

Online Data Supplement

Sex-specific impact of asthma during pregnancy on infant gut microbiota

Petya T. Koleva¹, Hein M. Tun¹, Theodore Konya², David S. Guttman³, Allan B. Becker⁴, Piush J. Mandhane¹, Stuart E. Turvey⁵,
Padmaja Subbarao⁶, Malcolm R. Sears⁷, CHILD Study Investigators⁸, James A. Scott², Anita L. Kozyrskyj¹

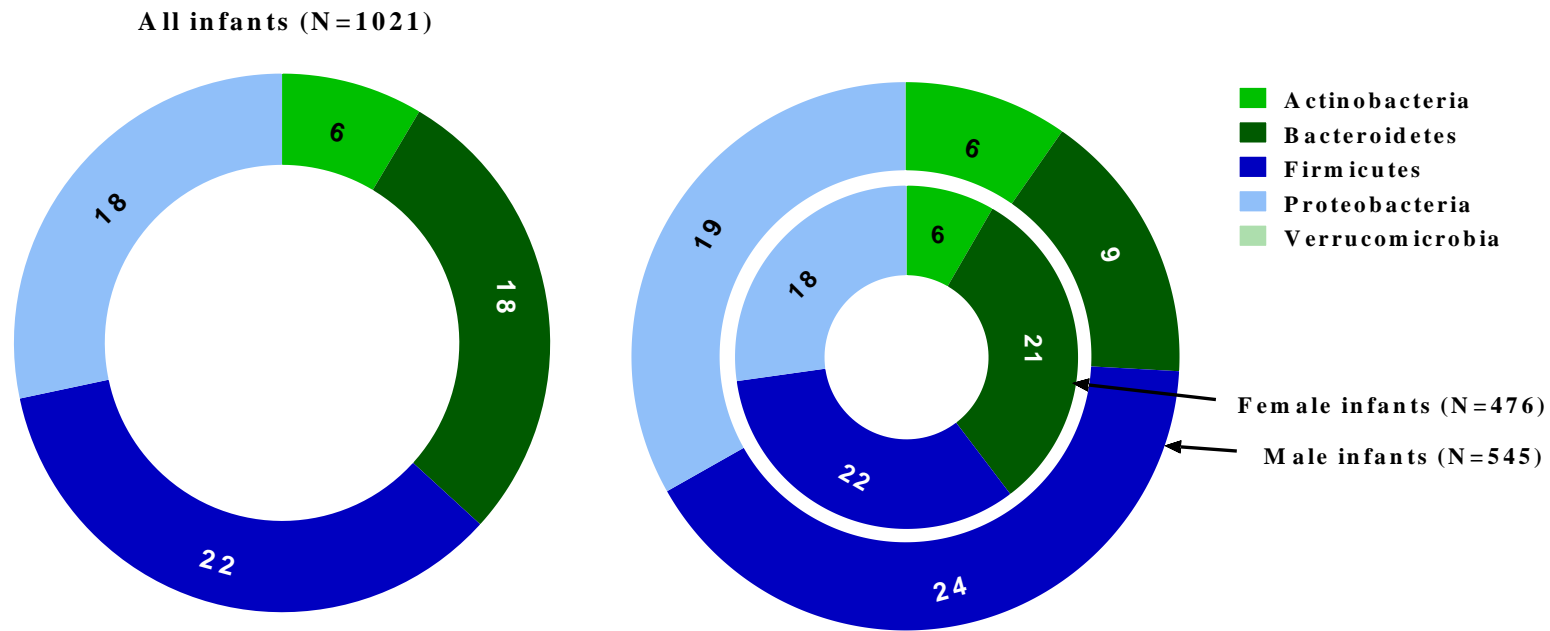


Figure S1. Median relative abundance of bacterial taxa at the phylum level in infant gut microbiota at 3-4 months, by infant sex.

Table S1. Median relative abundance of bacterial phyla, and microbial richness and diversity in infant gut microbiota at 3-4 months, according to maternal prenatal asthma and infant sex.

