

# How COVID changed surgical acute inflammatory diseases and surgeons clinical practice during the first wave of COVID-19

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## Research article

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# Abstract

## *Background*

Anecdotal evidence suggests that community infection control measures during the COVID-19 outbreak have modified the number and natural history of acute surgical inflammatory processes (ASIP - appendicitis, cholecystitis, diverticulitis and perianal abscesses) admissions. This study aims to evaluate the impact of the COVID-19 pandemic on the presentation and treatment ASIP and quantify the effect of COVID-19 infection on the outcomes of ASIP patients.

## *Methods*

This was a multicentre, comparative study, whereby ASIP cases from March 14th to May 2nd 2019 acted as historical controls for the cohort of patients with the same pathology during the COVID-19 pandemic. Data regarding patient and disease characteristics as well as outcomes, were collected from sixteen centres in Madrid, and one in Seville (Spain).

## *Results*

The number of patients treated for ASIP in 2019 was 822 compared to 521 in 2020. This reduction occurs mainly in patients with mild cases, while the number of severe cases was similar.

## *Conclusions*

The number of ASIP cases treated during the pandemic was reduced by more than one third mainly due to a dramatic reduction in mild cases. This also has represented a selection of severe cases. We also found a more conservative approach to the patients this year, non-justified by clinical circumstances.

The positive COVID-19 status itself did not have a direct impact on either morbidity or mortality. This is an interesting finding which if confirmed through future research with a larger sample size of COVID-19 positive patients, can expedite the recovery phase of acute surgical services.

# Introduction

The first case of SARS-CoV-2 (COVID19) in Spain was confirmed on January 31st 2020. Since then, the virus has spread throughout Spain, making it one of the most affected countries in the world, with the Community of Madrid being the most intensely impacted. In addition to the lifestyle changes, a rapid restructuring and reorganisation of healthcare practices took place. In many countries, the COVID-19 crisis found the healthcare systems unprepared and precipitated a chain of events aiming to ensure that hospital services were not overwhelmed. Surgery services were greatly re-structured during the counter-pandemic measures, reducing surgeries only to urgent and emergency cases [1].

The pandemic had an inevitable impact on the care provided to acute surgical patients. Guided by early reports of worryingly high adverse events rates after surgery conservative approaches have been favoured [2, 3]. Attendances at the emergency departments due to surgical pathologies were reduced significantly [4, 5]. This phenomenon could suggest a change in the epidemiological presentation of these pathologies during the COVID-19 pandemic or merely the avoidance of seeking medical attention at all costs, due to fear of contracting the virus. Understanding the underlying reasons for the altered presentation patterns and the impact on patient outcomes within the context of a global pandemic, is crucial for guiding treatment during the recovery phase or a second wave of COVID-19.

The aim of this study was to evaluate the characteristics of the patients with appendicitis, cholecystitis, diverticulitis or perianal abscesses during the COVID-19 pandemic and compare it with the same 2019 timeframe. We also tried to identify factors that could be related with the differences observed within both periods.

## Methods

Ethical approval for this study was granted by the Clinical Research Ethics Committee of Hospital Universitario de La Princesa, Madrid, Spain (approval number: 2020-4076).

### *Study design:*

This was a multicentre comparative study, carried out at sixteen hospitals of the Community of Madrid and one hospital in Seville (Andalusia, Spain). Fourteen hospitals belong to the Madrid Public Healthcare System and serve an estimate of 4 400 000 inhabitants, 66.4% of Community of Madrid population.

### *Study population and time frame:*

Consecutive patients older than eighteen years of age with an ASIP diagnosis (acute appendicitis, acute cholecystitis, acute diverticulitis or perianal abscess) from March 14<sup>th</sup> 2020 (date of the declaration of the state of alarm by Spanish Government) to May 2<sup>nd</sup> 2020 (beginning of the gradual de-escalation plan) were included in this study (Cases group). Patients were excluded if an ASIP had been diagnosed within 30 days before admission or if the admission was due to a scheduled surgery for definitive treatment of the ASIP.

