

RESEARCH NOTE

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Comparison of nasopharyngeal bacteriological profile between patients with diabetes and healthy individuals in Accra, Ghana

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Abstract

Background The nasopharynx is characterised by a rich microbial diversity, making it an important endogenous reservoir for respiratory infections. People living with diabetes (PLWD) have a high risk for acquisition of respiratory tract infections, but their nasopharyngeal bacterial flora have rarely been investigated.

Aim To investigate the nasopharyngeal bacterial flora among PLWD and non-diabetics at the Korle Bu Teaching Hospital in Accra.

Methodology This study was a case-control one, involving 130 each of PLWD and non-diabetics. Nasopharyngeal swab specimens were obtained from the participants and cultured for bacteria, which were identified using MALDITOF mass spectrometry.

Results The bacterial flora present in the anterior nares of the participants of both study groups was characterised by a rich diversity, comprising both Gram-positives and Gram-negatives. In the diabetics, the dominant bacteria were *Acinetobacter baumannii* (19.6%), *Staphylococcus epidermidis* (18.12%), *Staphylococcus aureus* (15.2%), and *Rahnella aquatilis* (12.3%). In the control group, however, the dominant bacteria were *Staphylococcus epidermidis* (21.9%), *Staphylococcus aureus* (19.0%), *Proteus mirabilis* (10.9%), *Pseudomonas aeruginosa* (10.2%), *Acinetobacter baumannii* (8.8%), and *Enterobacter cloacae* (7.2%). Between groups, *Acinetobacter baumannii* (19.6% vs. 8.8%, $p=0.014$) and *Rahnella aquatilis* (12.3% vs. 0.0%, $p<0.001$) recorded a significantly higher prevalence in the diabetes group than in the control group. On the contrary, *Klebsiella pneumoniae* (0.0% vs. 4.4%, $p=0.003$), *Proteus mirabilis* (2.2% vs. 10.9%, $p=0.006$), and *Pseudomonas aeruginosa* (0.7% vs. 10.2%, $p<0.001$) had significantly lower prevalence than in the control group.

Conclusion The nasopharyngeal bacterial flora of PLWD in Accra seems to have comparable diversities with those of non-diabetics. Nonetheless, the PLWD had a higher carriage rate of *Acinetobacter baumannii* but seem to have some protection against carriage of *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*.

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Keywords Nasopharynx, Bacteriological profiles, Diabetes, PLWD

Introduction

The nasopharynx is an anatomical conduit between the nose and the throat, specifically found behind the nasal cavity and above the soft palate and oropharynx [1]. It is a major ecological niche for a variety of bacteria – such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Nes- seiria meningitidis*, *Haemophilus influenzae*, and *Morax- ella catarrhalis* – which co-exist with each other in an intricately delicate symbiotic mix referred to as microbial homeostasis [2, 3]. This homeostasis is essentially a prod- uct of an interplay of antagonism, synergism, and com- petition among the various colonising species [4–10]. For example, hydrogen sulphide-mediated antagonism exists between *S. aureus* and *S. pneumoniae* [11, 12] and between *S. aureus* and *N. meningitidis* [4]. Other molecu- lar mechanisms of antagonism, insights of which remain unclear, exist between *S. aureus* and each of *H. influenzae* and *M. catarrhalis* [13]. In contrast, some sort of syner- gism exists among *H. influenzae*, *M. catarrhalis*, and *S. pneumoniae*, especially, within polymicrobial biofilms [7, 9, 10, 14].

The rich microbial diversity of the nasopharynx makes it an important endogenous reservoir for respiratory infections, which usually occur following major pertur- bations in the microbial homeostasis [15–17]. Examples of such homeostasis-disrupting events include increased antibiotic consumption and immune suppression [18– 21]. People living with diabetes (PLWD), who comprise about 10% of the global adult population, are a recog- nised immunocompromised group who have a high vul- nerability to hospitalisations and respiratory infections [22–25]. Prevention and proper management of these infections require an improved understanding of how the nasopharyngeal microbiota of PLWD differs from that of those with no diabetes, but such data are largely non- existent. To help fill the identified knowledge gap, this study provides a snapshot comparison of the microbiota of the nasopharynx between PLWD and non-diabetics at the largest tertiary care facility in Ghana.

