Clinical and Biochemical diagnosis of patients with febrile neutropenia attended Babylon Cancer Treatment center

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Abstract

Background: Febrile neutropenia define as an oral fever of more than 38.3°C or ≥ 38.0°C sustained for more than one hour, with absolute neutrophil count (ANC) should be <500/μL. FN associated with high rate of disease indisposition, mortality, affect chemotherapy price and doses, and leading to chemotherapy course interruptions, as well as affects the chemotherapy potency. Aim of study: This study was aimed to estimate the patients that have cancer and newly diagnosed with febrile neutropenia **Patients and methods**: A retrospective study that included one hundred and fifty patients already diagnosed with cancer who attended the outpatient clinic of Babylon Cancer Treatment Center, from 1st of January 2020 to 1st of January 2021. **Results**: From a total of 150 patients, age of patients ranged from 20-85 years, with mean age of 62.3±10.17 years, 63(42%) were males and 87(58%) were females. Breast cancer form 40%, as the most common solid cancers presented with febrile neutropenia, while head and neck cancer form 2%. We found 20% blood culture positive, and E. coli most bacterial isolated (40%), while 8.66% was positive urine culture and E. coli was form 84.6% also most commonly urine bacterial isolated, and only 2.66% sputum culture was positive and S. pneumonia is most common bacterial isolated (50%). 73.34% of patients presented with fever without localizing symptoms, while 12.66% of patients presented with respiratory system related symptoms. We found day 8th after last cycle of chemotherapy was the most day of starting fever (28.66%). **Conclusion**: FN is a leading cause of cancer related death, early management is required to decrease rate of mortality.

Keywords: febrile neutropenia, presentation, solid tumor.

Resumen

Antecedentes: la neutropenia febril se define como una fiebre oral de más de 38,3°C o ≥38,0°C sostenida durante más de una hora, con un recuento absoluto de neutrófilos (RAN) que debe ser <500/μL. La FN se asocia con una alta tasa de indisposición de la enfermedad, mortalidad, afecta el precio y las dosis de la quimioterapia, y conduce a interrupciones del curso de quimioterapia, así como también afecta la potencia de la quimioterapia. Objetivo del estudio: Este estudio tuvo como objetivo estimar los pacientes que tienen cáncer y recién diagnosticados con neutropenia febril **Pacientes y métodos**: Un estudio retrospectivo que incluyó a ciento cincuenta pacientes ya diagnosticados con cáncer que asistieron a la clínica ambulatoria del Centro de Tratamiento del Cáncer de Babylon, del 1 de enero de 2020 al 1 de enero de 2021. **Resultados**: De un total de 150 pacientes, la edad de los pacientes osciló entre 20 y 85 años, con una edad media de 62,3±10,17 años, 63 (42%) eran varones y 87 (58%) eran mujeres. El cáncer de mama forma el 40%, ya que los cánceres sólidos más comunes se presentan con neutropenia febril, mientras que el cáncer de cabeza y cuello forma el 2%. Encontramos un 20% de hemocultivo positivo, y E. coli la mayoría de las bacterias aisladas (40%), mientras que el 8,66% fue un urocultivo positivo y la E. coli fue del 84,6% también más comúnmente aislada de bacterias en la orina, y solo el 2,66% del cultivo de esputo fue positivo. y S. pneumonia es la bacteria aislada más común (50%). El 73,34% de los pacientes presentó fiebre sin síntomas localizadores, mientras que el 12,66% de los pacientes presentó síntomas relacionados con el sistema respiratorio. Descubrimos que el octavo día después del último ciclo de quimioterapia fue el que tuvo más días de inicio de la fiebre (28,66%). **Conclusión**: La FN es una de las principales causas de muerte relacionada con el cáncer, por lo que se requiere un manejo temprano para disminuir la tasa de mortalidad.

Palabras clave: neutropenia febril, presentación, tumor sólido.

