletal muscle mass, has been demonstrated to adversely affect FEV_1, FVC and peak flow, but not the FEV_1/FVC ratio, even in apparently healthy individuals.[9,10] The impact of sarcopaenia on lung function has not been adequately recognised or studied in ILD, unlike in COPD.[11] Many CTD-ILD patients have limitation of physical activity related to joint, muscle and skin disease, contributing to sarcopaenia. Sarcopaenia has been shown to be associated with poorer outcomes in patients with IPF and may not necessarily be associated with overt weight loss.[12] Decreased excursion of the diaphragm, the most important muscle of respiration and composed of skeletal muscle, has been shown to be predictive of muscle mass loss in sarcopaenia. Evaluation by ultrasound examination[13] may prove to be a useful tool in detecting this neglected component of chronic lung disease which impacts lung function, quality of life and survival.

An important message from this study confirms that the feared complication of methotrexate-induced pneumonitis has been overstated in previous literature. None of the patients who received methotrexate (7 605 patient-years of exposure) experienced this complication. A recent case-control study suggests that methotrexate use in RA may, in fact, delay or protect against the development of ILD.[14] However, clinicians should be mindful that the potentially fatal entity of methotrexate-induced hypersensitivity pneumonitis does exist.

There is an obvious need to identify patients with CTD in Africa and to detect CTD-ILD early by performing routine HRCT scans at diagnosis. In many CTDs, pulmonary complications are the most important factor responsible for mortality. We are living in an exciting era with the advent of anti-fibrotic drugs which have shown conclusively to slow decline in lung function in progressive fibrosing ILDs (PF-ILDs). The INBUILD trial[15] showed that administration of Nintedanib for 52 weeks resulted in a lower rate of FVC decline in PF-ILDs other than IPF. Autoimmune ILDs accounted for 24.7% of ILDs in the treatment arm.

The reasons for the paucity of data on CTD-ILD in Africa include delayed recognition, relative rarity compared with more pressing diseases (e.g. TB, malaria), the need for expensive and sophisticated technology (lung function equipment, CT scanners, lung biopsy, autoantibody tests), scarcity of specialists (pulmonologists, radiologists, clinical technologists and pathologists) and the unavailability of immunosuppressant drugs.

Lessons learned from Palalane *et al.*'s[2] study are (*i*) all newly-diagnosed patients with CTD should be investigated for ILD, irrespective of the absence of symptoms, preferably by HRCT scans; (*ii*) even in the absence of respiratory symptoms or HRCT scan abnormalities, such patients should be followed up for a minimum of 3 years to detect the development of ILD; and (*iii*) multidisciplinary collaboration is vital to improve the diagnosis and management of these patients.

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