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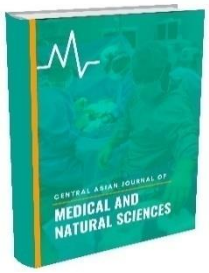

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The Relationship Between White Blood Cell Cunt and Mortality in Patients with Crimean–Congo Hemorrhagic Fever

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Key words: leukocytosis, leukopenia status, Platelets, Crimean–Congo hemorrhagic fever.

Abstract: **Aim:** Crimean–Congo hemorrhagic fever (CCHF) generally affects many organs. In this study a retrospective evaluation of white blood cell and platelet counts, cures, and deaths of CCHF patients was performed to determine the prognostic value of blood count at presentation. . Patients and methods: The records of 100 patients who admitted in Al Hussian Teaching hospital, Nasiriya, south of IRAQ from March to November 2022 were retrospectively analyzed. For each patient an evaluation was made for age, sex, White Blood cell count status. Platelet count (mild, moderate, sever and critical) and fate of the patients (cure or death) . A confirmed diagnosis of CCHF was made on determination by polymerase chain reaction.

Results: Of the 100 patients, 45 were female and 55 were male. Leukocytosis was present in only 7% while normal WBC value status in 38% (24 male & 14 female), while leukopenia status in 55% (27 male & 28 female). Regarding platelet count, most of the patients have severe or moderate thrombocytopenia (37% and 34% respectively) , while critical thrombocytopenia seen in 16% most of them are male. The present study showed that mild, moderate, sever and critical count of PLT in young age group 8%, 21%, 27%, and 9% respectively, while the lowest categories of thrombocytopenia in older age group,

Most patients with CCHF were cured 77%, while 23% of patients unfortunately died , also the most cure rate was reported among patients with leukopenia (out of 55 patients. 52 were survive) Compared to those with leukocytosis (out of 7. Only one survive), also among patients who have normal WBC count (out of 38 patients, 14 were died).

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In addition to that, the study noted most patients cure from disease with moderate PLT, while most death in those with severe thrombocytopenia. The results also noted a significant difference between status of leukocyte according hospital say of patients. The results noted a non-significant difference between status of platelets and hospital stay

Conclusions: This study shows a non-significant difference between status of leukocyte and platelets count according to sex, age group and hospital stay but, The results also noted a significant difference between status of leukocyte and platelets count according to fate of patients. Those who presented with normal or high white blood cell count may stay longer in the hospital and have higher risk of mortality.

Introduction

Viral Hemorrhagic Fever (VHF) is a group of acute zoonotic diseases with high fatality rates that are brought on by seven different virus families that can infect both people and animals. If untreated, VHF is marked by bleeding symptoms and fatal platelet failure. The majority of VHF is spread to people by a variety of vectors, including rodents, bats, ticks, voles, and mosquitoes. Infections like Dengue, Ebola, Yellow Fever, and Hantavirus are linked to some of the prevalent and fatal VHF. According to the International Health Regulations (IHR) 2005, a potentially lethal category of developing diseases known as viral hemorrhagic fevers (VHF) is one of the major public health emergencies of global concern. Crimean-Congo hemorrhagic fever (CCHF) is a viral infection that can be contracted through a tick bite or spread through contact with the blood or bodily fluids of infected individuals or domestic animals. In 1940, it was first observed in the Crimean Peninsula (Chris, 2004). Currently, it can be found in 30 nations in the Middle East, Africa, Asia, and Eastern Europe. Patients with CCHF typically contract the disease from tick bites or contact with the blood, bodily fluids, or tissues of animals or humans who have the virus. According to Khan et al. (1997), patients with CCHF may have fever, hemorrhage, and death.

They exhibit sudden onset, pain in the muscles and joints, fever, hemorrhage, and shock due to blood loss. Hemorrhaging from orifices and internal organs is a prominent sign in severe instances. The diagnosis of VHF is based on laboratory proof of the viruses in the bloodstream, such as the detection of antigens and antibodies or the isolation of the virus from the body, because VHF shares symptoms with many other diseases.

