Fecal calprotectin as a prognostic factor for gastrointestinal involvement in pediatric Henoch-Schölein purpura patients: a retrospective analysis

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Research article

Keywords: Gastrointestinal tract, Child, Calprotectin, Henoch–Schönlein purpura

Posted Date: April 9th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-21357/v1

Version of Record: A version of this preprint was published on August 8th, 2020. See the published version at https://doi.org/10.1186/s12887-020-02263-x.

Abstract

Background Henochchönlein purpura (HSP) is a systemic vasculitis occurring in children. HSP prognosis is usually good, but its recurrence is relatively common, and if the intestines get affected, severe complications could arise, including intussusception or intestinal perforation. Here, we investigated the value of fecal calprotectin (FC) in early screening of HSP and the usefulness of FC as a prognostic factor for GI manifestations.

Methods We retrospectively reviewed the medical records of pediatric patients who were diagnosed with HSP and had undergone FC testing during the acute phase. Subjects were categorized into gastrointestinal (GI) involvement and non-GI involvement groups based on their clinical symptoms. Moreover, GI involvement levels were divided as follows: upper GI tract up to the duodenum and lower GI tract from the ileocolic

Results Sixty-nine patients were diagnosed with HSP and underwent FC testing. Among them, 40 patients (58.0%) showed signs of GI involvement. The GI involvement group showed higher FC levels (379.9 ± 399.8 vs. 77.4 ± 97.6 mg/kg, P = 0.000). There were no significant differences in the relapse of HSP symptoms or GI symptoms. The cut-off value according to GI involvement was 69.10 mg/kg (P < 0.01). Patients with FC levels of >50 mg/kg more frequently showed GI involvement (77.8% vs. 20.8%, P = 0.000) and a more severe prognosis. Significant correlations were observed for abdominal pain duration, HSP clinical score, and abdominal pain severity (P = 0.002, P = 0.000, and P = 0.000, respectively). Additionally, FC levels were significantly higher in patients with lower GI tract involvement (214.67 ± 150.5 vs. 581.8 ± 510.1 mg/kg, P = 0.008), and the cut-off value was 277.5 mg/kg (P < 0.01).

Conclusion FC testing is useful for predicting the involvement of GI, location of involvement, and course of prognosis in pediatric HSP patients.

Background

Henoch–Schönlein purpura (HSP) is a systemic vasculitis involving small vessels, which is characterized by a peculiar skin rash, arthritis and gastrointestinal (GI) and renal symptoms.[1] Its annual incidence is estimated to be 14–20 cases per 100,000 persons, and over 90% of the incidents occur in children.[2] The prognosis of HSP is usually good, and most patients attain spontaneous remission after 4–5 weeks. However, recurrence is relatively common, and if the intestines or kidneys are affected, treatment may be needed.[3] The patient's intestines are affected in approximately 80% of all cases, and without appropriate treatment, it can lead to severe complications including intussusception or intestinal perforation.[4] Therefore, regular follow-up is important to prevent such complications. Abdominal pain, vomiting, melena, hematochezia, and other GI symptoms can be an evidence of GI involvement in HSP patients, but the symptoms may be nonspecific, and if the symptoms are not severe, it is challenging to make an early clinical diagnosis.[5]

Recently, some laboratory markers or clinical scoring systems have been used for determining the diagnosis or severity of HSP. Moreover, examination techniques such as abdominal ultrasonography (USG) and computed tomography (CT) may be used for diagnosing GI involvement in HSP patients.[6] Furthermore, invasive examination techniques, including esophagogastroduodenoscopy (EGD), have been used to substantiate the severity of GI involvement.[7] However, the existing diagnostic methods have limitations in terms of early diagnosis or accuracy and are invasive or inconvenient for follow-up examinations.

Calprotectin is a complex having high affinity for calcium, zinc, iron, and manganese.[8] It is predominantly found in neutrophilic granulocytes and its levels may be elevated in inflammatory conditions. Calprotectin can be detected in feces because the neutrophils migrate to the intestinal mucosa when intestinal inflammation occurs. Therefore, fecal calprotectin (FC) elevation indicates intestinal inflammation, and it has been used as a biomarker for diagnosing the activity of inflammatory bowel disease.[9] Furthermore, it can be used as an indicator for other intestinal diseases, including polyps, bacterial GI infection, and necrotizing enterocolitis.[10] We expected that FC levels could be used to identify GI involvement, severity, recurrence, and invasion site in HSP patients. Here, we investigated the value of FC in the early screening and diagnosis of complications among HSP patients and its usefulness as a prognostic factor for GI manifestations.

