The Association of Sleep-Related Breathing Disorders Among Pediatric Patients with Allergic Rhinitis: A Cross-Sectional Study in a University Hospital

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ABSTRACT

Introduction: Allergic rhinitis is a common condition in children linked to sleep-related breathing disorders (SRBD). Because of nasal congestion, it can cause obstructive sleep apnea, sleep fragmentation, and excessive fatigue. Studies regarding its association with SRBD is limited.

Objectives: To determine the association of allergic rhinitis with sleep-related breathing disorders.

Methodology: A cross-sectional analytical study involving pediatric patients diagnosed with allergic rhinitis was conducted. Allergic rhinitis severity was evaluated with the ARIA classification. SRBD was identified using the validated Filipino version of the pediatric sleep questionnaire. Potential association between allergic rhinitis and SRBD were assessed using the student's t-test, Fisher's exact test and odds ratio.

Results: A total of 66 children with mean age 8.2 years were included in the study. The mean age, weight, height, and BMI were comparable among participants who were positive or negative for obstructive sleep apnea (OSA). Among the perceived problems related to sleeping disorders, snoring

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loudly, heavy breathing, dry mouth of awakening, not listening, and difficulty organizing showed different responses (p<0.05) among the subgroups of allergic rhinitis. The odds ratio of snoring loudly, not listening, difficulty organizing, heavy breathing, and unfreshened in the morning were more likely among patients with mild persistent allergic rhinitis compared to patients with mild intermittent allergic rhinitis.

Conclusion: There was sufficient evidence to prove the association of SRBD with severity of allergic rhinitis using the validated Filipino version of the Pediatric Sleep Questionnaire. OSA shows a greater likelihood among patients with mild persistent allergic rhinitis compared to those with mild intermittent allergic rhinitis.

Key words: allergic rhinitis, sleep-related breathing disorders, obstructive sleep apnea, pediatric sleep questionnaire

INTRODUCTION

Sleep-related breathing disorders (SRBD) encompass conditions such as obstructive sleep apnea syndrome, central sleep apnea, upper airway resistance syndrome, and obesity hypoventilation syndrome. Common symptoms include loud snoring, paradoxical movement of the chest and abdomen, apnea during sleep, difficulty breathing with snorting, cyanosis, sweating, restless sleep, frequent awakenings, night terrors, daytime hypersomnolence, fatigue, reduced ability to function, and headache.[1]

The prevalence of SRBD among the pediatric population has constantly increased in the last few decades. This condition has significantly affected the quality of life of children and has been associated with neurobehavioral and cognitive problems, metabolic ailments (insulin resistance and hyperlipidemia), cardiovascular disorders (cor pulmonale, systemic and pulmonary hypertension), growth and developmental abnormalities, and death. Unfortunately, due to ignorance and/or lack of awareness of its clinical occurrence in children, SRBD remains underdiagnosed.[1] Thus, it is recommended that physicians be wary of its existence and exert vigilance in detecting SRBD in children to obviate the harmful consequences of the disease.

Overnight polysomnography remains the gold standard for the diagnosis of SRBD. However, it cannot predict clinically significant morbidity or disease burden in children.[2,3] In addition, not all institutions are equipped with sleep laboratories and many hospitals do not have in-house pediatric sleep specialists. Moreover, the time, effort, and expense of the procedure can be restrictive and burdensome for both the child and the family.[4] As such, alternatives in the form of questionnaires for the evaluation of SRBD have been formulated and validated.

The Pediatric Sleep Questionnaire (PSQ) Sleep Related Breathing Disorder Subscale is a 22-item questionnaire used as a screening tool. It has a sensitivity of 81% and a specificity of 87% in predicting SRBD, with good internal consistence and test-retest reliability.[4] It has been validated in several studies and has been shown to better predict neurobehavioral outcomes compared to overnight polysomnography. [2,3,5] It has also been translated into different languages to address the need for culturally appropriate and linguistically accessible questionnaires. Recently, a Filipino version of the pediatric sleep questionnaire was formulated and validated.[6]

Allergic rhinitis is a common chronic respiratory illness in children characterized by nasal congestion, sneezing, and nasal itchiness.[7] Inflammation of the nasal mucosa is the main pathophysiologic mechanism of allergic rhinitis that leads to clinical symptoms of nasal congestion, rhinorrhea, sneezing, and nasal itching, often worse at night. Consequently, patients develop manifestations similarly seen in patients with SRBD such as mouth breathing, arousing irritability, sleep fragmentation, headaches, and fatigue.[8]

To date, there are no local studies correlating SRBD with allergic rhinitis. It is therefore the objective of this study to determine the association of allergic rhinitis with SRBD in children. Using the validated Filipino version of the pediatric sleep questionnaire, early recognition of sleep-related breathing disorders in patients with allergic rhinitis is possible, enabling early referral to a specialist for appropriate management and consequently, preventing recognizable complications.

