Application of Mahalanobis-Taguchi System in Liver Function Profile of Methadone Flexi Dispensing Program

S N A M Zaini*, S K M Saad and M Y Abu
Faculty of Manufacturing and Mechatronic Engineering Technology, Universiti Malaysia Pahang, 26600 Pekan Pahang, Malaysia

Abstract

Patients under the methadone flexi dispensing (MFlex) program are required to do blood tests like liver function profile. A doctor assesses 3 parameters like Alk phosphatase, ALT (SGPT), and AST (SGOT) to ensure the patient has a liver problem. Consequently, the existing system does not have a stable ecosystem towards classification and optimization. The objective is to apply the Mahalanobis-Taguchi system (MTS) in the MFlex program. The data is collected at Bandar Pekan clinic with 34 parameters. Two types of MTS methods are used like RT-Method and T-Method for classification and optimization respectively. The average Mahalanobis distance (MD) of healthy is 1.00 and unhealthy is 352.58. A positive degree of contribution has only 1 parameter. 15 unknown samples have been diagnosed. Type 2 of 6 modifications has been selected as the best-proposed solution. In conclusion, a pharmacist from Bandar Pekan clinic confirmed that MTS is able to solve problems in the classification and optimization of the MFlex program.

Keywords: *Mahalanobis-Taguchi system, Methadone flexi dispensing program*

1. Introduction

In 2019, almost a million people died as a result of drug usage. More than half of the fatalities were caused by hepatitis C which is related to liver cancer, cirrhosis, and other chronic liver disorders, but the surge was also attributable to an increase in overdose deaths linked to the use of opioids like fentanyl [1]. Drug abuse involves various sections of society regardless of age, race, or level of education obtained by a drug addict. Nowadays, drug abuse in Malaysia is increasing and this matter not only involves the older generation but also the new generation even teenagers who are still in school also fall into this drug abuse [2]. The implementation of the methadone flexi dispensing program (MFlex) program has generally proven to be effective in HIV/AIDS issues and billing. The program manages to improve the lives of drug addicts. Methadone treatment is given daily as an outpatient. Participation in the MFlex program can also be a platform for patients to detect other health problems such as HIV, hepatitis, and tuberculosis. The percentage of new HIV cases as a result of injection drug addiction reported to the Ministry of Health has shown a significant decrease from 66% with 4,038 cases in 2005 to 16.8% with 561 cases in 2015 [3]. Patients under MFlex program are required to do 4 types of blood tests, such as FBC, liver function profile, lipid profile, and renal profile involving 34 parameters to determine whether the patient has other diseases or vice versa. In addition, to ensure that the patient has a liver problem, a doctor refers to 3 parameters as Alk phosphatase, ALT

* Corresponding author.
E-mail address: areena5582@gmail.com

Manuscript History:
Received 04 December, 2021, Revised 10 October, 2022, Accepted 11 October 2022, Published 31 October, 2022

https://doi.org/10.33736/jaspe.4283.2022

e-ISSN: 2289-7771

(SGPT), and AST (SGOT). This proves that the existing system does not have an accurate measurement method and there is a lack of justification of significant parameters.

The objective of this research is to analyze the classification and optimization factors in the liver function profile and to diagnose the unknown data of the MFlex program. The literature review section describes related studies on the Mahalanobis-Taguchi system (MTS), where the research gap on MTS is the most significant in this chapter. Next, the research methodology section explains the methods and strategies used to meet the goal or objectives of the research. Results and discussion elaborate on all the evidence obtained during data collection using the MTS method for classification and optimization. Lastly, the conclusion section concludes the final findings after the measurements have been handled and provide some recommendations for subsequent work.

2. Literature review

According to a recent global systematic study, 8.2 million individuals who inject drugs are HIV and hepatitis C virus (HCV) antibody-positive, including 2.8 million HIV-positive people. This equates to 52.3% and 17.8% of drug users worldwide, respectively [4]. In 2018, the major trend in Malaysian drug usage shifted from opiate-based drugs (heroin and morphine) to Amphetamine-Type Stimulant (ATS) drugs. In recent years, the usage of ATS, particularly Methamphetamine and ATS pills, has skyrocketed. Methamphetamine (in crystalline and pills forms) was used by 16,384 drug addicts in 2018, an increase of 10.8% from 14,785 in 2017. During the same time period, 7,746 drug addicts were discovered using heroin and morphine, compared to 10,154 drug addicts in 2017, suggesting a 23.7% reduction. However, the usage of ATS pills which comprise methamphetamine, ecstasy, and amphetamine has increased significantly by 50.8% with 1,152 drug addicts in 2018 compared to 764 drug addicts in 2017. Marijuana consumption increased by 5.3% in 2018 over the previous year with 1,122 drug addicts in a recent year compared to 1,066 in 2017 [5].

Table 1. Number of drug addicts in Malaysia, 2013-2018

Year	Opiate	Marijuana	Methamphetamine (crystalline)	Methamphetamine (pills)	Amphetamine-Type Stimulant	Psychotropic Group	Others	Total
2013	16,041	1,885	2,901	107	369	18	40	21,361
2014	14,502	1,919	4,117	1,239	535	8	35	22,355
2015	16,616	1,389	8,133	674	635	7	25	27,479
2016	16,985	1,236	10,107	2,631	764	18	23	31,764
2017	10,154	1,066	10,419	4,366	764	9	13	26,781
2018	7,746	1,122	11,513	4,853	1,152	26	19	26,449

The government implemented the MFlex Program as one of the components of the Harm Reduction Program in October 2005 to address the issue of HIV infection and other blood-borne diseases as well as to address the issue of opiate addiction in the country. The implementation of this program has proven successful in reducing HIV infection in Malaysia as observed in other countries such as Australia, United Kingdom, Hong Kong which earlier implemented this program. The program also proved to be cost-effective in terms of providing cost savings and returns [3].

MTS by Genichi Taguchi is the implementation of the Taguchi Methods concepts in multivariate applications that helps in quantitative decision making by constructing a multivariate scale of measurements using a data-analytical process [6]. MTS is used to distinguish normal and abnormal findings and to optimize different parameters at the workstation to generate a higher quality

product. The positive gain from signal-to-noise ratio (SNR) meant that the efficiency of the device was still in great condition once a significant variable had been removed [7].

There are two major variations in the distance between the Mahalanobis distance (MD) and the Euclidian distance (ED) as shown in Figure 1. MD is very sensitive to changes in the reference data [8]. MD is very adaptive to the partnership framework of the comparison group and it is used to find the "nearness" of the unknown point from the middle point of the group(s). ED also indicates the distance between the "unknown" point and the group mean point, and there are two limitations of the technique where ED does not have a mathematical calculation of how closely the unknown fits the reference range, and it calculates only a proportional distance from the mean point in the group but does not consider the distribution of the points in the group [9].

