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Medicine

FRONTLOADING SPUTUM MICROSCOPY: A RELEVANCE IN CASE DETECTION

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ABSTRACT **Background**: In 2019, 7.1 million new cases of Tuberculosis were reported to WHO which fell to 5.8million in 2020 owing to covid-19 pandemic. [1] The present standard sputum microscopy requires PTB suspect to submit a spot sputum sample and an early morning sample, for which he/she has to travel back the next day. This burdens the tuberculosis suspect and results in out-of-pocket expenditure. Hence many suspects drop out during the diagnosis are labelled as "diagnostic defaulters". Front-loaded microscopy is a strategy in which two smears are prepared from two sputum specimens obtained on the first day a patient is assessed. **Aim:** The present study aims to assess if front loading microscopy is as effective as the standard "spot-morning" strategy. **Methods:** This is an institution based cross sectional study that included 200 PTB suspects. Patients unable to produce sputum, relapse, defaulters and extra pulmonary tuberculosis cases were excluded. **Results:** In the present study, total of 143 males (71.50%) and 57 females (28.50%) were recruited. Sputum smear was positive in 36% of morning samples, 34.5% of first spot samples and 32% of second spot samples. Sensitivity of standard and frontloading methods was 93.6% and 87.4%. The specificity was 96.3% for both the methods. Three cases (1.5%) were missed by frontloading method. There is no evidence (p = 0.37) to show that front loading microscopy was less effective when compared to the standard strategy. The kappa value was 0.96, so the strength of agreement was very good. **Conclusion:** The frontloading sputum microscopy method does not require the patient to visit the health facility multiple times. Thus, will lead to lesser drop-out rates and since the report is available on the same-day, it ensures no delay in the initiation of treatment

KEYWORDS : Front-loading microscopy; Pulmonary Tuberculosis; Same day; spot-spot; spot-morning;

INTRODUCTION:

Pulmonary Tuberculosis is one among the most important health problems worldwide. Under the programme conditions, such as those endorsed by the World Health Organization (WHO) [2] and implemented successfully in high burden countries including Revised National Tuberculosis Control Programme (RNTCP) of Government of India [3], the initial diagnostic approach of PTB suspect is based on sputum smear examination. Sputum smear microscopy is a highly specific, inexpensive appropriate technology and is an essential component of the directly observed treatment, short- course (DOTS) strategy.

The program aimed to achieve early detection and treatment of 90% of the estimated cases by 2016.COVID-19 pandemic has threatened the progress achieved over years as seen by 18% fall in case detection worldwide which nearly levels back to 2012. [1] Improvement in the case detection rates will be possible only if there is optimal and adequate usage of quality assured sputum microscopy services

The present standard sputum microscopy requires a Pulmonary Tuberculosis suspect to submit a spot sputum sample and an early morning sample, for which he/she has to travel back the next day. This burdens the tuberculosis suspect and results in out-of-pocket expenditure in the form of transport costs, food and lost wages. Hence many tuberculosis

suspects drop out during the diagnosis labelled as "diagnostic defaulters" and remain untreated, providing more chances for transmission of the disease. [4,5,6]

Rapid culture-based methods for diagnosis of Tuberculosis include rapid automated liquid culture, where results may be available in a few weeks [7]; thin layer agar culture, which has an average turnaround time of 11.5 days [8] and Microscopic Observation Drug-Susceptibility Assay (MODS), which can provide results in an average of 9.2 days [8]. Phage based assays give results in two days. [9] While performance indicators of these techniques might be better than that of smear microscopy, turnaround times are longer. There are also requirements in terms of investment in infrastructure and equipment, leading to higher costs per test.

Nucleic Acid Amplification Tests (NAATs) known as Gene-Xpert attempt to provide accurate and rapid diagnosis of TB using a technology that provides improved sensitivity and specificity functions as compared to sputum smear microscopy. Unfortunately, NAATs have infrastructure and investment requirements that are often beyond the scope of most diagnostic facilities that offer TB diagnostics in rural areas.

TB diagnosis has been facing several challenges in the form of stigma, heath infrastructure awareness and covid-19 pandemic adds to this especially with redirection of health care services.

Front-loaded microscopy is a method in which two smears are prepared from two sputum specimens obtained on the first day a patient is assessed. When all samples are collected and the results are reported on first day, the strategy is termed same-day microscopy. [10]

Gammo M et al [11] in 2013 concluded that sensitivity and specificity of frontloading sputum microscopy is same as that of standard microscopy. Myneedu VP et al [12] in 2011 conducted a pilot study in Lala Ram Sarup Institute of Tuberculosis and Respiratory Diseases, New Delhi, concluded that same day smear microscopy for diagnosing tuberculosis by a proposed new method of smear examination in the case of suspected tuberculosis seems not only a promising step towards improving the quality of sputum smear examination but definitely improved patients' compliance.

