NASAL-PHARYNGEAL MUCOCILIARY CLEARANCE TIME AMONG HEALTHY NIGERIANS: AN UPDATE

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ABSTRACT

Background: *Nasal-Pharyngeal-Mucociliary-Clearance (NPMC) is the primary innate defence mechanism of upper airway. The aim of the study is to revalidate the use of saccharine for the assessment of the NPMC time based on age and sex among healthy Nigerians and establish a reference value.*

Methodology: *A prospective, cross-sectional, descriptive study carried out at Kogi State Specialist Hospital, Lokoja, over six-month period, following ethical approval. All participants were given information sheet and were then made to complete a modified version of the health-questionnaire as well as a semi-structured questionnaire and nasal endoscopy done to determine the most patent nasal cavity. The saccharine test was carried out using standard technique described by Andersen et al in 1974. Using a stop watch, time of introduction and time of perception of taste was documented. All information was entered into IBM-SPSS Statistics version 24 software and analysed descriptively and results presented in tables and figures.*

Results: *A total of 208 subjects filled out the modified respiratory health questionnaire and 201 were found fit. The age range was 10-65years (mean age of 29.79years) with 91 males and 110 Females. The duration of NPMC time ranged from 5-18 minutes with a mean NPMC time of 11.35minutes (SD=3.00±0.25minutes). The average NPMC time range was between 10-14 minutes for both gender with a P-value of 0.816 and chi square of 0.4084. The average duration NPMC time increased with age with 10-19 yrs with least average NPMC time of 10.43minutes, while 60-69yrs had an average of 14.50minutes with a $\alpha^2 = 28.45$ and a P-value of 0.000396.*

Conclusion: *The minimum time for NPMC was 5minutes and the maximum time was 18 minutes with a mean NPMC duration of 11.35minutes. There was positive correlation between -the age and NPMC time and no correlation between gender and NPMC time.*

Keywords: *Nasal; Pharyngeal; Mucociliary; Clearance; Time; Saccharine*

INTRODUCTION

The Nasal-Pharyngeal Mucociliary Clearance (NPMC) is an important defence mechanism in the human respiratory system as it protects the body against noxious inhaled materials.[1]
The nasal cavity is lined by ciliated cells and it is estimated that the mucous lining the airway trap up to 25 million particles an hour.[2]This function is coordinated by cilia beating in a metachronous fashion at a frequency of 7-16 Hz at normal body temperature[3, 4] to the throat called ciliary escalator, ciliary clearance or nasal-pharyngeal mucociliary clearance. This system transports the mucus from the nasal cavity to the nasopharynx, where after it is swallowed[5-7].
The impairment of this function, either acquired or genetically determined, can lead to mucous stagnation and subsequent chronic infection of the upper and lower airways [1, 2]. Appropriate nasal-pharyngeal mucociliary clearance is possible only when there is proper ciliary movement and an adequate mucous blanket especially in the upper airway like the nose and paranasal sinuses, while in the lower airway this is replaced by mechanisms like coughing[8].
James et al. in their study reported that the normal NMC time is determined to be up to 20 minutes. Duration of 30 minutes is considered as the cut-off point that discriminates normal subjects from subjects with impaired NMC[9].
NPMC has been reported to be affected by various factors, like aging, body temperature, drugs (like adrenaline, acetylcholine, corticosteroid, and intranasal medications), tobacco use and smoking, and environmental factors (like pollutant, smoke, and dust) affect this system, besides pathological conditions such as allergic rhinitis, acute or chronic rhinosinusitis, and deviated nasal septum.[10-13]
Various methods have been used to evaluate the NPMC time across, these include:

1. Mucociliary transit time with saccharin called Saccharin test which was used in our previous study and in this study as well to find out if there is any variation.
2. Mucus flow rate with - 99m Tc-labelled particles also called Rhinoscintigraphy - 99m Tc-labelled resin particle.
3. Mucus flow rate with radiopaque Teflon dicks.
4. Mucociliary transit time with colouring substances.
5. Mucociliary transit time with a combination of dye and saccharin.

