Insufficient Weight Gain During Pregnancy in Maternal IBD Predicts Adverse Pregnancy Outcomes: Results from The PIANO and Norwegian Registry

May-Bente Bengtson[1,4], Christopher F. Martin[2] , Geir Aamodt[3], Morten. H. Vatn[4], Uma Mahadevan[5]

1: Medical Department, Vestfold Hospital Trust, P.O. Box 2168, 3103 Tønsberg, Norway, 2: Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, 3: Norwegian University of Life Sciences, P.O. Box 5003, 1432 Ås, Norway

4: EpiGen-Institute, Faculty Division Akershus University Hospital, University of Oslo, Norway, 5: Division of Gastroenerology, University of California, San Francisco

Aim and Background

Mothers with inflammatory bowel disease (IBD) have an increased risk of adverse pregnancy outcomes, with disease activity as the strongest predictor. The aim of this study was to determine if inadequate weight gain during pregnancy is a predictor of adverse outcomes in two pregnancy cohorts, the prospective US PIANO IBD cohort and the population-based Norwegian Mother and Child Cohort (MoBa) .

Methods

PIANO comprises 922 IBD mothers with live birth followed during and after pregnancy at 30 US IBD centers. MoBa includes 107,000 pregnancies throughout Norway from 1999 to 2008. Sub-classification of disease, medication, disease activity, and complications during pregnancy and delivery were ascertained. The pre-pregnancy body mass index (BMI) (in kg/m^2) was categorized into four groups with recommended gestational weight gain (GWG) (Table 1). Gestational weight gain (GWG), was classified into three groups: inadequate, adequate and excessive, based on The US Institute of Medicine (IOM) recommendations.

Table 1 The American Institute of Medicine (IOM) recommendations for gestational weight gain (GWG)

Prepregnant categories of BMI	GWG (kg) according to IOM recommendations
BMI < 18.5	12.5 < GWG < 18
18.5 < BMI < 24.9	11.5 < GWG < 15
25 < BMI < 29.9	7 < GWG < 11.5
BMI > 30	5 < GWG < 9

The association between maternal IBD and GWG, between inadequate GWG and preterm birth (< 37 weeks), small for gestational age (SGA), or intrauterine growth restriction (IUGR) were analyzed in separate models, adjusted for diabetes, hypertension, smoking history, maternal age and education. The association between flares and inadequate GWG or GWG quartiles (< 18 kg) was explored.

US Piano IBD Cohort

The PIANO cohort included 559 CD and 363 UC mothers.

Inadequate GWG was associated with:

- *2.5-fold increased risk of preterm birth in maternal CD and UC*
- *3.3-fold increased risk of IUGR in maternal CD*
- *SGA in maternal CD (p =0.08)*

Flares were associated with preterm birth (OR = 1.5, CI: 0.6, 3.5, p = 0.09) and with inadequate GWG (OR = 1.6, CI: 1.2, 2.3), ***however adjusting for flares did not change the association of inadequate GWG and preterm birth.***

The PIANO Cohort
Descriptive data, mothers' disease and pregnancy outcomes in maternal IBD allocated by gestational weight gain groups

		N (%, mean, SD)	Inadequate	Adequate	Excessive	p-value
Age	N(mean, std)	922 (31.00, 4.62)	187 (30.61, 4.57)	296 (31.72, 4.56)	439 (30.67, 4.63)	0.0014
Education	1 High school	28 (5.1)	7 (25)	4 (14.3)	17 (60.7)	0.1803
	2 some college	75 (13.6)	17 (22.7)	16 (21.3)	42 (56.0)	
	3 Graduate from college	196 (35.5)	35 (17.9)	65 (33.2)	96 (49.0)	
	4 Graduate school	211 (38.2)	46 (21.8)	74 (35.1)	91 (49.0)	
	5 Unknown	42 (7.6)	6 (14.3)	14 (33.3)	22 (52.4)	
BMI groups	1 Underweight	51 (5.5)	15 (29.4)	30 (58.8)	6 (11.8)	< 0.0001
	2 Normal	631 (68.4)	154 (24.4)	223 (35.3)	254 (40.3)	
	3 Overweight	175 (19.0)	11 (6.3)	39 (22.3)	125 (71.4)	
	4 Obese	65 (7.0)	7 (10.8)	4 (6.2)	54 (83.1)	
Diabetes	no	865 (93.8)	173 (20.0)	270 (31.2)	422 (48.8)	0.0179
	yes	57 (6.2)	14 (24.6)	26 (45.6)	17(29.8)	
Hypertension	no	870 (94.4)	180 (20.7)	281 (32.3)	409 (47.0)	0.2696
	yes	52 (5.6)	7 (13.5)	15 (28.8)	30 (57.7)	
Smoking history	Current	22 (2.4)	3 (13.6)	6 (27.3)	13 (59.1)	0.0749
	Former	266 (28.9)	46 (17.3)	76 (28.6)	144 (54.1)	
	Never	633 (68.7)	138 (21.8)	214 (33.8)	281 (44.4)	
Preterm birth	no	847 (91.9)	160 (18.9)	269 (31.8)	418 (49.4)	0.0002
	yes	75 (8.1)	27 (36.0)	27 (36.0)	21 (28.0)	
IUGR	no	899 (97.5)	178 (19.8)	289 (32.1)	432 (48.1)	0.0604
	yes	23 (2.5)	9 (39.1)	7 (30.4)	7 (30.4)	
SGA	no	898 (99.1)	180 (20.0)	287 (32.0)	471 (48.0)	0.1053
	yes	8 (0.9)	4 (50.0)	2 (25.0)	2 (25)	