Methodology

This case-control study was done at the National Diabe- tes Management and Research Centre (NDMRC) which can be found on the premises of the Korle Bu Teach- ing Hospital (KBTH). The NDMRC is the biggest centre in Ghana dedicated to diabetes care and mainly offers outpatient services to its over 7500 registered patients, approximately 70–80 of whom visit the centre daily. The patients comprise PLWD referred from KBTH, as well as those from other healthcare facilities around the country.

In total, 130 each of PLWD and non-diabetic partici- pants were sampled from July 2022 to April 2023. The diabetes patients were expected to have clinically-proven diabetes and to be aged between 15 and 95 years. The non-diabetics were recruited based on their fasting/ran- dom blood sugar levels less than or equal to 7.0 mmol/l and less than or equal to 11.1 mmol/l for random blood sugar results (and not on glucose-lowering medica- tions), and were between 15 and 95 years old. Potential participants who had disease warranting hospitalisation and/or a recent (two weeks) history of antimicrobial therapy were excluded. Participants' data were gathered with a standard questionnaire. Nasopharyngeal swabs were taken by a qualified infectious disease nurse who had been trained to sample the nasopharynx during the COVID-19 pandemic, via rotation of sterile calcium alginate swabs at the anatomical site. The specimens were thereafter kept in vials containing 1 ml skim milk- tryptone-glucose-glycerin (STGG). Within four hours of collection, they were transported to the Department of Medical Microbiology, University of Ghana Medical School, which is about 500 m from the sampling site, for laboratory processing. The processing involved an ini- tial vortexing and a subsequent storage at -80 °C, until needed.

At the laboratory, specimen processing and bacterial identification were done as previously described [26, 27], with a few modifications. Plating of the samples was preceded by a pre-enrichment step. Media on which the samples were cultured included 5% sheep blood agar with and without gentamicin supplementation, choco- late agar, and mannitol salt agar. The blood and chocolate agar plates were incubated at 37 °C in 5% CO₂, whereas the MacConkey and mannitol salt agar plates were incu- bated aerobically at 37 °C, all for 24 to 48 h. Subcultur- ing was performed until pure cultures were obtained, followed by bacterial identification using MALDI-TOF mass spectrometry.

STATA 14 (Strata Corp, College Station, TX, USA) was used for the data analysis. Chi square and Fisher's exact tests were used in comparing the bacteriological profile between the diabetics and non-diabetics, at a 0.05 alpha level.

This study was approved by the Ethical and Pro- tocol Review Committee of the College of Health Sciences, University of Ghana (Unique identifier: "CHS- Et/M.1–4.7/2021–2022"). Written informed consent was also obtained from all the participants.

Results

In total, 130 each of PLWD and non-diabetic individuals participated in this study, and they had identical gender distributions – in each group, 17.7% ($n=23$) were males and 82.3% ($n=107$) were females. Similarly, the mean age was identical for both groups (59.4 ± 10.1 years), as was the age range (28 to 89 years), and the only existing co-morbidity was diabetes, which was present among participants of the diabetes group. Furthermore, the participants of the diabetes group mainly had Type 2 diabetes (95.4%, $n=124$), while just a few had Type 1 diabetes (4.6%, $n=6$); the duration of diabetes was less than 10 years for 33.1% ($n=43$), 10–20 years for 49.2% ($n=64$), and greater than 20 years for 17.7% ($n=23$) of the participants.

The bacterial flora present in the anterior nares of the participants of both study groups was characterised by

a rich diversity, comprising both Gram-positives and Gram-negatives (Table 1). In the PLWD, the dominant bacteria were *Acinetobacter baumannii* (19.6%), *Staphylococcus epidermidis* (18.12%), *Staphylococcus aureus* (15.2%), and *Rahnella aquatilis* (12.3%). In the control group, however, the dominant bacteria were *Staphylococcus epidermidis* (21.9%), *Staphylococcus aureus* (19.0%), *Proteus mirabilis* (10.9%), *Pseudomonas aeruginosa* (10.2%), *Acinetobacter baumannii* (8.8%), and *Enterobacter cloacae* (7.2%).