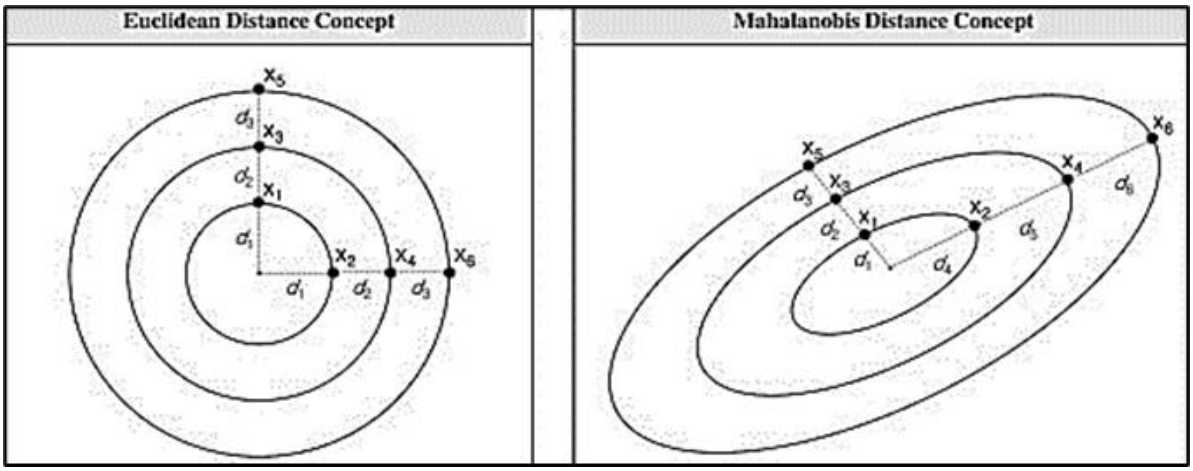

Figure 1. Comparison between MD and ED.

MTS is allowed to identify abnormalities even though learning data were classified as 'unlabelled' [10]. It is used to create a continuous scale of measurement and to calculate the abnormality degree [11], and it can define critical and non-critical variables [12]. On the other hand, MTS can handle issues with binary classification only, it can decide imperative features, but employments the difficult threshold to choose the features [13], and it lacks a strategy for evaluating an appropriate binary classification threshold [14].

According to Mota-Gutiérrez et al. (2018) [15], the research of MTS is grouped into 7 categories which are, introduction to the method, case of study/application, comparison with other methods, construction of Mahalanobis space (MS), integration and development with other methods, dimensional reduction, and threshold establishment. This work used these categories to summarize the research gap of the published work from the year 2011 to 2020 as shown in Figure 2. It can be seen that the integration and development with other methods had the highest percentage of 26% for the application fields using MTS. Then, followed by threshold establishment at 22%, dimensional reduction at 18%, compared with other methods at 15%, case study/application at 8%, introduction to the method at 6%, and construction of MS at 5%.

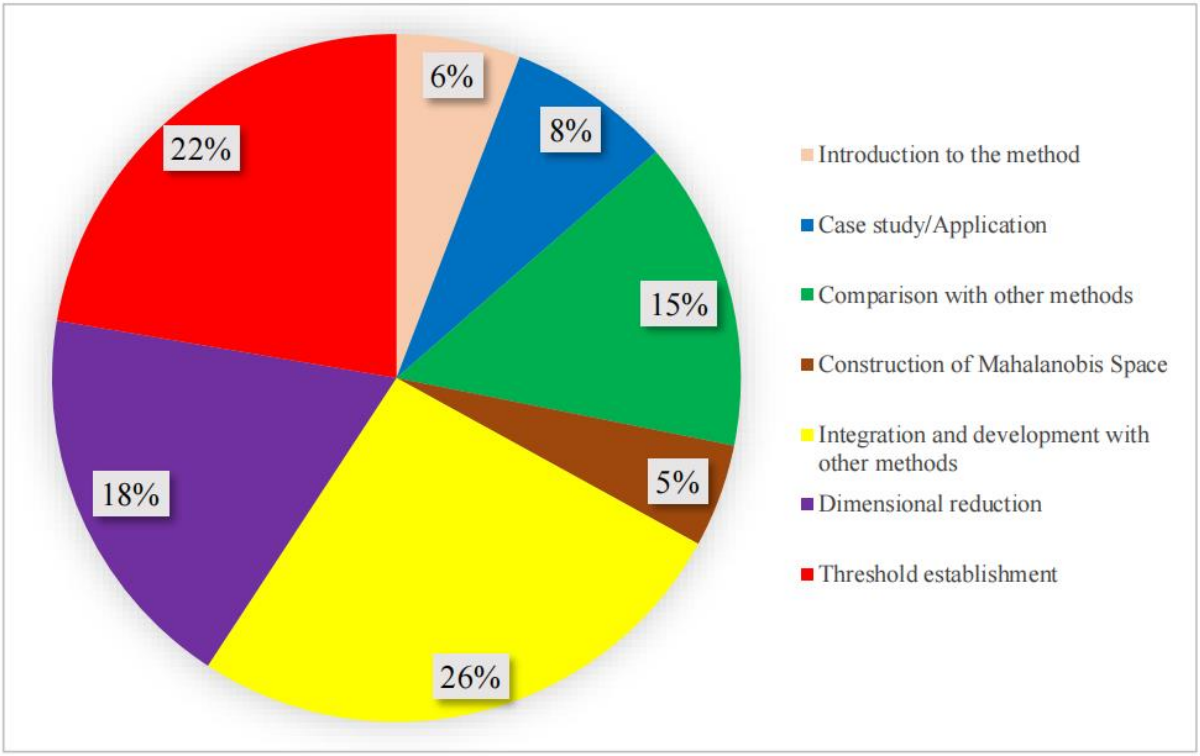

Figure 2. Variety of application fields in MTS

From the findings of the published work in Figure 2, the introduction to the method which is 6% has been chosen as the keyword to expand the research gap. This is because it is the most suitable to be implemented as it focuses on the complete MTS methodology starting from the classification until the optimization process. Based on Table 2, all the published work that contained the application introduction to the method in their literature studies have been listed out and sorted according to the methods they applied in their MTS.

Table 2. Elements introduction to the method

Author (Year)	Application	Method		
		Generate MD		Reduction of element
		Normal	Abnormal	
(Ohkubo & Nagata, 2019)	Unlabelled unit space	√	√	X
(Fukuda, 2017)	Human Motion Control	√	X	X
(Res´endiz-Flores & L´opez-Quintero, 2017)	Welding process	√	X	√
(Ketkar & Vaidya, 2014)	MBA program	√	X	√
(Piyush Shakya et al., 2014)	Bearing health status	√	X	√
(Dimitris Liparas et al., 2013)	Encephalographic	√	√	X

In the application of unlabelled unit space, [16] used the method for generating MD in their works. The collected historical data can detect anomalies using the MTS even when learning data is labelled as 'unlabelled'. However, the proposed procedure is not in accordance due to when there is a mix of mislabelled data, it can lead to unlabelled detection problems. A total research gap concludes that the MTS method is more suitable to be applied in their technology system studies. There is a gap in optimizing the unnecessary data due to no development of the reduction of the element. As a result, this work will need to focus on a selection of mixed labelled data.

Based on the study by Fukuda (2017) [17], he solely used the method to generate MD for normal to find the result of his finding in human body motion control. He proved that his work is suitable to measure movements quantitatively using MTS. MTS is a successful tool for human motion control because it makes it easier for humans to recognise their motions. A total research gap concludes that the MTS method is more suitable to be applied in their technology system studies. His research has a poor design and the tool used cannot support the middle and ending phase. As a result, this work will need to upgrade the current activity method by following the step by step of MTS method. Besides, this work will focus more on the abnormal finding and the reduction of the element's method to obtain the specific parameters that can be identified and the number of degrees of freedom can be reduced.

[18] were applied to generate MD for normal and reduce the element in their research work. They stated that MTS successfully minimised the number of dimensional variables to be regulated by introducing and applying the hybrid MTS technique using Gompertz Binary Particle Swarm Optimization (GBPSO) after the data has been collected and successfully classified into a healthy group. Consequently, in the welding area, MD could be used to classify welding faults between two groups normal and abnormal. However, there is a gap in generating MD for abnormal leads to the impact of the process since it is an essential step before reducing the element.

