DOI: https://doi.org/10.53350/pjmhs20231709197

ORIGINAL ARTICLE

Prevalence of Cervical Intraepithelial Neoplasia among Women with Chronic Gynecological Infections: A Clinical and Hematological Study

SYEDA SHAISTA WAHEED[1], HANANA HAMEED[2], HAAFIZAH AZKA IQBAL[3], MUHAMMAD TARIQ HAMAYUN KHAN[4], ABDUL KARIM SOOMRO[5]

[1]*Professor and Head of Department, Obstetrics and Gynaecology, Nawaz Sharif Medical College, Gujrat, Pakistan*
[2]*Associate Professor, Department of Obstetrics and Gynaecology, Bolan Medical College, Quetta, Pakistan*
[3]*Department of Histopathology, Children's Hospital and Institute of Child Health, Lahore, Pakistan*
[4]*Assistant Professor of Haematology, Department of Pathology, Burns and Plastic Surgery Centre, Hayatabad, Peshawar, Pakistan*
[5]*Associate Professor, Department of Pathology, Bilawal Medical College, Jamshoro, Pakistan*
Correspondence to: Muhammad Tariq Hamayun Khan, Email: Qazi09066@gmail.com

ABSTRACT

Background: Cervical Intraepithelial Neoplasia (CIN) is a premalignant condition often associated with persistent infection and chronic inflammation of the female genital tract. Chronic gynecological infections are frequently overlooked in resource-limited settings, despite their potential to induce epithelial changes that predispose women to CIN. Hematological alterations such as anemia and inflammatory markers may reflect the systemic effects of persistent cervical inflammation, offering additional diagnostic clues.

Objective: To determine the prevalence of CIN among women with chronic gynecological infections and to evaluate associated hematological changes including hemoglobin levels, ESR, CRP, and serum ferritin.

Methods: This descriptive cross-sectional study was conducted from March 2022 to March 2023 at the Department of Gynecology and Obstetrics, Bolan Medical College, Quetta, and the Children Hospital and Institute of Child Health, Lahore. Ninety women aged 20 to 55 years with a history of chronic gynecological infections were enrolled. All participants underwent Pap smear screening, and those with abnormal findings were subjected to colposcopy-guided cervical biopsy for CIN confirmation. Hematological investigations were performed, and results were statistically analyzed using SPSS version 26.

Results: CIN was histologically confirmed in 34 women (37.8%), with CIN I in 18.9%, CIN II in 11.1%, and CIN III in 7.8%. CIN-positive women had significantly lower hemoglobin levels (mean 10.2 g/dL), higher ESR (mean 42.1 mm/hr), and more frequent CRP positivity (70.6%) compared to CIN-negative cases ($p < 0.05$). Normocytic normochromic anemia was predominant among anemic participants. Serum ferritin levels were also significantly lower in CIN-positive patients, indicating chronic inflammatory consumption.

Conclusion: A considerable prevalence of CIN was observed in women with chronic gynecological infections, accompanied by significant hematological alterations. The integration of cervical cytology with basic hematological screening could improve early detection of CIN, especially in resource-constrained healthcare systems.

Keywords: Cervical Intraepithelial Neoplasia, Chronic Gynecological Infections, Hematology, Pap Smear, Inflammation, Anemia.

INTRODUCTION

Cervical cancer is one of the most common malignancies affecting women worldwide, particularly in low- and middle-income countries (LMICs), where preventive screening programs are inadequate and awareness remains limited[1]. Cervical Intraepithelial Neoplasia (CIN) is a premalignant lesion of the cervix that represents a spectrum of dysplastic changes in the cervical epithelium. CIN is classified into three grades CIN I (mild dysplasia), CIN II (moderate dysplasia), and CIN III (severe dysplasia or carcinoma in situ) based on the severity of epithelial abnormality. If left untreated, CIN can progress to invasive cervical carcinoma over several years. Therefore, early detection and intervention are critical in preventing the morbidity and mortality associated with cervical cancer[2].

