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Investigating The Association Of Demographic Factors On Methotrexate Delay-Clearance And Toxicity In Pediatric Oncology Patients: A Retrospective Chart Review

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INVESTIGATING THE ASSOCIATION OF DEMOGRAPHIC FACTORS ON METHOTREXATE DELAY-CLEARANCE AND TOXICITY IN PEDIATRIC ONCOLOGY PATIENTS: A RETROSPECTIVE CHART REVIEW

By

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A thesis submitted in partial fulfillment of the requirements
for Honors in the Major Program in Pediatric Oncology
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and in the Burnett Honors College
at the University of Central Florida
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Thesis Chair: Jacqueline Flores-Otero, Ph.D.

Abstract

High-dose methotrexate (HD MTX) is critical for treating pediatric malignancies such as acute lymphoblastic leukemia and neuro-carcinoma. However, its significant toxicity due to drug accumulation poses substantial risks. This retrospective study assesses the impact of demographic factors on MTX toxicity and clearance in pediatric oncology patients. Patient records from Saint Mary Hospital were analyzed, focusing on two MTX administration protocols: a 24-hour infusion followed by alkaline hydration and a 4-hour infusion followed by alkaline hydration. We hypothesize that factors such as age, body surface area (BSA), and body mass index (BMI) are associated with MTX clearance and toxicity. The study found no significant difference in clearance between genders, but females exhibited higher toxicity rates. Ethnicity comparisons showed Caucasians had the fastest clearance, followed by Hispanics, African Americans, and others, with Hispanics experiencing the highest toxicity rates. Patients with a BSA of less than one had a lower risk of delayed clearance, although toxicity levels were similar across BSA groups. BMI analysis indicated that patients with a BMI over 25 were at a higher risk of toxicity. Taken together, these findings suggest the need for personalized treatment plans in pediatric oncology to enhance therapeutic efficacy and reduce adverse effects. Future research should expand the sample size and develop a risk stratification guideline to identify patients suitable for outpatient treatment.

Keywords: Methotrexate, Pediatric Oncology, Toxicity, Clearance, Demographic Factors, Body Surface Area, Body Mass Index, Personalized Treatment.

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Introduction and Literature Review

Methotrexate (MTX) is a cornerstone chemotherapeutic agent widely used in pediatric oncology, notably for treating acute lymphoblastic leukemia (ALL), osteosarcoma, and other childhood cancers [1,2]. Its efficacy stems from its ability to inhibit DNA synthesis in rapidly proliferating cancer cells[3]. Despite its therapeutic benefits, the administration of high-dose methotrexate (HD MTX) is associated with significant toxicity, primarily due to drug accumulation in the body[4]. Understanding and mitigating these adverse effects are crucial for improving patient outcomes in pediatric oncology.

The pharmacokinetics and pharmacodynamics of HD MTX are critical for optimizing its therapeutic efficacy while minimizing toxicity[5,6]. Recent studies have highlighted the role of genetic polymorphisms and renal function in MTX metabolism and toxicity, suggesting that individual variability significantly affects treatment outcomes[7,8,9]. For instance, polymorphisms in genes such as MTHFR, RFC1, and ABCB1 have been associated with variations in MTX toxicity and efficacy[10,11]. Additionally, renal function, which is essential for MTX excretion, significantly influences drug clearance and toxicity risk; more than 90% of MTX clearance is mediated by the kidneys, while only about 10% is handled by the liver[8,12,13]. However, the association of demographic factors such as age, body surface area (BSA), and body mass index (BMI) on MTX clearance and toxicity remains underexplored, particularly in pediatric patients[14].

Several studies have attempted to elucidate the impact of demographic variables on pharmacokinetics. Age has been shown to affect drug metabolism and clearance, with younger patients often exhibiting higher clearance rates[15]. Body surface area (BSA) is a critical factor in

dosing calculations and has been linked to variations in pharmacokinetics[16]. Similarly, body mass index (BMI) can be associated with drug distribution and clearance, potentially affecting toxicity profiles[17]. However, the association of BMI and BSA is with drugs in general, not specifically with MTX.

Our study aims to fill this knowledge gap by investigating how demographic factors associate with MTX toxicity and clearance in pediatric oncology patients. We hypothesize that specific demographic variables, including ethnicity, sex, age, BSA, and BMI, associate with the rate of MTX clearance, thereby affecting the incidence of chemotherapy-related toxicity. This hypothesis is grounded in the understanding that physiological differences, associated with demographic factors, can significantly alter drug metabolism and clearance[18,19].

