

PREPROCESSING AND GENERATION OF ASSOCIATION RULES FOR PREDICTION OF ACUTE MYELOID LEUKEMIA FROM BONE MARROW DATA

¹D.MINNIE, ²S.SRINIVASAN

¹Madras Christian College, Department of Computer Science, Chennai, India

²Anna University: Chennai Regional Office Madurai, Department of Computer Science and Engineering, Madurai, India

E-Mail: ¹minniearul@yahoo.com, ²sriniss@yahoo.com

ABSTRACT

In this paper we analyze the components of the bone marrow and the structure of the bone marrow database. The Knowledge Discovery in Databases (KDD) steps are briefly explained. 18,000 bone marrow analysis records are collected from a reputed Hospital and this raw data is transformed into a preprocessed data using the pre-processing phases of KDD such as Data Cleaning, Data Selection and Data Transformation. Eliminate the tuple technique is used to clean the data. The attributes related to the bone marrow components are selected. The ranges of low, high and normal values for the individual attributes are used to transform the data. The Data Mining techniques are studied and the Apriori algorithm is selected for finding frequent item sets that are used for the generation of association rules.

Keywords: *Knowledge Discovery in Databases, Data Mining, Association Rule Mining, Haematology, Bone Marrow Analysis.*

1. INTRODUCTION

Huge volumes of automated medical data are currently available in various forms. This data are used along with various analysis techniques to generate results that can be used by the health care professionals in efficient decision making that can improve the quality of service in the medical fields.

Bone Marrow is the flexible tissue found in the interior of bones. It produces the cellular elements of the blood such as red blood cells, white blood cells and platelets. The bone marrow is used to diagnose diseases such as leukemia, anemia, neimem pick disease and so on.

Leukemia is a type of blood cancer that begins in the bone marrow. Leukemia leads to an uncontrolled increase in the number of white blood cells (leukocytes) that are used by the body to fight infections and other foreign substances. The cancerous cells prevent healthy red cells, platelets, and mature white cells (leukocytes) from being made. Life-threatening symptoms can then develop as normal blood cells decline. The cancer cells can spread to the bloodstream and lymph nodes. The main types of leukemia are:

- Acute lymphocytic leukemia (ALL)

- Acute myeloid leukemia (AML)
- Chronic lymphocytic leukemia (CLL)
- Chronic myeloid leukemia (CML)

AML is an acute form of leukemia that spreads very fast. An early detection can increase the survival rate of an infected person. A bone marrow aspiration and biopsy shows the presence of any leukemia cells. The bone marrow data can be used to predict the presence of leukemia [1].

Knowledge Discovery in Databases (KDD) is used to extract useful knowledge such as prediction from data. The data is to be preprocessed using the KDD preprocessing steps Data Cleaning, Data Transformation and the resultant preprocessed data is used to generate knowledge using the Data Mining techniques such as classification, clustering, association rule mining and prediction [2-5].

Classification is a supervised learning process and it maps data into known classes using Decision Trees, Neural Networks and Genetic Algorithms. Clustering is an unsupervised learning and it groups similar data into unknown clusters using K-Means, Nearest Neighbour and various other algorithms. Association Rule Mining (ARM) uncovers relationships among

data in a database [6-8]. Prediction generates models that are used to predict the outcome for a given input.

The data mining algorithms are used to generate knowledge from medical data. Clustering algorithms are used to mine temporal data to diagnose diabetes [9]. Association Rule Mining is used to diagnose hyperlipidemia disease [10], heart disease [11,12] and in the application of counseling and analyzing the help seeking behavior of adolescents [13]. Association rules are generated among the attributes of the Automated Blood Cell Counter Data [14].

A class discovery procedure using Leukemia classification automatically distinguishes between acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) with previous knowledge of these classes [15]. The association rule mining and classification techniques were used to predict the diseases and the association rule mining technique was found to be better than the classification algorithm [16].

This bone marrow data consist of numerical and categorical attributes. The numerical data are discretized and association rules are generated. The association rules are proposed to be used to predict the disease AML.

