# Factors Associated with Survival Outcomes of Febrile Neutropenia in Hematologic Malignancy Patients

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***Background:*** *Febrile neutropenia (FN) is a common, life-threatening complication of hematologic malignancy patients who receive chemotherapy. The assessment of the epidemiology and related factors are necessary to improve survival outcomes of FN.*
***Objective:*** *To determine the epidemiology of FN and investigate the factors that are associated with outcomes of FN.*
***Material and Method:*** *This study is a retrospective cohort study. Medical records between 2012 and 2014 of fifty FN patients of the Her Royal Highness (HRH) Princess Maha Chakri Sirindhorn Medical Center were reviewed.*
***Results:*** *Of the 50 episodes with FN, the median age was 35.5 years (range from 15 to 81 years), and 39 patients (78%) were younger than 60 years of age. Thirty-three patients (66%) were treated with the first-line chemotherapy. Source of infections could not be identified in 58% of patients. For patients with a definite source of infection, 14% were lower respiratory tract infections. Gram-negative bacteria were more common than gram-positive organisms as found in blood cultures. The multivariate analysis has confirmed a significant association with no weight loss greater than 5% within 1 month ($p<0.05$), no blood loss requiring intravenous fluid ($p = 0.01$), and low Acute Physiology and Chronic Health Evaluation (APACHE) II score ($p = 0.01$) associated with survival outcomes of FN. The overall mortality was 28%.*
***Conclusion:*** *There was a high mortality rate in neutropenic patients with fever. The no significant weight loss, no blood loss requiring intravenous fluid, and low APACHE II score at the time of diagnosed FN were found to be associated factors with survival outcomes.*

***Keywords:*** *Neutropenia, Agranulocytosis, Neutropenic fever, Hematologic malignancies*

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Febrile neutropenia (FN) is a serious common problem in hematologic malignancies for patients receiving chemotherapy. It can cause high mortality rates. The study about the incidence in Thailand from Teparat et al[1] done at Thammasat university hospital has shown a rate approximately 17.30%. Studies done in foreign countries mortality rates range from 4 to 30%[2-4]. Additional studies have shown the mortality rate in Thailand to be approximately 17.7 to 23%[5-8]. Teparat et al[1] have shown mortality rates of only 5% but the sample size in the study is dismal.

The most common cause of mortality is infection[9]. There is a study of 800 patients with bacteremia in the European Organization for Research and Treatment of Cancer-International Antimicrobial Therapy Group (EORTC-IATG) therapeutic trials done from 1978 until 1994 has found mortality rates to decrease from 21 to 7%[10]. The organisms causing mortality in foreign studies within 30 days are gram negative and gram positive bacteria, 10% and 6% respectively[11]. However, in Thailand, it has been found that the most common bacteria are gram negative organisms that account for 60% to 81.4% of the cases[1,5-7,12]. It is different from foreign studies that have found gram positive organisms. But, increasing gram positive organisms at 29.9% was found in a King Chulalongkorn Memorial hospital[8] and 35.5% in a study done in Khon Kaen hospital[7]. In contrast, the prevalence of fungal infection was found in 3.2% of patients in a study done by Phungtaharn et al[7] in 2006. This increased to 6.2% in a study done by Roongpoovapatr et al[8] in 2010.

Teparat et al[1] in Thammasat University showed that a history of FN is associated with FN after

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receiving chemotherapy. The Multinational Association for Supportive Care in Cancer (MASCC)[13] reported factors that are related with outcomes of FN in patients who have received chemotherapy. The study divided the patients into 2 groups defined as low risk and high risk for FN. The first group has favorable outcomes (fever resolved within 5 days with no severe complications) and another group with unfavorable outcomes (fever more than 5 days with severe complication, need to change antibiotic, expired from FN within 5 days). It has found good outcome of the mild burden of illness, no hypotension, no history of chronic obstructive pulmonary disease, solid tumor, no previous fungal infection, no dehydration requiring intravenous fluid, age less than 60 years defines as low risk of FN. It is similar to studies in Thailand that have determined low risk and high risk in KhonKaen hospital[7]. One report from Chayakulkeeree et al[6] in Siriraj hospital found that there were no differences.

The aim of this study is to define the epidemiology of FN and the factors that are related to the survival outcomes of FN in the HRH Princess Maha Chakri Sirindhorn Medical Center.

