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PATTERN OF INTERSTITIAL LUNG DISEASE DETECTED BY HIGH RESOLUTION COMPUTERISED TOMOGRAPHY
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PATTERN OF INTERSTITIAL LUNG DISEASE AS SEEN BY HIGH RESOLUTION COMPUTERISED TOMOGRAPHY

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ABSTRACT

***Background*: Diffuse lung diseases constitute a major cause of morbidity and mortality worldwide. High Resolution Computed Tomography (HRCT) is the recommended imaging technique in the diagnosis, assessment and followup of these diseases.**
***Objectives:* To describe the pattern of HRCT findings in patients with suspected interstitial lung disease.**
***Setting*: Kenyatta National Hospital (KNH), Nairobi Hospital and MP Shah Hospital; all situated in Nairobi, during the period February to August 2010.**
***Subjects*: One hundred and one patients sent for HRCT in the six month study period.**
***Results*: A total of 101 patients were recruited with age range 18 to 100 years, with a mean age of 53.6 (SD 19.7) years and a median age of 54 years. The male-female ratio was 1.2: 1. Cough [80.2% (n = 81)] was the most common presenting complaint followed by dyspnoea (53.5%, n=53) and chest pain [24.8% (n = 25)]. Overall, the predominant pattern of involvement on chest HRCT was reticular pattern seen in 56.1 % (n=82) of patients, followed by honey-comb pattern (37.8%, n=82).**
***Conclusion*: The study demonstrated marked lung parenchymal destruction in most cases; a poor prognostic indicator which could have been due to delayed referral. HRCT has a high pick up rate of subtle parenchymal lung lesions as well as defining the lesions and their distribution compared to plain chest radiography. This is important in narrowing the differential diagnosis as well as for pre-biopsy planning. The diagnosis of ILD requires a multidisciplinary approach including a detailed clinical history, physical findings, and laboratory investigations, radiological and histological assessment.**

INTRODUCTION

Interstitial Lung Disease (ILD) is a major cause of morbidity and mortality worldwide in patients with chronic lung diseases. They account for 8.8% of all chronic lung diseases (1). Early diagnosis and proper management has been shown to increase the chance of reversibility and prevent further damage to the lung parenchyma. Assessment of pulmonary diseases is therefore of paramount importance for the initial diagnosis, treatment and subsequent follow-up of patients. High Resolution Computerised Tomography (HRCT) is more sensitive in picking subtle lung parenchymal lesions that may not be detectable on radiographs. It offers more detailed information compared to the conventional chest radiograph in terms of lesions' characterisation and their distribution within the lung hence improving diagnostic accuracy.

Many people suffer from chronic lung diseases in Kenya; however, no emphasis has been put on ILD. The first and most readily available diagnostic modality for pulmonary conditions in most parts of Kenya is the chest radiograph which has low pick-up rate for subtle interstitial changes due to overlap of tissue shadows along the X-ray beam path.

Use of HRCT in the evaluation of lung disease dates back to the foundation laid by Itoh *et al*(2) who demonstrated the accurate anatomic depiction of the secondary pulmonary lobule and the anatomic distribution of small pulmonary nodules on post-mortem radiographs of thin lung sections. Initial clinical descriptions of HRCT in the evaluation of pulmonary disease are attributable to Todo *et al* from Japan and Nakata *et al* from England. They showed that HRCT was sensitive for the detection of diffuse peripheral lung disease and accurately correlated with the pathologic findings. HRCT encompasses

techniques that combine the thinnest attainable collimation with construction algorithms designed to produce high spatial resolution so that objects as small as 0.1mm can be resolved.

HRCT is the recommended imaging technique in the diagnosis, assessment, and followup of interstitial lung diseases. It also allows evaluation of the effectiveness of the medical therapy and the selection of the type and the location of the biopsy when required (3, 4, 5) as well as the best route of approach during biopsy (6, 7).

A special group of patients with suspected ILD is oncologic patients with pulmonary symptoms especially dyspnoea who may benefit from HRCT which excellently depicts features of lymphangitis carcinomatosa.

To maximise benefit from HRCT images isotropic data acquisition is used as it allows image reconstruction in any plane and at varying collimation. Expiratory images are used to assess air trapping and small airway disease. Prone images can be used to exclude dependent opacities that may mimic disease.

