

# Controlled clinical study to evaluate the utility of the platelet distribution width (PDW) in the diagnosis of acute appendicitis

## *Estudio clínico controlado para valorar la utilidad del ancho de distribución plaquetaria (PDW) en el diagnóstico de apendicitis aguda*

Rafael A. Espinosa-Campos<sup>1,2\*</sup>, Silvia G. De la O-Hernández<sup>3</sup>, María G. González-Zárate<sup>3</sup>, and Eduardo E. Montalvo-Javé<sup>2,4</sup>

<sup>1</sup>Division of Surgery, High Specialty Medical Unit No. 71, Instituto Mexicano del Seguro Social (IMSS), Torreón Coahuila; <sup>2</sup>Surgery Department, Faculty of Medicine, Universidad Nacional Autónoma de México, Mexico City; <sup>3</sup>General Surgery Department, Hospital General Dr. Fernando Quiroz Gutiérrez, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE), Mexico City; <sup>4</sup>General Surgery Department, Hepato-Pancreato-Biliary Surgery Clinic, Hospital General de Mexico Dr. Eduardo Liceaga, Mexico City, Mexico

### Abstract

**Introduction:** Acute appendicitis is the most common abdominal urgency around the world. Recent studies have investigated the efficacy of platelet distribution width (PDW) in the diagnosis of acute appendicitis. **Objectives:** The objectives of this study were to determine if there is a correlation between PDW and the diagnosis of patients with acute appendicitis and to define their relation to the phases of appendicitis. **Method:** A case-controlled study was conducted in two population groups with 41 patients older than 18 years of age diagnosed with acute appendicitis (Group I) and 41 healthy patients (Group II). Statistical analysis was performed using SPSS software version 21. **Results:** An average age of  $37.27 \pm 15.6$  years was observed. The largest number of cases with acute appendicitis was presented in phase III. The total number of leukocytes and the percentage of neutrophils presented significant differences in the statistics. It was observed that there is no association between the appendicitis phase and the PDW values. **Conclusion:** There are no differences between PDW values of patients with acute appendicitis compared to healthy patients, nor PDW ratio with the phases of appendicitis.

**Keywords:** Acute appendicitis. Diagnosis. PDW.

### Resumen

**Antecedentes:** La apendicitis aguda es la urgencia abdominal más común en el mundo. Estudios recientes han investigado la eficacia del ancho de distribución plaquetaria (PDW, platelet distribution width) en el diagnóstico de apendicitis aguda. **Objetivos:** Determinar si existe correlación entre el PDW y el diagnóstico de pacientes con apendicitis aguda, y definir su relación respecto a las fases de apendicitis. **Método:** Se realizó un estudio de casos y controles con dos grupos poblacionales, conformados por 41 pacientes mayores de 18 años con diagnóstico de apendicitis aguda (grupo I) y 41 sujetos sanos (grupo II). El análisis estadístico se realizó utilizando el programa SPSS versión 21. **Resultados:** Se observó una edad media de  $37.27 \pm 15.6$  años. La mayor cantidad de casos de apendicitis se presentaron en la fase III. La cifra total de leucocitos y el porcentaje de neutrófilos mostraron diferencias estadísticamente significativas. Se observó que no existe asociación entre

### Correspondence:

\*Rafael A. Espinosa-Campos

Dr. Balmis, 148

Col. Doctores, Del. Cuauhtémoc

C.P. 06720, Ciudad de México, México

E-mail: alejandro.escam@gmail.com

Date of reception: 13-12-2018

Date of acceptance: 24-05-2020

DOI: 10.24875/CIRUE.M22000175

Cir Cir (Eng). 2020;88(5):617-621

Contents available at PubMed

www.cirugiaycirujanos.com

2444-0507/© 2020 Academia Mexicana de Cirugía. Published by Permanyer. This is an open access article under the terms of the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

