

Developing Expert System for Tuberculosis Diagnose to Support Knowledge Sharing in the Era of National Health Insurance System

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Abstract. National Health Insurance has been implemented since 1st January 2014. A number of new policies have been established including multilevel referral system. The multilevel referral system classified health care center into three levels, it determined that the flow of patient treatment should be started from first level health care center. There are 144 kind of diseases that must be treat in the first level which mainly consists of general physicians. Unfortunately, competence of the physician in the first level may not fulfil the standard competence yet. To improved the physisians knowledge, government has created many events to accelerate knowledge sharing. However, it still needs times and many resources to give signifikan results. Expert system is kind of software that provide consulting services to non-expert users in accordance with the area of its expertise. It can improved effectivity and efficiency of knowledge sharing and learning. This research was developed a model of TB diagnose expert system which comply with the standard procedure of TB diagnosis and regulation. The proposed expert system has characteristics as follows provide facility to manage multimedia clinical data, supporting the complexity of TB diagnosis (combine rule-based and case-based expert system), interactive interface, good usability, multi-platform, evolutionary.

1. Introduction

Tuberculosis (TB) is an epidemic. Prevention and treatment of TB has been a national health program for years. It has been supported by the establishment of hospital and health center specifically for TB and other lung diseases, as well as the treatment of tuberculosis which is free for the community. Community leaders together with pulmonary physician associations through various foundations also actively conduct outreach activities to reduce the number of TB patients and the risk of TB transmission. All updated within national guidelines for TB control[1].

Since National Health Insurance (*Jaminan Kesehatan Nasional/JKN*) has been implemented in Indonesia, a number of new policies have been established, including multilevel referral system. The multilevel referral system classified health care center (*Pusat Pelayanan Kesehatan/PPK*) into three levels, namely the PPK-1, PPK-2 and PPK-3. It determined that the flow of patient treatment should be started from PPK-1, if PPK-1 was not able to handle, the patient will be referred to the PPK-2 or PPK-3. This change raises several issues including the readiness of stakeholders due to lack of knowledge[2]. According to the guide book of clinical treatment in PPK-1, general physicians in PPK-1 has to mastering the 144 kinds of diseases[3]. Unfortunately their competence may not fulfil yet. This may caused over diagnosis or under diagnosis, including when diagnosing TB. These are a series of problems



identified from our previous studies related to implementation of JKN and the possible impact on TB treatment.

Nowadays, Indonesian government through Ministry of Health held a variety of workshops to increase the knowledge of stakeholders in diagnosing and treating TB. These efforts of course takes time, costs and resources. To improve its effectiveness, this study proposes an information technology-based solution that is an expert system to support learning and sharing knowledge. Expert system is kind of software that providing consulting services to non-expert users in accordance with the area of its expertise. In this paper we propose a model of expert system for TB diagnosis which supports knowledge sharing and comply with the standard procedure of TB diagnosis and regulations of JKN and national guidelines for TB control.

2. Methodology

Expert system is a software application. Therefore the development of expert system can follow the life cycle of software engineering. Software engineering process is divided into five generic process framework: communication, planning, modeling, construction and deployment[4]. Communication is done to understand the goals and desires of stakeholders as well as obtaining the necessary data such as process flow system, stakeholders involved, documents and information required. In this study, data collection done through observation (seeing / observing) the flow of patient's treatment process and in-depth interviews with stakeholders (pulmonary specialists and general practitioners) in PPK-1 and PPK-2. Data collection in this research involved many stakeholders in some healthcare institutions.

Expert system to be developed is expert system to support sharing of knowledge from experts (lung specialist) to general physician / medical students who want to gain knowledge about TB diagnosis. TB diagnosis procedure adopted is standard procedure TB diagnostics[5], guideline services at primary health care center[3], and enriched by the internal knowledge of experts. System modeling consists of two stages: analysis and design. Analysis process was conducted to understand the existing system and defining the system requirements to be developed.

3. Results and Discussion

This section covers concepts, principles and processes of TB diagnosis. Sources of knowledge were collected from literature research [2][5][6] and deep interviewed with experts.

