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How well can signs and symptoms predict AMI in the Malaysian population?

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How well can signs and symptoms predict AMI in the Malaysian population?

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Abstract

The aim of the study was to use data from an electronic medical record system (EMR) to look for factors that would help us diagnose acute myocardial infarction (AMI) with the ultimate aim of using these factors in a decision support system for chest pain. We extracted 887 records from the electronic medical record system (EMR) in Selayang Hospital, Malaysia. We cleaned the data, extracted 69 possible variables and performed univariate and multivariate analysis. From the univariate analysis we find that 22 variables are significantly associated with a diagnosis of AMI. However, multiple logistic regression reveals that only 9 of these 22 variables are significantly related to a diagnosis of AMI. Race (Indian), male sex, sudden onset of persistent crushing pain, associated sweating and a history of diabetes mellitus are significant predictors of AMI. Pain that is relieved by other means and history of heart disease on treatment are important predictors of a diagnosis other than AMI. The degree of accuracy is high at 80.5%. There are 13 factors that are significant in the univariate analysis but are not among the nine significant factors in the multivariate analysis. These are location of pain, associated palpitations, nausea and vomiting; pain relieved by rest, pain aggravated by posture, cough, inspiration and exertion; age more than 40, being a smoker and abnormal chest wall and face examination. We believe that these findings can have important applications in the design of an intelligent decision support system for use in medical care as the predictive capability can be further refined with the use of intelligent computational techniques.

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Keywords: Acute myocardial infarction; Diagnosis; Prediction; Multiple logistic regression

1. Introduction

Acute chest pain in adults is a frequently encountered symptom in all healthcare settings [1]. It warrants immediate attention and assessment because of the high rates of morbidity and mortality associated with the pathology. It is a symptom that can be quite perplexing for the doctor because of the wide range of differential diagnoses possible for the patient. Differential diagnoses can range from the most life threatening of illnesses to simple problems that can be treated in the outpatient clinic. It is vital for the emergency physician not to miss a diagnosis of AMI as ischaemic heart disease is one of the leading causes of morbidity and mortality in the western world [2]. In a review of sudden deaths in England, it was found that for cases involving myocardial tissue, death was ascribed to ischaemic heart disease in 82.4% of cases [3]. In the elderly, hypertension and ischaemic heart disease have been found to be significant predictors of emergency room admissions [4].

There are many risk factors for AMI. In the elderly, for example it has been shown that hyperlipidaemia, smoking, hypertension, diabetes and a family history of heart disease are independently and strongly related to the risk of AMI [5]. In addition to these, males are often at substantially higher risk than females and renal impairment does appear to influence mortality for AMI [6]. Hypertension treatment has been shown to be of benefit in hypertensives with diabetes, ischaemic heart disease and high global cardiovascular risk although in smokers, these should be accompanied by efforts to induce smoking cessation [7]. Blood pressure was at least as strongly associated with
cardiovascular events in Asian populations compared to Australasian populations [8]. Throughout middle and old age, blood pressure is strongly and directly related to vascular (and overall) mortality, without any evidence of a threshold down to at least 115/75 mm Hg [9].

The importance of diabetes mellitus in the aetiology of AMI cannot be over-emphasised although the incidence varies between ethnic groups. A study of Turkish and Sirunam–Asian migrants in the Netherlands [10] showed a high prevalence of ischaemic heart disease in young migrant Asians with diabetes and in the Slovak Republic, every fifth diabetic patient has ischaemic heart disease [11].

Chest pain possesses the characteristic of occasionally being vague but sometimes it is fairly localised and having distinct characteristics that would immediately alarm an experienced physician. When this occurs, a confirmatory investigation such as an electrocardiogram (ECG) and/or cardiac enzymes is definitely warranted. Localisation of chest pain may have some limited value (although not that predictive) in the diagnosis of myocardial infarction [12] but a focused history and physical examination followed by an ECG remain the key tools for the diagnosis of myocardial infarction [13]. In children, the diagnosis of chest pain is less clear-cut and there are grounds for ordering further investigations like echocardiograms, ECG and chest X-rays especially when such children are seen for the first time for heart murmurs or chest pain. Nonetheless, these investigations are expensive and should be added only when clinically warranted by the history and physical examination [14].

