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Original Paper

ALTERATIONS IN GUT MICROBIOTA AFTER ANTIBACTERIAL TREATMENT DUE TO CONCOMITANT DISEASE AMONG AMBULATORY PAEDIATRIC PATIENTS

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*Antibacterial treatment is an important factor in shaping gut microbiota in children. The study aims to assess the effects of antibacterial therapy on microbiota composition. Parents of children with antibacterial treatment due to a concomitant disease submitted three children's faecal samples (before the treatment, one week, one month after the treatment). Relative Abundance (RA) of bacterial taxa (*16 rRNS*) was compared between baseline and follow-up samples. Among 20 participants (median age 22 months) shifts within a month were noted for* Bifidobacterium *(46.80% vs 28.93% vs 41.50%;* p *= 0.087);* Blautia *(10.80% vs 8.94% vs 11.50%;* p *= 0.06),* Anaerostipes *(3.70% vs 0.32% vs 7.31%;* p *= 0.032), and* Ruminococcaceae *UCG-004 (*p *= 0.020) at baseline/one week/one month, respectively. Median RA of* Eggerthellaceae *decreased from 0.08% at baseline to 0.01% at one month (*p *= 0.040), while RA of* Veillonellaceae *increased from 0.01% at baseline to 0.04% at one month (*p *= 0.022). In conclusion, among the studied toddlers, antimicrobial treatment was associated with temporal alterations of gut microbiota, although a tendency towards the recovery of the pre-treatment microbial composition was noted. Persistent shifts of certain bacterial families could be minor markers for long-term changes in microbiota composition that should be analysed in dynamics.*

Keywords: *gut dysbiosis, antibiotics, children,* 16S rRNA.

INTRODUCTION

Human gut microbiota is recognised as an important factor for health. Although the gut is colonised mainly at birth, microbiota develops throughout the first years of life, and it is still questioned when microbiota becomes stable (Korpela *et al*., 2018).

An important factor influencing microbiota is antibacterial treatment. However, antibiotics are often prescribed for children, thereby promoting gut dysbiosis. Although antibiotic-associated gut dysbiosis is linked to the development of diseases late in life (Vangay *et al.,* 2015), the mechanism is not fully understood. Moreover, some studies show spontaneous normalisation of microbiota after antibacterial therapy in children, and therefore understanding of specific effects of antibacterial treatment to microbiota could help tailor treatment and minimise the side effects of the treatment (Zimmermann *et al*., 2019).

Faecal sample microbiota was analysed as a proxy for gut microbiota. Up to now 16S rRNA gene profiling has been used to analyse and characterise microbiota in respect to bacterial composition.

The objective of the study was to identify short-term gut microbiota changes after antibacterial therapy in infants and toddlers.

MATERIALS AND METHODS

Study design. The present research was part of a longitudinal study "Gut microbiota composition in relation to extrinsic factors and health status in infants and toddlers". The study was carried out in a primary health care doctor praxis in Rīga, Latvia. Parents of consecutive children, who were prescribed antibacterial treatment due to a concomitant disease, were asked to answer a questionnaire and bring three faecal samples of their children (before the treatment, one week and one month after the treatment). Further, bacterial DNA was extracted and 16 rRNS gene sequencing was performed to identify the bacterial taxonomic units. The composition of the gut microbiota was evaluated and compared between baseline and two follow-up samples.

Participants. Inclusion criteria were the following: a previously healthy child (up to five years of age) visiting a doctor due to acute disease that further needed antibacterial therapy.

Exclusion criteria were a severe general status that needed hospitalisation and unwillingness to participate in the study.

Questionnaire. A structured questionnaire included questions about demographic data, perinatal history (including maternal antibacterial therapy during pregnancy), child's anthropometric data, health status, previous antibacterial treatment and side effects during the treatment.

Storage and sampling methodology. Faecal samples were frozen immediately; the frozen samples were transported and stored at –70 °C temperature regimen until DNA extraction.

Microbial DNA isolation and 16S rRNA gene sequencing. Molecular analyses were carried out at the Latvian Biomedical Research and Study Centre, Latvia.

Microbial DNA was extracted using a FastDNA Spin Kit for Soil (MP Biomedicals, Santa Ana, CA, USA), according to manufacturer's guidelines. The concentration of extracted DNA was measured using a Qubit 2.0 Fluorometer and Qubit dsDNA HS Assay Kit (Life Technologies, USA).