Between groups, *Acinetobacter baumannii* (19.6% vs. 8.8%, $p=0.014$) and *Rahnella aquatilis* (12.3% vs. 0.0%, $p<0.001$) recorded a significantly higher prevalence in the diabetes group than in the control group. On the contrary, *Klebsiella pneumoniae* (0.0% vs. 4.4%, $p=0.003$), *Proteus mirabilis* (2.2% vs. 10.9%, $p=0.006$),

Table 1 Comparison of the microbiota isolated from the PLWD and non-diabetics

Bacteria Isolated	Diabetes Group		Control Group		p value
	Number	Prevalence (%)	Number	Prevalence (%)	
Gram-negative bacteria					
<i>Acinetobacter baumannii</i> **	27	19.6	12	8.8	0.014
<i>Stenotrophomonas maltophilia</i>	5	3.6	0	0.0	0.06
<i>Rahnella aquatilis</i> **	17	12.3	0	0.0	<0.001
<i>Citrobacter koseri</i>	4	2.9	0	0.0	0.06
<i>Enterobacter cloacae</i>	8	5.8	10	7.2	0.81
<i>Enterobacter bugandensis</i>	1	0.7	0	0.0	0.99
<i>Escherichia coli</i>	1	0.7	5	3.6	0.21
<i>Aeromonas jandaei</i>	2	1.4	0	0.0	0.50
<i>Aeromonas veronii</i>	2	1.4	0	0.0	0.50
<i>Klebsiella pneumoniae</i> **	0	0.0	6	4.4	0.03
<i>Klebsiella aerogenes</i>	2	1.4	1	0.7	0.99
<i>Klebsiella variicola</i>	4	2.9	0	0.0	0.06
<i>Providencia stuartii</i>	0	0.0	3	2.2	0.25
<i>Pseudomonas aeruginosa</i> **	1	0.7	14	10.2	<0.001
<i>Proteus mirabilis</i> **	3	2.2	15	10.9	0.006
<i>Kosakonia cowanii</i>	0	0.0	1	0.7	0.99
Gram-positive					
<i>Enterococcus faecalis</i>	1	0.7	0	0.0	0.99
<i>Streptococcus pneumoniae</i>	1	0.7	1	0.7	1.00
<i>Streptococcus oralis</i>	4	2.9	0	0.0	0.12
<i>Staphylococcus aureus</i>	21	15.2	26	19.0	0.52
<i>Streptococcus peroris</i>	1	0.7	0	0.0	0.99
<i>Staphylococcus epidermidis</i>	25	18.12	30	21.90	0.54
<i>Staphylococcus haemolyticus</i>	5	3.6	6	4.4	0.99
<i>Staphylococcus cohnii</i>	1	0.7	0	0.0	0.99
<i>Staphylococcus schleiferi</i>	0	0.0	1	0.7	0.99
<i>Bacillus pumilus</i>	0	0.0	2	1.46	0.50
<i>Corynebacterium amycolatum</i>	1	0.7	0	0.0	0.99
<i>Micrococcus luteus</i>	0	0.0	1	0.7	0.99
<i>Streptococcus mitis</i>	1	0.7	0	0.0	0.99
<i>Staphylococcus hominis</i>	0	0.0	4	2.92	0.12
<i>Streptococcus vestibularis</i>	1	0.7	0	0.0	0.99

**Significant at 0.05 alpha level

and *Pseudomonas aeruginosa* (0.7% vs. 10.2%, $p < 0.001$) each had a significantly lower prevalence than in the control group.

Discussion

The nasopharynx is characterised by a rich microbial diversity, making it an important endogenous reservoir for respiratory infections [1–3, 15–17]. People with diabetes have high vulnerability to hospitalisations and respiratory infections [23–25], but have hardly been studied in connection with their nasopharyngeal microbiota. A well-rounded understanding of how the nasopharyngeal microbiota of PLWD differs from that of those without diabetes is crucial to effective prevention and management of respiratory infections that may arise among them. To help fill the identified knowledge gap, this study aimed to provide a snapshot comparison of the microbiota of the nasopharynx between PLWD and non-diabetics at the Korle Bu Teaching Hospital.

The richness in nasopharyngeal bacterial diversity in both study groups is consistent with what is generally known about the nasopharyngeal bacterial flora [1–3]. *Staphylococcus aureus* and *Staphylococcus epidermidis* were key colonisers in both study groups, with comparable relative proportions within each of the study groups. This is interesting, especially, given that they are known to be antagonistic to each other [28, 29]. Probably, when it comes to *Staphylococcus aureus* and *Staphylococcus epidermidis* colonisation in the nasopharynx, there are interplays introduced by age which are not necessarily cancelled out by diabetes status. It is noted that of the two, *S. aureus* is credited with a higher clinical significance, and especially in PLWD, it is the predominant cause of infections [30, 31]. This may, however, be of little relevance in the studied cohort of PLWD. This is because the proportions of the pathogen between them and their non-diabetic counterparts were not significantly different, which suggests that adults may generally share the same risks when it comes to *S. aureus* carriage, regardless of diabetes status. It remains to be seen whether this observation is universal for PLWD, given that a recent study published by Mizgala-Izworska et al. [32] in Poland also reported similar *S. aureus* carriage risks between PLWD and non-diabetics. Moreover, the ease of transmissibility of AMR determinants between the Staphylococci, especially, the methicillin resistance-conferring SCCmec-harboured *mecA* gene, suggests that *S. epidermidis* merits further clinical attention [33–35].

