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Detection of Misuse or Illegal Use of Medicines: A Study Example for Tacrolimus Active Ingredient

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ABSTRACT

Corruption and irregularity are situations that we may encounter in every field such as banking, insurance, security and health. Health expenditures are increasing every year all around the world. The amount of corruption and irregularity is parallel to this increase. Corruption and irregularities in the health sector both threaten human health and cause financial losses. With the help of methods for detecting corruption and irregularities, malpractices can be avoided and also financial losses can be prevented, thus contributing to the improvement of health service delivery. The aim of this study is to identify risky individuals who may be involved in drugs, which constitute an important part of health expenditures, and who may cause corruption and irregularities. Drugs with the Anatomical Therapeutic Chemical (ATC) code with the same active ingredient were examined. Anomaly detection, association analysis and rule-based data mining methods were used for the detection of corruption and irregularity. 24 physicians were identified as with high risk. Those who were found to be risky in the analysis were examined specifically and it was confirmed that all of them abused the drug with the relevant active ingredient, thus it means that the method used is 100% consistent and accurate.

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Keywords: Data mining, Corruption, Irregularity detection, Prescription fraud

INTRODUCTION

Data mining is the process of obtaining information from big data (Karimi, H.A. 2014). Health is a basic human right and access to health services is a fundamental right that every individual has just after birth (United Nations, (2022, June 02)). Health care is a type of service that costs to countries increasingly every year. According to 2020 data, approximately 250 billion Turkish Liras have been spent on health in the Republic of Türkiye (Türkiye Statistics Institution (2022, June 22)).

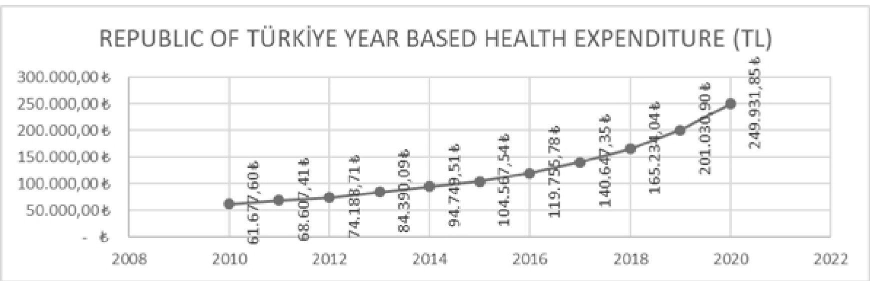


Figure 1: Year based health expenditures (2010-2020) (Türkiye Statistical Institute (TÜIK), 2022).

Drug use constitutes a significant part of health expenditures. Medicines are medical products which are open to abuse due to their financial burden and difficulties access to them. Drug corruption occurs when drugs are made to appear as if they were used while unused, over-prescribed drugs, off-label drugs are prescribed and with the cooperation of physicians with organizations such as companies or pharmacies (Thornton et al, 2013). It is important to detect unnecessary or illegally prescribed drugs, to prevent financial losses, and to prevent situations that may harm human health. The financial resource flowing to corruption and irregularity is an important factor that prevents people from getting a better service. Due to the high number of people receiving health services and the difficulty of detecting individual irregularities, it has become vital to conduct irregularities with data mining methods in the health sector. It has been shown that corruption and irregularity can be found in health with methods such as outlier detection, association rules among data mining methods (Capelleveen et al, 2016). The aim of this study is to identify risky individuals who may be involved in drug related corruption and irregularities by using data mining methods.

METHODOLOGY

In our literature review, it is observed that data mining methods are generally used in the health sector to detect corruption over insurance systems.

Namrata Ghuse has tried to detect corruption that may occur in health insurances with prediction algorithms and logistic regression models. The difficulties of working with raw big data are mentioned. It has been found to be more efficient than the classical audit approach in detecting corruption (Ghuse et al, 2017).

Verna's study is an experimental study and the purpose of the experimental study is to define and measure health insurance data. Statistical decision rules in two criteria based on abnormal demands and diseases, k-means clustering algorithm are applied on abnormal claims, anomaly detection and association algorithms are used on diseases. The results were found to be effective. 75 cases of corruption have been identified (Verma et al, 2017).

Kareem's study used classification, association (apriori algorithm) and data mining methods of support vector machines. No significant association was detected. The data of the University of Malaysia was used. He concluded that corruption detection methods should be developed (Kareem et al, 2017).

