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The Pattern of Compounded Medicines Prescribing For Pediatric Patients Using FP Growth Analysis in the Installation of Hospital Pharmacy

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Abstract - Shortages of available drugs suitable for pediatric patients (infants, children, and adolescents) play a central role in the increased demand for compounded medicines. A doctor tends to give the similar prescription for the patients with the same clinical condition. This will form a pattern in prescribing. This research aims to find the pattern of compounded medicines prescribing (in the form of association rules) done by the doctors and stored in forms of data mining using Algorithm FP Growth Analysis. The result of this pattern can be used as the proposal to determine the supplies of brand-name medicine in the hospital pharmacy.

Keywords: medicines, pediatric, data mining, FP-growth, hospital pharmacy.

I. INTRODUCTION

In Indonesia, compounded medicines have often been prescribed by the doctors, especially for pediatric patients (infants, children, and adolescents) both in Community Health Centre (*Puskesmas*) and hospitals. The prescribing has been based on the physiological and psychological condition of a patient. The differences of medicines formulation are in the consideration of the dosage, the ability to swallow in tablet/solid dosage forms, and the flavor of the medicine given orally (Wiedyaningsih, 2013). Compounded medicines were given because of the lack of specific supplies for pediatric patients both in Health Centre and pharmaceutical industries. The report by Nahata (1999) showed that some liquid dosage form for children were unavailable. Some countries that have limited financial resources face various obstacles in providing child drug formula. The drug dosage forms related closely to the prices. For example, drugs for asthma, an inhaler with a dose dosage form that can be set (*metered-dose inhaler*), is more expensive than the same drug given by mouth.

WHO launched the campaign of 'Make medicine child size' in December 2007. It aimed to raise the awareness and promote global action towards the needs to improve access for better and safer medicines for children under fifteen, especially in developing countries (Gray, 2009). The campaign target was related to the researches, developments, regulatory, legality including the needs to ensure that children receive the right medicine in the right dose at the right time (Gray, 2009). In collaboration with UNICEF, WHO published essential medicine lists and provided data sources and selected drugs price for children as the response to this campaign. The availability of medicines for the children has become worldwide concern (Chui et al., 2004). Several study groups have been formed to foster the cooperation between the researchers and stakeholders (policy maker, professionals, and customers/consumers) in order to optimize the use and development of new medicines for children (Ceci et al., 2009). New regulation of pediatrics in Europe reinforced pharmaceutical industries to conduct researches on pediatrics in hopes that it can increase the availability of the tested and accurate medicines for children (Ceci et al., 2009).

Compounded medicines will be used as long as the availability of medicine suitable for pediatric condition is still limited. Besides, the experience of the doctor will support the decision to give compounded medicines (Wiedyaningsih, 2013: 80). Based on the data used on this research object until December 2014, it was found that around 59.32% of the pediatric patients' prescription contained compounded medicines.

Having regard to the high frequent used of compounded medicine prescribing for pediatric patients and the high worldwide concerns toward the availability of medicines suitable for pediatric patients, this research attempts to find out the prescribing pattern of compounded medicines for pediatric patients using FP-Growth method. Hopefully, the findings can be used as the proposal of new medicine supply making suitable for pediatric patients.

II. LITERATURE REVIEW

A. The Previous Studies

One of the previous studies related to FP-Growth and/or pharmaceutical data mining was done by Khader and Yoon (2015), aiming to find the best implementation for lessening the time of FP-Growth execution on several applications using pharmaceutical data. The finding showed that the performance of sequential implementation and FP-Growth parallel depended on the preliminary determination of support minimum limitation. Besides, the execution of FP-Growth will be faster when transaction to null value is not included. Li, Haoyuan et al. (2008) conducted FP-Growth parallelism (PFP) on the distributed machine. The result showed that PFP was able to fulfill the virtually process speed and promised for promoting query recommendation on web search engine. Sindhu M.S and Kannan B (2013) used apriori algorithm and FP-Growth to detect drugs interaction.