**Material and Method**

To determine the epidemiology of FN and investigate the factors that are associated with survival outcomes of FN. The hematologic malignancies included are acute leukemia, chronic leukemia (CLL), multiple myeloma (MM), and non-Hodgkin lymphoma (NHL). The inclusion criteria include; age more than 15 years old, recently received chemotherapy, and developing FN. The exclusion criteria include; no receiving of chemotherapy, and non-hematologic malignancies.

A retrospective cohort study was conducted by collecting data from the medical records at the HRH Princess Maha Chakri Sirindhorn Medical Center from January, 2012 to June, 2014.

Data collection were age, gender, underlying disease, stage of cancer, types of cancer, status of disease, performance status, chemotherapy regimens, burden of disease, stress intolerance, hospitalization status, prophylaxis granulocyte stimulating growth factor (G-CSF), treatment, complete blood count (CBC), blood chemistry, imaging, complication and outcomes of treatments. For determining factors associated with survival outcomes of FN, we divided the patients into 2 groups at the time of patients' discharge from hospital. The first group has survival outcomes (survived from FN) and another group with expired outcomes (expired from FN). This is a retrospective study. This study was approved by the ethics committee from Srinakarinwirot University.

The Infectious Diseases Society of America (IDSA)[14] defines fever in neutropenic patients as a single oral body temperature (BT) more than 38.3 Celsius or more than 38.0 Celsius and sustain 1 hour. The neutropenia is defined by absolute neutrophil count (ANC) less than 500 cells/microL or ANC less than 1,000 cells/microL and predict to decrease until less than 500 cells/microL within 48 hours later[14]. The Performance status as defined by Eastern Cooperative Oncology Group (ECOG)[15] varying from 0-4. The fully active, able to carry on all pre-disease performance without restriction was defined as ECOG 0, the restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature was defined as ECOG 1, the ambulatory and capable of all self-care but unable to carry out any work activities; up and about >50% of waking hours was defined as ECOG 2, the capable of only limited self-care, confined to bed or chair >50% of waking hours was defined as ECOG 3 and the completely disabled; cannot carry on any self-care; totally confined to bed or chair was defined as ECOG 4.

The uncontrolled cancer was defined as absence of complete remission in leukemia, new lesions or increase of >25% of lesions or symptoms of progressive disease in lymphoma and multiple myeloma[13].

The Burdens of disease to define the severity of illness was estimated at presentation by the attending physician using visual analog scales that measure symptom severity. Categorical to no or mild symptom, moderate symptom and severe symptom[16].

The severity of illness to evaluated stress tolerance and physiologic reserve was estimated at first diagnosis of febrile neutropenia by the attending physician using visual analog scales. Categorized as extreme or most stress tolerable, trouble with the moderate stress, and trouble with mild stress or without stress[16].

The Talcott risk groups was developed by Talcott[2] to define the neutropenic patient varying from I-IV. The neutropenic patients with controlled cancer, no serious comorbidity, and outpatient were classified to low risk. The inpatient was defined as Talcott group I, the outpatient with comorbidity itself justifying hospitalization was defined as Talcott group II, the outpatient without cancer control but without comorbidity was defined as Talcott group III, and the

outpatient without comorbidity and without controlled cancer was defined as Talcott group IV.

The Acute Physiology and Chronic Health Evaluation (APACHE) II score to estimate mortality in the critically[17].

***Statistical analysis***

The descriptive analyses were performed to determined percentage, mean, and median. The Chi-square test was used to assess the significant correlation between age, gender, types of cancer, status of disease, performance status, chemotherapy regimens, burden of disease, stress intolerance, hospitalization status, prophylaxis G-CSF, CBC, blood chemistry, imaging, and treatment outcomes between groups. Difference between groups was calculated using the log-rank test for univariate analysis. Cox's proportional hazards model was used to analyze for independent prognostic factors. OS was calculated using the kaplan-Meier method. A *p*-value less than 0.05 is determined to be significant.

**Results**

We collected data of patients who were diagnosed with FN follow by ICD 10 code agranulocytosis (D70) from January, 2012 to June, 2014. Of the 50 episodes with hematologic malignancies who developed FN, the median age was 35.5 years (15-81 years) and 39 patients were younger than 60 years of age. Twenty-nine patients were males, and 21 patients were females. Thirty-one patients had acute leukemia, sixteen patients had NHL.