In Yang's study "Gradient Boosting Decision Tree (GBDT) and LHEM" were used as the decision tree model. Pharmaceutical data of health insurers in Jinhua city in 2019 and 2020 are used. Disease diagnosis and gender were evaluated together with medication. When the results of the two models were evaluated together, LHEM was found to be more effective in detecting health corruption (Yang et al, 2021).

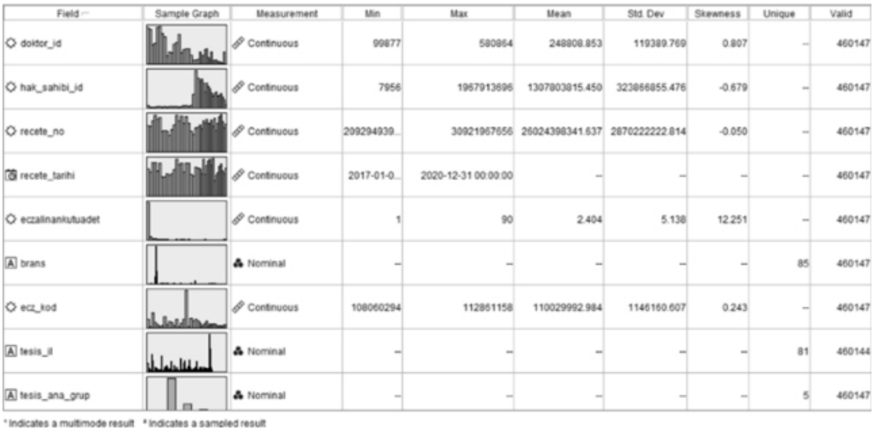
The subject of data mining has been examined by following the steps of data selection, data cleaning, data reduction, data integration, data transformation, modelling, model evaluation and information presentation (Han et al, 2012). The study was carried out using the IBM SPSS Modeler software.

Data Selection

Anonymized 9x235162 sized data of the Republic of Türkiye Ministry of Health was used for drugs containing tacrolimus active ingredient covering the years 2019-2020. Within the scope of this study, 16460 physicians and 24671 pharmacies were examined.

Pre-Processing and Cleaning the Data

Data quality was evaluated using the SPSS Modeler Data Audit tool.



Field	Sample Graph	Measurement	Min	Max	Mean	Std. Dev	Skewness	Unique	Valid
doktor_id		Continuous	99877	580864	248808.853	119389.769	0.807	–	460147
hak_sahibi_id		Continuous	7956	1967913696	1307803815.450	323866855.476	-0.679	–	460147
recete_no		Continuous	209294939...	30921967656	26024398341.637	2870222222.814	-0.050	–	460147
recete_tarihi		Continuous	2017-01-0...	2020-12-31 00:00:00	–	–	–	–	460147
eczalinankutuadet		Continuous	1	90	2.404	5.138	12.251	–	460147
brans		Nominal	–	–	–	–	–	85	460147
ecz_kod		Continuous	108060294	112861158	110029992.984	1146160.607	0.243	–	460147
tesis_il		Nominal	–	–	–	–	–	81	460144
tesis_ana_grup		Nominal	–	–	–	–	–	5	460147

* Indicates a multimode result * Indicates a sampled result

Figure 2: Data Audit result image

Physicians with empty branch data are combined under the "other" heading. The missing data were completed by taking the arithmetic mean of the other non-null physicians for the values with the null number of physician examinations and the total number of physician prescriptions.

Data Reduction and Integration

In order to prevent the effect of a small number of prescribers on the mean and standard deviation, the distribution of the number of prescriptions written by the physicians in their own branches was examined and the quarters were calculated. According to these quarters, physicians with prescription numbers less than the 1st quarter value were excluded from the data set (4 boxes) and analyzes were made with 75% of the physicians. Thus, physicians who write a small number of prescriptions are prevented from being among risky physicians. The data size is reduced to 9x215195.

Transforming Data

Data transformations were carried out within the framework of risk criteria.

