

Utility of Gastric Lavage for Diagnosis of Tuberculosis in Patients who are Unable to Expectorate Sputum

Parvaneh Baghaei, Payam Tabarsi, Parisa Farnia, Amir Hoseyn Radaei¹, Mehdi Kazempour, Yazdan Ali Faghani¹, Mehdi Mirsaiedi, Atieh Novin, Ehsan Chitsaz, Davoud Mansouri, Mohammad Reza Masjedi, Ali Akbar Velayati

Clinical Tuberculosis and Epidemiology Research Center, N. R. I. T. L. D, Masih Daneshvari Hospital, Shaheed Beheshti University of Medical Science and Health Services, ¹ Azad Medical University, Tehran, Iran

ABSTRACT

Background: There are number of patients who are unable to expectorate sputum specimens. In this study, we used gastric lavage (GL) test for diagnosis of tuberculosis (TB) in patients who were unable to produce sputum. **Materials and Methods:** Patients who were unable to produce sputum specimens were included in the study to confirm TB disease. Gastric lavage sampling was performed and sent for acid fast bacillus smear and culture under special laboratory conditions and sterilized methods. Further bronchoscopy for broncho-alveolar lavage was done on patients with negative GL smear results. Drug susceptibility tests were performed on 48 GL culture positive cases. **Results:** Eighty-five patients were included in the study; who were hospitalized at our referral center for suspected TB. GL smears were reported to be positive in 37 cases (66.07%) and culture in 85.7%. The total number of smear and culture-positive cases in this study was 48 (85.7%). Forty cases (87%) of drug-sensitive, 1 case (2.2%) of isoniazid and rifampin-resistant TB (multi-drug resistant; MDR), and 5 cases of resistant to one drug were detected. There have not been observed any complications after the GL method. **Conclusion:** It seems that regarding the high number of positive GL cultures (85.7%), GL can be effective for diagnosis of patients who have suspicious tuberculosis symptoms and are unable to produce sputum especially in resource limited areas.

Key words: Acid fast bacillus, Broncho-alveolar lavage, Gastric lavage, Isoniazid, Rifampin, Tuberculosis

INTRODUCTION

Increasing incidence of tuberculosis (TB) as well as the escalating trend of resistance to anti-TB drugs has attracted much attention during the past decades and has turned out the need for early microbiological confirmation of TB and drug sensitivity testing more than ever.^[1] On the other hand, approximately 50% of patients with suspected active TB are either unable to produce sputum or demonstrate a negative sputum smear for acid fast bacillus (AFB).^[2] Thus, in such cases developing alternative methods to obtain sputum specimens are necessary. Sputum induction (SI), bronchoalveolar lavage (BAL), and gastric lavage (GL) procedures are among the most common methods to obtain required samples. However,

each of these procedures have their own advantages and disadvantages. Bronchoscopy for BAL requires special facilities and is not accessible in many regions because of the limited resources. Additionally, bronchoscopy is not feasible for all patients due to its invasive nature.^[3,4] Although the SI method has yielded favorable results, its use mandates having access to isolation rooms with negative pressure which is not currently available in many health care facilities.^[3,5] The GL method is preferred in diagnosis of TB in children who swallow their sputum and cannot expectorate.^[6-8] However, this method has reportedly yielded different results in various studies. The main shortcoming is in most of the previous studies, the limited rate of positive culture in GL specimens which makes its positive smear results unreliable.^[9,10]

Therefore, in order to confirm the clinical and radiological findings in patients with suspected active TB who are not able to give sputum samples, we used GL to obtain specimens for bacteriologic confirmation.

Address for correspondence:

Dr. Parvaneh Baghaei, E-mail: pbaghaei@gmail.com

Access this article online

Quick Response Code:



Website:
www.jgid.org

DOI:
10.4103/0974-777X.91054

In this study, we attempted to determine the diagnostic accuracy of GL in the aforementioned population.

MATERIALS AND METHODS

The study was carried out in the Mycobacteriology Research Center at Masih Daneshvari Hospital which is the National Research Institute of Tuberculosis and Lung Disease (NRITLD); in Tehran, Iran from January 2008 to December 2008. Those patients, suspected for TB with clinical and radiological findings, were included in this study who met the following criteria: (1) being above 15 years of age; (2) having no history of receiving previous or current anti-TB medication; (3) being unable to expectorate sputum samples; and (4) having no immunodeficiency or HIV infection. GL was done once for any patient. All GL specimens were sent for AFB smear and culture. In the case of negative smear results, BAL was undertaken in order to obtain a conclusive diagnosis. Anti-TB treatment was initiated for patients whose smears turned positive for *Mycobacterium tuberculosis* (MTB).