Likewise, in the application of MBA program, [19] used MTS to generate MD for normal and optimally select criteria for evaluation. A total research gap concludes that MTS gives better performance in terms of finding the best-fitted candidates, gets closer to the criteria of the B-school, and increases the rating of college/university. Next, the proposed approach to bearing health status decreased the frequency of testing in a healthy state and raised it as the level of harm changes [20].

However, in their research, there is a gap in the full MTS method of generating MD abnormal before optimally selecting the criteria and identifying useful bearing elements respectively. Then, the work on MBA program will focus more on generating MD for abnormal to quantify candidates' scores, whereas the research work on bearing health status will also be focusing on generating MD for abnormal to classify the degradation level of health.

[21] used classification using generate MD method in the encephalographic application. The method approach proposed that underlying notions of healthiness and unhealthiness using MTS have made the use of single-trial (ST) brain reactions as healthy cases in combination with resting-state (RS) activations as unhealthy cases. A total research gap found in encephalography that MTS gave benefit from actual brain response qualifications and improvement. But, there is a gap in optimally the original data of brain responses due to no reduction of element. Then, this work will focus more on the optimization of response detection to obtain the classification of brain responses and decrease unnecessary response data.

3. Research methodology

This research work focused on the MFlex program under the Ministry of Health Malaysia in blood tests. The 34 parameters of blood tests are defined into four types namely, FBC, liver function profile, lipid profile, and renal profile which are used to identify the healthiness of methadone patients. The four types of diseases are for the classification of methadone patients whether they had one of the diseases in those four types during joining the MFlex program. Moreover, the significant parameters of the blood tests can be optimized. Table 3 shows the parameters of blood tests which

contain 34 parameters selection and reference range classified as a healthy group. The total numbers parameters for FBC, liver function profile, lipid profile, and renal profile are 17, 8, 4, and 5 respectively.

Table 3. Parameters in blood tests

Parameters	Unit	Reference range
Full Blood Count (FBC)		
1. White Blood Cell (WBC)	10^9/L	(4.0-11.0)
2. Red Blood Cell (RBC)	10^{12}/L	(3.5-5.6)
3. Haemoglobin (HGB)	g/dL	(11.5-16.4)
4. Hematocrit (HCT)	%	(36-47)
5. Mean Corpuscular Volume (MCV)	fL	(76-96)
6. Mean Corpuscular Haemoglobin (MCH)	pg	(27-32)
7. Mean Cell Haemoglobin Concentration (MCHC)	g/dL	(30-35)
8. Platelet Count (PLT)	10^9/L	(150-400)
9. Lymphocyte % (LYM%)	%	(20.0-45.0)
10. Lymphocyte # (LYM#)	10^9/L	(1.5-3.5)
11. MXD %	%	(3.0-10.0)
12. MXD #	10^9/L	(2.0-7.7)
13. NEUT %	%	(40.0-75.0)
14. NEUT #	10^9/L	(2.5-7.5)
15. MPV	fL	(5.0-10.0)
16. PDW	fL	(12.0-18.0)
17. Fasting Blood Sugar	mmol/L	(4.1-5.9)
Liver Function Profile		
18. Total Protein	g/L	(65-85)
19. Albumin	g/L	(35-52)
20. Globulin	g/L	(20-39)
21. A/G Ratio	-	(0.9-1.8)
22. Total Bilirubin	umol/L	(2-24)
23. Alk Phosphatase	U/L	(30-115)
24. ALT (SGPT)	U/L	(0-41)
25. AST (SGOT)	U/L	(0-41)
Lipid Profile		
26. Cholesterol	mmol/L	(3.60-5.20)
27. Triglycerides	mmol/L	(0.50-2.00)
28. HDL Cholesterol	mmol/L	(0.90-1.55)
29. LDL Cholesterol	mmol/L	(2.3-4.4)
Renal Profile		
30. BUN	mmol/L	(1.7-8.5)
31. Creatinine	umol/L	(62-150)
32. Sodium	mmol/L	(135-152)
33. Potassium	mmol/L	(3.5-5.5)
34. Chloride	mmol/L	(95-114)

The RT-Method could classify items into two categories which are within and outside the unit space. A unit space is a population that is homogeneous with respect to the target object, which is a normal population in many cases. If a normal state is defined as the unit space, and the object data is far removed from that space, it can be determined the situation is abnormal [22]. Unit data was chosen on the basis of the largest number of samples, among other samples. The RT-Method measured the value of the output, but the category is clear

when more than one unit spaces exist. The average value for each parameter is calculated as shown in equation (1), from *n* number of samples in the healthy group.

$$\text{Average, } \overline{X}_j = \frac{1}{n}\left(x_{1_j} + x_{2_j} + ... + x_{n_j}\right)(j = 1, 2, ..., k) \quad (1)$$

The sensitivity β, the linear formula L, and the effective divider r, are shown in equation (2), equation (3), and equation (4) respectively.

$$\text{Sensitivity, } \beta_1 = \frac{L_1}{r} \quad (2)$$

$$\text{Linear equation, } L_1 = \overline{x}_1 x_{11} + \overline{x}_2 x_{12} + ... + \overline{x}_k x_{1k} \quad (3)$$

$$\text{Effective divider, } r = \overline{x}_1^2 + \overline{x}_2^2 + ... + \overline{x}_k^2 \quad (4)$$

The total variations S_T, variation of proportional term S_β, error variation S_e, and error variance V_e, are shown in equations (5) - (8) respectively.

$$\text{Total variation, } S_{T1} = x_{11}^2 + x_{12}^2 + ... + x_{1k}^2 \quad (5)$$

$$\text{Variation of proportional term, } S_{\beta 1} = \frac{L_1^2}{r} \quad (6)$$

$$\text{Error variation, } S_{e1} = S_{T1} - S_{\beta 1} \quad (7)$$

$$\text{Error variance, } V_{e1} = \frac{S_{e1}}{k-1} \quad (8)$$

The standard signal-noise (SN) ratio η is then calculated as stated in equation (9). The greater the value of η, the stronger the relationship between the input and output.

$$\text{SN ratio, } \eta_1 = \frac{1}{V_{e1}} \quad (9)$$

The sensitivity β, and the standard SN ratio η, are then calculated in the healthy group, and the two variables Y_1 and Y_2 are calculated to generate a scatter diagram. Equations (10) and (11) show the value of Y_1 and Y_2 respectively.

$$Y_{i1} = \beta_i \quad (10)$$

$$Y_{i2} = \frac{1}{\sqrt{\eta_1}} = \sqrt{V_{ei}} \tag{11}$$

The prediction of origin is referred to the calculation of the average for Y_1 and Y_2 in equations (12) and (13) respectively.

$$\bar{Y}_1 = \frac{1}{n}\left(Y_{11} + Y_{21} + ... + Y_{n1}\right) \tag{12}$$

$$\bar{Y}_2 = \frac{1}{n}\left(Y_{12} + Y_{22} + ... + Y_{n2}\right) \tag{13}$$

Hence, equations (1) - (13) contributed to equation (14), through A^{-1} (correlation matrix), Y (normalized parameter), Y^T (transpose parameter) and *k (*number of variables). Finally, MD is calculated through equation (14).

$$\text{Mahalanobis distance, } D^2 = \frac{YA^{-1}Y^T}{k} \tag{14}$$

The methadone patients who are under monitoring were classified as an unhealthy group. To calculate the unhealthy group, a similar equation as a healthy group is repeated, but the difference between the two groups is in the normalization of the unhealthy group. The linear equation *L*', and the effective divider *r*', are calculated as the same equation in a healthy group which are equations (3) and (4) respectively. Note that the average values of samples and parameters $\bar{x}$, and the effective divider *r*', are the same values of the healthy group. Next, the value sensitivity β for each unhealthy group can be calculated as stated in equation (2).

