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Prenatal exposure to Hurricane Maria is associated with an altered infant nasal microbiome

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Abstract

Background: Prenatal adverse exposures have been associated with increased risks of development of respiratory diseases in children. The infant nasal microbiome is an important mechanism and indicator.

Objective: Our aim was to characterize and compare the nasal microbiome of infants who were *in utero* and exposed to Hurricane Maria in Puerto Rico during 2017 with that of infants who were conceived at least 5 months after the hurricane as controls.

Methods: We recruited 63 vaginally born infants, 29 of whom were in the exposure group and 34 of whom were in the control group. Nasal swab samples were collected and analyzed by using 16S ribosomal RNA gene sequencing at the community and taxon levels, respectively.

Results: Infants in the exposure group were more likely to harbor a *Staphylococcus-Streptococcus*–dominant microbial community in their nose. The richness and diversity of the microbiome was significantly higher in the exposure group than in the control group. In the exposure group, the bacterial genera *Rhodocista, Azospirillum, Massilia, Herbaspirillum, Aquabacterium,* and *Pseudomonas* were enriched, whereas *Corynebacterium* and *Ralstonia* were depleted. Food insecurity due to Hurricane Maria was associated with an increase in *Pseudomonas* in the infant nasal microbiome.

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Conclusion: Infants who were exposed to Hurricane Maria during gestation had an altered nasal microbiome, with a higher prevalence of environmental bacteria. More research is needed to evaluate the long-term impacts of extreme weather events occurring in the prenatal stage on a child's nasal microbiome and respiratory health.

Keywords

Prenatal maternal; *in utero* ; infant nasal microbiome; upper airway bacteria; nasal swab; respiratory infection; asthma; disaster; hurricane; extreme weather event

Prenatal maternal exposures to environmental or psychological stressors increase the risk of development of respiratory diseases, including wheezing and asthma, in children.[1,2] With the worldwide increases in the frequency and intensity of extreme weather events, which pose major environmental and psychological burdens in affected regions, it is essential to evaluate the risks of development of respiratory diseases among children who are exposed *in utero* to devastating climate events.

Extreme weather events, such as hurricanes and tropical storms, often increase the amount of pollutants, chemicals, and pathogens found in the atmosphere and environment.[3] Strong floods are also associated with high levels of inhalable particles, bacteria, allergens, and mold.[4] For example, after Hurricane Katrina struck New Orleans in 2005, there were large concentrations of airborne endotoxins, mold, and fungal glucans.[5–7] Before, during, and after the Okinawa typhoon season in Japan from June to October 2018, influxes of potentially pathogenic bacteria from the orders Flavobacteriales, Campylobacterales, and Vibrionales were identified in soil samples.[3] These powerful incidents also tend to cause widespread damage and devastation, such as power outages, disruptions in food and water access, and financial struggles, all of which may have negative health impacts directly or through psychological distress.[8–10]

The infant nasal microbiota (ie, a collection of all of the bacteria residing in the nasal passage) play a major role in priming the immune system in the respiratory tract and have been associated with respiratory disease risks in early childhood as a result of environmental exposures.[11,12] Having a balanced microbiome in the upper airways can be protective by controlling allergic airway inflammation and improving respiratory health.[13] On the other hand, dysbiosis in the infant nasal microbiota has been linked with severe outcomes of respiratory tract infections and pulmonary disorders, such as the development of rhinitis, wheezing, and childhood asthma.[14,15] Studies have shown that microbiota profiles dominated by *Corynebacterium* and *Dolosigranulum* in early infancy exhibited more stable compositions during the first 2 years of life and appeared to be protective, whereas the dominance of *Staphylococcus* and *Streptococcus* in the early nasal microbiome was associated with unstable microbial communities and pathogenic bacterial colonization.[16–18]

The infant microbiome may be influenced as early as at the prenatal stage.[19] Maternal inflammatory and metabolic dysregulation in response to adverse events, such as infections, dietary changes, and stress, during pregnancy may disrupt maternal microbial balance. Altered microbial metabolites can subsequently translocate into the placenta and affect the fetal immune profile, which can then influence the selection of the founding infant

microbiome.[20–22] Emerging evidence has also shown that bacteria, especially certain pathogenic bacteria, may directly penetrate the human placenta during gestation.[23,24] Although still being debated, several studies have reported a detection of microbial traces in human placenta and fetal tissues.[25–29] Live bacterial strains have also been extracted from fetal tissues during the second trimester and activated memory T cells *in vitro*.[30] Therefore, the infant nasal microbiome may likely be a major mechanism underlying prenatal adverse exposures and increased respiratory risks.

To evaluate the nasal microbiome of infants who were exposed prenatally to a devastating weather event, we conducted a study named Hurricane as the Origin of Later Alterations in Microbiome (HOLA) by recruiting a cohort in San Juan, Puerto Rico, that consisted of infants who were exposed *in utero* to Hurricane Maria and a control group of infants who were conceived at least 5 months after the hurricane. As one of the deadliest natural disasters in the United States, Hurricane Maria struck Puerto Rico on September 20, 2017, resulting in more than 4645 excess deaths and more than $90 billion of prolonged damages.[31,32] Many Puerto Ricans experienced posttraumatic stress due to a combination of physical and economic challenges.[33] Studies have also reported environmental changes after Hurricane Maria, with higher concentrations of debris, fuels, pesticides, sediments, bacteria, and chlorinated volatile organic matter in water samples.[34,35] In our HOLA study, we were among the first to characterize the nasal microbiome of infants who were exposed *in utero* to a devastating hurricane and compare it with that of infants who were not.

