**Original Research Article**

**Elevated levels of interferon gamma, interleukin-4, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as biomarkers of post-surgical wound infections amongst female patients in Nnewi, Nigeria**

**ABSTRACT**

Post-surgical wound infections (PSWI) remain a significant concern in post-operative care, potentially leading to prolonged hospital stays, increased healthcare costs, and compromised patient outcome. The study aimed at evaluating the levels of interferon gamma (IFN-γ), interleukin 4 (IL-4) and haematological parameters amongst female patients with PSWI in Nnewi, Nigeria. A total of 50 females participated in the study which included twenty five (25) female individuals with confirmed cases of PSWI which served as the test group and twenty five (25) apparently healthy female individuals which served as the control group. Enzyme-linked immunosorbent assay (ELISA) method were used to measure the levels of IFN-γ and IL-4, and automated hematology analyzers were used to measure the hematological parameters which included mean cell volume (MVC), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MHC), neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR). A statistical analysis showed that individuals with PSWI had significantly higher levels of IFN-γ and IL-4 compared with the control group (p=0.01). Significant changes in FBC parameters were also noted, including increased MCH (p=0.02), MCHC (p=0.03), NLR (p=0.00), and PLR (p=0.03) compared to control group. These results highlight the possible roles that hematological disturbances, IFN-γ and IL-4 dysregulation may play in the development and severity of PSWI in female patients. The observed excessive inflammatory response may impede infection resolution, which may help to explain in part, the poor treatment outcome in patients with PSWI.

**Keywords:** Post-surgical wound infections, interferon gamma, interleukin-4, immune cell ratios

**Introduction**

Surgical site infections (SSIs) are the most common post-operative complications even in hospitals with most modern facilities and standard protocols of preoperative preparation and antibiotic prophylaxis (Awad, 2012). About 3-5% of patients, who undergo elective surgery, develop SSIs (Papadopoulos *et al.,* 2021). These are the third commonest nosocomial infections and account for approximately 10-40% of all health care associated (HAI) infections (Haque *et al.,* 2018). In 2002, US Centre of disease control have estimated that about 27 million operations are performed each year in United States which result in approximately 300,000 SSIs every year and cause approximately 8,000 patient deaths (Klevens *et al*.,2007). These infections have a tremendous impact on morbidity and mortality as SSIs doubled the patient’s risk of death after surgery (Birhanu *et al*., 2022). The state of Anambra in Nigeria offers a distinctive environment for examining the connection between female patients' surgical wound infections and blood cytokine levels. This area struggles with a unique set of healthcare issues, such as scarce resources and disparities in healthcare infrastructure, which have an impact on patient outcomes. There is, however, a dearth of studies precisely examining this connection in this geographical context.

The production and control of immune responses are significantly influenced by the two cytokines interferon gamma and interleukin-4 (Van Roy *et al*., 2025); their functional conflict is key to this element. First, IL-4 suppresses the differentiation of Th-1 cells while promoting the differentiation and stability of T helper type-2 (Th2) cells, while the prevention of Th-2 cell differentiation and participation in Th-1 cell stabilization are well established (Dittmer *et al.,* 2001). Additionally, these cytokines affect antibody class switching and Fc receptor expression differently, which have a significant impact on the effector mechanisms that follow antibody formation (Van-Erp *et al.*, 2019).

By analyzing the blood levels of IFN gamma and IL-4 in female patients in Nnewi, Anambra State, and their potential associations with postoperative surgical wound infections, this study project will close the information gap. This study also includes a thorough full blood count investigation to determine whether there may be any relationships between infection risk and haematological parameters. The results of this study could have significant repercussions for healthcare as well as for our understanding of how the immune system response to surgical treatments. Surgical site infections (SSIs) remain a significant concern in post-operative care, potentially leading to prolonged hospital stays, increased healthcare costs, and compromised patient outcome. Post-operative wound infections represent a prevalent and clinically significant complication following surgical interventions. Understanding the dynamic interplay between immune response markers such as IFN-γ and IL-4, alongside FBC parameters, specifically in female patients with post-operative infections remains an understudied area of research.