Khader and Yoon (2014) used FP-Growth for identifying the possible relationship in prescribing for different patients in

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order to find the way to enhance the planogram process of Robotic Prescription Dispensing System (RPDS). This research showed the close relationship among paid medicines used for increasing distribution and dispenses allocation among robot units on pharmaceutical automation.

B. Medicines and Prescription

Medicine constitutes a substance or combination of substances used to diagnose, prevent, alleviate, treat, cure human or animal's deseases or sympthoms, injuries or physical and mental disorder, and make the body or part of the body more beautiful (Lestar et al., 2001).Lestar (2001) quoting Howard C. Ansel Ph. D. a pharmacist, that the prescription is an order given by a physician or medical personnel authorized to pharmacy staff to provide the appropriate medication for a patient .

Compounding has been known as the basic job description of the pharmacists since the USP/The United State Pharmacopeia firstly published in 1820 (Allen, 2003). The Compounding means combination, mixture, or change of one substance or medicine formulation as a response to the doctor's prescription in order to compound medicines that meet patients' condition (Pegues, 2006; Mullarkey, 2009). FDA stated that compounding is ethical and legal as long as it is prescribed by the lisenced doctors for particular patients and specific amount and also compounded by the lisenced pharmacists (Pegues, 2006).

Compounding has been also done in several developed countries. The survey conducted by Buurma et al (2003) in Netherlands, 2001, stated that there were compoundings in every drugstore per day in community drugstore. In 2002, FDA predicted that around 1-8% of compounding would be prescribed every year (Coyne et al., 2006).

C. Data Mining

Seidman, in his book of "Data Mining with Microsoft SQL Server 2000 Technical Reference" conveyed that data mining is a process for finding the sound pattern and hidden relationship inside of huge database. It was seldom to find the sound pattern by browsing through tables and notes. Therefore, the data, usually analyzed by automatic process, is often stated in terms of data mining as *Knowledge Discovery* (KD). By automating data mining, computer finds the pattern and trend appeared in data, while the people in charge will use this findings to determine the relevant pattern.

Data mining can be used to solve hundreds of business problems. According to this problem atribute, data mining can be classified into: a) Classification, b) Clustering, c) Association, d) Regression, e) Forecasting, f) Sequence Analysis, and g) Deviation Analysis

D. FP Growth Analysis

FP Growth Analysis is one of the algorithms that included in the group of Association. It is an algorithm that can be used to determine the frequent itemset. It implements FP-Tree in solving the problems. FP-Tree constitutes compressed data storage structure. The more transactions having the same items are, the more efective the compression process using FP-Tree structure is. The strength of FP-Tree compared to other algorithms in Association group is that it needs only twice transaction data scanning. FP-Growth algorithm finds the frequent itemset ended in particular suffix. In this research, frequent itemset will refer to medicine codes used in preparation of compounding. FP Growth algorithm consists of several steps: 1) Header Table Forming, 2) FP Tree Forming, 3) Conditional Pattern Base Forming, 4) Conditional FP-Tree Forming, and 5) Assosiation Rules Forming. Algorithm of FP-Growth is as follows:

```
Input:   D: Dataset
         Min_sup: Minimum threshold
Output: FP-tree
         IA: item array
         NA: node array

Begin
   FI ← () // List of the frequent itemsets
   H ← () // Header Table
   // Count frequent items
   for each (item i∈D) do
      Insert the item i in H
      H ← H ∪{i}
   for each (item i∈H) do
      if Support(i) < Min_sup

   Eliminate the infrequent item i from H
   Initialize it to 0
// it : the position of the label item i of the
node N in the item array
   for each (transaction t∈D) do
      for each (item i∈t) do
         if The item list in which appears i
         shares a common prefix with the
         existing path in FP-tree then
               The count of the node N in
            FP-tree is incremented by 1
               The count of the node N in node
            array is incremented by 1
      else
            Insert a new node N in FP-tree
            Insert the label item i of the node
         N in the item array IA
            Insert a new node N in the node
         array NA
            Increment it

   Delete (FP-tree)
End
```

III. METHODS

A. Data Description

The data was gathered from XYZ Hospital Pharmacy in Central Java, which its name remains unstated in consideration of privacy. The used database of prescription transaction was collected in the middle of February 2010 to August 2015, especially for pediatric patients (0 – 12 year-old children [5]). The used prescription transactions were only derived from compounded prescription transactions for outpatients. This research also encompasses the knowledge mapping of pharmacists doing medicine dispensing and interaction of medicines.