Crimean-Congo hemorrhagic fever (CCHF) is a severe virus-related illness that can infect humans when Hyalomma ticks bite them or when they come into direct contact with the blood of sick people or domestic animals. Additionally, reports of nosocomial illness transmission, primarily among medical staff, have been made. The virus that causes the disease belongs to the family Bunyaviridae's Nairovirus genus and contains a viral envelope (Ergonul, 2007; Ergönül et al., 2006). Direct contact with infectious material, such as bodily fluids containing infectious viruses, causes infections. Although aerosolized virus does induce rapidly deadly disease in experimentally infected non-human primates, airborne transmission is not believed to be a significant route of human infection (Osterholm et al., 2015).

After exposure, there is a 2–21 day incubation period, then a sudden, general viral illness with myalgia, chills, and fever. Prostatation, nausea, vomiting, stomach discomfort, and diarrhea emerge as the infection worsens. According to Feldmann and Geisbert (2010), coagulopathy and vascular leakage that results in hemorrhage characterize the disease's advanced phases. Following attachment, local viral replication occurs. The virus can infect the lung, hilar lymph nodes, and other organs. Interstitial infiltrates and edema do occur, but there is no pulmonary consolidation. Macrophages are initially infected. Widespread epithelial engagement follows this (Pigott, 2005**).**

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Patients and Methods

The records of 100 patients diagnosed with CCHF and admitted to the Infectious Diseases and Clinical Microbiology Clinic of Al-Hussein Teaching Hospital in Nasiriya city in Iraq between March and November 2022 were retrospectively analyzed. This study was approved by the ethics committee of our hospital. An evaluation was conducted for age, sex, leukocyte count status (a white blood cell count of 4000 – 11000 cell/ml consider as normal). the count of PLT (critical when count less than 10000/ml, severe when count from 10000 – 50000, moderate from 50000 – 100000 and mild with count between 10000 and 150000/ ml) ,cure and death and period of hospital stay and laboratory findings for each patient. During the acute and convalescent period, serum was collected from the patients and sent to the Central Virology Laboratory for serological and virological testing. CCHF was confirmed by polymerase chain reaction (PCR). The research sampling technique used consecutive 9-month sampling. . Measurement of platelet and leukocyte levels in the research subjects using the spectrophotometer method was performed in the Clinical Pathology Laboratory of Al-Hussein Hospital. Venous blood samples were collected from the cubital fossa after disinfection

Statistical Analysis

Statistical analysis of the study's data was performed using SPSS (Statistical Package of Social Science, version 26), using a descriptive Chi-Square test and p. value < 0.05.

Results

Leukocyte Status in Patients with CCHF According to Sex

The present study showed that leukopenia observed in 55% of patients (27 male & 28 female) while normal count in 38% most of the are male (24 versus 14). Leukocytosis observed in 7% (four of them are male & three are female). The results also noted a non-significant difference between status of leukocyte according to sex as in table 4-1.

Table 4-1: Leukocyte status according to sex

Sex / WBC Status	Male		Female		Total	
	No.	%	No.	%	No.	%
Leukocytosis	4	4	3	3	7	7
Normal WBC	24	24	14	14	38	38
Leukopenia	27	27	28	28	55	55
Total	55	55	45	45	100	100
$CalX^2$= 1.811		$TabX^2$= 5.99		DF= 2	p. value 0.404	

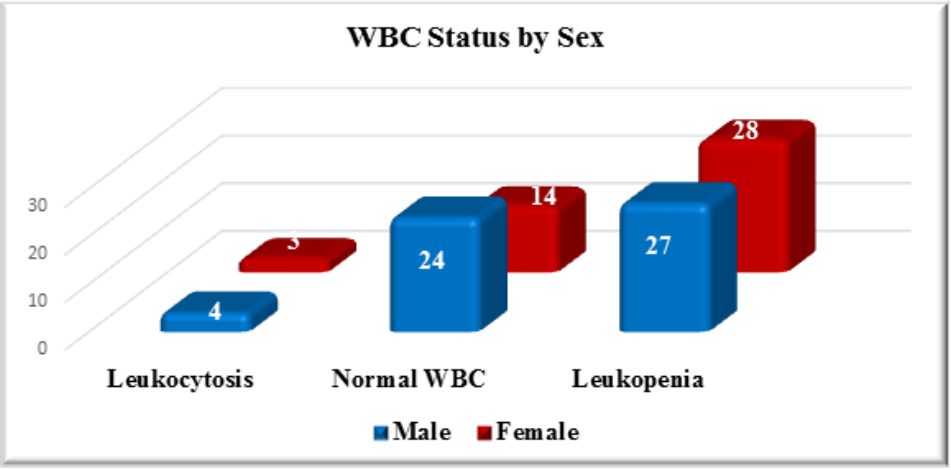

Figure 4-1: Leukocyte status according to sex

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Platelets Status in Patients with CCHF According to Sex

The present study showed the mild thrombocytopenia seen in only 13% of cases , while most of the Patients have moderate and severe thrombocytopenia (34% - most of them are female - & 37 % respectively) . Critical counts occur in 16% most of them are male (13 versus 3)The results also noted a non-significant difference between status of platelets according to sex as in table 4-2.