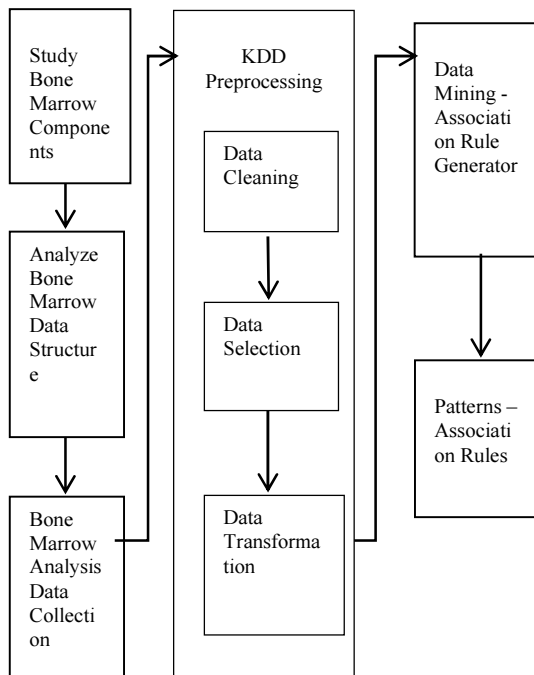


Figure 1 System Architecture

2. METHODS

2.1 System Architecture

The system architecture of this work is shown in figure 1 and it consists of studying the bone marrow components, analyse bone marrow data structure, bone marrow analysis data collection, KDD preprocessing steps data cleaning, data selection and data transformation and data mining using association rule generation.

2.2 Bone Marrow Components

The bone marrow contains various cells such as erythrocytes (red blood cells), blasts, promyelocyte, myeloblasts, plasma cells, white blood cells such as neutrophils, eosinophils, basophils and monocytes.

2.3 Data Collection

Eighteen thousand bone marrow data are collected from a Clinical Pathology department of a reputed hospital. The data is present as an excel file. The bone marrow analysis data is de-identified to preserve the privacy of the patient, doctor and the hospital. A sample of the data file is shown in figure 2.

2.4 Bone Marrow Data Format

The Bone Marrow Analysis data consists of values for each attributes such as erythrocytes, blasts, promyelocyte, myeloblasts, neutrophils, eosinophils, plasma cells, basophils and monocytes, the patient id, date in which the test is taken, hospital id, detailed description of the results and the final impression. The list of attributes along with a detailed description of the attributes is shown in table 1.

Table 1 Attributes of the Bone Marrow Data

Attribute Name	Description
bmid	Patient Id
date	Test Date
hsno	Hospital Number
eryth	Erythrocyte count
blasts	Blast cell count
promy	Promyelocyte count
myel	Myeloblast count
plasma	Plasma cell count
neutr	Neutrophil count
eosin	Eosinophil count
lymph	Lymphocyte count
baso	Basophil count
mono	Monocyte
txt	Test results
edit_name	Doctor's name
fin_name	Doctor's name
imp	Impression

2.5 Knowledge Discovery In Databases (KDD)

The data is subjected to the KDD processes to generate knowledge from it. The processes include Data Cleaning, Data Integration, Data Selection, Data Transformation, Data Mining, Generation of Patterns and Knowledge Interpretation.

In Data Cleaning the irrelevant data are removed from the collected data. In Data Integration data from multiple sources are combined into a data warehouse. The Data Selection process is involved with the selection of data relevant to the analysis and extracting them from the integrated data. The selected data is transformed to the appropriate form for the mining procedure.

The process of extracting useful and implicit information from the transformed data is referred to as Data Mining. In Pattern Evaluation interesting patterns are identified from the processed data. The discovered knowledge is visually presented to the user in the Knowledge Representation process.

2.6 Association Rule Mining (ARM)

ARM is used to find frequent patterns, associations and correlations among sets of items in databases and any other information repositories. Association Rule correlates the presence of one set of items with that of another set of items in the same transaction. The quality of an Association Rule is measured using its support and confidence values and several efficient methods are developed to generate association rules.

Let N be the number of records in a database, $N(I)$ be the number of records with item set I , X be an item set with k elements X_1, X_2, \dots, X_k and Y be an item set with h elements Y_1, Y_2, \dots, Y_h . An Association Rule $X \Rightarrow Y$ can be generated if the support of X and that of Y is above the minimum support value and also the confidence of the rule $X \Rightarrow Y$ is above the minimum confidence specified.