After that, the total variations S_T, variation of proportional term S_β, error variation S_e, and error variance V_e, are calculated through equations (5) - (8) respectively. The value of sensitivity β, and the standard SN ratio η, from the unhealthy group, are used for the calculation of variables Y_1 and Y_2 as well. The value of sensitivity β is used for Y_1 as stated in equation (10), meanwhile, the variable Y_2 is converted first as stated in equation (11) for allowing the evaluation of any scattering from the normal conditions. The average value for Y_1 and Y_2 are the same as shown in equations (12) and (13) respectively for the prediction of healthy group origin. Lastly, the MD value can be found based on the equation (14).

The T-Method is utilized as an evaluation of the same parameters towards the output of MD. The highest sample (the highest frequency) will be defined as a healthy group while the remaining number of samples will be defined as an unhealthy group. The average values for every parameter and the output average value from the number of samples in the healthy group are found are shown in equations (15) and (16) respectively.

$$\text{Average value, } \bar{x}_1 = \frac{1}{n}\left(x_{ij} + x_{zj} + ... + x_{nj}\right) \tag{15}$$

$$\text{Average output value, } \bar{y} = m_0 = \frac{1}{n}\left(y_1 + y_2 + ... + y_n\right) \tag{16}$$

The balance samples that belong to healthy group are defined as unhealthy group. After that, the unhealthy group has been normalized using the average value of every parameter and output that belong to the healthy group. The aim of normalization is to make the data more flexible by removing their redundancy. The calculation of normalized data for input and output are shown in equations (17) and (18) respectively.

$$X_{ij} = x'_{ij} - \overline{x}_j \tag{17}$$

$$M_i = y'_i - m_0 \tag{18}$$

The proportional coefficient β and SN ratio η for each parameter are calculated as shown in equations (19) - (25).

Effective divider, $r = M_1^2 + M_2^2 + ... + M_i^2$ (19)

Total variation, $S_{T1} = X_{11}^2 + X_{12}^2 + ... + X_{1k}^2$ (20)

Variation of proportional term, $S_{\beta 1} = \dfrac{\left(M_1 X_{11} + M_2 X_{21} + ... + M_i X_{i1}\right)^2}{r}$ (21)

Error variation, $S_{e1} = S_{T1} - S_{\beta 1}$ (22)

Error variance, $V_{e1} = \dfrac{S_{e1}}{i-1}$ (23)

Proportional Coefficient, $\beta_1 = \dfrac{M_1 X_{11} + M_2 X_{21} + ... + M_i X_{i1}}{r}$ (24)

SN ratio, $\eta_1 = \begin{cases} \dfrac{\frac{1}{r}\left(S_{\beta 1} - V_{el}\right)}{V_{el}} & \text{(when } S_{\beta 1} > V_{el}\text{)} \\ 0 & \text{(when } S_{\beta 1} \le V_{el}\text{)} \end{cases}$ (25)

A positive value of β means that the steepness is ascending to the right, while a negative value of β means that the steepness is descending to the right. The value of η should be a positive value, but if it turns out to be a negative value, it will be considered zero which means there is no longer a significant relationship between input and output.

The integrated estimate value of an unhealthy group is computed by using the proportional coefficient β and SN ratio η for each parameter. The calculation of the integrated estimate value is shown in equation (26). Note that, x_{j1}, x_{j2}, …, x_{j6} are the normalized value of each parameter.

$$\text{Integrated estimate value, } \hat{M}_1 = \frac{\eta_1 \times \frac{X_{i1}}{\beta_1} + \eta_2 \times \frac{X_{i2}}{\beta_2} + ... + \eta_k \times \frac{X_{i6}}{\beta_6} +}{\eta_1 + \eta_2 + ... + \eta_6} \quad (26)$$

The step by step for calculating the estimated SN ratio η is by using the following equations (27) - (33). The estimated SN ratio η is based on the suitability of the orthogonal array (OA).

$$\text{Linear equation, } L = M_1\hat{M}_1 + M_2\hat{M}_2 + ... + M_i\hat{M}_i \quad (27)$$

$$\text{Effective divider, } r = M_1^2 + M_2^2 + ... + M_i^2 \quad (28)$$

$$\text{Total variation, } S_T = \hat{M}_1^2 + \hat{M}_2^2 + ... + \hat{M}_i^2 \quad (29)$$

$$\text{Variation of proportional term, } S_\beta = \frac{L^2}{r} \quad (30)$$

$$\text{Error variation, } S_e = S_T - S_\beta \quad (31)$$

$$\text{Error variance, } V_e = \frac{S_e}{i-1} \quad (32)$$

$$\text{Estimated SN ratio, } \eta = 10\log\left[\frac{\frac{1}{r}\left(S_\beta - V_e\right)}{V_e}\right] \quad (33)$$

The relative importance of the parameter is evaluated in terms of the extent to which the estimated SN ratio deteriorates when the parameter is not used. Two-level OA which is level 1 and level 2 is used for an evaluation. The use of OA enables measurements to be made of the estimated SN ratio under various conditions. The two-level of OA means that level 1 is the parameter that will be used and level 2 is the parameter that will not be used. With respect to the estimated SN ratio, the difference between the averages of SN ratio for level 1 and level 2 for each parameter and on that basis determine the relative importance of the parameters. When the parameter is used with larger SN ratios and when the parameter is not used with smaller SN ratios, the degree of contribution turns out to be positive. Otherwise, when the parameter is used with lower SN ratios and when the parameter is not used with higher SN ratios, the degree of contribution turns out to be negative.

4. Results and discussion

The scatter diagrams of the blood tests between healthy and unhealthy groups are created. All the unhealthy groups are computed sample by sample through two variables of Y_1 and Y_2. The x-axis represents Y_1 (proportional coefficient β) and the y-axis represents Y_2 (SN ratio η). The blue dots on

the graph represent the healthy group with 5 samples while the orange dots represent the unhealthy group with 80 samples. These graphs consist of 34 blood test parameters and the number of samples for the liver function profile is 35. Figure 3 shows a scatter diagram of the liver function profile between healthy and unhealthy samples. The healthy and unhealthy samples form an aggregation of their own. From the scatter diagram, the unhealthy are scattered but still in a group of their own. Both healthy and unhealthy do not overlap with each other due to the MD values for both samples are not identical. The MD value of maximum and minimum for healthy are 5.66 and 0.01 respectively while for unhealthy are 476.67 and 150.70 respectively. Moreover, the average value of MD for healthy is 1.00 and for unhealthy is 352.58.

The value of correlation coefficient *r* for the unhealthy samples (orange dots) is 0.6704. This is a moderate positive correlation, which means there is a tendency for a high correlation between variables. Then, for the healthy samples (blue dots) the value of *r* is 0.0585. It is a positive correlation with a weak relationship.