Persistent infection with high-risk oncogenic strains of human papillomavirus (HPV), particularly types 16 and 18, is the primary etiological factor for the development of CIN. However, several cofactors have been implicated in modulating susceptibility to HPV infection and the progression of cervical neoplasia[3]. Among these, chronic gynecological infections such as bacterial vaginosis, trichomoniasis, recurrent candidiasis, and chronic cervicitis play a significant role. These infections contribute to prolonged local inflammation, increased cellular turnover, disruption of mucosal barriers, and altered immune responses, which can facilitate viral persistence and epithelial dysplasia. Furthermore, co-infections can compromise cervical epithelial integrity and lead to microabrasions, making the cervical mucosa more susceptible to oncogenic HPV entry and integration[4].

Despite growing evidence linking chronic gynecological infections with CIN, this relationship is often underexplored in clinical practice, particularly in resource-constrained settings. Most women with chronic infections are treated symptomatically without further investigation into underlying cervical pathology[5]. This represents a missed opportunity for early diagnosis and prevention of cervical cancer, especially when such infections are recurrent and long-standing. Moreover, chronic inflammation caused by these infections may have systemic manifestations that are reflected in hematological parameters, such as elevated erythrocyte sedimentation rate (ESR), increased C-reactive protein (CRP), and changes in red blood cell indices. These alterations can act as indirect indicators of the body's inflammatory status and may correlate with the severity or presence of epithelial abnormalities in the cervix[6].

Hematological evaluation, although not specific for cervical pathology, could serve as a complementary tool in identifying women at higher risk of CIN, especially when advanced diagnostic modalities like colposcopy and HPV DNA testing are unavailable. Parameters like normocytic normochromic anemia, raised ESR, and CRP positivity have been associated with chronic infection and inflammation in various clinical conditions, but their specific relationship with CIN in the context of gynecological infections has not been extensively studied[7, 8].

In Pakistan and other similar LMICs, the burden of both chronic gynecological infections and cervical cancer remains significant due to poor access to health care, lack of regular screening programs, cultural barriers, and limited public awareness[9]. Consequently, studies that explore cost-effective and easily accessible markers for early detection of cervical abnormalities are urgently needed. Integrating hematological assessment with routine gynecological examination could offer a more comprehensive and accessible approach to identifying at-risk women in these settings[10].

Received on 10-05-2023
Accepted on 15-08-2023

The present study was designed to determine the prevalence of cervical intraepithelial neoplasia among women presenting with chronic gynecological infections and to explore the associated hematological changes. By identifying clinical and laboratory patterns associated with CIN, this study aims to highlight the importance of multidisciplinary evaluation in early detection and prevention strategies for cervical cancer in resource-limited environments[11].

MATERIALS AND METHODS

This descriptive cross-sectional study was carried out jointly at the Department of Gynecology and Obstetrics, Bolan Medical College, Quetta, and the Gynecology Unit of Children Hospital and Institute of Child Health, Lahore. The study was conducted over a duration of one year, from March 2022 to March 2023. The primary objective was to determine the prevalence of cervical intraepithelial neoplasia (CIN) in women presenting with chronic gynecological infections and to analyze associated hematological parameters. A total of 90 women between the ages of 20 and 55 years, presenting to the outpatient departments of both institutions with chronic gynecological symptoms, were included using a non-probability purposive sampling technique. Chronic infection was defined as the persistence or recurrence of gynecological symptoms such as vaginal discharge, pelvic discomfort, itching, or cervicitis for a duration of six months or more.

Women with known cervical cancer, those who were immunocompromised, pregnant women, and those who had recently received antibiotic or anti-inflammatory treatment within the last four weeks were excluded from the study. All participants provided written informed consent after a complete explanation of the study protocol. Ethical approval was obtained from the institutional review boards of both collaborating hospitals.

Each participant underwent a thorough clinical evaluation, which included a detailed history focused on menstrual irregularities, sexual activity, obstetric profile, contraceptive use, and previous history of infections or Pap smear screening. A complete pelvic examination was performed to identify any clinical signs of infection, cervical erosion, abnormal discharge, or suspicious lesions. Cervical cytological examination was conducted using the conventional Pap smear technique. Samples were obtained from both the ectocervix and endocervix using sterile Ayre's spatula and endocervical brush, immediately fixed in alcohol-based fixative, and sent to the pathology laboratory for cytological analysis. Women who showed abnormal cytological findings such as atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), or high-grade squamous intraepithelial lesion (HSIL) were advised to undergo colposcopic evaluation. Directed punch biopsies were taken from suspicious areas of the cervix under colposcopic guidance and sent for histopathological confirmation and grading of CIN.