The significantly higher carriage prevalence of *A. baumannii* among the diabetes group is noteworthy, given the endured high importance of this coloniser as a priority pathogen in the context of AMR [36, 37]. Moreover, the pathogen has been implicated in respiratory tract infections involving PLWD [23–25]. Although pathogen

carriage does not necessarily result in infections, the probability that *A. baumannii* respiratory infections had origins from nasopharyngeal carriage is high [38–40]. That notwithstanding, longitudinal studies would be important to determine variations in the carriage of the pathogen over time and how these translate to infections. Insights on this epidemiological gap could be bolstered further if the sites for these studies are geographically diverse.

The significantly lower carriage prevalence of *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa* among the PLWD is noteworthy, as it suggests that diabetes probably confers some protection against carriage of these pathogens. It is unclear what the mechanism of this seeming protective advantage of diabetes is, and thus, further investigations are warranted. This is because these organisms are part of critical- and high-priority pathogens which have received a lot of attention for high AMR as well as high morbidities, mortalities, and healthcare costs [36, 37]. The mechanism(s) underlying this observation, if determined, could be exploited in the control of these pathogens.

Limitations

This study had a few limitations. First, owing to its cross-sectional nature, it does not distinguish persistent carriage from intermittent carriage, and does not provide information on spatio-temporal variation in the microbiota composition. Also, non-culturable bacteria may have been missed, as culture-based techniques were relied upon in the study. Future studies employing metagenomics techniques could allow for generation of more complete insights, which could cover in-depth information on the nasopharyngeal mycobiome and virome.

Conclusion

The nasopharyngeal bacterial flora of PLWD in Accra seems to have comparable diversities with those of non-diabetics. Nonetheless, the PLWD had a higher carriage prevalence of *Acinetobacter baumannii* but seem to have some protection against carriage of *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*.

Abbreviations

AMR	Antimicrobial resistance
KBTH	Korle Bu Teaching Hospital
MALDI-TOF	Matrix-assisted laser desorption/ionization
NDMRC	National Diabetes Management and Research Centre
PLWD	People living with diabetes
STGG	Skim milk-tryptone-glucose-glycerin

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Author contributions

Conceptualisation, E.S.D. and F.C.N.K.; methodology, N.T.K.D.D., Y.A., P.B.T.-Q., M.-M.O., F.C.N.K., and E.S.D.; validation, N.T.K.D.D., Y.A., P.B.T.-Q., M.-M.O., F.C.N.K., and E.S.D.; formal analysis, M.S.D.-D., N.T.K.D.D., F.C.N.K., and E.S.D.; investigation, Y.A., P.B.T.-Q., M.S.D.-D., M.-M.O., B.B.B., G.O.S., I.O.J., and E.S.D.; resources, F.C.N.K., N.T.K.D.D., Y.A., P.B.T.-Q., M.S.D.-D., M.-M.O., B.B.B., and E.S.D.; data curation, F.C.N.K., Y.A., M.S.D.-D., M.-M.O., B.B.B., G.O.S., I.O.J., and E.S.D.; writing—original draft preparation, F.C.N.K. and E.S.D.; writing—review and editing, F.C.N.K., N.T.K.D.D., Y.A., P.B.T.-Q., M.S.D.-D., M.-M.O., B.B.B., G.O.S., I.O.J., and E.S.D.; visualisation, F.C.N.K., N.T.K.D.D., P.B.T.-Q., M.S.D.-D., and E.S.D.; supervision, N.T.K.D.D., Y.A., and E.S.D.; project administration, E.S.D., N.T.K.D.D., and M.S.D.-D. All authors have read and agreed to the published version of the manuscript.

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Data availability

All relevant data are within the manuscript.

Declarations

Ethics approval

This study was approved by the Ethical and Protocol Review Committee of the College of Health Sciences, University of Ghana (Unique identifier: "CHS-Et/M.1–4.7/2021-2022").

Consent to participate

Written and oral informed consent were obtained from all the participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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