Methods

Patient selection

We retrospectively reviewed the medical records of pediatric patients aged < 18 years who were diagnosed with HSP and hospitalized at Chung-Ang University Hospital or Kyungpook National University Hospital between February 2015 and June 2019. Among these patients, the patients who underwent FC testing during the acute phase were selected as the study group. Cases of an uncertain HSP diagnosis and cases showing comorbidities, such as those with a positive stool culture result, which may affect FC levels were excluded from this investigation. Additionally, patients with indefinite GI symptoms and patients with abdominal pain that could have been caused by other factors, including fecal impaction, were excluded. Consequently, 69 patients were included in the study, and their clinical information, laboratory results, USG results, and CT results were reviewed.

Data extraction

Subjects were categorized into GI involvement and non-GI involvement groups based on clinical symptoms, including abdominal pain, vomiting, hematemesis, melena, and abdominal tenderness. In addition to the clinical symptoms, imaging results of USG, CT, and EGD were auxiliary to confirm GI involvement, and to determine involvement level. Consequently, GI involvement levels were categorized according to the two most frequently involved sites as follows: upper GI tract up to the duodenum and lower GI tract from the ileocolic.[4, 5] Medical records were reviewed to investigate the duration of

hospitalization, joint or kidney involvement, HSP activity scores, recurrence of symptoms, severity of GI involvement measured via HSP activity scores, and duration of steroid treatment.[11,12] Laboratory findings, including white blood cell count, absolute neutrophil count, erythrocyte sedimentation rate, C-reactive protein level, fibrin degradation product (FDP), D-dimer, and stool occult blood (SOB), were also checked.[13–14] FDP and D-dimer tests were only performed at Chung-Ang University Hospital and not at Kyungpook National University Hospital. FC (GEMINI, Strategic Biomedical, Germany) tests were performed on the first day of hospitalization, and the results were measured up to 2000 mg/kg at both hospitals. The FC levels of all the patients to be investigated were examined and confirmed according to their groups, and an inter-group comparison was also conducted based on a cut-off value of 50 mg/kg, which is considered as the normal threshold for children aged > 4 years.[8]

Ethics statement

This study was conducted after obtaining approval from the Institutional Review Board of Chung-Ang University Hospital (IRB no.: 1712-014-16123) and Kyungpook National University Hospital (IRB no.: 2020-03-019), and informed consent was waived owing to the retrospective nature of the study.

Statistical analysis

Statistical analysis was performed using SPSS 18.0 statistical software (SPSS Inc., Chicago, IL, USA). The chi-square test and Student's t-test were used to compare between the groups, and the corresponding data were presented as mean and standard deviation values. Linear regression test was used to compare the continuous variables. Correlation of FC levels with GI involvement and the involved part of the GI tract were investigated, and the ROC curve was used to determine the diagnostic cut-off values. *P* values of < 0.05 were considered to be statistically significant.

Results

Clinical features and laboratory results of pediatric HSP patients who underwent FC testing

Sixty-nine patients were diagnosed with HSP and underwent FC testing in both hospitals (57 patients at Chung-ang University Hospital and 12 patients at Kyungpook National University Hospital) (Tables 1 and 2). Of the 69 patients, 37 (53.6%) were males and 32 (46.4%) were females, and their mean age was 6.85 ± 2.93 years. The mean hospitalization period, HSP activity index, and FC level of the patients were 5.41 ± 5.27 days, 1.99 ± 1.53, and 252.7 ± 343.8 mg/kg, respectively. Of all the patients, 40 patients (58.0%) showed signs of GI involvement, including vomiting, abdominal pain, bloody stool, or significant test results from USG, CT, or EGD imaging studies, and 29 patients (42.0%) showed no evidence of GI involvement.

In total, 23 patients (33.3%) showed recurring symptoms related to the initial symptoms, including involvement of the skin, joints, and GI tract, and 19 patients (27.5%) showed recurring GI symptoms unrelated to the initial ones.