Therefore, this study has been formulated to characterize the frontloading microscopy technique in rural Indian background and determine its efficacy in resource limited country like ours. This study was conducted in Designated Microscopy Centre in Mamata General Hospital, Telangana to assess if front loading "spot-spot" microscopy is as effective as the standard "spot-morning" strategy in detecting sputum smear positive Tuberculosis and to evaluate & validate its efficacy in terms of its sensitivity & specificity.

MATERIAL AND METHODS

Study setting and Patient selection

This is an Institutional based cross- sectional study conducted over a period of two years (2013-2015) done on randomly selected two hundred Pulmonary Tuberculosis suspects. Adults who have symptoms suggestive of Pulmonary Tuberculosis: persistent cough with expectoration more than two weeks as per RNTCP guidelines were included. Patients unable to produce sputum: with extra Pulmonary Tuberculosis, already on antituberculosis treatment and with past history of Pulmonary Tuberculosis & HIV were excluded from this study.

In this study, patients who agreed for voluntary participation were enrolled. Patients were provided with sputum container and were asked to submit sputum specimens as per RNTCP guidelines i.e., one on the spot specimen at the time of first visit and second specimen collected at home the very next day morning and bring the sample to the laboratory. In the newer method, the same patient deposits second sample as spot specimen collected at the time of first visit collected one hour after first spot sample.

Quality control of the ZN smear was maintained by systematic and effective internal quality scheme as per RNTCP guidelines in order to maintain the error within acceptable limits.

Data analysis

The sensitivities, specificities, negative predictive values (NPV) and positive predictive values (PPV) of sputum smear microscopy for both methods were determined. Their 95% confidence intervals were also determined and the kappa statistic (with its p-value) was used to determine the level of agreement between the two methods. Microsoft Excel and SPSS software was used for analysis.

RESULTS:

In the present study, 143 males (71.50%) were more commonly affected than 57 females (28.50%) with male to female ratio of 2.5:1. The most common age group was found to be 51- 60 years i.e., 59 patients (26%) followed by 38 patients (19%) in 31-40 years age group, The mean age of presentation was 45.88 years.

Sputum smear was positive in 72 (36%) of morning samples, 69 (34.5%) of first spot samples and 64 (32%) of second spot samples. Smear grading was done as per WHO guidelines

Table 01-shows positive rates among the sputum sample

Sputum sample N=200	Morning	Spot 1	Spot 2
Positive	72(35%)	69 (34.5%)	64 (32%)
Negative	128	131	135

The sensitivity of frontloading method was 87.4% and to standard method was 93.6%. The specificity was 96.3% for both the methods. The positive predictive value for both methods was 0.93 and negative predictive value shows for standard method was 0.96 and frontloading method was 0.92. The total number of sputum smear positive cases by standard method was 72 cases (36%) whereas total number of sputum smear positive cases by frontloading method was 69(34.5%). In the present study three cases (1.5%) were missed by frontloading method in comparison with standard method.

There is no evidence (p = 0.37) to show that front loading "spot-spot" microscopy is less effective when compared to the standard "spot-morning" strategy in detecting sputum smear positive tuberculosis. Kappa value denotes strength of agreement between both the methods (k= 0.81-1 implies very good agreement). Kappa value in present study was 0.96. Statistical analysis of comparison of both the methods is depicted below.

Table 2 showing sputum smear grading in both conditions NPV negative predictive value PPV positive predictive value

Table 2	Standard method	Front loading method
Sensitivity	93.6	87.4
Specificity	96.3	96.3
PPV	0.93	0.93
NPV	0.96	0.92

Table 3-showing agreement between both the methods

Observed agreement	Expected agreement	Kappa	Standard error	Z-value	P-value
98.5%	54.34%	0.96	0.0188	0.3132	0.3771

DISCUSSION:

Sputum smear microscopy has been the primary method for diagnosis of pulmonary tuberculosis in low- and middle-income countries. It is a simple, rapid and inexpensive technique which is highly specific in areas with a very high prevalence of tuberculosis. [13] Hence, it has been an integral part of the global strategy for TB control.

Smear microscopy remains the cornerstone for the diagnosis of tuberculosis in developing countries (Schirm et al. 1995) as alternative diagnostic tests are associated with long turnaround times and or require complex technologies not suitable for the lower strata of health services where most patients are present. [14]

Strategies to improve the efficiency of sputum smear microscopy, the most widely available method for diagnosis of pulmonary tuberculosis, could improve rates of case detection and treatment initiation in countries with a high incidence of the disease.

