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Risk factors and prediction of the severity of respiratory diseases in domestic rabbits (*Oryctolagus cuniculus*)

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Abstract

This study examined the health information of domestic rabbits to find the risk factors and the relationship mortality rates due to respiratory diseases and to predict of the severity of the respiratory diseases by carrying out a prospective study. The study process involved collecting samples from healthy and sick rabbits with respiratory diseases. In total, there were 1,758 samples, which were divided into 1,000 healthy rabbits, 758 sick, and 210 dead rabbits. Age, sex, breed, density in rabbit husbandry, sanitation, and management had been related to illness. In order to investigate the relationship of the clinical symptoms, comparisons were made between the sick rabbits and those that had expired from respiratory diseases. The findings indicated that having the symptoms of oculonasal discharge and having a higher body condition score [Standard (Score=3) to obese (Score=5)] were not found in relation to the dead rabbits. The cause of the sick rabbits to have a higher mortality rate include 1) indicators of mental status, such as having depression or having a lower body condition score: [Emaciation (Score=1) to Underweight (Score =2)]; 2) increases in the respiratory rates and heart rates; 3) lung opacity pattern of interstitial, 4) an abnormal Complete blood count, and 5) blood chemistry parameters, such as Aspartate aminotransferase, Alanine aminotransferase, Alkaline phosphatase, Albumin, Gamma-glutamyltransferase, Blood Urea Nitrogen and creatinine. These values are used to predict the severity of respiratory diseases and to classify patient rabbits. This is the first report of severity index of respiratory diseases for domestic rabbits.

Keywords: Rabbits, Respiratory diseases, Risk factors, Severity

1. Introduction

Currently, having rabbits as household pets has become more popular for three main reasons: 1) rabbits are small animals that require only a little space in which to be kept, 2) they do not make loud noises, and 3) they are easily handled. From a retrospective survey conducted in the years between 2011-2016 by the Kwuncum Animal Hospital, it was found that the number of rabbits visiting the animal hospital had increased each year. The number of rabbits admitted had been 3,337 (17.56%), 5,736 (26.24%) and 8,155 (27.04%) for the years of 2011, 2012, and 2013, respectively. Therefore, it was discovered that more rabbits were succumbing to more illnesses due to various causes. During 2014-2015, it was found that the mortality rate from rabbit respiratory diseases had amounted to 40.32 percent. When conducting additional surveys in the years between 2016-2018, it was found that 8,371; 9,242; and 9,388 rabbits had been admitted, respectively. In total, there had been 27,001 rabbit admissions. After gastrointestinal diseases (27.5%, 7,425 cases), respiratory illnesses are the second most common disease at 25.5 percent (6,886 cases). Furthermore, the mortality rate from respiratory diseases was 38.32 percent (1,552 cases). The pathogen which often causes death in rabbits from respiratory diseases has been identified as *Pasteurella multocida* [2-5,7,10,16]. Based on the survey of bacteria found in rabbits that shows respiratory symptoms in Thailand from the deep nasal cavity, 12 different types of bacteria were identified consisting of: *Pasteurella multocida*, *Streptococcus* spp., *Staphylococcus* spp., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Corynebacterium* spp., *Escherichia coli*, *Micrococcus* spp., *Proteus* spp., *Moraxella* spp., *Enterobacter* spp., and *Klebsiella* spp [20]. In order to lower the mortality rates, the most important detail is to

provide the appropriate and fast-acting antibiotics [18]. However, in humans, the cause of death does not solely depend upon the pathogen and the severity of the infection. It is, however, dependent upon other risk factors, such as heart disease, kidney disease, and the age of the patient [1]. Accordingly, for humans, there are patient classification tools and severity indices for pneumonia, including Pneumonia severity index (PSI), the Severity Score estimates mortality of community-acquired pneumonia (CRB 65, and the CURB65) [8,9,11,12,14,15,17-19,22,24]. In order to evaluate and prognose any disease, it is important to consider various clinical parameters and environmental factors.

