ORIGINAL ARTICLE

Bacterial and antibiotic susceptibility test patterns and quality of life of diabetic foot ulcer patients

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ABSTRACT

Antibiotic resistance is a growing concern in the treatment of diabetic foot ulcers. To address this, this study analyzed antibiotic usage patterns, microbial profiles, antimicrobial susceptibility, and patient quality of life (QoL). This was a descriptive observational study. This study collected data prospectively at Bojonegoro Regional Hospital between October 2022 and January 2023. Of the 66 patients, all of them exhibited bacterial growth. Microbial sensitivity profiles were categorized as gram-positive in 21 patients (32%), gram-negative in 38 patients (58%), gram-positive - gram-positive in 1 patient (2%), gram-negative - gram-negative in 2 patients (3%), and gram-positive - gram-negative in 4 patients (5%). The use of antibiotics is sensitive to gram-positive drugs, such as: cefepime, ceftriaxone, imipenem, and meropenem. Levofloxacin and imipenem both work 100% in gram-negative bacteria. Antibiotic usage overall is 159.05 DDD/100 patient days. Of the 11 highest domains, 33 patients (50.0%) have a good QoL, while 19 patients (28.8%) have poor QoL. A comprehensive approach is necessary for the effective management of diabetic foot wound infections, and family support is essential for the improved patient's QoL.

Key words: Antibacterial agents, behavior, diabetic foot, disease susceptibility, patients, quality of life

INTRODUCTION

The International Diabetes Federation (2021) reports that diabetes affects 537 million people globally, with projections of 643 million by 2030 and 783 million by 2045. Indonesia ranks seventh among the top 10 countries in Southeast Asia.[1-3] Diabetic foot ulcer (DFU) infections are a common complication of diabetic microangiopathy, causing tissue damage and death.[4,5] Jain *et al*. observed that among their 30 patients, 19 presented with right-footed diabetic foot ulcers (DFU), 12 with wet gangrene, and 24 required amputation.[1] Systems biology offers a new perspective on antibiotic resistance, shifting from traditional single-target investigations to explore the complex, interconnected networks within bacterial cells that drive resistance mechanisms. This approach provides a comprehensive understanding of how bacteria respond to and evade antibiotics, revealing novel targets and strategies to combat this growing global health threat. Guidelines promote antibiotic use based on culture results and reduce infection spread.[5] The American Diabetes Association (2020) reports that polymicrobial bacteria, including *Staphylococcus aureus*, *Streptococcus*,

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and gram-negative bacteria, cause DFU infections. Dendy *et al*. identified *Proteus* sp. (36%), *Klebsiella* sp. (34%), *Pseudomonas* sp. (21%), and *Acinetobacter* sp. (9%) at Dr. M. Djamil Padang Hospital.[6,7] Rizqiyah *et al*. found that Wagner grade II ulcers were most common at Dr. H. Abdul Moeloek Hospital, with 85.7% monomicrobial and 14.3% polymicrobial infections, including 62% gram-positive (*S. aureus*) and 37.5% gram-negative bacteria.[8] Empirical antibiotics can be given in ischemia or trauma cases, regardless of culture results.

The World Health Organization reports a 65% overall increase in antibiotic use globally between 2000 to 2015 (165% per capita in low- middle- income countries and 28% in developing countries). Apridamayanti *et al*. found that *Pseudomonas aeruginosa* in grade III and IV DFU patients were resistant to cefadroxil and amikacin but sensitive to levofloxacin, norfloxacin, cefotaxime, ceftriaxone, ciprofloxacin, imipenem, and meropenem.[9] Inappropriate empirical therapy can increase re-hospitalization and mortality rates, emphasizing the need for accurate diagnosis, drug selection, and patient assessment. Drs. Kariadi and Dr. Soetomo Hospitals found 42% of inappropriate antibiotic use.[10] Dr. Mintoharjo Naval Hospital reported 27.78% appropriate antibiotic dose, 38.89% for indication, 8.33% for patient, and 13.89% for drug use, with no drug interactions in 72.22% of cases.[11-13] Empirical use of ceftriaxone and ciprofloxacin for more than 3–4 days without culture results should be monitored, as studies show resistance to these antibiotics in some bacteria. Rational antibiotic selection is crucial for DFU treatment.

