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P-38 - UNVEILING THE IMPACT ON IN UTERO EXPOSURE TO BIOLOGIC TREATMENTS FOR INFLAMMATORY BOWEL DISEASE (IBD) ON CHILDREN'S PSYCHOMOTOR DEVELOPMENT: INSIGHTS FROM THE DUMBO REGISTRY OF GETECCU

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Resumen

Introduction: Our aim was to evaluate the impact of the exposure of biologics in utero on the psychomotor development of children during the first year of life.

Methods: Data from children included in the DUMBO registry with complete AQS-3 available up to 12 months of age were analysed. DUMBO is a prospective, observational, and multicentre registry endorsed by GETECCU, which enrolls pregnant women with IBD throughout 5 years in 70 centres in Spain. Study protocol is summarized in figure 1a. Normal psychomotor development was defined by ASQ-3 scores above the lower limit of normality (referral zone) in all domains. Serious adverse events (SAE) were defined in accordance with the ICH Topic E 2 A Clinical Safety Data Management.

Results: 352 children born to 343 mothers were included (9 pair of twins) (tables 1a, 1b and 1c). 134 children (38%) had been exposed to biologics in utero; from them, 50 (37%) had been exposed to adalimumab, 44 (32%) to infliximab, 3 (2.2%) to certolizumab, 1 (0.7%) to golimumab, 28 (20%) to ustekinumab, and 10 (7.5%) to vedolizumab. 8% of the mothers were smokers during pregnancy; no other toxic consumption (alcohol or drugs) was recorded. The ASQ-3 results across different domains are presented in figure 1b, and the impact of the different factors associated with the neurodevelopment is summarised in table 1d. In the multivariate analysis, to have been born to a mother with CD (vs. UC) was associated with higher likelihood (OR = 2, 95%CI = 1.1-3.9), while to be premature was associated with lower likelihood (OR = 0.3, 95%CI = 0.1-0.6) of having ASQ-3 scores above the limit of normality in all domains at 12 months of age.

Table 1a. Characteristics of mothers at conception depending on the presence of biologic treatment.

		Non exposed to biologics	Exposed to biologics	
	Maternal age (years), mean ± SD	33 ± 5	32 ± 6	**p<0.001**
	Time since IBD diagnosis (years), mean ± SD	8.2 ± 6.3	9.8 ± 6.7	**p<0.05**
Type of IBD	Crohn´s disease, n (%)	88 (42)	104 (78)	**p<0.001**
	Ulcerative colitis, n (%)	120 (58)	29 (22)	
	Non classified, n (%)	2 (1)	0	
Crohn´s disease	Ileal (L1), n (%)	50 (57)	48 (45)	ns
	Colonic (L2), n (%)	8 (9)	12 (12)	
	Ileocolonic (L3), n (%)	30 (34)	45 (42)	
	Upper digestive tract involvement, n (%)	6 (7)	9 (9)	ns
	Perianal disease, n (%)	11 (13)	25 (24)	**p<0.05**
	Inflammatory behavior (B1), n (%)	61 (70)	62 (60)	ns
	Stenosing behavior (B2), n (%)	20 (23)	25 (24)	
	Fistulizing behavior (B3), n (%)	7 (8)	17 (16)	
Ulcerative colitis	Proctitis (E1) n (%)	52 (43)	2 (7)	**p<0.001**
	Left colitis (E2), n (%)	36 (30)	7 (24)	
	Extensive colitis (E3), n (%)	34 (28)	20 (69)	
	IBD activity (baseline), n (%)	10 (4.6)	4 (3)	ns
Maternal history	Previous surgical interventions, n (%)	30 (14)	36 (27)	**p<0.05**
	Comorbidities, n (%)	71 (34)	49 (37)	ns
	Anemia, n (%)	173 (84)	113 (86)	ns
	Previous pregnancies, mean ± SD	0.9 ± 1.3	0.8 ± 0.9	ns
	Previous miscarriages, n (%)	55 (25)	34 (25)	ns
	Previous fetal anomalies, n (%)	2 (1)	0	ns
	Previous fetal deaths, n (%)	3 (1)	1 (0.8)	ns
	Multiparous, n (%)	93 (43)	53 (40)	ns
Maternal weight at conception	Body Mass Index (BMI), mean ± SD	24 ± 5	24± 3.9	ns
	Normoweight (BMI 18.5-24.9), n (%)	134 (64)	82 (62)	
	Overweight (BMI 25-29.9), n (%)	39 (19)	32 (24)	
	Obesity (BMI <30), n (%)	19 (9)	9 (6.8)	
	Underweight (BMI <18.5), n (%)	18 (8.6)	9 (6.8)	

SD, standard deviation; IBD, inflammatory bowel disease; n.s., non-statistically significant.