In Veterinary Medicine, there is no study of risk factors and classification in animals with respiratory diseases. Therefore, there are limitations in assessing the severity and risk control and in determining the successful treatment of respiratory diseases. This study of the risk factors and severity assessment of respiratory diseases in rabbits, is the first study of its kind in Thailand. It is very likely that the proper way to manage respiratory diseases is to examine the important parameters (i.e., age, sex, species, raising the rabbits, and the sanitary conditions the rabbits live in, as well as their evaluating their clinical symptoms, hematological values, and radiographic images in accordance to the principles of the pneumonia severity index) in order to make comparisons among “healthy”, “sick”, and “dead” rabbits [11].

2. Materials and methods

2.1 Sample size

Sample collection from healthy and sick rabbits with respiratory problems took place at Kwuncum Animal Hospital. The criteria for screening of rabbits that had been diagnosed with respiratory diseases was used by relying on clinical symptoms, such as oculonasal discharge, respiration rates, lung sounds, and chest radiographs. To calculate the population in the study, the Epi Info program was used to determine the total sample size of 384 samples. For this study, there were a total of 1,758 samples, which were divided into three groups: 1,000 healthy rabbits, 758 sick rabbits, and 210 rabbits that died.

2.2 Methods

This prospective study was conducted based on information, such as taking the history and a physical examination, consisting of a body condition score, mucus membrane coloration, capillary refilling time, heart rate, respiration rate, oculonasal discharge, and the heart and lung sounds. The radiography was taken by the right lateral recumbency and the dorso-ventral position using the Kv value of 45-50 and the mAs value is 0.04-0.06, which depended upon the size of the rabbit (KELEX X-ray machine model MD 1100, 100 mA, 100 kV). Blood sample collection was taken from the saphenous vein to study the hematogram, such as the complete blood count (CBC) and blood biochemistry. At least 2 ml of blood was placed in the blood collection tube containing Ethylenediaminetetraacetic acid (EDTA) and heparin sodium. Then it was checked with the SHINNOWA automatic blood counting machine model HB 7021, which uses the principle of electro-impedance measurement. Moreover, the SHINNOWA automatic blood chemistry checker (Model DS 161) uses the principle of optical filtering by reading the wavelength at a range of 340-810 nm.

2.3 Statistics

The statistical analysis was performed by using Chi-square, One-way ANOVA, and the Post Hoc Test to analyze relative risk or Odds ratio using the SPSS version 25.

2.4 Ethics in the use of experimental animals

The animals were in the normal health examination and treatment process. The study of the experimental animals was carried out in *Category C* in which the rabbits are subjected to procedures that cause them no pain or distress, or only momentary or slight pain or distress. Therefore, the use of pain-relieving drugs had not been required.

3. Results

3.1 Risk factors between healthy rabbits and sick rabbits

The parameters of interest were age, gender, species, rabbit density, feeding type, water cup type, and sanitation management. This data was used to find the statistical relationships of the risk factors for respiratory

diseases in rabbits. The results indicated that all parameters had been risk factors and were significantly related to illness when compared to healthy rabbits ($p < 0.05$), which is shown in Table 1.

3.2 The relationship of clinical symptoms comparison between sick and dead rabbits with respiratory diseases

In order to study the factors that had resulted in higher severity and mortality rates, there were 210 rabbits that had died from respiratory diseases out of a collection of 758 rabbits suffering from respiratory diseases. The clinical symptoms, which the researchers were interested in studying, consisted of: nasal discharge, ocular discharge, mental status, body condition scores (BCS 1-5), body temperatures, anorexia, the color of mucous membranes, capillary refilling times (CRT), respiratory rates (RR), and heart rates (HR). The statistical relationships found that mental status, BCS 1-2, high body temperature, anorexia, mucous membrane, CRT, HR, and RR had all been associated with severity and that the mortality rate had been higher compared to the “sick” rabbits ($p < 0.05$). In contrast, other symptoms, such as oculonasal discharge, BCS 3-5, and low body temperatures, had not correlated with death in sick rabbits ($p > 0.05$), which is shown in Table 2.

Table 1 The association between the clinical criteria of the disease and the rabbits that died of respiratory diseases.

