Data Extraction for Associative Classification using Mined Rules in Pediatric Intensive Care Data

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Abstract: Based on the characteristics of health and medical informatics, data mining techniques that were designed to tackle healthcare problems are faced with new challenges. One such challenge is to prepare medical data for pattern mining or machine learning. In this paper, we present a feature engineering technique for the Associative Classification of the Systemic Inflammatory Response Syndrome (SIRS) in severely ill children by mining Associative Rules. SIRS is characterized as the body's excessive defense response due to malevolent stressors such as trauma, acute inflammation, infection, malignancy, and surgery. It can have an impact on the clinical outcome and elevate vulnerability for organ dysfunctions. We aim to extract the features from given datasets using the described extraction process. After the transformation, those features are used to mine rules using Association Rule Mining. Those rules are used to perform Associative Classification and evaluated with the result generated by SIRS criteria defined by the experienced clinicians. The mined rules provide better control over sensitivity and specificity than the SIRS criteria used in everyday medical practice..

Keywords: Data Mining; SIRS; Association Rule Mining; Associative Classification

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1 Introduction

Recently, patient monitoring and clinical documentation in the Intensive care unit (ICU) are performed with patient data management systems (PDMS). Sophisticated PDMS are able to directly present and analyze all incoming data, necessary for the diagnosis of a disease. Systemic inflammatory response syndrome (SIRS) was introduced along with the definition of sepsis for the adult in 1992 [Bo92] and SIRS criteria were modified for the children with age-specific norms in 2005 [Go05]. Four criteria were proposed to detect the presence of SIRS in children, which are a) hyperthermia or hypothermia, b) tachy- or bradycardia c) tachy- or bradypnoea or d) leukocytosis, leukopenia or increased immature neutrophile count [Go05]. Two of these four criteria must be evident, one of which has to be abnormal leukocyte count or temperature to be diagnosed with SIRS. For pediatricians, the recognition of SIRS in children is a challenging duty due to the nature of its definition, as there are different age-specific values for all these criteria except temperature. Age groups for some patients, especially newborn children, can even change multiple times within a short timespan i.e., during their stay on the pediatric intensive care unit (PICU) [In09]. Due to this complexity, it is difficult to diagnose SIRS in an early manner, especially in the stressful surroundings of a PICU. Several studies showed that any delay in recognizing SIRS and sepsis could increase mortality and morbidity significantly [Ha03]. Yet, by early identification of SIRS and sepsis, it is possible to prevent organ dysfunction and lead to a much better outcome for ICU patients.

In this work, a data mining technique is introduced to extract and transform different vital signs and laboratory tests from the 'cross-institutional and data-driven decision-support for intensive care environments' (CADDIE-2) dataset [Wu19] and to find associations between them. In clinical settings, these association rule mining approaches can be considered as supporting methods to better comprehend the disease patterns for the patients. Mainly, the goal of this work is four-fold: i) to explore a data extraction and transformation technique for SIRS, ii) to evaluate the extraction process using expert rules (SIRS criteria), iii) to get important features and iv) to find association rules for associative classification and evaluate it using the result produced by expert rules.

The rest of this article is organized as follows. Section 2 discusses prior work. We describe our feature engineering and extraction techniques in Section 3. In Section 4, we present the definition of expert rules and association rule mining (ARM). Results and discussion are provided in Section 5. Finally, we derive conclusions of the study in Section 6.

2 Prior Works

Hospital data are still, to a large extent, under-explored, despite growing awareness of their particular potential value in health analytics and risk modeling [De06, Ke13]. The variety and complexity of patient records present a substantial challenge for knowledge discovery. Generally, disease-specific data are gathered by various medical expertise; for instance, suicide risk assessments use a distinct data format than white blood cell counts.

It is apparent that hand-picking features for each analysis are inadequate, and it is also impossible to ensure that all substantial information in the data is incorporated. Nowadays, the use of Machine Learning (ML) approaches are escalating for knowledge discovery and prediction of biomedical data [Ta07, XJ19]. ARM is one of the areas of ML that can also be used for finding patterns in biomedical data; this commonly used data mining application determines the patterns of items or events [So17, Iv15]. To mine association rules for pattern discovery, several incremental techniques were presented recently [Aq19, LNFV21]. It was also utilized to solve various problems in the healthcare sector. Mainly, there are a number of links between patients' diseases and vital signs or symptoms. ARM can assist researchers to comprehend a disease effectively by finding those links. One study identified early childhood caries using ARM [Iv15]. Other authors [RN20] used ARM in conjunction with a keyword-based clustering strategy for the prediction of the disease. Risk factors of heart diseases were determined using ARM in some studies [Na13, So17]; while others [No18] identified the negative incidents caused by drug-drug interactions. The risk of diabetes mellitus was predicted using ARM in [Ka16]. Moreover, Borah et al. [BN18] identified different risk factors of breast cancer, hepatitis, and cardiovascular disease by applying dynamic rare ARM. However, the use of ARM to find a pattern for SIRS is absent in the literature which also highlights the importance of this work.