Risk 1: Physician prescribing a large number of boxes to patients with similar diseases compared to other physicians in his/her own branch

Indicator 1: Number of Boxes Per Prescription

I1 Calculation: (Number of Risky Boxes i)/(Number of Risky Drug Prescriptions i) , i=1.N(Number of physicians in the branch) (1)

Risk 2: The high share of prescriptions that the physician prescribes drugs with risky active ingredients in total prescriptions

Indicator 2: Risky Prescription Ratio

I2 Calculation: (Number of Risky Drug Prescriptions i)/ (Number of Prescriptions of All Medicines i) , i=1.N(Number of physicians in the branch) (2)

Risk 3: Physician always prescribes risky drugs to the same patients

Indicator 3: Number of Drug Boxes Per Different Patient

I3 Calculation: (Total Number of Boxes of Risky Drug i)/(Number of Different Patients i), i=11.N(Number of physicians in the branch) (3)

Risk 4: Physician prescribes medication for the same patient in a very short time (Note: It includes outpatients who are prescribed in 10 days or less, the medications given to inpatients are excluded.) Physicians who prescribe the same medication to the same patient more than once within 10 days are considered risky.

Indicator 4: Physician - Patient Relationship

I4 Calculation: Date of Prescribing Medication to a Single Patient-Previous Medication Date ≤10 (4)

Risk 5: Physician prescribes too many related drugs on the same day

Indicator 5: Prescribing drugs on the same day above the country's average

I5 Calculation: Number of physician's prescriptions per day≥3*(Number of Prescriptions Per Day)/ (Number of Active Physicians on the Same Day) (5)

Data Mining (Modeling) Phase

In this step of the process, data mining methods were applied according to the purpose of the study by using the data prepared in the previous steps. Data mining methods used in this study are:

Anomaly Detection:

Outliers, which can have significant effects on further analysis and modeling, occur between continuum situations (Čampulová et al, 2021). Outlier detection methods make an implicit assumption: normal objects are somehow "clustered". In other words, an unsupervised outlier detection method would expect normal objects to follow a pattern much more frequently than outliers. Normal objects do not need to fall into a group that shares high similarities. Instead, they can form multiple groups, where each group has different characteristics. However, an outlier would be expected to occur very far in the feature space from any of these normal object groups (Han et al, 2012). Anomaly Detection is a technique that enables the detection of unexpected situations in data. The detection of unexpected situations is revealed by determining over big data. These unexpected situations are called outliers, exceptions, or anomalies in the literature (Pang et al, 2021).

Association Analysis- Apriori Algorithm:

The Apriori algorithm is an impressive algorithm found by R. Agrawal and R. Srikant in 1994 for logical association relationships (Losarwar ve Joshi, 2012). Association analysis is a data mining and machine learning method that reveals the relationship between variables based on rules.

Each transaction set with the units in this data set, including the D data set and the $I=\{I1, I2,\cdots,Im\}$ unit set (Itemset), is $T\subseteq I$. Each transaction is represented by a TID number. With $A\subseteq I$, $B\subseteq I$, $A\neq\emptyset$, $B\neq A$, and $A\cap B=\emptyset$, the association rule of A and B units is shown as $A\supset B$. The expression to the left of the $\supset$ symbol in the rule notation is called antecedent, and the expression to the right is called the consequent. Association rules shown as antecedent A $\supset$ consequent *B* among the units in the D data set are defined by support, confidence, and lift values.

Support (A⇒B) = (Frequency Number (A, B)) / (N Number (Data Set))

Confidence (A⇒B) = (Frequency Number (A, B)) / (Frequency Number (A))

Lift (A⇒B) =(Support(A⇒B))/(Support(A)×Support(B)) (Momeni Kho et al, 2021).

The methods are implemented through the SPSS Modeler data mining product.

Rule Induction:

One of the known classification approaches in data mining is rule extraction. It is a key algorithm for building classification models with simple, yet effective, easy to understand rules. This algorithm was developed in 1987 based on the separation of data samples using existing class labels. Rule inference algorithms generally produce if-then classifiers with predictive performance comparable to other traditional classification approaches such as decision trees and relational classification.

Anomaly detection model was applied for branch and sector (public, private, and university) based evaluations via IBM SPSS Modeler Program for Boxes Per Converted Recipe, Risky Prescription Rate, and Number of Drug Boxes Per Different Patient. In the indicators of Physician-Patient Relationship and prescribing drugs above the country average on the same day, rule-based progress was made, and abnormalities were detected. The mean of frequency (μ) and standard deviation (σ) were calculated, and the risk score was given.