Support S , of X is a probability that a transaction contains X and is given in (1) and (2).

$$S(X) = P(X) \quad (1)$$

$$S(X) = N(X) / N \quad (2)$$

Support of $X \Rightarrow Y$ is a probability that a transaction contains both X and Y as given in (3) and (4).

$$S(X \Rightarrow Y) = P(X \cup Y) \quad (3)$$

$$S(X \Rightarrow Y) = N(X \cup Y) / N \quad (4)$$

Confidence C , of $X \Rightarrow Y$ is a conditional probability that a transaction that contains X contains Y also. Confidence can be calculated as in equations (5), (6) and (7).

$$C(X \Rightarrow Y) = P(X | Y) \quad (5)$$

$$C(X \Rightarrow Y) = N(X \cup Y) / N(X) \quad (6)$$

$$C(X \Rightarrow Y) = S(X \cup Y) / S(X) \quad (7)$$

Association Rule Mining consists of the two steps finding frequent item sets and generating association rules. The set of all item sets are called as candidate item sets. The item sets which occur frequently in a database are called frequent item sets. The frequent item sets satisfy the minimum support, min_sup specified by the user or designer. If the min_sup is 10%, then the item sets whose support % are greater than or equal to 10 are considered as frequent item sets.

The association rules are generated using the frequent item sets and they should satisfy the minimum confidence min_conf of 50%. Apriori algorithm is used to find frequent item sets in a database and to generate Association Rules from the frequent item sets. Apriori algorithm uses the apriori principle "All subsets of an infrequent item set are infrequent" and hence those subsets need not be considered for further processing.

2.7 Application Interface

The interface for this application to generate association rules between the attributes of the bone marrow analysis data are given in figure 3.

RESULTS AND DISCUSSION

3.1 Data Cleaning

The process of detecting and correcting or removing corrupt or inaccurate records from a record set, table, or database is Data Cleaning. The missing values or invalid values in the Bone Marrow data cannot be replaced by any other value and hence those records were eliminated from further process. 18,429 records out of 18,449 records were selected for further process as they have valid values.

3.2 Data Selection

The cleaned bone marrow data was taken as input for data selection. The numerical attributes representing the bone marrow components such as *bid*, *neutr*, *eosin*, *lymph*, *baso*, *mono*, *myel*, *plasma*, *eryth* and *impression* are identified for the generation of association

rules and hence they are selected for further process.

3.3 Training And Testing Data

The cleaned and transformed data is divided into two data sets Training Data and Testing Data. The training data consist of 9212 records and testing data consist of 9217 records. The training data is used to generate association rules and the testing data is used to measure the quality of the association rules generated

3.4 Data Transformation

In the Data Transformation stage the data are transformed or consolidated in to forms appropriate for mining.

The ranges of values for the bone marrow component attributes are used to find out whether the value is low, normal or high. New attributes low, normal and high are generated for each of the attributes. Hence the individual attribute values are used to generate the status of the attributes as low, normal or high. A value 0 is stored for the normal values, 1 is stored for the high values and -1 is stored for the low values for the newly generated attributes depending on the values of the corresponding attributes.

The disease AML data is collected from the impression attribute and a new attribute is inserted for AML that can hold Boolean values 0 for the absence of the disease AML and 1 for the presence of the disease AML for that record. The flattened data is shown in figure 4 and figure 5. Also the excel data was converted into a SQL Data base.

3.5 Attribute Combinations

The attributes have a normal, low and high support associated with them. Various combinations of these are considered for generating the association rules. The combination selected to produce association rules is shown in table 2.

3.6 Frequent Item Sets

The minimum support value is set as 0.1% to include all the item sets including outliers for the association rule generation process. The number of frequent 1 item sets, 2 item sets, 3 item sets and 4 item sets generated are given in Table 3.