Primers were designed for PCR amplification of the 16S rRNA V3–V4 region specific to the domain bacteria according to the 16S Metagenomic Sequencing Library Preparation protocol for Illumina MiSeq (Illumina Inc., USA). In brief, 4 ng of microbial DNA was amplified separately by V3 (341F) and V4 (805R) primers using a Phusion U Multiplex PCR Master Mix (Thermo Fisher Scientific, USA) with the following reaction conditions: denaturation at 98 °C for 30 s, 35 cycles of 98 °C for 10 s, 67 °C for 15 s, 72 °C for 15 s and fragment elongation at 72 °C for 7 minutes. The yield of PCR products was assessed using 1.2% agarose gel electrophoresis and purified using a NucleoMag NGS Clean-Up and Size Select kit (Macherey-Nagel, Germany). The concentration of the PCR product was measured using a Qubit dsDNA HS Assay Kit on a Qubit 2.0 Fluorometer. During the second stage of PCR, 4 ng of V3 and V4 PCR product was used to add Illumina MiSeq i7 and i5 indexes using a custom-ordered Nextera XT Index Kit (Illumina Inc.) primers (Metabion International AG, Germany). For this reaction, Phusion U Multiplex PCR Master Mix was used with thermal cycler reaction conditions as specified above. The 16S rRNA PCR products were then pooled and purified for the sequencing reaction using NucleoMag magnetic beads. The quality and yield of 16S rRNA V3–V4 amplicons was assessed using an Agilent High Sensitivity DNA kit on an Agilent 2100 BioAnalyzer (Agilent Technologies, USA), and using a Qubit dsDNA HS Assay Kit on a Qubit 2.0 Fluorometer. Before sequencing, all samples were diluted to 8 pM and pooled. Samples were paired-end sequenced using a 500 cycle MiSeq Reagent Kit v2 (Illumina Inc, USA) on Illumina MiSeq (Illumina Inc, USA). Each run was expected to produce at least 20,000 reads per sample.

16S sequence analysis. Sequence reads were de-multiplexed using Illumina's MiSeq Reporter Software (Illumina Inc, USA), and quality filtered using fastp (Chen *et al*., 2018). In brief, the first 30 nt from each read were trimmed to remove primer annealing sites; next, dynamic trimming was applied to remove up to 20 low-quality bases from both ends; and finally, bases with a quality score below 20 were removed, and reads shorter than 40 bp were discarded. All quality approved sequences were imported into the QIIME2 v.2022.08 environment for further analysis (Bolyen *et al.,* 2019). The DADA2 plugin (Callahan *et al*., 2016) was used to pair forward and reverse reads, as well as for extra sequence quality control and chimeric sequence removal using a pooled consensus method. The resulting feature table and sequences were used for de novo clustering, employing the search plugin (Rognes *et al.,* 2016) using a 97% identity threshold. Then, *de novo* multiple sequence alignment was performed using the MAFFT method (Katoh *et al*., 2013), while phylogenetic trees were constructed using FastTree2 (Price *et al*., 2010). *De novo* clustered sequences were used for taxonomic assignment with a pre-fitted sklearn-based taxonomy classifier based on the Silva v.132 database (Glöckner *et al*., 2017) trained with Naive Bayes classifier (Pedregosa *et al*., 2011).

Statistical analysis. The composition of gut microbiota in respect to median relative abundance (MRA) of taxa was analysed using software programs IBM SPSS Statistics 23 and MedCalc® Statistical Software version 22.007 (MedCalc Software Ltd, Ostend, Belgium).

The changes in abundance of taxa were analysed by a paired samples t-test or Wilcoxon test and by ANOVA or Friedman test (a parametric or non-parametric test was used, based on the D'Agostino-Pearson test for normal distribution). In addition, the independent samples t-test and Mann–Whitney test were used to compare relative abun-

dances of taxa at different time points. The p value 0.05 was considered significant.

Alpha diversity measures (Shannon and Simpson index) were calculated using the phyloseq v.1.46.0. package (McMurdie *et al*., 2013) in R environment. The Pairwise Wilcoxon Rank Sum test with Holm's p-value adjustment method was used to assess the significance of alpha diversity measures between sample time points. Principal Coordinate Analysis (PCoA) based on Bray–Curtis distances was performed using the phyloseq package. An ANOVA-like pairwise comparison permutation test was used from the vegan v.2.6-8 package to assess the global significance of sample time points on the composition of the infant gut microbiome. Pearson correlation analysis was performed to identify correlation patterns between bacterial genera and sample collection time points using the microbiome Seq v.0.1 package (Ssekagiri *et al*., 2023). A p-value threshold of 0.05 was applied, and the p-value were adjusted using the Bonferroni–Hochberg method, accounting for taxa and groups.