Gastric lavage

An appropriate-sized nasogastric (NG) tube was placed transesophageally in the stomach of a fasting patient early in the morning before getting out of the bed. The stomach was washed with 50 ml of normal saline pushed via NG tube, and then the gastric content was aspirated. The sample was collected in a sterile plate, placed on ice and delivered to the mycobacteriology laboratory immediately.

Bronchoalveolar lavage

Fiber-optic bronchoscopy was performed on fasting patients whose GL smear results were negative. Bronchoalveolar lavage (BAL) samples were collected from affected lung lobes. Approximately, 20-30 ml aliquots of sterile saline solution up to a total of 100 ml were aspirated of the affected segments and then about 10-15 ml aspiration samples were collected and placed on ice and delivered to the Mycobacteriology Laboratory immediately.

Clinical specimens

In the laboratory, the GL fluid samples were immediately adjusted to neutral pH using 100 mg sodium carbonate. Then, the specimens were cultured on Löwenstein-Jensen (LJ) slants. Briefly, for culture, the samples were digested and decontaminated, using the Petroff method, with sodium hydroxide at a 2% final concentration. After 15 minutes of digestion, the samples were centrifuged at

3000 g for 30 minutes and decanted, leaving a volume of 1-2 ml of sediment. Following this procedure, the sediment was neutralized with few drops of N-hydrochloric acid and washed with 10 ml phosphate buffered saline (0.067M, pH 6.8). The remaining sediment was reconstituted in 2 ml of sterile phosphate buffered saline. 200 µl of this suspension was inoculated into LJ culture slant. Smears were prepared from the concentrated sediment of the specimen for Ziehl-Neelsen (ZN) acid-fast microscopy. For all patients with positive culture ($n=48$), drug susceptibility test (DST) was done. DST for isoniazid (INH), rifampin (RMP), streptomycin, and ethambutol (EMB) was performed by the proportion method on LJ media at concentrations of 0.2, 40, 4.0, and 2.0 mg/ml, respectively. Resistance was labeled if number of the colonies on the drug-containing medium was more than 1% number of the colonies on drug-free medium. Susceptibility to pyrazinamide (PZA; 900 and 1200 mg/ml) was tested using a 2-phase medium where the strain was reported to be resistant to PZA if, on day 21, the proportion of drug resistant colonies was higher than the defined critical proportion. The method of DST was described in previous publications in the fullest detail.^[11,12] The positive smears and cultures were gathered and analyzed for sensitivity. Statistical analysis was performed using SPSS V.13 software. The scientific and ethics committee of NRITLD approved the study protocol.

RESULTS

Eighty-five patients were included in the study. The majority of the patients were women (80; 94%). Most patients (72; 84.7%) were Iranian and the remainder came (15.3%) from the neighboring country Afghanistan. The mean age of the patients was 61.9 ± 18.9 . Diagnosis of TB was confirmed in 56 patients with isolating MTB from their specimens. Out of confirmed 56 cases, 37 (66.07%; 95%CI: 53-77%) were revealed MTB in the smear of the specimens taken via GL. Sensitivity and specificity of GL smear were 66.07% (37/56) and 100% (29/29), respectively [Figure 1].

As well, GL specimens' culture for MTB became positive in 48 (85.7%; 95% CI: 74.2-99.2%) patients. Sensitivity and specificity of GL culture were 85.7% (48/56) and 100% (37/37) respectively.

Overall, a total of 48 (85.7%; 95% CI: 74.2-99.2%) patients had both smear and culture positive results for MTB in their GL specimens.

In 11 patients with negative GL smears, the culture of GL rendered positive results. DST was performed for the 46 patients with positive culture. The DST was not