The study employs a retrospective chart review of pediatric patients treated with HD MTX at Saint Mary Hospital in collaboration with the University of Central Florida (UCF). Two MTX administration protocols are examined: a 24-hour infusion followed by alkaline hydration and a 4-hour infusion followed by alkaline hydration. By analyzing clearance patterns and toxicity data, we aim to identify trends and correlations that could potentially suggest personalized treatment strategies. Understanding these interactions is vital for refining treatment protocols in pediatric oncology, where the goal is to maximize therapeutic efficacy while minimizing toxicity.

Previous research has provided valuable insights into the pharmacokinetic variability of MTX and its clinical implications. Studies have demonstrated that delayed MTX clearance is a significant predictor of toxicity and adverse outcomes[20]. Monitoring MTX plasma levels and adjusting doses based on real-time pharmacokinetic data have been recommended to mitigate toxicity risks[21].

Furthermore, supportive care measures, including leucovorin rescue and enhanced hydration, are critical components of managing MTX toxicity[22,23].

In summary, while genetic and renal factors are well-recognized determinants of MTX pharmacokinetics and toxicity, the role of demographic factors requires further investigation. Our study seeks to bridge this gap by exploring the association of ethnicity, sex age, BSA, and BMI on MTX clearance and toxicity in pediatric oncology patients.

Hypothesis and Aims

Hypothesis: We hypothesize that demographic factors like age, body surface area (BSA), and body mass index (BMI) induce faster clearance of methotrexate (MTX), leading to reduced chemotherapy-related toxicity in pediatric oncology patients.

Aim 1: To assess the correlation between MTX clearance rates and patients' demographic factors. **Hypothesis**: Demographic factors such as age, gender, and BMI significantly affect MTX clearance rates, with younger patients and those with smaller BSA exhibiting faster clearance.

1.1. Collect and analyze demographic data (age, gender, BSA, and BMI) from pediatric oncology patients treated with HD MTX at Saint Mary Hospital.

1.2. Analyze the incidence of Delay clearance of HD MTX across different demographic groups and identify any significant correlations

Aim 2: To compare the incidence of MTX-related toxicity across different demographic groups. **Hypothesis**: Demographic factors such as age, gender, BSA, and BMI significantly associate with the incidence of MTX-related toxicity, with specific groups showing higher toxicity rates.

2.1. Collect data on MTX-related toxicity (including mucositis, renal toxicity, and other adverse effects) from the same patient cohort.

2.2. Analyze the incidence of toxicity across different demographic groups and identify any significant correlations.

Additionally, this research is aimed at identifying individuals who belong to high-risk groups for delayed MTX clearance to determine if high doses of methotrexate can be administered to them as outpatients instead of inpatients. If it is found that patients who do not belong to high-risk groups can safely manage MTXHD administration as outpatients with follow-up bloodwork at 24 and 48 hours, it could significantly ease the burden on these patients and improve their quality of life. According to the current protocol, patients are required to stay in the hospital for at least three days during which MTX is administered, and bloodwork is conducted at 24 and 48 hours before discharge.

Methodology

Study Design: This study employs a retrospective chart review design. It examines pediatric patients treated with high-dose methotrexate (HD MTX) at Saint Mary Hospital in collaboration with the University of Central Florida (UCF).

Subjects: The study includes 54 pediatric patients, who received a total of 213 doses of HD MTX their underlying diagnoses include: Acute Lymphoblastic Leukemia (ALL), T-cell Lymphoma, Osteosarcoma (OS), and Non-Hodgkin Lymphoma (NHL).

Data Collection: Data were extracted from patient records, focusing on variables including:

1. **Subject Number**: Unique identifier assigned to each patient in the study.
2. **Diagnosis**: Type of cancer diagnosed in the patient.
3. **Year of Diagnosis**: Year in which the patient was diagnosed with cancer.
4. **Age**: Age of the patient at the time of diagnosis.
5. **Sex**: Biological sex of the patient.
6. **Race/Ethnicity**: Self-reported race or ethnicity of the patient.
7. **Body Surface Area (BSA)**: Body surface area of the patient in square meters.
8. **Number of HD MTX Treatments**: Total number of high-dose methotrexate treatments received by the patient.
9. **Delayed Clearance**: Whether the patient experienced delayed clearance of MTX. Delayed clearance occurs when MTX takes longer than expected to be removed from the patient's body.
10. **Toxicity**: Major toxic effects experienced by the patient.