Post processing techniques that are crucial for image evaluation include maximum intensity projection (MIP) that can differentiate pulmonary vasculature and pulmonary nodules showing the latter to advantage. Minimum intensity projection (min-IP) can be used to evaluate air trapping, emphysema and lung cysts.

One of the drawbacks of HRCT is high radiation dose which can be minimised by using low dose technique (120 kVP, 40 MAs). Another drawback is artifacts. Black and white bands (so called "Hurricane artifact") are seen on HRCT due to difference in attenuation of structures like blood vessels and adjacent lung. Motion artifact may also be a problem in dyspnoeic patients undergoing volumetric imaging. This can mitigate against by doing axial incremental HRCT

MATERIALS AND METHODS

A cross-sectional descriptive study was carried out over a period of six months between February and August 2010.All patients aged 18 years and above referred for HRCT of the chest and who met the selection criteria during the study period were included in the study after signing an informed consent. They all availed their preliminary plain chest radiographs for reporting.

The study was performed on three 16 slice multi-detector CT scanners, Brilliance Model, manufactured by Phillips. The parameters used included 1-2mm beam collimation, 35cm field of view, and matrix size of 512x512.

Each HRCT done was reviewed by the researcher and a consultant radiologist. The findings were recorded in the data collection form for each participant. Data entry preceded analysis that was done using a computer programme; SPSS 15. The results were presented in form of tables, graphs and charts followed by a comprehensive discussion.

RESULTS

During the six month-study period, a total of 101 adult patients with suspected diffuse pulmonary disease or diffuse pulmonary disease discovered on chest radiograph were identified and recruited into the study. The age distribution was between 18 and 100 years with a mean age of 53.6 (SD 19.7) years and a median age of 54 years. Most patients (23.8%, 95%CI 15.8%-33.2%) were aged 70 years and above followed by those aged between 60 and 69 years who accounted for 18.8% (95% CI, 11.7%-27.8%) of the sample.

Males represented 54.5% of all participants (male-female ratio of 1.2: 1). Slightly more male patients had suspected diffuse parenchymal lung disease compared to females (54.5% versus 45.5%), however the proportion of male to female patients with the diagnosis was not significantly different (difference in proportions = 8.9%, z = 1.27, p = 0.21).

Smoking history: Seventeen point eight percent (95%CI, 10.9-26.7) of patients with suspected diffuse parenchymal lung disease were smokers or had ever smoked at some stage in their life. Smoking was more common among male compared to female patients (32.7% versus 0%; chi = 18.3, p<0.0001). Patients aged between 30-59 years were also more likely to smoke compared to younger (18 to 29 years) or older (60 years and above) patients (p=0.05).

Findings of the occupational history of the patients presented showed that only three per cent (n=3) of patients engaged in industrial occupations. All the three patients in industrial occupation were male (p=0.24) and two out of the three industrial workers were aged between 18 and 29 years (p=0.07).

Presentation of patients and indications for HRCT chest examination: Cough [80.2% (n = 81)] was the most common presenting complaint followed by dyspnoea (53.5%, n=53) and chest pain [24.8% (n = 25)]. However, majority had a combination of complaints. One-fifth (20.8%, n =21) of patients had other co-existing systemic conditions. Minority of the patients had positive smoking history [17.8 % (n = 18)] or industrial-related occupation history [3% (n=3)]. The clinicians failed to indicate their impression of the cause of illness in one-third of the cases (33.7%, n =34) for which HRCT scans were requested.

Figure 1 shows the complaints on presentation among 101 patients with suspected diffuse lung disease.