RESULTS

Participant sample. In total, 22 children up to 3.5 years of life participated in the study. Of them, three did not provide the third faecal sample, and therefore, the final sample for analysis included 20 patients (F/M: 14/6) with median age of 22 months (95% CI for the median 18.000–24.090). The majority were vaginally delivered (n = 18) and had received exclusive breastfeeding for at least one month. Children were treated with sulfamethoxazole/trimethoprim (n = 16) or clarithromycin (n = 4) due to acute respiratory tract disease with mean duration of treatment of five days.

Diversity characteristics between sampling points. Sequencing analysis was successful for 60 samples, yielding an average of 54,242.2 ± 85,707.4 sequences per sample. After quality control, 59 samples passed, with an average of 43,167.6 ± 68,909.5 sequences per sample, representing 75.56% ± 13.20% of the raw sequence data. To ensure dataset homogeneity, all samples were rarefied to 4000 sequences per sample following quality control.

To estimate infant gut microbiome taxonomic richness and evenness, we calculated alpha diversity using the Shannon and Simpson indices, respectively (Fig. 1A). However, none of the alpha diversity metrics differed significantly across timepoints ($p > 0.05$). The median Shannon index was 3.79 (IQR 2.82–4.25) at baseline, compared to 3.37 (IQR 2.84 –3.97) and 3.48 (IQR 2.91–4.31) at one week and one month after treatment, respectively ($p = 0.340$; Friedman test). Similarly, the median Simpson index was 0.92 (IQR 0.75–0.95 at baseline, 0.91 (IQR 0.81–0.94) at one week, and 0.91 (IQR 0.87–0.96) at one month after treatment ($p = 0.378$; Friedman test).

Further on, we performed a beta diversity analysis in the form of Principal Coordination Analysis (PCoA) based on Bray–Curtis dissimilarity indices to explore the relationship between samples and sampling points. Analysis revealed that infant gut microbiome samples originating from different timepoints did not exhibit clustering patterns, thus indicating similar taxonomic structures across different sampling points (Fig. 1B). This observation was supported by pairwise comparisons, which revealed no significant differences between different time points ($p < 0.05$, 999 permutations).

The most abundant bacterial families (%, ±SD) in toddler gut microbiomes (Fig. 1C) were *Lachnospiraceae* (40.15% ± 27.23%), *Bifidobacteriaceae* (41.71% ± 28.05%), *Ruminococcaceae* (7.52% ± 13.33%), and *Streptococcaceae* (3.48% ± 5.515%). The most abundant bacterial genera (Fig. 1D) were *Bifidobacterium* (39.08% ± 25.97%), *Blautia* (16.20% ± 17.76%), *Anaerostipes* (7.85% ± 8.97%), and *Faecalibacterium* (5.94% ± 9.31%).

Impact of antibacterial therapy on family and genus-level microbial community abundance. In the family level, the mean abundance of one of the major taxon *Bifidobacteriaceae* decreased non-significantly from 39.96% (SD ± 0.27) at baseline to 25.16% (SD ± 0.23) one week after the treatment ($p = 0.098$), while no differences at all were observed one month after the treatment compared to baseline ($p = 0.42$). Further, the second most abundant family *Lachnospiraceae* did not show differences within one week but raised non-significantly from 40.15% (SD ± 27.41) to 45.52% (SD ± 28); $p = 0.520$); (paired sample t-test).

The most significant differences were observed in low-abundant bacterial families. For instance, the median relative abundance of *Eggerthellaceae* decreased from 0.08% (IQR 0–0.14) at baseline to 0.01% (IQR 0–0.04) after one month ($p = 0.04$). In contrast, the relative abundance of *Veillonellaceae* increased after one month compared to baseline (0.04% (IQR 0–0.29) vs 0.01% (IQR 0–0.05); $p = 0.022$), although it was absent after one week (0%; Hodges–Lehman median difference: –0.03). Lastly, *Coriobacteriaceae* decreased significantly just one week after the treatment (0.88% at baseline vs 0%; $p = 0.026$) (Wilcoxon test).