3.1. Multilevel referral system

BPJS card owner has the right to health check and treatment through multilevel referral system. There were no obstacles and difficulties for cardholders BPJS to use the benefits of the insurance throughout referral procedures gradually from the level of basic services Puskesmas (Pusat Pelayanan Kesehatan/ PPK-1), RS secondary type D, C (PPK-2), B and A (PPK-3). The Center for Lung Health Community (Balai Besar Kesehatan Paru Masyarakat/BBKPM) and the Center for Lung Health Community (Balai Kesehatan Paru Masyarakat BKPM) is a specialized health care facilities lung equivalent to RS type C (PPK-2).

3.2. Epidemiology TB

Tuberculosis (TB) is a disease caused by the bacteria *Mycobacterium tuberculosis* (*M. tuberculosis*). TB germs can attack various parts of the body such as the kidneys, bones, brain and lungs. Lung is the organ most frequently subjected. WHO estimates that, in Indonesia every year there are 500,000 new cases; 200,000 cases (40%) are around health centers, 250,000 (50%) of cases are found in the service of the Hospital or Clinic Government and Private sector, while the remaining 10% is not affordable health care units. TB bacilli are rod-shaped and are resistant to acid staining alcohol (so-called acid-fast bacilli or AFB, Basil Tahan Asam/BTA). BTA can be seen with a microscope.

3.3. Management of TB patients

TB patient management implemented by health centers, hospitals and hospital lung, BKPM and BBKPM, Physician Private Practice (DPS) and other service facilities. TB disease is inserted into the ability level 3A[3]. Physician graduates capable of making a clinical diagnosis and provide preliminary treatment on the state that is not an emergency; able to determine the most appropriate referrals for further care of patients and to follow up after returning from the referral.

3.4. Procedures of TB diagnosis

In the national TB program, the diagnosis of pulmonary tuberculosis for adults is confirmed by the discovery of the TB germs through microscopic examination of sputum (three times, in the time of the first day–in the morning of the second day-in the time of the second day; namely Sewaktu Pagi Sewaktu/SPS). While chest X-ray, culture and sensitivity can be carried out in accordance with the indication. It is not justified to diagnose TB only by radiographic examination because chest X-ray does not always give an typical of pulmonary TB, so often occurs overdiagnosis or underdiagnosis. To diagnose extrapulmonary TB, a bit difficult. Symptoms and complaints depending on which organs are affected, such as neck stiffness in TB meningitis, TB pleural chest pain (pleurisy), enlargement of the superficial lymph nodes in lymphadenitis tuberculosis and spinal deformity (gibbus) on TB spondylitis and others. The diagnosis is confirmed by clinical examination, bacteriological or histopathological taken from the body's tissues are exposed.

3.5. Pathogenesis

Tuberculosis germs that enter through the airway will be lodged in the lung tissue so it will nest pneumonic form, which is called the primary nest or primary affective. This primary nest may arise in any part of the lung, in contrast to the nest reactivation.

3.6. Classification of Diseases TB

Types of TB disease can be classified based on anatomical location and results of examination of sputum / bacteriology, and a history of previous treatment.

3.6.1. Location of anatomical disease

- Pulmonary tuberculosis, the TB cases that the lung parenchyma. Miliary tuberculosis is classified as pulmonary TB because the lesion is located in the lung.
- Extrapulmonary tuberculosis, the TB case on organs other than the lung such as pleura, lymph nodes (including mediastinal and/or hilum), abdomen, genitourinary tract, skin, joints, bones and meninges.

