



Published in final edited form as:

Asia Pac J Public Health. 2022 March ; 34(2-3): 258–261. doi:10.1177/10105395211060119.

Evaluation of Sputum-Culture Results for Tuberculosis Patients in the United States-Affiliated Pacific Islands

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Abstract

Sputum-culture confirmation guides tuberculosis (TB) diagnosis and patient management but has previously been reported to be low in the US-Affiliated Pacific Islands (USAPI). We evaluated factors associated with positive sputum-culture results by analyzing TB case surveillance and laboratory data, including sputa quality and quantity for diagnostic specimens from the USAPI. A lower proportion of sputum specimens were reported as culture positive from the USAPI (42%), compared with Hawaii (58%) and the United States (55%). Few (3%) sputa collected from TB patients in the USAPI had both optimal quality and quantity; 40% had optimal quality (mucoïd), and 7% had optimal quantity (>5 mL). Suboptimal sputum specimen quality and quantity contributed to fewer sputum-culture positive results in the USAPI. Improving sputum collection and handling might lead to more culture positive results and ultimately improve patient care and TB control in USAPI.

Keywords

clinical laboratory techniques; public health surveillance; sputum specimen; tuberculosis

Sputum-culture confirmation guides TB diagnosis and patient management.¹ However, the U.S.-Affiliated Pacific Islands (USAPI)¹ previously reported lower proportions of *M. tuberculosis* (*Mtb*) culture confirmation compared to the rest of the United States.^{2,3}

We hypothesized factors contributing to a low proportion of culture confirmation in USAPI could be due to (a) higher proportions of pediatric patients (age < 15 years) with

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Author Contribution

Smita Ghosh, Derrick Felix, Richard Brostrom, Angela Starks, and Ben Silk conceptualized the study. Smita Ghosh and Ben Silk drafted the manuscript. All co-authors revised it critically for important intellectual content and approved the final version for publication.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Supplemental Material

Supplemental material for this article is available online.

paucibacillary disease and sputum collection challenges⁴ and (b) more extrapulmonary TB patients for whom sputum tests may not be ordered.⁵ Additional factors included sub-optimal sputum quality and quantity resulting from specimen collection, handling, and transport to a remote off-island laboratory, contributing to specimen overgrowth (resulting from contamination with other bacteria).⁶⁻⁸

Understanding patient- and laboratory-related factors associated with low sputum-culture positive results can improve diagnoses and case management in USAPI.

Methods

We analyzed data from the National Tuberculosis Surveillance System (NTSS) for TB cases reported during 2010 to 2017 and USAPI specimen data collected during October 3, 2015 to September 26, 2018 from a commercial laboratory in Hawaii contracted by the Centers for Disease Control and Prevention (CDC). A TB case is verified by isolation of *Mtb complex* from a clinical specimen through culture, or a positive nucleic acid amplification test, or by a positive smear; otherwise TB is verified through clinical or provider diagnosis. USAPI includes the 3 US territories of American Samoa (AS), the Commonwealth of the Northern Mariana Islands (CNMI), and Guam (GU) as well as the independent nations of the Federated States of Micronesia (FSM), Republic of the Marshall Islands (RMI), and Republic of Palau (PW).

For each unique patient, a diagnostic specimen was defined as the first or second sputum specimen (i.e., initial diagnostic series) as indicated by the specimen collection date. Transport time was calculated as the median number of days from specimen collection to receipt. Diagnostic specimens were considered optimal quality and quantity if they were of mucoid consistency (determined by visual observation upon receipt) and >5 mL in volume, respectively.⁹ Volume cutoffs were pre-selected by the contracted laboratory.

We computed a Pearson's chi-square statistic to evaluate associations between quality and quantity of specimens and culture results. An $\alpha = 0.05$ was considered significant. CDC determined this public health surveillance activity to be non-research, as defined in 45 CFR 46.102.

Results

During 2010 to 2017, 82,285 TB cases were reported from USAPI (4%), Hawaii (1%), and the rest of the USA (95%) (Table 1). Among all reported cases, the proportion that were culture positive was lower in USAPI (42%) than Hawaii (58%) or the United States (55%). Higher proportions of TB patients in USAPI were verified by clinical or provider diagnosis (54%), compared with less than half of that proportion in Hawaii (24%) and the United States (21%) (Table 1). Among adult patients with pulmonary TB, fewer (57%) had sputum-culture-positivity in USAPI, compared with Hawaii (69%) and the United States (74%). A greater representation of pediatric patients in USAPI contributed, in part, to lower culture positivity in USAPI; adults, who make up 77% of TB cases, were the primary driver of lower sputum-culture positive proportions in USAPI (Supplementary Table 1).