	All infants			Female infants			Male infants		
	No Asthma (n=934)	Asthma (n=87)	Crude p	No Asthma (n=430)	Asthma (n=46)	Crude p	No Asthma (n=504)	Asthma (n=41)	Crude p
Alpha metrics									
Chao1 richness estimator	342.3 (285.4-403.8)	365.5 (300.6-400.3)	0.19	349.4 (289.6-409.0)	371.8 (304.4-411.3)	0.53	335.7 (283.7-395.6)	362.5 (298.8-396.1)	0.25
Shannon diversity index	3.1 (2.6-3.6)	3.1 (2.5-3.6)	0.90	3.1 (2.7-3.6)	3.2 (2.4-3.4)	0.70	3.1 (2.6-3.5)	3.0 (2.7-3.6)	0.61
Simpson diversity index	0.77 (0.66-0.83)	0.54 (0.42-0.63)	0.95	0.78 (0.67-0.84)	0.76 (0.65-0.84)	0.57	0.76 (0.65-0.83)	0.75 (0.70-0.85)	0.51
Bacterial phyla									
Actinobacteria	5.7 (1.4-15.3)	4.7 (1.4-15.0)	0.97	5.7 (1.6-14.7)	5.1 (1.7-15.0)	0.74	5.7 (1.2-17.3)	3.9 (1.4-14.6)	0.71
Bacteroidetes	17.7 (0.1-60.3)	24.1 (0.1-70.4)	0.20	19.1 (0.1-60.4)	34.8 (0.2-72.9)	0.08	12.0 (0.1-60.2)	0.8 (0.1-69.4)	0.99
Firmicutes	23.4 (9.0-44.8)	18.0 (7.5-41.2)	0.31	23.1 (9.7-47.0)	16.5 (5.6-31.3)	0.03	23.5 (8.9-43.5)	27.4 (10.6-52.6)	0.40
Proteobacteria	18.5 (7.9-40.4)	15.4 (8.2-35.1)	0.21	18.2 (8.4-40.1)	13.8 (8.2-32.6)	0.34	19.3 (7.7-40.4)	16.9 (7.0-35.1)	0.43
Verrucomicrobia	0.002 (0.0003-0.01)	0.002 (0.0004-0.01)	0.87	0.003 (0.0004-0.006)	0.002 (0.0-0.008)	0.95	0.002 (0.0003-0.006)	0.002 (0.0005-0.006)	0.88

Results are presented as median and inter quartile range in brackets. Comparisons were performed by Wilcoxon rank sum test. FDR was used to adjust p values for multiple testing, and p values <FDR p are indicated with ‘*’. P values <0.05 are indicated in boldface type.

Table S2. Median relative abundance of bacterial taxa in infant gut microbiota at 3-4 months, according to maternal prenatal asthma and infant sex. Comparisons were restricted to vaginally-delivered, breastfed infants not exposed to maternal antibiotics during birth.