B. Data Pre-processing

Pre-processing aims at transforming raw data inputs into suitable form for the next analysis. FP-Growth analysis involves data derivation of frequent items inside of pharmaceutical transaction database of XYZ Hospital to find association rules among different medicine combination. Therefore, data collection should be organized in the form of regulation suitable for market-based database transaction with two columns, where the first column showed transaction ID (in this research, it means prescription's number/code). Meanwhile, the second column showed the compounded medicine items. There are four main steps of pre-processing: 1) combining data, 2) cleaning data, omitting *null* transaction, 3) transforming data, 4) reducing data.

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This research does not discuss about discovered knowledge but only data mining approach. The problem in mining business-oriented transaction data set is the existence of null transaction. Null transaction is a transaction that does not contain any tested items [12]. In this research, the prescription consists of one single medicine. The existence of null transaction will influence on the processing time performance.

Table1. The example of preliminary data

Row No.	Date	ID	Item	Qty	Unit
84710	2012-12-01 15:52:39.000	12120106020022	C T M 4 MG TAB	1.00	TABLET
84711	2012-12-01 15:52:39.000	12120106020022	DEXAMETHASONE 0.5 MG TAB	1.00	TABLET
84712	2012-12-01 15:52:39.000	12120106020022	PARACETAMOL 500 MG TAB	1.00	TABLET
84713	2012-12-01 16:49:09.000	12120106020023	AMOXICILLIN 500 MG TAB (INH)	3.00	TABLET
84714	2012-12-01 16:49:09.000	12120106020023	DEXAMETHASONE 0.5 MG TAB	3.00	TABLET
84715	2012-12-01 16:49:09.000	12120106020023	PARACETAMOL 500 MG TAB	3.00	TABLET
84716	2012-12-02 13:00:14.000	12120206020001	L-BIO SACHET	3.00	SACHET
84717	2012-12-02 14:04:59.000	12120206020002	AMOXICILLIN 500 MG TAB (INH)	2.50	TABLET
84718	2012-12-02 14:04:59.000	12120206020002	AMOXICILLIN 500 MG TAB (INH)	2.50	TABLET
84719	2012-12-02 14:04:59.000	12120206020002	ONDANSETRON 8 MG TAB +	3.33	TABLET
84720	2012-12-02 14:04:59.000	12120206020002	ONDANSETRON 8 MG TAB +	3.33	TABLET
84721	2012-12-02 14:04:59.000	12120206020002	PARACETAMOL 500 MG TAB	2.50	TABLET
84722	2012-12-02 14:04:59.000	12120206020002	PARACETAMOL 500 MG TAB	2.50	TABLET
84723	2012-12-02 14:04:59.000	12120206020003	L-BIO SACHET	3.00	SACHET
84724	2012-12-02 14:04:59.000	12120206020003	L-BIO SACHET	3.00	SACHET
84725	2012-12-02 14:12:24.000	12120206020004	AMOXICILLIN 500 MG TAB (INH)	0.25	TABLET
84726	2012-12-02 14:12:24.000	12120206020004	AMOXICILLIN 500 MG TAB (INH)	0.25	TABLET
84727	2012-12-02 14:12:24.000	12120206020004	ONDANSETRON 8 MG TAB +	0.33	TABLET
84728	2012-12-02 14:12:24.000	12120206020004	ONDANSETRON 8 MG TAB +	0.33	TABLET
84729	2012-12-02 14:12:24.000	12120206020004	PARACETAMOL 500 MG TAB	0.25	TABLET
84730	2012-12-02 14:12:24.000	12120206020004	PARACETAMOL 500 MG TAB	0.25	TABLET

