CHAPTER IX

DISCUSSION

Tuberculosis is again becoming a major threat to worldwide public health. More people get infected and die of tuberculosis. Although medications and vaccines are widely available to combat tuberculosis, the current epidemic is actually being spread by drug-resistant strains of Mycobacterium tuberculosis. From our study of one hundred fifty three (153) patients, one hundred (100) manifested resistance to any or all of the four anti-tuberculosis drugs; fifty three (53) patients showed sensitivity to the four drugs. The high resistance rate must have contributed to the difficulty we encountered in gathering an adequate number of patients, particularly for the control group. The Bactec method for the culture of Mycobacterium tuberculosis was adapted in our hospital in the early 1990's and due to the expensive price of the procedure, not all the patients suspected of having tuberculosis could afford to have their sputum examined for culture and sensitivity tests. These somehow limited our sample population and size. The data analyzed were based on our patients' existing records. Therefore, the information given by the patient during history taking might not be exact. The patient's ability to recall accurately events that were related to the study might

not be sufficient enough. Although the historian could have taken the patient's history thoroughly, the patient's capacity to recall certain events exactly might add some bias to the study. The short time frame allotted for the study contributed to the inadequate number of patients gathered. In spite of the sample size obtained, analysis of one hundred (100) cases and fifty three (53) control patients was done.

The diagnosis of pulmonary tuberculosis was reviewed by an independent pulmonologist. It was not surprising to note the complete agreement (100%) when the computation for the kappa error was used. This could be explained by the fact that the 153 patients' charts reviewed already showed positive culture result for the Mycobacterium tuberculosis which is considered as the gold standard for the diagnosis. There were only ten chest x-rays available for review by the radiologist. This could be explained by the fact that most of the subjects included in the research were on an ambulatory setting. It was our practice to give the x-ray plates to the patients for their safe keeping. Therefore, only the x-ray films of patients who were confined in the hospital were available. Although the degree of agreement was high, the number of x-ray plates reviewed was not sufficient for the result to have a very good significance.

A simple descriptive analysis was done. The baseline characteristics of the subjects were summarized and could be seen on Table 6. It seemed that our control samples were not very good representative of an "ideal" control group.

Both drug-resistant and drug-sensitive pulmonary tuberculosis were common among the elderly patients. It was also observed that tuberculosis was predominant in the male population. The latter duplicates the observation done by D. Wosornu et al in 1990.

For the tuberculous patients who had previous intake of anti-tuberculosis regimen, compliance was evident in 72% of the cases and 82% of the control group. Our definition of good compliance meant that the patient has taken 80% of the required dose of drug at a specified time. Therefore, the datum for compliance depended greatly on how well the patients in the study remembered their drug intake habits and their honesty in answering the question during the interview. Occasionally, the attending physician did random pill count or checked the color of the patient's urine. These methods, however, covered only the period when the patients were only under our care. Since the history of a previous diagnosis of tuberculosis and previous treatment occurred sometime in the past, there's not enough objective basis to conclude that the patients were truly compliant. The only way we checked the veracity of their history as far as this aspect was concerned was to ask for the former physician's prescriptions. A few patients in our study still kept with them their doctor's prescription orders. We also asked them about the length of time they took the drug(s) and compared their reply with the dates appearing on the prescription form.

To see the relationship of each variable to drug-resistant or drug-sensitive tuberculosis, a univariate analysis was done. The results were summarized on Table 7. A history of tuberculosis in the past, a history of previous intake of rifampin and isoniazid showed a significant p value of < 0.05 with odds ratio of 2.12, 2.68, 2.53 respectively. All were within the 95% confidence limit. History of previous intake of pyrazinamide and alcohol for more than five years gave an odds ratio of 2.08 and 2.11 respectively. However, the p value of the aforementioned factors were greater than 0.05. Since these two data fell within the 95% confidence interval, we surmised that, clinically, they could have some significance.

One of our objectives was to identify risk factor(s) for drug-resistant pulmonary tuberculosis. Therefore, the ideal statistical design to show the relationship involving various factors was multiple logistic regression. This model also corrected for any confounding variables present in the study. A stepwise logistic regression using the BMDP was done. When the variables were entered, three factors had significant p value (< 0.05) namely: previous history of tuberculosis, previous intake of rifampin, and previous intake of INH. The entry of previous intake of INH in the model removed the significant p value of previous TB history and rifampin intake. Thus, the final analysis showed that only a previous intake of INH was statistically significant ($p = 0.025$). Since the odds ratio of previous history of

INH intake is equal to 2.53, we tend to believe that it is associated with the development of drug-resistant pulmonary tuberculosis. In the United States and Europe, individuals who are exposed to tuberculous patients, like household contacts, are given INH for chemoprophylaxis. However, in the Philippine setting, real life situation does not call for any prophylaxis for various reasons; topping the list, of course, is the lack of logistics. However, for the common Filipino, INH is not looked upon as an anti-TB treatment, but more for its vitamin content, since most INH available in the market contains Vitamin B_6 or other B complex vitamins.

If this were so, we believe that this factor may possibly be due to incessant intake of INH, which not only the patients, but everyone can easily procure from the drug stores without a doctor's prescription order. If we look at our data closely, non-compliance will not completely explain the development of resistance. Apparently, 72% of patients previously treated for tuberculosis was compliant with the therapeutic regimen. Yet, on culture, results showed development of resistance. The crux of the matter lies on the awareness of the patients regarding INH as an anti-TB drug. Some of them might have taken INH, not as a treatment for the tuberculous infection, but as a vitamin supplement which makes the pulmonary system "strong". Hence, when the patient finally gets the disease, he develops some kind of resistance to the drug. This seems tenable in as much as tuberculosis is a chronic illness, usually dormant and only

10-30% finally develops into a full blown case of active tuberculosis.

At this point, a final conclusion could not be made considering that the number of cases and control subjects were still not adequate. To achieve a stronger conclusion, the study needs to be continued until the desired sample size is reached. However, analysis of the data would involve a stricter alpha value, set at 0.025.

TABLE 7. SUMMARY OF RESULTS OF UNIVARIATE ANALYSIS

RISK FACTOR	P VALUE	ODDS RATIO	95% CONFIDENCE LIMIT	INTERPRETATION
Smoking	0.46	0.73	0.73, 1.51	Not significant
Alcohol intake				
≥ 5 years	0.24	2.11	0.68, 6.97	Not significant
BCG vaccination	0.73	1.20	0.58, 2.49	Not significant
History of exposure	0.43	1.46	0.64, 3.41	Not significant
Concomitant illness	0.27	1.59	0.73, 3.46	Not significant
Severity of illness	0.38	1.64	0.76, 3.5	Not significant
Previous history of TB	0.001	2.12	1.52, 7.8	Significant
Compliance	0.39	0.59	0.59, 2.76	Not significant
Previous intake of Rifampin	0.01	2.68	1.19, 6.14	Significant
Previous intake of Pyrazinamide	0.17	2.08	0.77, 5.78	Not significant
Previous intake of Ethambutol	0.16	1.84	0.81, 4.24	Not significant
Previous intake of INH	0.01	2.53	1.17, 5.25	Significant
Previous treatment with streptomycin	0.71	1.06	0.16, 8.68	Not significant