*la fase de apendicitis y los valores de PDW. Conclusiones: No hay diferencias entre los valores de PDW de pacientes con apendicitis aguda en comparación con sujetos sanos, ni relación del PDW con las fases de la apendicitis.*

**Palabras clave:** Apendicitis aguda. Diagnóstico. PDW.

## Introduction

Acute appendicitis clinical picture is the most common emergency surgical pathology worldwide. Its incidence increases between the second and fourth decades of life. Acute appendicitis diagnosis is clinically established with an accuracy rate of up to 85%. Clinical scales, such as the Alvarado score, have a diagnostic sensitivity of up to 88%, with a specificity of 75%. However, signs and symptoms are not specific and may vary depending on each patient, which makes it difficult for diagnosis to be accurately established<sup>1-3</sup>.

The rate of non-therapeutic laparotomy/laparoscopy due to probable appendicitis diagnosis is 15%, despite an increase in the use of diagnostic technologies, such as ultrasound and computed tomography (CT). Therefore, it is necessary for new complementary tests to be available for timely diagnosis. Some studies have examined the diagnostic efficacy of platelet distribution width (PDW), a blood count-measured platelet activation marker, as a new parameter that can be used for acute appendicitis diagnosis<sup>3-5</sup>.

PDW is an easily measurable and specific platelet activation marker, since it does not increase with platelet volume temporary changes (increase), as other markers do<sup>6</sup>. The platelet activation phenomenon causes morphological changes with volume increase since platelets acquire a larger surface area when changing from their discoid shape to a spherical shape with pseudopod formation<sup>7-9</sup>. Platelet size is correlated with their activity and function; larger platelets are more active than smaller ones, and PDW is an indicator of change in their size, which translates into a sign of platelet activation. PDW normal values in healthy individuals range from 10% to 17.9%<sup>10</sup>.

There are three studies in the literature that measure PDW diagnostic efficacy in patients with acute appendicitis. In 2013, Aydogan et al.<sup>5</sup> have the first group to carry out a retrospective study of 202 cases, without a control group, with patients being divided in two groups (complicated and uncomplicated appendicitis), with significantly higher PDW values being found in the complicated appendicitis group, thus concluding that PDW can be used as a marker for

appendiceal perforation risk early detection. In 2015, Dinc et al.<sup>3</sup> published the first case-control clinical trial, in which 295 cases were compared with two control groups, with a significant increase in PDW being observed in patients with acute appendicitis. They reported a sensitivity of 97.1% and specificity of 93%, which were higher than the sensitivity of leukocyte total count and neutrophil percentage (73.1% and 70%, respectively) and had a positive predictive value of 97.4% and negative predictive value of 92.1%. They conclude that it is possible for this test to be used as part of an initial battery of diagnostic tools for patients in whom appendicitis is suspected and thus reduce costs and loss of time in their diagnosis. In 2015, Fan et al.<sup>4</sup> published the second case-control study, which was the first to analyze only cases of complicated appendicitis. They observed a significant PDW increase in this group with regard to the control group of patients with uncomplicated appendicitis, with a sensitivity of 76.3% and specificity of 93.1% being reported, which was only surpassed by neutrophil percentage specificity, which was 96.9%. Their results confirm those obtained by Dinc et al.<sup>3</sup> and support that PDW is a parameter with high sensitivity for diagnosing cases of complicated appendicitis<sup>4</sup>.

These investigations have demonstrated a significant PDW increase in patients with acute appendicitis, suggesting this parameter as a marker that can be used for the early detection of this condition. However, it is necessary for prospective studies to be carried out to confirm these results. Herein, we present a case-control clinical study, in which the correlation existing between PDW and acute appendicitis diagnosis is demonstrated.