Of 50 episodes, 38 had ECOG performance status 0-1, and 12 had ECOG 2-4. Seven patients had diabetic mellitus, four patients had history of chronic blood loss, eleven patients had significant weight loss, sixteen patients had history of FN, six patients had dehydration, and two patients had a history of surgery. All patients' characteristics are shown in Table 1.

Thirty-three patients were treated with the first-line chemotherapy regimens and seventeen patients were treated with second line or salvage chemotherapy regimens. There were 16, 12, 8, and 3 patients who were treated with hyper CVAD alternating with methotrexate and cytarabine regimens, idarubicine plus cytarabine regimen, CHOP regimen, and etoposide plus mitoxantrone, respectively and these are shown in Table 2.

Baseline laboratory findings at the time of diagnosis of FN have shown a median hemoglobin of 8.5 g/dL (range 3.9-14, SD 2.07), median absolute

**Table 1.** Demographic characteristics of patients with febrile neutropenia (n = 50)

| Characteristic | No. of patients | Rate (%) |
|---|---|---|
| Sex | | |
| Female | 21 | 42 |
| Male | 29 | 58 |
| Cancer | | |
| Controlled | 28 | 56 |
| Uncontrolled | 22 | 44 |
| Cancer group | | |
| Acute leukemia | 31 | 62 |
| NHL | 16 | 32 |
| Others (CLL, MM) | 3 | 6 |
| Treatment setting | | |
| First line treatment | 33 | 66 |
| Second line treatment | 17 | 34 |
| Growth factor use | | |
| Growth factor administration | 25 | 50 |
| No growth factor administration | 25 | 50 |
| Expected further neutropenia duration | | |
| <7 days | 1 | 2 |
| 7-14 days | 27 | 54 |
| >14 days | 21 | 42 |
| ECOG performance status | | |
| 0-1 | 38 | 76 |
| 2-4 | 12 | 24 |
| Symptoms (Burden) | | |
| No or mild symptom | 19 | 38 |
| Moderate symptom | 26 | 52 |
| Severe symptom | 5 | 10 |
| Stress tolerance | | |
| Extreme or most stress tolerable | 19 | 38 |
| Moderate stress tolerable | 24 | 48 |
| Mild stress or without stress tolerable | 7 | 14 |
| Hospitalization status | | |
| Outpatient | 18 | 36 |
| Inpatient | 32 | 64 |
| Temperature | | |
| <39°C | 26 | 52 |
| ≥39°C | 24 | 48 |
| Fever duration | | |
| ≤24 hours | 45 | 90 |
| >24 hours | 5 | 10 |
| Infection | | |
| No infection site | 29 | 58 |
| Presence of infection site | 21 | 42 |
| Chest x-ray | | |
| No abnormality | 42 | 84 |
| Abnormal, tumor and infection | 8 | 16 |
| Hypotension | | |
| No | 50 | 100 |
| Yes | 0 | 0 |

**Table 1.** Cont.

| Characteristic | No. of patients | Rate (%) |
|---|---|---|
| Pulse | | |
| <120 beats/min | 40 | 80 |
| ≥120 beats/min | 10 | 20 |
| Respiratory rate | | |
| ≤24 breaths/min | 47 | 94 |
| >24 breaths/min | 3 | 6 |
| Surgery | | |
| No surgery within 6 weeks | 48 | 96 |
| Within 6 weeks | 2 | 4 |
| Cardiac disease or comorbidity | | |
| No | 50 | 100 |
| Yes | 0 | 0 |
| Chronic obstructive pulmonary disease | | |
| No | 49 | 98 |
| Yes | 1 | 2 |
| Diabetes | | |
| No | 43 | 86 |
| Yes | 7 | 14 |
| Confusion or alteration of mental state | | |
| No | 48 | 96 |
| Yes | 2 | 4 |
| Blood loss requiring IV therapy | | |
| No | 46 | 92 |
| Yes | 4 | 8 |
| Dehydration requiring IV therapy | | |
| No | 44 | 88 |
| Yes | 6 | 12 |
| Weight loss of >5% within 1 month | | |
| No | 39 | 78 |
| Yes | 11 | 22 |
| Previous febrile neutropenia | | |
| No | 34 | 68 |
| Yes | 16 | 32 |
| Previous fungal infection | | |
| No | 46 | 92 |
| Yes | 4 | 8 |
| Antifungal therapy within 6 months | | |
| No | 44 | 88 |
| Yes | 6 | 12 |
| Antiviral therapy within 6 months | | |
| No | 45 | 90 |
| Yes | 5 | 10 |
| Others serious comorbidity | | |
| No | 48 | 96 |
| Yes | 2 | 4 |
| Talcott group | | |
| I | 48 | 96 |
| II | 2 | 4 |
| IV | 0 | 0 |
| I-III | 50 | 100 |