Difference according to GI involvement

The clinical manifestations of the GI involvement group and the non-GI involvement group are compared in Table 1. There was no difference in the mean age or sex between the two groups, but the mean hospitalization period was longer in the GI involvement group (7.25 ± 6.05 vs. 2.79 ± 1.97 days, P = 0.000). Patients with GI involvement exhibited a more frequent occurrence of joint symptoms (40.0% vs. 65.5%, P = 0.036) but showed no correlation with kidney involvement. The GI involvement group showed higher HSP clinical scores (2.65 ± 1.59 vs. 1.07 ± 0.80, P = 0.000) and higher FC levels (379.9 ± 399.8 vs. 77.4 ± 97.6 mg/kg, P = 0.000). There were no significant differences with regard to the recurrence of HSP or GI symptoms. The value of the area under the ROC curve for FC level was 0.844, which was statistically significant (P < 0.01) and had a diagnostic accuracy with sensitivity and specificity values of 87.5% and 72.4%, respectively, when the cut-off value for FC level was 69.10 mg/kg (Figure 1). Additionally, SOB, FDP, and D-dimer levels were different between the two groups (P = 0.000, P = 0.064, and P = 0.036, respectively).

Difference according to FC levels

The clinical manifestations of patients with FC levels over and under 50 mg/kg are compared in Table 2. Patients with FC levels of >50 mg/kg showed more frequent GI involvement (77.8% vs. 20.8%, P = 0.000), longer hospitalization duration, and longer GI symptom duration (P = 0.043 and P = 0.001). Moreover, HSP clinical score, GI symptom severity, fasting duration, steroid treatment, and steroid duration also differed (P = 0.005, P = 0.000, P = 0.040, P = 0.012, and P = 0.003, respectively). However, FC levels were not related to the involvement site or HSP or GI symptom recurrence.

As shown in Table 3, no significant difference in the mean FC level was observed when compared in the context of HSP recurrence and GI symptom recurrence (P = 0.218 and P = 0.176). However, significant correlations were noted with regard to the abdominal pain duration, HSP clinical score, and abdominal pain severity (P = 0.002, P = 0.000, and P = 0.000, respectively). Additionally, FC levels were significantly higher in patients with lower GI tract involvement than in patients with upper GI tract involvement (up to the duodenum) (214.67 ± 150.5 vs. 581.8 ± 510.1 mg/kg, P = 0.008). The value of the area under the ROC curve for FC level was 0.768, which was statistically significant (P < 0.01) and had a diagnostic accuracy with sensitivity and specificity of 77.8% and 77.3%, respectively, when the cut-off value for FC level was 277.5 mg/kg (Figure 2). Fasting status, fasting duration, steroid use, and steroid duration also showed statistically significant correlations (P = 0.047, P = 0.004, P = 0.001, and P = 0.000, respectively). The mean levels of FC were not correlated with other inflammatory markers, except SOB.

Test results of patients with joint or kidney involvement

There was no significant difference in the mean FC levels between patients with joint or kidney involvement (Table 4). Furthermore, other laboratory inflammatory markers could not predict joint or kidney involvement or its severity.

Discussion

Calprotectin is a 36.5-kDa long calcium- and zinc-binding protein consisting of heterodimers of the S100A8 (MRP-8) and S100A9 (MRP-14) subunits.[15–17] It is commonly found in neutrophilic granulocytes and may be elevated in inflammatory conditions. In particular, FC remains stable in feces for more than 1 week, and thus, it is a useful marker for intestinal inflammatory reactions. FC test is widely used to diagnose the activity of inflammatory bowel disease, and nowadays, it is gradually being used to diagnose infectious gastroenteritis, necrotizing enteritis, and other intestinal diseases.[18–22]

FC was used to investigate the association between HSP GI involvement and other clinical symptoms of HSP and to determine the prognosis and progression of the disease. Other prospective studies have explored the association between FC and HSP.[13, 23] Because these studies were prospective in nature, they were able to determine the changes in FC levels caused by improvements in HSP symptoms; contrastingly, because our study had a retrospective design, we could not determine such changes. Our study, however, may have had an advantage in objective identification of disease prognosis or progression because the medical records of our patients were retrospectively reviewed. Moreover, because our study group comprised only HSP patients and not healthy controls, identifying the prognosis of GI involvement or recurrence in HSP patients proved to be advantageous. Our results revealed that FC levels were significantly correlated with GI involvement, GI symptom duration, fasting state/steroid treatment durations, and GI involvement site. FC results also showed a positive correlation with HSP clinical score, including the GI severity score. However, there was no correlation between joint or kidney involvement scores and FC levels, and unlike previous studies, there was no correlation between FC levels and inflammatory markers such as white blood cell count, absolute neutrophil count, and C-reactive protein or kidney involvement itself.[13, 23] This can be attributed to the difference between the investigation groups. Because not all HSP patients, but only FC-tested patients, were included in the study, many other patients need to be investigated, including all HSP patients with a simple rash.