A lower proportion of patients had exclusively extrapulmonary disease in the USAPI (15%) and Hawaii (13%), when compared with the United States (21%). In USAPI, pediatric TB patients represented a higher proportion of all TB patients among those with exclusively pulmonary (21%), exclusively extrapulmonary (28%), or pulmonary with extrapulmonary disease (25%) than corresponding proportions in the United States (6% each). (Supplementary Table 1).

The vast majority (97%) of 11,137 specimens evaluated from USAPI were sputa. Two-thirds (66%) were diagnostic specimens (n = 7145) (Supplementary Figure 1, available online).

Overall, 3% of USAPI specimens had both optimal quality and quantity (Table 2). Less than half (40%) of specimens had optimal (mucoïd) quality; 7% of specimens had optimal quantity (>5 mL) (Table 2). In FSM (27%) and RMI (47%), less than half of the specimens had optimal quality and a smaller proportion (5%) were of optimal quantity. While American Samoa had the highest proportion of sputum specimens with optimal quality (79%), Palau had the highest proportion with optimal quantity (18%) (Supplementary Table 1, available online). The median transport time for receipt at the off-island laboratory was 5.6 days (IQR: 3.2-7.6 days). Only 315 (8%) of the 3,848 watery specimens were culture positive, compared with 504 (18%) of the 2,863 mucoïd specimens (Table 2). Among 5,259 specimens with 1 to 5 mL, 721 (14%) were culture positive; 80 (6%) of the 1,357 specimens with <1 mL were culture positive.

Discussion

Our systematic evaluation of surveillance and laboratory data indicates that 42% of TB patients reported in USAPI had positive sputum-culture positive results during 2010 to 2017. Although a greater proportion of TB cases were pediatric in USAPI (22%) compared to the United States (5%), culture positivity was similar (13% and 11%, respectively). We excluded the effect of HIV status from the analysis due to small numbers (7 HIV positive cases [0.2%] in USAPI). We conclude that pediatric patients and extrapulmonary cases do not account for substantial differences in sputum-culture positivity rates.

We found that 3% of the diagnostic specimens collected during the study period had both optimal quality and quantity. Future evaluations that match diagnostic specimen results to patient surveillance records could provide further insights. Because 3 years may be insufficient to monitor trends, additional long-term monitoring is recommended. Programmatic and laboratory interventions, particularly patient education on sputum collection, and staff training on routine reviews of sputum quality and quantity data, revision of laboratory requisition forms, and monthly reports to monitor trends in transport time and contamination have been implemented. Furthermore, the Australian Respiratory Council has collaborated with the Pacific Island TB Nurses Network to start the “USAPI Sputum Project” with practice guidelines, competency standards, and education resources [Resources-Australian Respiratory Council (thearc.org.au)].

Policies and procedures for optimizing specimen and data collection as well as collaboration and coordination between clinicians, laboratorians, and program staff are essential steps

toward improving laboratory results. Routine quality improvement and assurance activities as well as coaching and/or mentorships through virtual communities of practice models¹⁰ might help establish a sputum quality and quantity improvement framework that counters laboratory and programmatic challenges.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We are grateful to the TB controllers, program managers, and laboratory colleagues in USAPI who inspired this work. We thank Lori Armstrong for her many contributions to the analysis and for her dedication to improving and expanding NTSS, including support to the USAPI. We appreciate careful editorial review by C. Kay Smith. Finally, we thank Mayleen Ekiek, Risa Bukbuk, Connie Olikong, Lance Chinna, and the many USAPI and off-island laboratory staff for their collaborations with this important work and their efforts in improving surveillance and laboratory activities in the USAPI.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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What We Already Know

- Sputum-culture confirmation is the reference standard for diagnosing pulmonary tuberculosis (TB) disease and guiding programmatic decisions for TB control. Yet, demographic and clinical differences as well as challenges with sputum collection may lead to lower rates of culture confirmation in the United States-Affiliated Pacific Islands (USAPI) compared with Hawaii and the rest of the USA.

What This Article Adds

- Among 82,285 TB cases reported to the National Tuberculosis Surveillance System during 2010–2017, the proportion of sputum-culture positive cases was lower in USAPI (42%) than Hawaii (58%) or USA (55%).
- Pediatric patients and extrapulmonary cases did not account for these substantial differences in sputum-culture positivity rates.
- Among 7,119 diagnostic sputum specimens from USAPI, the majority (75%) were culture negative; a small proportion (3%) had both optimal quality and quantity.
- Policies and procedures, routine quality-improvement activities, and virtual communities of practice models to optimize specimen, data collection, collaboration and coordination between clinicians, laboratorians, and TB program staff will be critical steps toward improving laboratory results, which may ultimately impact TB control in USAPI.

Table 1. Demographic and Clinical Characteristics of TB Patients, USAPI, Hawaii, and the Rest of the USA, 2010–2017.