The aim of the study was to see how well factors from history and physical examination predict a diagnosis of acute myocardial infarction (AMI) in Malaysians with the further aim of later using these factors in researching a decision support system for chest pain.

2. Materials and methods

2.1. Source of data

We obtained the dataset from Selayang Hospital, a tertiary level hospital in Malaysia. This hospital is unique in that it is the first hospital in Malaysia to use an electronic medical record (EMR) system and thus is able to record and store accurate and comprehensive details about a patient’s illness in an electronic database right from the point of entry until discharge. The hospital information system (HIS) has source On-line Transaction Processing (OLTP) data stored in a large database. Basically the entire EMR consists of forms created by hospital staff before the hospital began operations 4 years ago. There are a number of forms used for this purpose and depending on the type of illness, there are a number of fields that are required for the project. All records of patients seen in the Emergency Department for chest pain from 20 August 1999 (when the hospital opened) to 9 August 2002 and clerked using the chest pain clerking form were extracted for this study.

Selayang Hospital has a specific form for patients with chest pain and the database is a rich source of data on which many studies can be done. All data from this form was extracted for records which fitted the criteria above. No identification data other than the medical record number (MRN) and financial number were required to identify the record. This ensured that confidentiality was preserved.

To extract the dataset from the hospital we used a specialised data-mining tool called Speedminer as the database was constructed for flexibility rather than for easy data mining. After processing the information using Speedminer, we extracted a total of 887 records, which was exported into an MS Excel spreadsheet and subsequently exported to MS Access.

2.2. Data cleaning and pre-processing

Data cleaning and pre-processing was performed before any analysis was carried out. This involved accuracy checking, treatment of missing values, recategorisation and recoding of fields and feature construction. The data was then analysed using various statistical techniques. A total of 77 variables were analysed with respect to AMI. Frequency tables and descriptive statistics were run for all the variables and relevant graphs such as scatter plots and histograms were used to examine the data distribution and to detect outliers in the data. Outliers were carefully checked against the original data and were only corrected where it was felt that they were clearly errors in entry. We used the diagnosis on discharge as the definitive diagnosis. This is the diagnosis as confirmed by specialist physicians after taking into consideration ECG readings and other laboratory investigations. Physicians who provided the definitive diagnoses were not necessarily the same ones who treated the subjects in the Emergency Department as they came from the Medicine Department rather than the Emergency Department and all cases of AMI were treated as inpatients.

2.3. Missing value analysis and treatment

Some data was missing, probably because the attending doctor did not see any need to fill in such data. The range of missing data was variable and depended on the variable but ranged between 0% and 10%. We were able to analyse and treat for missing values in numeric fields. First the distributions of the variables were examined to see whether they deviated from known distributions. To do this, histograms, P–P plots and Q–Q plots of the numeric fields were created. Histograms can be used for looking at the distribution is a general way but comparison with any distribution is less precise. To be more precise, one can use P–P plots and Q–Q plots where there is a comparison with the expected values if such a field is normally distributed. Alternatively, one can use a statistical test like the One-
sample Kolomogorov–Smirnov test. This test is used to test the hypothesis that a sample comes from a particular distribution (Uniform, Normal, or Poisson). The value of the Kolomogorov–Smirnov Z is based on the largest absolute difference between the observed and the theoretical cumulative distributions. The downside is that deviations from the theoretical distribution caused by outliers will be a problem so practically speaking, one might like to use a combination of graphs and the Kolomogorov–Smirnov test to determine whether a field approximates some sort of known distribution or not. If the data does not deviate too much from a normal distribution, then the mean will be a good value to use as a replacement for the missing values. Otherwise, if it deviates too much from the Normal distribution, then a global constant or the median may be a better value to use to replace the missing values. The distributions appear to be more or less normal in shape. The values of the constants are taken to be the average of the maximum and minimum normal values and as these values are normally distributed in the population, these should be fair values to use. An analysis of the means before and after replacement of missing values see little change in the means, leading to the conclusion that replacing the missing values will have little impact on the overall result. However, for the statistical analysis of the data, the actual values are used so as not to distort the true picture.