Factors	Morbidity rate %	<i>p</i> value for trend	
		Chi-square ($\alpha = 0.05$)	Odd ratio
Age		< 0.05	2.18
≤ 4 years	45.9		
> 4 years	54.1		
Gender		< 0.05	2.02
Female	54.4		
Male	45.6		
Number of crowns		< 0.05	2.25
> 1 animal	43.11		
Only 1	38.9		
Place		< 0.05	22.22
Indoors	12.7		
Outdoors	76.2		
Type of Feeder		< 0.05	4.18
A bowl	28		
A rack	61.9		
Water filling characteristics		< 0.05	7.39
A bottle	18.2		
A bowl	63.9		
Sanitation		< 0.05	7.14
The tray was changed every 24 h	21.5		
The tray was changed over 24 h	66.2		
Breeds		< 0.05	
Holland Lop and Thai	86.43 / 13.57		3.52
Holland Lop and Netherland Dwarf	73.27 / 26.73		2
Holland Lop and Mini Rex	100 / 0		-
Holland Lop and Mixed	76.38 / 23.61		1.8

Table 2 The association between the clinical criteria of disease and the rabbits that died from respiratory diseases.

Factors	Mortality rate %	<i>p</i> value for trend	
		Chi-square ($\alpha = 0.05$)	Odd ratio
Nasal Discharge		0.98	1
Nasal discharge	81		
No nasal discharge	19		
Ocular Discharge		0.45	1
Ocular discharge	33.33		
No ocular discharge	66.7		
Mental Status		< 0.05	
Depressed and alert	87.5 / 12.5		3.84
Stuporous and alert	71.4 / 28.6		6.84

Factors	Mortality rate %	<i>p</i> value for trend	
		Chi-square ($\alpha = 0.05$)	Odd ratio
Body Condition Scores			
Body condition scores of 1 and 3	95.1 / 4.9	< 0.05	6.65
Body condition scores of 2 and 3	98.6 /1.4	< 0.05	7.23
Body condition scores of 4 and 3	71.4 / 28.6	0.485	1.81
Body condition scores of 5 and 3	91.7 / 8.3	0.06	0.26
Body Temperatures			
Low and Normal Body temperatures	7.1 / 92.9	0.08	1.91
High and Normal Body temperatures	35 / 65	< 0.05	4.15
Anorexia		< 0.05	7.19
Anorexic	90.5		
Non- Anorexic	9.5		
Mucous Membranes			
Pale and pink	57.9 / 42.1	< 0.05	1.68
Cyanotic and pink	74.2 / 25.8	< 0.05	2.76
Capillary Refilling Time		< 0.05	
CRT ≤ 2 s and CRT >2 s	61.9 / 38.1		5
Respiratory rates			
Low and Normal respiratory rates	59.1 / 40.9	< 0.05	8.84
High and Normal respiratory rates	75.5 / 24.5	< 0.001	3.82
Heart rates			
Low and Normal heart rates	17.8 / 82.2	< 0.05	3.33
High and Normal heart rates	16.9 / 83.1	< 0.05	1.93

3.3 The relationship of chest radiographs compared to sick and dead rabbits with respiratory diseases

There was a noticeable value -28% of the rabbit with abnormal radiographs had died, while those with normal chest radiographs showed a mortality rate of only 5%. However, after the statistical analysis had been performed, it was found that there had been no significant difference ($p > 0.05$). When only the interstitial pattern and the normal radiographic images were compared, it was found that there was a statistically significant difference ($p < 0.05$), which is shown in Table 3.

3.4 Relation of hematological values of sick and dead rabbits with respiratory diseases

The hematological data was collected by applying complete blood count and biochemical values from 3,049 rabbits. These were divided into three groups: healthy rabbits (2,095), sick rabbits (757), and dead rabbits (210). This data was used to discover the statistical relationships so that the factors that result in severe and higher mortality rates in respiratory diseases could be identified