Regarding the genus level, the median abundance of several bacterial entities decreased significantly (Wilcoxon paired test) one week after the treatment, such as *Colinsella* (0% at week one vs 0.21% at baseline, $p = 0.011$), *Dialister* (0% at week one vs 0.03% at baseline; $p = 0.028$), *Eggerthella* (0% at week one vs 0.03% at baseline; $p = 0.039$), *Lachnospiracae* UCG 004 (0% at week one vs 0.01% at baseline; $p = 0.018$), candidate generaXIII AD3011 from the order *Clostridiales* (0% at week one vs 0.04% at baseline; $p = 0.005$), and *Ruminococcaceae* UCG-004 (0.01% at week one vs 0.03% at baseline; $p = 0.028$). The mean abundance of *Bifidobacterium* decreased non significantly (paired samples t-test) from 45.19% at baseline to 28.93% at week one ($p = 0.093$), while the difference was significant comparing the

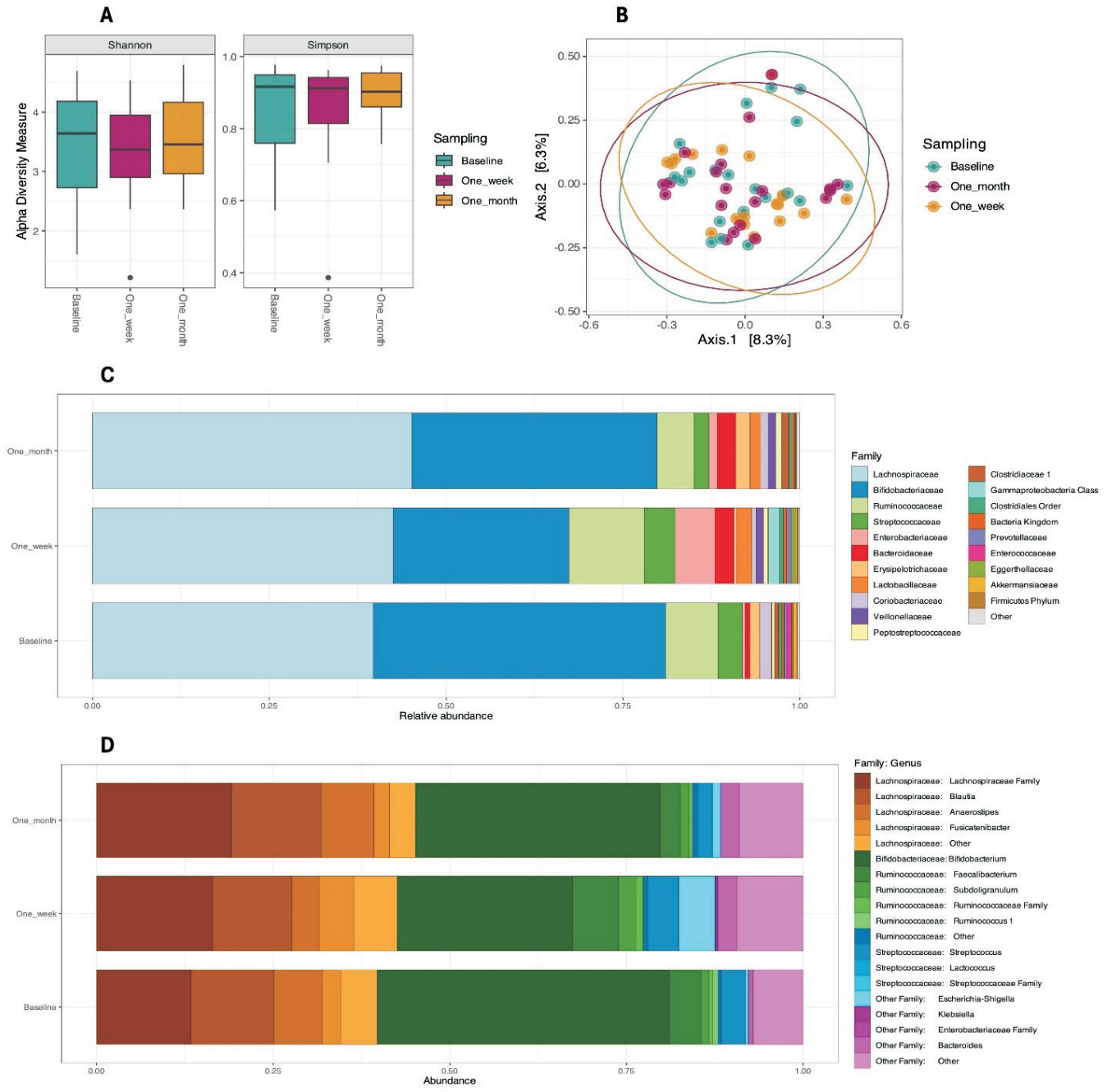

Fig. 1. Taxonomic composition and diversity characteristics. Panel **A** – genus-level alpha diversity, represented by Shannon and Simpson indices. Panel **B** – beta diversity in the form of Principal Coordinate Analysis (PCoA) based on Bray–Curtis distances. Panel **C** – family-level taxonomic composition of infant gut microbiome averaged by sampling points. Panel **D** – genus-level taxonomic composition of infant gut microbiome averaged by sampling points.

abundance in both groups by the independent sample t-test (35.65% at week one vs 44.42% at baseline, $p = 0.046$).