Table 4-2: Platelets status according to sex

Sex / PLT Status	Male		Female		Total	
	No.	%	No.	%	No.	%
Mild	8	8	5	5	13	13
Moderate	14	14	20	20	34	34
Sever	20	20	17	17	37	37
Critical	13	13	3	3	16	16
Total	55	55	45	45	100	100
$CalX^2$= 7.318		$TabX^2$= 7.81		DF= 3	p. value 0.062	

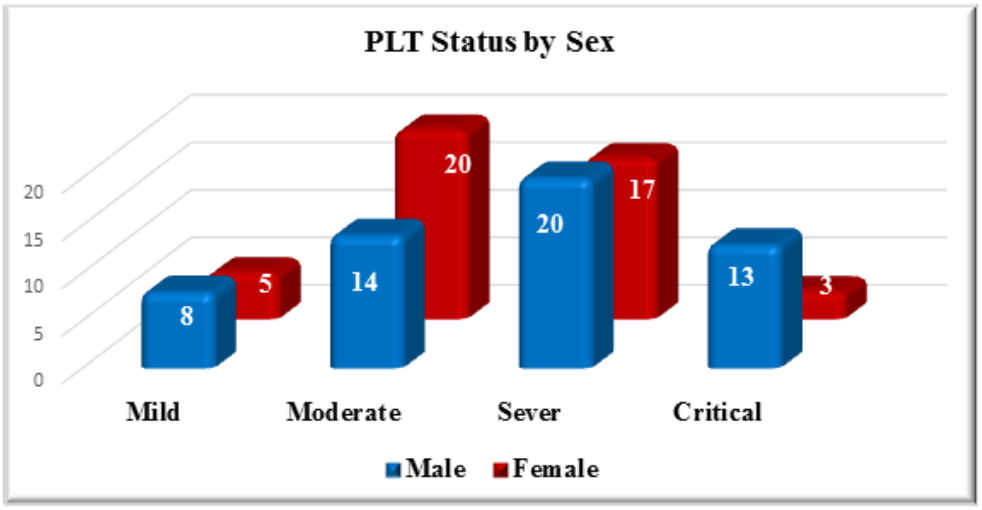

Figure 4-2: Platelets status according to sex

Leukocyte Status in Patients with CCHF According to Age Groups

The present study showed the most of the patient was young (age from 18 - 45 years) most of them have low or normal leukocyte count (38 & 24 respectively) , while lowest status of leukocyte in older age group The results also noted a non-significant difference between status of leukocyte according to age groups as in table 4-3.

Table 4-3: Leukocyte status according to age groups

Age / WBC Status	18-45 years		46-65 years		> 65 years		Total	
	No.	%	No.	%	No.	%	No.	%
Leukocytosis	3	3	2	2	2	2	7	7
Normal WBC	24	24	12	12	2	2	38	38
Leukopenia	38	38	14	14	3	3	55	55
Total	65	65	28	28	7	7	100	100
$CalX^2$= 5.996		$TabX^2$= 9.49			DF= 4		p. value 0.199	