FC test has low specificity but high sensitivity for the early detection of intestinal inflammation.[8] Owing to the nature of FC testing, we expected that FC testing might facilitate the prediction of GI involvement site or GI symptoms in patients who did not initially have GI symptoms. Mostly, HSP patients with GI involvement showed invasion in the upper parts of the GI tract including the duodenum. However, compared with the patients who experienced invasion limited to the upper parts of the GI tract, patients who experienced invasion to the lower parts of the GI tract, including the colon, showed a significantly high FC level (214.7 ± 150.5 vs. 581.8 ± 510.1 mg/kg; $P = 0.008$). Contrastingly, there was no significant difference in the clinical manifestations and prognosis between patients with positive FC results (> 50 mg/kg) and those with negative FC results (< 50 mg/kg). In our study, the cut-off FC level for GI

involvement was 69.10 mg/kg, which was much lower than the value reported by Teng et al., i.e., 264.5 mg/kg. [23] This result was similar to the cut-off level for lower GI involvement reported in our study, i.e., 277.5 mg/kg, and it is evident that this is an interesting finding as opposed to the previous study. Therefore, if FC levels are elevated in HSP patients with GI symptoms, it is necessary to more carefully check the possibility of lower GI complications such as intussusception. Moreover, there was no correlation between HSP relapse and GI symptom recurrence. We expected that elevated FC levels would be a predictor of future GI symptoms in patients with only simple purpura, but no correlation was found.

Kanik et al. previously reported that FC levels were also associated with renal involvement.[13] Hence, we identified the association of FC with kidney or joint involvements, which are other major symptoms of HSP. However, no significant associations were confirmed in our results. Moreover, these manifestations showed no correlation with severity of GI symptoms. Because FC is a marker for intestinal inflammation, it is believed that it has no correlation in cases where only kidney or joint involvement alone occurs while GI involvement is lacking. Furthermore, in another study by Teng et al., only the association of FC with GI involvement had been reported.[23]

In a study conducted by Hong et al.,[14] various inflammatory markers, including FDP and D-dimer, showed correlations with GI involvement in HSP, but in our study, only FDP and D-dimer levels were higher when GI involvement occurred. It was also difficult to find relevance to FC levels and other symptoms. SOB and FC levels seemed to be the most meaningful laboratory results that showed highest correlation with GI symptoms.

Although we proved that FC is related to the characteristics and prognosis of GI involvement in HSP patients, our study had some limitations. First, the GI involvement group was retrospectively classified based on clinical symptoms, physical examinations, and imaging test results. Although patients who had abdominal pain likely caused by factors other than HSP were excluded from the study group, there still remains a possibility that these patients were included. However, of the 40 patients with abdominal pain, only one patient did not undergo ultrasonography, CT, or endoscopy. Contrastingly, no imaging tests were conducted when GI symptoms were absent; therefore, some patients with GI involvement might have been classified into the non-GI involvement group. It is especially likely that patients with high FC levels were classified into the non-GI involvement group. Second, FC was prescribed at the time of admission, but there were cases in which FC was prescribed only 2–3 days later. Furthermore, FC levels were tested only in inpatients and not in outpatients with only simple purpura or mild symptoms. However, this does not change our results because all such cases are expected to have a lower FC level than that noted for our study group, and if these limitations were not present, our results would be more strongly supported. Finally, in our results, of the 23 relapsed patients, GI symptoms relapsed in 19 patients. However, because many patients with simple purpura alone are likely to not visit the hospital, symptoms such as simple rash are expected to be reported more frequently than GI symptoms among all HSP patients.