Notable shifts in the abundance of bacterial genera within a month were observed for *Bifidobacterium* (46.80% at baseline, 28.93% at week one, 41.50% at one month; $p = 0.087$); (ANOVA test); as well as *Blautia* (10.8% at baseline, 8.94% at week one, 11.50% at one month; $p = 0.06$), *Anaerostipes* (3.7% at baseline, 0.32% at one week, 7.31% at one month; $p = 0.032$), and *Ruminococcaceae* UCG-004 (mean rank 2.289–1.684 - 2.026; $p = 0.20$); (Friedman test).

Correlation analysis. The abundance of *Bifidobacteriaceae* correlated negatively with abundance of *Lachnospiraceae* at all time points: at baseline (rho = (–0.82); $p = 0.001$), at one week (rho = (–0.62), $p = 0.005$) and at one month (rho = (–0.89); $p = < 0.001$) (Spearman correlation).

The abundance of *Eggerthellaceae* at one week after the treatment correlated negatively with the abundance of *Bifidobacteriaceae* one month after the treatment (rho = (–0.52); $p = 0.023$) and positively with the abundance of *Lachnospiraceae* at one month (rho = 0.63; $p = 0.004$).

Correlation analysis between genus-level entities and the three sample collection time points (baseline, one week, and one month) revealed that none of the bacterial genera exhibited a significant correlation with any time point ($p > 0.05$).

DISCUSSION

Overall, our participant sample composition of gut bacteria resembled a healthy toddler microbiota dominated by *Bifidobacteriacae* and *Lachnospiraceae.* Although several changes in gut microbiota shortly after antimicrobial treatment were identified, a trend towards recovery of microbiota after one month was noted.

Nevertheless, significant shifts of some low-abundant bacterial families could possibly be minor markers for the start of long-term changes in microbiota composition, thus illustrating the complexity of early-life microbiome development.

In general, studies demonstrate less diverse microbiota after antibacterial treatment (Yassour *et al*., 2016). However, in the present patient sample we did not identify significant changes in diversity among the samples at different time points. This could be explained partly by the antibiotic used in our patients, since the majority of children were treated with trimethoprim/sulfamethoxazole. A recent systematic review of studies concluded that trimethoprim/sulfamethoxazole has the least pronounced effect on strain diversity after antibacterial treatment (Wurm *et al*., 2024); therefore lack of changes in bacterial (alpha and beta) diversity after the treatment could be related to the antibiotic.

Further, a systematic review concluded that the most commonly prescribed antibiotics in primary care show an effect on *Bifidobacterium,* demonstrating decreased abundance even after 2–6 months in the majority (but not all) of studies (Elvers *et al*., 2020). In the present sample, we also observed certain shifts in the abundance of *Bifidobacterium* at baseline level and one week after the therapy. However, the statistical significance was demonstrated only in the independent sample test, while the difference was marginal ($p < 0.09$) in the paired sample test. This could be explained by inconsistent paired differences due to low *Bifidobacterium* abundance in the baseline sample in some patients, possibly due to sample storage problems in these participants. Thus, interpatient variations could also influence the result. However, alterations in *Bifidobacteriacae* abundance should be studied further.

Although only non-significant differences in the abundance of *Lachnospiraceae* were observed among different points (possibly, due to a small patient sample size), significant shifts after one week were observed for some genera belonging to *Lachnospiraceae* like *Blautia* and *Anaerostipes*. In total, significant differences after one week were observed for some other genera from *Clostridiales* for example, *Family XIII* AD301 ($p = 0.005$) and *Ruminococcaceae* UCG-004 (0.013).

Our results are consistent with data showing depletion of *Clostridiales* and other bacteria that are important in fibre fermentation and SCFA production (Bokulich *et al*., 2016). Butyrate producers are important in improving the epithelial barrier, thus increasing susceptibility to pathogens. Therefore, temporal shifts in the abundance of these bacteria could increase susceptibility to infections during the convalescence period after antibacterial therapy.

In addition, temporal shifts after the treatment were observed also for the genera *Collinsella* ($p = 0.032$) and *Dialister* ($p = 0.012$).