The PIANO Cohort
ORs for pretem birth, IUGR and SGA among IBD mothers with inadequate gestational weight gain

	N (obs)	Inadequate GWG	Preterm birth	OR (95 %CI)	p-value	Adjusted OR (95 %CI)	p-values
IBD	922	187	75	2.41 (1.46,3.99)	0.0006	2.48 (1.49, 4.11)	0.0005
CD	559	104	46	2.31 (1.19, 4.45)	0.0128	2.50 (1.28, 4.90)	0.0072
UC	363	83	29	2.62 (1.19, 5.72)	0.0163	2.53 (1.15,5.62)	0.0217
	N (obs)	**Inadequate GWG**	**SGA**	**OR (95 %CI)**	**p-value**	**Adjusted OR (95 %CI)**	**p-values**
IBD	906	184	8	3.98 (0.98, 16.10)	0.052	4.11 (0.99, 17.01)	0.0506
CD	549	102	6	4.49 (0.89, 22.55)	0.069	4.49 (0.83, 24.35)	0.0810
UC	357	82	2	3.38 (0.21, 54.68)	0.39	4.11 (0.25, 68.16)	0.324
	N (obs)	**Inadequate GWG**	**IUGR**	**OR (95 %CI)**	**p-value**	**Adjusted OR (95 %CI)**	**p-values**
IBD	922	187	23	2.60 (1.11, 6.11)	0.028	2.51 (1.05, 5.99)	0.038
CD	559	104	14	3.42 (1.16, 10.08)	0.026	3.32 (1.09, 10.04)	0.034
UC	363	83	9	1.71 (0.42, 7.00)	0.45	1.51 (0.348, 6.57)	0.58

Adjusted for education, mothers' age, diabetes, hypertension and smoking history

The Norwegian Mother and Child Cohort
Descriptive data, mothers' disease, smoking history and pregnancy outcomes in maternal CD and UC, compared to control

		CD		UC	
		N (%, mean, SD)	p-values	N (%, mean, SD)	p-values
Age	N (mean, std)	166 (30.35, 4.13)	0.91	218 (30.96, 4.15)	0.011*
Education groups	High school or less	55 (35.3)		60 (29.1)	
	College 3 years	71 (45.5)	0.83	101 (49.0)	0.06
	Master or higher	30 (19.0)	0.25	45 (21.8)	0.78
Diabetes	Yes	1 (0.6)	0.39	3 (1.4)	0.97
	No	165 (99.4)		215 (98.6)	
Hypertension	Yes	8 (4.8)	0.62	10 (4.6)	0.47
	No	158 (95.2)		208 (95.5)	
Smoking history	Current	18 (11.7)	0.01*	6 (3.1)	0.14
	Former	4 (2.6)	0.9	4 (2.1)	0.46
	Never	132 (85.7)		181 (94.8)	
Gestational age	N (mean, std)	39.27 (1.9)	0.057	39.43 (1.5)	0.39
Gestational weight gain	N (mean, std)	13.56 (6.7)	0.006*	13.97 (5.8)	0.038*
Prepregnant BMI	N (mean, std)	23.42 (4.1)	0.98	23.74 (3.9)	0.97
Preterm	Yes	13 (7.8)	0.039*	10 (4.60)	0.93
	No	153 (92.2)		208 (95.4)	
SGA	yes	17 (10.2)	0.048*	18 (8.3)	0.27
	No	186 (89.8)		200 (91.7)	

P-values compared to controls, plural birth and GWG > 50 and GWG < -50 excluded

The Norwegian Mother and Child Cohort
Maternal CD and UC, compared to control, allocated by gestational weight gain in BMI groups according to the American Institute of Medicine (IOM) recommendations