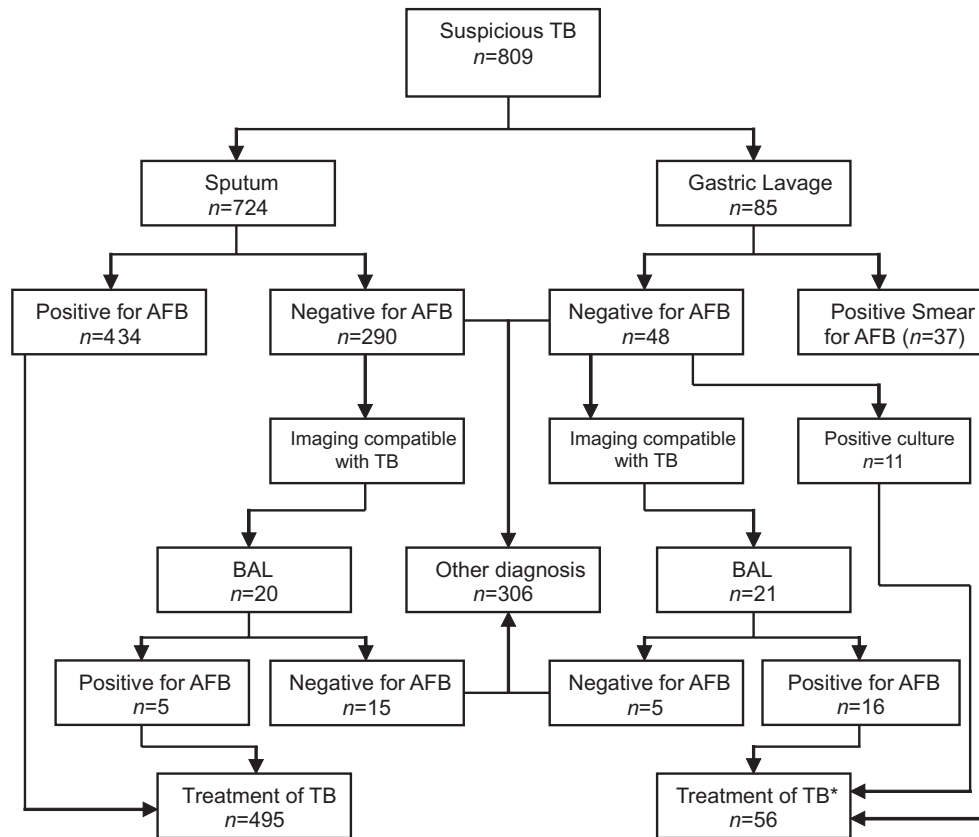


Figure 1: The algorithm of diagnosis of tuberculosis in suspicious patients, AFB: acid fast bacilli, BAL: broncho-alveolar lavage, *8 patients with BAL smear positive were GL culture positive so the total of TB patients was 56

done for two culture positive patients because technical problems happened in the Mycobacteriology Labor. MTB was sensitive to all drugs in 40 cases (87%), was resistant to one drug in five cases (10.9%), and the pathogen was multidrug-resistant (MDR) in one case (2.2%). We performed polymerase chain reaction (PCR) to confirm the presence of MTB in the suspected MDR case which had ultimately a positive PCR. There were no adverse effects reported during or after GL in the study.

DISCUSSION

Even though clinical and radiological findings can provide to some extent, useful information on diagnosis of TB, isolating MTB from the patients' specimens is crucial. In addition, the separation of the mycobacterium is needed in order to perform DST.^[1,13] Meanwhile, microbiological confirmation of TB in patients who are unable to produce sputum is problematic.^[2] In this regard, a number of methods including GL, BAL, and sputum induction (SI) exist to facilitate the sample collection. Heather *et al* stated SI is better than GL in children because three GL were necessary to obtain the same yield as one induced sputum

specimen and the risk of nosocomial transmission is lower in children than in adults.^[14] But SI should be done in a room with adequate ventilation and personal respiratory protection.^[15] On the other hand, bronchoscopy causes coughing and leads to an increased risk of respiratory dissemination of TB.^[16] The GL method is found to be an efficient and beneficial which does not require specific facilities. This method is commonly used among children; however, its utility and results have varied among adults.^[6,7,9,10] In our study, there were no complications after GL.

The main drawback with the previous studies was observing low numbers of positive GL cultures in comparison to their corresponding positive GL smears results obtained in the patients.^[3,10,13,17] For instance, in Rizvi *et al*'s study the sensitivity of GL smear was determined approximately to be 90%, whereas positive cultures were present in only 40% of the cases. In our study, these values were found to be 66.07% and 85.7%, respectively. A summary of our results compared to other studies is depicted in Table 1.

There were possibly two reasons for low rates of positive GL culture despite high rates of concomitant positive smears in the previous studies.

Table 1: The used procedures in the literature and their results compared to our findings

Studies	Patients	The used procedures in studies					
		GLs [†] positive	GLc [†] positive	BALc ^{**}	SLc ^{**} positive	Sc [†] positive	All procedures*
Norrman <i>et al</i> ^[9]	63 adults	-	7 (12)	13 (21)	-	-	-
Rizvi <i>et al</i> ^[20]	20 adults	16 (80)	6 (30)	14 (70)	-	-	-
Okutan <i>et al</i> ^[23]	107 adults	30 (61)	15 (31)	47 (81)	-	-	-
Zar <i>et al</i> ^[24]	250 children	17 (7)	38 (15)	-	51 (20)	-	-
Uskul <i>et al</i> ^[26]	38 adults	-	17 (49)	18 (55)	-	23 (66)	36 (95)
Singh <i>et al</i> ^[20]	58 children	-	10 (17)	12 (21)	-	-	20 (34)
Jones <i>et al</i> ^[23]	155 adults	-	59 (30)	-	176 (51)	-	176 (51)
Our study	85 adults	37 (66)	48 (86)	-	-	-	-