Nevertheless, a trend towards recovery of initial microbiota (reflected by non-significant changes after one month following an initial decrease in abundance) was observed, supporting the idea of a spontaneous recovery of microbiota after antibacterial treatment. A study on adults demonstrated recovery to near-baseline composition within 1.5 months after the depletion of *Bifidobacterium* species and butyrate producers (Palleja *et al*., 2018)

Despite a trend for recovery after an initial decrease in abundance, significant changes were observed for some low-abundant bacterial families.

For example, lower abundance after one month was observed for *Eggerthellaceae.* Several members of *Eggerthellaceae* have been reported to be able to convert *in vitro* ellagic acid into metabolite isolecithine-A, which exerts anti-inflammatory, anti-carcinogenic, cardioprotective, and neuroprotective properties (Bourke *et al*., 2019). Therefore, recently *Eggerhtellaceae* strains have been suggested even as new-generation probiotics. Moreover, a study on pediatric patients with ulcerative colitis showed that some species belonging to *Eggerthellaceae* were depleted in patients compared to controls. (Zuo *et al*., 2022) Thus, a decrease of the abundance could be evaluated as a negative side effect of antibacterial treatment. Interestingly, a negative correlation between *Eggerthelacea* and *Bifidobacteriaceae* suggests the interaction of different taxa in the struggle for sources and stabilisation of microbiota, thus emphasising the role of diet during convalescence after infections in children.

Another low-abundant bacterial family that showed shifts after one month was *Veillonellacae*, with an increase in abundance after a month. It has been demonstrated that *Veillonellaceae* abundance may be higher in obesity due to altered gut fermentation patterns, as well as in patients with inflammatory bowel disease (Luo *et al*., 2025). Thus, we could speculate that possibly gut microbiota alterations in individuals with overweight and autoimmune diseases could be driven by minor shifts after antibacterial treatment.

However, we have to recognise that only short-term shifts were demonstrated in the present patient sample; therefore it would be important to study long-term changes in gut microbiome of the same participants in dynamics. In addition, the rather small sample without differences in relation to type of delivery and feeding did not allow analyses of other factors that could influence the alterations. Moreover, some clinically important changes could have lost signifi-

cance due to the sample size. It would also be important to analyse the effect of other commonly prescribed antibiotics with a higher number of participants using different kinds of antibiotic.

Nevertheless, this is one of the first studies analysing gut microbiota changes after antibacterial therapy in the paediatric Latvian population. Further, only a few studies about the changes in gut microbiome after antibacterial treatment have been performed in adults in Latvia, the largest being within the GISTAR study, which showed only modest differences in gut microbiota composition between individuals before and after *H. pylori* eradication therapy (Gudra *et al*., 2020). Since systematic reviews about changes of microbiome after antibacterial treatment demonstrate inconsistent results in different countries (Elvers *et al*., 2020), it is important to study the alterations in different populations.

Finally, an important aspect of studying faecal microbiota changes after early antibiotic exposure in children is an increase in antibiotic resistance genes, which could lead to resistance problems in the future. Thus, gut microbiota in paediatric age could play an important role in health status among adults and in the whole society.

CONCLUSIONS

In toddlers concomitant antimicrobial treatment can be associated with temporal alterations in key beneficial bacteria (e.g., *Bifidobacterium*, *Collinsella*) one week post-treatment.

Despite antimicrobial therapy, both alpha and beta diversity remained stable, indicating that the structure of the toddler gut microbiome was largely flexible.

A tendency toward the recovery of the pre-treatment microbial composition within one month was noted, possibly due to the resilience of the baseline gut microbiome in the studied paediatric patient sample.

Significant persistent shifts of certain low-abundant bacterial families (*Eggerthellaceae* and *Veillonellaceae)* could possibly be the first minor markers for long term changes in microbiota composition, which should be further analysed in dynamics.

ETHICS

The study was approved by the Life and Medical Sciences Research Ethics Committee of the University of Latvia, document No. 71-35/50. Parents of children signed informed consent prior to inclusion in the study

DATA AVAILABILITY

Raw sequence data have been deposited at the European Nucleotide Archive under study accession No. PRJEB87327.

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REFERENCES

Bokulich, N. A., Chung, J., Battaglia, T., Henderson, N., Jay, M., Li, H., Lieber, A. D., Wu, F., Perez-Perez, G. I., Chen, Y., *et al.* (2016). Antibiotics, birth mode, and diet shape microbiome maturation during early life. *Sci. Transl. Med.*, **8** (343), 343ra82. https://doi.org/10.1126/scitranslmed.aad7121.