	Controls	UC		CD	
Underweight BMI < 18.5	N (%)	N (%)	p-value (vs controls)	N (%)	p-value (vs controls)
Inadequate (< 12.5)	714 (30.8)	1 (16.7)	0.48	4 (66.7)	0.04*
Adequate (12.5<GWG< 18)	1075 (46.4)	3 (50)	0.97	2 (33.3)	0.87
Excessive (>18)	529 (22.8)	2 (33.3)	0.65	0 (0)	0.30
Normal weight 18.5 < BMI < 24.9					
Inadequate (< 11.5)	11527 (21.1)	50 (32.6)	< 0.0001*	46 (39.3)	<0.0001*
Adequate (11.5<GWG< 15)	21134 (40.5.)	55 (36.9)	0.63	35 (29.9)	0.10
Excessive (>15)	19555 (37.4)	44(29.5)	0.13	36 (30.8)	0.38
Overweight 25 < BMI < 29.9					
Inadequate (< 7)	1571 (9.1)	3 (7.0)	0.52	5 (15.2)	0.34
Adequate (7<GWG< 11.5)	3733 (21.6)	8 (18.6)	0.47	12 (36.4)	0.12
Excessive (>11.5)	11957 (69.3)	32 (74.4)	0.87	16 (48.5)	0.05*
Obese BMI > 30					
Inadequate (< 5)	1319 (18)	4 (21.1)	0.84	2 (20.0)	0.64
Adequate (5<GWG< 9)	1603 (21.8)	3 (15.8)	0.49	4 (40.0)	0.72
Excessive (>9)	4422 (60.2)	12 (63.2)	0.94	4 (40.0)	0.08

Plural birth and GWG >50 and GWG < -50 excluded from the analyses

The Norwegian Mother and Child Cohort

MoBa included 215 CD and 287 UC mothers.
Risk of inadequate GWG was increased in CD compared to controls (OR =1.4, CI: 1.2, 1.7).

- ***Inadequate GWG was associated with*** *3.5 to 4.4-fold increased risk of SGA in maternal UC and CD*
- ***Weight gain was a protective factor against preterm birth*** *in CD mothers with inadequate GWG* (OR = 0.66, CI: 0.45, 0.96).
- ***Flares in IBD*** were more likely with the two lowest GWG quartiles compared to the highest (OR = 2.6, CI: 1.1, 6.4, OR = 2.5, CI: 1.1, 5.6).

The Norwegian Mother and Child Cohort
ORs for preterm birth and SGA among IBD mother with inadequate gestational weight gain

	N (obs)	Inadequate GWG	Preterm birth	OR (95 %CI)	p-value	Adjusted OR (95% CI)	p-values
IBD	489	115	31	1.59 (0.72, 3.49)	0.24	1.39 (0.55, 3.54)	0.48
CD	207	57	17	1.51 (0.53, 4.28)	0.44	1.16 (0.34, 4.08)	0.80
UC	280	58	14	1.57 (0.74, 5.2)	0.46	1.3 (0.43, 8.23)	0.40
	N (obs)	**Inadequate GWG**	**SGA**	**OR (95 %CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-values**
IBD	486	115	45	2.91 (1.55, 5.47)	0.001	3.91 (1.87, 8.17)	< 0.0001
CD	207	57	21	2.69 (1.07, 6.73)	0.035	4.40 (1.42, 13.62)	0.01
UC	280	58	24	3.09 (1.29, 7.39)	0.01	3.48 (1.26, 9.64)	0.016

Adjusted for education, mothers' age, diabetes, hypertension, smoking history

Conclusion

In both the US PIANO and the Norwegian MoBa cohorts:

- *Inadequate weight gain during pregnancy was highly associated with adverse pregnancy outcomes*
- *disease activity reduced weight gain*

In the US PIANO cohort:

- *The strong association between inadequate GWG and preterm birth was not influenced by disease activity*

In MoBa:

- *The risk of inadequate GWG was increased in CD mothers compared to controls*

Despite different IBD patient cohorts, inadequate GWG represented a predictor of adverse events in pregnancy.

Authors listed below DO NOT have any financial or other relationship(s) to disclose:May-Bente Bengtson, Christopher F. Martin, Geir Aamodt, Morten H. Vatn,
Uma Mahadevan: Janssen-Cilag, Self: Consulting fee, Advisory Committees or Review Panels, Abbvie, Self: Consulting fee, Advisory Committees or Review Panels, Takeda, Self: Consulting fee, Advisory Committees or Review Panels, UCB Pharma, Self: Consulting fee, Advisory Committees or Review Panels, Genentech Inc., Self: Consulting fee, Advisory Committees or Review Panels, Prometheus Laboratories Inc., Other financial benefit, Grant/ Research Support, Takeda Pharmaceutical Company Ltd, Other financial benefit, Grant/ X : 55172SDISC 03-22-15 22:24:34 PDT : 22778 : o Page 79 79 Name Disclosure Research Support, GlaxoSmithKline, Other financial benefit, Grant/ Research Support