Table 1: Risk Scoring Table

$\mu + 0,5\ \sigma \leq$ Indicator Result $< \mu + 0.75$	σ	1 score
$\mu + 0.75\ \sigma \leq$ Indicator Result $< \mu + 1$	σ	2 scores
$\mu + 1\ \sigma \leq$ Indicator Result $< \mu + 1.25$	σ	3 scores
$\mu + 1.25\ \sigma \leq$ Indicator Result $< \mu + 1.5$	σ	4 scores
$\mu + 1.5\ \sigma \leq$ Indicator Result $< \mu + 1.75$	σ	5 scores
$\mu + 1.75\ \sigma \leq$ Indicator Result $< \mu + 2$	σ	6 scores
$\mu + 2\ \sigma \leq$ Indicator Result $< \mu + 2.25$	σ	7 scores
$\mu + 2.25\ \sigma \leq$ Indicator Result $< \mu + 2.5$	σ	8 scores
$\mu + 2.5\ \sigma \leq$ Indicator Result $< \mu + 2.75$	σ	9 scores
$\mu + 2.75\ \sigma \leq$ Indicator Result		10 scores

In addition, the apriori algorithm for the patient-patient relationship was used to observe the relationship between physicians and pharmacies and block movements between patients (repeated block movements of patients who prescribed the same drug to the same doctor on the same day and bought this drug from the same pharmacy).

RESULTS

Calculation and Findings

Finding 1: Number of Boxes Per Recipe

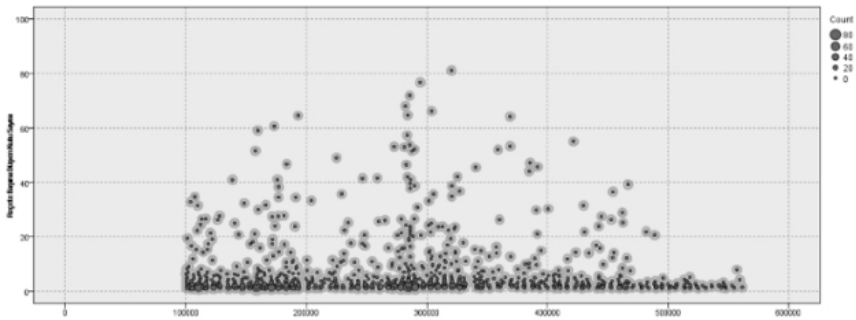


Figure 3: Boxes Per Prescription Ratio Scatter Chart

Table 2: Number of Boxes Per Prescription Data Characteristics

Count	3,327
Mean	2.07
Min	1.00
Max	76.67
Range	75.67
Variance	5.54
Standard Deviation	2.35
Standard Error of Mean	0.04

In the Number of Boxes Per Prescription indicator, the overall average was 2.073, and physicians who deviated from the general average were scored according to their standard deviation. From Indicator 1, out of 2354 physicians, 16 physicians attained the high-risk physician status by obtaining a risk score of 9-10, 5 physicians attaining the status of risky physician with a risk score of 7-8, 5 physicians attaining the status of medium-risk physician with a risk score of 5-6 and 2328 physicians attaining the status of low risk-no risk physician with a risk score of 1-4 were identified. 1.1% of physicians were identified as risky.

Finding 2: Risky Prescription Ratio

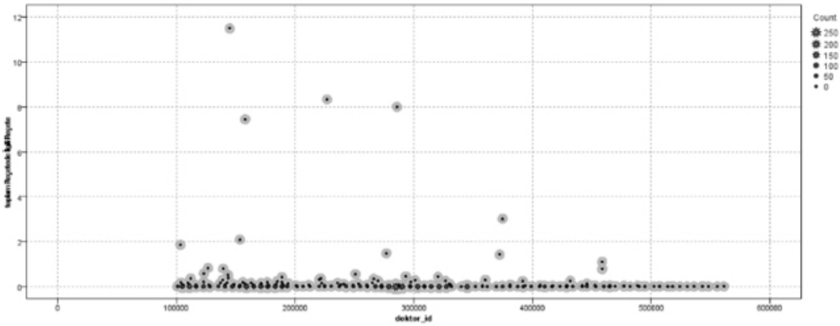


Figure 4: Relevant Prescription Ratio in the Whole Prescriptions Scatter Chart

Table 3: Relevant Prescription Ratio in Whole Prescriptions Data Attributes

Count	3,327
Mean	0.006
Min	0.000
Max	0.149
Range	0.149
Variance	0.000
Standard Deviation	0.010
Standard Error of Mean	0.000

In the indicator of Relevant Prescription Ratio in the whole prescriptions, the general average was 0.006, and the physicians who deviated from the general average were scored according to their standard deviation. From Indicator 2, out of 2354 physicians, 66 physicians entered the high-risk physician status by obtaining a risk score of 9-10, 29 physicians attained the status of risky physician with a risk score of 7-8, 51 physicians attaining the status of medium-risk physician with a risk score of 5-6 and 2208 physicians attaining the status of low risk-no risk physician with a risk score of 1-4 were identified. 6% of physicians were identified as risky.