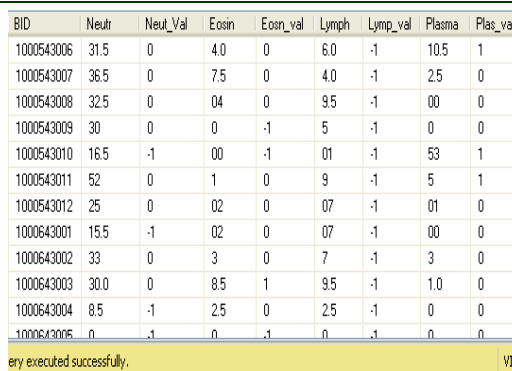


Figure 4 Flattened Bone Marrow Numerical Data base – Sample Screenshot

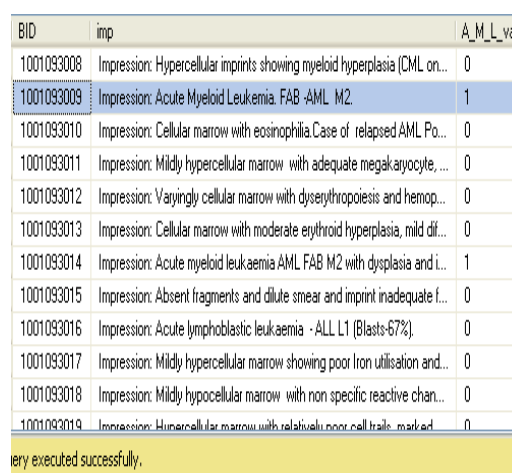


Figure 5 Flattened Bone Marrow Categorical Disease Data base – Sample Screenshot

Table 2 Combinations of Levels selected for attributes

Attributes	Levels	Support value	Support percentage (%)
Neutrophils	Low	4101	44.51802
Eosinophils	Low	1211	13.1459
Lymphocytes	Normal	4152	45.07165
Monocytes	Low	3291	35.72514
Blasts	High	1104	11.98437
Myeloblast	High	7560	82.06687
Plasma Cells	Normal	4868	52.84412
Erythrocyte	High	6378	69.23578
A M L	Present	1052	11.41989

Table 3 Frequent Item Set Generation Count

Item sets	Count
Frequent 1 item sets	9
Frequent 2 item sets	36
Frequent 3 item sets	84
Frequent 4 item sets	121

3.7 Association Rules Generated Without Disease Detail

The minimum confidence is set as 50% to select strong association rules that are formed using the numerical attributes of the bone marrow data and the categorical disease data is not considered.

The associations generated with 2 attributes are given in Table 4, with 3 attributes are given in Table 5 and are shown graphically in figure 6. The 4 attribute associations and the 5 attribute association rules have the confidence level lesser than the minimum confidence of the confidence level lesser than the minimum confidence of 50% and hence they are not discussed.

Table 4 Association rules with 2 Attributes and without Disease Details

Association Rule	Confidence
Neut Eosn -> Mono	73.43
Neut Eosn -> Myel	53.96
Neut Eosn -> Plas	62.5
Neut Lymp -> Myel	91.23
Neut Lymp -> Plas	55.8
Neut Lymp -> Eryt	81.53
Neut Mono -> Myel	75.09
Neut Mono -> Plas	70.49
Neut Mono -> Eryt	64.68
Neut Blas -> Myel	51.97
Neut Myel -> Plas	55.24
Neut Myel -> Eryt	82.79
Neut Plas -> Eryt	74.78
Eosn Lymp -> Mono	63.74
Eosn Lymp -> Myel	83.94
Eosn Lymp -> Plas	63.74
Eosn Lymp -> Eryt	66.18
Eosn Mono -> Myel	62.42
Eosn Mono -> Plas	70.44
Eosn Blas -> Plas	64.48
Eosn Myel -> Plas	64.32
Eosn Myel -> Eryt	75.52
Eosn Plas -> Eryt	54.92
Lymp Mono -> Myel	94.15
Lymp Mono -> Plas	74.43
Lymp Mono -> Eryt	80.55
Lymp Blas -> Myel	63.35
Lymp Myel -> Plas	60.6
Lymp Myel -> Eryt	83.89
Eryt -> Lymp Myel	51.61
Lymp Plas -> Eryt	84.49
Mono Blas -> Myel	52.36
Mono Blas -> Plas	71.57
Mono Myel -> Plas	73.84
Mono Myel -> Eryt	82.46
Mono Plas -> Eryt	76.29
Blas Myel -> Plas	52.92
Myel Plas -> Eryt	84.94
Eryt -> Myel Plas	59.72