In Indonesia, mortality rates from gangrene and amputations in diabetes mellitus (DM) patients range from 17% to 32% and 15% to 30%. Quality of life (QoL) metrics assess treatment responses, which are negatively impacted by amputation.[14] All domains will be evaluated objectively for health status and subjectively for health perception, though subjective perceptions may skew objective assessments, affecting true QoL representation. This study aims to determine antibiotic use, pathogen mapping, culture tests, antimicrobial sensitivity, and patients' QoL.

METHODS

This descriptive observational study collected data on diabetic foot wound infections from October 2022 to January 2023 at Dr. R. Sosodoro Djatikoesoemo Bojonegoro Regional Hospital. Data included treatment records, medication, laboratory results, sensitivity tests, and microbiological cultures. Primary outcomes were antibiotic use (DDD/100 patient days), bacterial culture results, antibiotic appropriateness, and QoL. The sample included adult DFU patients with comorbidities, on antibiotics for at least 3 days, and treated at the hospital, excluding those with additional infections.

Determining the minimum sample size uses the sample size formula.

The method for determining the number of samples uses the sample size formula for descriptive research (ordinal data), namely:

$$n = \frac{z^2 1 - \frac{\alpha}{2} p(1-p)}{d^2}$$

whereas

n = Minimum number of samples

$Z^2 1 - \frac{\alpha}{2}$ = Degree of significance 95%, hence Z = 1.96

p = The probability of error is expressed in odds of 0.1

d = The error precision level used is 0.1

So that the number of samples obtained for the research for 3 months of research is as follows:

$$n = \frac{1,96^2 - 0,1(1-0,1)}{(0,1)^2} = 34,5744 \sim 35 .$$

Descriptive statistics analyzed antidiabetic medication use and QoL. Proportions represented nominal data, and interval data was shown as mean ± standard deviation and median (range). The P = 0.1 value was chosen as a conservative estimate based on preliminary data and similar DFU studies, where a 10% event rate is common. With no prior data, this assumption ensures adequate statistical power. We are open to refining it as more localized data becomes available.

Questionnaire development

Validation testing ensured the checklist's legitimacy with face and content validity. The checklist, based on previous research, was tested with 10 patients for face validity. Content validity was verified by experts using corrected item-total correlation ($r \geq 0.30$). Reliability testing with a split-half technique and Cronbach's alpha >0.60 showed high reliability (0.543–0.921). The study used the Diabetic Foot Scale questionnaire by Abetz *et al.* (2002), validated and translated by ULC Universitas Surabaya, covering 58 questions across 11 domains of QoL.[15]

RESULTS

From October 2022 to January 2023, 66 DFU patients at Dr. R. Sosodoro Djatikoesoemo Bojonegoro Regional Hospital met the criteria [Table 1]. Wound specimens were collected before antibiotics. Total antibiotic use was 159.05 DDD/100 patient days [Table 2], with imipenem (41.42

DDD/100 patient days) being the most used, followed by metronidazole (30.30 DDD/100 patient days) and cefuroxime (18.51 DDD/100 patient days). Cefixime 100 mg was the most used oral antibiotic (33.54 DDD/100 patient days). Culture results showed 100% bacterial growth, and antibiotic use aligned with the hospital's 2021 pathogen map [Table 3].

The QoL of patients showed the following results across different domains: In the comfort domain, 29 patients (43.9%) rated as "quite comfortable" (category 3); in physical health, 33 patients (50.0%) rated as "healthy" (category 4); in daily activities, 52 patients (78.8%) rated as "quite independent" (category 3); in emotions, 36 patients (54.5%) rated as "quite good" (category 3); in noncompliance, 36 patients (54.5%) rated as "quite obedient" (category 3); in family, 37 patients (56.1%) rated as "harmonious" (category 4); in friends, 34 patients (51.5%) rated as "quite good" (category 3); in care, 38 patients (57.6%) rated as "quite good" (category 3); in satisfaction, 37 patients (56.1%) rated as "quite satisfied" (category 3); in positive attitude, 36 patients (54.5%) rated as "quite positive" (category 3); in finances, 36 patients (54.5%) rated as "quite problematic" (category 3). Overall, 33 patients (50.0%) had a "good" total QoL (category 4), while 19 patients (28.8%) had a "not good" QoL (category 2) [Table 4]. Table 4 shows six questions on daily activities. Most respondents (78.8%, or 52 of 66) rated themselves as "moderately independent," indicating they are somewhat independent but still rely on others for tasks like cooking, cleaning, and leaving the house and experience longer task completion times and restricted daily routines.