Table 2. Data sample after transforming

	TRIN 250 TAB +	CEFIXIME 100 MG CAP (INH)	CURCUMA 200 MG FCT	C T M 4 MG TAB	IKAMICTEN 20 MG/G SALEP KULIT (15G)	IKAGEN 0.1% CREAM (10G)	ZOFREDAL 2 MG TAB ASKES
8448	0	0	0	0	0	0	0
8449	0	0	0	0	0	0	0
8450	0	0	0	0	0	0	0
8451	0	0	0	0	0	0	0
8452	0	0	0	0	0	0	0
8453	0	0	0	1	0	0	0
8454	0	0	0	0	0	0	0
8455	0	0	0	0	0	0	0
8456	0	0	0	0	0	0	0
8457	0	0	0	0	0	0	0
8458	0	0	0	0	0	0	0
8459	1	0	0	0	0	0	0
8460	0	0	0	0	0	0	0
8461	0	0	0	0	0	0	0
8462	0	0	0	0	0	0	0
8463	0	0	0	0	0	0	0
8464	0	0	0	0	0	0	0
8465	0	0	0	0	0	0	0
8466	0	0	0	1	0	0	0
8467	0	0	0	0	0	0	0

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Table 3. The result of frequent itemset

Size	Support	Item 1	Item 2	Item 3
2	0.042	GLYCERIL GUAICOLAT 100 MG TAB	AMBROXOL 30 MG TAB	
2	0.041	GLYCERIL GUAICOLAT 100 MG TAB	C T M 4 MG TAB	
2	0.030	GLYCERIL GUAICOLAT 100 MG TAB	DEXAMETHASONE 0.5 MG TAB	
2	0.035	GLYCERIL GUAICOLAT 100 MG TAB	DEXTROMETHORPHAN TAB	
2	0.033	INTERHISTIN 50 MG TAB	AMINOPHYLLIN 200 MG TAB/ERPHAFILIN	
2	0.062	INTERHISTIN 50 MG TAB	VECTRINE 300 MG CAP	
2	0.044	INTERHISTIN 50 MG TAB	SIRPLUS SYR	
2	0.039	AMINOPHYLLIN 200 MG TAB/ERPHAFILIN	SALBUTAMOL 2 MG TAB	
2	0.047	VECTRINE 300 MG CAP	SIRPLUS SYR	
3	0.040	INTERHISTIN 50 MG TAB	VECTRINE 300 MG CAP	SIRPLUS SYR

A single medicine transaction was not used as the data in this research because collected prescription data should be in the form of compound items.

IV. FINDINGS

The process of FP-Growth algorithm resulting frequent itemset is then followed by the searching of pattern using the association rule done by RapidMiner.

Process of Architecture - Architecture processing used in this research can be depicted in Figure 2 below:

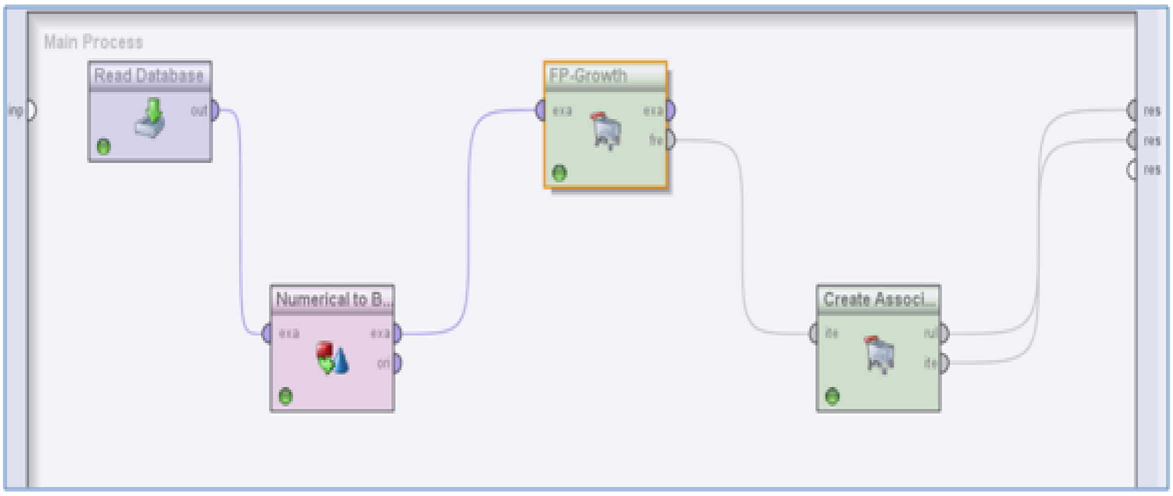


Figure 2. Process of Architecture

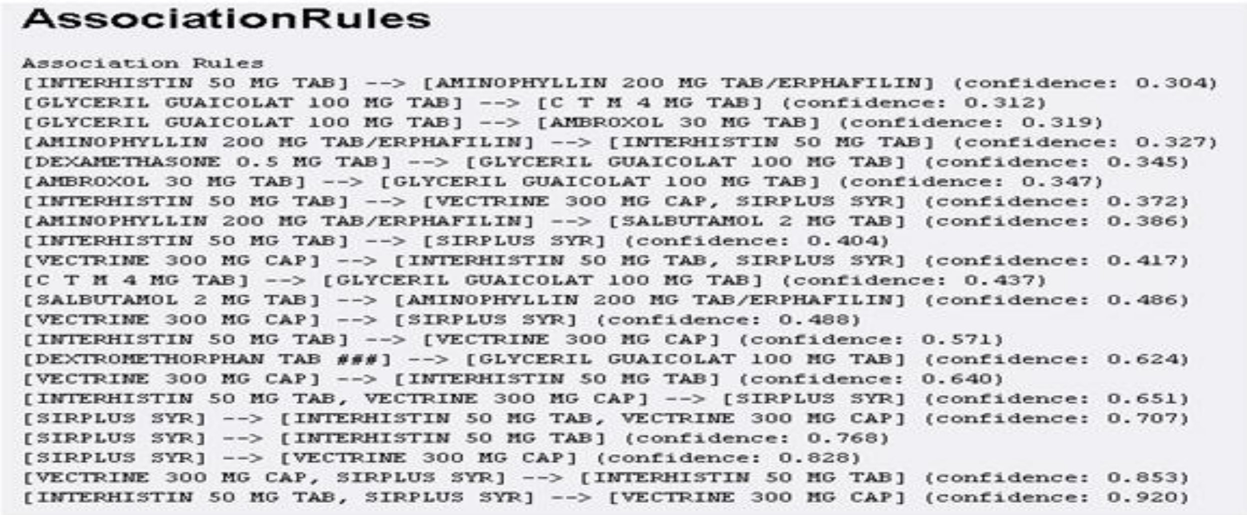
Experimental Result - Numbers of attributes = 654, numbers of processed lines = 54.165, duration of the processing = 21 minutes The value of minimum support = 3% , minimum confidence = 30%, generated frequent itemset results as follows in Table 3. On the other hand, the pattern/rule formed is as follows in Table 4: There were 22 formed rules with two minimum and three maximum attributes like in Figure 3.

Rule [VECTRINE 300 MG CAP] → [INTERHISTIN 50 MG TAB] has support value more than 6% and confidence value by 57.1%. For the rule with 3 attributes was derived on the pattern [VECTRINE 300 MG CAP] → [INTERHISTIN 50 MG TAB, SIRPLUS SYR] with the confidence value by 41.7%. Rule graph in Figure 4 has confidence value above 70% and there are only three dominant attributes from the result of formed association regulation VECTRINE 300 MG CAP, SIRPLUS SYR and INTERHISTIN 50 MG TAB.