METHODS

Study participants

The HOLA study was approved by the institutional review board of San Juan City Hospital (identifier EPDC-Microbiome); it did not meet the federal definition of being engaged in human subject research per the Washington University in St Louis institutional review board, as only coded data and samples were used for analysis. The inclusion criteria for both groups were (1) full-term birth (≥36 weeks of gestational age), (2) birth by vaginal delivery, (3) age between 2 to 6 months, (4) residence in Puerto Rico throughout the mother's pregnancy, and (5) not currently taking any medications. The exclusion criteria for both groups were (1) delivery by cesarean section, (2) premature birth (<36 weeks of gestational age), (3) admission to a neonatal intensive care unit, (4) acute illness at the time of acquisition of the samples, (5) airway or pulmonary malformations, (6) identified chromosomal or genetic abnormalities, and (7) low birthweight (<2500 g).

Sampling and questionnaires

At the San Juan City Hospital Clinical Research Unit, each of the infants' mothers provided written informed consent and completed a Spanish questionnaire on her personal history and adverse exposures as a result of Hurricane Maria. The questions were adapted from various sources, including instruments used by psychology researchers in Puerto Rico during that time and personal experiences of the research team members. The Edinburgh Postnatal Depression Scale (EPDS) was used as a standard psychological instrument to

detect depressive symptoms, in which an EPDS score was calculated and agreed on by 2 researchers.[36]

During this visit, a clinical research coordinator also collected nasal swab samples from the infants by inserting a sterile swab into both nostrils of the infants against the nasal mucosa. The swab was immediately placed into a DNA/RNA Shield collection tube (Zymo Research, Irvine, Calif) with DNA and RNA stabilization solutions that preserved the nucleic acid integrity of the samples. All collection tubes were shipped within 2 weeks to Washington University in St Louis and immediately stored in a freezer at −80°C until they were processed.

Microbial DNA extraction, 16S recombinant RNA gene sequencing, and data processing

After all of the samples were received, microbial DNA was extracted from each of them by using a ZymoBIOMICS DNA Miniprep Kit (Zymo Research). A Quick-16S NGS Library Prep Kit (Zymo Research) was used to amplify and barcode the V3 to V4 regions of the 16S ribosomal RNA gene. The samples were then pooled and sequenced based on the Illumina MiSeq platform (2 × 250 standard runs; Washington University DNA Sequencing Innovation Lab, St Louis, Mo). The amplicon sequencing variances (ASVs) were inferred by using the merged forward and reverse reads from demultiplexed fastq files and the DADA2 R package.[37] Taxonomy assignments were based on the Ribosomal Database Project's training set 16.[38] The negative control samples yielded very low sequencing reads (<40 reads per sample) and were removed for further analysis. The ASV counts, taxonomy assignments, phylogeny, and sample metadata were combined to generate a PhyloSeq object.[39] The DADA2 pipeline calculated bacterial richness, Shannon index, weighted UniFrac distance and unweighted UniFrac distance between each pair of samples, and principal coordinates in RStudio (R version 4.1.1). The 16S ribosomal RNA sequencing files have been deposited in the European Nucleotide Archive (accession code PRJEB49831).

Statistical analysis

Demographics, maternal information, and feeding methods were compared between the exposure and control groups by using the nonparametric Wilcoxon rank sum test for continuous variables and chi-square test for categoric variables. The Wilcoxon rank sum test was used to compare the Shannon diversity and richness between groups. β-Diversity was based on the weighted or unweighted UniFrac distance matrix, and significance was evaluated by using the analysis of similarities test. α-Values less than 0.05 were considered statistically significant. Community typing was based on the Dirichlet multinomial mixture model by using the core bacterial genera (present in ≥10% of the samples with a relative abundance of ≥0.1%).[40] Differential bacteria genera were detected by using the generalized linear regression model with a logarithmic link that followed a negative binomial distribution in the R package DESeq2.[41] RStudio (R version 4.1.1) was used for statistical analyses, and ggplot2 was used for visualization. ASVs not assigned to any genus were removed in the DESeq2 analysis.

RESULTS

Characterization of the participants

This study included 63 infants, of whom 29 were in the exposure group, as they were *in utero* during the course and sequelae of Hurricane Maria, and 34 were in the control group, as they were conceived ≥5 months after Hurricane Maria occurred. All of the participants resided in the San Juan metropolitan area. Fig 1 shows the municipalities in which the infants from the exposure and control groups were located.

The characteristics of the participants from both groups are compared in Table I. The infants in the exposure group were enrolled between March and August 2018, and those in the control group were enrolled between February and September 2019. There were no significant differences in infant age at the time of sampling, gestational age, presence of siblings living in the same household, breast-feeding status, or mothers' EPDS score between both groups. However, there were significantly more male infants in the control group than in the exposure group ($P = .05$). The infants were all Latino and born vaginally.

In the exposure group, 72.41% of the infants' mothers were in their second trimester in pregnancy when Hurricane Maria occurred, whereas 27.59% were in their first trimester. During their pregnancy, all of the mothers experienced power outages and were exposed to fumes, mold, or debris due to Hurricane Maria. Some of the mothers also experienced displacement (27.59%), food insecurity (27.59%), and drinking water insecurity (34.38%) for at least 1 month after the hurricane.

Sequencing reads and community types

We had a total of 1,357,087 raw sequencing reads. After quality control procedures in the DATA 2 pipeline, 909,647 high-quality reads were retained for downstream analysis. The exposure group had 423,428 high-quality reads for 29 of the samples, and the mean read number was 14,601. The control group had 486,219 high-quality reads for 34 of the samples, and the mean read number was 14,301. The read numbers of each sample and rarefaction curve are listed in Fig E1, A and B (see the Online Repository at www.jaci-global.org).