Table 1b. Characteristics of babies depending on the exposure to biologic treatment.

		Non exposed to biologics	Exposed to biologics	
Birth	Female sex, n (%)	113 (52)	69 (51)	ns
	Gestational age (weeks), mean ± SD	38.4 ± 2.5	39 ±1.8	ns
	Vaginal delivery, n (%)	114 (75)	56 (52)	**p<0.05**
	Cesarean delivery, n (%)	38(25)	34 (38)	
	Size at birth (cm), mean ± SD	49 ± 3	50 ± 2.6	ns
	Birth weight (kg), mean ± SD	3.1 ± 0.6	3.21 ± 0.5	ns
	Low birth weight, n (%)	31 (14)	10 (7.5)	ns
	Apgar ≥7 at 5 minutes, n (%)	213 (98)	129 (96)	ns
	Apgar ≥7 at 10 minutes, n (%)	217 (99.5)	134 (100)	ns
Feeding in the 1st month of life	Exclusive breastfeeding, n (%)	141 (65)	78 (58)	ns
	Mixed breastfeeding, n (%)	28 (13)	19 (14)	
Feeding in the 6th month of life	Exclusive breastfeeding, n (%)	43 (22)	23 (21)	ns
	Mixed breastfeeding n (%)	19 (9.7)	5 (4.5)	
Feeding (with complementary feeding) in the 12th month of life	Exclusive breastfeeding, n (%)	9 (6)	4 (4.4)	ns
	Mixed breastfeeding, n (%)	2 (1.3)	1 (1)	
Follow-up first 12 months of life	Hearing impairment, n (%)	16 (7.3)	12 (9)	ns
	Visual impairment, n (%)	1 (0.5)	2 (1.5)	ns
	Family concern about behavior, mean ± SD	0.5 ± 1	0.2 ± 0.6	ns
	Health problems according to parents, mean ± SD	1.6 ± 1.9	1.4 ± 1.5	ns
	Daycare attendance, n (%)	88 (40)	45 (34)	ns
	Serious adverse events, n (%)	61 (28)	25 (19)	**p<0.05**
	Hospital admission, n (%)	58 (27)	24 (18)	ns
	ICU admission, n (%)	14 (6.4)	5 (3.7)	ns
	Surgical intervention, n (%)	8 (3.7)	5 (3.7)	ns
	Complete vaccination, n (%)	215 (99)	131 (98)	ns
	Allergies, n (%)	12 (5.5)	7 (5.2)	ns
	Infections, n (%)	17 (7.8)	9 (6.7)	ns
	Malformations, n (%)	2 (0.9)	0	ns
	Neoplasms, n (%)	0	0	

SD, standard deviation; ICU, intensive care unit; n.s., non-statistically significant.

Table 1c. Characteristics of pregnancies depending on the presence of biologic treatment.

		Non exposed to biologics	Exposed to biologics	
Mother´s information during pregnancy	Natural pregnancy, n (%)	185 (88)	120 (90)	ns
	Fertility treatment, n (%)	26 (12)	14 (10)	
	Difference in BMI from baseline on last ultrasound scan, mean ± SD	0.1 ± 0.9	0.1 ± 0.7	ns
	Hospital admission, n (%)	8 (3.7)	9 (6.7)	ns
	Surgical interventions, n (%)	6 (2.8)	1 (0.8)	ns
	IBD activity, n (%)	28 (13)	11 (8.2)	ns
	Smoking habit, n (%)	15 (6.9)	13 (9.7)	ns
	Daily cigarettes consumption, mean ± SD	3.8 ± 4.5	3.4 ± 3.4	ns
Paternal antecedents	Relevant disease, n (%)	24 (11)	13 (10)	ns
	Known genetic alteration, n (%)	1 (0.5)	0	ns
	Treatment at the time of conception, n (%)	22 (10)	11 (8.2)	ns

SD, standard deviation; BMI, Body Mass Index; n.s., non-statistically significant.

Table 1d. Distribution of factors according to psychomotor development at 12 months, according to normality in all domains of the ASQ-3 questionnaire.