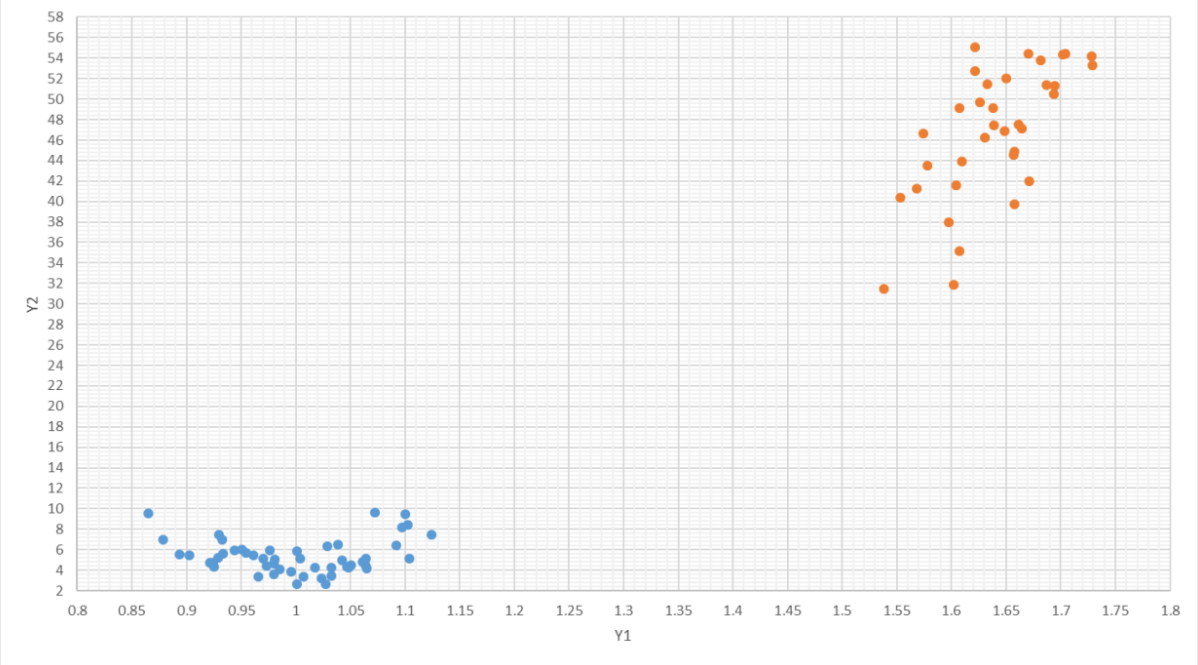

Figure 3. Scatter diagram of liver function profile between healthy and unhealthy.

In the liver function profile of blood tests, the number of healthy and unhealthy samples are 5 and 80 respectively with 34 parameters. The data is organized in the ascending order of output value, as shown in Figure 4. Sample number 11 turns out to be the smallest with 0.011 while sample number 58 turns out to be the with 476.667. That means sample numbers 51, 52, 53, 64, and 79 are set to be the centre point in blue and red dots.

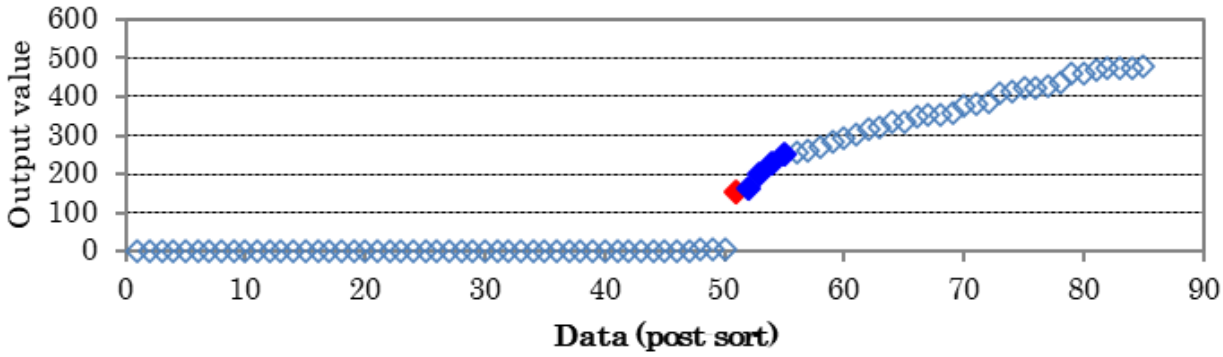

Figure 4. Data (post-sort) for liver function profile in blood tests.

The relationship between parameters and their output values is shown in Figure 5. The x-axis represents the normalized output values and the y-axis represents the normalized parameters' values. To determine which of the parameters would be useful for evaluation, parameter by parameter computation of the proportional coefficient β and SN ratio η were carried out. The T-Method calculates SN ratios η and proportional coefficients β based on the relationship between the normalized output value and the normalized parameter value. According to Teshima, S. et al. (2012) [22], the greater the SN ratio η produces the stronger relationship or in the other words, the distribution is closer to a blue line. Since Figure 5 (A) which represents the parameter of A/G ratio has 0.000007 SN ratio η, so the distribution is far away from a blue line whereas Figure 5 (B) which represents the parameter of Alk phosphatase has 0.0015 SN ratio η, so the distribution is approaching to the blue line. This proves that the greater value of SN ratio, the closer the distribution to a blue line in a graph.

Furthermore, [22] also stated that ascending the line from left to the right indicates the parameter has a positive value of proportional coefficients β whereas descending the line indicates the parameter has a negative value of proportional coefficients β. This has been proven through Figure 5 (A) which represents the parameter of A/G Ratio has -0.0004 of proportional coefficient β whereas the remaining 33 parameters have a positive value of proportional coefficient β. As a result, those parameters are well suited to the purpose of calculating integrated estimate value. This study would derive the value of integrated estimate value by using those proportional coefficient β and SN ratios η values. Therefore, the higher the SN ratio η, the greater the degree to which it contributes to the integrated estimates of MD value which is closer to the actual normalized MD value. Since none of those parameters has a negative SN ratio η value, subsequently all those parameters are considered in integrated estimate value.

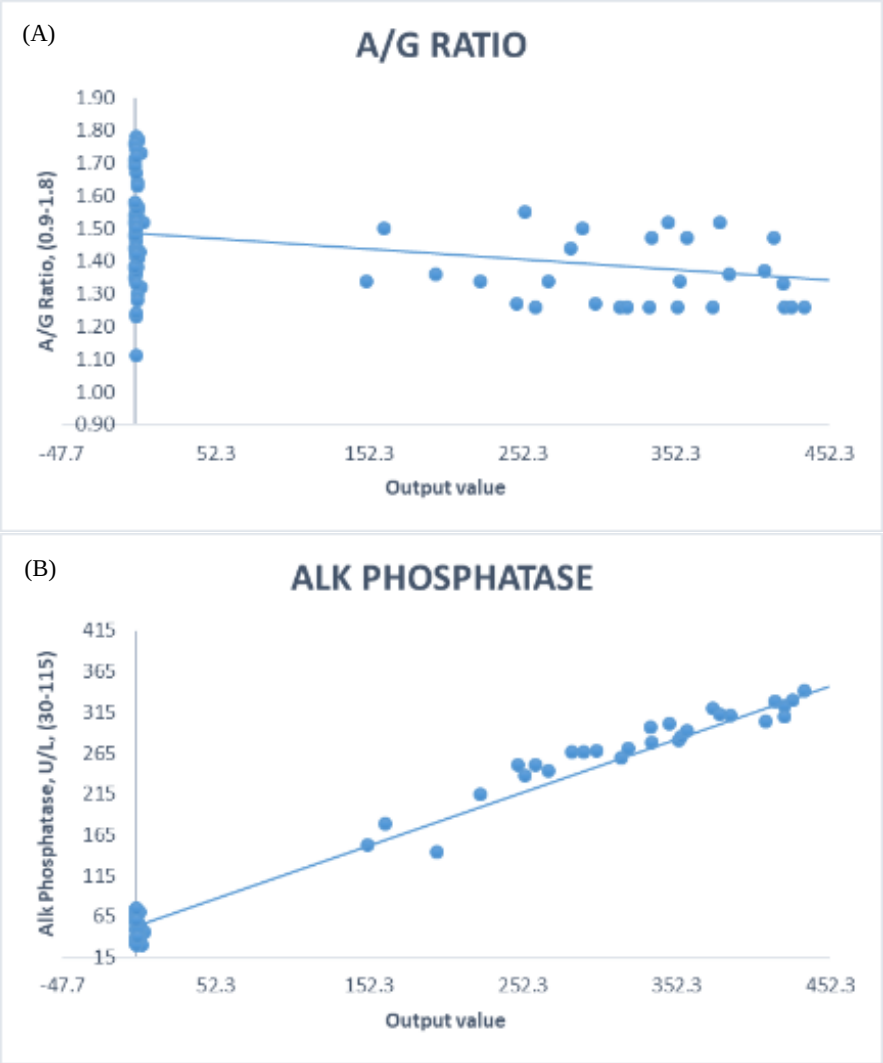

Figure 5. Scatter of normalized output and parameter values of liver function profile.