Bacterial taxa	Female infants			Male infants		
	Restricted to vaginally-delivered, breastfed infants, not exposed to maternal antibiotics during birth			Restricted to vaginally-delivered, breastfed infants, not exposed to maternal antibiotics during birth		
	No Asthma (n=186)	Asthma (n=21)	Crude p	No Asthma (n=208)	Asthma (n=11)	Crude p
Actinobacteria	7.0 (2.0-19.0)	6.4 (2.5-13.5)	-	6.8 (2.3-18.5)	12.7 (2.0-26.6)	-
<i>Actinomycetaceae</i>	0.03 (0.005-0.1)	0.01 (0.003-0.03)	0.07	0.01 (0.001-0.06)	0.02 (0.002-0.09)	-
<i>Actinomyces</i>	0.03 (0.003-0.1)	0.007 (0.001-0.02)	0.08	0.008 (0.001-0.04)	0.009 (0.002-0.03)	-
<i>Bifidobacteriaceae</i>	6.6 (1.8-18.4)	6.4 (1.7-13.4)	-	6.2 (2.0-17.8)	12.2 (1.8-26.6)	-
<i>Bifidobacterium</i>	6.6 (1.8-18.4)	6.4 (1.7-13.4)	-	6.2 (2.0-17.8)	12.2 (1.8-26.6)	-
Bacteroidetes	33.2 (0.8-63.2)	65.3 (28.1-78.5)	0.01*	40.2 (0.5-67.8)	50.3 (0.2-78.8)	-
<i>Bacteroidaceae</i>	27.1 (0.3-60.8)	52.3 (28.1-76.8)	0.02*	35.6 (0.4-60.8)	22.6 (0.1-58.7)	-
<i>Bacteroides</i>	27.1 (0.3-60.8)	52.3 (28.1-76.8)	0.02*	35.6 (0.4-60.8)	22.6 (0.1-58.7)	-
<i>Porphyromonadaceae</i>	0.006 (0.002-0.2)	0.007 (0.002-2.4)	-	0.005 (0.001-0.7)	0.02 (0.002-13.7)	-
Firmicutes	16.0 (7.2-33.9)	9.3 (3.4-17.1)	0.05	14.6 (5.9-30.6)	21.5 (6.8-34.9)	-
<i>Lactobacillaceae</i>	0.003 (0.0002-0.07)	0.003 (0.0003-0.03)	-	0.003 (0.0-0.05)	0.0005 (0.0-0.002)	0.06
<i>Lactobacillus</i>	0.003 (0.0002-0.07)	0.003 (0.0003-0.03)	-	0.003 (0.0-0.05)	0.0005 (0.0-0.002)	0.06
<i>Clostridiaceae</i>	0.2 (0.02-2.2)	0.2 (0.03-0.7)	-	0.07 (0.01-0.8)	0.4 (0.02-2.5)	-
<i>Clostridium</i>	0.02 (0.004-0.7)	0.005 (0.002-0.5)	-	0.006 (0.002-0.1)	0.008 (0.002-0.4)	-
<i>Lachnospiraceae</i>	1.8 (0.03-7.9)	0.7 (0.3-4.5)	-	1.1 (0.03-5.8)	2.1 (0.3-15.6)	-
<i>Blautia</i>	0.0006 (0.0-0.003)	0.001 (0.0-0.02)	-	0.0007 (0.0-0.003)	0.001 (0.0-0.1)	-
<i>Dorea</i>	0.0003 (0.0-0.002)	0.001 (0.0003-0.005)	0.03*	0.0004 (0.0-0.002)	0.0 (0.0-0.002)	-
<i>Ruminococcaceae</i>	0.03 (0.003-0.7)	0.06 (0.004-1.9)	-	0.04 (0.002-0.7)	0.03 (0.003-1.1)	-
<i>Ruminococcus</i>	0.0006 (0.0-0.04)	0.0005 (0.0-0.05)	-	0.0009 (0.0-0.05)	0.0003 (0.0-0.01)	-
<i>Veillonellaceae</i>	3.2 (0.4-12.2)	1.6 (0.5-4.3)	-	2.3 (0.4-12.7)	2.6 (0.4-10.9)	-

<i>Dialister</i>	0.0007 (0.0-0.006)	0.001 (0.0-0.005)	-	0.0004 (0.0-0.003)	0.0003 (0.0-0.02)	-
<i>Megasphaera</i>	0.001 (0.0-0.006)	0.0006 (0.0-0.001)	0.11	0.0009 (0.0-0.005)	0.0005 (0.0003-0.006)	-
<i>Veillonella</i>	1.9 (0.2-11.1)	1.3 (0.1-4.2)	-	1.5 (0.2-7.4)	0.5 (0.1-2.6)	-
Proteobacteria	19.4 (10.0-35.7)	9.8 (8.2-22.6)	0.04	16.2 (7.4-41.2)	13.8 (10.8-28.2)	-
<u><i>Enterobacteriaceae</i></u>	17.8 (7.0-34.2)	9.7 (5.5-16.5)	0.03*	15.1 (5.9-39.6)	13.8 (6.8-27.9)	-
Verrucomicrobia	0.001 (0.0004-0.005)	0.002 (0.0-0.006)	-	0.002 (0.0002-0.006)	0.0007 (0.0-0.003)	-
<u><i>Verrucomicrobiaceae</i></u>	0.001 (0.0004-0.005)	0.002 (0.0-0.006)	-	0.002 (0.0002-0.006)	0.0007 (0.0-0.003)	-
<i>Akkermansia</i>	0.001 (0.0004-0.005)	0.002 (0.0-0.006)	-	0.002 (0.0002-0.006)	0.0007 (0.0-0.003)	-

Results are presented as median and inter quartile range in brackets. Comparisons were performed by Wilcoxon rank sum test. FDR was used to adjust p values

for multiple testing, and p values <FDR p are indicated with '*'. P values <0.05 are indicated in boldface type.