Systemic conditions among patients with interstitial

Figure 1
Chest HRCT patterns of ILD obtained in 82 out of 101 patients

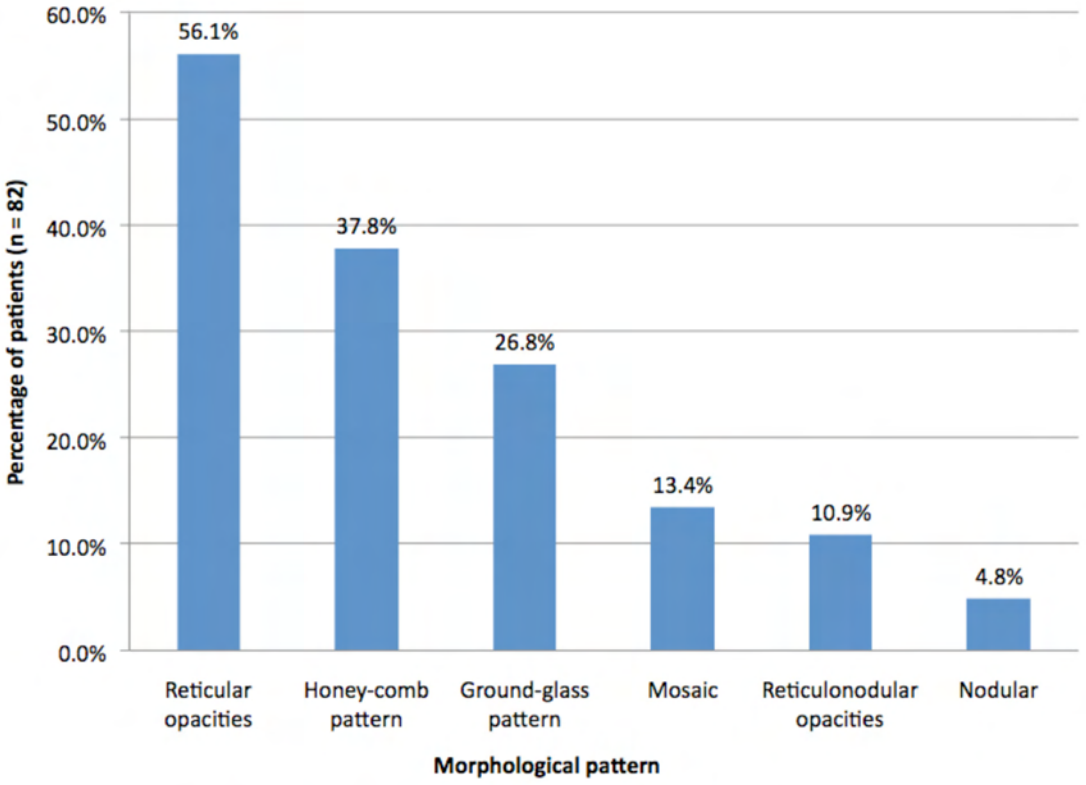


Table 1
Lung zones affected by disease as seen on HRCT in patients with suspected ILD

Lung zone	Frequency	Percent (95% CI)
Lower	56	68.2% (57-78.1)
Middle	18	21.9% (13.5-32.4)
Upper, mid and lower	8	9.7% (4.3-18.3)
Total	82	100

Table 2
Radiological diagnosis among 101 patients investigated using chest HRCT

Radiological diagnosis	Frequency	Percent (95%CI)
Interstitial lung disease	37	36.6(27.3-46.8)
Tuberculosis	14	13.8(7.8-22.1)
Pneumonia	13	12.8(7-21)
Chronic bronchitis	6	6(2.2-12.4)
Bronchiectasis	4	4(1-9.8)
Emphysema	3	3(0.6-8.4)
Lung metastases	2	1(0.2-6.9)
COPD	2	1(0.2-6.9)
PCP	1	1(0.2-5.4)
Normal	19	18.8(11.7-27.8)
Total	101	100

Figure 2
81 year old female who presented with cough, dyspnoea and chest pain. Chest radiographic findings were indeterminate. HRCT chest showed bibasal reticular pattern in peripheral distribution. No honey-combing. Radiological diagnosis of ILD was made

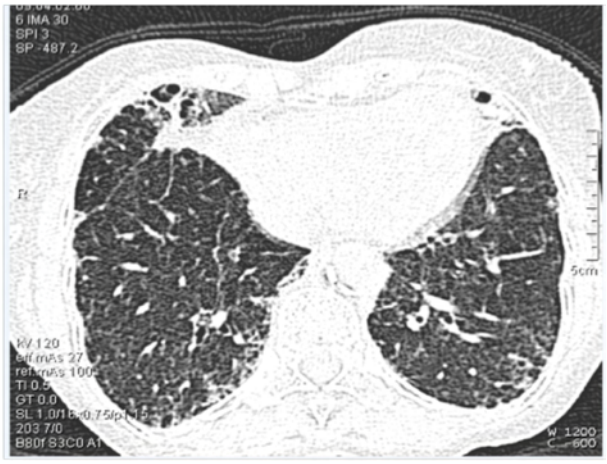


Figure 3
A 27 year old female with history of persistent cough and chest pain. Chest radiographic findings were indeterminate. HRCT chest showed a tree-in-bud pattern with associated ground glass opacification in the left lung. There was upper lobe predominance. Radiological diagnosis of endobronchial pulmonary tuberculosis was made