A total of 971 ASVs were detected in all 63 nasal swab samples. Of the 971 ASVs, 189 appeared in both the exposure and control groups, 589 appeared only in the exposure group, and 193 appeared only in the control group. The 189 ASVs that appeared in both groups accounted for most of the taxa in the samples (89.7% across all samples). The top 4 most abundant bacterial phyla, which corresponded to 99% of the reads, included Firmicutes (44.6%), Actinobacteria (36.2%), Proteobacteria (17.9%), and Bacteroidetes (0.9%). A comparison of the top 5 phyla is presented in Table E1 (see the Online Repository at www.jaci-global.org); there were no remarkable differences regarding their relative abundances between the 2 groups. The top 10 most abundant bacterial families were Corynebacteriaceae (35.1%), Carnobacteriaceae (22.6%), Staphylococcaceae (12.2%), Streptococcaceae (8.5%), Moraxellaceae (7.8%), Neisseriaceae (5.4%), Pasteurellaceae (2.3%), Veillonellaceae (0.8%), Prevotellaceae (0.6%), and Enterobacteriaceae (0.5%). Of these, Staphylococcaceae ($P = .04$), Moraxellaceae ($P = .008$), Streptococcaceae ($P < .001$),

and Veillonellaceae ($P = .002$) were significantly more abundant in the exposure group than in the control group (see Fig E2 in the Online Repository at www.jaci-global.org).

We then partitioned the microbial data into community types by using the Dirichlet multinomial mixture model. Four different microbial community types were identified (Fig 2, A). Interestingly, community type A was enriched with samples from infants in the control group (72%), whereas community type B was enriched with samples from infants in the exposure group (73%). Community types C and D both had relatively similar numbers of infants from both groups. As shown in Fig 2, B, community type A was codominated by *Dolosigranulum* and *Corynebacterium*, community type B was codominated by *Staphylococcus* and *Streptococcus*, community type C was dominated by *Corynebacterium,* and community type D was dominated by *Moraxella*. Community type B had significantly higher numbers of observed ASVs and a higher Shannon index value (an indicator of community richness) than the other 3 community types did (Fig 2, C). In addition, the bacterial compositions represented by the principal coordinate analysis (PCoA) among the 4 community types were significantly different ($P = .001$ for both weighted UniFrac and unweighted UniFrac distances [Fig 2, D]).

Comparison of the 2 groups at the community level

As shown in Fig 3, A, the number of observed ASVs in the nasal swab samples was significantly higher in the exposure group than in the control group ($P < .001$), which was also confirmed by Shannon index value ($P = .002$). These α-diversity differences were largely attributable to the phyla Proteobacteria and Firmicutes (Fig 3, B). Fig 3, C displays the PCoA based on the weighted and unweighted UniFrac distance matrixes, respectively. The bacterial compositions between the exposure and control groups were significantly different ($P = .04$ for the weighted UniFrac and $P = .001$ for the unweighted UniFrac). The unweighted UniFrac distances determine similarities based solely on the presence or absence of a taxon in the 2 groups, whereas the weighted UniFrac distances also consider the differences in the abundance of a taxon. The more significant results from the unweighted UniFrac distance–based PCoA analysis than from those from the weighted UniFrac distance–based analysis indicate that the major microbial compositional differences may be due to the presence of a unique taxon in each group, in which their relative abundances were relatively small.

We then performed subgroup analyses to examine whether the community differences between the exposure and control groups appeared only under certain circumstances. As shown in Fig 4, A, similar significant trends in both the number of observed ASVs and Shannon index values were seen in most of the subgroups that were stratified by exclusive breast-feeding status, infant age, infant sex, or presence of siblings at home. Fig 4, B shows the β-diversity of these subgroup analyses. Similarly, PCoA analyses based on unweighted UniFrac distances were still significant in all subgroups. For PCoA analysis based on weighted UniFrac distance, significant compositional differences between these 2 groups were observed among infants aged 16 weeks or older ($P = .01$) and infants who did not have siblings present in the same household ($P = .002$).

Comparison of the 2 groups at the genus level

Next, we applied a generalized linear regression model using DESeq2. The model included all 207 genera to identify bacterial genera with significantly differential abundances between the exposure and control groups. After adjustment for multiple comparisons, 8 bacterial genera, namely, *Aquabacterium* (adjusted $P = 1.06 \times 10^{-8}$), *Pseudomonas* (adjusted $P = 1.41 \times 10^{-6}$), *Corynebacterium* (adjusted $P = .023$), *Herbaspirillum* (adjusted $P = .013$), *Azospirillum* (adjusted $P = .026$), *Massilia* (adjusted $P = .023$), *Rhodocista* (adjusted $P = .020$), and *Ralstonia* (adjusted $P = .023$), showed significantly differential abundances (Fig 5, A). Of those 8 genera, *Rhodocista spp*, *Azospirillum spp*, *Massilia spp*, *Herbaspirillum spp*, *Aquabacterium spp*, and *Pseudomonas spp* were enriched, whereas *Corynebacterium* spp and *Ralstonia spp* were depleted in the exposure group versus in the control group. The $\log_2$ fold change and SE of each genus are shown in Fig 5, B. Comparisons of the species within each identified genus are shown in Fig E3 (in the Online Repository at www.jaci-global.org).

We further examined whether the identified bacterial genera were associated with maternal prenatal adverse experiences due to Hurricane Maria, including displacement during gestation, food insecurity, and drinking water insecurity. As shown in Fig 5, C, *Pseudomonas* was increased in the nasal microbiome of infants who were exposed to food insecurity *in utero*. However, these adverse exposures were not associated with other identified genera (see Fig E4 in the Online Repository at www.jaci-global.org).