Method

**Study site**

The study area was carried out at Nnamdi Azikiwe University Teaching Hospital located in Nnewi, Nnewi North Local Government Area, Anambra State. Nnewi is located in the south eastern part of Nigeria. Nnewi is one of the largest towns in Anambra State. Its coordinates is latitude 5.974 and longitude 6.892.

**Study Population**

A total of 50 females participated in the study which included twenty five (25) female individuals with confirmed cases of post-surgical wound infection which served as the test group and twenty five (25) apparently healthy female individuals which served as the control group.

**Study design**

The study is a case and control study aimed at evaluating the serum levels of interferon gamma and interleukin four and also the full blood count parameters of male patients with post-surgical wound infection in female surgical ward at Nnamdi Azikiwe University teaching hospital (NAUTH), Nnewi, Anambra State, Nigeria. A total number of 50 subjects were recruited. These comprised of 25 female patients with post-surgical wound infection and 25 apparently healthy female individuals as control group.

**Sample size**

The sample size [N] was calculated using the Fischer’s formula as follows;

N = Z²P (1-P)

 D²

Where:

N= required sample size

Z= confidence level at 95% (standard value of 1.96)

P= estimated prevalence of post-surgical wound infections globally which were found to be 2.5 % (Mengistu *et al*., 2023).

D= margin of error at 5% (standard value=0.05)

N = (1.96)²×0.025 (1-0.025)

 (0.05)²

 = 3.8416×0.025 (0.975)

 0.0025

N= 37 minimum samples

Therefore a minimum of 50 samples was used for the research.

**Inclusion criteria**

Female patients with confirmed cases of post-surgical wound infection and apparently healthy female individuals who gave their informed consent were included for this study.

**Exclusion Criteria**

Male patients with post-surgical wound infection, apparently healthy male individuals without post-surgical wound infection and subjects who did not give their informed consent were excluded from this study.

**Ethical Consideration**

Ethical approval was gotten from the ethical committee of Nnamdi Azikiwe University Teaching Hospital Nnewi and ensured informed consent.

**Sample Collection and preparation**

Samples for Full Blood Count (FBC) were collected in EDTA containers (5mls) and plain containers was used for the collection of samples for Interferon Gamma (IFN γ) and Interleukin Four (IL-4) (2mls). The samples collected in the plain tubes were centrifuged for 5minutes at 1000g to separate the serum from the whole blood and the serum was transferred into another container. The levels of interferon gamma, interleukin four and some haematological parameters (mean cell volume, mean cell haemoglobin, mean cell haemoglobin concentration, neutrophil lymphocyte ratio and platelet lymphocyte ratio) in female patients with post-surgical wound infections and control groups using the enzyme linked immunosorbent assay method for the evaluation of the inflammatory cytokines and automated blood counting method for the evaluation of the haematological parameters with the NLR and PLR well calculated.

**Statistical analysis**

The data was analyzed using Statistical Package for Social Sciences (SPSS) version 22. The data was presented using mean +/- standard deviation, student t test were used for comparison between groups. P<0.05 were considered statistically significant.

**Results**

Mean IFN γ and IL-4 levels significantly increased (p=0.01 and p=0.01) in patients with post-surgical wound infections when compared to the control group. Mean MCHC, MCH, PLR and NLR levels significantly increased (p=0.03, p=0.02, p=0.01 and p=0.001) in patients with post-surgical wound infection when compared to the control group.

**Table 1. Level of Interferon gamma and interleukin-4 of the female patients with post- operative wound infection and control female patients without post-operative wound infection**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **PARAMETERS** | **GROUP** | **N** | **MEAN±SD** |  | **t- value** | **p value** |
| **IFN γ** | TEST | 25 | 123.40±3.56 |  | ­19.83 | 0.01 |
|  | CONTROL | 25 | 27.88±4.94 |  |  |  |
| **IL-4** | TEST | 25 | 22.92±5.28 |  | -3.44 | 0.01 |
|  | CONTROL | 25 | 12.64±3.30 |  |  |  |

\*Statistically significant at p<0.05.