Bolyen, E., Rideout, J. R., Dillon, M. R., Bokulich, N. A., Abnet, C. C., Al-Ghalith, G. A., Alexander, H., Alm, E. J., Arumugam, M., Asnicar, F., *et al.* (2019). Reproducible, interactive, scalable and extensible microbiome data science using QIIME 2. *Nature Biotechnol*., **37** (8), 852–857. 10.1038/s41587-019-0209-9). Author Correction in *Nature Biotechnol.*, **37** (9). https://doi.org/10.1038/s41587-019-0252-6.

Bourke, C. D., Gough, E. K., Pimundu, G., Shonhai, A., Berejena, C., Terry, L., Baumard, L., Choudhry, N., Karmali, Y., Bwakura-Dangarembizi, M., *et al.* (2019). Cotrimoxazole reduces systemic inflammation in HIV infection by altering the gut microbiome and immune activation. *Sci. Transl. Med.*, **11** (486), eaav0537. https://doi.org/10.1126/scitranslmed.aav0537.

Callahan, B. J., McMurdie, P. J., Rosen, M. J., Han, A. W., Johnson, A. J. A., Holmes, S. P. (2016). DADA2: High-resolution sample inference from Illumina amplicon data. *Nature Meth.*, **13** (7). https://doi.org/10.1038/nmeth.3869.

Chen, S., Zhou, Y., Chen, Y., Gu, J. (2018). Fastp: An ultra-fast all-in-one FASTQ preprocessor. *Bioinformatics*, **34** (17). https://doi.org/10.1093/bioinformatics/bty560.

Elvers, K. T., Wilson, V. J., Hammond, A., Duncan, L., Huntley, A. L., Hay, A. D., van der Werf, E. T. (2020). Antibiotic-induced changes in the human gut microbiota for the most commonly prescribed antibiotics in primary care in the UK: A systematic review. *BMJ Open*, **10** (9). https://doi.org/10.1136/bmjopen-2019-035677.

Glöckner, F. O., Yilmaz, P., Quast, C., Gerken, J., Beccati, A., Ciuprina, A., Bruns, G., Yarza, P., Peplies, J., Westram, R., Ludwig, W. (2017). 25 years of serving the community with ribosomal RNA gene reference databases and tools. *J. Biotechnol.,* **261**, 169–176. https://doi.org/10.1016/j.jbiotec.2017.06.1198.

Gudra, D., Pupola, D., Skenders, G., Leja, M., Radovica-Spalvina, I., Gorskis, H., Vangravs, R., Fridmanis, D. (2020). Lack of significant differences between gastrointestinal tract microbial population structure of Helicobacter pylori-infected subjects before and 2 years after a single eradication event. *Helicobacter*, **25** (5), e12748. https://doi.org/10.1111/hel.12748.

Katoh, K., Standley, D. M. (2013). MAFFT multiple sequence alignment software version 7: Improvements in performance and usability. *Mol. Biol. Evolut.,* **30** (4), 772–780. https://doi.org/10.1093/molbev/mst010.

Korpela, K., de Vos, W. M. (2018). Early life colonization of the human gut: Microbes matter everywhere. *Curr. Opin. Microbiol.,* **44**, 70–78. https://doi.org/10.1016/j.mib.2018.06.003.

Luo, Y., Li, M., Luo, D., Tang, B. (2025). Gut microbiota: An important participant in childhood obesity. *Adv. Nutr.,* **16** (2), 100362. https://doi.org/10.1016/j.advnut.2024.100362.

McMurdie, P. J., Holmes, S. (2013). Phyloseq: An R]ackage for reproducible interactive analysis and graphics of microbiome census data. *PLoS ONE*, **8** (4), e61217. https://doi.org/10.1371/journal.pone.0061217.

Palleja, A., Mikkelsen, K. H., Forslund, S. K., Kashani, A., Allin, K. H., Nielsen, T., Hansen, T. H., Liang, S., Feng, Q., Zhang, C., *et al.* (2018). Recovery of gut microbiota of healthy adults following antibiotic exposure. *Nat. Microbiol.,* **3** (11), 1255–1265. https://doi.org/10.1038/s41564-018-0257-9.

Pedregosa, F., Varoquaux, G., Gramfort, A., Michel, V., Thirion, B. (2011). Scikit-learn: Machine learning in Python. *J. Machine Learn. Res.,* 12, 2825–2830. https://dl.acm.org/doi/10.5555/1953048.2078195.