3 Data Preparation

This section provides an overview of the used dataset, extraction and transformation of the features for ARM. The overall procedure is illustrated in Figure 1.

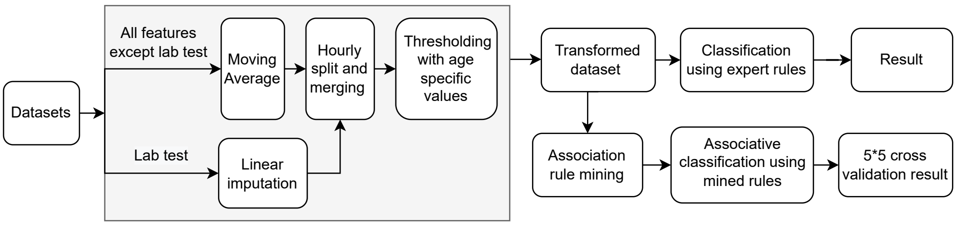

Fig. 1: Block diagram for the overall procedure.

3.1 Initial Dataset

In the context of this work, we use routine data from the PICU of the Hannover Medical School [Wu21]. The data is not currently available for public use, but within the ELISE project we are creating an Evolutionary Open Pediatric Intensive Care Dataset [Rü22]. The dataset consists of various vital parameters like temperature values, heart and respiration rates as well as laboratory test results and information from medical devices such as cooling blankets, ventilation and pacemaker for each of the included 168 pediatric patients. The patients can be distinguished from one another by a unique identifier (study number) that was generated as part of the pseudonymization. Laboratory test results include leukocyte, platelet and neutrophil counts as well as INR values derived from the prothrombin time. All measurements in the dataset come with a timestamp documenting its time of measurement by which a temporal sequence is ensured. Furthermore, the age of the respective patients is given. These parameters are supplemented by blood pressure values. In addition to the existing data, there is also a gold standard for the existence of SIRS for the respective patients for the period of the documented data available [Wu19, Wu21]. For the generation of this gold standard, two experienced pediatric intensive care physicians assessed the patients according to SIRS diagnostic rules defined by the International Pediatric Sepsis Consensus Conference (IPSCC) [Go05]. The clinician's decision on the presence of SIRS has been documented for each day that a particular patient was stationed at the PICU. In addition to this day-based gold standard, SIRS episodes were precisely documented in terms of time in order to provide an additional episode-based gold standard. The data set includes 168 patients from the pediatric intensive care in 243 days corresponding to a total of 1,998 days of stay within the ward. From those 1.998 days of stay, 460 days were labeled as SIRS within the day-wise gold standard [Wu21]. According to the gold standard 101 out of 168 patients suffered from SIRS during their hospitalization corresponding to a proportion of approximately 60%. The distribution of the sex is 106 to 62 in favor of male patients.

3.2 Feature Extraction

We work with five different vital signs named temperature, pulse rate, respiration rate and systolic and diastolic pressures, and one lab test result. We use these features due to the orientation along with the IPSCC criteria. Birthdate, disease diagnosis and gender information of the patient are also being taken for further analysis. All of these features are extracted from their respective datasets and merged into a single table based on timestamps for further processing. The extraction process is described in the following subsections.

3.2.1 Moving Average

In this approach, we obtain the moving average (MA) for temperature, pulse, respiration, systolic and diastolic pressures data, and used these averages for further processing. However, we do not apply MA to laboratory test values (leukocyte counts), as very few observations are available for it. Sometimes, there are only one or two laboratory values per 24 hours. A MA is a type of finite impulse response filter which is normally used in technical analysis by constructing a sequence of averages of different subsets of the full dataset. There are different variations existing in the literature (e.g., simple [Hy11], exponential [Br57], weighted [Hy11], etc.). In our work, we have used the standard version of moving average of order m can be written as [Hy11],

$$\hat{T}_t = \frac{1}{m} \sum_{i=-k}^{k} y_{t+i} \text{ where } m = 2k + 1 \tag{1}$$

MA eliminates randomness in the data, leaving behind a consistent trend-cycle component. The trend-cycle at time t is estimated by taking the average of the values of the time series within k periods (in minutes) of t. We try to find the optimal k and experiment with different values from $k = 10$ to $k = 30$. Based on the experiment, we choose $k = 15$, as the result remains almost unchanged when $k > 15$. We do not apply the MA operation to the lab-test dataset due to the unavailability of sufficient data points. The effect of the moving average is shown in Figure 2. It also improves the overall classification result as shown in Section 5.