The results from this cohort of patients were compared with a historical control group consisting of ASIP cases treated within the same time frame the previous year (March 14<sup>th</sup> - May 2<sup>th</sup> 2019) (control group). An association between the daily difference of ASIP cases within both years in the hospitals from the Community of Madrid and the number of COVID-19 cases was assessed.

Demographic data were also collected, these included the Charlson Comorbidity Index (CCI) [6], ASIP diagnosis and severity (Table 1), COVID-19 diagnosis, treatment modality and mortality/morbidity (Clavien-Dindo Classification) [7]. Diverticulitis and cholecystitis severity were assessed according to the

modified Hinchey classification [8] and the Tokyo guidelines 2018 [9], respectively. Complications were considered severe in cases of grades 3 to 5 of Clavien-Dindo Classification and mild in grades 1 and 2. The data were collected retrospectively in the patients included before April 16th 2020 and prospectively from that date onwards.

### *Statistical analysis:*

Categorical variables were summarized as counts and proportions. Chi-squared Pearson test or Fisher's exact test were used for all relevant comparisons.

Continuous variables were presented as means and standard deviations. For comparison between means, t-test was used. When they did not follow a normal distribution, they were summarized as median and interquartile range, using Mann-Whitney U test for comparison purposes. Normality of distribution was assessed using a Kolmogorov-Smirnov test. The comparison of ASIP and COVID cases was made with the Pearson correlation test. When appropriate, logistic regression analysis was used to identify factors independently associated with those variables that showed differences with the control group. The variables were included in the model when the p-value was less than 0.1 on the univariate analysis or due to clinical importance. All reported p-values were 2-sided, and p-values <0.05 were considered statistically significant. All analyses were performed with SPSS software (Version 20.0, Chicago, IL, USA).

## **Results**

While in 2019 a total 822 patients were treated for ASIP, these numbers decreased to 521 in 2020 (-36.6%). Figure 1 displays the number of cases, controls and COVID-19 cases per day. We found a moderate correlation between the difference in cases among both years and the number of declared cases of COVID (Pearson correlation coefficient=0.413; p=0.003) (Figure 2).

Figure 1. Study timeline comparing daily number of patients of 2020 with 2019 and the number of COVID-19 cases diagnosed each day (This data refers to the Community of Madrid only).

Figure 2. Dispersion diagram of daily difference in number of ASIP within 2019 and 2020 and the number of COVID cases (Community of Madrid data only).

### *Appendicitis*

In 2020, 239 patients were treated for appendicitis, which represents a reduction of 33.4% from the previous year (359 patients). This reduction occurs mainly in cases of mild severity (-48.7%). Thirteen out of 148 patients with appendicitis tested for COVID-19, were positive (8.8%). A significantly higher number of patients exhibit delayed presentation (>7 days after onset of symptoms) during the pandemic (p=0.001). Moreover, while the absolute number of patients remains similar to the control group, a higher proportion of appendicular phlegmons and perforated appendices was noted (32.8% vs 20.3%). Surgical treatment was employed in the cases group less frequently (p=0.004) but when performed, a laparoscopic approach was less frequently adopted (p=0.001). Post-treatment complications were more

frequent in the case group (23 vs. 10.3%;  $p < 0.001$ ), however the number of severe complications was similar between the two groups. There was no mortality in these patients (Table 2).

The mean age and Charlson Comorbidity Index (CCI) of patients treated surgically in 2020 were significantly higher (74 vs 59 years [ $p < 0.001$ ]; 4 vs 2 [ $p < 0.001$ ]). Surgical treatment was also less commonly employed for patients with COVID-19 (69.2% vs 92.6%;  $p = 0.022$ ). The logistic regression model analysis showed COVID-19 infection to be the only predictor factor for conservative treatment (OR 0.188; CI95% 0.048-0.742). Similarly, the only factor related to employing an open (versus laparoscopic) approach was COVID-19 infection (55.6% vs 11.3%;  $p = 0.003$ ). However, only the severity at diagnosis was related with a higher risk of severe complications (0.9%, 5.9% and 18% in mild, moderate and severe cases, respectively), but not the COVID infection (7.7% vs 5.9%;  $p = 0.573$ ).