METHODOLOGY

The research was a cross-sectional analytical study conducted in the University of Santo Tomas Hospital ambulatory care services or private clinics.

Children aged 1-17 years and 364 days old diagnosed with allergic rhinitis were included in the study. Participants with craniofacial or neuromuscular anomalies, chronic hypertrophic tonsils, those who underwent tonsillectomy, and participants on corticosteroid, leukotriene receptor antagonist or antihistamine therapy were excluded.

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines [9] was used for allergic rhinitis diagnosis and classification. Participants were classified as either mild intermittent, mild persistent, or moderate persistent according to the chronicity of the symptoms, and if these symptoms have significant effect on daily activities.

The study used the validated Filipino version of the SRBD subscale within the PSQ (Appendix A). It contains 22 items documenting the presence or absence of symptoms such as snoring, observed apneas, difficulty in breathing during sleep, daytime sleepiness, and inattentive or hyperactive behavior. The positive responses will be scored as 1 and negative responses as 0. The overall score will be divided by 22 to provide a final value. A cut-off value of eight positive responses is thought to be most effective in identifying OSA. Permission was acquired from the author through electronic mail granted on August 15, 2018. A license agreement for digital downloading was likewise obtained.

The study commenced with the approval by the Research Ethics Committee. Informed written consent, verbal assent and/or simplified assent were obtained. Baseline demographic and clinical data were recorded. The validated Filipino version of the SRBD subscale within the PSQ was given to the parent/guardian of the participant to answer and was collected afterwards.

Statistical Analysis

Mean and standard deviation were used to summarize the age, weight, height, BMI, and score in the pediatric questionnaire. Counts and percentages were used in gender, classification of BMI, severity of allergic rhinitis, and sleeping disorders. The Student's t-test was used in comparing age, weight, height, and BMI of patients with and without OSA. Fisher's exact test was used in comparing the sex and BMI classification of those with and without OSA. Fisher's exact test, including odds ratio, was used in association of sleeping disorders and severity of allergic rhinitis.

All statistical tests were performed in R ver 3.6.1, at 5% level of significance.

RESULTS

A total of 66 patients were included in the study, with mean age of 8.2 years (range, 1 to 17). There were 33 (50%) males and 33 (50%) females with mean weight of 30.7 Kg (range, 9.0 to 83.40), mean height of 126.2 (range, 70 to 173) and mean BMI of 17.6 (range, 10.5 to 29.4). Five (7.6%) patients had BMI above the normal range and six (9.1%) below the normal range (Table 1).

Based on their pediatric sleep questionnaire responses, they had a mean positive response (score) of 5.4 (range, 1 to 11). Eighteen (27.3%) had at least eight positive responses indicating positive OSA, while 48 (72.7%) had less than eight positive responses indicating negative OSA.

The mean age (p=0.125), weight (p=0.059), height (p=0.110), and BMI (p=0.053) did not significantly differ among patients who were positive or negative for OSA. Likewise, there were no correlations between sex (p=0.783) and BMI classification (p=0.103) with OSA.

Participants were classified as mild intermittent, mild persistent, or moderate persistent according to the ARIA classification. There were sufficient evidences to prove the association of OSA with severity of allergic rhinitis (p<0.001). Data showed that patients with mild persistent allergic rhinitis had an odds ratio of 9.1 [95% CI: 2.3 to 44.9] or 90.9% chance of having OSA (p<0.001). On the contrary, patients with mild intermittent allergic rhinitis had an odds ratio of 0.02 [95% CI: 0.00 to 0.19] or were 98% less likely to have OSA (p<0.001). However, this correlation was not observed among patients with moderate persistent allergic rhinitis (p=0.441) (Table 2).

Demographics	ALL	Obstructive sleep apnea		p-value	
		Positive (score ≥8)	Negative (score <8)		
Number of Patients	66	18 (27.3%)	48 (72.7%)		
Age	8.2 ± 5.2	9.8 ± 4.7	7.6 ± 5.3	0.125	
Sex: Male	33 (50.0%)	8 (44.4%)	25 (52.1%)	0.783	
Female	33 (50.0%)	10 (55.6%)	23 (47.9%)		
Weight (in kg)	30.7 ± 18.6	37.8 ± 20.8	28.1 ± 17.3	0.059	
Height (in cm)	126.2 ± 28.4	135.3 ± 24.1	122.7 ± 29.4	0.110	
BMI (in kg/m²)	17.6 ± 4.1	19.1 ± 5.8	17.0 ± 3.0	0.053	
BMI-for-age Classification:					
Obese	1 (1.5%)	1 (5.6%)	0 (0%)	0.103	
Overweight	4 (6.1%)	4 (22.2%)	0 (0%)		
Normal	55 (83.3%)	12 (66.7%)	43 (89.6%)		
Wasted	4 (6.1%)	0 (0%)	4 (8.3%)		
Severely wasted	2 (3.0%)	1 (5.6%)	1 (2.1%)		

Table 1. Demographic profile of participants with allergic rhinitis with or without sleep-related breathing disorders.

