Manage TB
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Lecture - 41
Management of Patients with HIV-TB Coinfection
Session 01

Dear colleagues I am Dr. Narendran, I work as scientist E medical in the Department of Clinical Research in National Institute of Research in Tuberculosis.

I am going to concentrate on management of patients with HIV-TB coinfection, talking about the catastrophic comradeship between the two diseases, going by the statistics you know thanks to the program. Now, measures have been taken that HIV epidemic is a declining epidemic as of now.

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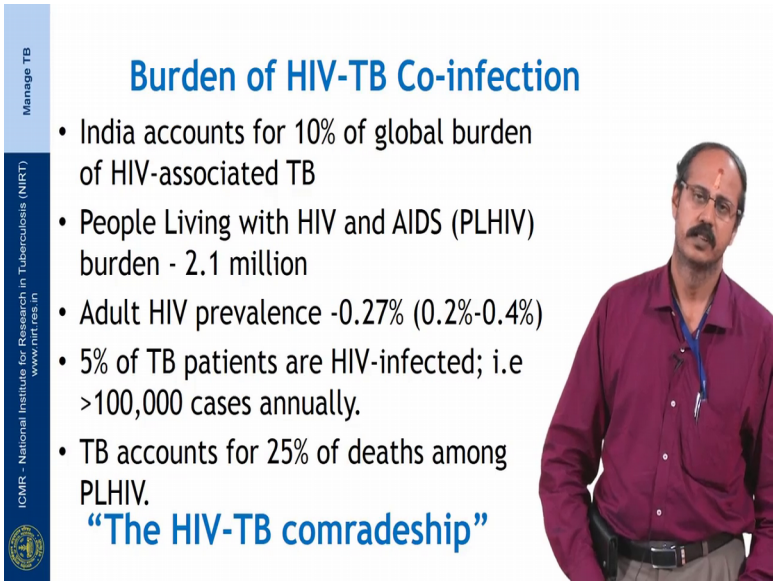

But still because of the rampant progression of TB, we still have importance to this dual diseases, it is a perfect syndromic I tell you because the reason is that, if you take HIV, HIV reduces immunity of the patient, as the CD 4 goes down you have TB creeping. In fact, in all stages of HIV if the CD 4 quite high, you have typical TB with typical manifestations. If you have CD 4's between 200 to 400 or 100 to 200, you have typical

TB with a typical manifestations. As you touch the RBS, you have CD 4 less than 100 you have all other non tuberculosis mycobacteria with both typical and a typical manifestations.

If you look at what TB does to HIV because of the inflammatory cytokines, which are released into the blood, they act like proactive growth factors increasing viral replication. The statistics are here for you to read, HIV complicates every aspect of TB starting from diagnosis up till management. Hence, starting the diagnostic issues even though, pulmonary TB is the commonest TB in HIV also.

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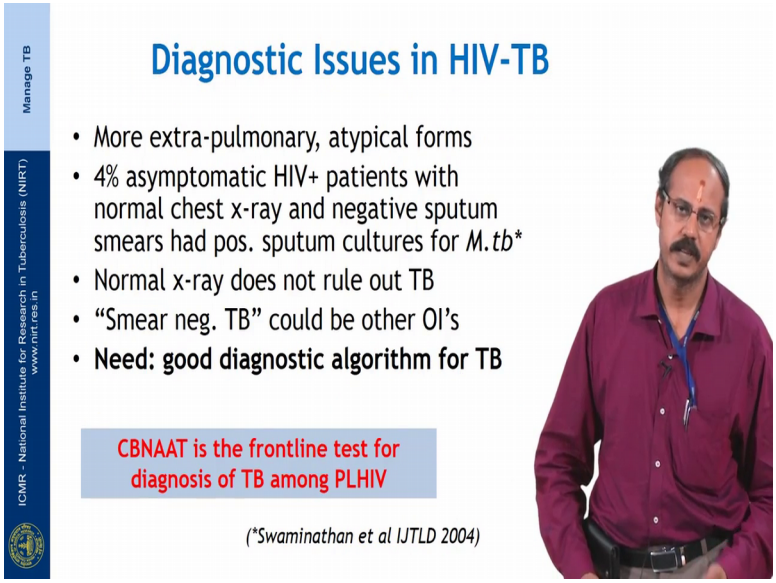

Surprisingly, you will see that there are more extra pulmonary forms, as well as isolated extra pulmonary forms, which are much more frequent than in patients without HIV infection, 4 percent of them asymptomatic HIV we have been able to isolate culture positive for tuberculosis from the paper by Dr. Swaminathan.