3.5 Complete blood count

The rabbits were divided into three groups: healthy (Group 1), sick (Group 2), and dead rabbits (Group 3). It was found that the following changes in the hematological data had had an effect on increasing mortality: white blood cells (WBC), lymphocytes (LY), monocytes (MO), granulocytes (GR), the neutrophil lymphocyte ratio (LY ratio), monocyte lymphocyte ratio (MO ratio), the hemoglobin (HGB), the hematocrit (HCT), and the mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), reticulocyte distribution width by standard deviation (RDWsd) and the platelets (PLT) ($p < 0.05$). Nonetheless, some parameters had not shown any effects on the mortality rate, such as the red blood cells (RBC), reticulocyte distribution width by coefficient of variation (RDWcv), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) ($p > 0.05$). The MO ratio, GR, and MCH were found to be different between the three groups, which had been classified as “healthy” and which distinguished the “dead” from the “sick” and from the “healthy”. These parameters had affected the increased mortality rates between the three groups. LY, HGB, HCT, and MCHC had distinguished “healthy” and from the “sick”. WBC, MO, and the LY ratio were used to distinguish between the sick and dead from healthy rabbits. However, no difference was found between the “sick” and the “dead”. The MCV and the RDWsd were the only differences found between the

“healthy” and the “sick”. There was no difference between the dead. As shown in Table 4, there were no differences between the groups with respect to PLT. As shown in Table 4.

Table 4 The association between the complete blood count of the disease and the rabbits that died from respiratory disease.

Complete Blood Count		<i>p</i> value for trend	No. different among groups	Groups
WBC	Between Groups	.000	2	1,2 1,3
LY ratio	Between Groups	.000	2	1,2 1,3
Mo ratio	Between Groups	.000	3	1,2 1,3 2,3
LY	Between Groups	.000	2	1,3 2,3
MO	Between Groups	.000	2	1,2 1,3
GR	Between Groups	.000	3	1,2 1,3 2,3
RBC	Between Groups	.631	-	-
HGB	Between Groups	.000	2	1,3 2,3
HCT	Between Groups	.000	2	1,3 2,3
MCV	Between Groups	.000	1	1,2
MCH	Between Groups	.000	3	1,2 1,3 2,3
MCHC	Between Groups	.000	2	1,3 2,3
RDWcv	Between Groups	.594	-	-
RDWsd	Between Groups	.000	1	1,2
PLT	Between Groups	.039	-	Not different
MPV	Between Groups	.456	-	-
PDW	Between Groups	.209	-	-
PCT	Between Groups	.491	-	-

*ANOVA analysis, group comparisons, and POST HOC TEST. The comparison of individual differences.

3.6 Blood chemistry

It was found that changes in blood chemistry, consisting of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), Blood Urea Nitrogen (BUN), Creatinine (Creat), Albumin (ALB), and Gamma-glutamyltransferase GGT ($p < 0.05$), had affected the increased mortality rate, while total protein (TP) had shown no significant difference ($p > 0.05$). When the three groups were compared, it was found that AST, ALT, BUN, Creatinine, and Albumin had differed between the three groups or had separated the “sick” from the “healthy” and had distinguished the “dead” from the “sick” and the “dead” from the “healthy”. ALP and GGT had distinguished the dead from the “healthy” and the “sick”, but no difference was found between the “sick” and the “healthy” as shown in Table 5.

Table 5 The association between the blood chemistry of the diseases and the rabbits that died from respiratory diseases.

Blood Chemistry		<i>p</i> value for trend	No. different among groups	Groups
AST	Between Groups	.000	3	1,2 1,3 2,3
ALT	Between Groups	.000	3	1,2 1,3 2,3
ALP	Between Groups	.000	2	1,3 2,3
BUN	Between Groups	.000	3	1,2 1,3 2,3
Creat	Between Groups	.000	3	1,2 1,3 2,3
TP	Between Groups	0.45	-	-
ALB	Between Groups	.000	3	1,2 1,3 2,3
GGT	Between Groups	.000	2	1,3 2,3

* ANOVA analysis, group comparison, and the POST HOC TEST. A Comparison of individual differences.

4. Discussion

It was found that those rabbits, which were older than four years, were at risk of getting respiratory diseases at 2.18 times greater than those less than four years of age. Females had a risk factor of 2.02 times that of males. However, these factors have not been reported in rabbits before. Although it has been found that age is associated with pneumonia in humans, the exact relationship in rabbits cannot be determined. It was found that humans over the age of 65 have a higher risk of severe pneumonia. Also, sex affects the disease, which is often caused by risky

behaviors associated with sexual activities. For example, males are more vulnerable to pneumonia than females due to their smoking behaviors [17,18].