Despite these limitations, FC testing is useful for predicting GI involvement, the involvement site, and the course of prognosis in pediatric HSP patients. Better results can be expected if a larger number of

patients are investigated, including those with simple skin rashes alone.

Abbreviation List

HSP: Henoch–Schönlein purpura, GI: gastrointestinal, USG: ultrasonography, CT: computed tomography, EGD: esophagogastroduodenoscopy, FC: fecal calprotectin, FDP: fibrin degradation product, SOB: stool occult blood

Declarations

Ethics approval

This study was conducted after obtaining approval from the Institutional Review Board of Chung-Ang University Hospital (IRB no.: 1712-014-16123) and Kyungpook National University Hospital (IRB no.: 2020-03-019), and informed consent was waived owing to the retrospective nature of the study.

Acknowledgements

We thank Essay Review Language Editing Services for reviewing the manuscript and for editorial assistance.

Funding: This study had no funding source.

Competing interests

The authors declare that they have no competing interests.

Author contributions

Data analysis: BK and DYY. Writing of the manuscript: EYP and DYY. Designing of the study: BHC and DYY.

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Tables

Table 1: Result-*Clinical features and laboratory results of pediatric HSP patients who underwent FC testing,* Result- *Difference according to GI involvement*

Table 1. Clinical manifestations and laboratory results of HSP patients with and without GI involvement

Variable	Total HSP patients (n = 69)	GI involvement (n = 40)	Non-GI involvement (n = 29)	*P* value
Age (years)	6.85 ± 2.93	7.11 ± 2.67	6.48 ± 3.27	0.380
Male sex	37 (53.6%)	21 (52.5%)	16 (55.2%)	0.826
Duration of admission (days)	5.41 ± 5.27	7.25 ± 6.05	2.79 ± 1.97	0.000*
Patients with joint symptoms	35 (50.7%)	16 (40.0%)	19 (65.5%)	0.036*
Patients with kidney involvement	16 (23.2%)	10 (25.0%)	6 (20.7%)	0.675
HSP clinical score	1.99 ± 1.53	2.65 ± 1.59	1.07 ± 0.80	0.000*
HSP recurrence	23 (33.3%)	15 (37.5%)	8 (27.6%)	0.389
GI symptom recurrence	19 (27.5%)	12 (30.0%)	7 (24.1%)	0.591
Positive SOB result	17 (24.6%)	17 (42.5%)	0 (0%)	0.000*
Fecal calprotectin (mg/kg)	252.7 ± 343.8	379.9 ± 399.8	77.4 ± 97.6	0.000*
WBC count (10^6/L)	11757 ± 5133	12365 ± 6015	10889 ± 3434	0.246
ANC (μL)	7673 ± 4388	8476 ± 4716	6526 ± 3652	0.071
ESR (mm/h)	23.74 ± 12.46	25.50 ± 12.62	21.04 ± 11.95	0.157
C-reactive protein (mg/L)	5.87 ± 6.39	5.18 ± 5.65	6.87 ± 7.31	0.285
FDP (μg/mL) (n = 57)	9.14 ± 9.16	11.08 ± 11.14	6.73 ± 5.07	0.064
D-dimer (μg/mL) (n = 57)	2.34 ± 2.45	2.93 ± 2.89	1.61 ± 1.50	0.036*

HSP: Henoch–Schönlein purpura, GI: gastrointestinal, SOB: stool occult blood, WBC: white blood cell, ANC: absolute neutrophil count, ESR: erythrocyte sedimentation rate, FDP: fibrin degradation product

*Significant findings at $P < 0.05$

Table 2: Result-*Clinical features and laboratory results of pediatric HSP patients who underwent FC testing,* Result-*Difference according to FC levels*

Table 2. Clinical manifestations of HSP patients with increased fecal calprotectin levels