Based on the analysis of the suitability of antibiotic use with the 2021 hospital pathogen map, it shows that the appropriateness of antibiotics is 100% (66 patients).

Table 1: Demographic characteristics

Variable	Number of cases (%)
Gender	
Male	19 (28)
Female	47 (72)
Age	
18–45 (adult)	6 (9)
46–59 (preaging)	40 (61)
>60 (elderly)	20 (30)
Duration of foot wound (day)	
<10	46 (70)
10–20	6 (9)
>20	14 (21)
Length of stay (day)	
1–7	30 (45)
8–14	27 (41)
>14	9 (14)
Degree of foot wound	
I	13 (20)
II	17 (26)
III	9 (14)
IV	22 (32)
V	5 (8)
Outcome (therapy)	
Improvement	62 (94)
Death	4 (6)

DISCUSSION

The age group of individuals with DFU infections is predominantly 46–59 years old, constituting 61% of cases, while 30% are over 60 years old and only 9% are under 45 years old, consistent with the increased prevalence of DFU with advancing age. This may be due to reduced circulation, muscle strength, and nerve function from aging. Behavioral factors such as poor blood sugar control, low activity, and lack of awareness, along with life

Table 2: Antibiotic drug usage profile

ATC code	Name	DDD WHO	DDD	DDD/100 patient days
J01DB05	Cefadroxil tablet	2	3	0.26
J01DC02	Cefuroxime injection	3	317	18.51
J01DD04	Ceftriaxone injection	2	89	7.79
J01DD08	Cefixime capsule	0.4	76.6	33.54
J01DE01	Cefepime injection	4	11.7	0.51
J01DH02	Meropenem injection	3	61	3.56
J01DH51	Imipenem infusion	2	473	41.42
J01FF01	Clindamycin capsule	1.2	8.1	1.18
J01GB06	Amikacin injection	1	57	9.98
J01MA02	Ciprofloxacin tablet	1	5	0.88
J01MA12	Levofloxacin infusion	0.5	12	4.20
J01XD01	Metronidazole infusion	1.5	259.5	30.30
P01AB01	Metronidazole tablet	2	79	6.92
	Total (patient days: 571)		1451.9	159.05

WHO: World Health Organization, DDD: Defined Daily Dose, ATC: Anatomical Therapeutic Chemical

Table 3: Pathogen map and antimicrobial resistance (number sensitive/number isolates)

Antibiotic	Gram positive		Gram negative			
	Staphylococcus aureus	*Staphylococcus haemolyticus*	*Escherichia coli*	*Klebsiella pneumoniae ssp. pneumoniae*	*Proteus mirabilis*	*Pseudomonas aeruginosa*
Ceftriaxone	-	-	-	4/57	6/86	1/33
Meropenem	-	-	8/100	8/100	6/100	5/71
Imipenem	-	-	-	-	-	-
Clindamycin	11/100	2/67	-	-	-	-
Amikacin	-	1/100	8/89	8/100	8/100	7/100
Ciprofloxacin	7/70	-	-	3/38	5/83	5/83
Levofloxacin	7/64	-	-	-	-	-

Table 4: Patients with diabetic wound infections and their quality of life

Domain	Scale 1	Scale 2	Scale 3	Scale 4	Scale 5	Interpretation
Comfortability (5 questions)	6	21	29	10	0	Very uncomfortable (1) - very comfortable (5)
Physical health (6 questions)	7	1	23	33	2	Very unhealthy (1) - very healthy (5)
Daily activity (6 questions)	3	7	52	4	0	Extremely dependent (1) - extremely independent (5)
Emotion (17 questions)	7	18	36	2	3	Awful (1) - excellent (5)
Compliance (2 questions)	3	23	36	0	4	Uncompliant (1) - compliant (5)
Family (2 questions)	4	21	23	37	1	Disharmonious (1) - harmonious (5)
Friends (5 questions)	3	23	34	1	5	Unhealthy friendship (1) - healthy friendship (5)
Care (4 questions)	4	21	38	0	3	inadequate attention (1) - adequate attention (5)
Satisfaction (1 questions)	2	19	37	8	0	Not content (1) - very content (5)
Positive attitude (5 questions)	4	19	36	7	0	Negative (1) - very bright (5)
Financial stability (2 questions)	6	0	36	22	2	Sufficient (1) - unsufficient (5)
QoL (11 domain)	3	19	10	33	1	Unwell (1) - well (5)