Figure 4

A 72 year old male presented with history of cough and dyspnoea. No history of smoking. Plain chest radiographic findings were indeterminate. HRCT showed bibasal reticular pattern with honey combing in Sub-pleural distribution. A radiological diagnosis of ILD was made

Figure 5

A 74 year old male patient with positive smoking history presented with cough and dyspnoea. Chest radiographic findings were indeterminate. HRCT chest revealed predominant bibasal reticular pattern in peripheral distribution. There was associated honey-combing. Radiological diagnosis of ILD was made

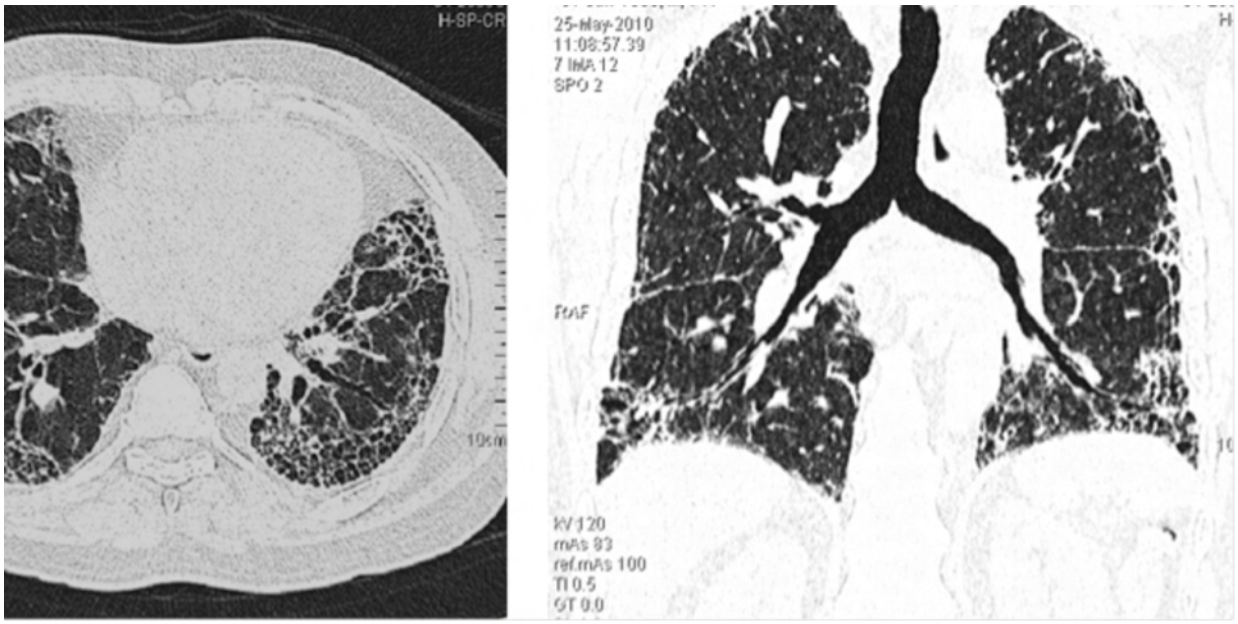


Figure 6

A 79 year old male with positive smoking history presented with history of progressive dyspnoea. His chest radiographic findings were indeterminate. HRCT showed predominantly low attenuation and mosaic pattern of the left lower lobe with paucity of vessels. Radiological diagnosis of emphysema was made