DISCUSSION

The infant nasal microbiome may be a sensitive indicator of respiratory disease risks during childhood.[13] Although accumulating evidence has shown that hurricanes and other extreme weather events lead to a series of adverse changes in the environmental and socioeconomic status of affected regions, only a few studies have evaluated the infant microbiome in postdisaster settings.[19] This cohort study characterized for the first time the nasal microbiome of infants who were exposed *in utero* to a devastating hurricane. The HOLA cohort comprised an exposure group of 29 infants whose mothers were in their first or second trimester when Hurricane Maria struck Puerto Rico and a control group of 34 infants who were conceived at least 5 months after the hurricane. Our results show that infants in the exposure group harbored more species abundance and diverse bacteria in their nasal passages than did those in the control group. The compositions of the microbial communities also differed significantly between the exposure and control groups, indicating that an alteration of the nasal microbiome may exist among infants who were exposed *in utero* to Hurricane Maria.

On the basis of the major genera in the infant nasal microbiome, 4 different community types were identified in the 63 nasal swab samples. Among them, the samples from the exposure group were remarkably different from those in the control group in terms of 2 community types. In the community codominated by *Dolosigranulum* and *Corynebacterium*, 72% of the samples were from the control group, whereas in the community codominated by *Staphylococcus* and Streptococcus, 73% of the samples were from the exposure group. Many studies have demonstrated that infants with *Dolosigranulum* and *Corynebacterium* dominant in their nose have decreased risks of having severe respiratory infections,

wheezing, and asthma, compared with infants who have *Staphylococcus* and *Streptococcus* dominant in their nose.[16] Our results indicated that infants who were exposed *in utero* to Hurricane Maria were more likely to be in the high-risk group, as they had a *Staphylococcus*- and *Streptococcus*-dominated microbiota in their nose. This may provide primary evidence that infants exposed to a devastating hurricane may have increased risks for development of respiratory diseases during childhood.

Previous studies have identified several factors that could influence the infant nasal microbiome, such as mode of delivery, feeding methods, and the presence of siblings at home.[13,17,42] In this study, we restricted our inclusion criteria to only vaginally born infants to avoid this strong influencer on the nasal microbiome being a confounder. Regarding other potential factors, we performed subgroup analyses to examine whether the differences that we observed between the exposure and control groups existed only under certain conditions. Similar differences were seen in all of the subgroups stratified by feeding methods, infant age, infant sex, and having siblings at home, suggesting that alterations of the nasal microbiome in the exposure group were a relatively common phenomenon.

In addition to the differences identified at the community level, we found 8 bacterial genera with significantly differential abundance between the exposure and control groups. As *Corynebacterium* has been repeatedly verified as a beneficial bacteria genus in the infant nasal microbiota in many studies, the significant decrease in *Corynebacterium* in the exposure group versus in the control group in our study further alerts us that infants who were prenatally exposed to a devastating hurricane may harbor fewer beneficial bacteria in their nose during early life, which can increase their risks of developing respiratory diseases.[16,43] In our study, 6 bacterial genera, namely, *Pseudomonas, Aquabacterium, Herbaspirillum*, *Azospirillum, Massilia*, and *Rhodocista*, were also significantly increased or uniquely present in the samples from the exposure group. These genera have been found primarily in soil, water, and detritus, but some have also been previously detected in human respiratory samples, indicating that the nasal passage can be a niche for them.[44–47] A study reported that *Pseudomonas* was the dominant genus discovered in the beach sand at the land point during and after a strong typhoon event.[48] However, after 3 months, the presence of *Pseudomonas* significantly decreased to undetectable levels.[48] Taken together, the data indicate that because *Pseudomonas* and several other environmental bacteria were more prevalent and abundant in the exposed infants than in the control infants, maternal exposure to high concentrations of bacteria in a posthurricane setting during gestation may cause those bacteria to be transmitted to the offspring. Interestingly, we also found that food insecurity during pregnancy was significantly associated with the increase in *Pseudomonas* in the infant nasal microbiome. It is possible that food insecurity experienced after a hurricane is a way of selecting for those most exposed to environmental consequences. This may also be related to prenatal maternal distress. Depression and stress can pose great risks for development of impaired immunity, and this may subsequently disrupt the stability of a developing microbiome and allow the capacity of environmental bacteria to become persistent and cause dysbiosis.[49,50] Hurricane Maria caused devastating mental health outcomes for many years, especially in urban areas, but very few studies have addressed the impact of environmental microbes (bacteria as well as fungi) in causing perturbations to a normal microbiome development.[8]

The observed alterations in the nasal microbiome of infants who were exposed *in utero* to Hurricane Maria indicate an increased risk of development of respiratory diseases. Our study highlighted the importance of monitoring the respiratory health of children in postdisaster settings. Further, our results provide a potentially promising method in using the nasal microbiome to predict the risks of respiratory diseases in children who were exposed *in utero* to a devastating hurricane. Predicting and detecting respiratory outcomes early in life is beneficial to identify appropriate treatment and interventions that can prevent the progression of disease and reduce morbidity and mortality. This may also improve quality of life and lung function.

This was a preliminary study with several limitations. The main limitation was the relatively small number of participants in our cohort, owing to the many difficulties in recruiting participants in a postdisaster setting. However, given that research on the associations between devastating climate events and the infant nasal microbiome are currently limited, we believe that our study highlights important results that may help us better evaluate the impacts of disasters on development of respiratory diseases among children. Another limitation was the inability to collect environmental samples. Indoor and outdoor samples of the water and air in the aftermath of Hurricane Maria would have allowed us to better understand the increased diversity of the nasal microbiome in the exposure group. In addition, some other variables, such as exposure to secondhand smoke, maternal diet, and obesity, as well as parental medical history and socioeconomic status, were not evaluated, but they may have been potential moderators of the association between prenatal exposures and the nasal microbiome.