Introduction

Febrile neutropenia (FN) is define myelo suppressed patients with fever, even though an extensive variety of temperature and neutrophil cutoff have been used to recognize such incidents[1,2]. FN define as an oral fever of more than 38.3°C or ≥ 38.0°C sustained for more than one hour, with absolute neutrophil count (ANC) should be <500/μL. or <1000/μL with fast decrease <500/μL[3,4]. Febrile neutropenia associated with high rate of disease indisposition, mortality, affect chemotherapy price and doses, and also leading to chemotherapy course interruptions[4,5], as well as affects the chemotherapy potency[6,7].

The frequency of FN arising during the first cycle of treatment is around (23%–36%)[8], although most patients complained from mild events, the frequency of severe complications range (25–30%) and mortality (9–12%)[9]. While the progressions in helpful care of patients have cancer development, decrease death due to FN from 40% in 1970 to (1-3%) currently[10,11]. Most local[12], national[13], and international[14-17] guideline groups have suggested that routine primary FN prophylaxis be used for treatments with an FN risk 20 %[13].

Prompt empirical therapy with broad-spectrum antibiotics is standard of care and lethality is 10% in adult patients[17,18]. FN remains the important cause of emergency hospitalization[19]. Immediately must be sending for full blood count to determine the neutrophil count beside other investigations is essential in guiding early management[20,21]. When patients at low-risk, may be treated in outpatient with oral empirical antibiotic, while high-risk patients need hospital admission for IV antibiotic medications[22]. Infections due to Candida species may occur later in the course of neutropenia, particularly as a result of gastrointestinal (GI) mucositis[22,23]. The NCCN Guidelines Panel advises that fluoroquinolone prophylaxis (levofloxacin is preferred) be considered in patients with an expected duration of neutropenia (ANC 1000 neutrophils/μL) for more than 7 days. This is in agreement with the recommendations of the recent IDSA guidelines for the use of antimicrobial agents in neutropenic patients with cancer[24,25]. This study was aimed to estimate the patients that have cancer and newly diagnosed with febrile neutropenia to help them and medical staff for proper management and decrease rate of morbidity and mortality.

Methods

A retrospective study that included 150 patients already diagnosed with cancer who attended the outpatient clinic of Babylon Cancer Treatment Center, from 1st of January 2020 to 1st of January 2021. All patients had underlying solid malignancy with absolute neutrophil count ≤0.5 x10/L^9 plus either: Body temperature ≥38.3 C for a single measure or ≥38.0 C sustained over one hour following chemotherapy.

All patients in this study were sent for the following tests: Complete blood count with WBC differential, Chest X-ray (PA view), GUE and Microbiological tests: Blood culture and sensitivity to identification of blood by using routine usual laboratory methods, other culture and sensitivity such as sputum, urine and stool cultures (when appropriate). For blood culture, 2 blood samples were sent acquired from two different peripheral blood vessels; 5 ml was aspirated for each sample.

Ethical consideration: The study was conducted in accordance with ethical principles that have their origin in the declaration of Helsinki. It was carried out with patients verbal and analytical approval before the sample was taken. The study protocol and the subject information and consent from were reviewed and approved by the local ethics committee.

Statistical analysis done by SPSS 22 frequency and percentage used for categorical data, mean and SD for continuous data.

Results

The age of patients ranged from 20 - 85 years, with mean age of 62.3±10.17 years, age groups are shown in table 1. Of the total 150 patients included in the study 63 (42%) were males and 87 (58%) were females as shown in figure 1.

Table 1: Frequency distributions of age for patients have solid malignancy with febrile neutropenia

Age group	Number	Percentage
< 40 years	21	14%
41– 60 years	45	30%
61-80 years	72	48%
>70	12	8%
Total	150	100%

201

Figure 1: Frequency distributions of males and females among patients have FN and solid malignancy.

87 (58 %)   63 (42 %)

- MALE
- FEMALE
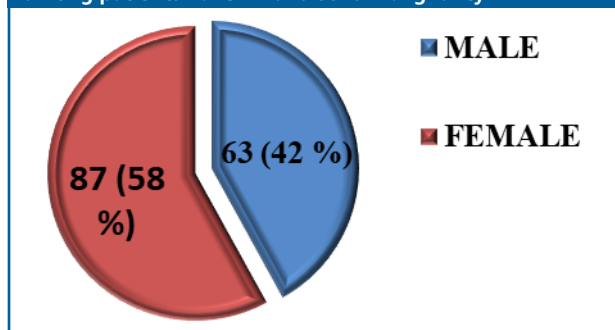
Figure 2: Frequency distribution of Febrile Neutropenia among solid malignancy.