11. **Action Taken**: Interventions implemented in response to delayed clearance or major toxicity.
12. **Creatinine Level at Time of Delay**: Serum creatinine level at the time of delayed MTX clearance.
13. **Baseline Creatinine Level**: Baseline serum creatinine level before MTX treatment.
14. **BMI > 25**: Whether the patient's body mass index (BMI) is greater than 25.

Statistical Analysis: Data will be analyzed using chi-square tests to determine associations between categorical variables. Significant figures will be calculated to identify meaningful differences. The p-value will be set at 0.05 for determining statistical significance.

1. **Chi-Square Test**: To analyze the association between demographic factors (age, sex, race/ethnicity, comorbidities) and outcomes (delayed clearance, major toxicity).
2. **Significant Figures**: To highlight significant results from the statistical tests.
3. **P-Value**: A p-value of less than 0.05 will be considered statistically significant
   - If the p-value is less than the significance level α we reject the null hypothesis.
   - If the p-value is equal or greater than the significance level α we fail to reject the null hypothesis.

Software: The statistical analysis will be performed using EXCEL, ensuring rigorous data handling and accurate results.

Ethics: This study was conducted following ethical guidelines and approved by the relevant institutional review board (IRB# STUDY00006186). Patient confidentiality was maintained throughout the study, and no personal identifiers were used in data analysis.

Results

A) Demographic Factors and Toxicity Frequencies:

1) Ethnicity and Toxicity Frequencies Chi-Square Calculation:

Table 1 Ethnicity and Toxicity Frequencies Observed Data

Ethnicity	No Toxicity	Toxicity
Caucasians	14	4
African Americans	12	1
Hispanics	15	6

Table 2 Ethnicity and Toxicity Frequencies Expected Data

Ethnicity	No Toxicity	Toxicity
Caucasians	14.192	3.808
African Americans	10.250	2.750
Hispanics	16.558	4.442

Table 3 Ethnicity and Toxicity Frequencies Chi-Square Contributions

Ethnicity	No Toxicity	Toxicity	Total Contribution
Caucasians	0.003	0.010	0.013
African Americans	0.306	1.111	1.417
Hispanics	0.147	0.556	0.703

Table 4 Ethnicity and Toxicity Frequencies Statistic Result

Statistic	Value
Overall Chi-Square	2.133
p-value	0.347

Table 5 Ethnicity and Toxicity Frequencies Implications

Ethnicity	Implication
Caucasians	The chi-square contribution from Caucasians is 0.013, indicating that the observed frequencies of toxic and non-toxic cases are very close to the expected frequencies.
African Americans	The chi-square contribution from African Americans is 1.417, which is higher, suggesting a greater difference between the observed and expected frequencies, particularly for the Toxic category.
Hispanics	The chi-square contribution from Hispanics is 0.703, indicating some difference in the frequencies of toxic and non-toxic cases compared to the expected frequencies
	Overall Ethnicity is not statistically significant

2) Sex and Toxicity Frequencies Chi-Square Calculation:

Table 6 Sex and toxicity Frequencies Observed Data

	No Toxicity	Toxicity	Total
Female	13	6	19
Male	30	5	35
Total	43	11	54

Table 7 Sex and toxicity Frequencies Expected Data

	No Toxicity	Toxicity	Total
Female	15.12963	3.87037037	19
Male	27.87037	7.12962963	35
Total	43	11	54

Table 8 Sex and toxicity Frequencies Chi-Square Contributions

	No Toxicity	Toxicity
Female	0.29976427	1.171805777
Male	0.162729	0.636123136

Table 9 Sex and toxicity Frequencies Statistic Result

Statistic	Value
Overall Chi-Square	2.27
p-value	0.132

Table 10 Sex and toxicity Frequencies Implication

Sex	Implication
Female	The chi-square contribution from females for No Toxicity is 0.2998 and for Toxicity is 1.1718. This indicates that the observed frequencies cases among females show some differences from the expected frequencies, with a more notable difference in Toxicity category.
Male	The chi-square contribution from males for No Toxicity is 0.1627 and for Toxicity is 0.6361. This suggests that the observed frequencies of cases among males are relatively close to the expected frequencies, though there is a slight difference in the Toxicity.
	Overall Sex is not statistically significant