In conclusion, this study compared the nasal microbiome of infants who were *in utero* when Hurricane Maria struck Puerto Rico with that of infants who were conceived at least 5 months afterward. Our results show that the exposure group’s bacterial composition at the community and genus levels differed significantly from that of the control group and that the environmental bacteria persisted longer in those who had *in utero* exposure to the event. Infants who were exposed to Hurricane Maria during gestation had an altered nasal microbiome, with a higher diversity and prevalence of environmental bacteria. Extreme weather events, such as devastating hurricanes, may be associated with increased risks of development of childhood respiratory diseases in the unborn. These findings can be used to strengthen strategies preventing the development of respiratory diseases in children in postdisaster settings. Follow-up studies are clearly needed to assess the long-term impacts of prenatal maternal exposures to Hurricane Maria on the offspring nasal microbiome and respiratory health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations used

ASV	Amplicon sequencing variance
EPDS	Edinburgh Postnatal Depression Scale
HOLA	Hurricane as the Origin of Later Alterations in Microbiome
PCoA	Principal coordinate analysis

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Key messages

- Infants who were exposed *in utero* to Hurricane Maria had more environmental bacteria in their nasal microbiome and were more likely to harbor a *Staphylococcus-Streptococcus*–codominant community type than were infants conceived at least 5 months after the hurricane.
- The richness and diversity of the nasal microbiome was significantly higher in infants who were exposed to Hurricane Maria during gestation than in the control group.
- This study provides insights into the infant nasal microbiome in a postdisaster setting and characterizes the alterations in the infant nasal microbiome that are associated with prenatal maternal exposures to an extreme weather event.

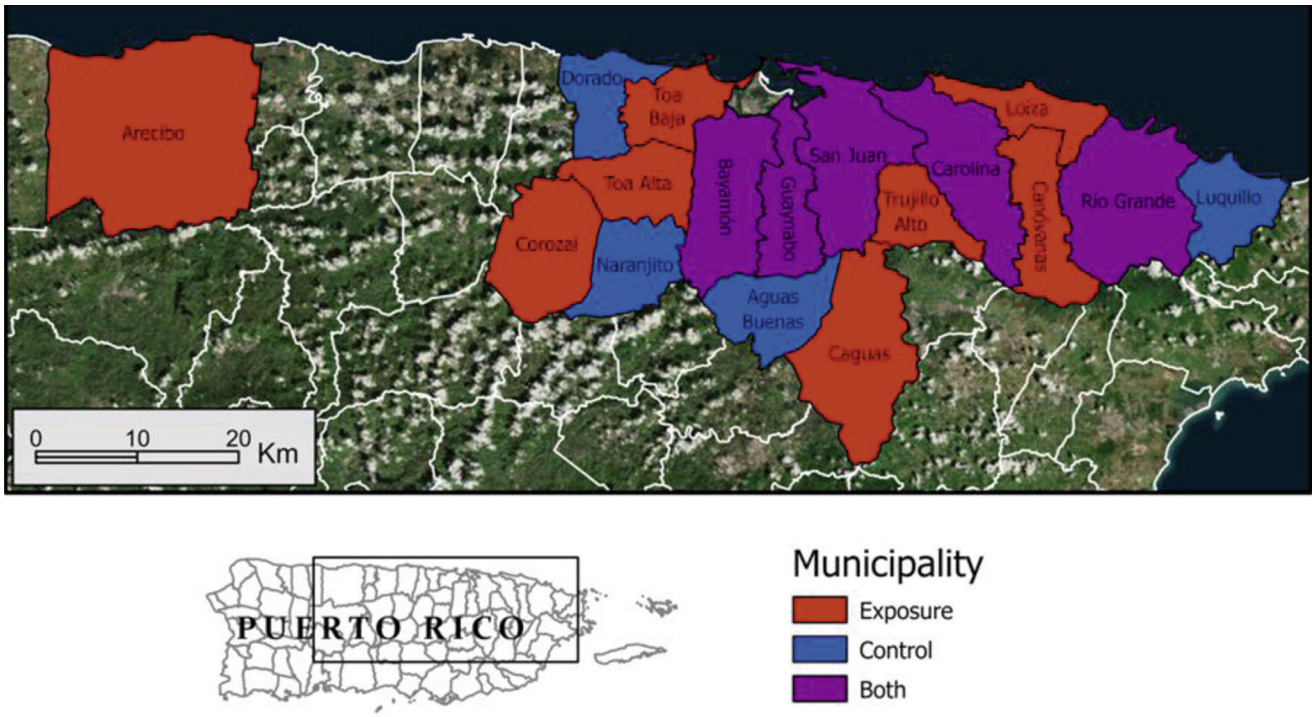

FIG 1.

Location of the study area and municipalities in Puerto Rico in which the study participants resided.