Normal X-rays do not rule out TB, if you look at the X-ray in HIV patient as the CD 4 goes down, if the CD 4 is below 100. The typical CD 4 angle it is which is required for you to produce, an inflammation an inside an opacity in the X-ray is not actually there, that is the reason in which in fact, that X-ray is may be normal.

Smear negative TB could be due to wide spectrum of other opportunistic infections, which could infect the patient with HIV. Hence, we are close to getting a good diagnostic algorithm, but still there is a long way to go. The CBNAAT has been a lime line test and has been helpful in various ways, which has been now advocated in the program for HIV patients, one you are able to diagnose very little amount of TB infection.

So, you are able to start treatment very early to your able to diagnose MDR TB at a very very early stage and, try to start the patients or change the management treatment in this patients. More importantly if there is an immune a constraint inflammatory syndrome, CBNAAT will help you to differentiate resistance from iris.

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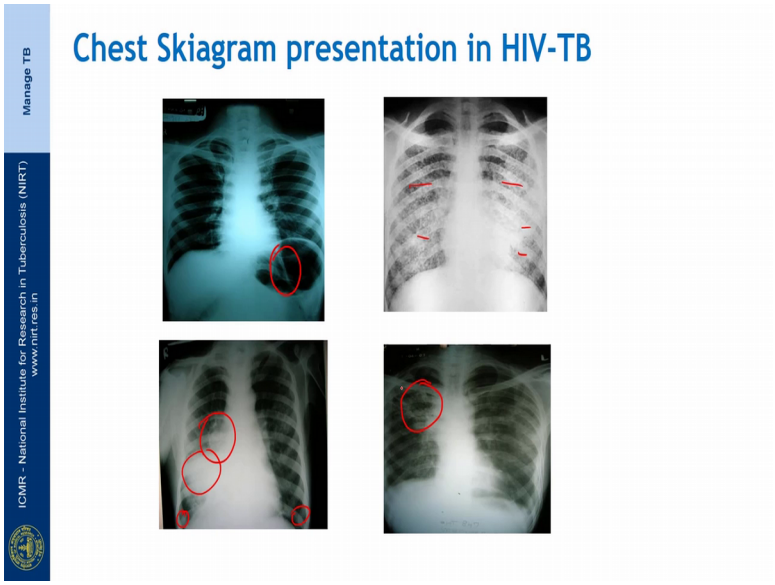

Coming to chest X-rays, you have wide spectrum of presentations, they can range from absolutely normal chest X-ray to complete whiteout of the lungs as in military.

If you look at the chest X-ray in the left, you see it is almost normal, but all that you see which I would like you to appreciate is the (Refer Time: 03:44) shadow almost overlapping the (Refer Time: 03:47) shadow, which shows that beneath the stomach bed, where the plunge shadow is supposed to be there it is absent, which is actually a surrogate marker of immunodeficiency.

If you look on the right you have typical miliary pattern, almost involving the entire lung. Most often you see multitude of lesions, where you have mediastinal adenopathy consolidation floral effusion, floral effusion usually are bilateral, but there absolutely asymmetric. You never have symmetric effusions in HIV, looking at the cavities well dilated well demarcated cavities are conspicuous by their absence, all that you see is small areas of consolidation coalescing to form cavities.

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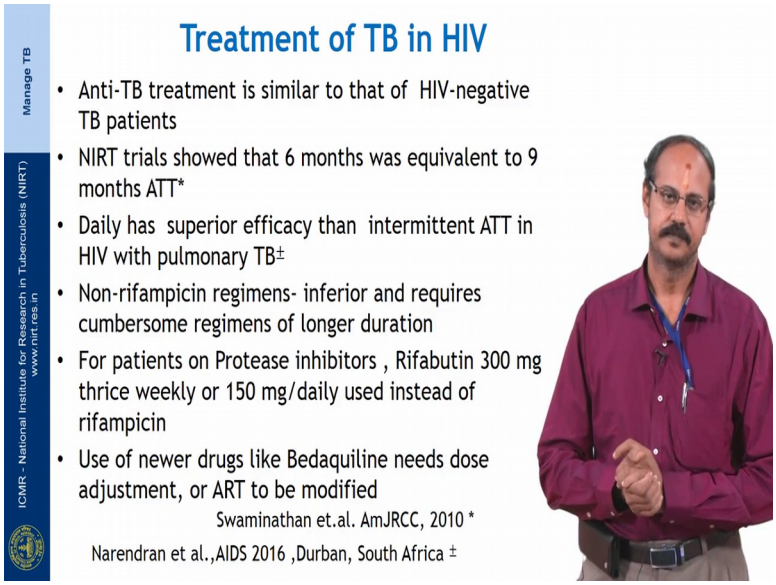