3) BMI and Toxicity Frequencies Chi-Square Calculation:

Table 11 BMI and Toxicity Frequencies Observed Data

	No Toxicity	Toxicity	Total
BMI > 25	5	4	9
BMI ≤ 25	41	4	45
Total	46	8	54

Table 12 BMI and Toxicity Frequencies Expected Data

BMI	No Toxicity	Toxicity
BMI > 25	7.667	1.333
BMI ≤ 25	38.333	6.667

Table 13 BMI and Toxicity Frequencies Chi-square Contributions

BMI	No Toxicity	Toxicity	Total Contribution
BMI > 25	0.928	5.333	6.261
BMI ≤ 25	0.186	1.067	1.253

Table 14 BMI and Toxicity Frequencies Statistic Results

Statistic	Value
Overall Chi-Square	7.514
p-value	0.0061

Table 15 BMI and Toxicity Frequencies Implications

BMI	Implication
BMI > 25	The chi-square contribution from the BMI > 25 group is 6.261, indicating a significant difference between the observed and expected frequencies, particularly for the Major Toxicity category.
BMI ≤ 25	The chi-square contribution from the BMI ≤ 25 group is 1.253, suggesting some difference between the observed and expected frequencies.
	Overall BMI is statistically significant

4) BSA and Toxicity Frequencies Chi-Square Calculation:

Table 16 BSA and Toxicity Frequencies Observed Data

Category	No Toxicity	Toxicity	Total
BSA > 1	31	4	35
BSA ≤ 1	19	0	19
Total	50	4	54

Table 17 BSA and Toxicity Frequencies Expected Data

Category	No Toxicity	Toxicity	Total
BSA > 1	32.41	2.59	35
BSA ≤ 1	17.59	1.41	19
Total	50	4	54

Table 18 BSA and Toxicity Frequencies Chi-Square Contributions

Category	No Toxicity	Toxicity
BSA > 1	0.061	0.764
BSA ≤ 1	0.113	1.407

Table 19 BSA and Toxicity Frequencies Statistic Results

Statistic	Value
Overall Chi-Square	2.345
p-value	0.126

Table 20 BSA and Toxicity Frequencies Implication

BSA	Implication
BSA > 1	The chi-square contribution is 0.061 for No Toxicity and 0.764 Toxicity This indicates that the observed frequencies cases in this group are relatively close to the expected frequencies, with a slightly higher difference in the Toxicity category.
BSA ≤ 1	The chi-square contribution is 0.113 for No Toxicity and 1.407 for Toxicity This suggests that the observed frequencies cases in this group also show some differences from the expected frequencies, particularly in the Toxicity category.
	Overall BSA is not statistically significant

B) Demographic factors and delay clearance

1) Ethnicity and MTX Delay Clearance Frequencies Chi-Square Calculation:

Table 21 MTX Delay Clearance Frequencies Observed Data

Ethnicity	No Delay Clearance	Yes	Total
African American	6	8	14
Hispanic	9	14	23
Caucasian	10	9	19

Table 22 MTX Delay Clearance Frequencies Expected Data

Ethnicity	No Delay Clearance	Delay Clearance
African American	6.94	7.06
Hispanic	9.72	9.28
Caucasian	8.33	10.67

Table 23 MTX Delay Clearance Frequencies Chi-Square Contributions

Ethnicity	No Delay Clearance	Delay Clearance	Total Contribution
African American	0.13	0.08	0.21
Hispanic	0.05	0.23	0.28
Caucasian	0.32	0.21	0.53

Table 24 MTX Delay Clearance Frequencies Statistic Results

Statistic	Value
Overall Chi-Square	2.10
p-value	0.35

Table 25 MTX Delay Clearance Frequencies Implications

Ethnicity	Implication
African American	The chi-square contribution from African Americans is 0.21, indicating that the observed frequencies of delay clearance cases are very close to the expected frequencies.
Hispanic	The chi-square contribution from Hispanics is 0.28, indicating some difference between the observed and expected frequencies.
Caucasian	The chi-square contribution from Caucasians is 0.53, indicating that the observed frequencies of delay clearance cases are somewhat different from the expected frequencies.
	Overall Ethnicity is not statistically significant

2) Sex and MTX Delay Clearance Frequencies Chi-Square Calculation:

Table 26 Sex and MTX Delay Clearance Frequencies Observed Data

Sex	No Delay Clearance	Delay Clearance
Female	7	12
Male	16	19

Table 27 Sex and MTX Delay Clearance Frequencies Expected Data

Sex	No Delay Clearance	Delay Clearance
Female	8.09	10.91
Male	14.91	20.09

Table 28 Sex and MTX Delay Clearance Frequencies Chi-Square Contributions

Sex	No Delay Clearance	Delay Clearance
Female	0.14	0.12
Male	0.11	0.1

Table 29 Sex and MTX Delay Clearance Frequencies Statistic Results

Statistic	Value
Overall Chi-Square	0.40
p-value	0.53

Table 30 Sex and MTX Delay Clearance Frequencies Implication

Sex	Implication
Female	The chi-square contribution from females for No Delay Clearance is 0.14 and for Delay Clearance is 0.12. This indicates that the observed frequencies are close to the expected frequencies, with minimal differences.
Male	The chi-square contribution from males for No Delay Clearance is 0.11 and for Delay Clearance is 0.10. This suggests that the observed frequencies are also close to the expected frequencies, with slight differences.
	Overall delay clearance is somewhat different between males and females, but Sex does not appear to significantly affect MTX delay clearance rates.

3) BMI and MTX Delay Clearance Frequencies Chi-Square Calculation:

Table 26 BMI and MTX Delay Clearance Frequencies Observed Data

Category	No Delay Clearance	Delay Clearance
BMI > 25	1	8
BMI ≤ 25	21	24

Table 27 BMI and MTX Delay Clearance Frequencies Expected Data

Category	No Delay Clearance	Delay Clearance
BMI > 25	4.5	4.5
BMI ≤ 25	22.5	22.5

Table 28 BMI and MTX Delay Clearance Frequencies Chi-Square Contributions

Category	No Delay Clearance	Delay Clearance
BMI > 25	2.722	2.722
BMI ≤ 25	0.1	0.1

Table 29 BMI and MTX Delay Clearance Frequencies Statistic Results

Statistic	**Value**
Overall Chi-Square	5.644
p-value	0.039

Table 30 BMI and MTX Delay Clearance Frequencies Implication

BMI	Implication
BMI > 25	The significant association between BMI over 25 and delayed clearance indicates that individuals with a BMI over 25 are more likely to experience delayed clearance.
BMI ≤ 25	The lack of a significant association between BMI below 25 and delayed clearance suggests that BMI below 25 does not associate with the likelihood of delayed clearance.
	Overall BMI is statistically significant

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4) BSA and MTX Delay Clearance Frequencies Chi-Square Calculation:

Table 31 BSA and MTX Delay Clearance Frequencies Observed Data

BSA Category	No Delay Clearance	Delay Clearance
BSA > 1	15	20
BSA ≤ 1	8	11

Table 32 BSA and MTX Delay Clearance Frequencies Expected Data

BSA Category	No Delay Clearance	Delay Clearance
BSA > 1	14.91	20.09
BSA ≤ 1	8.09	10.91

Table 33 BSA and MTX Delay Clearance Frequencies Chi-Square Contributions

BSA Category	No Delay Clearance	Delay Clearance
BSA > 1	0.0007	0.0040
BSA ≤ 1	0.0010	0.0008

Table 34 BSA and MTX Delay Clearance Frequencies Statistic Results

Statistic	Value
Overall Chi-Square	0.0065
p-value	0.9361

Table 35 BSA and MTX Delay Clearance Frequencies Implications

BSA	Implication
BSA > 1	The chi-square contributions for both No Delay Clearance and Delay Clearance in the BSA > 1 category are negligible, indicating that the observed and expected frequencies are almost identical.
BSA ≤ 1	The chi-square contributions for both No Delay Clearance and Delay Clearance in the BSA ≤ 1 category are also negligible, indicating that the observed and expected frequencies are almost identical.
	Overall BSA is not statistically significant

Discussion

The chi-square analysis revealed no significant association between ethnicity and MTX toxicity, with a p-value of 0.347. However, the data indicated that Caucasians had the fastest clearance rates, while Hispanics experienced the highest toxicity rates. This finding aligns with previous research suggesting ethnic differences in drug metabolism, possibly due to genetic polymorphisms affecting MTX pharmacokinetics. The lack of statistical significance in this study may be attributed to the relatively small sample size (N=54), which limits the power to detect significant differences across ethnic groups. The analysis indicated a higher incidence of toxicity in females compared to males, although the difference was not statistically significant (p-value = 0.132). The lack of statistical significance suggests that while there may be a trend, it is not strong enough to be confirmed with the current dataset. Larger scale studies are needed to explore this potential sex-based difference further and determine whether specific adjustments in MTX dosing are warranted for female patients.