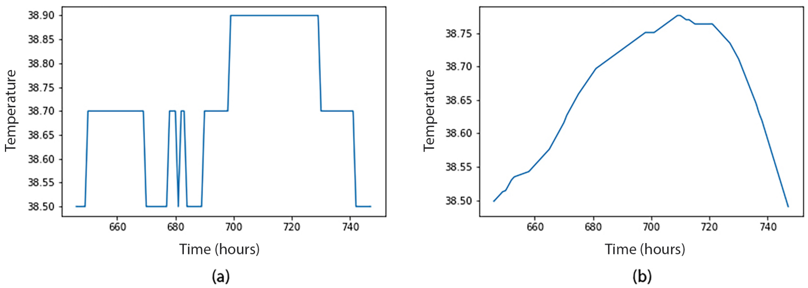

Fig. 2: The effect of moving average of the temperature data within a particular stay for a specific study number. (a) raw data. (b) after applying MA operation to the raw data of (a)

3.2.2 Hourly split

The features are split on an hourly basis after obtaining the moving average and merged into a single table. This produces missing values for laboratory tests due to a lack of hourly observation as mentioned previously. Table 1 shows the imputation for the feature ‘leukocyte count’. The column named Lab test represents the actual leukocyte measurement in each hour. The missing values are imputed before any further processing on this data as follows,

- The missing values between any two numerical observations are imputed by the equally spaced numbers of those two observations (linear imputation).

$$X_{\text{val}} = A_{\text{val}} + \frac{B_{\text{val}} - A_{\text{val}}}{\textit{Number of observation between } A_{\text{val}} \textit{ and } B_{\text{val}} \textit{ (inclusive)} - 1} \tag{2}$$

where, X_{val} is the missing value, A_{val} is the actual assessment taken prior to X_{val}, and B_{val} is the the actual assessment taken after X_{val}.

- If a column starts with missing values, all the missing values prior a numerical observation are imputed with the same value of that observation.
- If a column ends with missing values, we look for the last observation with a numerical value and impute all the missing values after that with the same value of that observation.

Tab. 1: Imputation for lab test (leukocyte count). The actual lab test measurement and the imputed values are shown in Lab Test and Imputed columns, respectively.

Study	Lab Test	Date-time From	Date-time To	Imputed
2		2018-08-01 16:00:00	2018-08-01 17:00:00	8
2	8	2018-08-01 17:00:00	2018-08-01 18:00:00	8
2		2018-08-01 18:00:00	2018-08-01 19:00:00	8.4
2		2018-08-01 23:00:00	2018-08-01 00:00:00	8.8
2	9.2	2018-08-02 00:00:00	2018-08-01 01:00:00	9.2
2		2018-08-02 01:00:00	2018-08-01 02:00:00	9.2

3.2.3 Thresholds for numerical values

Initially, we convert the age into age groups using Table 2. This table defined the High (H.), Low (L.) and Normal (N.) thresholds for the body vitals and laboratory test. Using these thresholds, we also convert the needed features (Temperature (Temp.), Pulse, Respiration (Resp.), Leukocytes (Leuk.), etc.) to categorical features.

3.3 Feature Transformation

One of our objectives is to apply expert rules to the extracted dataset that contains maximum, minimum, mean and median values for the vital signs and lab tests for the individual study numbers in a stay- and day-wise manner. We use the birth date from the Electronic Health Record (EHR) dataset and calculate the age in weeks for the specific study number by looking at the day/stay-based Gold standard datasets. Gender information is added as well from the Gender dataset. Feature Transformation transforms numerical values to categories using thresholds for numerical values.