60(40%) 21(14%) 18(12%) 15(10%) 15(10%) 12(8%) 6(4%) 3(2%)

Breast Cancer, Lung Cancer, Bladder Cancer, Pancreatic Cancer, Ovarian Cancer, STS, CUP, HAN Cancer

- Breast Cancer
- Lung Cancer
- Bladder Cancer
- Pancreatic Cancer
- Ovarian Cancer
- STS
- CUP
- HAN Cancer

Figure 3: fever onset day after starting last cycle of chemotherapy in patients with febrile neutropenia.

9 (6%) 21 (14%) 43 (28.66%) 30 (20%) 27 (18%) 12 (8%) 6 (4%) 2 (1.34%)

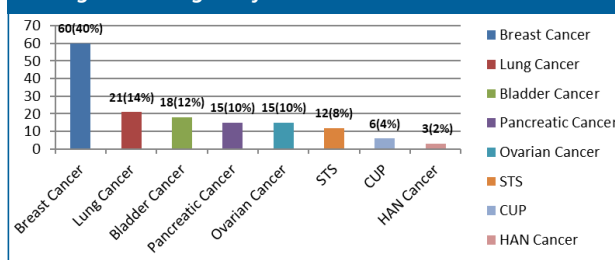6th day 7th day 8th day 9th day 10th day 11th day 12th day 13th day

Table 2: Frequency distributions of blood, sputum and urine culture results among patients have solid malignancy with febrile neutropenia.

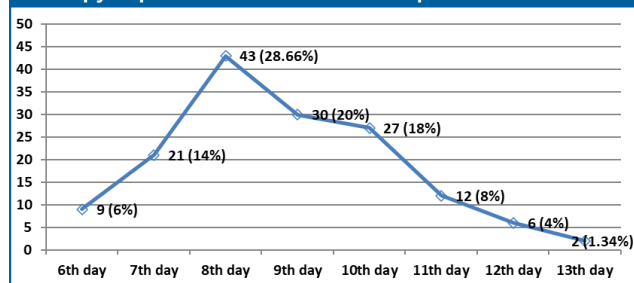|	Blood Culture		Sputum Culture		Urine Culture	
Results	N0.	%	N0.	%	N0.	%
Positive	30	20	4	2.66	13	8.66
Negative	120	80	146	97.34	137	91.34
Total	150	100	150	100	150	100

Table 3: frequency distribution of bacterial type isolated from blood, urine and sputum cultures among patients with solid malignancy and febrile neutropenia.

Type of bacterial isolated	Blood culture		Urine culture		Sputum culture	
	N0.	%	N0.	%	N0.	%
E. coli	12	40	11	84.6	-	-
Klebsiella pneumonia	9	30	-	-	-	-
Staphyllococcus aureus	5	16.66	-	-	-	-
Pseudomonas aeruginosa	1	3.34	-	-	-	-
Streptococcal pneumonia	3	10	-	-	2	50
Streptococcal viridans	-	-	-	-	1	25
Moragnella morganii	-	-	-	-	1	25
Proteus species	-	-	1	7.69	-	-
Klebsiella species	-	-	1	7.69	-	-
total	30	100	13	100	4	100

Table 4: Frequency distribution of system related clinical symptoms in patients with solid malignancy.