Treatment of TB in HIV, if you look at the anti tuberculosis treatment it is more or less similar to what is being driven in HIV negative patients, based on the trials we have evidence that a 6 months regimen of anti tuberculosis therapy, even if intermittent has got as equivalent results as a 9 months ATT, but we had bacteriological recurseness more, because of the because the study was done in the pre heart era.

Ours is the only global evidence to stay that daily regimen has a better efficacy than intermittent ATT, especially in HIV with pulmonary tuberculosis, but there was a small price to pay in the form of increased nephrotoxicity.

More importantly if you look at the risks and benefits, daily regimen has got the advantage of preventing emergence of drug resistance, which is very very important in

HIV, non rifampicin regimens are quite inferior, they require longer duration of action and more more cumbersome.

And as let to not of non adherence and defaults during drug intake, for patients on protease inhibitors because, they either do not tolerate an ARTs, or they have failed therapy rifabutins an ideal choice, it has been to be given 300 milligram thrice weekly, or can be given 150 milligram daily. It is a very good to substitute for rifampicin because, it has interactions with protease inhibitors

Internationally people have even started giving rifabutin 300 milligram daily looking at the newer drugs bedaquiline and delamanid, they also need to be adjusted when ART is given a efavirenz reduces bedaquiline levels whereas, protease inhibitors increases bedaquiline levels, hence they need to be very closely titrated.

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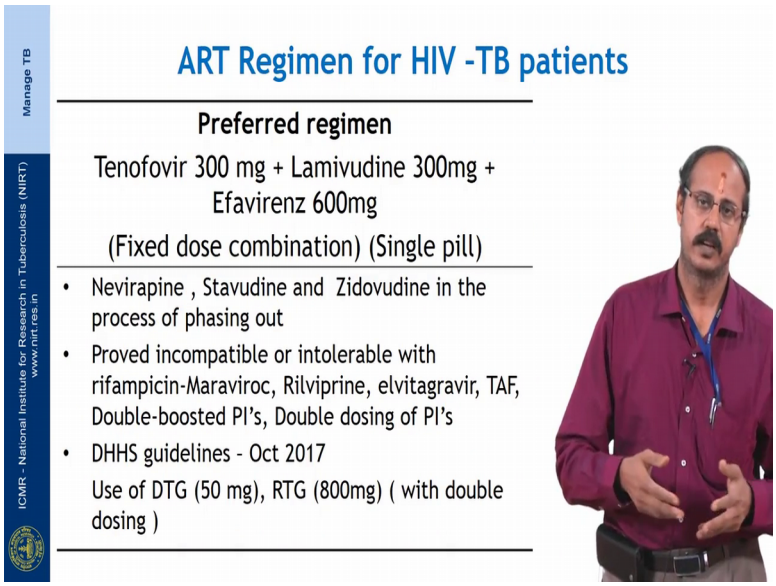

If you look at ART what regimens to give in patients with TB. The preferred choices tenofovir disoproxil, along with lamivudine and efavirenz of course, lamivudine can be substituted with (Refer Time: 06:32).

The advantage is you have an FDC, it is a single pill the pill button is reduced, the lots of

drugs which are getting faced out recently stavudine has already been faced out, nevirapine zidovudine all are because of their side effects. Recent trials have proved that among second line and reserved drugs, there are certain drug which could not be given with rifampicin the CCR 5 inhibitor, maraviroc, rilviprine the integrase inhibitors elvitagravir, more importantly tenofovir, alafenamide even though there is definite advantage of using TAF instead of tenofovir.

Because one tenth of the dose is more than enough and, there is huge reduction and a drastic reduction in renal toxicity as well, as bone marrow density reduction. Now, all these side effects are actually taken care of the TAF, but unfortunately when you are giving it along with rifampicin, it is not possible because TAF doses are reduced to sub therapeutic levels.