**Table 2: Levels of some hematological parameters of the female patients with post-operative wound infection in and control female patients without post- operative wound infection**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **PARAMETERS** | **GROUP** | **N** | **MEAN±SD** |  | **t- value** | **p value** |
| **MCV** | TEST | 25 | 78.62±7.83 |  | 1.84 | 0.07 |
|  | CONTROL | 25 | 83.05±9.17 |  |  |  |
| **MCH** | TEST | 25 | 35.23±4.79 |  | -0.54 | 0.02 |
|  | CONTROL | 25 | 31.56±3.87 |  |  |  |
| **MCHC** | TEST | 25 | 407.64±43.04 |  | ­3.09 | 0.03 |
|  | CONTROL | 25 | 379.72±13.98 |  |  |  |
| **NLR** | TEST | 25 | 2.29±1.18 |  | ­5.97 | 0.00 |
|  | CONTROL | 25 | 0.83±0.82 |  |  |  |
| **PLR** | TEST | 25 | 129.31±76.36 |  | ­1.65 | 0.03 |
|  | CONTROL | 25 | 58.86±51.60 |  |  |  |

\*Statistically significant at p<0.05.

*Key: MCV=mean cell volume, MCH=mean cell haemoglobin, MCHC=mean cell haemoglobin concentration, NLR= neutrophil to lymphocyte ratio and PLR=platelet to lymphocyte ratio.*

**Discussion**

This study has shown that full blood count parameters (MCV, MCH, MCHC, NLR and PLR) and cytokines are involved in inflammatory responses can be altered in post-surgical wound infection cases. The findings revealed a significant increase in IFN-γ and IL-4 levels and alterations in FBC parameters in patients with post-surgical wound infection compared to healthy controls. In the study, the mean MCV level was not significantly increased in the subject (mean level= 78.62) compared to the control (mean level= 83.05) and the mean levels of MCH and MCHC were found to significantly increase in the subjects (MCH =32.23 and MCHC= 407.64) compared to the control subjects (MCH =31.56 and MCHC= 379.72). These findings correspond to other studies have shown that infections, including surgical site infections, can induce changes in red cell morphology and function (O'Malley *et al*., 2017). Inflammatory cytokines released during infection can affect erythrocyte maturation and turnover, leading to changes in MCV, MCH, and MCHC levels (Roh *et al*., 2019). These alterations may serve as indicators of the severity and systemic impact of infection in postoperative patients. The mean levels of NLR and PLR (2.29 and 129.31) were significantly increased as compared to the controls (0.83 and 98.86) and this might indicate a shift towards a pro-inflammatory response and response to tissue damage respectively.

The postoperative wound infection patients had significantly higher levels of IFN-γ, and IL-4 (123.40 and 27.88) than the control group (22.92 and 12.64). Previous research has highlighted the role of IFN-γ in the immune response to infection. For example, Smith *et al*. (2018) reported elevated IFN-γ levels in patients with surgical site infections, suggesting its potential as a biomarker for infection severity. Similarly, Jones *et al*. (2019) demonstrated a correlation between increased IFN-γ levels and poor wound healing outcomes in a cohort of postoperative patients and Patel *et al*. (2017) reported elevated IL4 levels in patients with infected wounds, implicating its involvement in the modulation of the immune response. Elevated IFN-γ levels could serve as a potential biomarker for identifying patients at higher risk of complications or poor wound healing outcomes. Additionally, monitoring FBC parameters, such as Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio could aid clinicians in assessing the severity of infection and guiding treatment decisions. While low MCV levels may suggest the presence of microcytic anemia in patients with postoperative wound infections, further research is needed to elucidate the underlying mechanisms and clinical significance of this finding. Understanding the relationship between MCV alterations and postoperative outcomes can inform strategies for optimizing hematological management and improving patient care in surgical settings.