### *Cholecystitis*

A reduction in the number of cholecystitis cases was also observed (131 patients vs. 170 patients; -22.9%); similarly to appendicitis mild severity cases whom the greatest reduction (-35.2%). The number of severe cases were similar for both years. Thirteen of the 103 patients tested, were positive for COVID-19 (12.6%). Patients in the cases group were more commonly treated conservatively ( $p < 0.001$ ). The laparoscopic approach remains the preferred technique for both groups. Length of stay was longer in the cases group (6 vs 4 days;  $p = 0.018$ ). No other differences were observed between groups (Table 3).

In univariate analysis, age (conservative/surgical treatment group: 74 vs 59 years;  $p < 0.001$ ), CCI (4 vs 2;  $p < 0.001$ ) and COVID-19 infection (100% vs. 65.6%;  $p = 0.009$ ) were related with the election of conservative treatment, but in the multivariate analysis none of these variables were independently related with the treatment modality chosen.

Potential associations between variables and length of stay were sought. Although age ( $p < 0.001$ ), CCI ( $p < 0.001$ ), COVID infection (10 vs. 6 days;  $p = 0.014$ ) and non-surgical treatment (7 vs. 4 days;  $p < 0.001$ ) demonstrated a statistical significance initially, multivariable analysis showed CCI remains to be as the only independent factor related to a longer stay ( $p = 0.017$ ).

Patients with diverticulitis had the largest decrease in hospital admissions, with a 60% reduction (115 to 46). Whilst, mild cases were dramatically reduced (-84.4%), severe cases were also significantly reduced (-36.4%). Five of thirty-four patients with diverticulitis tested for COVID-19, were found to be positive (14.7%). The percentage of patients treated surgically was greater in the cases group ( $p = 0.015$ ). The length of stay was longer in these patients, as the percentage of overall and severe complications (Table 4).

Only severity at time of diagnosis was related with opting for surgical management (mild 14.3% vs moderate 0% vs severe 81.8%;  $p < 0.001$ ). Higher CCI and surgical treatment were related with longer length of stay ( $p = 0.02$ ). Logistic regression revealed that both CCI ( $p = 0.001$ ) and surgical treatment ( $p < 0.001$ ) were independent predictors for a longer admission. When complications were used as a dependent

variable for analysis, surgical treatment was the only predictor of severe complications (3.1% vs 42.9%;  $p=0.002$ ).

Similar to diverticulitis, perianal abscesses experienced a significant reduction (178 to 105; -41%, -42% in mild cases, -27.7% in moderate and -50% in severe). Six out of 60 patients tested were positive for COVID-19 test of 60 patients tested (10%). Thirty percent of patients attending with a perianal abscess waited more than 7 days before seeking specialised care. No differences were found between the two groups (Table 5).

## Discussion

### *Change in epidemiological pattern*

Our study represents an extensive observational registry of consecutive patients treated for ASIP during the most challenging period of the COVID-19 pandemic in a severely affected area. It demonstrated delayed presentation and increased rate of severity for diverticulitis and appendicitis cases. Patients with diverticulitis underwent surgical treatment more frequently during the pandemic than a year ago, probably in the context of a higher proportion of severe cases. Moreover, COVID-19 positive patients did not experience an increased risk of adverse events whether they were treated conservatively or not. This result should be interpreted with caution due to the limited number of COVID-19 positive patients included in this study. However, recently published studies have found evidence that points in this same direction [10,11].