Systems related symptoms	No.	Percentage
Respiratory (cough, dyspnea)	19	12.66
GIT (diarrhea)	13	8.66
GUS (dysuria)	8	5.33
No system identified	110	73.34

Discussion

n this study among 150 patients with febrile neutropenia following chemotherapy, we found positive blood culture result was 30 (20%), this result was consistent to what had been reported by Hughes WT et al[28] who reported that the incidence of positive blood culture reaching to 20% and also this study was consistent with Al-Zubaidy AS et al[29] who found that the incidence was 18%, while our result disagree to what had been reported by Abhayakumar SM et al[30] that reported in their study a lower incidence of positive blood culture reaching to 12%, this difference might be due to better infection control and different in sample size. Regarding urine culture, in our study we find the urine culture was positive in 13(8.66%) and was negative in 137(91.33%), this study was similar to that of Abhayakumar SM et al[30] who reported slightly a lower incidence of positive urine culture and also consistent with Salam et al[29] who reported the positive urine culture in 4%. Among the patients of this study, 2.66% were found to be positive sputum culture, this result showed an agreement with that of Al-Zubaidy AS et al[29] who found that the results of sputum culture in solid malignancy was (0%). In addition, the result of this study was disagreed with that of Abhayakumar SM et al[30] who reported a higher incidence of positive sputum culture reaching to 9.7%. This difference might be due to smaller sample size in our study. Regarding the overall culture positivity results in our study were obtained in 31.32% (20% for blood cultures, 8.66% for urine cultures and 2.66% for sputum cultures) which was comparable to the results obtained by Abhayakumar SM et al[30] and Al-Zubaidy AS et al[29] were found 25% and 22% overall culture positivity, respectively. We found the predominant bacterial pathogens were gram negative bacteria forming 73.33 % for blood culture and 100% of urine culture and gram positive bacteria forming 26.66% in blood culture, 0% in urine culture and 100% for sputum culture. We noted a higher gram negative infection probably due to absence of use of central venous catheter and low frequency of ciprofloxacin used as prophylactic treatment, this result in agreement to what had been reported by Al-Zubaidy AS et al[29] who stated the predominant bacterial pathogens were gram negative bacteria forming 81.81%

and gram positive bacteria identified only in 18.18%. In addition, this results were consistent with the Safdar A et al[31] who also found that gram negative microbe isolates were most predominant accounted 63.3% while gram positive accounted only 36.7%, we noted in both our study and Safdar A et al[31] study that gram negative bacteria were more common than gram positive bacteria but in different percentage while Naurois JD et al[32] found that positive cultures were typically gram positive bacteria in 70%, this also this might be related to the use of central venous catheter and use of prophylactic treatment. Regarding the type of bacterial infection, E.coli was the most common type of gram negative bacteria and staphylococcus aureus was the only type of gram positive bacteria identified in blood culture, and also E coli was the most common type of bacteria identified in urine culture , these result agreed with the result in study mentioned above conducted by Abhayakumar SM et al[30] who also reported that E. coli was the most common type of gram negative bacteria and staphylococcus aureus was the most common type of gram positive bacteria identified in blood culture also E coli was the only type of bacteria identified in urine culture. Among the patients of this study, 73.34% patients presented clinically, with fever without localizing signs or symptoms and this result is comparable with slightly higher incidence to what has been reported by Oktay Y et al[33] who reported higher incidence reaching to 60%, while Rolston KV et al[34] who found 40% of patients presented clinically, with fever without localizing signs or symptoms. Also in our study, 26.65% patients presented clinically, with fever and system related clinical symptoms and most commonly 12.66% with respiratory symptoms such as dyspnea or cough followed by 8.66% with gastrointestinal symptoms (as diarrhea) and 5.33% patient with genitourinary symptoms (as dysuria), and these result differed from the result reported by Rolston KV et al[23] who found that gastrointestinal symptoms (diarrhea) was the most common symptom present in (29.5%) followed by respiratory symptom (20%) , sinus and ear infection (5%), skin and soft tissue infections (4.5%) and urinary tract symptoms(2%). In our study we found the onset of fever occur most commonly on 8th day followed by 9th day after starting last cycle of chemotherapy that causing febrile neutropenia. This result was consistent with Al-Zubaidy AS et al[29] who found that the most common day of fever onset occur on 9th day followed by 8th day post chemotherapy cycle.

Conclusions

FN is a leading cause of cancer related death. High index of suspicion is essential, and early treatment with antibiotics depending on local area susceptibility and sensitivity is needed to decrease rate of morbidity and mortality and hospital stay.

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