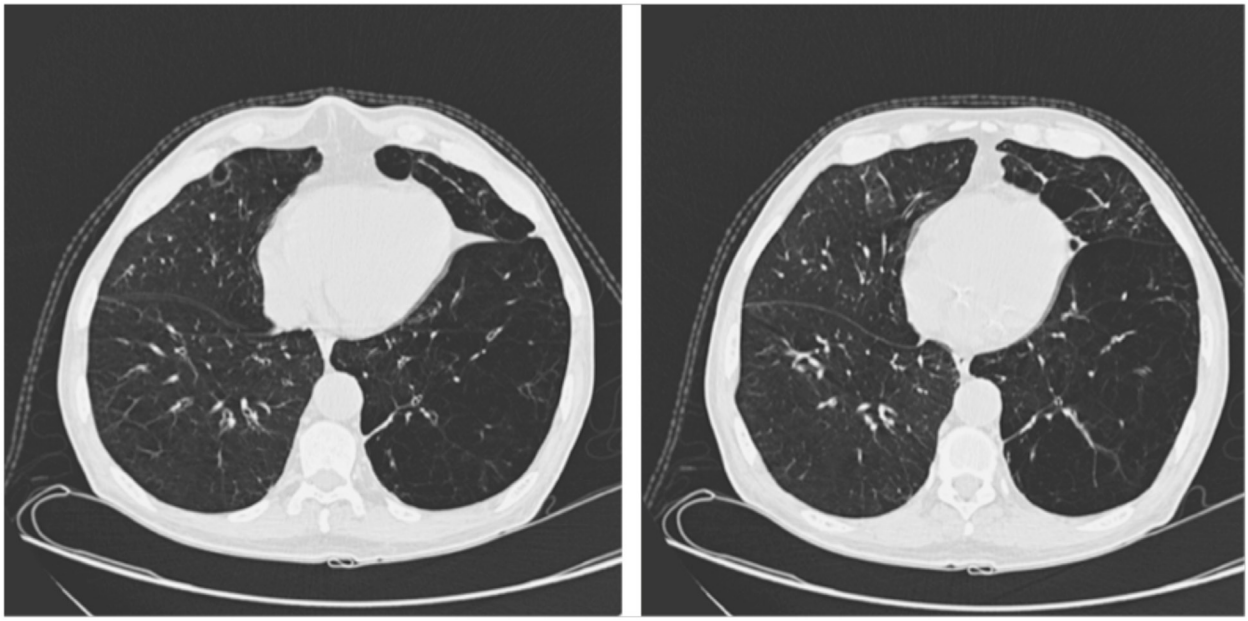
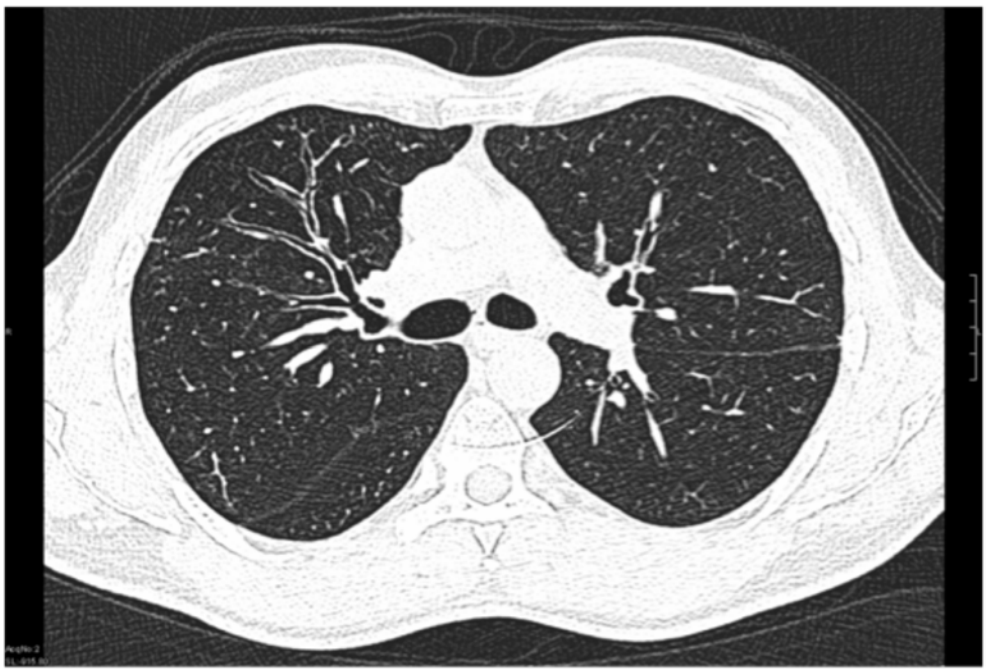