2.4. Analysed variables

Variables selected for analysis were all variables thought to have any relationship to AMI. Table 1 displays and groups these variables.

2.5. Statistical tests

The t-test and the Mann–Whitney U-test (where the variances were not homogenous) were performed to compare the means of AMI and non-AMI patients for these variables—age, pulse rate, systolic and diastolic blood pressure (BP) [15]. Before the t-test was used, normality assumptions were assessed using the Kolmogorov–Smirnov test and homogeneity of variances were tested using the Levene’s test. The χ² test (with continuity correction for 2×2 tables) and odds ratios (ORs) were performed to look for relationships between categorical variables [16]. These variables are divided into various groups—demographic factors, nature of chest pain, radiation of chest pain, relieving factors, associated factors, aggravating factors, cardiac risk factors and examination factors. Multiple logistic regression was carried out for all categorical variables with respect to acute myocardial infarction as the dependent variable [17]. Three different logistic regression techniques were used—the enter method, forward likelihood ratio and backward likelihood ratio. Interaction was carefully examined and likely interaction terms were tested before the final model was produced.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Independent variables selected for the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>Fields</td>
</tr>
<tr>
<td>Demographic</td>
<td>Age, citizen, race, sex, marital status</td>
</tr>
<tr>
<td>Nature of chest pain</td>
<td>Location, onset, pattern, quality</td>
</tr>
<tr>
<td>Radiation of pain</td>
<td>Jaw, left arm, laterally, neck, locally, other parts</td>
</tr>
<tr>
<td>Relieving factors</td>
<td>Leaning forward, sitting up, GTN, rest, other means</td>
</tr>
<tr>
<td>Aggravating factors</td>
<td>Posture, meals, coughing, inspiration, exertion</td>
</tr>
<tr>
<td>Associated heart/lung symptoms</td>
<td>Cough, dyspnoea, oedema, orthopnoea, palpitations</td>
</tr>
<tr>
<td>Other associated symptoms</td>
<td>Collapse, headache, dizziness, fever, numbness, nausea, sweating, vomiting, fainting</td>
</tr>
<tr>
<td>Cardiac risk factors</td>
<td>Age &gt;40, diabetes mellitus, family history, hypertension, physical inactivity, obesity, smoking, known case defaulted treatment, known case on treatment, high cholesterol levels</td>
</tr>
<tr>
<td>General examination</td>
<td>Pulses, pulse rate, respiratory rate, systolic BP, diastolic BP</td>
</tr>
<tr>
<td>Heart/lung examination factors</td>
<td>Air entry, breath sounds, chest expansion, chest wall, crepitations, heart sounds, JVP, percussion, pleural rub, prae, ronchi</td>
</tr>
<tr>
<td>Other examination factors</td>
<td>Abdomen, central nervous system (CNS), eye, face</td>
</tr>
</tbody>
</table>

All univariate statistical tests were carried out using a significance level of 0.05. All multiple logistic regression models were built using p=0.05 for entry and p=0.10 for removal.

2.6. Biases and limitations

There are some limitations to our analysis. We are aware that the data is from a hospital and does not include those who suffered from and died of AMI outside the hospital or those who suffered from silent myocardial infarcts and were not admitted to the hospital. It is, however, difficult to obtain data from such patients and there is no way of determining what proportion of patients has been missed in this way. We are not also able to provide information about the number of subjects in the sample who had not been appropriately treated in the Emergency Department or had been misdiagnosed as such information was not available.

3. Results

A total of 887 records were analysed. The mean age of patients was 53.84 years (standard deviation 13.09). There were 649 males (73.2%) and 238 females (26.8%). Malays formed the biggest proportion of patients (43.4%), followed by Chinese (27.1%), Indians (25.7%) and other races (3.8%). Almost all the patients were Malaysians (98.5%).
3.1. Quantitative variables

Table 2 looks at the difference in certain quantitative variables between AMI patients and non-AMI patients. The \( t \)-test was applied for all quantitative variables except where assumptions of normality and homogeneity of variance for its use could not be met. Where the assumptions were not met, the Mann–Whitney \( U \)-test was used. Four quantitative variables were analysed—age, pulse rate, systolic and diastolic blood pressure (BP). All of them except for diastolic BP are significantly different in both AMI and non-AMI groups. AMI patients are on average older than non-AMI patients, have a significantly lower mean pulse rate and lower mean systolic BP.