Sickness is related to the number of pets being raised together. The risk of sickness is 2.25 times greater when raising a group of pets versus a single pet rabbit. Raising rabbits outdoors has a risk of 22.22 times that of raising groups indoors. The density of the rabbits and the place where the rabbits are being kept are related to illness, and might increase the likelihood of infection. Feeding them using a hay rack has a risk, which is 4.18 times greater than those groups that use food cups. The risk using a cup of water has a risk factor of 7.93 times than those groups that use water bottles. Such studies have helped to identify that food and water feeding factors have a relationship with illness. However, the possible causes could not be determined. It is possible that the using a hay rack could cause a diffusion of dust from the hay, which could cause allergic reactions and respiratory diseases. When drinking water from cups, rabbits would be more likely to dip their faces or touch water until they are wet, which would not occur when water bottles were used [3,7]. The group that changed the toilet tray for longer than 24 h had a risk of 7.14 times the group that changed the tray every 24 h. This indicated that in preventing illnesses, sanitary factors are important. Due to the accumulation of droppings and urine, the smell of sewage was more severe. As the time between changing the trays increases, there are greater chances for infections of the respiratory system. Although no reports have been found to confirm this, it is believed that the concentration of ammonia levels result in increased rates of respiratory diseases [7]. Holland Lop varieties have a higher risk of illness than other species, such as Thai, Netherland Dwarf, and mixed species, which had risk factors of 3.52, 2, and 1.8 times, respectively. The Lop have gained popularity and have more parties than other varieties. This has causing the population of Lop to be studies more than any other species.

The oculonasal discharge, which is a symptom found in respiratory diseases, was not found to be associated with death, but was not related to the severity of illness or the risk of death in sick rabbits. Mental status was found to be an indicator that was related to death. When a comparison was carried out, it was found that the depression group had had a 2.34 times greater chance of death than the alert group, while the stupor group had had 6.85 times greater chance than the alert group. This is in accordance with reports on humans that focus on mental status, resulting in more severity in patients [17,18]. BCS 2 (underweight) had been related to death 7.23 times greater than the BCS 3 (standard), while both the BCS 4 (overweight) and BCS 3 had not been found to correlate with death. The results showed that a lower BCS compared with standard had a higher correlation to death than others. It is possible that rabbits with chronic infections often require more energy from the body's inflammation, which would include the use of energy for cytokines and Tumor Necrotic Factor Alpha (TNF- α). In humans, weight loss is always found in patients with chronic obstructive bronchitis [21]. Moreover, this also includes the state of anorexia or poor nutrition, which corresponds to this study in which it was found that rabbits that are anorexic are also at risk of death.

For the groups with normal body temperatures and low body temperatures, it was found that had been no correlation with death. The risk rate was 1.91 times that of group with normal body temperatures. Regarding the risk factors from an examination of various information at the level of more than one or nearby, it was found that some factors did not correlate with death ($p > 0.05$). However, it was statistically found that if the risk rate is greater than one, it is normally considered to be a risk or the negative effects of the factors. Yet, it is not considered a clear risk factor. This finding conflicts with reports about humans with low fevers or high fevers and whether or not it is an important factor in the assessment of systemic inflammatory response syndrome (SIRS) or sepsis, which is similar to tools used in this study (PSI or Acute Physiology and Chronic Health Evaluation II (APACHE II) scores). The high body temperature group was shown to have a risk rate of 4.154 times that of a normal body temperature group, which is consistent with reports on humans [11,13]. It was found that the condition of anorexia had been related to death due to the fact that the risk rate had been 7.19 times that of appetite group. In addition, it was found that the mucous membrane coloration had been associated with death. Pale indicated a risk rate of 1.65, while cyanosis indicated a risk rate of 2.76 times that of the normal pink mucosal color. It was discovered that the group at CRT > 2 seconds had a 4.8 times greater risk than that of the group at CRT ≤ 2 seconds, which was related to the problem of vital signs in humans, and both the color of the mucous membranes and CRT. If the blood circulation worsens, it will result in reduced oxygen supply to various parts of the body and then there will be shock. A CRT > 2 seconds indicates severe decompensatory shock that may not be easily corrected [13].