Variable	Total HSP patients (n = 69)	FC > 50 mg/kg (n = 45)	FC < 50 mg/kg (n = 24)	*P* value
Duration of admission (days)	5.41 ± 5.27	6.33 ± 5.88	3.61 ± 3.22	0.043*
Patients with GI symptoms	40 (58.0%)	35 (77.8%)	5 (20.8%)	0.000*
Upper GI involvement	22/40 (55.0%)	19/35 (54.3%)	3/5 (60.0%)	1.000
Lower GI involvement	18/40 (45.0%)	16/35 (45.7%)	2/5 (40.0%)	
Duration of GI symptoms (days)	2.88 ± 4.02	3.89 ± 4.35	1.00 ± 2.41	0.001*
HSP clinical score	1.99 ± 1.53	2.36 ± 1.61	1.29 ± 1.08	0.005*
GI involvement score	0.93 ± 0.93	1.27 ± 0.89	0.29 ± 0.62	0.000*
Fasting patients	25 (36.2%)	20 (44.4%)	5 (20.8%)	0.052
Duration of NPO (days)	0.86 ± 1.56	1.09 ± 1.8	0.42 ± 0.88	0.040*
Patients on steroid treatment	40 (58.0%)	31 (68.9%)	9 (37.5%)	0.012*
Duration of steroid use (days)	5.03 ± 7.85	6.69 ± 8.98	1.92 ± 3.53	0.003*
HSP recurrence	23 (33.3%)	18 (40.0%)	5 (20.8%)	0.108
GI symptom recurrence	19 (27.5%)	15 (33.3%)	4 (16.7%)	0.167
Positive SOB result	17 (24.6%)	16 (35.6%)	1 (4.2%)	0.003*

HSP: Henoch–Schönlein purpura, GI: gastrointestinal, NPO: nothing by mouth, SOB: stool occult blood

*Significant findings at $P < 0.05$

Table 3: Result-*Difference according to FC levels*

Table 3-1. Fecal calprotectin levels resulting from different clinical manifestations

Variable	Fecal calprotectin (mg/kg)		*P* value
GI involvement (yes : no evidence)	379.9 ± 399.8	77.4 ± 97.6	0.000*
Part of GI involvement (upper : lower)	214.7 ± 150.5	581.8 ± 510.1	0.008*
Fasting status (non-fasting : fasting)	177.6 ± 214.7	385.0 ± 473.1	0.047*
Steroid treatment (none : yes)	106.0 ± 116.4	359.1 ± 410.8	0.001*
HSP recurrence (none : recur)	216.5 ± 361.5	325.3 ± 299.8	0.218
GI symptom recurrence (none : recur)	218.1 ± 349.4	344.0 ± 319.5	0.176
SOB result (negative : positive)	149.3 ± 170.4	569.3 ± 518.2	0.004*

Table 3-2. Fecal calprotectin levels resulting from different clinical manifestations

Variable	R^2	*P* value
Hospitalization period (days)	0.053	0.060
Abdominal pain duration (days)	0.137	0.002*
HSP clinical score	0.278	0.000*
GI involvement score	0.380	0.000*
Fasting duration (days)	0.117	0.004*
Steroid treatment duration (days)	0.197	0.000*

HSP: Henoch–Schönlein purpura, GI: gastrointestinal, SOB: stool occult blood

*Significant findings at $P < 0.05$

Table 4: Result-*Test results of patients with joint or kidney involvement*)

Table 4. Fecal calprotectin and other inflammatory markers in patients with joint and kidney involvement

	Joint (+) (n = 35)	Joint (-) (n = 34)	*P* value	Kidney (+) (n = 16)	Kidney (-) (n = 53)	*P* value
FC (mg/kg)	243.2 ± 378.5	262.6 ± 309.6	0.817	317.1 ± 411.7	233.3 ± 322.5	0.397
FC > 50 mg/kg (n= 45)	19 (54.3%)	26 (76.5%)	0.053	12 (75.0%)	33 (62.3%)	0.390
WBC count (10^6/L)	11479 ± 6626	12020 ± 3234	0.668	11853 ± 5597	11445 ± 3320	0.783
ANC (µL)	7734 ± 5554	7615 ± 2985	0.911	7655 ± 4697	7729 ± 3318	0.954
ESR (mm/h)	26.75 ± 12.09	20.91 ± 12.30	0.056	24.06 ± 12.86	22.67 ± 11.35	0.707
CRP (mg/L)	6.75 ± 7.10	5.05 ± 5.62	0.274	6.34 ± 6.36	4.35 ± 6.43	0.279
FDP (µg/mL) (n = 57)	10.01 ± 11.67	8.28 ± 5.78	0.493	9.67 ± 9.91	6.85 ± 4.20	0.385
D-dimer (µg/mL) (n = 57)	2.69 ± 3.05	1.99 ± 1.64	0.304	2.52 ± 2.63	1.56 ± 1.26	0.267