Table 5 Association rules with 3 attributes and without disease details

Association Rule	Confidence
Neut Eosn -> Mono	73.43
Neut Eosn -> Myel	53.96
Neut Eosn -> Plas	62.5
Neut Lymp -> Myel	91.23
Neut Lymp -> Plas	55.8
Neut Lymp -> Eryt	81.53
Neut Mono -> Myel	75.09
Neut Mono -> Plas	70.49
Neut Mono -> Eryt	64.68
Neut Blas -> Myel	51.97
Neut Myel -> Plas	55.24
Neut Myel -> Eryt	82.79
Neut Plas -> Eryt	74.78
Eosn Lymp -> Mono	63.74
Eosn Lymp -> Myel	83.94
Eosn Lymp -> Plas	63.74
Eosn Lymp -> Eryt	66.18
Eosn Mono -> Myel	62.42
Eosn Mono -> Plas	70.44
Eosn Blas -> Plas	64.48
Eosn Myel -> Plas	64.32
Eosn Myel -> Eryt	75.52
Eosn Plas -> Eryt	54.92
Lymp Mono -> Myel	94.15
Lymp Mono -> Plas	74.43
Lymp Mono -> Eryt	80.55
Lymp Blas -> Myel	63.35
Lymp Myel -> Plas	60.6
Lymp Myel -> Eryt	83.89
Eryt -> Lymp Myel	51.61
Lymp Plas -> Eryt	84.49
Mono Blas -> Myel	52.36
Mono Blas -> Plas	71.57
Mono Myel -> Plas	73.84
Mono Myel -> Eryt	82.46
Mono Plas -> Eryt	76.29
Blas Myel -> Plas	52.92
Myel Plas -> Eryt	84.94
Eryt -> Myel Plas	59.72

3.8 Association Rules Generated With Disease AML

The minimum confidence is set as 50% to select strong association rules. The association rules are generated with the disease AML and other attributes of the bone marrow analysis data.

The associations generated with AML and 1 attribute is given in Table 6, 2 attributes are given in Table 7, with 3 attributes are given in Table 8. The 4 attribute ones are shown in Table 9 and all associations are shown in figure 7

Table 6 Association rules with AML and 1 Attribute

Rule	Confidence
A_M_L -> Neut	69.29
Blas -> A_M_L	62.4
A_M_L -> Blas	65.49
A_M_L -> Myel	52.09

Lymp Blas Plas -> A_M_L	64.61
Mono Blas Myel -> A_M_L	60.47
Mono Blas Plas -> A_M_L	60.97
Mono Blas Eryt -> A_M_L	51.64
Blas Myel Plas -> A_M_L	60.06
Blas Plas Eryt -> A_M_L	51.35

Table 7 Association rules with AML and 2 Attributes

Association Rules	confidence
Neut Blas -> A_M_L	66.44
A_M_L -> Neut Blas	55.89
Eosn Blas -> A_M_L	66.97
Lymp Blas -> A_M_L	64.88
Mono Blas -> A_M_L	62.59
Blas Myel -> A_M_L	60.48
Blas Plas -> A_M_L	63.08
Blas Eryt -> A_M_L	52.23

Table 8 Association rules Generated with AML and 3 Attributes

Association Rule	Confidence
Neut Eosn Blas -> A_M_L	69.1
Neut Lymp Blas -> A_M_L	69.78
Neut Mono Blas -> A_M_L	66.29
Neut Blas Myel -> A_M_L	66.52
Neut Blas Plas -> A_M_L	67.85
Neut Blas Eryt -> A_M_L	55.87
Eosn Lymp Blas -> A_M_L	73.83
Eosn Mono Blas -> A_M_L	67.07
Eosn Blas Myel -> A_M_L	72.95
Eosn Blas Plas -> A_M_L	68.11
Eosn Blas Eryt -> A_M_L	66.66
Lymp Mono Blas -> A_M_L	65.58
Lymp Blas Myel -> A_M_L	59.43