Finding 3: Number of Drug Boxes Per Different Patient

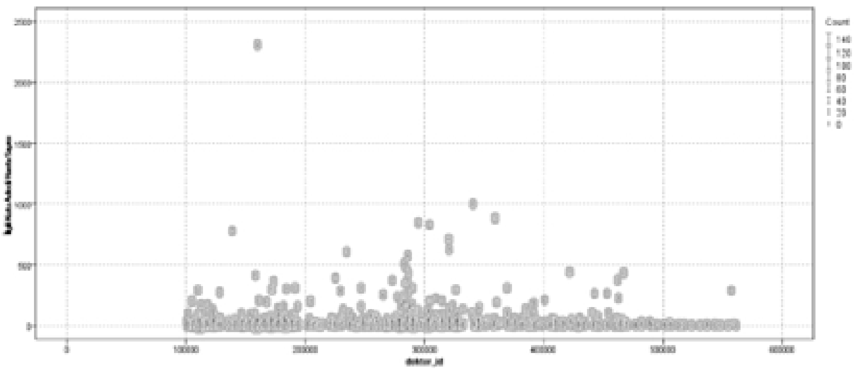


Figure 5: Number of Boxes Per Different Patient Ratio Scatter Chart

Table 4: Number of Boxes Per Different Patient Ratio Data Attributes

Count	3,327
Mean	4.34
Min	1.00
Max	161.00
Range	160.00
Variance	54.62
Standard Deviation	7.40
Standard Error of Mean	0.13

In the indicator of number of boxes per different patient, the overall average is 4.336, and physicians who deviate from the general average are scored according to their standard deviation. From Indicator 3, out of 2354 physicians, 29 physicians entered the high-risk physician status by obtaining a risk score of 9-10, 10 physicians attained the status of risky physician with a risk score of 7-8, 10 physicians who attained the status of medium-risk physician with a risk score of 5-6, and 2305 physicians attaining the status of low risk-no risk physician with a risk score of 1-4 were identified. 2.08% of the physicians were identified as risky.

Finding 4: Physician Patient Relationship

Table 5: Physician Patient Relationship Results

patient id	physician id	Number of drug prescription for less than 10 days
1401592710	924780	4
344468574	2589444	4
1300046880	1895838	4
762594054	960120	4
1438197570	1644612	3
1763156016	1872726	3
9806514	1895838	3
1807953708	1895838	3
1468176342	1488270	3
1130521644	1895838	3
1052406702	3214986	3

Among the physicians who prescribed this drug group for less than 10 days to the same patient, the first physician, who was considered the riskiest, prescribed the drug to 87 different patients in less than 10 days. The 2nd physician prescribed drugs to 47 different patients, the 3rd physician to 21 different patients, the 4th physician to 14 different patients, the 5th physician to 12 different patients, and the 6th physician to 10 different patients. In this way, 46 physicians were considered to be risky.

Finding 5: Prescribing drugs above more than 3 times of the country average on the same day

Table 6: Physician Average Number of Exceeded Days

physician id	Exceeded Days
945744	249
1514028	224
1895838	150
1146864	129
1636224	87
996204	85
898710	81
712596	67
834468	64
894642	63
1580226	61

The number of days of the physicians who prescribed the drug more than 3 times of the average of the number of prescriptions per day was determined. It was found that 4 high-risk physicians wrote prescriptions for more than 100 days above the national average and 7 physicians wrote prescriptions for more than 50 days above the national average.