QoL: Quality of life

experiences and limited healthcare access, also contribute to the increased risk. The prevalence of diabetic ulcers rises by 3% at age >40 years and by 6% at age > 60 years.[2] Ages 45–65 years, marking menopause, are linked to a decline in estrogen production, which increases the risk of metabolic, cardiovascular, and cancerous conditions. Al-Rubeaan *et al*. found that age ≥45 years increases the risk of DM. Beta *et al*. (2022) reported that most DM patients with gangrene at Abdoel Wahab Sjahranie Hospital were aged 39–59 years (57%). Preelderly diabetic foot wound infection patients often experience vascular changes, reduced muscle mass, and decreased insulin secretion, leading to slower wound healing and impaired skin regeneration.[16-18]

Based on the number of antibiotic uses, the findings indicated that 44 patients (67%), or those who received a combination of two types of antibiotics, were the most likely to do so. Of these, 40 patients (91%), or 23 patients (52%), received infusions of metronidazole and imipenem. The DDD/100 patient days metric for DFU antibiotic use has limitations, not accounting for dose, duration, or patient factors, and not distinguishing between appropriate and inappropriate use. Alternatives such as DOT, DDD/1000 patient days, AUD, and the Point Prevalence Survey (PPS) offer more accurate insights.

Imipenem is a broad-spectrum antibiotic effective against most gram-positive, gram-negative, and anaerobic bacteria, as well as protozoa, which are major causes of infections in diabetic foot wounds. Imipenem is a carbapenem effective against gram-negative bacteria such as *P. aeruginosa* and *Escherichia coli*, as well as gram-positive bacteria like *S. aureus*. It inhibits cell wall synthesis and is effective against resistant strains due to low resistance in gram-negative bacteria. Imipenem resistance develops through beta-lactamase production, protein modification, efflux pump activation, and gene mutations. Antibiotic resistance, primarily driven by overuse and misuse, and the proliferation of resistant bacteria, necessitates stringent adherence to correct dosing, appropriate treatment duration, and comprehensive patient monitoring to preserve therapeutic efficacy.

According to the study's findings, infections are typically caused by gram-negative bacteria. Factors contributing to high gram-negative bacteria in DFU include patient health (age and poor blood sugar control), wound characteristics (large, deep, and chronic ulcers), bacterial factors (virulent strains such as *Pseudomonas*, *E. coli*, and *Klebsiella*), and environmental factors (moisture and bacterial exposure). This finding contradicts the findings of Putri *et al.* (2013) at RSAL in DKI Jakarta in 18 patients with diabetic gangrene, who reported that

S. aureus 47.46% of the pathogens in these patients were gram-positive;[19] meanwhile, the results of observations at RSI Surabaya Jemursari in the period 2012–2016 showed that the *Klebsiella pneumoniae* bacteria were the cause of the most infections (27%) among the five other causative bacteria, namely *S. aureus* (18%), *Staphylococcus non-haemolyticus* (18%), *Enterobacter aerogenes* (18%), *Burkholderia cepacia* (9%), and *E. coli* (9%).[20] gram-positive bacteria *S. aureus* (11 patients), gram-negative bacteria *K. pneumoniae* ssp. *pneumoniae* (8 patients), and *Proteus mirabilis* (8 patients) were the most often found types of bacteria in improved therapeutic outcomes. During the chronic period, wound infections frequently happen. Therapy results might be impacted by several things, including resistance to antibiotics.

Antibiotic resistance in Indonesia is rising, with 76 of 90 antibiotics exceeding resistance thresholds due to overuse and poor monitoring. In 2015, the Antimicrobial Stewardship Program was implemented in hospitals. Despite progress, more efforts in surveillance, education, and rational use are needed. Hospital pathogen mapping optimizes antibiotic use, reduces resistance, and raises awareness through data collection, analysis, strategy development, and training. Limited resources, poor infrastructure, and low awareness hinder its implementation, but it is essential for controlling resistance.

Antibiotics can cause resistance in DFU infections, complicating treatment. Proper antibiotic choice based on sensitivity tests is crucial. Tissue damage from *P. aeruginosa* worsens infections, and comorbidities like poor blood sugar control hinder healing. Delayed diagnosis and treatment reduce success, while early intervention improves outcomes. New diagnostic technologies enhance pathogen identification, offering faster, more accurate results and better detection of antibiotic resistance, leading to more effective treatment.