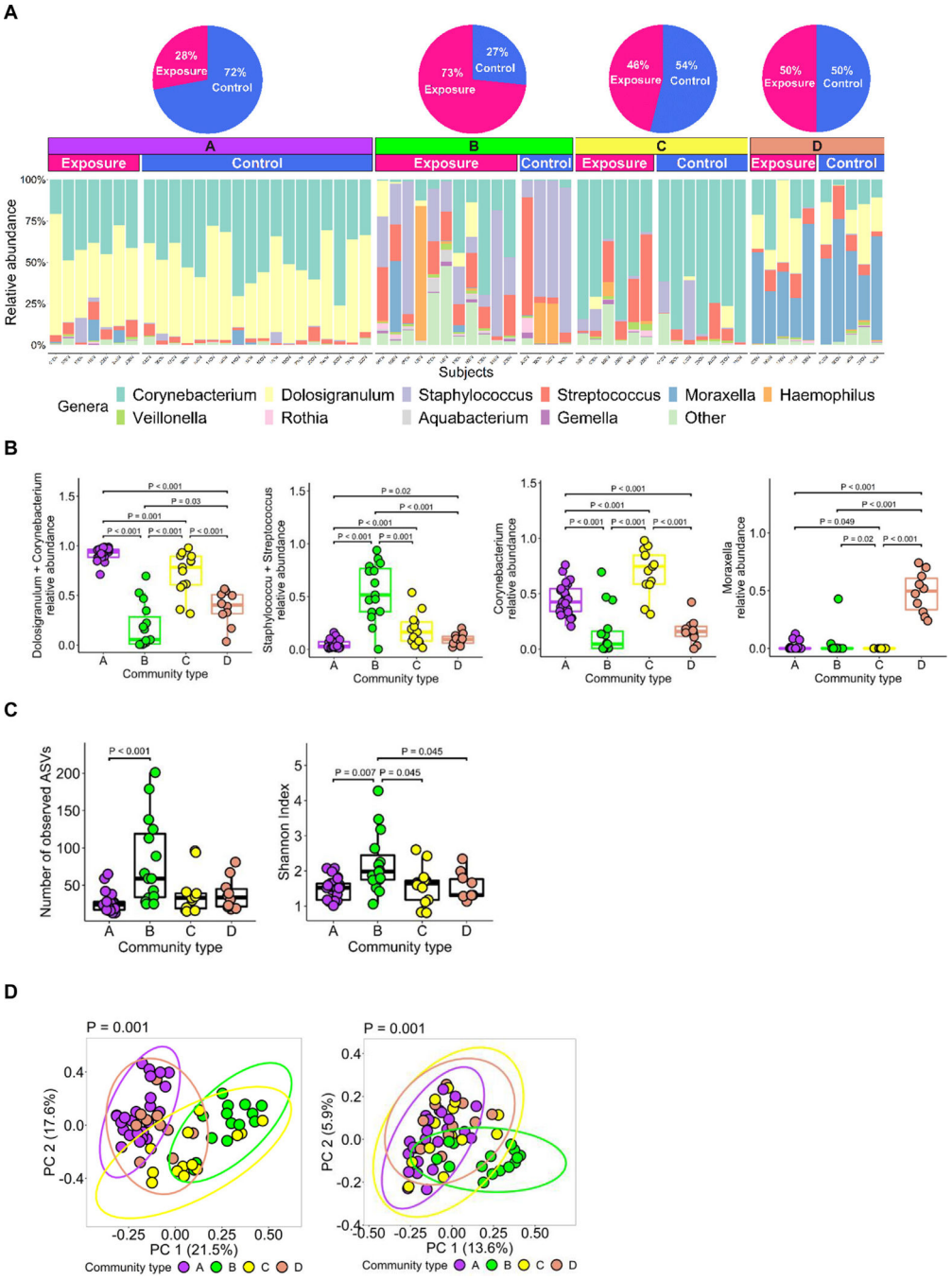

FIG 2.

Characterization of the infant nasal microbiome by community type. **A**, Stacked plots showing the average relative abundances of the top 10 bacterial genera detected in each nasal swab sample grouped by the community types. Community type A is codominated by *Corynebacterium* and *Dolosigranulum*, community type B is codominated by *Staphylococcus* and *Streptococcus*, community type C is dominated by *Corynebacterium,* and community type D is dominated by *Moraxella*. **B**, The relative abundance of dominated genera in each community type. **C**, α-Diversity analyses (observed number of taxa and

Shannon index value) by community type. **D**, PCoA plot based on the weighted UniFrac distance matrix and unweighted UniFrac distance, (analysis of similarities; $P = .001$). Statistical significance in (**B**) and (**C**) was determined by using the pairwise Wilcoxon rank sum test; *P* values were adjusted by using the Benjamini and Hochberg method. Statistical significance in (**D**) was determined by using the analysis of similarities test. *PC*, Principal coordinate.