FC: Fecal calprotectin, WBC: white blood cell, ANC: absolute neutrophil count, ESR: erythrocyte sedimentation rate, FDP: fibrin degradation product Significant findings at $P < 0.05$

Figures

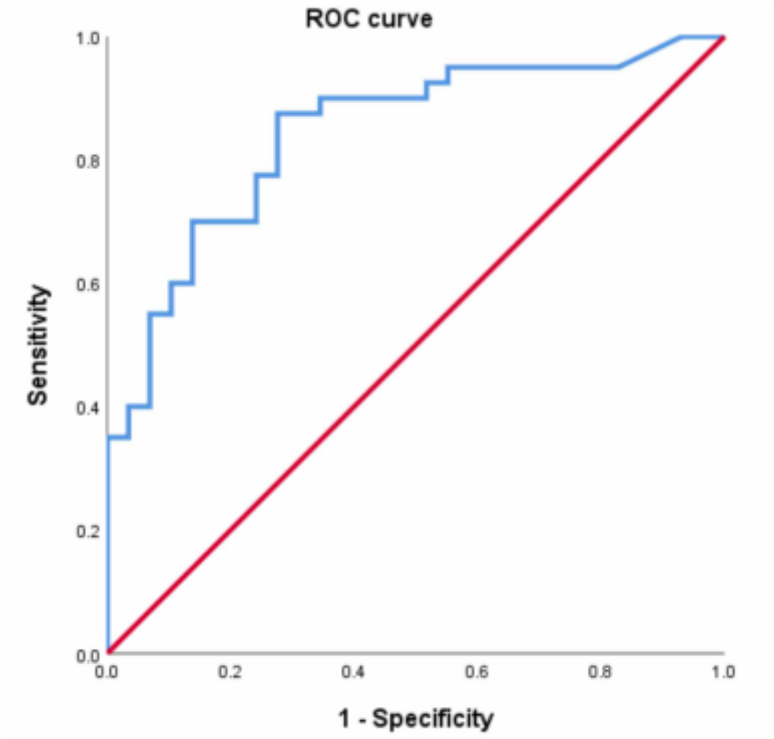

Figure 1

ROC curve of fecal calprotectin levels for diagnosing GI involvement in pediatric HSP patients

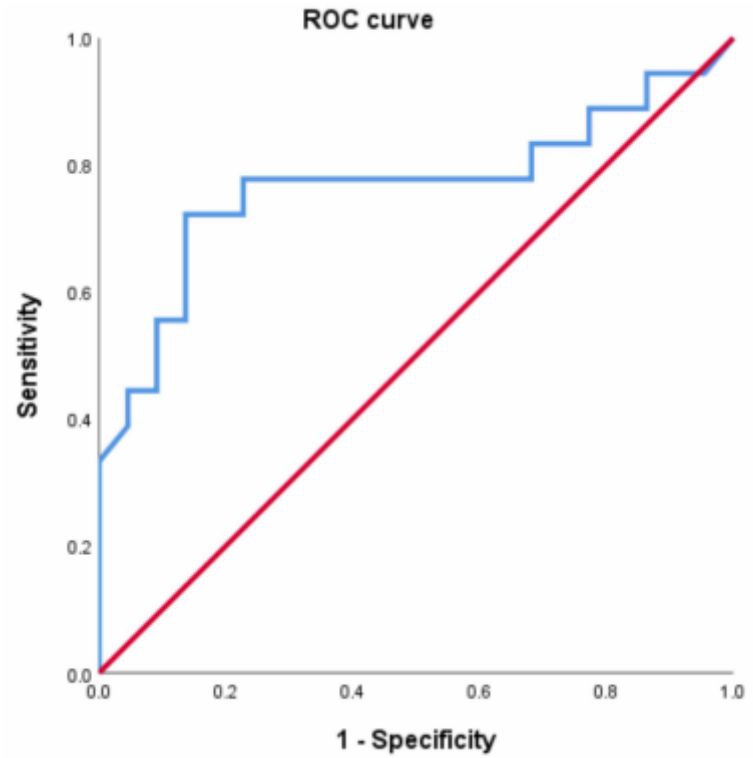

Figure 2

ROC curve of fecal calprotectin levels for diagnosing lower GI involvement in pediatric HSP patients