At Dr. R. Sosodoro Djatikoesoemo General Hospital, antibiotic use showed 96.97% compliance with the 2022 guidelines and 100% adherence to the 2021 microbial map. Among 66 patients, 50% reported a "good" QoL, 28.8% "poor," and 4.5% "very poor." DFUs significantly impact emotional, financial, and daily life, highlighting the need for comprehensive care. Effective management involves proper wound care, antibiotic use, and addressing risk factors.[21] Antibiotic selection should be based on bacterial culture and resistance testing. Empirical antibiotics are used initially, with polymicrobial interactions affecting treatment, requiring careful antibiotic selection, combination therapy, and regular resistance monitoring. Polymicrobial interactions between gram-positive and gram-negative bacteria can impact diabetic foot infection treatment, involving synergy, competition, and antimicrobial production. Treatment requires proper antibiotic selection, combination therapy, and regular monitoring for resistance.

Of 66 respondents, 50% rated their QoL as "good" (score 4), 28.8% as "less good" (score 2), and 4.5% as "not good" (score 1). Most had a good QoL despite leg issues, though some had lower quality. Patients with diabetic foot ulcers (DFUs) not only experience a low quality of life (QoL) that profoundly affects their daily activities, finances, and emotions, but studies also found they performed worse across all domains compared to the general population, even more so than individuals with diabetes but without foot ulcers. Good wound care, competent nursing care, pain management, psychological support, and physical rehabilitation are all components of a holistic strategy. In order to assist patients in managing the emotional and social effects they encounter, patient education and family support are equally crucial.[14,22,23]

Inclusion and exclusion criteria significantly affect study outcomes in DFU infection research. They can introduce selection bias, limit the generalizability of results, and influence sample size, which impacts statistical power, potentially affecting the reliability and relevance of findings. A larger, more diverse sample improves accuracy, reduces errors, and ensures better representation, enhancing QoL and resistance pattern data. It helps identify key QoL factors and complex resistance patterns, supporting the development of effective treatment strategies.

CONCLUSION

From October 2022 to January 2023, DFU patients at RSUD Dr. R. Sosodoro Djatikoesoemo Bojonegoro had a total antibiotic use of 159.05 DDD/100 patient days. Bacterial growth was observed in 100% of 66 samples (32% gram-positive, 58% gram-negative, and mixed types). Empirical antibiotics were continued as definitive therapy based on culture results in line with the hospital's 2021 pathogen map. Regarding QoL, 50% of patients reported a good score, while 28.8% reported a poor score. Hospital antimicrobial stewardship, especially pathogen mapping, is key to optimizing antibiotic use and reducing resistance, but challenges such as limited resources and infrastructure affect full implementation in Indonesia. Antibiotic resistance isn't just about one gene; it's a complex network of connections that mathematical modeling in computer science and bioinformatics is now helping us understand better.[24] Nonetheless, pathogen mapping remains essential for improving antibiotic use and combating resistance.

Informed consent statement

Patient consent was written along with the questionnaire, and the analysis used anonymous clinical data.

Ethical clearance

This research can be conducted based on permission from the hospital in response to the cover letter from the Head of the Master of Pharmacy Program, Faculty of Pharmacy, University of Surabaya, Number: Ref S-102/VIII/2022, and ethical clearance from the Dr. R. Sosodoro Djatikoesoemo Bojonegoro Regional General Hospital with Number: 445/366/412.202.38/SK/2022.

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Conflicts of interest

There are no conflicts of interest.

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India Universities and research institutions in India Media Ranking in India	Pharmacology, Toxicology and Pharmaceutics Pharmaceutical Science	Wolters Kluwer Medknow Publications	0.347 Q2 H-INDEX 48

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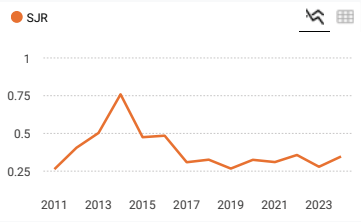