## Methods

A case-control study was carried out with patients from Dr. Fernando Quiroz Gutiérrez General Hospital, of the Institute of Social Security and Services for State Workers, in the period comprised from March 1 to September 30, 2016. The study was submitted to and approved by the ethics committee of said hospital. Two study groups were included, with the sample being calculated using demographic data and

previous 10 years cumulative incidence, which were made up of 41 patients older than 18 years with a diagnosis of acute appendicitis confirmed by histopathology (Group I) and 41 healthy subjects without comorbidity, who belonged to the donor population of the hospital blood bank (Group II). Patients with incomplete analyses and those who did not accept the surgical procedure were excluded from the study. Patients in whom surgical findings did not correspond to acute appendicitis, as well as those with histopathological studies not consistent with this diagnosis, were censored from the study.

Venous blood samples were taken from all patients by trained personnel, which were processed in test tubes with EDTA anticoagulant, using the hospital blood count equipment (SYSMEX, ROCHE brand, model XN-1000, serial number 14791), which is an automated and certified equipment. The samples were processed within a time period not exceeding 2 h.

Analyzed variables included age, gender, acute appendicitis phase, PDW, total leukocyte count, and neutrophil percentage. The Excel program was used to generate the database. Statistical analysis was performed using IBM® SPSS® Statistics v. 21 program.

Changes in PDW, total leukocyte count, and neutrophil percentage were measured in patients with acute appendicitis and in the control group, as well as PDW differences between men and women in both groups. Mann-Whitney's U statistical test was used, since the analyzed variables did not have a normal distribution, and a linear regression was carried out to determine the relationship of PDW, leukocyte total count, and neutrophil percentage with acute appendicitis phases. Finally, a comparison of the found data with those reported in medical international literature was carried out.

## Results

Mean age was  $37.27 \pm 15.6$  years; there was a larger number of patients aged <50 years (Fig. 1). With regard to distribution by gender, a higher frequency of the female gender was observed, with 56% of total sample in the group of cases (Fig. 2). As for the appendicitis phase at which variables were measured, the largest number of cases were at phase III, with 34% of total sample (Fig. 3). Leukocyte count and neutrophil percentage showed statistically significant differences in comparison with the control group (Tables 1 and 2). No

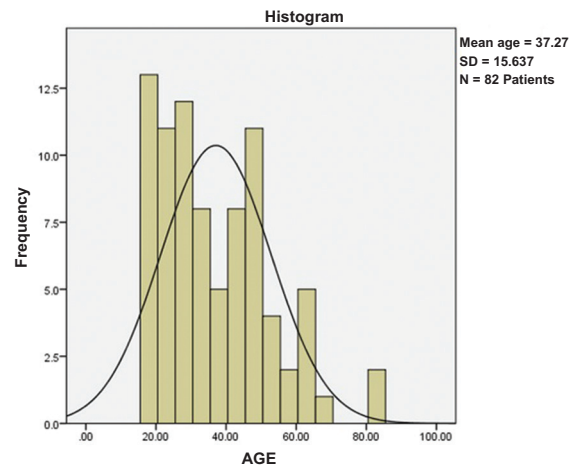


**Figure 1.** Study patients age distribution. The y-axis represents the frequency of presentation and the x-axis represents age. SD: standard deviation.