The use of saccharine for the assessment of the mucociliary clearance time from previous studies has established this method to a valid and reliable measure of mucociliary clearance[14,15].

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MATERIAL AND METHODS

This was a prospective, cross-sectional, descriptive study that was carried out at the family medicine and Otorhinolaryngology clinics of Kogi State Specialist Hospital, Lokoja, North-Central Nigeria over six-month period (March 2020 and August 2020).
The study was approved by the Ethical review committee of the hospital, and written informed consent was obtained from participants following one-on-one detailed explanation on the objective and methodology.

Study Population

The study sample was drawn from healthy residents of Lokoja, the state capital of Kogi state in North-central Nigeria. These Participants were Nigerian non-smokers aged over 10 – 65 years selected from among the consenting hospital workers, well adult patients attending well adult clinic of the hospital, Patient's relatives who accompanied patients to the hospital. Age 10 years was used as the lower limit to allow for cooperation with the investigation to be carried out. A non-smoker was defined as an individual who had never smoked. All individuals participated voluntarily, did not receive any payment, were not compelled to undertake the test and their refusal did not have any effect on the activities they came to do in the hospital. We excluded individuals with anatomic abnormalities of the upper respiratory tract, history of nasal surgery or nasal trauma, chronic nasal or respiratory disease, acute respiratory tract disease of either upper or lower tract infections within 6 weeks prior to the test and altered taste (due to the on-going COVID-19 pandemic).We also excluded smokers, tobacco usersand those addicted to other drugs (determined from taking history) and those receiving medications that might influence mucociliary clearance such as decongestants, topical nasal spray with anticholinergic or

adrenergic agents [10-13]. Pregnant women were also excluded from the study.

All participants were counselled on the nature and aim of the test after which the test was conducted, and the significance of the results were discussed with them. All participants and guardians signed a written informed consent, and assent obtained from participants under the age of 18. During the selection phase, all participants were made to complete a modified version of the health questionnaire described in the Epidemiology Standardization Project where the principles for assessing the state of respiratory health were established[16]. Nasal endoscopy was done using zero-degree rigid endoscope to access the most patent nostril with least resistance to physiological airflow which was used for the study (Figure 1). Once it had been established that the individual was healthy and did not meet any exclusion criteria, NPMCtime was measured by the saccharine test according to the standard technique described by Andersen et al in 1974[17] further modified by Rutland & Cole[8]as described below. It is the standard technique of measurement of NMCT which is reproducible. All the participants were studied at similar room temperatures between 18ºC and 30ºC and relative humiditybetween 40% and 70% and in the same posture by the same investigator to minimise human errors. The stopwatch was checked from time to time to ensure that it was working properly.

Saccharine Test Method

The participants were asked to sit head upright with their head tipped slightly forward while breathing quietlythrough the nose with their mouth closed (not forced), without sneezing or blowing their nose, and without taking any substances that might interfere with the test and to swallow every 30 seconds. A saccharine granule 1 mm in diameter was placed approximately 1 cm posterior from the anterior end of the inferior turbinate. The exact time of saccharine placement or introduction was noted and recorded. They were told to indicate when they first notice any change in taste. The actual taste they were to expect was not specified to avoid false positives. The saccharine particle was carried by means of ciliary transport along the entire nostril until it reached the oropharynx, whereupon a characteristic sweet taste could be perceived. The time elapsed was recorded to the nearest minute and the test was considered complete. If the participant did not detect any taste after 60 minutes, the saccharine was placed on the tongueto confirm that the participant does not have any taste abnormality and the absence of taste orally led to exclusion from the study.

All information was entered into IBM SPSS Statistics version 24 software, analysed descriptively and results presented in tables and figures

RESULTS

A total of 208 subjects filled out the modified respiratory health questionnaire, 201 were found fit and underwent the Nasal-Pharyngo-Mucociliary test. Three did not complete modified respiratory health questionnaire, one had upper respiratory tract infection, three did not perceive the taste after 60minutes and still could not recognise the taste when placed on the tongue thus were excluded.