3.2. Demographic factors and nature of chest pain

Table 3 looks at demographic factors and nature of chest pain. Four demographic factors were examined (Malaysian citizenship, marital status, race and sex) and four factors related to the nature of the chest pain were examined here (location, onset, pattern and quality). Of the demographic factors, only sex shows a definite relationship with AMI. Males are more likely to be diagnosed with acute myocardial infarction compared to females (OR 2.48, 95% CI 1.66, 3.71).

As far as nature of chest pain is concerned, location of pain is associated with AMI with those reporting retrosternal pain more likely to have AMI compared to those who complained of any other site (OR 1.51, 95% CI 1.11, 2.05). Those with sudden onset pain are also more likely to have AMI compared to other manner of onset (OR 3.34, 95% CI 2.36, 4.74) and persistent pain is more likely to be diagnosed as AMI compared to any other pattern (OR 4.35, 95% CI 2.99, 6.35). Patients with crushing pain are more likely to be diagnosed as AMI compared to other quality of pain (OR 2.96, 95% CI 2.16, 4.06).

3.3. Radiation of chest pain

Six factors related to radiation of chest pain were examined—radiation to jaw, radiation to left arm, radiation laterally, radiation to neck, radiation locally and radiation to other parts. None of these factors are significantly associated with AMI (not shown in any table).

3.4. Relieving and associated factors

We considered relieving and associated factors for AMI. Five ways whereby chest pain could be relieved were examined (leaning forward, sitting up, glyceryl trinitrate or GTN, rest and other means). The results are shown in Table 4.

Pain that is relieved by rest is less likely to be diagnosed as AMI (OR 0.54, 95% CI 0.36, 0.80). However, pain that is relieved by other means is more likely to be diagnosed as
AMI (OR 1.98, 95% CI 1.40, 2.79). Five cardiac or respiratory associated symptoms were examined in this category—cough, dyspnoea, oedema, orthopnoea, and palpitations. Of these, only palpitations are significantly associated with AMI but in an inverse relationship. Patients with palpitations are less likely to be diagnosed with AMI (OR 0.18, 95% CI 0.02, 0.76). Other than cardiac/respiratory factors, nine other associated symptoms were examined—collapse, headache, dizziness, fever, nausea, numbness, sweating, vomiting and fainting. Of these, patients complaining of nausea (OR 1.80, 95% CI 1.40, 2.39), vomiting (OR 2.26, 95% CI 1.46, 3.50) are more likely to be diagnosed with AMI. Patients over the age of 40 are more likely to be diagnosed with AMI (OR 1.46, 95% CI 1.05, 2.02). Smokers are also more likely to be diagnosed with AMI (OR 2.11, 95% CI 1.51, 2.94). However, patients who are known heart cases on treatment are less likely to be diagnosed with AMI (OR 0.40, 95% CI 0.27, 0.58).

3.5. Aggravating factors

Five aggravating factors of chest pain were examined—posture, meals, cough inspiration and exertion. Patients complaining that their chest pain is aggravated by posture (OR 0.65, 95% CI 0.46, 0.91) are less likely to be diagnosed with AMI. Because little meaningful analysis can be performed here, we have omitted presenting this in a table.

3.6. Cardiac risk factors

Table 5 illustrates results for cardiac risk factors. Ten cardiac risk factors were examined—age more than 40, diabetes mellitus, family history of heart disease, hypertension, physical inactivity, obesity, smoking, known case of heart disease defaulted treatment, known case of heart disease still on treatment and high cholesterol levels. Patients over the age of 40 are more likely to be diagnosed with AMI (OR 1.46, 95% CI 1.05, 2.02). Smokers are also more likely to be diagnosed with AMI (OR 2.11, 95% CI 1.51, 2.94). However, patients who are known heart cases still on treatment are less likely to be diagnosed with AMI (OR 0.40, 95% CI 0.27, 0.58).