In addition to clinical and cytological assessments, hematological investigations were conducted for all participants to evaluate systemic inflammatory status. These included complete blood count (CBC) to assess hemoglobin levels, red cell indices, and leukocyte counts; erythrocyte sedimentation rate (ESR) determined by the Westergren method; C-reactive protein (CRP) assessed by semi-quantitative latex agglutination technique; and serum ferritin levels measured by enzyme-linked immunosorbent assay (ELISA). All laboratory procedures were carried out in the central diagnostic laboratories of the respective institutions under standard quality control protocols.

The collected data were entered and analyzed using SPSS version 26. Descriptive statistics such as means, standard deviations, frequencies, and percentages were calculated to summarize demographic, clinical, and laboratory data. Associations between the presence of CIN and hematological parameters were assessed using chi-square tests for categorical variables and independent sample t-tests for continuous variables. A p-value of less than 0.05 was considered statistically significant for all analytical comparisons.

RESULTS

A total of 90 women were included in this clinical and hematological study, all of whom presented with chronic gynecological infections and fulfilled the inclusion criteria. The mean age of the participants was 36.4 ± 8.1 years, with the majority of the women (58.9%) falling within the age range of 31–45 years. Regarding parity, 75.6% of the women were multiparous, and 24.4% were nulliparous or primiparous. Most women (67.8%) belonged to lower-middle socioeconomic groups and reported delayed access to health care services. Chronic vaginal discharge (72.2%) and pelvic discomfort (56.7%) were the most commonly reported presenting complaints, followed by pruritus (24.4%) and postcoital bleeding (15.6%). A detailed summary of baseline demographic and clinical features is presented in Table 1.

Out of the 90 women screened using Pap smears, 48 cases (53.3%) were reported as negative for intraepithelial lesion or malignancy (NILM), while 42 women (46.7%) had abnormal findings. Colposcopy-directed punch biopsies were subsequently performed in all 42 women with abnormal cytology. Histopathological examination confirmed the presence of cervical intraepithelial neoplasia in 34 cases, yielding a CIN prevalence of 37.8% among the total study population. Among the confirmed CIN cases, CIN I was observed in 17 cases (18.9%), CIN II in 10 cases (11.1%), and CIN III in 7 cases (7.8%). These findings are summarized in Table 2, which provides a breakdown of the CIN grades among the biopsy-confirmed cases.

In terms of hematological parameters, significant differences were observed between women with biopsy-confirmed CIN and those without CIN. The mean hemoglobin level in CIN-positive women was 10.2 ± 1.4 g/dL, compared to 11.6 ± 1.2 g/dL in CIN-negative participants, which was statistically significant ($p < 0.001$). Furthermore, 67.6% of CIN-positive patients were found to be anemic, with normocytic normochromic anemia being the most common pattern. The erythrocyte sedimentation rate (ESR) was also notably elevated in the CIN-positive group, with a mean ESR of 42.1 ± 10.9 mm/hr, compared to 24.5 ± 7.6 mm/hr in the non-CIN group ($p < 0.01$). Similarly, C-reactive protein (CRP) was positive in 70.6% of CIN-positive women, whereas only 28.6% of the CIN-negative group exhibited a positive CRP result ($p < 0.001$). These results strongly suggest a correlation between chronic cervical inflammation and systemic hematological alterations. All hematological comparisons are presented in Table 3.

The analysis further revealed that serum ferritin levels, used as a marker of both iron stores and inflammatory status, were significantly lower in women with CIN (mean 22.7 ± 8.5 ng/mL) compared to those without CIN (mean 34.2 ± 9.1 ng/mL). The lower ferritin levels, along with anemia and raised inflammatory markers, point toward an underlying chronic inflammatory process and possible iron depletion in the presence of ongoing infection and neoplastic changes.