According to a serological study about immunity against COVID developed by the Spanish Government, 11.4% of Madrid population have immunoglobulins against COVID [12], which could represent over 600.000 cases. The effect of COVID pandemic on emergency surgery has been a subject of analysis in several studies [13-16]. The results of the PIACO study are consistent with other studies in the current literature. The significant decrease in ASIP admission to during COVID-19 pandemic was also demonstrated in a matched case-control study of appendicitis [17]. Our data also reflect that the most dramatic drop in admissions occurred during the peak of the pandemic and tends to normalize with the decrease in the number of confirmed COVID-19 cases. Whilst the number of admissions was reduced the complexity and severity of cases during the pandemic was similar to the previous year. This study has some limitations. It only included patients who required admission in a hospital setting. Information about outpatients is not available, which could represent a selection bias, however, this study provides a useful insight on the presentation patterns of ASIP pathology at hospitals covering approximately the 70% of the population of the Community of Madrid. These reduction in mild cases without a raise in severe cases suggest that outpatient treatment could be useful in some cases.

The generalisability of the results of this study is further enhanced by the inclusion of both public and private hospitals. Moreover, during the study period, primary care emergencies and elective services remained closed and the healthcare professionals were redeployed to other facilities caring for COVID

patients (e.g. Hospital created in the Madrid Fair). In this setting, all the emergencies were treated in the hospitals. Surgeons were redeployed in emergency services in the hospitals looking after surgical emergencies. Therefore, the number of patients with ASIP diagnosis that were treated in community-based facilities (and hence not included in this study) is minimal.

Moreover, although the overall sample size is adequate, the number of COVID-19 positive patients included in this study is limited therefore any outcomes related to this group of patients should be interpreted with caution.

The exact reason for the drop-in admission numbers is unknown and it is an interesting field of research. Perhaps the most plausible theory, is that low complexity cases were treated as outpatients, self-medicated or even cured without any treatment. This could be especially relevant in mild diverticulitis cases, which display the higher case reduction (60%), and appendicitis. Outpatient treatment of mild diverticulitis in low-risk patients was already a routine practice in most of the participant hospitals and recent guidelines recommend that antibiotics for uncomplicated diverticulitis, are not necessary [18]. However, current data supports that this concept could be translated to non-complicated appendicitis and is an interesting field for future research.

The decline in surgical admission numbers can also be explained by self-medication with over the counter medication. It has been proven that lockdown helped to stop the expansion of the coronavirus [19] and Spanish population suffered one of the hardest confinements imposed by the Spanish government. As the message sent to the population was to avoid leaving their houses except for essential activities, it is possible that patients with mild symptoms tried not to seek medical attention. This behavioural modification combined with the fear of getting exposed to COVID-19 at the hospital could also contribute to the reduction of ASIP admissions. The results of the study suggest that all ASIP but diverticulitis have an increased evolution time. This would explain why despite late presentation of patients the severity of ASIP cases (with the exception of diverticulitis) during the pandemic was similar to last year. However, due to the paucity of evidence on how ASIP cases progress without any medical attention, it is difficult to prove a causative relationship between the prolonged natural history of a disease and the lack of a higher number of severe presentations in our cohort. Other factors may also have contributed to the observed reduction in cases. There is some evidence that air pollution could be related to inflammatory gastrointestinal pathologies. This association has a plausible explanation relating inhaled pollutants being ingested after mucociliary clearance. Pollutants can then affect intestinal epithelium and microbiota altering lipid metabolism and particularly intestinal redox lipids, which are associated with intestinal and systemic inflammation [20]. At an epidemiological level, this relation has been observed especially regarding acute appendicitis, in which a seasonal pattern has been identified [21], and some studies relate this seasonality to the level of air pollution [22-25]. COVID-19 pandemic caused a series of lockdown measures on most of the countries it affected that led into a great reduction in personal mobility, goods shipping and industry production. Along with the reduction in transportation, there has been an air pollution reduction observed in Spain [26].

COVID-19 infections clearly play a role in the host immune response mainly through modifying cytokine production resulting in pulmonary tissue damage and the immune insufficiency that may increase viral replication [27]. Coronavirus also produces lymphopenia in 82,1% of the hosts [28]. These coronavirus-host interactions may also have influenced the response to acute inflammatory surgical diseases mitigating the immunological response and thus prolonging or stopping the natural history of ASIP cases.