Until 2007, WHO recommended that individuals with suspected pulmonary tuberculosis provide three sputum specimens for smear microscopy on two consecutive days, with one spot specimen collected immediately and one early morning spot and one additional spot specimen collected the next day.

At that time, noting that the third specimen increases cumulative sensitivity by only two- five percent [15], WHO began recommending that quality-assured laboratories examine only two sputum specimens.[16] This policy sought to decrease laboratory workloads and costs [17] and to increase time for smear examination [18,19] but did not address another disadvantage of smear microscopy: the need for the patient to visit a health center more than once.

The high costs of transportation, food, and lost wages associated with diagnostic visits can approach 50% of the household income of patients with suspected tuberculosis, which is a burden that measurably worsens poverty levels for these patients and their families, and leads a large proportion (13–95%) to drop out of the diagnostic pathway before completing sputum examination, receiving results, or starting treatment. [4,5,6, 20-26]

In 2009, WHO convened an Expert Group to summarize the evidence supporting same- day smear microscopy for the Strategic and Technical Advisory Group for Tuberculosis (STAG- TB), which subsequently issued a new policy. [10]

Davis et al cited in their meta-analysis that same-day and front-loaded diagnostic strategies are a relatively new idea. All identified studies were done recently, with the earliest publication from 2007. [27]

The various studies done along with present study showed that frontload sputum microscopy was equally effective as standard sputum microscopy shown below

Table 04- Various Studies Comparing Sensitivities And Specificities Of Standard Method And Frontload Method

	Standard method		Frontloading method	
	sensitivity	Specificity	Sensitivity	Specificity
Present study	93.6%	96.3%	87.4%	96.3%
Miremba P et al [28]	91%	91.7%	91%	86.2%
Ramsay et al Nepal [29]	69%	98 %	67%	99%
Ramsay et al Nigeria [29]	58 %	98 %	56 %	98 %
Ramsay et al Yemen [29]	71 %	100 %	67%	100 %
Cattamanchi et al [30] Uganda	56 %	97 %	55%	98 %
Cuevas et al Ethiopia [31]	64%	96 %	62%	97 %
Cuevas et al Nepal [31]	86 %	99 %	80 %	99 %
Cuevas et al Nigeria [31]	62 %	96 %	70%	96 %
Cuevas et al Yemen [31]	65 %	99 %	60%	98 %
S Hirao et al [32]	57.7%	64.8%	56.4%	63.6%
Myneedu VP et al [12]	58.25	99.5%	40.07	99.5%

This study was undertaken to improve case detection in resource limited settings. But it also seems appropriate in covid-19 pandemic. Lock downs, transportation difficulties, multiple contacts, loss of employment, salary deductions, stigma and fear of Covid-19 infection

has fuelled TB epidemic. Hence the frontload sputum microscopy needs to be emphasized and is relevant along with the development of broader policies that prioritize infection control measures, minimize covid related disruptions and fastrack diagnosis of Tuberculosis.

CONCLUSION

Frontloading microscopy was equally effective as standard approach. It would increase the patient's compliance and help in reducing the diagnostic defaults.

The development of diagnostic approaches that are responsive to the needs of the population may be feasible, and larger studies are urgently required to validate the findings of this study under operational conditions.

Developing strategies to improve the efficiency and sensitivity of smear microscopy is an urgent priority for global TB control.

Although tremendous improvement has occurred in the control of TB in India, much more is to be achieved and we need to be determined to improvise, innovate and act to move forward.

Limitations

The development of diagnostic approaches that are responsive to the needs of the population may be feasible, and larger studies are urgently required to validate the findings of this study under operational conditions.

If the findings of this study are confirmed, smear microscopy services should be front loaded in the interests of equity and improved TB control.

In this study, drop-out rate was not considered which may be relevant with present scenario.

There could be concerns about the potential effects of same-day microscopy on tuberculosis and other disease transmission, because patients could spend additional time at the health facility on the day of initial assessment while submitting a second specimen and waiting for results.

Ultimately, if same-day microscopy can ensure that all smear-positive patients receive immediate tuberculosis treatment, the benefits in reduced tuberculosis transmission in the community would probably outweigh the nosocomial transmission risk arising from having patients waiting for an additional one hour.

Under field conditions or in the microscopy center, not enough time is spent in motivating the patient to bring out a good quality sputum sample, which is the mainstay of the whole RNTCP programme.

Morning specimens have repeatedly shown greater bacillary load and high sensitivity than spot samples. Hence, the majority of the clinicians are reluctant to rely on the negative result of spot specimens.

Of course, ethically and ideally, one should not miss out on any case but if this loss of positivity against the advantage of returning the patients and preventing dropouts, this scheme of same-day microscopy is justified.

Moreover, this same day diagnostic approach for pulmonary TB can help to initiate therapy on the same day and can save time as well as resources of the patients.

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