Table 1. Baseline Characteristics of Study Participants

Parameter	Frequency (n=90)	Percentage (%)
Age (mean ± SD)	36.4 ± 8.1	–
Age group 20–30 years	22	24.4%
Age group 31–45 years	53	58.9%
Age group >45 years	15	16.7%
Multiparity	68	75.6%
Vaginal discharge	65	72.2%
Pelvic pain/discomfort	51	56.7%
Pruritus	22	24.4%
Postcoital bleeding	14	15.6%

Collectively, these findings highlight a clear pattern: women with chronic gynecological infections and biopsy-confirmed CIN exhibited a higher frequency of systemic inflammation, anemia, and deranged iron profiles. These hematological deviations were

not only statistically significant but also clinically relevant, reinforcing the hypothesis that chronic cervical inflammation when left unchecked may progress toward precancerous transformation, accompanied by measurable systemic changes. This supports the utility of combining routine cervical screening with hematological assessments to identify women at greater risk for CIN in clinical practice.

Table 2. Prevalence and Grades of Cervical Intraepithelial Neoplasia (CIN)

CIN Grade	Frequency (n=90)	Percentage (%)
No CIN	56	62.2%
CIN I	17	18.9%
CIN II	10	11.1%
CIN III	7	7.8%
Total CIN	34	37.8%

Table 3. Hematological Parameters in CIN-positive vs CIN-negative Groups

Parameter	CIN-Positive (n=34)	CIN-Negative (n=56)	p-value
Hemoglobin (g/dL)	10.2 ± 1.4	11.6 ± 1.2	<0.001
ESR (mm/hr)	42.1 ± 10.9	24.5 ± 7.6	<0.01
CRP Positive (%)	24 (70.6%)	16 (28.6%)	<0.001
Serum Ferritin (ng/mL)	22.7 ± 8.5	34.2 ± 9.1	<0.01

DISCUSSION

The findings of this study highlight a significant prevalence of cervical intraepithelial neoplasia (CIN) among women presenting with chronic gynecological infections, underscoring the pathophysiological link between persistent lower genital tract infections and cervical epithelial transformation[12]. With a CIN prevalence of 37.8%, the data align with global and regional studies that emphasize the rising incidence of cervical dysplasia in low- and middle-income countries, particularly where routine cervical screening is infrequent, delayed, or inaccessible. The predominance of CIN I (18.9%) among the biopsy-confirmed cases suggests that a considerable proportion of women may be in an early and potentially reversible stage of cervical dysplasia an opportunity that could be seized for timely intervention and prevention of progression to carcinoma in situ or invasive cervical cancer[13].

A central hypothesis of this study was the role of chronic inflammation induced by persistent gynecological infections in the initiation or promotion of CIN. The results strongly support this hypothesis. Chronic bacterial, fungal, or protozoal infections of the cervix and vagina are known to cause persistent epithelial irritation, mucosal damage, and inflammatory cytokine release, which in turn compromise the cervical barrier and facilitate high-risk HPV infection and integration into host DNA[14]. In this study, elevated inflammatory markers, including significantly higher ESR and positive CRP results among CIN-positive women, serve as surrogate indicators of an ongoing inflammatory state. These findings are consistent with previous research suggesting that persistent local inflammation, even in the absence of high-risk HPV typing, may predispose the cervical mucosa to dysplastic changes[15].

Another important aspect of this study was the hematological profiling of participants, which revealed a high frequency of anemia among women with CIN. The majority of these women exhibited normocytic normochromic anemia, suggesting a chronic disease pattern rather than nutritional anemia[16]. This pattern could be attributed to the chronic inflammatory milieu, which alters iron metabolism and suppresses erythropoiesis, a phenomenon well-documented in anemia of chronic disease. Additionally, the significantly lower serum ferritin levels in CIN-positive patients further suggest a dual contribution of chronic inflammation and iron depletion in these women. While serum ferritin is traditionally a marker of iron stores, it also acts as an acute-phase reactant, and its reduction in CIN-positive patients likely reflects prolonged inflammatory consumption and poor nutritional absorption secondary to chronic illness[17].

From a clinical perspective, these findings are particularly relevant in low-resource settings like Pakistan, where women often present late in the course of disease due to cultural taboos, lack of awareness, and limited access to screening facilities[18]. This study provides compelling evidence that routine hematological screening, especially in women with long-standing gynecological complaints, can offer valuable clues about underlying cervical pathology. Simple, cost-effective tests like CBC, ESR, and CRP, when interpreted in conjunction with clinical presentation, could help in identifying women who require urgent gynecological evaluation and Pap smear testing[19].