		Anormal ASQ-3	Normal ASQ-3	
Mother´s factors	Biologic treatment, n (%)	13 (25)	77 (41)	**p<0.05**
	Thiopurine treatment, n (%)	20 (38)	60 (32)	ns
	Crohn´s disease, n (%)	23 (43)	112 (59)	**p<0.05**
	Ulcerative colitis, n (%)	30 (57)	75 (40)	**p<0.05**
	IBD mother activity during pregnancy, n (%)	3 (5.7)	18 (9.2)	ns
	Comorbidities	10 (19)	24 (13)	ns
	Natural pregnancy n (%)	44 (83)	167 (88)	ns
	Fertility treatment n (%)	9 (17)	22 (12)	
	Multiparous, n (%)	30 (57)	92 (49)	ns
	Miscarriages, n (%)	0.3 (0.6)	0.3 (0.7)	ns
	Smoking habit n (%)	2 (3.8)	15 (8)	ns
Father´s factors	Known genetic alteration, n (%)	0	1 (0.5)	ns
	Father´s treatment at the time of conception, n (%)	1 (1.9)	16 (8.5)	ns
Babies factors	Male sex, n (%)	28 (53)	92 (49)	ns
	Female sex, n (%)	25 (47)	97 (51)	
	Prematurity, n (%)	13 (25)	18 (9.5)	**p<0.05**
	Vaginal delivery, n (%)	38 (72)	132 (70)	ns
	Cesarean delivery, n (%)	15 (28)	57 (30)	
	Low birth weight, n (%)	11 (21)	21 (11)	ns
	Apgar ≥7 at 5 minutes, n (%)	50 (94)	182 (96)	ns
	Apgar ≥7 at 10 minutes, n (%)	52 (98)	189 (100)	ns
	Exclusive breastfeeding ≤ 3months, n (%)	7 (33)	31 (33)	ns
	Daycare attendance, n (%)	24 (45)	79 (42)	ns
	Hearing impairment, n (%)	5 (9.4)	23 (12)	ns
	Visual impairment, n (%)	1 (1.9)	2 (1)	ns
	Family concern about behavior, mean ± SD	0.7 ± 1.2	0.3 ± 0.8	**p<0.001**
	Other family concerns, mean ± SD	0.9 ± 1.7	0.5 ± 1.4	**p<0.05**
	Health problems according to parents n (%)	1.7 ± 1.9	1.5 ± 1.7	ns
	Serious adverse events n (%)	21 (40)	40 (21)	p<0.05
	Hospital admission n (%)	19 (36)	41 (22)	**p<0.05**
	ICU admission n (%)	6 (11)	9 (4.8)	ns
	Surgical intervention n (%)	2 (3.8)	6 (3.2)	ns
	Complete vaccination n (%)	50 (100)	188 (99.5)	ns
	Allergies, n (%)	3 (5.7)	11 (5.8)	ns
	Infections, n (%)	5 (9.4)	16 (8.5)	ns
	Malformations, n (%)	1 (1.9)	0	ns
	Neoplasms, n (%)	0	0	

SD, standard deviation; ICU, intensive care unit; IBD, inflammatory bowel disease; n.s., non-statistically significant.

Figure 1a. Summary of the DUMBO registry protocol.

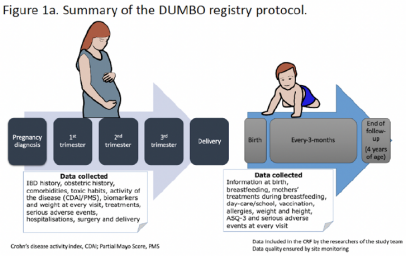
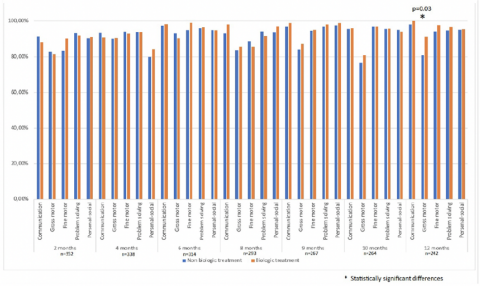


Figure 1b. Normal neurodevelopment based on ASQ-3 questionnaires.



Conclusions: In the multicenter, prospective DUMBO registry, the exposure to biologics for the treatment of IBD in utero (including anti-TNF and non-anti-TNF agents) did not impair the psychomotor development of the children.