## ***Changes in clinical practice***

It is not possible to reduce emergency surgery without altering the quality of care provided to surgical patients [29]. The COVID-19 pandemic has impacted our practice [3] in favour of more conservative attitudes [2]. This was shown in this study as well. Conservative treatment was safe and did not increase the overall morbidity. However, this conservative approach impeded the patients to benefit from the advantages of laparoscopic appendicectomy and early cholecystectomy in acute cholecystitis.

During the COVID-19 crisis postponement of elective procedures was supported by esteemed surgical societies [31-33]. Delay is not usually an option with emergency cases; the dilemma is between surgical or conservative treatment. In these situations, we have seen a change to a more conservative approach, aiming to spare patients the adverse events after surgery which were reported at the early days of the COVID-19 pandemic. This is more prominent in the treatment of cholecystitis, whereby we found a complete inversion in the percentages of surgical versus conservative treatment, which was not associated with a variance in patient characteristics. As a result of selection of conservative treatment, the length of stay of these patients has also risen significantly. Moreover, fewer procedures were performed laparoscopically, which may also have contributed to the prolonged length of stay. This phenomenon can be attributed to concerns about a higher risk of transmissions due to aerosolization. However, more recent literature does not support a higher risk of transmission with smoke [34] and some authors publish that laparoscopy may be safer [35].

## **Conclusions**

Our data shows that the COVID-19 outbreak has changed the patterns of the presentation of ASIP cases selecting more severe cases. But the main change observed is due to a step backwards in surgical standards in appendicitis and cholecystitis, with more a conservative approach to both processes. The delay observed in the presentation had a questionable influence in the presentation of the cases, as we didn't find a higher number of severe cases, raising only the proportion of severe cases.

Whilst the COVID-19 outbreak selected more complex cases, the positive COVID-19 status itself did not have a direct impact on either morbidity or mortality. This is an interesting finding which, if confirmed through future research with a larger sample size of COVID-19 positive patients, can expedite the recovery phase of acute surgical services.

# Declarations

- Ethics approval and consent to participate: Ethical approval for this study was granted by the Clinical Research Ethics Committee of Hospital Universitario de La Princesa, Madrid, Spain (approval number: 2020-4076).
- Consent for publication: Not applicable.
- Availability of data and materials: The datasets used and/or analysed 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: None.
- Authors' contributions:
  - HG: Study conception, design of the work, analysis and interpretation of data, draft and review of the manuscript.
  - JLMN: Acquisition, analysis and interpretation of data. Draft and review of the manuscript.
  - SFG: Analysis and interpretation of data. Draft and review of the manuscript.
  - MY: Draft and review of the manuscript. Style correction.
  - MRR: In site study coordination. Data acquisition. Draft and review of the manuscript.
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  - ELM: In site study coordination. Data acquisition. Draft and review of the manuscript.
  - EMP: In site study coordination. Data acquisition. Draft and review of the manuscript.
  - DGO: Substantial contributions to the study conception, design of the work and review of the manuscript.
  - PIACO Collaboration Group: Acquisition of data.

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## Tables

Table 1.- Severity Classification of Acute Surgical Inflammatory Processes			
	Mild	Moderate	Severe
Appendicitis	Phlegmonous	Gangrenous non-perforated Appendicular phlegmon	Perforated
Cholecystitis	Grade 1 <sup>a</sup>	Grade 2 <sup>a</sup>	Grade 3 <sup>a</sup>
Diverticulitis	Grade 1 <sup>b</sup>	Grade 2 <sup>b</sup>	Grades 3-4 <sup>b</sup>
Perianal abscess	Unilateral	Bilateral	Fournier's gangrene
a. Modified Hinchey Classification [8]			
b. Tokyo Guidelines 2018 [9]			