Finding 6: Physician-Pharmacist-Patient Association Analysis

Table 7: Physician-Pharmacist Association Analysis Results

pharmacy id	physician id	Support	Confidence	Lift
109864290	1895838	0.006	100%	17804%
108068646	651744	0.002	91%	63387%
110118972	1278096	0.002	70%	54370%
112385400	2368296	0.001	87%	84035%
112385400	2573940	0.002	62%	64902%
110079612	698370	0.001	63%	70778%
110094816	2154708	0.001	98%	112168%
109864896	2807646	0.001	97%	114407%
109864548	2294304	0.001	99%	124032%
109864350	605796	0.001	100%	171991%
109862982	1836270	0.001	100%	174906%
109267548	2275428	0.001	100%	179782%
108970476	1065024	0.001	86%	170852%
111660474	657732	0.001	94%	189696%
109864548	2949792	0.000	90%	246878%
109864350	686850	0.000	100%	286652%
112385400	2642670	0.000	100%	291511%

Physicians with higher than 50% confidence in the association analysis and prescribing more than 100 boxes were included in the risky category. No block movement of patient was observed.

DISCUSSIONS and CONCLUSIONS

Similar studies were examined. Aral et al., in their study "A fraud detection model", developed a model using data mining methods to detect prescription irregularities. Data titles are market price of the prescribed drug, prescription number, age, sex and diagnosis. The work is coded in MATLAB. 26,419 prescriptions were analyzed. Classification models are used. The established model showed high success with 77.4% true positive rate and 6% false positive rate for counterfeit prescriptions (Aral et al, 2012).

In the study "The evaluation of trustworthiness to identify health insurance fraud in dentistry" by Wang et al., rule-based data mining methods were used to detect this situation due to the fact that dentists harm health insurance companies due to false statements. The model works according to the reliability score of a dentist, the amount of procedure and the type of procedure. The treatment practices of dentists with patients through their social networks were evaluated. It has been evaluated that the model is capable of reducing insurance fraud (Wang et al, 2017).

In their study, Kirlidog and Asuk "A fraud detection approach with data mining in health insurance" aimed to detect situations that may cause fraud and corruption by making false statements in order to gain benefit from health insurance companies, by using data mining methods. By examining the historical data, anomaly detection and support vector machine models and possible corruption and irregularities have been determined. The study was carried out through Oracle. As a result of the study, it has been evaluated that anomaly detection methods and situations with the possibility of corruption and irregularity can be separated in big data and come to a conclusion in detailed analysis and examinations (Kirlioglu and Asuk, 2012)

The relationship between risk criteria such as physicians' risk score averages, high risk criteria, number of prescription drugs, clustering in certain healthcare facilities and provinces, physician/pharmacy relationship, and of block patient movements were evaluated. In addition, a final evaluation was made with experts on the subject and suggestions were made.

In our study, scenarios suitable for drug corruption were applied using data mining algorithms. 16460 physicians and 24671 pharmacies were examined and 26 physicians were selected from the Number of Boxes Per Prescription criteria, 146 physicians from the Rate of Related Prescription in All Prescriptions criteria, 49 physicians from the Ratio of the Number of Boxes per Different Patient, 46 physicians from the criteria of prescription drugs in less than 10 days, and 11 physicians from prescribing the drugs more than 3 times of the average number of prescriptions per day criteria were found to be high risk. It was also evaluated the pharmacy-physician relationship. As a result of the association analysis, physicians who prescribed more than 100 boxes of drugs with confidence above 0.50 were filtered out. As a result, 38 physicians and 29 pharmacies were evaluated as high risk.

When all the results were evaluated together, a total of 24 physicians were found to be at high risk and were ranked according to their risk levels. Each physician and pharmacy found to be at risk in the analysis was examined by the inspector, and it was confirmed that all of them abused the drug with the relevant active ingredient. For this reason, it has been observed that the method used is 100% consistent and accurate.

Due to the fact that unsupervised methods are generally used in the detection of corruption and irregularity with data mining methods, an inspector examination is needed after the risk focus is determined in the studies. The accuracy of the studies can only be revealed as a result of the inspection of the inspector.

In this study, unlike other corruption and irregularity detection studies, association algorithms and anomaly detection methods are used as a hybrid model. In addition, the criteria created for corruption and irregularity scenarios were evaluated together and achieved high success.

Ethical Approval: Ethics committee approval was not required for this study. The data used in the study were encrypted by the Ministry of Health Inspection Board and given to the authors with the letter dated 15.04.2022 and numbered 2946. The study started after data collection.

Authors' Contributions: The first author, Ahmet KOÇAK, coordinated the entire study, provided the data, performed the literature review and model building, operation and testing for accuracy. The second author, Hüseyin Erkin SÜLEKLİ was responsible for creation, operation, and accuracy of the model.

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Conflict of Interest Statement: The authors declare that there is no conflict of interest for this study.

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