**Table 1.** Cont.

| Characteristic | No. of patients | Rate (%) |
|---|---|---|
| Hemoglobin level | | |
| ≥8 g/dL | 32 | 64 |
| <8 g/dL | 18 | 36 |
| Absolute neutrophil count | | |
| ≥100/µL | 18 | 36 |
| <100/µL | 32 | 64 |
| Platelet count | | |
| ≥5,000/µL | 45 | 90 |
| <5,000/µL | 3 | 6 |
| Bilirubinemia | | |
| <2 mg/dL | 37 | 74 |
| ≥2 mg/dL | 2 | 4 |
| Albumin level | | |
| ≥2.5 g/dL | 36 | 72 |
| <2.5 g/dL | 2 | 4 |
| APACHE score | | |
| <40 | 48 | 96 |
| ≥40 | 2 | 4 |

**Table 2.** Chemotherapy regimens (n = 50)

| Chemotherapy regimens | No. of patients |
|---|---|
| HyperCVAD/methotrexate and cytarabine regimen | 16 (32%) |
| Idarubicin plus cytarabine (7+3 regimen) | 12 (24%) |
| CHOP regimen | 8 (16%) |
| Etoposide and mitoxantrone regimen | 3 (6%) |
| ALL protocol, ICE, ESHAP, DHAP | 11 (22%) |

HyperCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone; CHOP = cyclophosphamide, doxorubicin, vincristine, prednisolone; ICE = Ifosfamide, carboplatin, etoposide; ESHAP = etoposide, cisplatin, mannitol, methylprednisolone, cytarabine; DHAP = dexamethasone, high dose cytarabine

neutrophil count (ANC) of 39.9 cells/microL (range 0-949, SD 278.8), median platelet count of 31 X $10^9$/L (range 2-424 X $10^9$/L, SD 85830.12), median AST of 20 U/L (range 7-146, SD 30.67), median ALT of 21 U/L (range 8-317, SD 60.95), median alkaline phosphatase of 85.50 U/L (range 37-240, SD 47.1) median bilirubin of 0.79 mg/dL (range 0.15-6.95, SD 1.07) and median albumin of 3.7 g/dL (range 1.68-4.80, SD 0.67).

Source of infections could not be identified in most of patients. For patients with a definite source of

infection, the most common site were lower respiratory tract infections as shown in Table 3. Gram-negative bacteria were more common than gram-positive organisms as found in blood cultures. The causative organisms could not be detected in 90% of patients. However, three organisms had been detected, two patients had methicillin resistance *Staphylococcus aureus* (MRSA) septicemia, two patients had *Acinetobacter baumannii* pneumonia, and one patients had *Proteus mirabillis* urinary tract infection.

The antibiotics prescribed were ceftazidime plus amikacin for empirical antibiotic therapy, cefoperazone/sulbactam, piperacillin/tazobactam, vancomycin, fosfomycin, meropenem and levofloxacin were found in 30 (60%), 10 (20%), 4 (8%), 3 (6%), 1 (2%), 1 (2%), 1 (2%), at the first time of diagnosed FN, respectively.

After 72 hours follow-up of the treatments; thirty-four patients (68%) had shown clinical improvement, and sixteen patients (32%) had shown no clinical improvement. Of 50 patients, 14 patients (28%) died from infections at the time of discharge from hospital. The mortality rate is 28% in our study. The median duration of hospitalization from diagnosis of FN until expiration or survival is 39 days (95% CI 24.23-53.77, SE 7.54).

By univariate analysis, survival outcomes of FN were significantly high in patients with no antimicrobial prophylaxis used, no weight loss greater than 5% within 1 month, no dehydration requiring intravenous fluid, no blood loss requiring intravenous fluid, high albumin level, receiving first line chemotherapy, and low APACHE II score at the time of diagnosed FN. These data are shown in Table 4. The other factors such as age, gender, type of malignancy, G-CSF used, ECOG performance status, burden of disease, stress tolerance, hospitalization, body temperature, location of infection, and duration of FN to diagnosis were not related with survival outcomes.