3.6.2. The results of examination of sputum or bacteriologists

- smear positive pulmonary tuberculosis (BTA +), ie if:
 - at least one of at least two times a sputum examination showed positive results in laboratory qualified external quality assurance (EQA). Preferably one that comes from the sputum expectoration morning.
 - In countries or regions that do not have a laboratory on condition EQA, then pulmonary TB smear positive are: Two or more results of sputum smear-positive, or the results of sputum smear-positive and supported the results of radiographic fit the description TB set by the clinician, or the results of sputum smear positive plus positive M. tuberculosis cultures.
- smear negative pulmonary tuberculosis (BTA-), if:
 - negative sputum examination results but positive culture results. At least two sputum smear negative result at a qualified laboratory EQA. It is advisable culture examination on sputum smear negative test results to confirm the diagnosis, especially in areas with HIV prevalence > 1% or TB patients with pregnancy \geq 5% OR

- sputum smear examination twice negatif, in case no culture of M. Tuberculosis facility
- radiographic results in keeping with active tuberculosis and:
 - Test results are HIV positive or HIV laboratory correspond, or
 - HIV negative (or unknown HIV status or HIV prevalence is low)
- The case of former TB, if:
 - the results of smear examination (culture-negative if any) and the radiological picture smear negative test results (also negative cultures if any) and pulmonary radiological picture shows TB lesions that are not active, or photo series (within 2 months) show picture settled. OAT adequate treatment history will be more supportive.
 - In cases of doubt the radiological picture and have received treatment OAT two months but on the chest radiograph was no change in the radiological picture.

3.6.3. Previous treatment history

- Treatment history is very important to know to look at the risk of drug resistance or MDR. In this group is necessary to check the culture and sensitivity test OAT.
 - New patient: patient who had not received prior treatment for TB or have been getting OAT less than one month. Patients with sputum smear result is positive or negative with the disease at any anatomic location.
 - Patient with a history of previous treatment: patients who have received prior TB treatment for at least one month, with the results of sputum smear positive or negative by anatomic location of disease in any area, consisting of:
 - Relapse: patients who previously had received treatment for TB and has been declared cured or treatment is complete, re-diagnosed with smear-positive
 - Default: patients who have been treated and broke treatment 2 months or more with BTA+.
 - Failure: patients with sputum examination results remained positive in the fifth month or more during treatment
 - Transfer: patients were transferred to another register to continue treatment.
 - Other cases are all cases that do not satisfy the above conditions, as the unknown history of previous treatment, been treated but it is not known the results of treatment, and re-treated with smear negative.

3.7. The process of TB diagnosis

Physicians need some data obtained from several stages of examination:

- Anamnesa, in the form of questions posed to the patient to determine the clinical symptoms experienced by the patient. It can be divided into two groups, local symptoms and systemic symptoms. Local symptoms correspond organ involved when the organ affected is the lung, the local symptoms are respiratory symptoms.
 - Respiratory Symptoms: ≥ 2 weeks cough, coughing up blood, shortness of breath, and chest pain.
 - Systemic symptoms: fever, malaise, night sweats, anorexia and weight loss.
 - Extrapulmonary TB symptoms depend on the organs involved, such as tuberculous lymphadenitis will enlargement is slow and painless of the lymph nodes. In TB meningitis will see symptoms of meningitis. While the TB pleurisy symptoms are shortness of breath and sometimes chest pain in the side of the cavity pleuranya there is fluid.
- Physical examination, there are four methods: a) inspection (viewed at a glance); b) palpation / touched by hand; c) percussion (tap and listen to the sound produced); d) auscultation (listening to sounds). The technique is taught in basic medical education for signs / physical symptoms of

certain diseases. In pulmonary tuberculosis, abnormalities obtained depending on the area of structural abnormalities of the lung. In the beginning (early) development of the disease is generally not (or difficult) find abnormalities.