The age range was 10-65years with a mean age of 29.79years (SD = 11.28±0.80) (Table 1). There were 91males and 110 females with M:F ratio of 1:1.2. From our studies the minimum time for the nasal-pharyngo-mucociliary clearance time was 5minute and the maximum time was 18 minutes with a mean duration of Clearance from our study was 11.35minutes (SD=3.00±0.25minutes) the mean duration of clearance group was 11-.15 minutes.

The NPMC time-Gender frequency table showed that over 80% of the participants had NPMCT between 5 -14minutes and about 10.5% of those with NPMC time above 15minutes were females while 7.5% of them were males as seen in Table 2. From the cross-tabulation of Gender and NPMC time, majority of the participants who had NPMC time above 15minutes were females and constituted about 10.5% while the males constituted 7.5% and statistical analysis showed a Chi square (α^2) = 0.4084 with P-value = 0.815, since P-value> 0.05 thus not statistically significant (Table 2).

Using the cross tabulation of age-sex with the duration of mucociliary clearance, it was observed that there is an increase in the clearance time duration relative to increase in the age of the participants. The correlation showed a chi square of 28.45 with P-value of 0.000396 (P<0.05) which is statistically significant thus indicating a positive relationship between the age and the duration of mucociliary clearance (Table 3).

The Mean NPMC time for the age groupings was observed to increase with increasing age among the participants'and the statistical analysis showed α^2 =28.45 with a P-value of 0.000396Since P-value is < 0.05 thus the relationship between Age and Duration of clearance is statistically significant (table 4)

DISCUSSION

The mucociliary mechanism is the natural best air cleaner, protecting the upper and lower respiratory tracts and the susceptible alveoli. The mucociliary mechanism constitutes the initial line of the airway defence system against harmful particles and other agents in the air. [17] Our study looked at the healthy population from Nigeria and the age group spanned from 10 years to 65 years which covered all the age groupings except those below the age of 10 years which the investigators felt might not cooperate for the insertion of the sodium saccharine into the nasal cavity or may not be able to accurately observe change in taste of the mucous in the pharynx. Ours was hospital based using the patient without ear, nose, and throat complaints to forestall any form of hypersensitivity reaction to sodium saccharine which can be easily managed and to control the environmental condition such as humidity, temperature that can affect the clearance of this agent from the nasal cavity.[6]

The mean age in our study was 29.79years (SD = 11.28±0.80) which is comparable to a study in Kenya [18] with a slightly lower mean and difference may be related to the study population. The Male to Female ratio was 1:1.2 which was insignificant. The modal age group was among the young adult constituting more than 50% of the participants.

Most of the participants were students constituting one-third of the study population while the least were the pensioners which was about 1.5% of the study population. This may be because the institution where the study was carried out is close to a higher institution. A community-based study may be required to look at the various occupations and the NPMC from where an inference can be drawn.

Average clearance time for an adult, free from nasal disease, was 7–15 min based on a saccharin test[1,18–21]. If the subjects were fasting (e.g., waiting to go to a nasal procedure) the average clearance was measured to be 13.3 min (5.3–32.5 min) which is still higher than the average NPMC time in our study. Patients having allergy or rhinitis are likely to have accelerated mucociliary transport, which is mainly due to changes in the physiologic properties of the mucus in addition to an increased ciliary beat frequency

The NPMC timein our study varied between 5min as the minimum clearance time and 18minutes as the maximum clearance time from this study compared to an earlier study that found the maximum time to be 43 minutes[15]. The mean clearance time in this study was found to be 11.35minutes, this is slightly higher compared to recent study in France that compared smokers and non-smokers and found an average saccharine transit time of 7.26minutes[22]among non-smokers and is lower than a similar study done among the COVID patients[23]which however concluded that COVID did not have any effect on mucociliary clearance. The mean NPMC time for our study for both sexes were 11.35minute and Standard deviation (SD=3.00±0.25) which still fall within the existing reference value [2, 3,11,19-21] but higher than the study carried out in Kenya [18]that found a value of 7.51minutes.