As we have mentioned, five vital signs and one laboratory test are used in our experiment due to the fact that the SIRS criteria (expert rules / IPSCC criteria) only utilize those variables. Actually, blood pressure is not explicitly used in the four IPSCC criteria, although Goldstein et al. [Go05] listed norm-values for blood pressure. Therefore, we slightly modify the SIRS criteria by adding systolic and diastolic blood pressures to it. It increases the feature count as well as provides us with the impact of systolic and diastolic pressure on SIRS in rule mining. For each feature, four simple descriptive statistical summaries are

Tab. 2: Thresholds for age-specific vital signs and laboratory tests [Go05].

Age Groups	Pulse High (Beat/m)	Pulse Low (Beat/m)	Resp. (Breath/m)	Leuk. High	Leuk. Low	Sys. Normal	Dias. Normal	Temp. High	Temp. Low
Newborn (0d-1wk)	>180	<100	>50	>34	-	60-90	20-60	>38.5	<36
Neonate (1wk-1m)	>180	<100	>40	>19.5	<5	87-105	53-66	>38.5	<36
Infant (1m-1y)	>180	<90	>34	>17.5	<5	95-105	53-66	>38.5	<36
Toddler (2-5y)	>140	<60	>22	>15.5	<6	95-110	56-70	>38.5	<36
School age (6-12y)	>130	<60	>18	>13.5	<4.5	97-112	57-71	>38.5	<36
Adolescent (13-18y)	>110	<60	>14	>11	<4.5	112-128	66-80	>38.5	<36

obtained (Maximum (Max), Minimum (Min), Median and Average (Avg)). Hence, only one summary at a time is used by the expert rules. For example, after transforming the maximum values of the Temperature (Temp.), Pulse, Respiration (Resp.), Systolic (Sys.) and Diastolic (Dias.) pressure, and Leukocytes (Leuk.) along with the age groups, the data looks like Table 3. Afterwards, the results (specifically accuracy, sensitivity and specificity) of expert rules are acquired for each summary.

Tab. 3: An example of a transformed dataset after thresholding.

Pulse	Resp.	Temp.	Leuk.	Sys.	Dias.	Age	Diagnosis
Tachyc.	High	Normal	Normal	High	Normal	Neonate	No SIRS
Tachyc.	High	High	Normal	High	Normal	Neonate	SIRS
Normal	High	Normal	Normal	Normal	Normal	Newborn	No SIRS

4 Exploring Rules

Initially, the definition of SIRS criteria is presented. Then, frequency-based association rule mining along with their definitions is illustrated and associative classification is described.

4.1 SIRS criteria

The definition of SIRS is depicted here in simple terms. For diagnosing SIRS, at least two of the following four criteria must be present, one of which has to be abnormal leukocyte count or temperature [Go05]. (1) Pulse: high (tachycardia) or low (bradycardia); (2) Temperature: high or low (3) Respiration: high (4) Leukocyte count: high or low. We modify the expert rules (SIRS criteria) by adding a new rule for blood pressure: (5) Blood pressure: diastole high or diastole low and systole high or systole low. Here, high or low value means above or below age-specific norm values, respectively. The purpose of applying these expert rules is to understand the quality of the dataset and choose statistical features (maximum, minimum, average and median) for ARM.

4.2 Association Rule Mining

In ARM, association rules are extracted by mining transaction data to find out the relationships of different items inside the dataset. Assume, we have a transaction dataset with n transactions, $T = \{t_1, t_2, t_3 \ldots, t_n\}$ and m items, $I = \{i_1, i_2, i_3 \ldots, i_m\}$. Here, each transaction is a set of items, therefore, $t_c \in T$ with a distinct identifier TID is a subset of I. A transaction dataset is derived from the transformed dataset of Table 3 is shown in Table 4.

Tab. 4: A transaction dataset derived from Table 3.

TID	Transaction
t_1	(Pulse tachyc.:1), (Resp. high:1), (Temp. normal:1), (Leuko normal:1), (Syst. high:1), (Diast. Normal:1), (No SIRS:1)
t_2	(Pulse tachyc.:1), (Resp. normal:1), (Temp. high:1), (Leuko high:1), (Syst. high:1), (Diast. Normal:1), (SIRS:1)
..	

Suppose, X and Y are the sets of items. Therefore, a rule is inferred by $X \rightarrow Y$. Here X and Y are known as antecedent and consequent, respectively. Also, $X \cap Y = \emptyset$ and $X, Y \subset I$. We use support and confidence for rule mining.