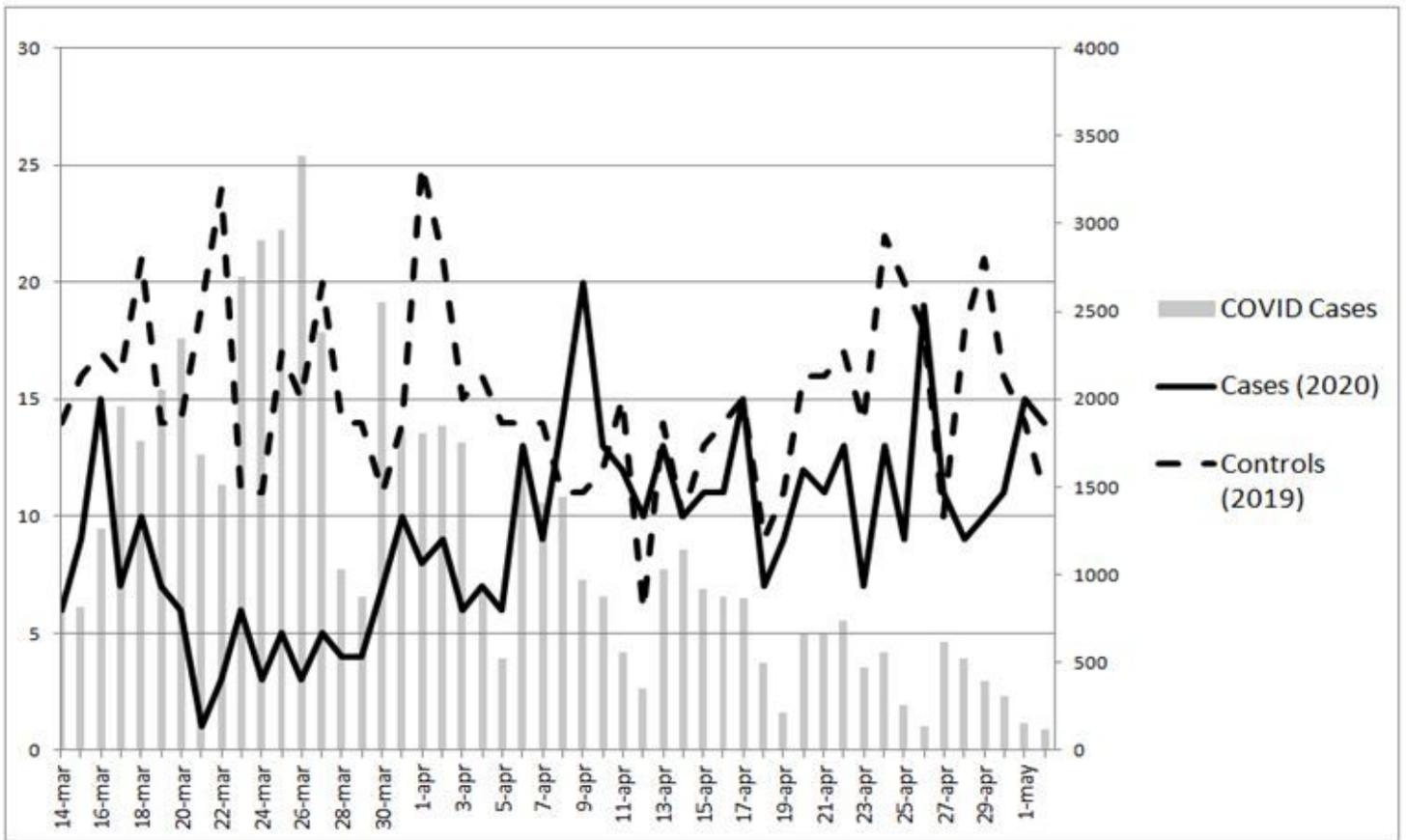
Table 2.- Appendicitis patients characteristics			
	Cases (2020)	Controls (2019)	p-value
Male gender n (%)	138 (57.7)	175 (48.7)	<b>0.031</b>
Age (years) median (IQR)	27 (39-54)	27 (37-51)	0.285
CCI median (IQR)	0 (0-1)	0 (0-1)	0.387
Delay >7 days n (%)	19 (7.9)	8 (2.3)	<b>0.001</b>
Severity at diagnosis			
Mild n (%)	117 (49.8)	228 (63.5)	<b>0.003</b>
Moderate n (%)	67 (28.5)	81 (22.6)	
Severe n (%)	51 (21.7)	50 (13.9)	
Appendicular lump n (%)	26 (11.1)	23 (6.4)	<b>0.043</b>
Surgical treatment n (%)	221 (92.5)	350 (97.5)	<b>0.004</b>
Laparoscopic approach n (%)	183 (83.2)	324 (92.6)	<b>0.001</b>
Length of stay (days) median (IQR)	2 (1-5)	2 (1-4)	0.054
Complications (any grade) n (%)	55 (23)	37 (10.3)	<b>&lt;0.001</b>
Severe complications (grade 3-5) n (%)	14 (5.9)	11 (3.1)	0.097