From our study there was a strong correlation between the age and the NPMC time in which the longest duration was observed in the elderly age group. This may be due to impaired lung defence by mucociliary clearance mechanisms impairment with age and is similar to a study carried out in India. [24]

Our study with 201 evenly distributed healthy individuals according to age, showed a positive correlation (P<0.05) between age and nasal-pharyngealmucociliary clearance time measured with the saccharine test.

A NPMC time of more than 60 minutes is generally regarded as abnormal and only three participants had this value but were excluded as they could still not recognize the taste when placed on the tongue. They were thus were further evaluated for COVID infection in-line with COVID-19 protocols at the time of this study.

All previous researchers generally agreed that individuals with a nasal MCT greater than 60 minutes should be studied to rule out any disease of the mucociliary system. [25]

In conclusion, our study of healthy Nigerians using Andersen technique modified by Rutland revealed an average nasal-pharyngeal mucociliary clearance time range of 11.0 – 15.0minuteswith a mean duration of 11.35minutes, slightly higher in females than males. There was positive correlation between Age and NPMC time with P-value of 0.000396. However, there was no correlation between gender and NPMC time.

Table 1 - Socio-demographic characteristics n = 201

Age (years)	Frequency (%) Male (%)	Female (%)	Frequency (%) Total
10-19	13 (6.5)	21 (10.5)	34 (17.0)
20-29	43 (21.4)	34 (16.9)	77 (38.3)
30-39	19 (9.5)	33 (16.4)	52 (26.0)
40-49	08 (4.0)	16 (8.0)	24 (12.0)
50-59	03 (1.5)	06 (3.0)	09 (4.5)
60-69	05 (2.5)	0 (0.0)	05 (2.5)
Total	**91 (45.3)**	**110 (54.7)**	**201 (100)**

Occupation	Frequency (%)
Students	68 (34)
Civil servants	58 (29)
Artisans	32 (16)
Unemployed	15 (7.4)
Trading	14 (6.9)
Housewife	09 (4.3)
Pensioner	5 (2.5)
Total	**201 (100)**

Educational Levels	Frequency (%)
None	2 (0.5)
Primary	61 (30.3)
Secondary	118 (58.5)
Tertiary	20 (10.6)
Total	**201 (100)**

Mean Age = 29.79years
SD = 11.28±0.80
Median Age = 29.00yrs
Model age = 30.00 years
Age range 10-65 years

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Table 2 – Nasal-Pharyngeal Mucociliary Clearance Time (NPMC) **n= 201**

Clearance Time Range (Minutes)	Frequency (%) Male	Female	Statistics
5-9	33 (16.4)	20 (10.0)	Chi square (α^2) = 0.4084
10-14	43 (21.4)	69 (34.3)	P-value = 0.815
15-19	15 (7.5)	21 (10.5)	P-value> 0.05 thus not
Total	**91**	**110**	statistically significant

Table 4 – Cross-Tabulation of the Age group with their Mean Nasal Pharyngeal Mucociliary Clearance Time by Sex (n= 201)

Age group (years)	Mean Nasal-Pharyngeal Mucociliary Clearance time (Min) Male	Female	Cumulative Average (Minutes)	Statistics
10-19years	8.61	12.25	10.43	**α^2 =28.45 P-value = 0.000396 Since P-value is < 0.05 thus the relationship between Age and Duration of clearance is statistically significant**
20-29years	10.80	10.30	10.55	
30-39years	10.11	11.03	10.57	
40-49years	11.13	12.25	11.69	
50-59years	12.00	14.00	13.00	
60-69years	14.50	0.00	14.50	

Table 3 – Cross-tabulation of NPMC with Age and Sex of the population n = 201

NPMC (MIN) AGE (YRS)	05-09 M	F	10-14 M	F	15-19 M	F	Total M	F
10-19	10	03	01	11	02	07	**13**	**21**
20-29	13	06	23	23	08	05	**44**	**34**
30-39	09	10	08	17	01	06	**18**	**33**
40-49	0	01	07	13	01	02	**08**	**16**
50-59	01	0	01	05	01	01	**03**	**06**
60-69	0	0	03	0	02	0	**05**	**0**
Total	**3320**		**43**	**69**	**15**	**21**	**91**	**110**

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