**Table 3.** Sites of infection (n = 50)

| Sites of infection | No. of patients |
|---|---|
| Upper respiratory tract | 1 (2%) |
| Lower respiratory tract | 7 (14%) |
| Urinary tract | 2 (4%) |
| Central nervous system | 1 (2%) |
| Others (skin and mucocutaneous, thrombophleblitis, perianal abscess) | 10 (20%) |
| Unknown | 29 (58%) |

The multivariate analysis has confirmed a significant association with no weight loss greater than 5% within 1 month, no blood loss requiring intravenous fluid, and low APACHE II score. Survival outcomes of FN are shown in Table 4 and 5.

**Discussion**

In our study, we found that acute leukemia is the common underlying disease of patients with FN that accounting for 62%. This is similar to the past studies done in Thailand and foreign countries[7,8,13,18,19]. The unknown source of infection was at 58%, similar to Khon Kaen Hospital[7] study as 52.1%, respectively. We found the most common infections are pneumonia (14%) similar to a Thammasat University Hospital study[1] as that had found the most common infections are pneumonia which accounted for 15.55%. This is different from studies done in King Chulalongkorn Memorial Hospital[8] and Suratthani Hospital[18] where the most common problem is septicemia.

Most common antibiotics prescribed are ceftazidime and amikacin, similar from other Thailand studies[7,18], may be due to the standard treatment of FN following Infectious disease society of America (IDSA) guidelines[14]. The appropriate use and sensitivity of antibiotics were not determined due to poor medical record. Two patients had MRSA septicemia from central venous catheters for chemotherapy infusion, 2 patients had *Acinetobacter baumannii* pneumonia, and 1 patient had *Proteus mirabillis* urinary tract infection. Indeed, 2 of 3 organisms were antibiotic resistant. The increased rates of antibiotic resistance were 17.95% from Srinakharind Hospital[5] from 1994-1995 had found proportions of *Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (17.9 %, 17.9 %, 14.9%). A study was done in King Chulalongkorn Memorial hospital[8] in 2006 that had found *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Coagulase-negative staphylococcus (*28%, 11.7%, 7%). Both studies had found different organism from our study.

Suratthani hospital[18] study in 2011-2013 and Thammasat University Hospital[1] study 2012-2013 had found similarly increased *Acinetobacter baumannii* at 11.3% and 11.42%, respectively.

The mortality rate in this study is 28% which is higher than mortality rate in Siriraj[6], Suratthani[18] and Khon Kaen[7] which are 17.7%, 19.1% and 19.7%, respectively. However our results are nearly equal to