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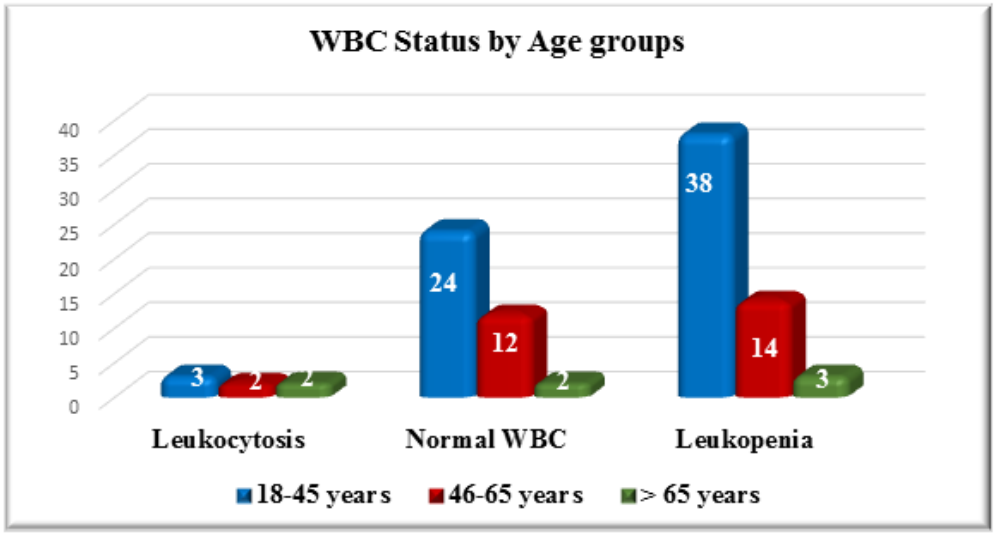

Figure 4-3: Leukocyte status according to age groups

Platelets Status in Patients with CCHF According to Age Groups

The present study showed the mild, moderate, sever and critical count of PLT in young age group 8%, 21%, 27, and 9% respectively, while the lowest categories of PLT in older age group, also noted neither mild nor critical status in third age group. The results also noted a non-significant difference between status of platelets according to age group as in table 4-4.

Table 4-4: Platelets status according to age groups

Age / Platelets Status	18-45 years		46-65 years		> 65 years		Total	
	No.	%	No.	%	No.	%	No.	%
Mild	8	8	5	5	0	0	13	13
Moderate	21	21	8	8	5	5	34	34
Sever	27	27	8	8	2	2	37	37
Critical	9	9	7	7	0	0	16	16
Total	65	65	28	28	7	7	100	100
$CalX^2$= 8.384		$TabX^2$= 12.59			DF= 6		p. value 0.211	

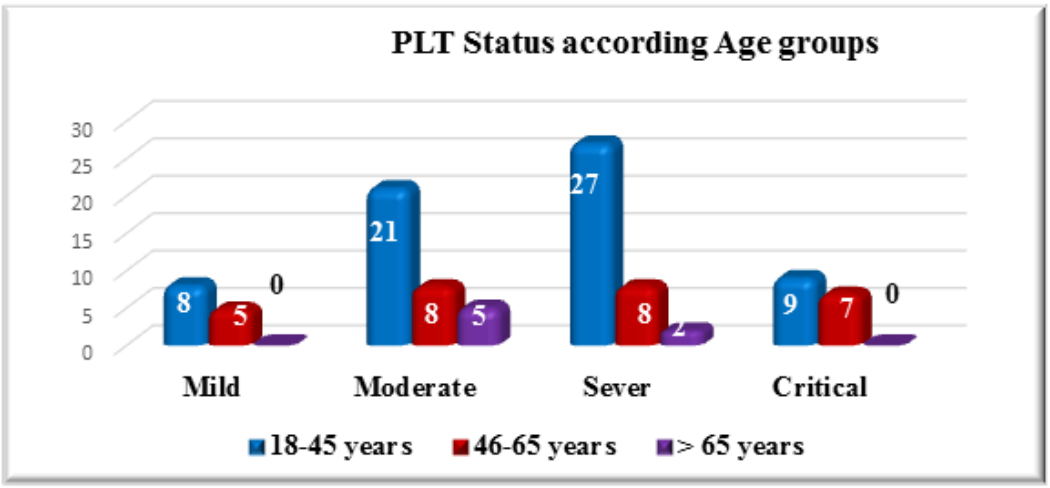

Figure 4-4: Platelets status according to age groups

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Leukocyte Status in Patients with CCHF According to Fate of Patients

The present study showed the most patients with CCHF were accepted cure 77%, while 23% of patients unfortunately die, also the most cure patients with leukopenia 52%, while most died patients have normal or high WBC count. The results noted a significant difference between status of leukocyte according to fate of patients as in table 4-5.