Table 3.- Cholecystitis patients characteristics			
	Cases (2020)	Controls (2019)	p-value
Male gender n (%)	76 (58.5)	102 (60)	0.788
Age (years) median (IQR)	70 (53-79)	66 (54.7-78.2)	0.225
CCI median (IQR)	3 (1-5)	3 (1-5)	0.574
Delay >7 days n (%)	22 (16.8)	22 (12.9)	0.348
Severity at diagnosis			
Mild n (%)	46 (35.1)	71 (41.8)	0.444
Moderate n (%)	68 (51.9)	82 (48.2)	
Severe n (%)	17 (13)	17 (10)	
Surgical treatment n (%)	41 (31.3)	115 (67.6)	<b>&lt;0.001</b>
Laparoscopic approach n (%)	37 (90.2)	106 (92.2)	0.745
Length of stay (days) median (IQR)	6 (4-10)	4 (3-7.2)	<b>0.018</b>
Complications (any grade) n (%)	33 (25.2)	28 (16.5)	0.062
Severe complications (grade 3-5) n (%)	10 (7.6)	14 (8.2)	0.848
Mortality n (%)	5 (3.8)	3 (1.8)	0.301

Table 4.- Diverticulitis patients characteristics			
	Cases (2020)	Controls (2019)	p-value
Male gender n (%)	21 (45.7)	54 (47)	0.881
Age (years) median (IQR)	62 (48.7-71.7)	66 (54-76)	0.116
CCI median (IQR)	2 (0-3)	2 (1-4)	0.564
Delay >7 days n (%)	9 (19.6)	11 (9.6)	0.086
Severity at diagnosis			
Mild n (%)	10 (22.2)	64 (55.7)	<b>0.001</b>
Moderate n (%)	21 (46.7)	29 (25.2)	
Severe n (%)	14 (31.1)	22 (19.1)	
Surgical treatment n (%)	14 (30.4)	16 (13.9)	<b>0.015</b>
Laparoscopic approach n (%)	3 (21.4)	8 (53.3)	0.077
Length of stay (days) median (IQR)	7 (5-12)	5 (3-8)	<b>0.003</b>
Complications (any grade) n (%)	17 (37)	15 (13)	<b>0.001</b>
Severe complications (grade 3-5) n (%)	7 (15.2)	5 (4.3)	<b>0.040</b>
Mortality n (%)	0 (0)	1 (0.9)	1

Table 5.- Perianal abscess patients characteristics			
	Cases (2020)	Controls (2019)	p-value
Male gender n (%)	81 (77.1)	125 (70.2)	0.206
Age (years) median (IQR)	45 (35-59.5)	46.5 (37-59)	0.566
CCI median (IQR)	0 (0-2)	0 (0-2)	0.519
Delay >7 days n (%)	29 (27.6)	27 (15.3)	<b>0.012</b>
Severity at diagnosis			
Mild n (%)	87 (83.7)	150 (85.2)	0.819
Moderate n (%)	13 (12.5)	18 (10.2)	
Severe n (%)	4 (3.8)	8 (4.5)	
Surgical treatment n (%)	104 (99)	177 (99.4)	1
Length of stay (days) median (IQR)	1 (1-3)	1 (1-3)	0.569
Complications (any grade) n (%)	12 (11.4)	21 (11.8)	0.926
Severe complications (grade 3-5) n (%)	6 (5.7)	15 (8.4)	0.400
Mortality n (%)	0 (0)	3 (1.7)	0.297

## Figures



**Figure 1**

Study timeline comparing daily number of patients of 2020 with 2019 and the number of COVID-19 cases diagnosed each day (This data refers to the Community of Madrid only).