Support It provides the notion of how frequent or popular an itemset is in all transactions.

$$\text{Support}(X \rightarrow Y) = \frac{\textit{Number of transactions containing both X and Y}}{\textit{Total number of transactions}} \tag{3}$$

Confidence This metric specifies how regularly the association rule is identified to be authentic: for a given antecedent, it finds out the likelihood of occurrence of the consequent.

$$\text{Confidence}(X \rightarrow Y) = \frac{\textit{Number of transactions containing both X and Y}}{\textit{Number of transactions containing X}} \tag{4}$$

Following algorithm is used for association rule mining:

$Input$:
min_conf : $threshold\ value\ for\ minimum\ confidence$;
$itemset\ 1$: $I1$;
$itemset\ 2$: $I2$;
$Output$:
$Association\ Rule$: $I1 \rightarrow I2$;

$X \leftarrow I1$
$Y \leftarrow I2$
if $X \subseteq Y$ **then**
  $Confidence \leftarrow Support(X) \div Support(Y)$
  if $Confidence \geq min\_conf$ **then**
    $Association\ Rule \leftarrow I2 \rightarrow I1$
  end
end
Return $Association\ Rule$

Algorithm 1: ARM algorithm

4.3 Associative classification

By using a set of provided rules, specifically the class association rules, it is possible to design a rule-based classifier consisting of two phases [AT14]. Initially, the ARM technique is used to obtain a set of rules for the classifier. Afterwards, the rules are refined and joined together in order to construct the finalized rule-based classifier. Refining the rules requires pruning, tuning and ranking operations. The evaluation of the classifier can be performed on the test set using standard metrics. In this work, the accuracy, the sensitivity or true positive rate (TPR) and the specificity or true negative rate (TNR) are obtained for evaluation.

5 Results and Discussion

Tab. 5: Classification results of expert rules.

Using MA	Summary	Accuracy	Sensitivity (TPR)	Specificity (TNR)
Yes	Maximum	0.87	0.76	0.93
Yes	Median	0.86	0.76	0.93
Yes	Average	0.86	0.76	0.93
Yes	Minimum	0.86	0.76	0.92
No	Maximum	0.86	0.76	0.92
No	Median	0.86	0.75	0.93
No	Average	0.86	0.75	0.92
No	Minimum	0.83	0.72	0.90

We now assess the extraction process using expert rules, find association rules for classification and evaluate it with the result produced by expert rules. We analyse the effect of

MA as part of extraction process. The definition of expert rules from Section 4.1 is applied to the transformed datasets (with and without MA) and the results are shown in Table 5. We can see that applying MA during data extraction, gives us the increments of 1% in Accuracy and Specificity while considering Maximum summary. For median and average summaries, Accuracies remain the same, however, Sensitivities improve while applying MA. For minimum summary, we get better results in all three metrics while applying MA. Therefore, the result justifies the use of moving average to the features.

Tab. 6: Classification results of mined rules.

summary	Confidence	Accuracy	Sensitivity (TPR)	Specificity (TNR)
Maximum	0.709	0.70	0.96	0.43
	0.712	0.72	0.92	0.52
	0.715	0.77	0.85	0.69
	0.724	0.79	0.83	0.76

For associative classification, we perform 5×5 cross validation with the mined rules and the results are shown in Table 6. We consider the Maximum summary, as it gives the best result for expert rule in terms of Accuracy, Sensitivity and Specificity (see Table 5). We can see that Confidence 0.724 gives us better accuracy whereas Confidence 0.709 has lower accuracy but higher Sensitivity. In our work, we prioritize Sensitivity over Specificity. Sensitivity corresponds to the true positive rate for SIRS. Therefore, it is crucial that we do not miss a significant amount of diagnosis regarding SIRS. However, we also want the difference between Sensitivity and Specificity to be minimized. Therefore, Confidence 0.712 is more preferable, as Sensitivity and Specificity are more than 0.90 and 0.50, respectively.

Tab. 7: Top 10 generalized rules (N=14920, Rules=103, Min.confidence=0.71).