[†]GLs: gastric lavage smear; [†]GLc: gastric lavage culture; ^{**}BALc: broncho-alveolar lavage culture; ^{**}SLc: sputum induction culture; [†]Sc: sputum culture, *When the procedures are used together, these procedures complement each other and increase positive culture and double the diagnosis yield; Figures in parenthesis are in percentage

1. Effect of not neutralizing samples and the collection of the specimens for the period of 1-2 weeks, that makes some microorganisms die in the presence of the gastric acid (low pH).
2. Inappropriate decontamination: Which may cause the mycobacterium to be trapped in the mucus and make its growth in culture media improper.^[10]

In this study, our samples were immediately transferred to the laboratory following having been collected, and the neutralization and decontamination were done as described earlier. Therefore, this may be the likely cause that we have observed higher rates of positive GL culture in comparison to other studies. Interestingly, this rate of positive GL culture (with GL sampling once) is comparable to the results obtained by BAL sampling in other studies.^[10,18] Against GL without any inhibitor, using topical anesthetics such as tetracaine and lidocaine during bronchoscopy inhibit the growth of MTB and other bacteria.^[19] In a study by Singh *et al* is shown that there are no differences in mycobacterial isolation rates from GL and BAL.^[20]

In previous studies, some authors have proposed that disproportionate GL smear and culture results can be presumed as the consequence of nontuberculous mycobacteria (NTM).^[10,13] Since the patients under our study had clinical and radiological manifestations suggestive for TB, it is most likely that the AFB observed in the smear was MTB.^[13] On the other hand, in GL positive cultures, the characteristics of MTB in culture plate (slow grower, nonpigmented, nonchromogen, rough, waxy, dry, Niacin and NO₃ reduction test positive) were detected and the DST demonstrated that in most of the cases MTB was sensitive to the first-line drugs. Therefore, considering the fact that most NTM are resistant to the first-line drugs, our finding confirmed that isolates obtained from the GL positive cases in our study were in fact MTB.^[21]

As well, in one suspected MDR case, we confirmed the presence of the MTB, rather than NTM, by PCR. This demonstrates that GL is efficient for the microbiological confirmation of TB and high rates of culture positive cases yield the possibility to perform DST.^[10] Another noteworthy factor was the absence of complications due to GL during our study. Notably, it can be compared to major adverse events of bronchoscopy in a study by Dang *et al* that they stated this technique is safe and they had less major complications like pneumothorax just in three patients occurred within 4 hours of bronchoscopy.^[22] However the aim of this study was not to evaluate the efficacy of BAL procedure, there were no major complication of BAL in 21 patients.

Another issue was that the most patients unable to give sputum specimens were female whose rationalization is not addressed here.

The hypothesis that performing GL for several times would increase its sensitivity is not investigated in most of previous studies.^[10,17] So, this indicates the need for further studies on the subject to reveal much more features and capacity of this diagnostic method.

Our study also carried some limitations. The study is undertaken in the national referral. So, at least in part, the findings may not be the exact representation of the general population. As well, we did not perform BAL for all patients, a factor that may affect the findings in different ways.

CONCLUSION

In summary, MTB can be isolated for smear and culture using a simple, rapid, and economic procedure; GL. In this study MTB was detected in 85.7% of cases suspected for TB who could not efficiently expectorate to give sputum samples. Additionally, a substantially high rate of positive cultures obtained in our study is of note. Thus,

GL seems to be an appropriate tool to obtain samples for mycobacteriologic confirmation of TB in patients with suspected TB who cannot produce sputum especially in resource limited areas.