WBC Table 4-5: Leukocyte status according to fate of patients

Fate Status	Cure		Death		Total	
	No.	%	No.	%	No.	%
Leukocytosis	1	1	6	6	7	7
Normal WBC	24	24	14	14	38	38
Leukopenia	52	52	3	3	55	55
Total	77	77	23	23	100	100
$CalX^2$= 29.217		$TabX^2$= 5.99		DF= 2	p. value < 0.001**	

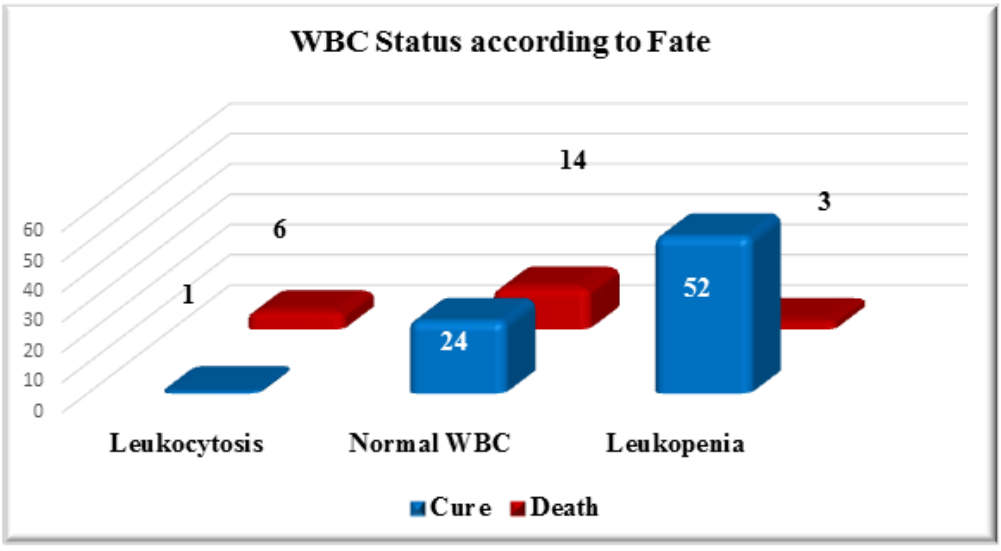

Figure 4-5: Leukocyte status according to fate of patients

Platelets Status in Patients with CCHF According to Fate of Patients

The present study showed the most patients with CCHF were accepted cure 77%, while 23% of patients die, also the study noted most patients cure from disease with mild or moderate thrombocytopenia , while most die patients with severe and critical thrombocytopenia . The results noted a significant difference between status of platelets according to fate of patients as in table 4-6.

Table 4-6: Platelets status according to fate of patients

Fate / PLT Status	Cure		Death		Total	
	No.	%	No.	%	No.	%
Mild	13	13	0	0	13	13
Moderate	30	30	4	4	34	34
Sever	22	22	15	15	37	37
Critical	12	12	4	4	16	16
Total	77	77	23	23	100	100
$CalX^2$= 12.771		$TabX^2$= 7.81		DF= 3	p. value 0.005**	

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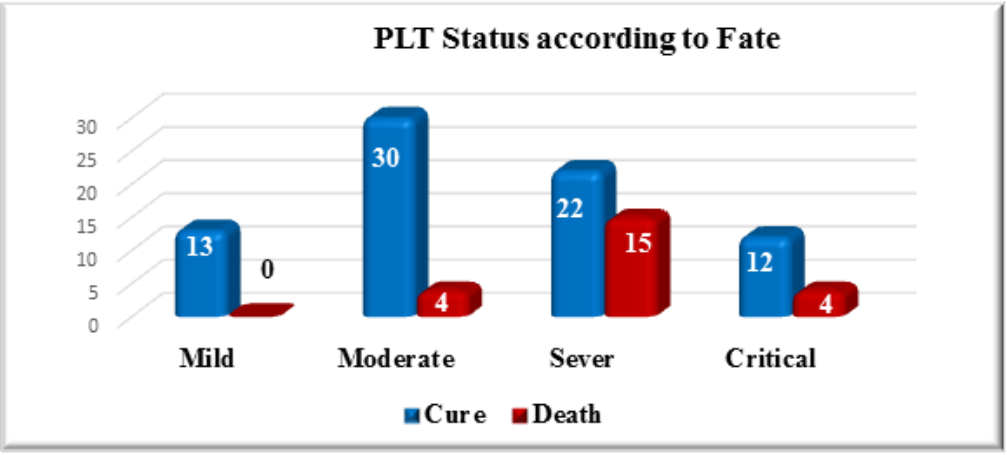

Figure 4-6: Platelets status according to fate of patients

Leukocyte Status in Patients with CCHF According to Hospital Stay

The present study showed the most patients with CCHF were stay < 5 days 48%, while lowest patients stay > 7 days 14%, also the most leucopenia patients with 26%, stay 5-7 days, while hospital-stay patients more than 7 days seen more among patients with normal WBC count. The results also noted a significant difference between status of leukocyte according hospital stay of patients as in table 4-7.