LHS	RHS	Confidence
Leukocyte high, Respiration high, Temperature low	SIRS	1.0
Leukocyte high, Pulse tachycardia, Respiration high		1.0
Leukocyte high, Respiration high, Temperature high		1.0
Leukocyte low, Respiration high		1.0
Leukocyte high, Respiration high		0.971
Leukocyte high, Pulse tachycardia		0.967
Respiration high, Temperature low		0.923
Leukocyte high, Temperature high		0.913
Pulse normal, Respiration high, Temperature high		0.909
Respiration high, Temperature high		0.905

Figure 3 shows the frequency of the features or items in the itemsets. From this figure, we can see the importance of the features which is crucial for the validation of the SIRS criteria. In the SIRS criteria, abnormal leukocyte count and temperature is given higher importance as mentioned in Section 4.1. From Figure 3, we can see, both features are at the top. The third, fourth, and fifth features are pulse tachycardia, high respiration and normal diastolic pressure, respectively. Naturally, the normal categories are in the bottom. Normal diastolic pressure is in the fourth place, which tells us that in many SIRS cases diastolic pressure remains normal when other parameters are abnormal (either high or low). We discover rules for SIRS patients using ARM techniques and the top 10 mined rules are shown in Table 7. Our study reports a relatively higher proportion of abnormal Leukocyte count, temperature and pulse in SIRS patients. Applying these mined rules to the transformed dataset gives us better results than the SIRS criteria in terms of Sensitivity. As we present the top 10 rules, most of the rules are aligned with the SIRS criteria which also validates the criteria itself.

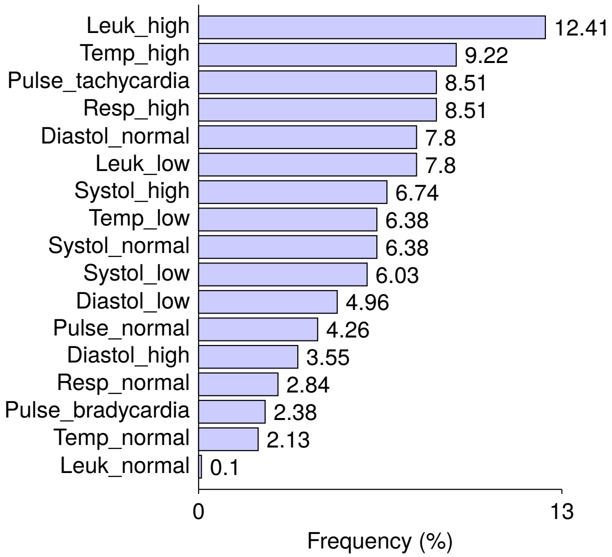

Fig. 3: Frequency of vital signs and lab test (items in the itemsets).

Better accuracy does not imply better results. From the experiment, we see that the expert rules have an accuracy at most 0.87 (Table 5). However, for that accuracy, we have a Sensitivity around 0.76 and Specificity around 0.93. As we prioritize Sensitivity over Specificity, the result of the mined rules with Maximum summary is more favorable. It can also be noted that the Sensitivity (TPR) and the Specificity (TNR) have a reciprocal relationship. With increasing confidence, Sensitivity (TPR) reduces whereas Specificity (TNR) escalates. Therefore, we can easily choose a confidence that can give us Sensitivity over 0.9 and Specificity over 0.5.

6 Conclusion

This work demonstrated a data mining technique in terms of feature extraction and transformation for finding association rules using Apriori algorithm. These rules are used to perform Associative Classification and compared with the results found using SIRS criteria.

Using SIRS criteria on the transformed dataset also showed the quality of the extraction process. We analyzed the effect of Moving Average (MA); it was found that MA improved the result to some extent in terms of Accuracy, Sensitivity and Specificity when applying SIRS criteria. In simple terms, we extracted a feature set with four summaries (Maximum, Minimum, Median and Average). Then we applied the SIRS criteria with a set of thresholds for age-specific vital signs and laboratory variables from the literature to see which summary is better. Then we used that summary for rule mining. After generating a set of rules, we again applied the mined rules for classification. This experiment was carried out to show the efficacy of mined rules while evaluated with expert rules (SIRS criteria).

Due to the nature of the diagnosis, Sensitivity was given more priority than Specificity and they showed a reciprocal relationship. By tuning the confidence of the mined rules, we gained control over Sensitivity and Specificity. From the SIRS criteria, the best result was found with Accuracy, Sensitivity and Specificity up to 0.87, 0.76 and 0.93, respectively for the Maximum summary. While applying mined rules with varying Confidence, we were able to achieve higher Sensitivity up to 0.96. However, Accuracy and Specificity were reduced to 0.70 and 0.43, respectively. Therefore a Confidence with 0.712 was more suitable where the Accuracy, Sensitivity and Specificity were around 0.72, 0.92 and 0.52, respectively.

In future work, we plan to explore other ways of feature extractions and perform a comparative analysis with SIRS criteria. We will also apply different Machine Learning algorithms like Decision Tree, Random Forest, Support Vector Machine.

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