- lung disorders are generally located in areas particularly the apex of the superior lobe and posterior segments (S1 and S2), and the apex of the inferior lobe (S6). On physical examination can be found bronchial breath sounds, breath sounds weakened amforik, wet crackles, signs of withdrawal lungs, diaphragm, and mediastinum.
- On TB pleurisy, fission examination abnormalities depending on the amount of fluid in the pleural cavity. In dim or found percussion dullness, auscultation breath sounds weakened until no sound on the contained liquid.
- In TB lymphadenitis, visible enlarged lymph nodes, common in the neck area (think of the possibility of tumor metastasis), sometimes in the armpit area. Enlargement of the gland can be cold abscess.
- Investigations: examination using laboratory facilities, such as bacteriological examination, radiology, pleural fluid, histopathology, blood, etc.
 - Examination of bacteriology: Regular microscopic examination using Ziehl-Nielsen and microscopic fluorescence using auramin-rhodamine staining. Examination of the bacteria culture using the egg base media, the Lowenstein-Jensen, Ogawa, and Kudoh. Molecular test such as PCR-Based Methods of IS6110 Genotyping. Sensitivity test like Hain test (test sensitivity to R and H), molecular beacon testing (test sensitivity to R), and gene x-pert (test sensitivity to R). Examination using the culture medium is more sensitive than microscopic examination. The other test: Tuberculin test, IGRA, T-SPOT TB and Serology test, but currently, serologi test was not significant for TB diagnosis.
 - Radiological examination: the standard tests is chest radiograph. Other checks on the indication that lateral photo, top-lordotic, oblique, or CT scan.
 - Other Investigations: Pleural fluid analysis, Histopathological examination of tissues, and Blood tests.

Patient said as Suspect TB, if the results of the anamnesis and physical examination showed symptoms of TB disease. Patients are said to be suffering from TB if have found the evidence of *M. tuberculosis* germs. Figure 1 shows the flow of TB diagnosis.

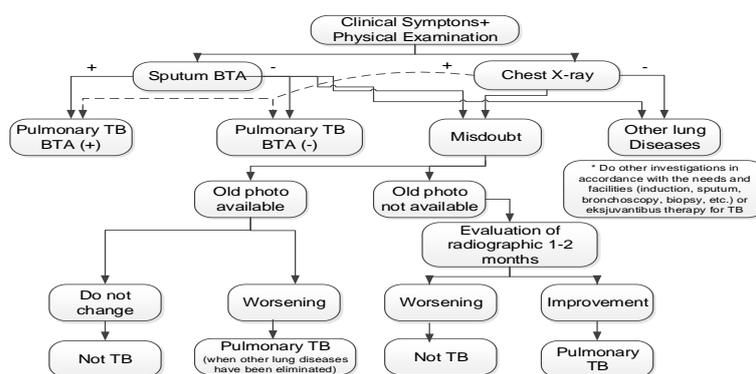


Figure 1. Flow of TB diagnosis [5]

3.8. Flow of TB diagnosis and treatment in PPK

Chronology of TB diagnosis in Figure 1 does not show the level of competence of doctors who deal with appropriate referral systems storied JKN. Flow TB diagnosis and treatment with JKN determined by the case and the gravity of the disease and the availability of supporting facilities at PPK. According to the flow of process, a general physician at PPK-1 is expected to make a diagnosis of TB disease in

the case of BTA +, ie if clinical symptoms +, examination +, sputum smear +, meaning it can proceed with treatment but if anamnesa +, examination + but smear (confusing/ suspected TB smear) then the doctor PPK-1 can make a referral to PPK-2.

At PPK-2, after registration, patients are first handled by general physicians in the PPK-2. General physicians here have been equipped with the ability to read an X-ray photograph (can handle cases of TB smear). Here re-examination of microscopic sputum (can use the results of PPK-1 if believed), and radiological / chest X-ray). If the chest X-ray results (confusing / doctors are not sure), the general physicians in the PPK-2 can refer to a pulmonary specialist, if the result of chest X-ray + then continued with the treatment and the patient was referred back to the PPK-1. If the results of radiographic equivocal or negative, the pulmonary specialist can perform the inspection again from the beginning, including sputum culture-as well as requesting additional examinations such as histopathological tissue by means of biopsy or analysis of pleural fluid, usually for cases of TB outside the lungs (extra-pulmonary TB), blood test is not done anymore. In addition to treatment, medical specialists may also perform some non medical action of drugs such as puncture namely tube placement (WSD) to remove fluid. If the diagnosis stating the patient needs surgery or hospitalization, the patient will be referred to the PPK-3.