The study found a significant association between higher BMI and increased MTX toxicity (p-value = 0.039). Patients with a BMI over 25 were at a higher risk of experiencing toxicity. This finding underscores the importance of considering BMI in treatment planning to optimize dosing and minimize adverse effects. It also reinforces the current practice and highlights the need for further research to develop specific dosing guidelines for patients with higher body weight. BMI.

The chi-square analysis showed no significant association between BSA and MTX toxicity (p-value = 0.126). Despite this, patients with smaller BSA were observed to have faster drug clearance rates, potentially leading to reduced toxicity. The findings were not statistically significant.

The analysis found no significant association between gender and delayed MTX clearance (p-value = 0.53). Both males and females exhibited similar rates of delayed clearance, indicating that gender does not significantly associate with MTX clearance in this cohort. Consistent with our previous results, the absence of a significant relationship in this study could be due to the limited sample size, which may not adequately capture subtle differences. Larger studies are needed to confirm these findings and explore potential mechanisms underlying the observed differences.

The chi-square test showed no significant association between race and delayed MTX clearance (p-value = 0.35). This finding suggests that race does not significantly affect MTX clearance in this patient population. The study found a significant association between BMI over 25 and delayed MTX clearance (p-value = 0.039). Patients with higher BMI were more likely to experience delayed clearance, consistent with previous findings that higher BMI can affect drug metabolism and excretion. This highlights the need for careful monitoring and potential dose adjustments for patients with higher BMI to prevent delayed clearance and associated toxicities. No significant association was found between BSA and delayed MTX clearance (p-value = 0.9361).

Limitations of Current Study and Future Considerations

- **Increase Sample Size:** Future research should involve a larger sample size will improve statistical power and reliability of the results.
- Multi-Center Approach: Conducting the study across multiple centers will ensure a diverse patient population and enhance the generalizability of findings.
- **Incorporate Additional Variables:** Including other relevant variables such as genetic polymorphisms, renal function, and detailed dietary intake could provide a more comprehensive analysis.
- **Advanced Statistical Methods:** Utilizing advanced statistical techniques, such as multivariate analysis, will help control for potential confounding factors and better understand relationships between demographic factors and methotrexate outcomes.
- **Detailed Toxicity Assessments:** Performing more detailed and standardized assessments of methotrexate-related toxicities, including grading the severity of adverse effects, will facilitate more precise comparisons.

Endnotes

Since the data for the “Other” category is too small, we excluded it from the calculation in both Ethnicity and MTX Delay Clearance Frequencies Chi-Square Calculation and Ethnicity and MTX Toxicity Frequencies Chi-Square Calculatio

Appendixes

UNIVERSITY OF CENTRAL FLORIDA

Institutional Review Board
FWA00000351
IRB00001138, IRB00012110
Office of Research
12201 Research Parkway
Orlando, FL 32826-3246

APPROVAL

January 2, 2024

Dear Jacqueline Flores:

On 1/2/2024, the IRB reviewed the following submission:

Type of Review:	Initial Study, Category 5; Waiver of Consent, Waiver of HIPAA Authorization
Title:	Demographic Study of The Incidence of Delayed Methotrexate Clearance and Severe Toxicity.
Investigators:	Jacqueline Flores Belal Alabdul Razzak
IRB ID:	STUDY00006186
Funding:	None
IND, IDE, or HDE:	None
Documents Reviewed:	• IRB approve from hospital , Category: Other; • Study 6186 UCF IRB-BAR and JFO V04, Category: IRB Protocol;

The IRB approved the protocol on 1/2/2024.

In conducting this protocol, you are required to follow the requirements listed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the IRB system. Guidance on submitting Modifications and a Continuing Review or Administrative Check-in is detailed in the manual. If continuing review is required and approval is not granted before the expiration date, approval of this protocol expires on that date.

When you have completed your research, please submit a Study Closure request so that IRB records will be accurate.

If you have any questions, please contact the UCF IRB at 407-823-2901 or irb@ucf.edu. Please include your project title and IRB number in all correspondence with this office.

Sincerely,

Renea Carver
Designated Reviewer

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