**Table 4.** Univariate analysis of factor associated with survival outcomes of febrile neutropenia (n = 50)

| Characteristic | No. of patients (%) | Survival outcome | | | |
|---|---|---|---|---|---|
| | | No. of patients (%) | HR | 95% CI | *p*-value |
| Age (year) | | | | | |
| ≤60 years | 39 (78) | 29 (74.4) | 2.23 | 0.65-7.68 | 0.21 |
| >60 years | 11 (22) | 7 (63.6) | | | |
| Sex | | | | | |
| Female | 21 (42) | 14 (66.7) | 0.53 | 0.18-1.59 | 0.26 |
| Male | 29 (58) | 22 (75.9) | | | |
| Cancer | | | | | |
| Controlled | 28 (56) | 22 (78.6) | 1.22 | 0.41-3.67 | 0.72 |
| Uncontrolled | 22 (44) | 14 (63.6) | | | |
| Cancer group | | | | | |
| Acute leukemia | 31 (62) | 21 (67.7) | 0.71 | 0.21-2.44 | 0.59 |
| NHL, CLL, MM | 19 (38) | 15 (79.0) | | | |
| Treatment setting | | | | | |
| First line treatment | 33 (66) | 28 (84.8) | 3.44 | 1.15-10.32 | 0.03 |
| Second line treatment | 17 (34) | 8 (47.1) | | | |
| Growth factor use | | | | | |
| Growth factor administration | 25 (50) | 20 (80) | 1.09 | 0.36-3.34 | 0.88 |
| No growth factor administration | 25 (50) | 16 (64) | | | |
| Expected further neutropenia duration | | | | | |
| <7 days | 1 (2) | 1 (100) | 22.66 | 0.00-1423067.9 | 0.58 |
| ≥7 days | 48 (98) | 34 (70.8) | | | |
| ECOG performance status | | | | | |
| 0-1 | 38 (76) | 30 (78.9) | 2.63 | 0.89-7.76 | 0.08 |
| 2-4 | 12 (24) | 6 (50) | | | |
| Symptoms (Burden) | | | | | |
| No or mild symptom | 19 (38) | 18 (94.7) | 6.76 | 0.88-52.12 | 0.07 |
| Moderate or severe symptom | 31 (62) | 18 (58.1) | | | |
| Stress tolerance | | | | | |
| Extreme or most stress tolerable | 19 (38) | 15 (78.9) | 1.21 | 0.37-3.94 | 0.76 |
| Mild or moderate stress tolerable | 31 (62) | 21 (67.7) | | | |
| Hospitalization status | | | | | |
| Outpatient | 18 (36) | 13 (72.2) | 1.12 | 0.37-3.44 | 0.84 |
| Inpatient | 32 (64) | 23 (71.9) | | | |
| Temperature | | | | | |
| <39°C | 26 (52) | 22 (84.6) | 2.16 | 0.67-6.94 | 0.20 |
| ≥39°C | 24 (48) | 14 (58.3) | | | |
| Fever duration | | | | | |
| ≤24 hours | 45 (90) | 33 (73.3) | 2.43 | 0.52-11.35 | 0.26 |
| >24 hours | 5 (10) | 3 (60) | | | |
| Infection | | | | | |
| No infection site | 29 (58) | 23 (79.3) | 1.77 | 0.59-5.28 | 0.31 |
| Presence of infection site | 21 (42) | 13 (61.9) | | | |
| Chest x-ray | | | | | |
| No abnormality | 42 (84) | 30 (71.4) | 0.83 | 0.18-3.77 | 0.81 |
| Abnormal, tumor and infection | 8 (16) | 6 (75) | | | |
| Antimicrobial prophylaxis | | | | | |
| No | 43 (86) | 33 (76.7) | 4.14 | 1.16-14.78 | 0.03 |
| Yes | 7 (14) | 3 (42.9) | | | |

**Table 4.** Cont.

| Characteristic | No. of patients (%) | Survival outcome | | | |
|---|---|---|---|---|---|
| | | No. of patients (%) | HR | 95% CI | *p*-value |
| Pulse | | | | | |
| <120 beats/min | 40 (80) | 28 (70) | 0.65 | 0.14-2.98 | 0.58 |
| ≥120 beats/min | 10 (20) | 8 (80) | | | |
| Respiratory rate | | | | | |
| ≤24 breaths/min | 47 (94) | 34 (72.3) | 1.17 | 0.15-9.15 | 0.88 |
| >24 breaths/min | 3 (6) | 2 (66.7) | | | |
| Surgery | | | | | |
| No surgery within 6 weeks | 48 (96) | 35 (72.9) | 10.20 | 1.05-99.51 | 0.05 |
| Within 6 weeks | 2 (4) | 1 (50) | | | |
| Confusion or alteration of mental state | | | | | |
| No | 48 (96) | 35 (72.9) | 7.23 | 0.75-69.67 | 0.09 |
| Yes | 2 (4) | 1 (50) | | | |
| Blood loss requiring IV therapy | | | | | |
| No | 46 (92) | 35 (76.1) | 5.41 | 1.35-21.68 | 0.02 |
| Yes | 4 (8) | 1 (25) | | | |
| Dehydration requiring IV therapy | | | | | |
| No | 44 (88) | 34 (77.3) | 4.72 | 1.38-16.17 | 0.01 |
| Yes | 6 (12) | 2 (33.3) | | | |
| Weight loss of >5% within 1 month | | | | | |
| No | 39 (78) | 32 (82.1) | 8.94 | 2.31-34.61 | 0.002 |
| Yes | 11 (22) | 4 (36.4) | | | |
| Previous febrile neutropenia | | | | | |
| No | 34 (68) | 22 (64.7) | 0.22 | 0.05-1.00 | 0.05 |
| Yes | 16 (32) | 14 (87.5) | | | |
| Previous fungal infection | | | | | |
| No | 46 (92) | 32 (69.6) | 0.04 | 0.00-765.89 | 0.53 |
| Yes | 4 (8) | 4 (100) | | | |
| Antifungal therapy within 6 months | | | | | |
| No | 44 (88) | 30 (68.2) | 0.04 | 0.00-99.27 | 0.42 |
| Yes | 6 (12) | 6 (100) | | | |
| Antiviral therapy within 6 months | | | | | |
| No | 45 (90) | 31 (68.9) | 0.04 | 0.00-362.80 | 0.50 |
| Yes | 5 (10) | 5 (100) | | | |
| Others serious comorbidity | | | | | |
| No | 48 (96) | 34 (70.8) | 0.04 | 0.00-1025.04 | 0.54 |
| Yes | 2 (4) | 2 (100) | | | |
| Hemoglobin level | | | | | |
| ≥8 g/dL | 32 (64) | 24 (75) | 0.93 | 0.31-2.82 | 0.90 |
| <8 g/dL | 18 (36) | 12 (66.7) | | | |
| Absolute neutrophil count | | | | | |
| ≥100/μL | 18 (36) | 12 (66.7) | 0.68 | 0.23-2.04 | 0.49 |
| <100/μL | 32 (64) | 24 (75) | | | |
| Platelet count | | | | | |
| ≥5,000/μL | 45 (90) | 34 (75.6) | 0.94 | 0.12-7.39 | 0.95 |
| <5,000/μL | 3 (6) | 2 (66.7) | | | |
| Bilirubinemia | | | | | |
| <2 mg/dL | 37 (74) | 26 (70.3) | 1.44 | 0.18-11.63 | 0.73 |
| ≥2 mg/dL | 2 (4) | 1 (50) | | | |