Table 4. The result of association rule

No	Premises	Conclusion	Support	Condidence	LaPlace	Gain	p-s	Lift
1	INTERHISTIN 50 MG TAB	AMINOPHYLLIN 200 MG TAB/ERPHAFILIN	0.033	0.304	0.932	-0.185	3.007	1.291
2	GLYCERIL GUAICOLAT 100 MG TAB	C T M 4 MG TAB	0.041	0.312	0.920	-0.220	3.347	1.317
3	GLYCERIL GUAICOLAT 100 MG TAB	AMBROXOL 30 MG TAB	0.042	0.319	0.921	-0.219	2.654	1.292
4	AMINOPHYLLIN 200 MG TAB/ERPHAFILIN	INTERHISTIN 50 MG TAB	0.033	0.327	0.938	-0.169	3.007	1.324
5	DEXAMETHASONE 0.5 MG TAB	GLYCERIL GUAICOLAT 100 MG TAB	0.030	0.345	0.947	-0.146	2.642	1.327
6	AMBROXOL 30 MG TAB	GLYCERIL GUAICOLAT 100 MG TAB	0.042	0.347	0.930	-0.199	3.007	1.330
7	INTERHISTIN 50 MG TAB	VECTRINE 300 MG CAP, SIRPLUS SYR	0.040	0.372	0.938	-0.177	2.642	1.516
8	AMINOPHYLLIN 200 MG TAB/ERPHAFILIN	SALBUTAMOL 2 MG TAB	0.039	0.386	0.944	-0.163	2.654	1.497

9	INTERHISTIN 50 MG TAB	SIRPLUS SYR	0.044	0.404	0.942	-0.174	7.842	1.582
10	VECTRINE 300 MG CAP	INTERHISTIN 50 MG TAB, SIRPLUS SYR	0.040	0.417	0.948	-0.154	4.808	1.639
11	C T M 4 MG TAB	GLYCERIL GUAICOLAT 100 MG TAB	0.041	0.437	0.952	-0.146	7.062	1.544
12	SALBUTAMOL 2 MG TAB	AMINOPHYLLIN 200 MG TAB/ERPHAFILIN	0.039	0.486	0.962	-0.122	4.808	1.747
13	VECTRINE 300 MG CAP	SIRPLUS SYR	0.047	0.488	0.955	-0.147	8.537	1.842
14	INTERHISTIN 50 MG TAB	VECTRINE 300 MG CAP	0.062	0.571	0.958	-0.155	5.887	2.105
15	DEXTROMETHORPHAN TAB	GLYCERIL GUAICOLAT 100 MG TAB	0.040	0.624	0.980	-0.077	4.780	2.314
16	VECTRINE 300 MG CAP	INTERHISTIN 50 MG TAB	0.062	0.640	0.968	-0.132	5.887	2.478
17	INTERHISTIN 50 MG TAB, VECTRINE 300 MG CAP	SIRPLUS SYR	0.040	0.651	0.980	-0.084	11.374	2.698
18	SIRPLUS SYR	INTERHISTIN 50 MG TAB, VECTRINE 300 MG CAP	0.040	0.707	0.984	-0.074	11.374	3.196
19	SIRPLUS SYR	INTERHISTIN 50 MG TAB	0.044	0.768	0.987	-0.070	7.062	3.845
20	SIRPLUS SYR	VECTRINE 300 MG CAP	0.047	0.828	0.991	-0.067	8.537	5.258
21	VECTRINE 300 MG CAP, SIRPLUS SYR	INTERHISTIN 50 MG TAB	0,040	0.853	0.993	-0.054	7.842	6.066
22	INTERHISTIN 50 MG TAB , SIRPLUS SYR	VECTRINE 300 MG CAP	0.040	0.920	0.997	-0.047	9.480	11.252