Figure 7

A 54 year old male presented with history of dyspnoea and chest pain. He had been working in a tyre-tube industry. Plain chest radiographic findings were indeterminate. HRCT revealed bronchial dilatation and wall thickening. Radiological diagnosis of cylindrical bronchiectasis was made



lung disease: One-fifth (20.8%, 95%CI, 13.3%-30%) of patients presenting to the three study sites with suspected ILD had other co-existing systemic conditions. The most common systemic conditions included: hypertension (n = 9), diabetes (n = 6) and HIV (n = 4). Other conditions which were seen in the sample, although less frequently were: SLE (n=1), scleroderma (n=1), rheumatoid arthritis (n=1), renal disease (n =1) and metastases (n = 3). There were no statistically significant differences between the patients with systemic conditions and those without these conditions in terms of their age, t=0.96, p=0.34, or gender, chi =0.5(1), p=0.62.

Chest HRCT patterns in suspected diffuse lung disease: Chest HRCT scans revealed abnormalities in 82 of 101 patients (81.2%, 95% CI 72.2-82.2) with suspected ILD. The predominant pattern of involvement on HRCT among ILD patients with abnormal scans was reticular opacities (n=46, 56.1%). Areas of honey-combing as well as ground-glass patterns were seen in 37.8% and 26.8% of all abnormal HRCTs, respectively. The other patterns recorded in 13.4, 10.9 and 4.8% of scans were mosaic pattern, reticulo-nodular opacities and nodular pattern respectively. In addition to the reported patterns, some patients showed additional abnormalities like septal thickening (n = 3), bronchial wall thickening (n = 2), and consolidation (n = 1).

The frequencies of six HRCT patterns seen in this study are presented in Figure 1. Patients commonly exhibited a polymorphous spectrum of patterns resulting in a higher total number of findings (120 recorded findings) compared to the number of patients (n=82) with HRCT abnormalities in the study.

Anatomical and zonal distributions of HRCT opacities: A combination of both central and peripheral abnormalities was seen in 41.5% (95%CI, 30.7-53.4) followed by peripheral abnormalities present in 37.8%. Involvement of central sites only was seen in 17 (21.5%, 95% CI 13-32.2) patients.

The lung zones affected by ILD as seen at high resolution CT among the 82 patients with an abnormality are presented in Table 1. The lower lung zone was the most (68.2%, 95%CI 57-78.1) commonly affected on HRCT followed by the upper lung zone (21.9%, 95%CI 13.5-32.4). All the three zones of the lungs (upper, mid and lower) were simultaneously affected by disease in only eight (9.7%, 95%CI 4.3-18.3) out of the 101 patients studied.

Radiological diagnosis: One-third (36.6%) of all patients (n=101) with suspected ILD had a radiological diagnosis of interstitial lung disease based on HRCT findings.The other common radiologic diagnoses were tuberculosis (13.8%) and pneumonia (12.8%). Lung metastases and pneumoconiosis were seen less frequently (Table 2).

All cases were assigned a radiological diagnosis based on typical features for specific diagnoses and any supporting clinical history. Cases that had nodular pattern in peribronchial distribution and tree-in bud appearance were diagnosed as tuberculosis. Chronic bronchitis had bronchial wall thickening with or without pulmonary artery enlargement. Non-tapering dilated bronchi with or without bronchial wall thickening was classified as bronchiectasis most of which were of cylindrical type. Pneumocystis Jiroveci Pneumonia (PJP/PCP) had ground glass opacification with a positive history of HIV/AIDS. A diagnosis of COPD (chronic obstructive pulmonary disease) was made in cases that had mosaic pattern and hypo-attenuating areas on expiratory HRCT scans with or without bronchial wall thickening or bronchiectasis. On the other hand emphysema was seen as areas of abnormal low attenuation without distinct walls with associated paucity of pulmonary vessels.

Comparison of plain radiographic chest findings with HRCT findings: Plain radiographic chest findings were available for all the patients in the study. These findings show that 30.7% of patients had a normal radiograph. The finding of HRCT reported above indicated that only 19 (18.7%, 95%CI 11.7-27.8) patients had normal scans findings demonstrating a 12% absolute improvement in identification of patients with normal lung fields.