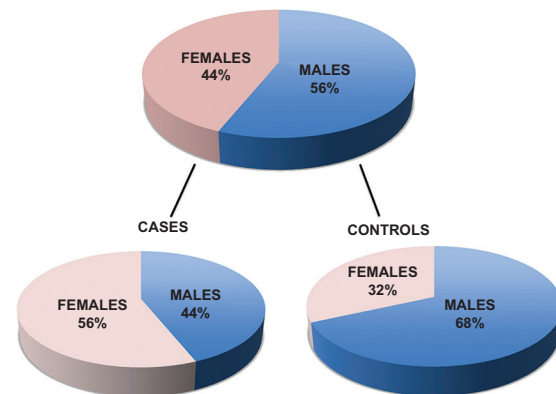


**Figure 2.** Study patients distribution by gender.

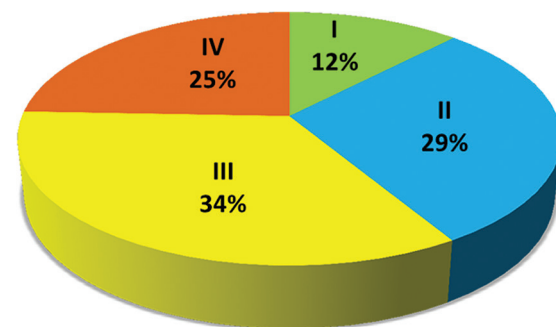


**Figure 3.** Distribution of the frequency of appendicitis phases at which the studied cases presented with.

association was observed between PDW values and the acute appendicitis phase, but there was a

**Table 1. Distribution of central tendency values and dispersion of variables analyzed in blood count**

| Variable                    | Cases |                    | Controls |                    |
|-----------------------------|-------|--------------------|----------|--------------------|
|                             | Mean  | Standard deviation | Mean     | Standard deviation |
| Platelet distribution width | 13.54 | 3.1                | 13.53    | 1.06               |
| Total leukocyte count       | 13.35 | 4.42               | 7.07     | 1.61               |
| Neutrophil percentage       | 79.97 | 8.34               | 58.79    | 9.33               |

**Table 2. Hypothesis testing for variables analyzed in blood count**

| Variable                    | Mann-Whitney value | Wilcoxon | P      |
|-----------------------------|--------------------|----------|--------|
| Platelet distribution width | 634.5              | 1,495.5  | 0.54   |
| Leukocyte total count       | 125                | 986      | 0.0001 |
| Neutrophil percentage       | 109.5              | 970.5    | 0.0001 |

**Table 3. Appendicitis phase linear regression with platelet distribution width, leukocyte total count, and neutrophil percentage**

| Variables in the model      | B      | p      |
|-----------------------------|--------|--------|
| Leukocyte total count       | 0.754  | 0.0001 |
| Neutrophil percentage       | 0.735  | 0.0001 |
| Platelet distribution width | -0.018 | 0.95   |

**Table 4. Hypothesis testing for platelet distribution width and gender in patients with appendicitis**

| Variable | Mann-Whitney | p     |
|----------|--------------|-------|
| Gender   | 145          | 0.101 |

directly proportional association for leukocyte total count and neutrophil percentage with appendicitis phases (Table 3). Regarding the association of PDW with patient gender, no differences were found either (Table 4).

## Discussion

Acute appendicitis is the most common cause of acute abdomen in all age groups. Rapidly and accurately establishing acute appendicitis diagnosis is

important, because lengthening of the time from symptom onset to patient admission to the operating room increases the risk of complications, such as appendiceal perforation, peritonitis, abdominal sepsis, and even death. Therefore, laboratory tests with high sensitivity and specificity are crucial for establishing reliable differential diagnoses<sup>1-3</sup>.

Leukocyte count is one of the most commonly used tests, as it is the first parameter to rise during an appendicular process; in the present study, the cutoff value was  $13.35 \times 10^9/L$ , which is consistent with those reported in the literature<sup>11</sup>. Similarly, numerous studies have evaluated the efficacy of differential neutrophil count for the diagnosis of patients with appendicitis; in this study, the cutoff value was 79.97%, similar to that internationally reported.

There are three studies in the literature that correlate PDW with acute appendicitis: the study by Aydoğan et al.<sup>5</sup> carried out in 2013, that by Dinc et al.<sup>3</sup> carried out in 2015, and that by Fan et al.<sup>4</sup> also performed in 2015. These investigations demonstrated a significant increase in PDW, suggesting that it is a marker that can be used for early detection of patients with acute appendicitis.

In the present prospective study, the sample was calculated, which allows to determine that the differences that were not found are not due to a sample size problem, but rather to the fact that there are no differences in observed PDW values. The patient age suggests that acute appendicular pathology occurs mainly in young adults, which allows assuming that possible concomitant conditions did not bias the results herein presented.