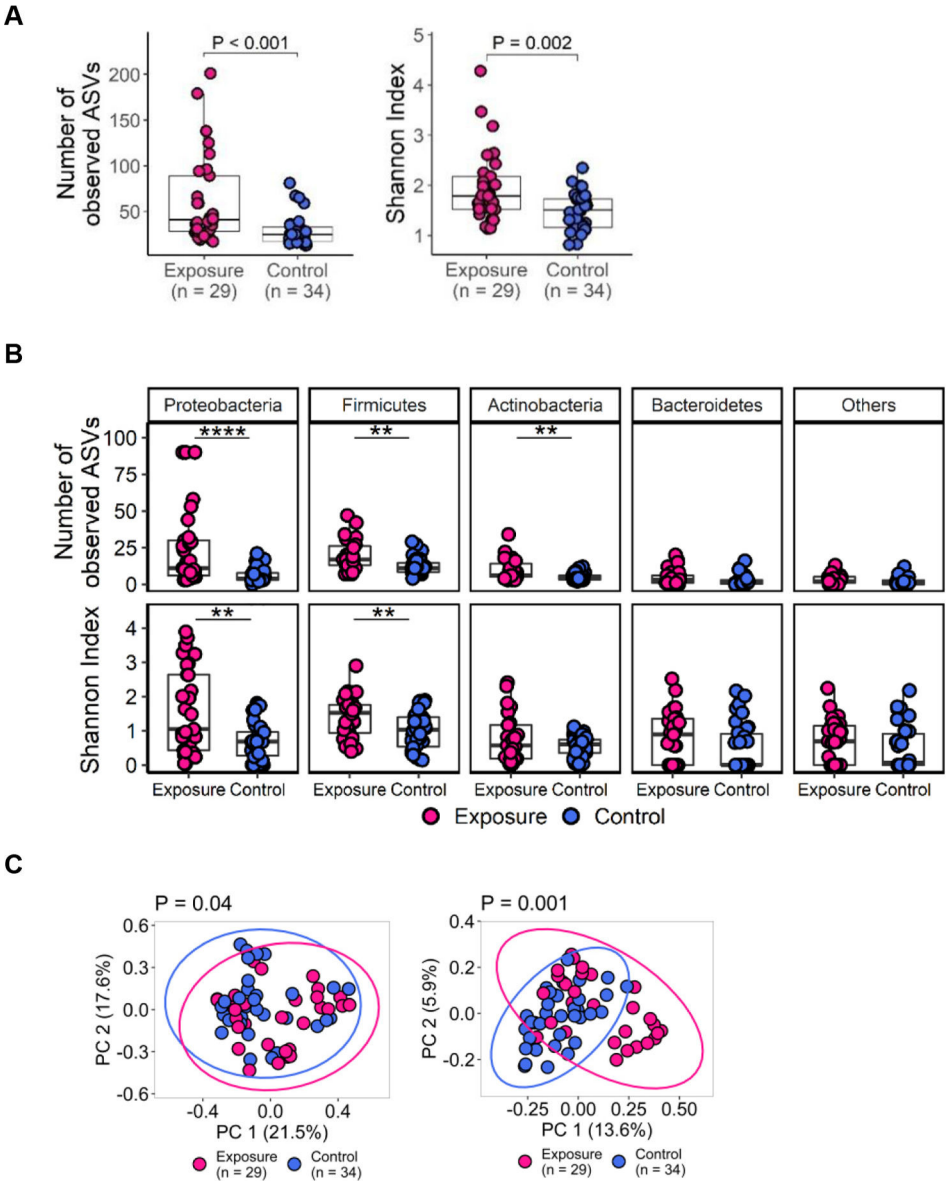

FIG 3.

Evaluation of the infant nasal microbiome at the community level by exposure status. **A**, α-Diversity analyses (observed number of taxa and Shannon index value) between the exposure and control groups. **B**, α-Diversity of the infant nasal microbiome for each phylum by exposure status. **C**, PCoA plot by exposure status based on the weighted UniFrac distances or unweighted UniFrac distances. Statistical significance in (**A**) and (**B**) was determined by using the Wilcoxon rank sum test. Statistical significance in (**C**) was determined by using the analysis of similarities test. *PC*, Principal coordinate.

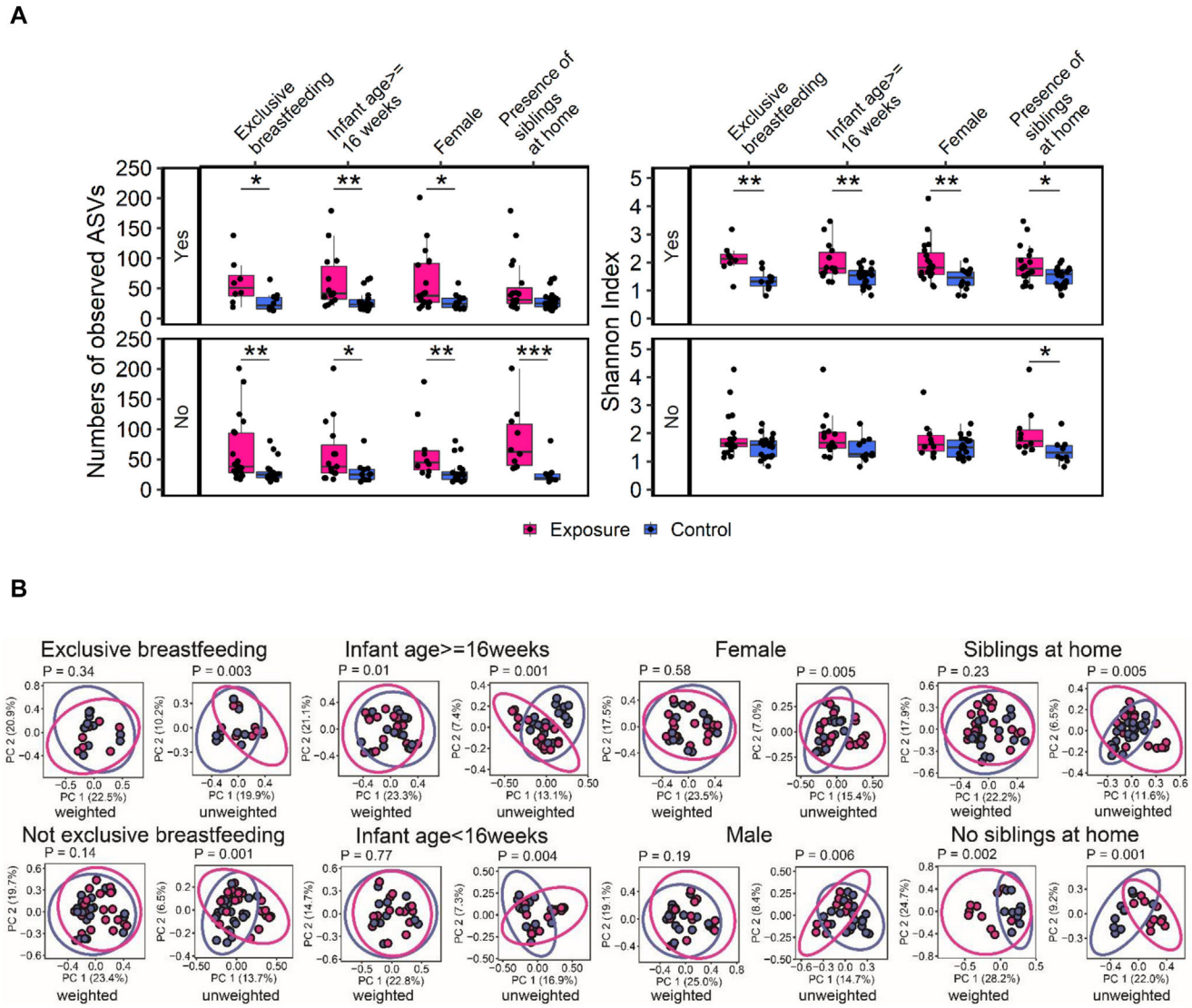

FIG 4.