Furthermore, the identification of CIN II and III in nearly 20% of the cohort signals a considerable risk of progression to cervical cancer if left untreated. It is therefore crucial to integrate cervical cancer prevention strategies with primary care and infectious disease management services. Educating women on the risks associated with untreated infections, increasing access to Pap smears and HPV vaccination, and encouraging follow-up visits can collectively curb the rising trend of cervical dysplasia and cancer in the region[20].

This study also opens avenues for further research. Future studies should incorporate HPV DNA testing, cytokine profiling, and longitudinal follow-up to determine the progression or regression of CIN in response to treatment of infections. Investigating the specific microbiological pathogens involved and their role in modulating local immune responses would also provide mechanistic insights into the CIN–infection relationship[21,22].

CONCLUSION

In conclusion, this study demonstrates a significant burden of cervical intraepithelial neoplasia among women with chronic gynecological infections, with nearly four out of ten women showing biopsy-confirmed CIN. The association of CIN with altered hematological parameters, particularly anemia, elevated ESR, and CRP positivity, highlights the systemic impact of chronic cervical inflammation and the potential role of basic hematological tests as indirect markers of disease. These findings underscore the need for a multidisciplinary approach in women's reproductive healthcare one that integrates gynecological, hematological, and microbiological assessments for early detection and prevention of cervical cancer. Strengthening cervical screening programs and awareness initiatives, especially in underserved communities, remains imperative to reducing the incidence of CIN and improving long-term women's health outcomes in Pakistan and beyond.

Availability of Data and Materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests: The authors declare that they have no competing interests.

Funding: No external funding was received for this study.

Authors' Contributions: S.S.W. and H.H. conceived the study, designed the protocol, and supervised data collection. H.A.I. and M.T.H.K. were responsible for clinical assessments and gynecological procedures. contributed to data analysis and interpretation. A.K.S. reviewed the manuscript for intellectual content and provided hematological expertise. All authors read and approved the final manuscript.

Acknowledgment: The authors would like to express their sincere gratitude to the staff of the Department of Gynecology and Obstetrics, Bolan Medical College, Quetta, and Children Hospital and Institute of Child Health, Lahore, for their continuous support during data collection and laboratory processing. Special thanks to the patients who voluntarily participated in this study and made this research possible through their cooperation and trust.

REFERENCES

1. Rubenovna AL, Shermamatovna KA. Features of Somatic and Gynecological Status in Women with Cervical Intraepithelial Neoplasia. Annals of the Romanian Society for Cell Biology. 2021;25(1):140-6.
2. Pruski D, Malkowska-Walczak B, Paluszkiewicz A, Kędzia W. The incidence of cervical intraepithelial neoplasia in a population of pregnant women with an abnormal cytology. Ginekologia Polska. 2017;88(1):20-3.