**Table 4.** Cont.

| Characteristic | No. of patients (%) | Survival outcome | | | |
|---|---|---|---|---|---|
| | | No. of patients (%) | HR | 95% CI | *p*-value |
| Albumin level | | | | | |
| ≥2.5 g/dL | 36 (72) | 26 (72.2) | 7.25 | 1.45-36.32 | 0.02 |
| <2.5 g/dL | 2 (4) | 0 (0) | | | |
| APACHE score | | | | | |
| <40 | 48 (96) | 36 (75) | 5.25 | 1.10-24.92 | 0.04 |
| ≥40 | 2 (4) | 0 (0) | | | |

**Table 5.** Multivariate analysis of factor associated with survival outcomes of febrile neutropenia (n = 50)

| Factors | HR | 95% CI | *p*-value |
|---|---|---|---|
| No weight loss >5% within 1 month | 11.56 | 2.77-48.23 | 0.001 |
| No blood loss requiring IV therapy | 7.92 | 1.74-36.08 | 0.01 |
| APACHE score <40 | 11.66 | 1.92-70.63 | 0.01 |

the Srinakarind study (24%)[3]. The cause of high mortality rate in this study may be due to we selected only FN in hematologic malignancy patients, and most patients suffered from acute leukemia. The acute leukemia patients had a bone marrow failure and patients will have received intensive treatments of chemotherapy. So they have a high risk of FN and high mortality rates in a cases with prolonged neutropenia. No weight loss greater than 5% within 1 month, no blood loss requiring intravenous fluid, and low APACHE II score have been associated with survival outcomes different to another studies done in Thailand and foreign countries[1,6,7,13].

The limitations of our study are this is a retrospective study with a small sample size, collected from medical record, and only patients who were treated in the HRH Princess Maha Chakri Sirindhorn medical center.

## Conclusion

There were high mortality rates in neutropenic patients with fever in this study. No significant weight loss, no blood loss requiring intravenous fluid, and low APACHE II score at the time of diagnosed FN were found to be associated factors with better survival outcomes.

## What is already known on this topic?

FN in hematologic malignancies is a high mortality complication.

## What this study adds?

The no significant weight loss, no blood loss requiring intravenous fluid, and low APACHE II score at the time of diagnosed FN were found to be associated factors with better survival outcomes.


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## Potential conflicts of interest

None.