Characteristic	USAPI (n = 3422)		Hawaii (n = 968)		United States (n = 77,895)	
	No.	(%)	No.	(%)	No.	(%)
Age groups (years)						
0-4	346	(10)	15	(1)	2221	(3)
5-14	408	(12)	19	(2)	1649	(2)
15-24	556	(16)	104	(11)	7807	(10)
25-44	926	(27)	204	(21)	24,262	(31)
45-64	904	(26)	310	(32)	24,233	(31)
65	280	(8)	316	(33)	17,708	(23)
Unknown/missing	2	(1)	0	(0)	15	(0)
Sex						
Male	1847	(54)	552	(57)	47,579	(61)
Female	1572	(46)	416	(43)	30,300	(39)
Unknown/missing	3	(<1)	0	(0)	16	(<1)
Sputum acid-fast bacilli smear results						
Positive	1200	(35)	360	(37)	28,688	(37)
Negative	1756	(51)	529	(55)	36,170	(46)
Not performed	457	(13)	79	(8)	12,972	(16)
Unknown/missing	9	(1)	0	(0)	65	(1)
Sputum-culture results						
Positive	1430	(42)	560	(58)	42,685	(55)
Negative	1259	(37)	329	(34)	21,381	(27)
Not performed	666	(20)	79	(8)	13,420	(17)
Unknown/missing	67	(1)	0	(0)	409	(1)
Culture results from other sources^a						
Positive	88	(3)	266	(28)	28,307	(36)
Negative	77	(2)	81	(8)	8158	(10)
Not performed because sputum was collected	3191	(94)	620	(64)	41,092	(53)
Unknown/missing	66	(2)	1	(<1)	338	(1)

Characteristic	USAPI (n = 3422)		Hawaii (n = 968)		United States (n = 77,895)	
	No.	(%)	No.	(%)	No.	(%)
Verification criteria for TB diagnosis^b						
Culture	1488	(43)	715	(74)	60,083	(77)
Nucleic acid amplification test	71	(2)	16	(1)	1228	(1)
Smear	30	(1)	5	(1)	377	(1)
Clinical	1020	(30)	198	(20)	12,149	(16)
Provider	813	(24)	34	(4)	4058	(5)
Disease site						
Pulmonary only	2755	(80)	730	(75)	53,918	(69)
Extrapulmonary only	505	(15)	129	(13)	16,153	(21)
Pulmonary with extrapulmonary involvement	160	(5)	109	(11)	7765	(10)
Unknown/missing	2	(<1)	0	(0)	59	(<1)
Chest radiograph results						
Abnormal	3103	(91)	880	(91)	61,511	(79)
Normal	180	(5)	73	(8)	12,905	(17)
Not performed	89	(3)	15	(1)	3143	(3)
Unknown/missing	50	(1)	0	(0)	336	(1)
Provider type						
Public health department	2692	(79)	735	(76)	46,035	(59)
Private provider/other	37	(1)	132	(14)	16,811	(22)
Both	2	(<1)	52	(5)	7441	(10)
Unknown/missing	691	(21)	49	(5)	7608	(10)

Abbreviations: TB, tuberculosis; USAPI, US-Affiliated Pacific Islands.

^aMost common sources cultured other than sputum are gastric aspirates, tissue samples, and cerebrospinal fluid.

^bVerification criteria are hierarchical surveillance criteria that include diagnosis of TB by laboratory confirmation, clinical criteria, or provider diagnosis (see text).

Table 2.

Quality and Quantity of Diagnostic Sputum Specimens by Culture Results, USAPI, October 2015-September 2018.^a

	Total n = 7119	Culture positive n = 879 (12%)	Culture negative n = 5360 (75%)	Overgrowth n = 880 (12%)	P-value
Quality of specimen (%)^b					
Mucoid (optimal)	2,863 (40%)	504 (57%)	2,041 (38%)	318 (36%)	<.0001
Saliva	408 (6%)	60 (7%)	313 (6%)	35 (4%)	
Watery	3,848 (54%)	315 (36%)	3,006 (56%)	527 (60%)	
Quantity of specimen (%)^b					
>5 mL (optimal)	503 (7%)	78 (9%)	360 (7%)	65 (8%)	<.0001
1-5 mL	5,259 (74%)	721 (82%)	3,884 (72%)	654 (74%)	
<1 mL	1,357 (19%)	80 (9%)	1,116 (21%)	161 (18%)	
Optimal quality and quantity (mucoid + >5 mL) (%)^c	194 (3%)	35 (18%)	132 (68%)	27 (14%)	0.03

Abbreviations: USAPI, US-Affiliated Pacific Islands.

^aDiagnostic specimens are defined as any sputum specimens with an initial or second collection date irrespective of culture results. Culture results missing for 26 specimens.

^bColumn percentages are reported.

^cRow percentages are reported.