Cases of tuberculosis resistant to anti-TB drugs (OAT) or multi-drug resistance (MDR TB), due to inadequate treatment handled directly by a specialist in the PPK-2, with a special procedure. Detailed guidelines in making the diagnosis and management in Indonesia has been available in print (book), issued by the Association of Pulmonary Specialist Indonesia. This book contains the standards for diagnosis of TB, the standard for the treatment of TB and standards for public health, the reference book for the entire pulmonary specialist in Indonesia. This book also discussed various TB treatment in special circumstances (TB Comorbidity / Tb with comorbidities), namely: i) TB Millier, ii) Eufusi pleural TB, iii) pulmonary tuberculosis with diabetes mellitus, iv) pulmonary TB with HIV / AIDs , v) pulmonary tuberculosis in Pregnancy, Breastfeeding and User Hormonal Contraception, vi) Pulmonary TB in kidney failure, vii) pulmonary tuberculosis with liver abnormalities. And also cases of TB with few complications both before treatment and after treatment should be referred to adequate facilities.

3.9. Complexity and potential inaccuracies in diagnosis of TB

Variations of TB disease specific circumstances affect the diagnosis and treatment process, namely:

- TB with comorbidities, is TB that occur together with other diseases and influence each other, such as TB with HIV, TB with Diabetes Mellitus, Kidney TB, TB in children;
- TB complications: TB is getting worse, may have an impact on organs outside the lungs so that handling is also more complicated as MDR (multi drugs resistance).

TB disease with special circumstances this causes the process of diagnosis and treatment is more complex that needs to be handled by a specialist.

Difficulty in TB diagnosis also located in anamnesis and physical examination. This needs to be done cleverly and conscientiously to produce an accurate diagnosis. It is not enough to rely on a literal understanding but also the ability of analysis supported by extensive knowledge and experience of the doctor. For example, when identifying patients who are less willing to be frank so that incorrectly states the clinical symptoms (eg, patients with symptoms of HIV/ AIDs). In this case, doctor should be good at digging up information using combination of communication techniques and analytical skills. The ability to diagnose and examination have been taught but the opportunity to get a unique cases very rarely. Anamnesis and physical examination helps the doctor to determine the location of disease.

3.10. The previous researchs and The proposed TB-diagnose expert system

Based on the characteristics of the system (flow diagnostic process should be in accordance with the standard procedures, medical data, problems and complexities in the process of diagnosis). Several approaches in the development of systems for disease diagnosis have been developed. Some previous researchs have contributed to develop the interface model that increases physician convenience in entering and accessing data during the process of medical diagnosis. They developed an interface dialog-based model which more interactive, fast and easy to entry the physical examination data for skin

diseases. Data could be represented in text and images (shapes of abnormal skin taken from photos and its location which is taken by touching the location of the disease in the photo)[7]. A system architecture that supports sharing clinical documents between doctors for consulting diagnosis of disease was purposed[8]. Some special features are provided to process medical image documents including store, access, transfer and medical image processing to identified abnormal areas and other processes that support analysis of disease.

Some software systems for detection of pulmonary TB was developed. An application using image processing techniques to distinguish normal and not normal lung picture based on cavity found at the upper region of thoracs[9]. Another knowledge-based system was developed to detect TB disease also through chest X-ray combined with a learning algorithm. It involves experts to improve the learning system finds the disease[10]. Nevertheless, lung specialist that we was interviewed said the detection of TB disease only through chest X-ray is not in accordance with the applicable standards for TB diagnosis. TB diagnosis should be confirmed by examination of sputum (BTA). The other rule-based expert system for TB diagnose designed to translate tuberculosis patients' symptomatic data for online (web-based) pre-laboratory screening to help medical practitioners reduce patient-doctor ratio in hospitals[11].

A rule-based expert system combined with image analysis techniques to detect and recognize facial expression was developed[12]. The system architecture is divided into three parts, namely processing: preprocessing (face detection) include elements / detection parameters, expert system (facial expression recognition) and post-processing (evaluation). This system architecture is inspired to develop TB diagnosis expert system architecture which is in accordance with standard diagnostic procedures and diversity of medical data is generated and used for diagnosis.