Table 9 Association rules with AML and 4 attributes

Association Rule	Confidence
Neut Eosn Lymp Blas -> A_M_L	77
A_M_L -> Neut Eosn Lymp Blas	7.319
Neut Eosn Mono Blas -> A_M_L	68.66
A_M_L -> Neut Eosn Mono Blas	15.2
Neut Eosn Blas Myel -> A_M_L	79.04
Neut Eosn Blas Plas -> A_M_L	70.1
Neut Eosn Blas Eryt -> A_M_L	69.81
Neut Lymp Mono Blas -> A_M_L	69.85
Neut Lymp Blas Myel -> A_M_L	66.01
Neut Lymp Blas Plas -> A_M_L	70.3
Neut Lymp Blas Eryt -> A_M_L	54.38
Neut Mono Blas Myel -> A_M_L	67.45
Neut Mono Blas Plas -> A_M_L	64.34
Neut Mono Blas Eryt -> A_M_L	56.09
Neut Blas Myel Plas -> A_M_L	66.66
Neut Blas Myel Eryt -> A_M_L	50.23
Neut Blas Plas Eryt -> A_M_L	55.9
Eosn Lymp Mono Blas -> A_M_L	70.23
Eosn Lymp Blas Myel -> A_M_L	75.86
Eosn Lymp Blas Plas -> A_M_L	72.22
Eosn Lymp Blas Eryt -> A_M_L	66.66
Eosn Mono Blas Myel -> A_M_L	72.41
Eosn Mono Blas Plas -> A_M_L	67.03
Eosn Mono Blas Eryt -> A_M_L	65

4. CONCLUSION AND FUTURE WORK

The KDD steps for preprocessing were applied on the Bone Marrow Analysis Data and two sets of association rules were generated one without the disease details and another with the disease details. The association rules generated with the disease details were used to predict the disease AML. Eight bone marrow cell attributes in different ranges were considered for the generation of the association rules.

The combination that gives a good association rule is presented in this paper. The project can be extended to include all possible combinations of the cell attributes and a comparative study can be done.

The associations between various bone marrow cell structures are presented in this paper. They can be used for missing value imputation of attribute values.

The association rules can also be generated for the records with other diseases such as malaria, MMM and ALL.

Eosn Blas Myel Plas -> A_M_L	73.49
Eosn Blas Myel Eryt -> A_M_L	60.86
Eosn Blas Plas Eryt -> A_M_L	68.42
Lymp Mono Blas Myel -> A_M_L	64.64
Lymp Mono Blas Plas -> A_M_L	61.26
Lymp Blas Myel Plas -> A_M_L	59.55
Mono Blas Myel Plas -> A_M_L	58.55