Subgroup analyses of the infant nasal microbiome at the community level. A, a-Diversity (observednumber of taxa and Shannon index value) in subgroup analyses between the exposure and control groups.B, PCoA plots in subgroup analyses between the exposure and control groups. Statistical significance in (A)was determined by using the Wilcoxon rank sum test. Statistical significance in (B) was determined by using the analysis of similarities test. PC, Principal coordinate.

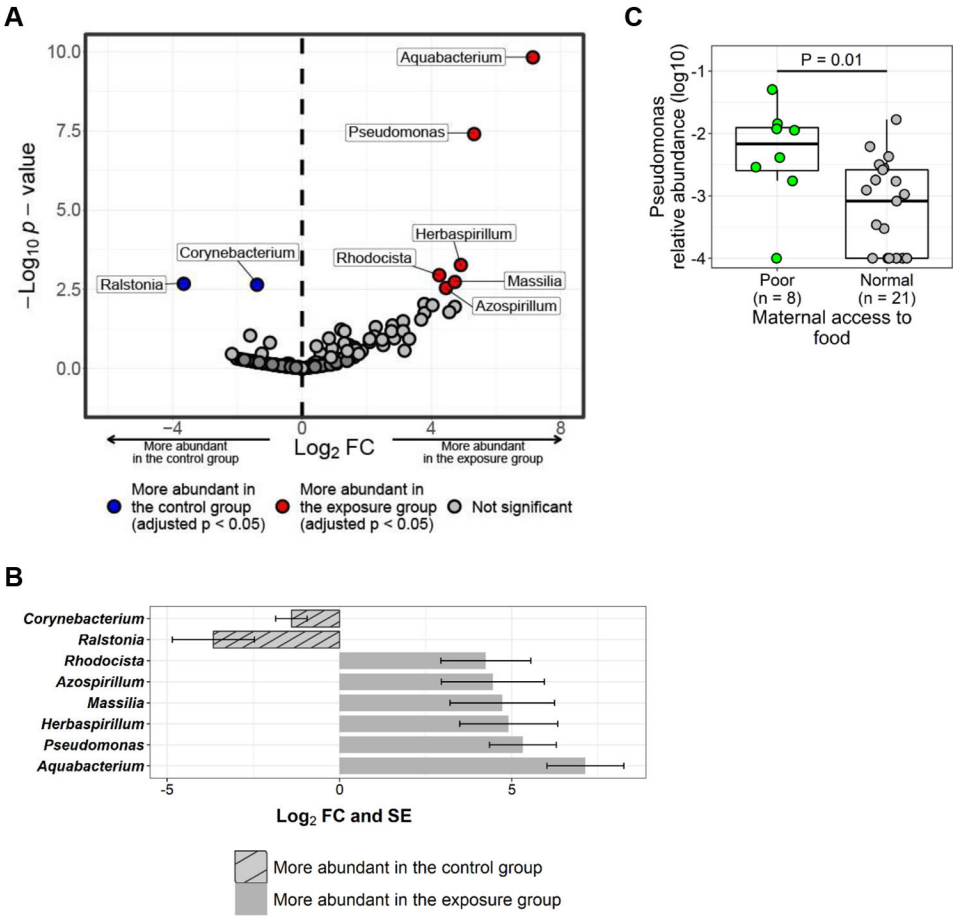

FIG 5.

Differentially abundant bacterial genera identified in the nasal microbiome between infants whowere exposed to Hurricane Maria in utero with those who were not. A, Volcano plot showing the fold change(FC) and P values of all of the genera using the DESeq2 algorithm. The dots in red or blue represent significantgenera identified after adjustment for multiple comparisons using the Benjamini and Hochbergmethods. B, Bar plot showing the FC and SE of the significantly different genera. C, The relative abundance of Pseudomonas by maternal prenatal food access in the exposure group (n = 29).

TABLE I.

Characterization of the study participants

Variables	Exposure group (n = 29)	Control group (n = 34)	*P* value
Enrollment dates	March-August 2018	February-September 2019	—
Infant sex: male, no. (%)	10 (34.48)	20 (58.82)	.05
Infant ethnicity: Latino, no. (%)	29 (100)	34 (100)	—
Vaginally delivered, no. (%)	29 (100)	34 (100)	—
Gestational age (wk), mean (SD)	38.86 (1.00)	38.83 (1.36)	.80
Presence of siblings at home, no. (%)	19 (65.52)	24 (70.59)	.67
Exclusive breast-feeding, no. (%)	8 (27.59)	10 (29.41)	.87
Maternal EPDS score, mean (SD)	5.45 (4.85)	4.68 (3.76)	.72
Trimester in pregnancy on the day of Hurricane Maria			
First, no. (%)	8 (27.59)	—	—
Second, no. (%)	21 (72.41)	—	—
Maternal adverse experience from Hurricane Maria			
Power outages, no. (%)	29 (100)	—	—
Exposed to fumes/mold/debris, no. (%)	29 (100)	—	—
Displacement, no. (%)	8 (27.59)	—	—
Food insecurity, no. (%)	8 (27.59)	—	—
Drinking water insecurity, no. (%)	10 (34.38)	—	—

Significance was evaluated on the basis of the Wilcoxon rank sum test and chi-square test.