Table 4-7: Leukocyte status according to hospital stay

Hospital Stay / WBC Status	< 5 days		5 – 7 days		> 7 days		Total	
	No.	%	No.	%	No.	%	No.	%
Leukocytosis	7	7	0	0	0	0	7	7
Normal WBC	18	18	12	12	8	8	38	38
Leukopenia	23	23	26	26	6	6	55	55
Total	48	48	38	38	14	14	100	100
$CalX^2$= 11.407		$TabX^2$= 9.49			DF= 4		p. value 0.022*	

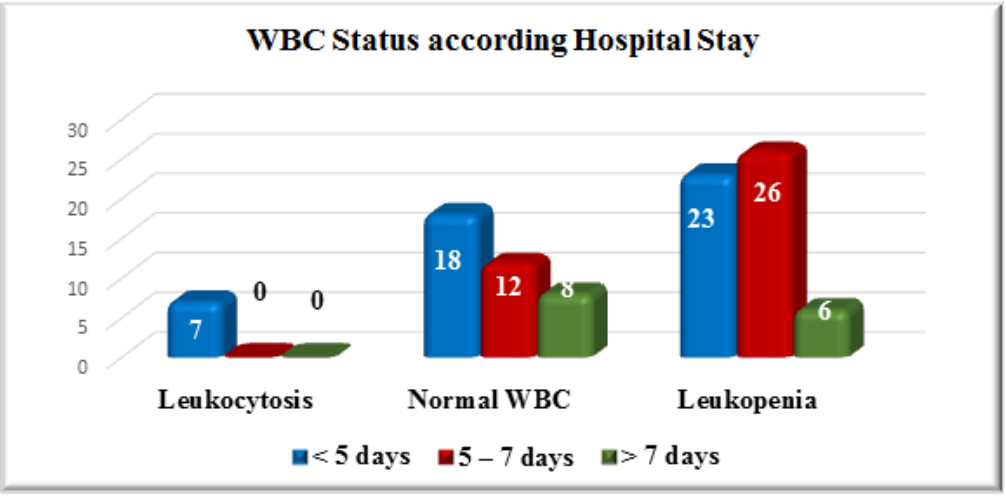

Figure 4-7: Leukocyte status according to hospital stay

Platelets Status in Patients with CCHF According to Hospital Stay

The present study showed the most patients with CCHF were stay < 5 days 48%, while lowest patients stay > 7 days 14%, also the study noted most patients stay < 5 days with severe PLT, while most

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patients stay 5-7 days with severe and moderate PLT. The results also noted a non-significant difference between status of platelets according to hospital stay as in table 4-8.

Table 4-8: Platelets status according to hospital stay

Hospital Stay platelet Status	< 5 days		5 – 7 days		> 7 days		Total	
	No.	%	No.	%	No.	%	No.	%
Mild	7	7	6	6	0	0	13	13
Moderate	16	16	13	13	5	5	34	34
Sever	18	18	13	13	6	6	37	37
Critical	7	7	6	6	3	3	16	16
Total	48	48	38	38	14	14	100	100
$CalX^2$= 2.691		$TabX^2$= 12.59			DF= 6		p. value 0.874	