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P1	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
	bmld	date	hsno	eryth	blasts	promy	myel	neutr	eosin	lymph	plasma	adn	baso	mono	txt	edit_name
2	710113014	06-08-2004	631694C	24		16.5	26.5	17	2	13.5	0.5				Fragments: Normocellular	DR.E DR
3	711013004	06-10-2004	630099C	23		21.5	32	9.5	5.5	7	1.5				Fragments: Normocellular	DR.E DR
4	711013006	06-10-2004	703928A	26		21	18	11	3	19	2				Fragments: Cellular	DR.F DR
5	711013009	06-10-2004	637661C	3.5	90.5	0.5	1	1	0.5	3					Fragments: Scanty.	DR.E DR
6	711013010	06-10-2004	615633C	47		12	14	19		8					Fragments: Hypercellular.	DR.F DR
7	711013011	06-10-2004	636655C	50		10	9	20	11						Fragments: Hypercellular.	DR.F DR
8	711013014	06-10-2004	637516C	12	71			2		12	3				Fragments: Hypercellular.	DR.F DR
9	710023004	06-12-2004	637542C	48		22	11	10		9					Fragments: Cellular	DR.F DR
10	710023006	06-12-2004	627947C	28		26	12	26.5		7.5					Fragments: Normocellular	DR.E DR
11	710023007	06-12-2004	630226C	20.5		20.5	32	15	2.5	6	3.5				Fragments: Normocellular	DR.E DR
12	710023009	06-12-2004	637556C	44		22	10	14		10					Fragments: Hypercellular.	DR.F DR
13	710023010	06-12-2004	637099C	49		9	5	1		33	3				Fragments: Markedly	DR.F DR
14	710023015	06-12-2004	634619C	40		6	16	24		14					Fragments: Cellular	DR.F DR
15	707133002	13/06/2004	637656C	41		22.5	11	10.5	3.5	10	1.5				Fragments: Solidly cellular	DR.E DR
16	707133011	13/06/2004	626637C	34			19	21	1	10					Fragments: Normocellular	DR.E DR
17	707143010	14/06/2004	633930C	22			15	18	1.5	7.5	0.5				Fragments: Normocellular	DR.E DR
18	707153000	15/06/2004	631965C												Trial bm report.	DR.E
19	707153007	15/06/2004	633402C	18		4	40	13		4	2				Fragments: Cellular	DR.F DR
20	707153008	15/06/2004	636618C	25.5		13.5	23	17	4.5	16.5					Fragments: Markedly	DR.A DR
21	707153009	15/06/2004	546530B	20.5		22	27.5	18.5	2	9	0.5				Fragments: Moderately	DR.A DR
22	707163001	16/06/2004	636203C												Fragments: Cellular	DR.B
23	707163002	16/06/2004	632921C	41.5		6	15	24.5	5.5	1.5	.5				Fragments: Cellular	DR.C
24	707163006	16/06/2004	806380C	28.5	6.5	7	15	17	9	3.5	6.5				Fragments: Cellular	DR.C
25	707173003	17/06/2004	965046B	20.5		10.5	16	31	2.5	9.5	10				Fragments: Normocellular	DR.D DR