We have already clearly rolled out in various trails the double boosted PI's, or double dosing of PI's cannot overcome the problem of rifampicin interaction, recently double dosing of integrase inhibitors both dolutegravir, as well as raltegravir can be safely given with rifampicin, but the trails are still going on for effective conclusion.

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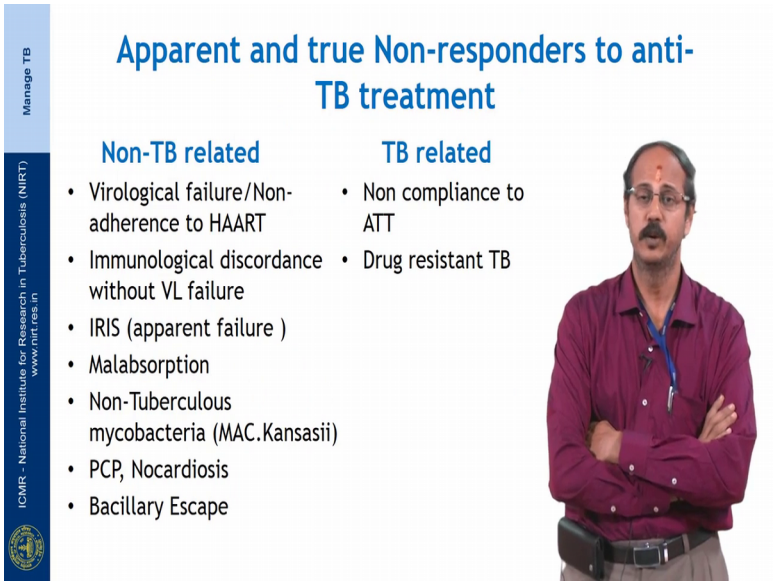

How do we know that the patient has responded, or not this is an important slide for

practising clinicians in HIV and TB care? There are situations in which the patient may respond, but you may take it that the patient is not responding, because of the symptoms and signs that have been presented to you, or it could be that patient is really deuterating, how do you find out now this list is not all inclusive, but the main reasons which need to be evaluated or listed here. You know the TB related is very easy, patient is not taking anti tuberculosis treatment mostly because of alcoholism and drug abuse, or he has developed resistant to TB.

But if you look at the non TB related causes, they are much more important much more frequent for you to see, because they are usually not present, or not overtly presented by the patient. The most important is biological failure, if the patient is failing ART because, he is being take taking the drugs for a month he has been suffering drugs for a month. If you do not ensure adherence, if there is non-adherence if is virological suppression is not perfect, then again there is resurgence of viremia, which can lead to a CD 4 breakdown and that can lead to TB recurrence of failure.

More importantly is the CD 4 level if a if in patients with immunological discordance and the CD 4 does not come up, even though there is effective virological suppression still, you could see that the patient is not responding. He cannot clear the TB bacilli, or any opportunistic infection unless the immunity comes up.

The other is cryptic non adherence due to malabsorption, if the levels are low he is not able to absorb due to various reasons including HIV enteropathy diarrhea with decreased gastric transit time, there could be lots of reasons, but if the levels are low then the tissue levels are much more low that leads to failure.

Coming back to apparent non responders, where the TB has responded. Most important is immune recursion inflammatory syndrome that, because of the inflammation created by the restitution of immunity, you think that the patient has developed symptoms and signs, but actually he is doing well.

The next is non tuberculous mycobacteria, as I told you if the CD 4 is quite low, you can have non tuberculous mycobacteria, where the smear may be positive, but cannot be

caught on the regular conventional cultures we do for M tuberculosis, we need special strains and reagents to prove it is non tuberculosis mycobacteria. In such situations you may think that the patient is not responding. The other mimics or PCP are nocardiosis especially, if there is a pleuropulmonary involvement.

Bacillary escapes are very unique situation, which we find where you have minimal colonies, which are totally resistance you do not have to panic. The classical thing is that the patient is asymptomatic usually.

The cultures and smears have already converted and, suddenly you see a culture less than a grade with a few colonies, throwing up in the sputum examination which is totally resistance that is what we call as bacillary escapes, which can occur in non HIV also. I finish the end of my first session, in the second session, I will try we trying to get into the interaction, or the influence of each of the diseases and what it creates, how it creates problems to the physicians during management.

Thank you.