Figure 6 shows a scatter diagram reflecting what happens when actual values are expressed in x-axis terms, and the estimated values in y-axis terms. If estimated values line up above a straight line, it indicates that a good estimation has been made. Furthermore, the graph will offer additional information regarding an approximately straight line and its attributes. The model contributes to 0.9147 of R^2 or -37.49 db of SN ratios η in general estimation. It means the correlation is high and the distribution is closer to the green line. The equation of the line is shown in equation (34).

$$y = 0.7729x \tag{34}$$

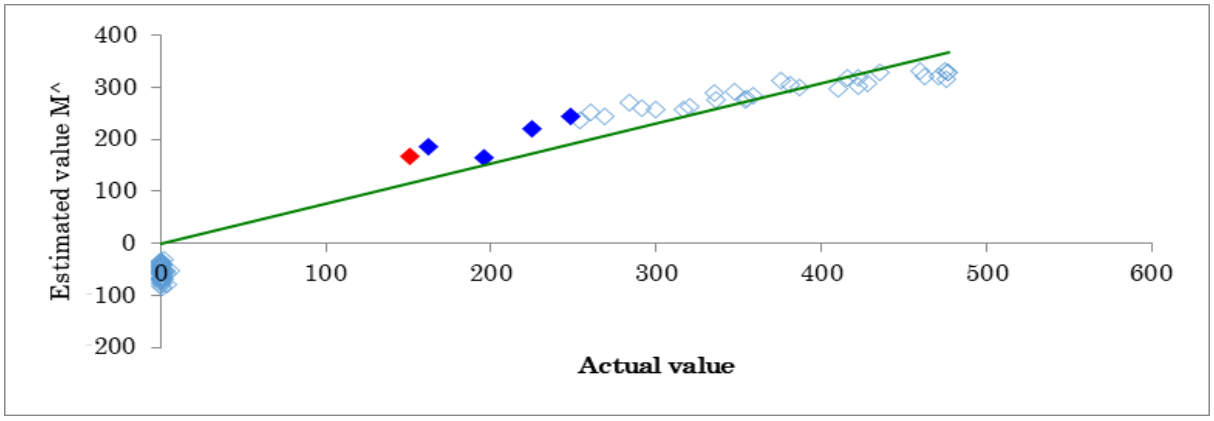

Figure 6. Distribution of actual and estimated signal data values of liver function profile.

Nevertheless, some of those parameters are useful for integrated estimation, while others are not. Hence, parameters assessment is performed by utilizing L_{64} of OA with level 1 indicating the parameter that will be utilized and level 2 indicating the parameter that will not be utilized. The value -37.49 db of integrated estimate SN ratio η refers to the first run in L_{64}. Subsequently, the degree of contribution is translated into a bar graph as shown in Figure 7. From that, it shows how the parameters are significant to the output. When the parameter 22 which represents Alk phosphatase has been used (level 1) with a greater relationship (SN ratio = -34.77 db) to the output and when the parameter has not been used (level 2) with a smaller relationship (SN ratio = -43.29 db) to the output, the parameter would obtain a higher degree of contribution (8.52 db) which is a positive contribution to the output. On the other hand, when parameter 1 which represents white blood cell (WBC) has been used (level 1) with a smaller relationship (SN ratio = -39.17 db) to the output and when the parameter has not been used (level 2) with a greater relationship (SN ratio = -38.89 db) to the output, the parameter would obtain a lower degree of contribution (-0.28 db) which is a negative contribution to the output.

A positive degree of contribution means that the use of a parameter produces the effect of elevating the output of MD whereas a negative degree of contribution means that the use of a parameter produces the effect of lowering the output of MD. Consequently, parameter 22 is positive degree of contribution whereas parameter 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, and 34 are negative degree of contribution. This research suggests that in order to obtain lower MD, the positive degree of contribution should be decreased while the negative degree of contribution should be increased.

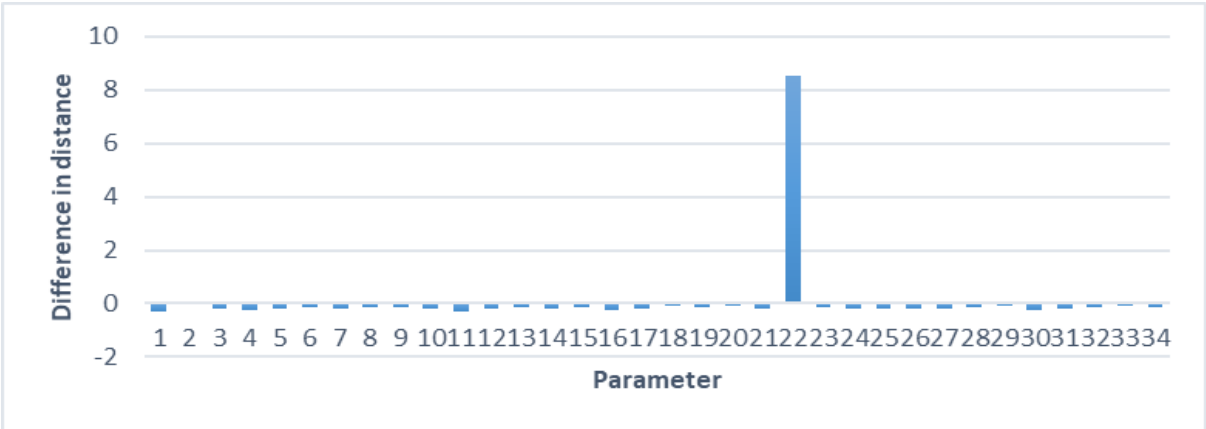

Figure 7. Degree of contribution of liver function profile.

The purpose of diagnosis of unknown data is to measure the MD and evaluate their parameters for each sample. The normalization is performed by subtracting from the average value of the parameters in the healthy group. The results of the estimated value $M\hat{}$ or MD for unknown data (random data) are calculated through equation (26) and subsequently, can be seen in Table 4.

Table 4. The estimated value $M\hat{}$ (MD) for unknown data in the liver function profile

No. of sample	Estimated value M^ (MD)
1	-94.47
2	-63.81
3	-24.93
4	-44.67
5	-53.04
6	87.52
7	113.57
8	128.08
9	113.34
10	119.99
11	41.37
12	42.50
13	40.92
14	40.28
15	41.46

Figure 8 shows a scatter diagram of the estimated values after being subjected to the ecosystem which has been developed during optimization of the liver function profile of blood tests. The x-axis represents the actual values of the output, M and the y-axis represents the estimated values of the output, $M\hat{}$. Since the actual values are unknown, the positions of unknown data on the x-axis use the same values as the estimated values. The position of 15 samples of unknown data is marked as a green triangle in Figure 8. It can be concluded that 5 unknown samples closely belong to the healthy group, 5 unknown samples belong to the unhealthy group, and another 5 unknown samples belong to the outlier.