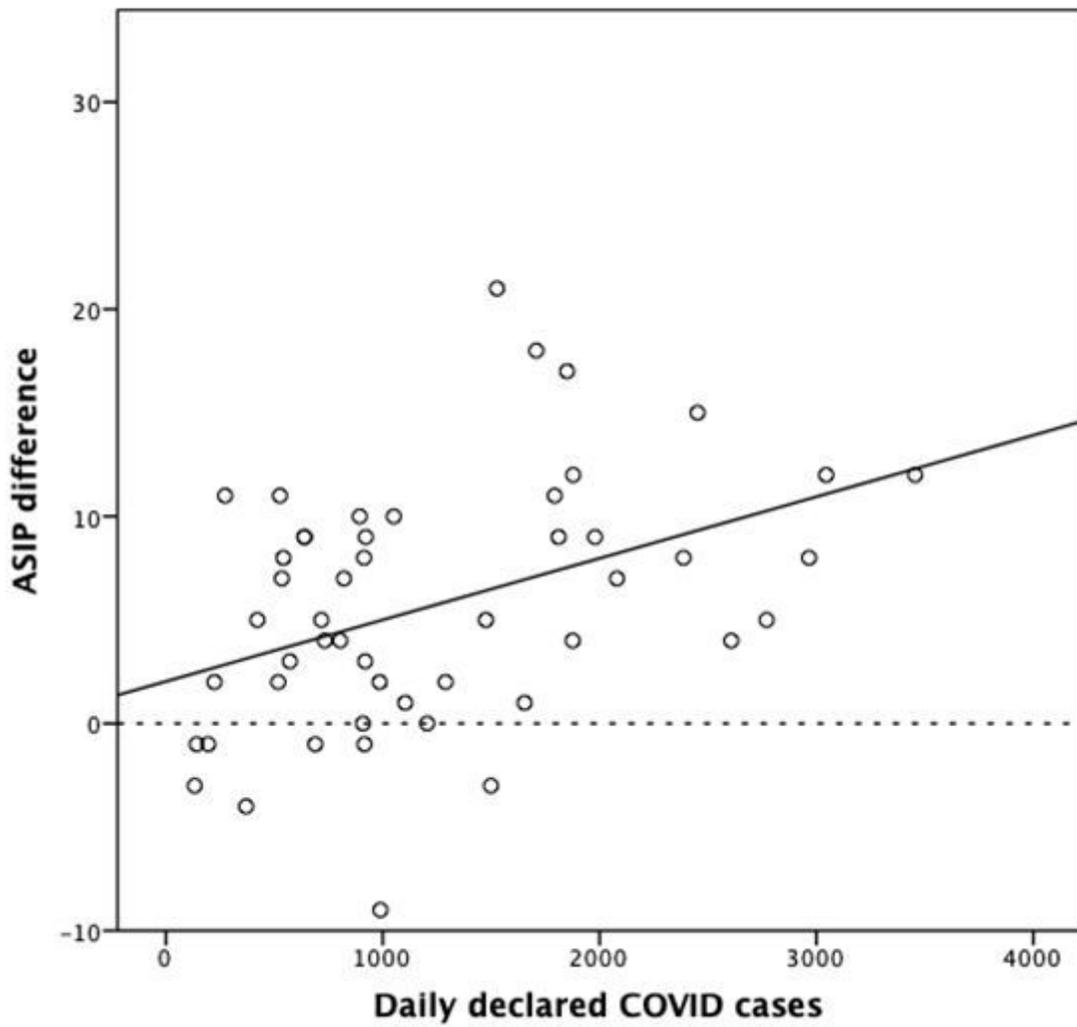


Figure 2

Dispersion diagram of daily difference in number of ASIP within 2019 and 2020 and the number of COVID cases (Community of Madrid data only).