An hybrid version of knowledge-based systems (expert systems) was developed for automatic classification of images echo images (B-scans) generated by ultrasonic scanning system[13]. This expert systems are made by combining rule-based expert system with case-based reasoning systems (CBR) for image classification. CBR is an expert system that is working to find a solution by calculating the proximity of a combination of symptoms in certain case by a combination of symptoms in cases-based. CBR is suitable to solve new problems. This hybrid system is also suitable to adopt in the development of TB-diagnosis expert systems. The field will always find a combination of symptoms (case) just because of disease progression and the development of techniques of diagnosis and treatment.

Treatment adherence is a particular problem in tuberculosis. Although tuberculosis is not a chronic disease, its prevention and cure require the use of medications for long periods, 6-9 months. A state of the art about the fails in tuberculosis treatment and strategy to improve patient adherence was conducted by Sumartojo using social behavioral methods[14]. The results of this research was very significant to formulate the new methods of TB treatment and control that is DOT (Directly Observed Therapy). DOT is one component of DOTS (Directly Observed Treatment Shortcourse, is the name given to the tuberculosis control strategy recommended by the World Health Organization. The others used new technology or tools to improve the efficiency and effectiveness of TB diagnosis[15][16].

Some ideas that can be inferred regarding the characteristics and system architecture system that will be developed are as follows:

1. Flow TB diagnosis process is quite complex and it must be in accordance with the standard procedures set by Indonesian pulmonary physician association and it must pay attention to the referral system and the rules relating to the implementation of JKN. The diagnosis of TB will not use radiographic image processing techniques as the only evidence for the diagnosis of TB. Image processing techniques can be used to improve the accuracy of diagnosis or just for learning.
2. The diagnosis of tuberculosis requires the support of clinical data obtained from the three stages of the examination including various type of data: anamnesa (description/text), physical examination (description or sound), and investigations (image and its description). So that, the proposed system could store, access and processing of multimedia data.

3. The interface module is designed to accelerate the process of entering data in various formats, improve the accuracy of diagnosis and supports the sharing of knowledge, interesting and comfortable to the users.
4. Implementing a hybrid system that combines rule-based expert system with case-based reasoning (CBR) expert system for consultation facilities, provide teaching facilities to improve the knowledge and ability of physicians to perform examination and analysis of clinical data (learning modul as pre-diagnosis) and supports knowledge sharing (direct consultation with experts) using communication facilities.
5. An expert system needs to be developed in stages. The process model used is prototyping in order to quickly capture the user's needs and to develop an expert system which has high usability.
6. Knowledge base consists of a set of rules derived from the flow of TB diagnosis were obtained from source of expertise, that was collected from manual diagnosis and expert's knowledge gained from in-depth interviews. Understanding the data, we conclude the complexity of the diagnostic process should not be ignored by simply using a simple interface model in the consultation process, especially when entering the various results of the examination (anamnesis, physical examination and investigations). Amenities interface to display the conclusion/ diagnosis should be supported by interactive-explanation facility. In particular, the expert system supporting multimedia data. Building for mutli-platform (desktop, web or mobile). If the chosen platform allows, expert systems will provide facilities to share knowledge directly (direct consultation).

4. Conclusions

This paper represents the conceptualization of TB-diagnosis expert system in JKN era and its development process. The process including some main activities like data collection, literature study, analysis and modeling. TB-diagnosis expert system required due to TB is an epidemiology, TB diagnosis is a complicated process and potentially give inaccurate result especially in the JKN era. This expert system is required to support knowledge sharing between lung specialists to general physicians or medical students. The proposed TB-diagnosis expert system characteristics as follows provide facility to store, access, and process multimedia clinical data, supporting the complexity of TB diagnosis (combine rule-based and case-based expert system), provide interactive interface, pay attention to usability, multi-platform, using evolutionary process model. Further research will be focused on prototype development, including design and construction of every component in accordance with the characteristics of the proposed system.

Acknowledgement

This paper was prepared based on the research funded by the Ministry of Research, Technology and Higher Education of the Republic of Indonesia. Facility support was also obtained from the Engineering Faculty of Pasundan University. The author would like to thank especially to dr. Yun Amril, SpP for information, expertise and time shared during this research.