Determining differences were only possible for leukocyte total count and neutrophil percentage, with p-values < 0.05, as well as a statistically significant association of increase in both these variables with appendicitis phases, a situation that was expected given that the comparison group is a healthy group, but PDW showed no statistically significant differences.

Acute appendicitis diagnosis should always combine clinical findings with laboratory and imaging investigations, and although a biomarker can be an important evaluation parameter, it always has to be correlated with symptoms (pain migration, vomiting, etc.), signs on physical examination (right iliac fossa pain, McBurney's sign, or equivalents), laboratory tests (leukocytosis

and neutrophil percentage increase) and imaging studies (plain abdominal radiography, ultrasound, and tomography).

The purposes of this research were to observe PDW modifications in patients with acute appendicitis, its relationship with appendicitis phase and the differences between men and women with this condition. These goals were met when no PDW changes were observed in any of the evaluated parameters.

## Conclusion

There are no differences between PDW values of patients with acute appendicitis in comparison with healthy subjects, and neither is there a relationship between PDW and appendicitis phases, which is why we consider, according to the results obtained in the present study, that PDW is not a useful marker for acute appendicitis diagnosis. However, further prospective, multicenter studies need to be conducted to confirm these results.

## Acknowledgment

The authors would like thanks to the blood bank staff at Hospital General Dr. Fernando Quiroz Gutiérrez for availability and help provided for the conduction of this study. To doctors Carlos Alberto Pantoja Meléndez, Jazmin Escobar Juárez and Axel Edmundo Guzmán Cedillo, for their support for statistical and methodological analysis

## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Funding

The authors declare that they have not received any sponsorship to carry out this article.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this research.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

## References

1. Paulson EK, Kalady MF, Pappas TN. Clinical practice. Suspected appendicitis. *N Engl J Med*. 2003;348:236-42.
2. Rebollar González RC, García Álvarez J, Trejo Téllez R. Apendicitis aguda: revisión de la literatura. *Rev Hosp Jua Mex*. 2009;76:210-6.
3. Dinc B, Oskay A, Dinc SE, Bas B, Tekin S. New parameter in diagnosis of acute appendicitis: platelet distribution width. *World J Gastroenterol*. 2015;21:1821-6.
4. Fan Z, Pan J, Zhang Y, Wang Z, Zhu M, Yang B, et al. Mean platelet volume and platelet distribution width as markers in the diagnosis of acute gangrenous appendicitis. *Dis Markers*. 2015;2015:542013.
5. Aydoğan A, Akkucuk S, Arica S, Motor S, Karakus A, Ozkan OV, et al. The analysis of mean platelet volume and platelet distribution width levels in appendicitis. *Indian J Surg*. 2015;77(Suppl 2):495-500.
6. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. *Hippokratia*. 2010;14:28-32.
7. Shah AR, Chaudhari SN, Shah MH. Role of platelet parameters in diagnosing various clinical conditions. *Nat J Med Res*. 2013;3:162-5.
8. Sachdev R, Tiwari AK, Goel S, Raina V, Sethi M. Establishing biological reference intervals for novel platelet parameters (immature platelet fraction, high immature platelet fraction, platelet distribution width, platelet large cell ratio, platelet-X, plateletcrit, and platelet distribution width) and their correlations among each other. *Indian J Pathol Microbiol*. 2014;57:231-5.
9. Gasparian AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des*. 2011;17:47-58.
10. Farias MG, Schunck EG, Dal Bó S, Martins de Castro S. Definition of reference ranges for the platelet distribution width (PDW): a local need. *Clin Chem Lab Med*. 2010;48:255-7.
11. Al-Gaithy ZK. Clinical value of total white blood cells and neutrophil counts in patients with suspected appendicitis: retrospective study. *World J Emerg Surg*. 2012;7:32.