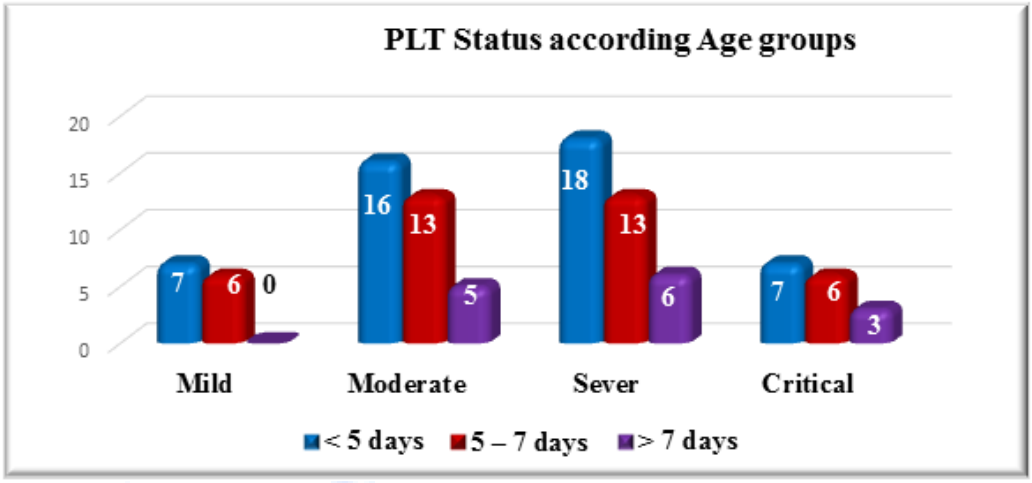

Figure 4-8: Platelets status according to hospital stay.

Discussion

Crimean-Congo hemorrhagic fever (CCHF) is a severe viral disease that is spread to humans by Hyalomma ticks or through direct contact with the blood of infected people or domestic animals. There have been isolated instances or CCHF outbreaks reported in the Middle East, Africa, South East Asia, and Africa, among other places. Some of the signs and symptoms of the illness include acute fever, nausea, vomiting, headache, myalgia, elevated liver enzymes, and hemorrhagic manifestations that can range from mucocutaneous bleeding to potentially lethal severe hemorrhage with disseminated intravascular coagulation (DIC) and hemophagocytosis. Similar to other viral hemorrhagic disorders, the pathogenesis and prognosis of CCHF are greatly impacted by the activation of lymphocytes, monocytes, macrophages, and excessive cytokine release.

In present study ,the leukocytosis and normal WBC value status observed in 45% of patients while leukopenia status in 55% of them. Only 3 patients from those with leukopenia were died with a survival rate of about 94.5% while those with normal or high WBC count carry poor outcome with a survival rate of 55.6%. This high mortality rate especially in those with leukocytosis (in this study, only one out of seven patients was survive). These results are consistent with studies from another study that leukocytosis is one of the factors linked to fatal outcomes, according to Swanepoel et al. This finding was only seen in patients who passed away on the eighth day after being admitted to the hospital. (Swanepoel *et al.* ,1989).

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This study shows that 47% of patients with CCHF have only mild or moderate thrombocytopenia while 53% have severe or critical thrombocytopenia with a platelet count 0f less than 20000/ml. The survival rate among those with account of more than 20000/ml was 91.5% while it was 64.2% among those with platelet count less than 20000/ml. These finding are expected especially when we are dealing with hemorrhagic fever where fatal bleeding is the major cause of mortality , Swanepoel and colleagues (13), developed the criteria for mortality. Leukocyte count greater than 10,000/mm3, thrombocyte count less than 20,000/ml, ALT levels greater than 150 U/L, and active partial thromboplastin time greater than 60 are required.

In this study, out of seven patients with leukocytosis only one patient was survive and he was young (age less than 45 years) raising our think to consider leukocytosis especially in those older than 45 years may be an ominous risk for poor prognosis and mortality in those with CCHF and may be with longer stay in the hospital although this study shows the reversed regarding hospital stay but this can be explained simply because of their critical state majority were died in the first week of hospitalization

Also in other study researchers found in patients with leukopenia, there are increased AST, ALT, LDH, and CPK levels. All laboratory tests for surviving patients returned to normal within 5–9 days (Hatipoglu *et al.*, 2010).

According to an in vitro study by Ojha et al., dengue thrombocytopenia is dependent on the degree of platelet activation (Ojha et al., 2017). Recently, we discovered that both severe and non-severe forms of dengue altered activated platelet fatty acids. The other distinguishing feature, vascular dysfunction, is reported to play a significant role in the severity of dengue, along with thrombocytopenia. According to a study, dengue infection increases ICAM-1 levels, which in severe situations causes endothelial cell activation and vascular leakage. (Khongphatthanayothin *et al.*, 2006; Azeredo *et al.*, 2006).

Conclusion :In present study noted a non-significant difference between status of leukocyte and platelets according to sex, groups ages and hospital stay but, The results also noted a significant difference between status of leukocyte and platelets according to fate of patients. Patients with high or normal WBC count may have higher mortality than those with leukopenia.

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