Figure 2 Sample Bone Marrow Analysis Data

Figure 3 Application interface for Association Rule Generation for AML

Confidence

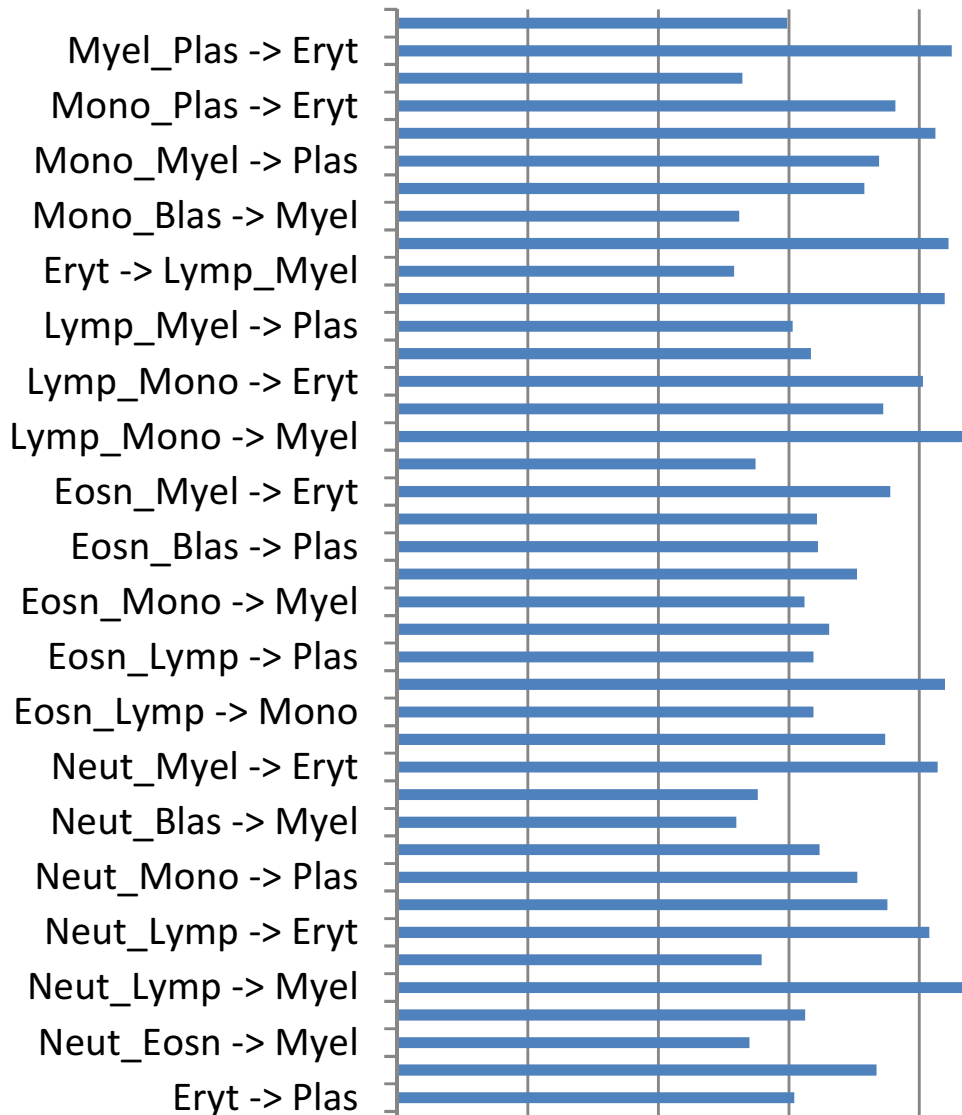


Figure 6. Confidence Of Association Rules Generated Without Disease Details

Confidence

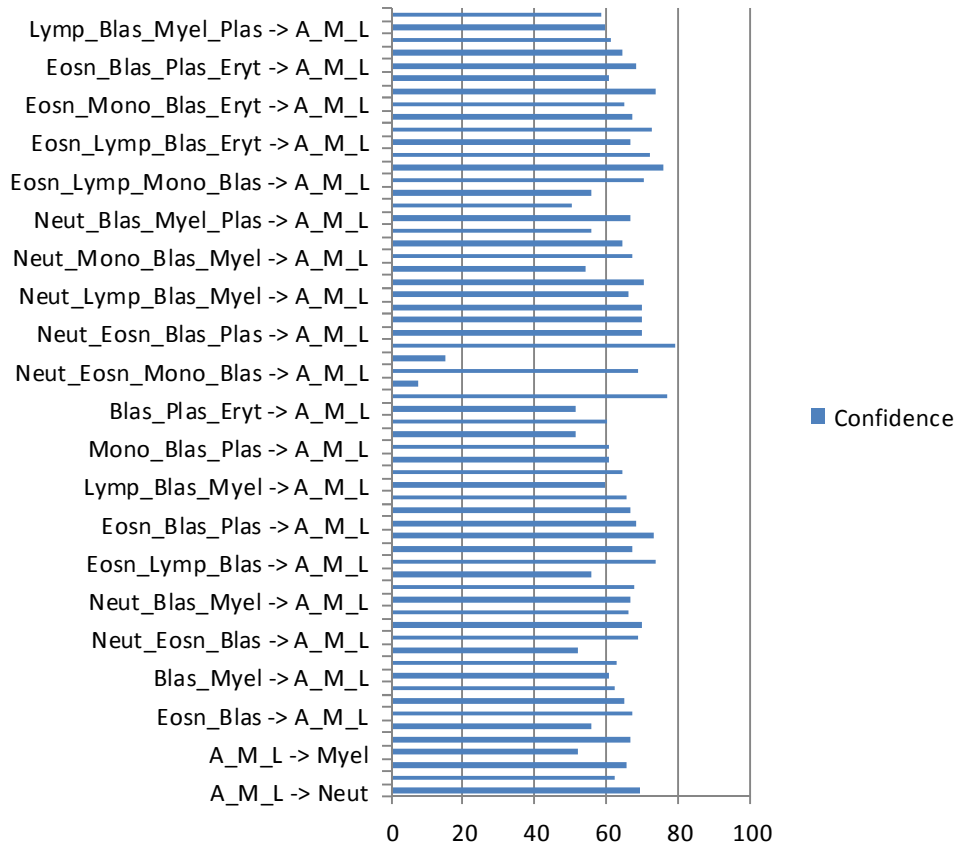


Figure 7. Confidence Of Association Rules Generated With Disease AML