Lower respiratory rate (RR) was associated with death, and the risk rate was 8.84 times greater than that of the group at the normal respiratory rate. Higher RR was also found to correlate with death with a risk rate of 3.824 times that of the normal RR. In humans, it was found that respiration rate is one of the most important vital signs. As compared with groups with the normal heart rates, the abnormalities of low heart rates and fast heart rates were associated with death at 3.33 and 1.93 times greater, respectively. This vital sign is also consistent with human studies [13].

Based on the study of most factors, it was found that they are associated with the assessment of the severity of pneumonia in humans. Both the Severity Index or PSI were found to be very consistent. Therefore, it is possible that these factors could be applied and used as a tool to assess the state of health in rabbits as well.

The factors, which are related to chest radiography, examined all four pattern of the lungs, such as normal, alveolar, bronchial, and interstitial. As compared to the alveolar and bronchial patterns, the normal pattern was not found to be correlated with death ($p > 0.05$), while the risk rate was as high at 5.21 and 3.32 times, respectively, as compared to the normal pattern. Yet, the interstitial pattern was associated with 8.54 times greater risk rate for death in the normal group ($p < 0.05$). In humans, it was found that the most dangerous pattern of the alveoli causes lobar pneumonia, which affects the exchange of air. Depending upon the nature of the lung infiltration and the opacity of the lungs, it may be difficult to distinguish the lung patterns [6].

The WBC had a relationship, which classified the severity of the disease differently when compared to the healthy group. The higher ratios of LY ratio and MO ratio correlated and distinguished the severity of the disease in the “sick” and “dead” rabbits from the “healthy” ones. The increase and decrease of the normal values of the white blood cells, such as lymphocytes, monocytes, and granulocytes, are associated with and can determine the severity of the disease, which is the difference between a “healthy” and a “sick” rabbit. As compared to the “sick” rabbits, the following indicated the degree of severity: 1) the higher amounts of white blood cells, such as lymphocytes and monocytes, in the “dead” rabbits and 2) the decrease in granulocytes in the “dead” rabbits. This was found to be consistent with studies conducted on humans [13].

The reduced amount of hemoglobin has a relationship with the severity of the disease, which indicates anemia because hemoglobin is present in red blood cells, which makes it directly related to the volume of red blood cells. [2] The value of the hematocrit has a relationship and could determine the severity of the disease for the “healthy” rabbits, which differed from the “sick” and the “dead” rabbits. This increased blood concentration may have been caused by dehydration. MCV could not be measured against those that had died, but it does indicate respiratory illness. MCH was related to the severity of the disease of the “dead” rabbits, which is different from the “healthy” and the “sick” rabbits. There is a relationship with anemia called hyperchromic anemia because there is more MCH than normal. In humans, this is caused by larger red blood cells, which corresponds to higher MCV values in the “sick” and “dead” rabbits in this study. The larger MCV values can be derived from the amount of hemoglobin in the cells as well [2]. This corresponds to MCHC, which is related to the severity of the disease of the “dead” rabbits and which is different from the “healthy” and the “sick” rabbits. Due to the need for hemoglobin to transport oxygen to various tissues, this condition in humans is often associated with pale mucous membranes. From this study, it was also found that for the rabbits, which were sick, the color of their mucous membranes was pale and cyanotic, and this was associated with an increased risk of death. This condition of low oxygen transport is also associated with dyspnea, tachypnea, or hyperpnea; faster heart rates; weakness; depression; and with deep stupor. The red cell distribution width (RDWcv) helps in assessing anemia in which the red blood cells have different types of blood cells. There was no difference found because this value is related to the anisocytosis. The normal values in humans are 11-14.5 percent. The values found in rabbits are similar, and might indicate the normal condition [23].