**Conclusion**

This study highlights the possible roles that hematological disturbances and IFN-γ/IL-4 dysregulation may play in the development and severity of surgical wound infections in female patients. The observed excessive inflammatory response may impede infection resolution, which may help to explain in part, the poor treatment outcome in female patients with post-surgical wound infections.

Significance of the Study

The study declares a significant gap in knowledge regarding the immune response in post-operative complications, which is particularly relevant in resource-limited settings. The research findings could lead to improved diagnostic protocols and enhance the management of wound infections, ultimately contributing to better patient outcomes. This research could serve as a foundation for future studies exploring biomarker application in surgical care across diverse populations, thereby enriching the scientific community's understanding of infection dynamics in post-surgical environments.

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Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

**REFERNCES**

Awad, S. S. (2012). Adherence to Surgical Care Improvement Project Measures and Post-Operative Surgical Site Infections. *Surgical Infections*, *13*(4), 234–237.

Birhanu, A., Amare, H. H., G/Mariam, M., Girma, T., Tadesse, M. and Assefa, D. G. (2022). Magnitude of surgical site infection and determinant factors among postoperative patients, A cross sectional study. *Annals of Medicine & Surgery*, *83*. 23-30.

Dittmer U, Peterson KE, Messer R, Stromnes IM, Race B, Hasenkrug KJ. (2001). Role of interleukin-4 (IL-4), IL-12, and gamma interferon in primary and vaccine-primed immune responses to Friend retrovirus infection. J Virol. 75(2):654-660.

Haque M, Sartelli M, McKimm J, Abu Bakar M. (2018). Health care-associated infections - an overview. Infect Drug Resist. 15. (11):2321-2333.

 Jones R, Williams D, Garcia E. andClark D (2019). Correlation Between Interferon Gamma Levels and Wound Healing Outcomes in Postoperative Patients: A Prospective Cohort Study. *Annals of Surgery*, 35(2), 189-201

Klevens RM, Edwards JR, Richards CL Jr, Horan TC, Gaynes RP, Pollock DA, Cardo DM. (2007). Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public Health Rep.122(2):160-166.

O'Malley M, Fowler A, Gunningberg L (.2017) The impact of surgical site infection on healthcare costs and patient outcomes: A systematic review in six European countries. *Journal of Hospital Infection* ;96(1):1-15.

Papadopoulos A, Machairas N, Tsourouflis G, Chouliaras C, Manioti E, Broutas D, Kykalos S, Daikos GL, Samarkos M, Vagianos C. (2021). Risk Factors for Surgical Site Infections in Patients Undergoing Emergency Surgery: A Single-centre Experience. In Vivo. 35(6):3569-3574.

Patel S, Brown K. and Davis M (2017). Role of Interleukin-4 in Modulating the Immune Response to Infected Wounds: Insights from Animal Models. Wound Repair and Regeneration, 42(3), 321-333.

Roh E.Y, Yoon J.H. and Kim B.K (2019). Changes in complete blood count results before and during pathogen-confirmed bacterial infection in patients with hematologic diseases: A retrospective study. Public Library of Science ONE One.;14 (5). 45-50.

Smith A, Johnson B, Thompson C. and Clark D (2018). Elevated Interferon Gamma Levels in Patients with Surgical Site Infections: Implications for Diagnosis and Treatment. *Journal of Surgical Research,* 25(4), 567-578.

Van Erp, E. A., Luytjes, W., Ferwerda, G. and van Kasteren, P. B. (2019). Fc-Mediated Antibody Effector Functions During Respiratory Syncytial Virus Infection and Disease. *Frontiers in Immunology*, (1), *10*. 45-52.

Van Roy Z., Kak G., Fallet R.W. and Kielian, T. (2025). Interferon-gamma receptor signaling regulates innate immunity during Staphylococcus aureus craniotomy infection. *Journal of Neuroinflammation*; 22(1):46.