Table 6 Multiple logistic regression (backward stepwise) of AMI as dependent variable

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>β (S.E.)</th>
<th>p-value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>−3.653 (0.331)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Race (Indian)</td>
<td>−0.508 (0.218)</td>
<td>0.020</td>
<td>0.60 (0.39, 0.92)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.665 (0.228)</td>
<td>0.004</td>
<td>1.95 (1.24, 3.04)</td>
</tr>
<tr>
<td>Onset (sudden)</td>
<td>0.665 (0.210)</td>
<td>0.002</td>
<td>1.94 (1.29, 2.94)</td>
</tr>
<tr>
<td>Pattern (persistent)</td>
<td>0.969 (0.218)</td>
<td>&lt;0.001</td>
<td>2.63 (1.72, 4.04)</td>
</tr>
<tr>
<td>Quality (crushing)</td>
<td>0.850 (0.193)</td>
<td>&lt;0.001</td>
<td>2.34 (1.60, 3.42)</td>
</tr>
<tr>
<td>Relieved by others</td>
<td>0.673 (0.192)</td>
<td>&lt;0.001</td>
<td>1.96 (1.34, 2.86)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.386 (0.201)</td>
<td>0.055</td>
<td>1.47 (0.99, 2.18)</td>
</tr>
<tr>
<td>Sweating</td>
<td>0.879 (0.194)</td>
<td>&lt;0.001</td>
<td>2.41 (1.65, 3.52)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0.459 (0.261)</td>
<td>0.078</td>
<td>1.58 (0.95, 2.64)</td>
</tr>
<tr>
<td>Aggravated by posture</td>
<td>−1.303 (0.776)</td>
<td>0.093</td>
<td>0.27 (0.06, 1.24)</td>
</tr>
<tr>
<td>Aggravated by inspiration</td>
<td>−1.236 (0.677)</td>
<td>0.068</td>
<td>0.29 (0.08, 1.10)</td>
</tr>
<tr>
<td>Age &gt; 40</td>
<td>0.359 (0.190)</td>
<td>0.059</td>
<td>1.43 (0.99, 2.08)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.592 (0.230)</td>
<td>0.010</td>
<td>1.81 (1.15, 2.84)</td>
</tr>
<tr>
<td>Heart disease on treatment</td>
<td>−1.027 (0.221)</td>
<td>&lt;0.001</td>
<td>0.36 (0.23, 0.55)</td>
</tr>
<tr>
<td>Abdomen</td>
<td>−1.751 (1.087)</td>
<td>0.107</td>
<td>0.17 (0.02, 1.46)</td>
</tr>
<tr>
<td>Overall percentage correct (Step 48)</td>
<td>80.5%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.7. Examination factors

Fifteen examination factors were examined—abdomen, air entry, breath sounds, central nervous system (CNS), chest expansion, chest wall, lung crepitations, eye, face, heart sounds, jugular venous pressure (JVP), chest percussion, presence of pleural rub, appearance of praecordium and presence of rhonchi. Due to the nature of the electronic medical record, examination of the patient was recorded as either normal or abnormal or signs were present or absent. Where findings were abnormal, some comments would be attached to the notes. However, in many cases, we were not able to eliciting meaningful comments about the types of abnormalities observed so we are unable to analyse these properly. Of the heart/lung examination factors, only examination of the chest wall is significantly related to diagnosis of AMI. Patients with an abnormal chest wall is less likely to be diagnosed with AMI (OR 0.13, 95% CI 0, 0.79). Other examination findings are not related to increased or decreased likelihood of being diagnosed with AMI. Because little meaningful analysis can be performed here, we have omitted presenting this in a table.