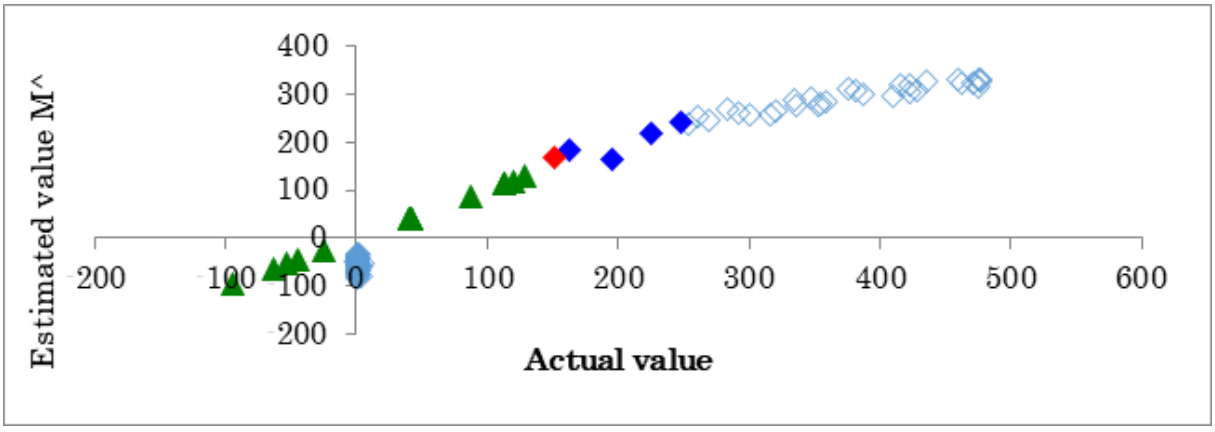

Figure 8. Interpretation of unknown data in liver function profile.

Figure 9 shows the degree of contribution in the first sample of unknown data in the liver function profile. Consequently, parameter 2, 4, 6, 8, 9, 13, 15, 22, 23, and 24 are positive degree of contribution whereas parameter 1, 3, 5, 7, 10, 11, 12, 14, 16, 17, 18, 19, 20, 21, 25, 26, 27, 28, 29, 30,

31, 32, 33, and 34 are negative degree of contribution. This research suggests that in order to obtain lower MD, the positive degree of contribution should be decreased while the negative degree of contribution should be increased.

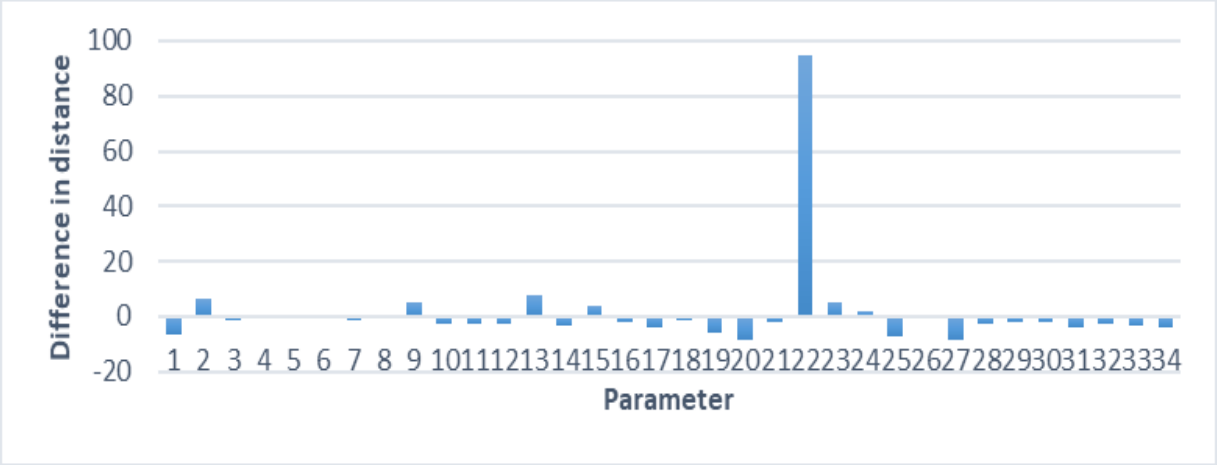

Figure 9. Degree of contribution in the first sample of unknown data in liver function profile.

There are two types of degrees of contribution. First is the positive degree of contribution indicating that the use of this parameter produces the effect of elevating the output. It means by increasing the value of this parameter, the MD value will be increased as well. Second is the negative degree of contribution indicates that the use of this parameter produces the effect of lowering the output. It means by decreasing the value of this parameter, the MD value will be decreased as well. The purpose of this section is to prove that the purpose solution to the Bandar Pekan clinic which is lowering the degree of contribution is the best solution. Thus, this research has selected blood tests (liver function profile) sample 1 as a subject matter as shown in Figure 9. The original output for sample 1 liver function profile is -94.47 as shown in Table 5. The value is compared with 6 types of modification.

Table 5. Comparison between original and types of modification

Original	MD	Modification	MD
1	-94.47	Type 1	-120.56
		Type 2	-56.41
		Type 3	-401.56
		Type 4	-274.82
		Type 5	-80.26
		Type 6	-134.78

The MD value for type 1 modification is -120.56 which is smaller than the original sample. This modification means the higher positive degree of contribution is added with two points (parameter 2, 9, 13, 22, and 23) while lower positive degree of contribution is added with one point (parameter 4, 6, 8, 15, and 24). On the other hand, the higher negative degree of contribution is subtracted with two points (parameter 1, 19, 20, 25, and 27) while the lower negative degree of contribution is subtracted with one point (parameter 3, 5, 7, 10, 11, 12, 14, 16, 17, 18, 21, 26, 28, 29, 30, 31, 32, 33, and 34). Consequently, this modification as a proposed solution has been rejected.

The MD value for type 2 modification is -56.41 which is higher than the original sample. This modification means the higher positive degree of contribution is subtracted with two points (parameter 2, 9, 13, 22, and 23) while the lower positive degree of contribution is subtracted with one point (parameter 4, 6, 8, 15, and 24). On the other hand, the higher negative degree of contribution is added with two points (parameter 1, 19, 20, 25, and 27) while the lower negative degree of contribution is added with one point (parameter 3, 5, 7, 10, 11, 12, 14, 16, 17, 18, 21, 26, 28, 29, 30, 31, 32, 33, and 34). Consequently, this modification as a proposed solution has been accepted.

The MD value for type 3 modification is -401.56 which is smaller than the original sample. This modification means the higher positive degree of contribution is added with two points (parameter 2, 9, 13, 22, and 23) while the lower positive degree of contribution is added with one point (parameter 4, 6, 8, 15, and 24). On the other hand, the higher and lower negative degree of contribution is set as 0. Consequently, this modification as a proposed solution has been rejected.

The MD value for type 4 modification is -274.82 which is smaller than the original sample. This modification means the higher and lower positive degree of contribution is set as 0. On the other hand, the higher negative degree of contribution is subtracted with two points (parameter 1, 19, 20, 25, and 27) while the lower negative degree of contribution is subtracted with one point (parameter 3, 5, 7, 10, 11, 12, 14, 16, 17, 18, 21, 26, 28, 29, 30, 31, 32, 33, and 34). Consequently, this modification as a proposed solution has been rejected.

The MD value for type 5 modification is -80.26 which is higher than the original sample. This modification means the higher positive degree of contribution is added with two points (parameter 2, 9, 13, 22, and 23) while the lower positive degree of contribution is added with one point (parameter 4, 6, 8, 15, and 24). On the other hand, the higher and lower negative degree of contribution maintained their value. Consequently, this modification as a proposed solution has been rejected.