Price, M. N., Dehal, P. S., Arkin, A. P. (2010). FastTree 2 - Approximately maximum-likelihood trees for large alignments. *PLoS ONE*, ***5*** (3), 9490. https://doi.org/10.1371/journal.pone.0009490

Rognes, T., Flouri, T., Nichols, B., Quince, C., Mahé, F. (2016). VSEARCH: A versatile open source tool for metagenomics. *Peer J.*, **4**, e2584. https://doi.org/10.7717/peerj.2584.

Ssekagiri, A. (2023). microbiomeSeq: Microbial community analysis in an environmental context. GitHub. http://www.github.com/umerijaz/microbiomeseq.

Vangay, P., Ward, T., Gerber, J. S., Knights, D. (2015). Antibiotics, pediatric dysbiosis, and disease. *Cell Host Microbe*, **17** (5), 553-564. https://doi.org/10.1016/j.chom.2015.04.006

Wurm, J., Curtis, N., Zimmermann, P. (2024). The effect of antibiotics on the intestinal microbiota in children: A systematic review. *Frontiers Allergy*, 5. https://doi.org/10.3389/falgy.2024.1458688.

Yassour, M., Vatanen, T., Siljander, H., Hämäläinen, A. M., Härkönen, T., Ryhänen, S. J., Franzosa, E. A., Vlamakis, H., Huttenhower, C., Gevers, D., Lander, E. S., Knip, M., Xavier, R. J. (2016). Natural history of the infant gut microbiome and impact of antibiotic treatment on bacterial strain diversity and stability. *Sci. Transl. Med.*, **8** (343), 343ra81. https://doi.org/10.1126/scitranslmed.aad0917.

Zimmermann, P., Curtis, N. (2019). The effect of antibiotics on the composition of the intestinal microbiota: a systematic review. *J. Infect.*, **79** (6), 471-489. https://doi.org/10.1016/j.jinf.2019.10.008.

Zuo, W., Wang, B., Bai, X., Luan, Y., Fan, Y., Michail, S., Sun, F. (2022). 16S rRNA and metagenomic shotgun sequencing data revealed consistent patterns of gut microbiome signature in pediatric ulcerative colitis. *Sci. Rep.,* **12** (1)., 6421. https://doi.org/10.1038/s41598-022-07995-7.

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IZMAIŅAS ZARNU TRAKTA MIKROBIOTĀ BĒRNIEM PĒC ANTIBAKTERIĀLAS TERPAIJAS

Antibakteriāla terapija var būtiski ietekmēt bērnu zarnu trakta mikrobiotas attīstību. Pētījuma mērķis bija analizēt mikrobiotas izmaiņas pēc antibakteriālas terapijas saņemšanas. Pētījuma ietvaros aicinājām vecākus, kuru bērni saņēma antibakteriālu ārstēšanu saistībā ar kādu blakusslimību, savākt bērna fēču paraugus pirms terapijas, nedēļu pēc tās sākuma un vienu mēnesi pēc ārstēšanas. Baktēriju taksonu relatīvo biežumu (16S rRNS) salīdzinājām paraugos pirms un pēc ārstēšanas. Analizējot fēču paraugus 20 dalībniekiem (mediānais vecums – 22 mēneši), tika novērotas izmaiņas *Bifidobacterium* (46,80% pret 28,93% pret 41,50%; p = 0,087), *Blautia* (10,80% pret 8,94% pret 11,50%; p = 0,06), *Anaerostipes* (3,70% pret 0,32% pret 7,31%; p = 0,032) un *Ruminococcaceae* UCG-004 (p = 0,020) relatīvajā biežumā (attiecīgi, sākotnēji, pēc vienas nedēļas un pēc viena mēneša). Mediānais *Eggerthellaceae* relatīvais biežums samazinājās no 0,08% līdz 0,01% (p = 0,040), savukārt *Veillonellaceae* relatīvais biežums palielinājās no 0,01% līdz 0,04% (p = 0,022), attiecīgi, sākotnēji un pēc viena mēneša. Lai gan bērniem antibakteriāla terapija var būt saistīta ar īslaicīgām izmaiņām zarnu mikrobiotas sastāvā, novērota tendence uz pirmsārstēšanas baktēriju sastāva atjaunošanos, kas varētu liecināt par zarnu mikrobiotas noturību. Tomēr izmaiņas atsevišķu baktēriju dzimtu biežumā mēnesi pēc ārstēšanas var norādīt uz mikrobiotas ilgtermiņa sastāva izmaiņu sākumu, kuras būtu jāanalizē dinamikā.