The distinct patterns identified on HRCT for the 12 patients who had initially been classified as normal using plain radiographs were: Reticular, honey comb, ground glass, mosaic and reticulo-nodular patterns.

Conversely, 69.3% (95%CI, 59.3-78.1) of all patients had indeterminate findings on their plain radiographic chest films, Figure 6. With the exception of a single film (1%), all the remaining indeterminate plain film radiographs had a pattern identified on HRCT. This single indeterminate radiograph was classified as normal using HRCT.

DISCUSSION

This study showed that the age range in suspected ILD patients is wide with a mean age of 53.6 years (SD 19.7) and a median of 54 years (inter-quartile range 38-69) and majority (24%) aged 70 years and above. These findings compare with a study done by Raghu *et al*, which showed that the prevalence of IPF that is the most common form of ILD increases with advancing age (7). Gender prevalence was seen in this study with a male to female ratio of 1.2:1
The most common clinical presentation was cough

(80.2%, 95% CI, 71%-87.4%) followed by dyspnoea (53.5%, 95%CI 42.2%-62.5%) and chest pain (24.8%, 95%CI, 16.7%-34.3%). Only 35.6% of these patients presented with a single complaint among the three. The relatively high frequency of cough could have been due to the manifestation of ILD or superimposed infection. Similar findings have been reported by Raghu *et al* (8).

Most clinicians did not provide their clinical impression (34%) or adequate clinical information which is useful in narrowing the differential diagnosis. Only 31% had a clinical impression of ILD. Additional information was obtained from the patients or the patients' files in particular the in-patient files.

There was no relation of ILD to either smoking or occupation. Only 18% reported to have ever smoked and only 3% reported to have ever worked in an industry. These figures raise suspicion that the suspected ILD could have been due to other causes and /or risk factors other than smoking and occupation. Passive smoking was not excluded in this study and therefore the actual percentage of smoking related ILD might be higher.

The predominant HRCT pattern of findings was divided into three; the morphologic pattern, the distribution pattern of lesions within the affected lung and their zonal distribution. Reticular pattern was the predominant morphologic pattern (56.1%, 95%CI, 44.7-67) followed by honey-comb (37.8%), ground-glass (26.8%), mosaic (13.4%), reticulo-nodular (10.9%) and nodular patterns (4.8%). These findings showed that majority of the referrals had irreversible lung parenchymal changes or advanced disease probably due to late referral. Various studies have reported similar findings (9, 10).Reticular pattern together with honey-comb pattern are associated with poor prognosis (11, 12).

Zonal distribution of the morphologic patterns showed that the lower zone was predominant (68.2%) followed by the middle (21.9%) zone and a combination of all zones in only 8% cases. These findings are similar to other studies that have cited IPF to be the most common form of ILD especially in the elderly with lower lobe predominance (13, 14). Peripheral distribution of lesions was seen in 37.8% (95%CI, 27.3-49.1)), central distribution in 21.5 %(95%CI, 13-32.2) and a combination of both in41.5 %(95%CI, 30.7-53.4).

A radiological diagnosis was provided for each HRCT chest findings in relation to the pattern of findings and the clinical history provided. A diagnosis of ILD was made in 36.6 % (95%CI, 27.3%-46.8%) of the HRCT chest done while the rest included pulmonary tuberculosis (13.8%), pneumonia (12.8%), and bronchitis (6%) among others. There was no lung biopsy done to correlate with the radiological diagnosis.

HRCT demonstrated superiority over conventional radiography in picking subtle lesions and demonstrating their distribution and this compared with various studies (15, 16). Majority of the radiographic findings were indeterminate (69.3%) while the remaining 30.7% were reported as normal (Figure 4). HRCT demonstrated distinct lesions in 81.2% and normal findings in18.8 % (Figure 2). HRCT has been reported to have high sensitivity and specificity in comparison to plain radiography (16, 17).

CONCLUSION AND RECOMMENDATIONS

There is evidence of advanced disease and irreversible lung parenchymal changes in patients referred for HRCT with the majority of cases aged 40 years and above. This could either due to low index of suspicion and therefore late referrals. There is therefore need for early and thorough diagnostic work-up of all patients suspected to have ILD.

