View Abstract

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ABSTRACT

TITLE: DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME: SERUM CYTOKINE LEVELS AND CLINICAL CORRELATION

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ABSTRACT BODY:

Abstract Body: Introduction: The pathophysiology of irritable bowel syndrome (IBS) is not completely understood; however, dysregulation of the brain-gut axis is believed to lead to IBS. Despite there is a growing evidence indicating that IBS patients show altered cytokine profiles, the results of published studies are not consistent.

Objectives: Explore differences in serum cytokine levels in IBS- diarrhea predominant (IBS-d) patients and healthy controls (HC) and correlate with symptoms, anxiety, depression, and somatization.
Methods: We included 106 patients aged over 18 years referred to tertiary hospital outpatient with Rome IV criteria for IBS-d and 52 HC (mainly patients relatives) with no history or symptoms of gastrointestinal disorders. Clinical data and blood samples were collected. 27 pro and antiinflammatory cytokines (Bio-Plex Pro™, Bio- Rad) were measured in serum. IBS-d patients complete the following questionnaires: IBS severity score, number of bowel movements per day, anxiety and depression score (HADS), PHQ-15 for somatization and a five-point Likert scale for the evaluation of pain and distension. The comparison of cytokine levels between IBS-d and HC adjusted for age, sex, and BMI was analyzed by linear regression. For correlations between levels of cytokines and symptoms Spearman coefficient was used.

Results: IBS-d patients had a mean age of 56 ± 17, (F=76%), HC 51 ± 7, (F=63%). After adjusting for age, sex and BMI, significantly higher levels were observed between IBS-d and HC, in the following cytokines: IL-1ra, IL-2, IL-5, IL-6, IL-8, IL-10, IL-12, IL-15, eotaxin, GM-CSF, IFN-γ, MCP-1, RANTES and VEGF. In addition, significantly lower levels were observed in the following cytokines IL-1b, IL-4, IL-7, IL-9, FGF-basic, IP-10, MIP-1β and TNF-α.
IL-13, IL-17, G-CSF, MIP-1α and PDGF-bb showed no difference.
In patients with IBS-d, a negative correlation was observed between IBS severity and IL-1ra (Rho –0.22, p=0.04) and TNF-α (Rho -0.21, p=0.05). A positive correlation was observed between the number of bowel movements per day and the following cytokines: IL-6 (Rho 0.23, p= 0.03), IL-8 (Rho 0.23, p= 0.02) and VEGF (Rho 0.20, p= 0.05). Also positive correlation was found between anxiety and IL-1b (Rho 0.20, p=0.05), FGF-basic (Rho 0.24, p=0.02) and G-CSF (Rho 0.22, p=0.04) and between somatization and IL-1b (Rho 0.26, p=0.02). A negative correlation was observed between the degree of distension and the following cytokines: IL-1ra (Rho -0.20, p=0.05), IL-8 (Rho -0.26, p=0.01), IL-10 (Rho -0.24, p=0.02), IFN-γ (Rho -0.29, p=0.005), TNF-α (Rho -0.27, p=0.01).

Conclusions: In patients with IBS-d we observed an alteration in serum cytokines compared to HC, regardless of age, sex, and BMI. The level of some cytokines was correlated with stool frequency, symptoms severity, distension, anxiety, and somatization.

	IBS-d (n=106)	Healthy controls (n=52)	p
Age, mean ± sd, y	56 ± 17	51 ± 7	0,07
Sex, No.(%)			
Female	81 (76)	33 (63)	
Male	26 (24)	19 (37)	0,11
Body Mass Index (BMI)			
BMI, median (IQR), kg/m^2	26 (23-31)	27 (24-32)	0,43
BMI>30 kg/m^2, No.(%)	43 (40)	17 (33)	0,36
Bristol Scale (IQR)	7 (6-7)		
Number of bowel movements/day (IQR)	4 (2-5)		
Likert Distension (IQR)	4 (2-5)		
Likert pain (IQR)	4 (2-5)		
Likert IBS (IQR)	4 (2-5)		
IBS severity score (IQR)	250 (190-325)		
Somatization (PHQ-15) (IQR)	11 (8-16)		
Depression (IQR)	8 (5-11)		
Anxiety (IQR)	10 (8-13)		

CYTOKINE pg/ml (IQR)	IBS-d (n=106)	Healthy controls (n=52)	p*
IL-1b	0 (0-0,91)	1,51 (0,91-2,08)	0,000
IL-1ra	436,55 (335,14-533,92)	0 (0-83,12)	0,000
IL-2	2,49 (1,86-3,68)	0 (0-0,19)	0,000
IL-4	1,7 (1,15-3,14)	4,95 (3,25-7,12)	0,000
IL-5	11,56 (6,22-19,11)	0 (0-6,18)	0,000
IL-6	2,78 (1,69-3,96)	0 (0-0,17)	0,000
IL-7	16.19 (11,19-21,24)	18,18 (12,19-29,58)	0,004
IL-8	7,98 (5,24-11,12)	4,49 (2,32-6,61)	0,009
IL-9	159,01 (109,35-303,2)	469,89 (412,37-492,96)	0,009
IL-10	2,46 (1,38-3,86)	0 (0-0)	0,000
IL-12(p70)	2,53 (1,28-4,54)	0,68 (0,18-2,38)	0,009
IL-13	1,15 (0,48-1,93)	1,07 (0,09-1,8)	0,96
IL-15	189,11 (0-235,84)	0 (0-0)	0,000
IL-17	9,62 (7,44-12,22)	11,27 (7,44-14,76)	0,32
Eotaxin	170,6 (125,29-261,45)	73,1 (57,22-99,15)	0,000
FGF ba1c	13,29 (9,73-38,45)	53,4 (40,71-61,77)	0,000
G-CSF	99,6 (64,92-167,31)	71,62 (47,55-99,28)	0,41
GM-CSF	1,22 (0,52-1,77)	0 (0-0,98)	0,000
IFN-Y	45,36 (27,14-59,97)	7,08 (5,83-8,75)	0,000
IP-10	241,36 (142,9-416,23)	682,31 (522,02-965,84)	0,000
MCP-1(MCAF)	167 (111,01-273,56)	26,82 (16,51-36,5)	0,000
MIP-1α	1,06 (0,7-1,41)	1,65 (0,98-2,22)	0,12
MIP-1β	87,88 (62,96-228,43)	285,05 (263,9-316,61)	0,000
PDGF-bb	1596,72 (992,72-2849,51)	1803,41 (1399,9-2144,53)	0,28
RANTES	34486,77(11565,31-102893,1)	13544,92 (11148,55-16220,63)	0,000
TNF-α	40,68 (29,69-50,35)	52,03 (40,86-64,06)	0,000
VEGF	349,96 (224,46-546)	0 (0-0)	0,000
* Adjusted p value (age, sex, bmi)			

DISCLOSURE

The following authors have completed their 2022 DDW disclosure: Maria Piskorz: Disclosure completed | HARUMI HASHIMOTO: Disclosure completed | Tatiana Uehara: Disclosure completed | FEDERICO BAZAN: Disclosure completed | Adriana Tevez: Disclosure completed | Juan Olmos: Disclosure completed | Esteban Gonzalez Ballerga: Disclosure completed | Jorge Olmos: Disclosure completed