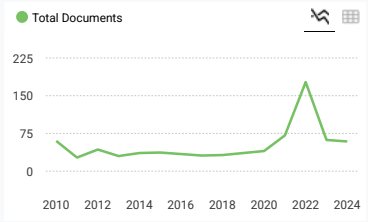

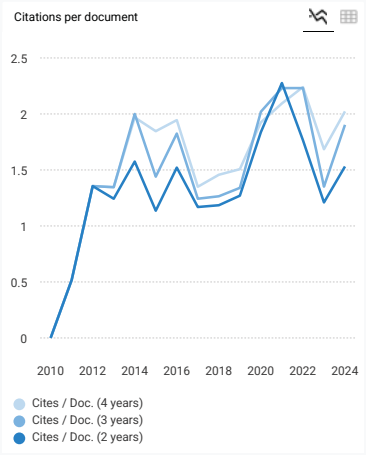

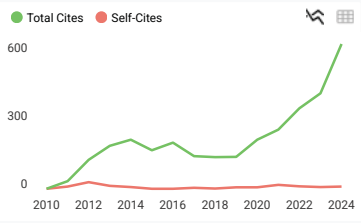

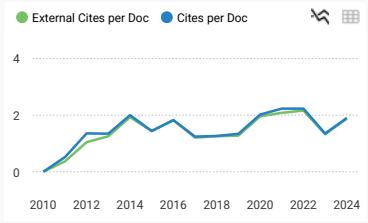

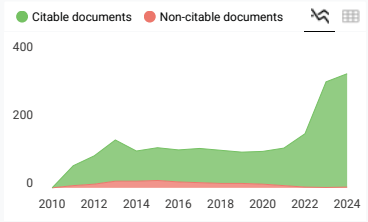

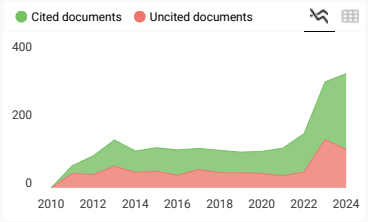

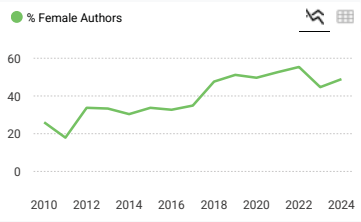

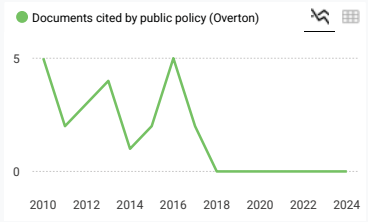

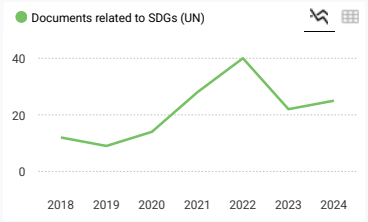

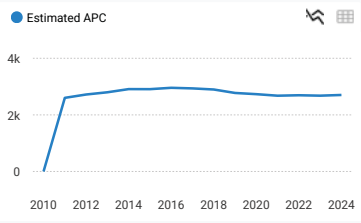

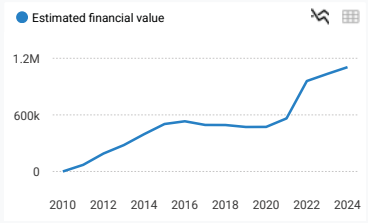

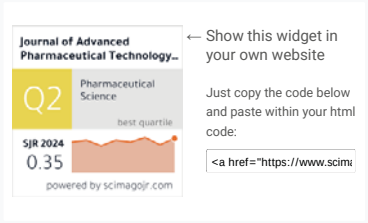

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expected time for the response.

Kind Regards

reply

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Best Regards, SCImago Team

B

Beatriz G. 5 years ago

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De antemano agradezco su respuesta

reply

SCImago Team

Melanie Ortiz 5 years ago

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E

eden fisha 6 years ago

good

reply

SCImago Team

Melanie Ortiz 6 years ago

Dear Eden, thanks for your participation! Best Regards, SCImago Team

A

Amina 6 years ago

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i would like to ask a question about this journal
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Regards..

reply

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A **Amina** 6 years ago

Hi
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Regards

reply

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Melanie Ortiz 6 years ago

Dear Amina, you can see the updated information just above. Best Regards, SCImago Team

M **Mohamed** 6 years ago

http://www.japtr.org/

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Melanie Ortiz 6 years ago

Dear Mohamed, thanks for your participation! Best Regards, SCImago Team

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