There was significant number of chest radiographs reported as normal yet HRCT findings were abnormal. This confirms that HRCT is superior to plain radiography in demonstrating parenchymal lesions and should therefore be recommended for all patients who present with persistent dyspnoea and/or cough with inconclusive or normal plain radiographic features.

None of the patients had a lung biopsy done. ILD is a major cause of morbidity in Kenya; lung biopsies should therefore be carried out in those patients who are likely to benefit from evidence based results and management.

Correlation of the HRCT findings with lung biopsy is also important and this would form a basis for another study to find out the incidence and prevalence of ILD in Kenya.

REFERENCES

1. Demedts M., Interstitial lung diseases: an epidemiological overview. *Eur Resp J* 2001; 32: 2s
2. Itoh H, Tokunga s, Asamoto h, *et al*: Radiologic-pathologic correlations of small pulmonary nodules with special reference to peribronchiolar nodules, *Am J Roentgeno*l 1978:**130**:223-231.
3. King TE Jr. Clinical advances in the diagnosis and therapy of the interstitial lung disease. *Am J Respir Crit Care Med*.2005; **172**:268-279
4. Raniga S, SharmaS, AroraA, *et al*.The epidemiology Utility of high resolution computed tomography (HRCT) in diagnosis and management of idiopathic pulmonary fibrosis - a study of 10 cases of interstitial lung diseases Chest 2006; **16**: 841-846
5. Bonelli FS, Hartman TE, Swensen SJ, Sherrick A: Accuracy of high-resolution CT in diagnosing lung diseases. *Am.J. Roentgenol* 1998; **170**: 1507-1512
6. Bergin CJ, Muller NL. CT of interstitial lung disease: a diagnostic approach. *Am J Roentgenol* 1987; **148**: 9-15

7. Corcoran HL, Renner WR, Milstein MJ. Review of HRCT of the lung. Radiographics 1992; 12: 917-939
8. Ganesh R, Derek Weycker, John Edelsberg, Williamson Z. Bradford, Oster G. Incidence and Prevalence of Idiopathic Pulmonary Fibrosis. *Am J Respir Crit Care* Med.2006; **174**:810-816
9. Padley SPG, Rubens MB: Diffuse lung disease. In Sutton David: Textbook of Radiology and Imaging. 7thEd 2003; 1: 187-215
10. Wesolowski S, Oniszh K, Kus J. Clinical significance of pattern types of high resolution computerised tomography images of patients with Idiopathic Pulmonary Fibrosis. *Pneumonol Alergol Pol*. 2000; **68** :434-40
11. Flaherty KR; Toews GB; Travis WD; Colby TV; Kazerooni EA; Gross BH; Jain A; Strawderman RL3rd;Paine R; Flint A; Lynch JP 3rd ; Martinez FJ:Clinical significance of histological classification of idiopathic interstitial pneumonia. *Eur Respir J* 2002;**19**: 275-83
12. Flaherty KR, Thwaite EL, Kazerooni EA, *et al*: Radiological versus histological diagnosis in UIP and NSIP: survival implications. *Thorax* 2003; **58**:143-148.
13. Colby TV, Swensen SJ. Anatomic distribution and histopathologic patterns in diffuse lung diseases: correlation with HRCT. *J Thorac Imaging*. *Spring* 1996; **11**: 1-26.
14. Ryu JH, Olson EJ, Midthun DE, Swensen SJ. Diagnostic approach to the patient with Diffuse Interstitial Disease. *Mayo Clin Proc*.2002; 77:1221-1227.
15. Epler GR, McLoud TC, Gaensler EA, *et al*. Normal chest roentgenograms in chronic diffuse interstitial lung disease. *N. Engl J Med* 1978; **298**: 934
16. Nyamande K; Lalloo U G; Vawda F Comparison of plain chest radiography and high-resolution CT in human immunodeficiency virus infected patients with community-acquired pneumonia: a sub-Saharan Africa study. *Brit. J. of radiol.* 2007;**80**:302-306
17. Mathieson JR, Mayo JR, Staples CA, Muller NL. Chronic diffuse infiltrative lung disease: comparison of diagnostic accuracy of CT and chest radiography. *Radiology* 1989; **171**: 111-116