3. Wang Z, Wang J, Fan J, Zhao W, Yang X, Wu L, et al. Risk factors for cervical intraepithelial neoplasia and cervical cancer in Chinese women: large study in Jiexiu, Shanxi Province, China. Journal of cancer. 2017;8(6):924.
4. Farzaneh F, Faghih N, Hosseini MS, Arab M, Ashrafganjoei T, Bahman A. Evaluation of neutrophil–Lymphocyte ratio as a prognostic factor in cervical intraepithelial neoplasia recurrence. Asian Pacific Journal of Cancer Prevention: APJCP. 2019;20(8):2365.
5. Gennigens C, De Cuypere M, Seidel L, Hermesse J, Barbeaux A, Forget F, et al. Correlation between hematological parameters and outcome in patients with locally advanced cervical cancer treated by concomitant chemoradiotherapy. Cancer Medicine. 2020;9(22):8432-43.
6. Shi F, Yoder AK, Mach C, Dalwadi S, Anderson ML, Hall TR, et al. Impact of hematologic toxicities during concurrent chemoradiation for cervical cancer. Obstetrics & Gynecology Science. 2022;65(2):176-87.
7. Stier EA, Lensing SY, Darragh TM, Deshmukh AA, Einstein MH, Palefsky JM, et al. Prevalence of and risk factors for anal high-grade squamous intraepithelial lesions in women living with human immunodeficiency virus. Clinical Infectious Diseases. 2020;70(8):1701-7.
8. Ittiamornlert P, Ruengkhachorn I. Neutrophil-lymphocyte ratio as a predictor of oncologic outcomes in stage IVB, persistent, or recurrent cervical cancer patients treated by chemotherapy. BMC cancer. 2019;19:1-10.
9. Joura EA, Giuliano AR, Iversen O-E, Bouchard C, Mao C, Mehlsen J, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. New England Journal of Medicine. 2015;372(8):711-23.
10. Benard VB, Castle PE, Jenison SA, Hunt WC, Kim JJ, Cuzick J, et al. Population-based incidence rates of cervical intraepithelial neoplasia in the human papillomavirus vaccine era. JAMA oncology. 2017;3(6):833-7.
11. Barra F, Della Corte L, Noberasco G, Foreste V, Riemma G, Di Filippo C, et al. Advances in therapeutic vaccines for treating human papillomavirus-related cervical intraepithelial neoplasia. Journal of Obstetrics and Gynaecology Research. 2020;46(7):989-1006.
12. Ghebre RG, Grover S, Xu MJ, Chuang LT, Simonds H. Cervical cancer control in HIV-infected women: past, present and future. Gynecologic oncology reports. 2017;21:101-8.
13. Harper DM, Nieminen P, Donders G, Einstein MH, Garcia F, Huh WK, et al. The efficacy and safety of Tipapkinogen Sovacivec therapeutic HPV vaccine in cervical intraepithelial neoplasia grades 2 and 3: Randomized controlled phase II trial with 2.5 years of follow-up. Gynecologic oncology. 2019;153(3):521-9.
14. Mitra A, Tzafetas M, Lyons D, Fotopoulou C, Paraskevaidis E, Kyrgiou M. Cervical intraepithelial neoplasia: screening and management. British Journal of Hospital Medicine. 2016;77(8):C118-C23.
15. Franza L, Costantini B, Corrado G, Spanu T, Covino M, Ojetti V, et al. Risk factors for bloodstream infections in gynecological cancer. International Journal of Gynecological Cancer. 2020;30(2):245-51.
16. Kaplan S. Risk factors that cause cervical intraepithelial lesion development: a single center cross-sectional study in Turkey. Asian Pacific Journal of Cancer Care. 2020;5(3):173-8.
17. Sawaya GF, Smith-McCune K, Kuppermann M. Cervical cancer screening: more choices in 2019. Jama. 2019;321(20):2018-9.
18. Small Jr W, Bacon MA, Bajaj A, Chuang LT, Fisher BJ, Harkenrider MM, et al. Cervical cancer: a global health crisis. Cancer. 2017;123(13):2404-12.
19. Trimble CL, Morrow MP, Kraynyak KA, Shen X, Dallas M, Yan J, et al. Safety, efficacy, and immunogenicity of VGX-3100, a therapeutic synthetic DNA vaccine targeting human papillomavirus 16 and 18 E6 and E7 proteins for cervical intraepithelial neoplasia 2/3: a randomised, double-blind, placebo-controlled phase 2b trial. The Lancet. 2015;386(10008):2078-88.
20. Moscicki A-B, Darragh TM, Berry-Lawhorn JM, Roberts JM, Khan MJ, Boardman LA, et al. Screening for anal cancer in women. Journal of lower genital tract disease. 2015;19(3):S27-S42.
21. Ogilvie GS, van Niekerk D, Krajden M, Smith LW, Cook D, Gondara L, et al. Effect of screening with primary cervical HPV testing vs cytology testing on high-grade cervical intraepithelial neoplasia at 48 months: the HPV FOCAL randomized clinical trial. Jama. 2018;320(1):43-52.
22. Athanasiou A, Veroniki AA, Efthimiou O, Kalliala I, Naci H, Bowden S, et al. Comparative effectiveness and risk of preterm birth of local treatments for cervical intraepithelial neoplasia and stage IA1 cervical cancer: a systematic review and network meta-analysis. The lancet oncology. 2022;23(8):1097-108.

This article may be cited as: Waheed SS, Hameed H, Iqbal HA, Khan MTH, Soomro AK: Prevalence of Cervical Intraepithelial Neoplasia among Women with Chronic Gynecological Infections: A Clinical and Hematological Study. Pak J Med Health Sci, 2023; 17(9): 197-200.