3.8. Multiple logistic regression

Table 6 shows logistic regression for AMI performed using the backward stepwise method. We used three different methods (enter, forward stepwise and backward stepwise) to determine which of the three would be the most suitable and parsimonious. After evaluation of these three methods, the
best and the most parsimonious model would appear to be backward stepwise model as this model offers all significant factors which are common to all three models while retaining sufficiently high overall percentage which is correct. We entered 62 variables into the model and evaluated the results. At each step we specified \( p = 0.05 \) for entry and \( p = 0.10 \) for removal from the model. \( p \)-values in the table are final multivariate \( p \)-values, which are obtained after adjustment for all other variables in the model. All nine common factors, which are found to be significant in the logistic regression analysis, are significant in the univariate analysis, indicating that they are not confounded by other factors. The variables are race (Indian), sex (male), sudden onset of pain, pattern of pain (persistent), quality of pain (crushing), pain that is relieved by other means, associated sweating, history of diabetes mellitus and history of heart disease on treatment. The degree of accuracy is quite high at 80.5%. This means that less than 20% of cases cannot be predicted by these factors and would require input of other factors.

There are 13 factors which are significant in the univariate analysis but are not among the nine significant factors in the multivariate analysis. These are location of pain, associated palpitations, nausea and vomiting; pain relieved by rest, pain aggravated by posture, cough, inspiration and exertion; age more than 40, being a smoker and abnormal chest wall and face examination.

4. Discussion

There are a few interesting findings in this analysis. Quite a number of factors investigated here have been well studied before and it is thus not surprising to find them to be significant. We would naturally expect to find AMI patients to be older than non-AMI patients. We would not, however, expect to find lower pulse rates and lower diastolic blood pressure in AMI patients unless there has been some deterioration in cardiac function. However, this is not borne out in the diagnosis made by the attending physician and clinically speaking we really should not expect to find these to be different so perhaps further study needs to be done on these. We had expected to find sex and ethnicity (Indians) to be significant factors in Malaysia as literature from other countries including neighbouring Singapore [18–20] have reported these to be risk factors for AMI. Sex is definitely associated with AMI (both univariate and multivariate analyses confirm this to be true) but univariate analysis fails to show any relationship between AMI and ethnicity. However, Indians are shown to have a lower (and not higher) risk of having AMI in the multivariate analysis. This is surprising and we cannot offer any explanation for this. We are not that surprised to find that the location of pain; although significant in the univariate analysis, is not significant after adjustment for other effects as this is a subjective symptom and similar findings elsewhere bears this out [12]. Having said that, we tend to conclude that persistent, crushing pain of sudden onset accompanied by sweating (most likely an autonomic response to pain) remain strong predictors of AMI and may be more important than localisation of pain. We are not surprised to find that pain relieved by rest is not statistically significant after adjustment for other variables as this is more characteristic of angina rather than AMI. Aggravation of pain by any means does not stand up to multivariate analysis and we would tend to conclude that aggravating factors may not be important as predictors of AMI. We do find the non-significance of age >40 and smoking in the multivariate analysis odd as both are highly significant risk factors in the univariate analysis. This needs to be looked into carefully in the future. Diabetes, as expected, remains a very important predictor of AMI [21,22] and we are not at all surprised by these results. On the other hand, we failed to find a relationship between AMI and high cholesterol levels, family history and hypertension despite studies confirming the existence of these. Whether this is peculiar to the sample we had or is purely by chance is not possible to determine at this point.

We found in this sample that having heart disease but still on treatment made it less likely for a patient to be diagnosed as a case of AMI. This could be due to some other diagnosis being made, such as stable or unstable angina and needs to be looked into carefully. We put this down to the lower likelihood of getting AMI for heart patients who are on proper follow-up treatment. We are not surprised to find that examination factors are less important compared to other factors in diagnosing AMI as there are few (if any) specific signs that a patient is suffering from AMI.

The factors studied in this paper confirm the value of a good history in diagnosing AMI. The importance of this cannot be over-emphasised as the high predictive value (80% of diagnoses can be predicted from just these data alone) based on only a few important points raises the possibility of AMI diagnosis based on history reinforced by ECG and cardiac enzyme markers.

We realise that there are some limitations to our analysis. The possibility of some bias occurring because we have limited our sample to hospital patients cannot be excluded. However, our main aim was to obtain some predictive signs and symptoms to enable us to develop a decision support system relevant to the Malaysian population so we believe that this is possibly the best way we can go about accomplishing this. We also believe that these findings can have important applications in the design of an intelligent decision support system for use in medical care as the predictive capability can be further refined with the use of intelligent computational techniques.

Acknowledgments

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References