AssociationRules

Association Rules
[INTERHISTIN 50 MG TAB] --> [AMINOPHYLLIN 200 MG TAB/ERPHAFILIN] (confidence: 0.304)
[GLYCERIL GUAICOLAT 100 MG TAB] --> [C T M 4 MG TAB] (confidence: 0.312)
[GLYCERIL GUAICOLAT 100 MG TAB] --> [AMBROXOL 30 MG TAB] (confidence: 0.319)
[AMINOPHYLLIN 200 MG TAB/ERPHAFILIN] --> [INTERHISTIN 50 MG TAB] (confidence: 0.327)
[DEXAMETHASONE 0.5 MG TAB] --> [GLYCERIL GUAICOLAT 100 MG TAB] (confidence: 0.345)
[AMBROXOL 30 MG TAB] --> [GLYCERIL GUAICOLAT 100 MG TAB] (confidence: 0.347)
[INTERHISTIN 50 MG TAB] --> [VECTRINE 300 MG CAP, SIRPLUS SYR] (confidence: 0.372)
[AMINOPHYLLIN 200 MG TAB/ERPHAFILIN] --> [SALBUTAMOL 2 MG TAB] (confidence: 0.386)
[INTERHISTIN 50 MG TAB] --> [SIRPLUS SYR] (confidence: 0.404)
[VECTRINE 300 MG CAP] --> [INTERHISTIN 50 MG TAB, SIRPLUS SYR] (confidence: 0.417)
[C T M 4 MG TAB] --> [GLYCERIL GUAICOLAT 100 MG TAB] (confidence: 0.437)
[SALBUTAMOL 2 MG TAB] --> [AMINOPHYLLIN 200 MG TAB/ERPHAFILIN] (confidence: 0.486)
[VECTRINE 300 MG CAP] --> [SIRPLUS SYR] (confidence: 0.488)
[INTERHISTIN 50 MG TAB] --> [VECTRINE 300 MG CAP] (confidence: 0.571)
[DEXTROMETHORPHAN TAB ###] --> [GLYCERIL GUAICOLAT 100 MG TAB] (confidence: 0.624)
[VECTRINE 300 MG CAP] --> [INTERHISTIN 50 MG TAB] (confidence: 0.640)
[INTERHISTIN 50 MG TAB, VECTRINE 300 MG CAP] --> [SIRPLUS SYR] (confidence: 0.651)
[SIRPLUS SYR] --> [INTERHISTIN 50 MG TAB, VECTRINE 300 MG CAP] (confidence: 0.707)
[SIRPLUS SYR] --> [INTERHISTIN 50 MG TAB] (confidence: 0.768)
[SIRPLUS SYR] --> [VECTRINE 300 MG CAP] (confidence: 0.828)
[VECTRINE 300 MG CAP, SIRPLUS SYR] --> [INTERHISTIN 50 MG TAB] (confidence: 0.853)
[INTERHISTIN 50 MG TAB, SIRPLUS SYR] --> [VECTRINE 300 MG CAP] (confidence: 0.920)

Figure 3. The formed Association Rules

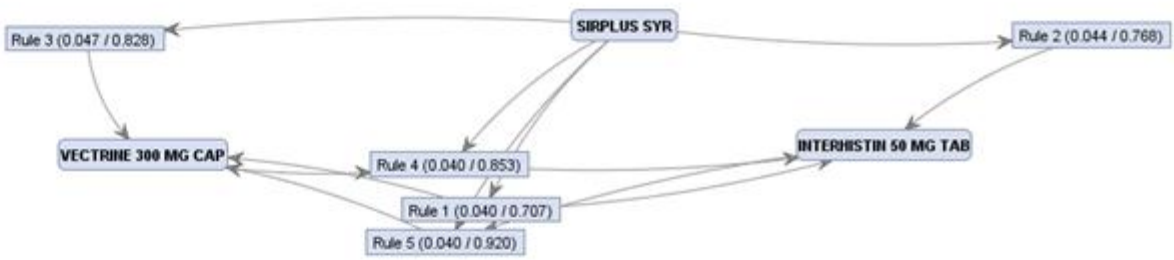


Figure 4. Association Rules Graph

V. CONCLUSIONS

Based on the above experimental result, it can be concluded that the pattern of medicine use (rules) on the compounded prescribing for pediatric patients can be produced using FP-Growth Algorithm and Association Rules with the highest strong confidence by 92%. On the other hand, formed maximum attributes was three (medicine items). As a continuation of this research is how to make the pattern of drug use that is formed can be a guide for hospital pharmacy to form the new drug dosage forms with paying attention to the minimum dosage the drugs.

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