REFERENCES

- Mirsaeidi M, Tabarsi P, Farnia P, Ebrahimi G, Morris M, Masjedi M, *et al.* Trends of drug resistant *Mycobacterium tuberculosis* in a tertiary tuberculosis center in Iran. *Saudi Med J* 2007;28:544-50.
- Sputum-smear-negative pulmonary tuberculosis: Controlled trial of 3-month and 2-month regimens of chemotherapy. *Lancet* 1979;1:1361-3.
- Brown M, Varia H, Bassett P, Davidson R, Wall R, Pasvol G. Prospective study of sputum induction, gastric washing, and bronchoalveolar lavage for the diagnosis of pulmonary tuberculosis in patients who are unable to expectorate. *Clin Infect Dis* 2007;44:1415-20.
- Kent R, Uttley A, Stoker N, Miller R, Pozniak A. Transmission of tuberculosis in British centre for patients infected with HIV. *BMJ* 1994;309:639-40.
- Larson J, Ridzon R, Hannan M. Sputum induction versus fiberoptic bronchoscopy in the diagnosis of tuberculosis. *Am J Respir Crit Care Med* 2001;163:1279-80.
- Abadco D, Steiner P. Gastric lavage is better than bronchoalveolar lavage for isolation of *Mycobacterium tuberculosis* in childhood pulmonary tuberculosis. *Pediatr Infect Dis J* 1992;11:735-8.
- Somu N, Swaminathan S, Paramasivan C, Vijayasekaran D, Chandrabhooshanam A, Vijayan V, *et al.* Value of bronchoalveolar lavage and gastric lavage in the diagnosis of pulmonary tuberculosis in children. *Tuber Lung Dis* 1995;76:295-9.
- Shingadia D, Novelli V. Diagnosis and treatment of tuberculosis in children. *Lancet Infect Dis* 2003;3:624-32.
- Norrman E, Keistinen T, Uddenfeldt M, Rydström P, Lundgren R. Bronchoalveolar lavage is better than gastric lavage in the diagnosis of pulmonary tuberculosis. *Scand J Infect Dis* 1988;20:77-80.
- Rizvi N, Rao N, Hussain M. Yield of gastric lavage and bronchial wash in pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2000;4:147-51.
- Canetti G, Froman S, Grosset J, Hauduroy P, Langerova M, Mahler HT, *et al.* Mycobacteria: Laboratory methods for testing drug sensitivity and resistance. *Bull World Health Organ* 1963;29:565-78.
- Kubica GP. Susceptibility testing of tubercula bacilli. In: Bondi A, Bartola JT, Prier JE, editors. *The clinical laboratory as an aid in chemotherapy of infections diseases*. Baltimore, USA: University Park Press; 1977. p. 107-14.
- Okutan O, Kartaloglu Z, Kilic E, Bozkanat E, Ilvan A. Diagnostic contribution of gastric and bronchial lavage examinations in cases suggestive of pulmonary tuberculosis. *Yonsei Med J* 2003;44:242-8.
- Zar H, Hanslo D, Apolles P, Swinger G, Hussey G. Induced sputum versus gastric lavage for microbiological confirmation of pulmonary tuberculosis in infants and young children: A prospective study. *Lancet* 2005;365:130-4.
- Jensen P, Lambert L, Iademarco M, Ridzon R. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR Recomm Rep* 2005;54:1-141.
- Uskul B, Turker H, Kant A, Partal M. Comparison of bronchoscopic washing and gastric lavage in the diagnosis of smear-negative pulmonary tuberculosis. *South Med J* 2009;102:154-8.
- Dickson S, Brent A, Davidson R, Wall R. Comparison of bronchoscopy and gastric washings in the investigation of smear-negative pulmonary tuberculosis. *Clin Infect Dis* 2003;37:1649-53.
- Baughman RP, Dohn MN, Loudon RG, Frame PT. Bronchoscopy with bronchoalveolar lavage in tuberculosis and fungal infections. *Chest* 1991;99:92-7.
- Conte BA, Laforet EG. The role of the topical anesthetic agent in modifying bacteriologic data obtained by bronchoscopy. *N Engl J Med* 1962;267:957-60.
- Singh M, Moosa NV, Kumar L, Sharma M. Role of gastric lavage and broncho-alveolar lavage in the bacteriological diagnosis of childhood pulmonary tuberculosis. *Indian Pediatr* 2000;37:947-51.
- Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, *et al.* An official ATS/IDSA statement: Diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med* 2007;175:367-416.
- Dang D, Robinson P, Winnicki S, Jersmann H. The safety of flexible fiberoptic bronchoscopy and proceduralist-administered sedation: A tertiary referral center experience. *Intern Med J Epub* 2010 May 11.
- Jones FJ. The relative efficacy of spontaneous sputa, aerosol-induced sputa, and gastric aspirates in the bacteriologic diagnosis of pulmonary tuberculosis. *Dis Chest* 1966;50:403-8.

How to cite this article: Baghaei P, Tabarsi P, Farnia P, Radaei AH, Kazempour M, Faghani YA, *et al.* Utility of gastric lavage for diagnosis of tuberculosis in patients who are unable to expectorate sputum. *J Global Infect Dis* 2011;3:339-43.

Source of Support: Nil. **Conflict of Interest:** None declared.