*Comparison of *Lactobacillaceae* family was the primary hypothesis.

Table S3. Median relative abundance of bacterial taxa at phylum, family and genus level in fecal microbiota at 3-4 months according to maternal asthma during pregnancy, restricted to Caucasian mothers and stratified by prenatal maternal allergy status.

Bacterial taxa	Maternal allergies during pregnancy Restricted to Caucasian mothers			No maternal allergies during pregnancy Restricted to Caucasian mothers		
	No Asthma (n=429)	Asthma (n=64)	Crude p	No Asthma (n=278)	Asthma (n=10)	Crude p
Actinobacteria	6.1 (1.5-16.9)	4.7 (1.4-18.6)	-	5.5 (1.5-15.1)	4.6 (0.7-36.1)	-
<i>Actinomycetaceae</i>	0.03 (0.005-0.1)	0.03 (0.008-0.09)	-	0.03 (0.004-0.1)	0.003 (0.0008-0.03)	<0.04
<i>Actinomyces</i>	0.02 (0.004-0.09)	0.02 (0.005-0.09)	-	0.03 (0.004-0.1)	0.003 (0.0008-0.03)	<0.04
<i>Bifidobacteriaceae</i>	5.4 (1.3-16.1)	4.3 (1.3-15.0)	-	4.9 (1.1-13.8)	4.5 (1.1-21.7)	-
<i>Bifidobacterium</i>	5.4 (1.3-16.1)	4.3 (1.3-15.0)	-	4.9 (1.1-13.8)	4.5 (1.1-21.7)	-
Bacteroidetes	13.3 (0.1-57.6)	32.6 (0.2-72.4)	0.08	24.3 (0.1-68.1)	0.4 (0.09-34.2)	-
<i>Bacteroidaceae</i>	8.4 (0.07-53.0)	28.0 (0.1-67.2)	0.09	18.0 (0.09-61.7)	0.1 (0.06-34.2)	-
<i>Bacteroides</i>	8.4 (0.07-53.0)	28.0 (0.1-67.2)	0.09	18.0 (0.09-61.7)	0.1 (0.06-34.2)	-
<i>Porphyromonadaceae</i>	0.005 (0.002-0.2)	0.006 (0.002-1.0)	-	0.004 (0.002-0.09)	0.006 (0.003-0.02)	-
Firmicutes	22.2 (10.1-44.7)	17.2 (7.8-35.8)	-	24.4 (7.8-47.6)	26.8 (3.2-75.5)	-
<i>Lactobacillaceae</i>	0.002 (0.0-0.05)	0.0005 (0.0-0.009)	0.03*	0.003 (0.0-0.05)	0.0009 (0.0-0.003)	-
<i>Lactobacillus</i>	0.002 (0.0-0.05)	0.0005 (0.0-0.009)	0.03*	0.003 (0.0-0.05)	0.0009 (0.0-0.003)	-
<i>Clostridiaceae</i>	0.3 (0.03-2.5)	0.2 (0.02-2.0)	-	0.5 (0.06-2.5)	0.3 (0.09-0.8)	-
<i>Clostridium</i>	0.02 (0.003-0.5)	0.01 (0.003-0.4)	-	0.03 (0.004-0.8)	0.007 (0.004-0.3)	-
<i>Lachnospiraceae</i>	2.9 (0.1-9.8)	2.4 (0.2-9.6)	-	3.1 (0.05-10.8)	3.9 (0.2-32.0)	-
<i>Blautia</i>	0.002 (0.0-0.07)	0.001 (0.0-0.04)	-	0.001 (0.0-0.03)	0.02 (0.0-0.1)	-
<i>Dorea</i>	0.0004 (0.0-0.003)	0.0004 (0.0-0.004)	-	0.0005 (0.0-0.003)	0.002 (0.0-0.03)	-
<i>Ruminococcaceae</i>	0.1 (0.006-1.6)	0.1 (0.004-1.2)	-	0.09 (0.003-1.7)	0.1 (0.005-4.2)	-
<i>Ruminococcus</i>	0.001 (0.0-0.07)	0.0004 (0.0-0.04)	-	0.0007 (0.0-0.06)	0.02 (0.0005-0.06)	-
<i>Veillonellaceae</i>	4.0 (0.7-15.4)	4.9 (1.0-14.0)	-	4.8 (0.8-16.8)	0.7 (0.2-4.3)	-
<i>Dialister</i>	0.0006 (0.0-0.004)	0.0004 (0.0-0.003)	-	0.0004 (0.0-0.003)	0.0001 (0.0-0.01)	-
<i>Megasphaera</i>	0.001 (0.0-0.007)	0.0005 (0.0-0.003)	0.02*	0.0008 (0.0-0.006)	0.002 (0.0-0.004)	-