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## ปัจจัยที่ผลต่อผลการรอดชีวิตของผู้ป่วยโรคมะเร็งทางโลหิตวิทยาที่ได้รับการวินิจฉัยภาวะไข้และเม็ดเลือดขาวต่ำ

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***ภูมิหลัง:*** *ภาวะไข้และเม็ดเลือดขาวต่ำเป็นภาวะแทรกซ้อนที่มีอันตรายถึงแก่ชีวิตที่พบได้บ่อยในผู้ป่วยมะเร็งทางโลหิตวิทยาที่ได้รับยาเคมีบำบัด การศึกษาถึงระบาดวิทยาและปัจจัยที่มีความเกี่ยวข้องกับการรอดชีวิตของผู้ป่วยนั้นมีความสำคัญต่อผลลัพท์ของการรักษาเพื่อทำให้ผลลัพธ์ของการรักษาดีขึ้น*

***วัตถุประสงค์:*** *เพื่อศึกษาถึงระบาดวิทยาและศึกษาถึงปัจจัยที่มีผลเกี่ยวข้องกับการรอดชีวิตของผู้ป่วยที่มีภาวะไข้และเม็ดเลือดขาวต่ำ*

***วัสดุและวิธีการ:*** *การศึกษานี้เป็นการศึกษาย้อนหลังเชิงพรรณนาโดยมีการทบทวนเวชระเบียนผู้ป่วยที่เข้ารับการรักษาที่ศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดาฯ สยามบรมราชกุมารี ระหว่างปี พ.ศ. 2555-2557 จำนวนทั้งหมด 50 คน*

***ผลการรักษา:*** *จากจำนวนครั้งของการเกิดไข้และเม็ดเลือดขาวทั้งหมด 50 ครั้ง พบว่ามีค่ามัธยฐานอายุของผู้ป่วยอยู่ที่ 35.5 ปี โดยอยู่ระหว่าง 15 ถึง 81 ปี พบว่า 39 คน คิดเป็นร้อยละ 78 อายุน้อยกว่า 60 ปี พบว่าผู้ป่วย 33 คน คิดเป็นร้อยละ 66 ได้รับการรักษาด้วยยาเคมีบำบัดเป็นแผนแรก เมื่อมาดูถึงตำแหน่งที่ติดเชื้อพบว่าร้อยละ 58 ของผู้ป่วยทั้งหมด ไม่พบตำแหน่งที่ติดเชื้อชัดเจน สำหรับผู้ป่วยที่มีตำแหน่งที่ติดเชื้อชัดเจนพบว่าร้อยละ 14 ติดเชื้อที่ทางเดินหายใจส่วนล่าง สำหรับผลเพาะเชื้อนั้น พบว่ามีการติดเชื้อแบคทีเรียชนิดแกรมลบมากกว่าชนิดแกรมบวก ผู้ป่วยส่วนใหญ่คิดเป็นร้อยละ 60 ได้รับยาปฏิชีวนะเป็น ceftazidime ร่วมกับ amikacin เมื่อมาวิเคราะห์ถึงปัจจัยต่างๆ ที่มีผลต่อการรอดชีวิตมาวิเคราะห์ multivariate analysis พบว่าปัจจัยที่มีผลต่อการรอดชีวิตของผู้ป่วยได้แก่ ผู้ป่วยที่ไม่มีประวัตินำหนักลดมากกว่าร้อยละ 5 ในระยะเวลา 1 เดือน โดยมีค่านัยสำคัญทางสถิติที่น้อยกว่า 0.05 ไม่มีประวัติเสียเลือดที่จำเป็นต้องได้รับสารน้ำ โดยมีค่านัยสำคัญทางสถิติที่ 0.01 และมีค่า APACHE II score น้อยกว่า 40 คะแนน โดยมีค่านัยสำคัญทางสถิติที่ 0.01 สำหรับอัตราการตายของผู้ป่วยนั้นคิดเป็นร้อยละ 28*

***สรุป:*** *ผู้ป่วยที่มีภาวะไข้และเม็ดเลือดขาวต่ำพบว่ามีอัตราการตายสูง ปัจจัยที่มีผลต่อการรอดชีวิตได้แก่ ผู้ป่วยที่ไม่มีประวัตินำหนักลดมากกว่าร้อยละ 5 ในระยะเวลา 1 เดือน ไม่มีประวัติเสียเลือดที่จำเป็นต้องได้รับสารน้ำและมีค่า APACHEII score ต่ำ จะมีอัตราการรอดชีวิตมากกว่าอย่างมีนัยสำคัญทางสถิติ*