The MD value for type 6 modification is -134.78 which is smaller than the original sample. This modification means the higher and lower positive degree of contribution maintained their value. On the other hand, the higher negative degree of contribution is subtracted with two points (parameter 1, 19, 20, 25, and 27) while the lower negative degree of contribution is subtracted with one point (parameter 3, 5, 7, 10, 11, 12, 14, 16, 17, 18, 21, 26, 28, 29, 30, 31, 32, 33, and 34). Consequently, this modification as a proposed solution has been rejected.

Therefore, the best solution for the Bandar Pekan clinic is modification type 2 because it shows the highest MD value than others which is nearest to the positive value. However, the proposed solution also might be influenced by the total number of positive and negative degrees of contribution, and the total number of higher and lower degrees of contribution. Also, the proposed solution might be different in real practice. The interview session with the pharmacist at Bandar Pekan clinic is done to ask her opinions about the classification and optimization using MTS in MFlex program. The question and the response were as stated below.

Question: In your opinion, does the RT-Method make it easier for the health department to classify between healthy and unhealthy patients in providing treatment?

Answer: Yes, because it gives benefits which is we know the patients are in the healthy group or in the unhealthy group. Besides, it will improve assisting the doctor in comparing whether the patient has recovered or not.

5. Conclusion

From this research, MTS can classify between healthy and unhealthy data. Besides, it can identify the significant parameters for the liver function profile in the blood tests. In other words, it proved that MTS can analyse the significant factors in the blood tests of the MFlex program. In the liver function profile, the average MD of healthy is 1.00 and unhealthy is 352.58. The positive degree

of contribution is parameter 22 whereas the negative degree of contribution is parameter 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, and 34. There are 6 types of modification to prove the proposed solution and type 2 modification has been selected as the best solution. A pharmacist from Bandar Pekan clinic has confirmed that MTS is able to solve a problem in classification and optimization in the MFlex program. It might be interesting if the RT-Method and T-Method of MTS can be applied for system updates, determination of medications, and ascertainment of patients from previous facilities.

Acknowledgements

This study was supported by Universiti Malaysia Pahang under PGRS220364 and the Ministry of Health, Malaysia.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

[1] Waly, G. (2021). *World Drug Report 2021. United Nations: Office on Drugs and Crime*. http://www.unodc.org/unodc/en/data-and-analysis/wdr2021.html

[2] Buntat, Y., & Rahaman, D. R. (2014). Addiction profile among addicts detained at CRCC throughout Malaysia. *Jurnal Antidadah Malaysia*, 12(1), 110-121. ISSN: 1985-1707

[3] Yuswan, F., & Dazali, M. N. M. (2016). Policies and Standard Operating Procedures Methadone Treatment Program. 7-42.

[4] Peacock, A., Leung, J., Larney, S., Colledge, S., Hickman, M., Rehm, J., & Degenhardt, L. (2018). Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. *Addiction*, 113(10), 1905-1926. https://doi.org/10.1111/add.14234

[5] Ministry of Health of Malaysia. (2019). Malaysia Country Report on Drug Issues 2019. *Alternative Development towards a Drug-Free ASEAN Community*, 1-27.

[6] Taguchi, G. (2001). Taguchi methods in LSI fabrication process. *6th International Workshop on Statistical Methodology*, 1-6. https://doi.org/10.1109/IWSTM.2001.933815

[7] Safeiee, F. L. M., & Abu, M. Y. (2020). Optimization using Mahalanobis-Taguchi System for inductor component. *Journal of Physics: Conference Series*, 1529, 1-7. https://doi.org/10.1088/1742-6596/1529/5/052045

[8] Ghasemi, E., Aaghaie, A., & Cudney, E. A. (2015). Mahalanobis Taguchi system: a review. *International Journal of Quality & Reliability Management*, 32(3), 291-307. https://doi.org/10.1108/IJQRM-02-2014-0024

[9] Taguchi, G., & Jugulum, R. (2002). The Mahalanobis-Taguchi Strategy: A Pattern Technology System. *John Wiley and Sons, Inc.* https://books.google.com.my/books?hl=en

[10] Ohkubo, M., & Nagata, Y. (2019). Anomaly detection for unlabelled unit space using the Mahalanobis Taguchi system. *Total Quality Management & Business Excellence*, 1-15.

[11] Chang, Z. P., Li, Y. W., & Fatima, N. (2019). A theoretical survey on Mahalanobis-Taguchi system. *Measurement*, 501-510. https://doi.org/10.1016/j.measurement.2018.12.090

[12] Abu, M. Y., Nor, E. E. M., & Rahman, M. S. A. (2018). Costing improvement of remanufacturing crankshaft by integrating Mahalanobis-Taguchi System and Activity based Costing. *IOP Conference Series: Materials Science and Engineering*, 342, 1-10. https://doi.org/10.1088/1757-899X/342/1/012006

[13] Wang, N., Zhipeng, W., Limin, J., Yong, Q., Xinan, C., & Zuo, Y. (2018). Adaptive Multiclass Mahalanobis Taguchi System for Bearing Fault Diagnosis under Variable Conditions. *Sensors (Basel)*, 19(1), 1-16. https://doi.org/10.3390/s19010026

[14] El-Banna, M. (2017). Modified Mahalanobis Taguchi System for Imbalance Data Classification. *Computational Intelligence and Neuroscience*, 1-15. https://doi.org/10.1155/2017/5874896

[15] Mota-Gutiérrez, C. G., Reséndiz-Flores, E. O., & Reyes-Carlos, Y. I. (2018). Mahalanobis-Taguchi system: state of the art. *International Journal of Quality & Reliability Management*, 35(3), 596-613. https://doi.org/10.1108/IJQRM-10-2016-0174

[16] Ohkubo, M., & Nagata, Y. (2019). Anomaly detection for unlabelled unit space using the Mahalanobis Taguchi system. *Total Quality Management & Business Excellence*, 1-15.

[17] Fukuda, S. (2017). A Mahalanobis Taguchi Approach to Human Motion Control. *Advances in Intelligent Systems and Computing*, 65-71. https://doi.org/10.1007/978-3-319-60495-4_7

[18] Res´endiz-Flores, E. O., & L´opez-Quintero, M. E. (2017). Optimal identification of impact variables in a welding process for automobile seats mechanism by MTS-GBPSO approach. *Int J Adv Manuf Technol*, 437–443. https://doi.org/10.1007/s00170-016-9395-5

[19] Ketkar, M., & Vaidya, D. O. S. (2014). Evaluating and Ranking Candidates for MBA program: Mahalanobis Taguchi System Approach. *Procedia Economics and Finance*, 654 - 664. https://doi.org/10.1016/S2212-5671(14)00231-7

[20] Shakya, P., Kulkarni, M. S. & Darpe, A. (2014). A novel methodology for online detection of bearing health status for naturally progressing defect. *Journal of Sound and Vibration*, 333(21), 5614-5629. https://doi.org/10.1016/j.jsv.2014.04.058

[21] Liparas, D., Laskaris, N. & Angelis, L. (2013). Incorporating resting state dynamics in the analysis of encephalographic responses by means of the Mahalanobis–Taguchi strategy. *Expert Systems with Applications*, 40(7), 2621–2630. https://doi.org/10.1016/j.eswa.2012.11.014

[22] Teshima, S., Hasegawa, Y., & Tatebayashi, K. (2012). Quality Recognition and Prediction: Smarter Pattern Technology with the Mahalanobis-Taguchi System. *Momentum Press LLC*, 1-220. ISBN 1606503421