<i>Veillonella</i>	2.8 (0.4-13.6)	3.0 (0.3-12.4)	-	2.8 (0.4-14.6)	0.7 (0.1-4.3)	-
Proteobacteria	18.7 (8.5-40.9)	14.5 (8.0-32.0)	0.09	16.0 (6.5-34.0)	19.6 (10.1-32.6)	-
<u><i>Enterobacteriaceae</i></u>	16.3 (6.8-39.3)	10.4 (4.6-21.4)	0.01 *	15.0 (4.5-32.0)	19.6 (8.7-32.6)	-
Verrucomicrobia	0.001 (0.0004-0.006)	0.001 (0.0-0.004)	0.11	0.002 (0.0004-0.007)	0.01 (0.005-0.01)	0.02
<u><i>Verrucomicrobiaceae</i></u>	0.001 (0.0004-0.006)	0.001 (0.0-0.004)	0.11	0.002 (0.0004-0.007)	0.01 (0.005-0.01)	0.02*
<i>Akkermansia</i>	0.001 (0.0004-0.006)	0.001 (0.0-0.004)	0.11	0.002 (0.0004-0.007)	0.01 (0.005-0.01)	0.02

Results are presented as median and inter quartile range in brackets. Comparisons were performed by Wilcoxon rank sum test. FDR was used to adjust p values

for multiple testing, and p values <FDR p are indicated with '*'. P values <0.05 are indicated in boldface type.

*Comparison of *Lactobacillaceae* family was the primary hypothesis.

Table S4. Median relative abundance of bacterial taxa at phylum, family and genus level in fecal microbiota at 3-4 months according to maternal asthma during pregnancy, restricted to Caucasian mothers and stratified by maternal pre-pregnancy weight.