References

- [1] Direktorat Jendral Pengendalian Penyakit dan Penyehatan Lingkungan, “Pedoman Nasional Pengendalian Tuberkulosis,” Katalog Dalam Terbitan : Kementerian Kesehatan Nasional. pp. 1–210, 2014.
- [2] Y. Amril, “Efektivitas Sosialisasi Peraturan Menteri Kesehatan No. 5 Tahun 2014 Pada Dokter di Layanan Primer di Kota Bandung tahun 2015,” Universitas Indonesia, 2015.
- [3] Kementerian Kesehatan Republik Indonesia and Ikatan Dokter Indonesia, Panduan Praktik Klinis bagi Dokter di Fasilitas Pelayanan Kesehatan Primer: Panduan Pelayanan di Fasilitas Kesehatan Tingkat Pertama, Pertama. Jakarta, 2013.
- [4] Roger S Pressman, *Software engineering: a practitioner’s approach*, Seventh. New York: McGraw-Hill Higher Education, 2010.
- [5] Perhimpunan Dokter Paru Indonesia, *Tuberkulosis: pedoman diagnosis dan penatalaksanaan di Indonesia*. Jakarta, 2011.
- [6] C. for D. C. and Prevention, “Core Curriculum on Tuberculosis : What the Clinician Should Know,” *Centers Dis. Control Prev. Natl. Cent. HIV/AIDS, Viral Hepatitis, STD, TB Prev. Div. Tuberc. Elimin.*, pp. 1–320, 2013.
- [7] F. Suryani, I. Muhimmah, and S. Kusumadewi, “Preferred model of dialog style in expert system of physical examination of skin disease,” in *Proceedings - 2015 International Conference on Science in Information Technology: Big Data Spectrum for Future Information Economy, ICSITech 2015, 2016*, pp. 247–252.
- [8] N. H. Minh, B. Yi, I. K. Kim, J. H. Song, and P. V. Binh, “Embedding the shapes of regions of interest into a Clinical Document Architecture document.,” *Health Informatics J.*, vol. 21, no. 1, pp. 57–72, 2015.
- [9] Poornimadevi CS. and Helen Sulochana C., “Automatic detection of pulmonary tuberculosis using image processing techniques,” in *2016 International Conference on Wireless Communications, Signal Processing and Networking (WiSPNET), 2016*, pp. 798–802.
- [10] J. Melendez, B. Van Ginneken, P. Maduskar, R. H. H. M. Philipsen, H. Ayles, and C. I. Sánchez, “On Combining Multiple-Instance Learning and Active Learning for Computer-Aided Detection of Tuberculosis,” *IEEE Trans. Med. Imaging*, vol. 35, no. 4, pp. 1013–1024, 2016.
- [11] V. C. Osamor, A. A. Azeta, and O. O. Ajulo, “Tuberculosis-Diagnostic Expert System: An architecture for translating patients information from the web for use in tuberculosis diagnosis,” *Health Informatics J.*, vol. 20, no. 4, pp. 275–287, 2014.
- [12] M. Pantic and L. J. M. Rothkrantz, “An Expert System for Recognition of Facial Actions and their Intensity,” *Image Vis. Comput.*, vol. 18, no. May, pp. 881–905, 2000.
- [13] J. Jarmulak, E. J. H. Kerckhoffs, and P. P. Van Veen, “Hybrid knowledge based system for automatic classification of B-scan images from ultrasonic rail inspection,” *IAAI-98 Proc.*, 1998.
- [14] E. Sumartojo, “When Tuberculosis Treatment Fails: A Social Behavioral Account of Patient Adherence,” *Am. Rev. Respir. Dis.*, vol. 147, no. 5, pp. 1311–1320, May 1993.
- [15] I. Langley, B. Doulla, H. H. Lin, K. Millington, and B. Squire, “Modelling the impacts of new diagnostic tools for tuberculosis in developing countries to enhance policy decisions,” *Health Care Manag. Sci.*, vol. 15, no. 3, pp. 239–253, 2012.
- [16] A. D. Baughn and K. Y. Rhee, “Tuberculosis Diagnostics: State of the Art and Future Directions,” *Microbiol. Spectr.*, vol. 4, no. 5, pp. 1–16, Oct. 2016.