When carrying out evaluations by adding parameters RDWsd, it is used as a guideline for detecting anisocytosis, as well as RDWcv, which is not influenced by MCV values. Therefore, it provides better measurement accuracy. From the results of the RDWsd study after it had been analyzed by ANOVA, the comparison between groups showed a significant difference between the three groups ($p < 0.05$), as well as had indicated that these values could not determine the differences of severity in the “dead” rabbits. Normal values in humans are equal to 39-47 percent, while this study indicated a higher value than the normal values found in humans. The findings showed that in all groups of rabbits had had a range of 69.42-70.43 fL. The same effects are used in humans (higher than normal MCV values and high RDW values) to indicate anemia due to deficiencies in Vitamin B12 and Folate and serious diseases, such as autoimmune diseases in the blood system (Autoimmune hemolytic anemia: AIHA) [23], which is a short-lived erythrocyte. However, this study was unable to confirm the origin of the cause. Yet, it is clear that anemia is an important factor that can be used to classify severity. Moreover, it would increase the risk of death.

AST has a relationship with the severity of the disease and shows the difference between “dead” rabbits and “healthy” and “sick” rabbits. AST is an enzyme that can be detected from many tissues including the liver, red blood cells, the heart, muscles, kidneys, and the pancreas. Although AST is not only found in the liver, the liver is an organ that is sensitive to damage. Therefore, it is the first organ that causes this value to increase, and it will rise within 6-10 h and remain for about 24-36 h. It will return to normal if the liver cells are not damaged within 3-7 d. However, cases of chronic injuries can still be found. In rabbits, this value is a specific value for liver function measurement and damage. It is also used in conjunction with other values in humans and other animals [2]. In this study, AST in “sick” and “dead” rabbits showed a very high difference as compared to the number of “healthy” rabbits. ALT can be found in many organs as well, but the values are not high except when there is liver damage. In humans, it is used in combination with other parameters to determine liver disease. However, in rabbits, ALT is less specific than AST [16]. From this study, it was found that there was a relationship with liver problems because the two values had been very abnormally high. This showed that when the diseases occur in the respiratory system, the liver is an important organ to examine. From this complication, the condition becomes more severe. Most of the elements of ALP are ALP1, which comes from the liver. When liver damage occurs, it

causes the ALP1 to rise and affects the total ALP, whereas ALP2 and ALP3 come from other organs, such as the bones, mucous membranes and kidneys. Therefore, in the “dead” rabbits, the ALP value from this study had been at a high level and had corresponded to the AST and ALT values, as well as the three values in the same manner. In addition, the level of albumin had decreased, which can occur for many reasons. However, it is always found due to the fact that hepatitis causes protein synthesis to decrease, which is caused by leakages in the capillary wall and burning too much energy. Moreover, GGT is synthesized from amino acids, and inside the cell, the greatest production source from the liver is at the area of the bile ducts. Therefore, it is often used as an indicator of liver cell abnormalities by helping to identify only bile duct inflammation and obstruction [16]. GGT values were found to be consistent with the liver-related values in this study, which, therefore, indicates that the liver is an important organ that can cause further complications and can increase the frequency of death.

The BUN is related to the severity of the disease as shown in the “dead” rabbits and was different from the “healthy” and “sick” rabbits. This indicates that urea and nitrogen in the bloodstream can cause toxicity, which is a complication that can increase the severity and the risk of death. Increased creatinine values indicate increased levels of damage or decreases in renal function. This is created by the muscles and is excreted through the urinary system. Although rabbits have uncomplicated kidneys (unipapillate kidneys), they have the ability to adjust to urinate well. Compared to other animals, the creatinine values are, therefore, often at an unusually high-level and can be reduced. However, if the damage persists, the creatinine will remain at the wrong level. From the results of the study, it was found that the BUN and creatinine can help to identify kidney damage, which is a major complication that can cause severe consequences and can lead to death [16].

5. Conclusion

This study has been helpful in identifying the severe conditions of respiratory diseases in rabbits with many risk factors and important parameters, which are also consistent with human prediction tools. Moreover, it was found that most of the health factors had had an effect on the mortality rate and had also been used to identify “sick” animals and to distinguish them from those animals that are in good health.

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