Bacterial taxa	Overweight / Obese before pregnancy Restricted to Caucasian mothers			Normal pre-pregnancy weight Restricted to Caucasian mothers		
	No Asthma (n=291)	Asthma (n=33)	Crude p	No Asthma (n=407)	Asthma (n=36)	Crude p
Actinobacteria	6.2 (1.8-15.5)	5.4 (1.8-22.2)	-	5.1 (1.0-16.3)	4.6 (1.0-14.1)	-
<i>Actinomycetaceae</i>	0.03 (0.006-0.1)	0.02 (0.007-0.08)	-	0.02 (0.004-0.1)	0.03 (0.002-0.09)	-
<i>Actinomyces</i>	0.03 (0.005-0.1)	0.02 (0.005-0.07)	-	0.02 (0.003-0.09)	0.02 (0.002-0.09)	-
<i>Bifidobacteriaceae</i>	5.2 (1.2-14.4)	4.9 (1.6-21.5)	-	4.9 (0.8-15.8)	4.3 (0.8-14.0)	-
<i>Bifidobacterium</i>	5.2 (1.2-14.4)	4.9 (1.6-21.5)	-	4.9 (0.8-15.8)	4.3 (0.8-14.0)	-
Bacteroidetes	23.1 (0.09-63.3)	32.6 (0.2-77.3)	-	12.4 (0.1-59.5)	26.1 (0.1-67.4)	-
<i>Bacteroidaceae</i>	14.0 (0.07-55.8)	31.8 (0.09-68.4)	-	6.8 (0.07-55.3)	23.4 (0.09-56.5)	-
<i>Bacteroides</i>	14.0 (0.07-55.8)	31.8 (0.09-68.4)	-	6.8 (0.07-55.3)	23.4 (0.09-56.5)	-
<i>Porphyromonadaceae</i>	0.005 (0.002-0.3)	0.004 (0.002-0.8)	-	0.005 (0.002-0.1)	0.007 (0.003-0.5)	-
Firmicutes	21.1 (9.1-43.1)	10.9 (6.2-33.0)	-	24.3 (8.9-47.5)	21.3 (10.1-47.1)	-
[‡] <i>Lactobacillaceae</i>	0.001 (0.0-0.04)	0.0004 (0.0-0.004)	<0.04	0.003 (0.0-0.06)	0.001 (0.0-0.009)	0.10
[‡] <i>Lactobacillus</i>	0.001 (0.0-0.04)	0.0004 (0.0-0.004)	<0.04	0.003 (0.0-0.06)	0.001 (0.0-0.009)	0.10
<i>Clostridiaceae</i>	0.5 (0.06-2.3)	0.2 (0.04-1.0)	-	0.3 (0.03-2.8)	0.5 (0.009-3.3)	-
<i>Clostridium</i>	0.02 (0.003-0.3)	0.01 (0.003-0.3)	-	0.02 (0.004-1.0)	0.01 (0.003-0.6)	-
<i>Lachnospiraceae</i>	3.9 (0.5-10.0)	3.2 (0.2-9.2)	-	2.0 (0.04-10.7)	2.7 (0.1-13.6)	-
<i>Blautia</i>	0.002 (0.0-0.3)	0.0007 (0.0-0.05)	-	0.001 (0.0-0.007)	0.001 (0.0002-0.1)	-
<i>Dorea</i>	0.0006 (0.0-0.008)	0.0009 (0.0-0.009)	-	0.0004 (0.0-0.002)	0.0003 (0.0-0.002)	-
<i>Ruminococcaceae</i>	0.3 (0.009-2.1)	0.4 (0.006-2.1)	-	0.07 (0.003-1.3)	0.02 (0.004-0.8)	-
<i>Ruminococcus</i>	0.003 (0.0-0.09)	0.002 (0.0-0.06)	-	0.0005 (0.0-0.06)	0.0004 (0.0-0.04)	-
<i>Veillonellaceae</i>	4.1 (0.8-15.8)	2.6 (0.5-7.8)	-	4.2 (0.6-16.8)	9.0 (1.1-18.2)	-

<i>Dialister</i>	0.0005 (0.0-0.004)	0.0 (0.0-0.003)	-	0.0005 (0.0-0.004)	0.0007 (0.0-0.003)	-
<i>Megasphaera</i>	0.001 (0.0-0.007)	0.0004 (0.0-0.001)	0.009*	0.001 (0.0-0.005)	0.0009 (0.0-0.004)	-
<i>Veillonella</i>	2.4 (0.3-13.2)	2.6 (0.2-7.7)	-	3.2 (0.4-15.1)	3.6 (0.3-14.0)	-
Proteobacteria	16.4 (6.5-38.9)	16.6 (5.5-24.8)	-	19.1 (9.3-39.5)	14.1 (9.9-33.3)	-
<u><i>Enterobacteriaceae</i></u>	14.4 (4.7-36.7)	14.8 (1.9-21.8)	-	17.6 (7.2-37.2)	10.4 (6.5-31.8)	-
Verrucomicrobia	0.002 (0.0006-0.007)	0.003 (0.0009-0.01)	-	0.002 (0.0004-0.006)	0.002 (0.0-0.004)	-
<u><i>Verrucomicrobiaceae</i></u>	0.002 (0.0006-0.007)	0.003 (0.0009-0.01)	-	0.002 (0.0004-0.006)	0.002 (0.0-0.004)	-
<i>Akkermansia</i>	0.002 (0.0006-0.007)	0.003 (0.0009-0.01)	-	0.002 (0.0004-0.006)	0.002 (0.0-0.004)	-

Results are presented as median and inter quartile range in brackets. Comparisons were performed by Wilcoxon rank sum test. FDR was used to adjust p values

for multiple testing, and p values <FDR p are indicated with '*'. P values <0.05 are indicated in boldface type.

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