Values expressed as mean ± SD, or counts (%). p-values are based on Student's t-test or Fisher's exact test.

Allergic Rhinitis	ALL	Obstructive sleep apnea			
		Positive (score ≥8)	Negative (score <8)	p -value	Odds Ratio (95% Cl)
Moderate Persistent	4 (6.1%)	3 (16.7%)	1 (2.1%)	0.441	3.1 (0.04 – 250.5)
Mild Persistent	27 (40.9%)	14 (77.8%)	13 (27.1%)	<0.001	9.1 (2.3 – 44.9)
Mild Intermittent	35 (53.0%)	1 (5.6%)	34 (70.8%)	<0.001	0.02 (0.00 – 0.19)

 Table 2. Correlation between OSA with severity of allergic rhinitis.

p-values are based on Fisher's exact test. **95% CI** - 95% confidence interval

Among the perceived problems related to sleeping disorders, snoring loudly, heavy breathing, dry mouth on awakening, not listening, and difficulty organizing showed different responses (p<0.05) among the subgroups of allergic rhinitis.

Snoring loudly (OR = 0.06; 95% CI: 0.00 - 0.51), heavy breathing (OR = 0.11; 95% CI: 0.01 - 0.60), dry mouth on awakening (OR = 0.72; 95% CI: 0.09 - 0.85), not listening (OR = 0.20; 95% CI: 0.05 - 0.67) and difficulty organizing (OR = 0.00; 95% CI: 0.00 - 0.90) were less likely to be observed among patients with mild intermittent allergic rhinitis compared to patients with mild persistent allergic rhinitis.

On the contrary, the odds ratio of snoring loudly (OR 8.93, 95% CI: 1.61 - 93.35), not listening (OR 4.07, 95% CI: 1.25 - 14.30), difficulty organizing (OR 19.31, 95% CI: 1.02 - 365.55), heavy breathing (OR 14.64, 95% CI: 1.05 - 829.03) and unrefreshed in the morning (OR 18.70, 95% CI: 1.33 - 1073.00) were more likely among patients with mild persistent allergic rhinitis compared to patients with mild intermittent allergic rhinitis.

DISCUSSION

This study, using the 22-item SRBD subscale of the PSQ demonstrated an association between the subgroups of allergic rhinitis and SRBD. Patients with mild persistent allergic rhinitis tend to have symptoms related to sleep disordered breathing such as loud snoring, heavy breathing, daytime sleepiness, and inattentiveness compared to patients with mild intermittent allergic rhinitis. This correlation, however, was not observed among patients with moderate persistent allergic rhinitis probably because of the small number of participants enrolled in this category. The study by Leger, et al. [10] which aimed to assess whether duration and severity of allergic rhinitis were associated with sleep impairment concluded that sleep was significantly more impaired in patients with severe AR than in those with the mild type. However, the duration of allergic rhinitis (intermittent or persistent) had no effect on sleep.

Allergic rhinitis, an IgE-mediated hypersensitivity reaction, is a common allergic disease characterized mainly by nasal congestion and obstruction. This nasal mucosal manifestation results from activation of TH2 lymphocytes, basophils, and mast cells, release of cytokines and chemical mediators, and influx of inflammatory cells, especially eosinophils causing vasodilatation, mucosal edema, increased vascular permeability, and mucus secretion, all of which are characteristic features of allergic inflammation.[11]

With an inflamed nasal mucosa and nasal congestion, increased effort is needed to inhale through the nose. This generates a negative pressure during inspiration in the nasal airway leading to nasal collapse and airway obstruction. The increase in nasal resistance and the change in the patency of the nasal airway can have significant effects on breathing manifested as episodes of apnea, hypopnea, arousals, and/or snoring. Total or neartotal nasal obstruction can lead to oral respiration which causes dry mouth upon awakening, a significant observation in this study.

While nasal airway resistance is relatively constant, oral airway resistance varies during waking hours and sleep. During sleep, relaxation and flaccidity of the oral and pharyngeal muscles narrows the airway diameter, resulting in increased oral airway resistance and increased risk of collapse of the upper airway. Since the nose is the preferred route of breathing during sleep, the effect in patients with allergic rhinitis with nasal congestion becomes

				Seventy	of Allergic Rhinitis		
		I PIW	ntermittent	Mik	d Persistent	Mode	rate Persistent
			n=35)		(n=27)		(n=4)
3		Positive		Positive		Positive	
Perceived problems	ALL	Responses	OR (95% CI)	Responses	OR (95% CI)	Responses	OR (95% CI)
Snorng					0		
Q1. Usually snores	16 (24.2%)	5 (14.3%)	0.31 (0.07 - 1.14)	10 (37.0%)	3.17 (0.87 - 12 61)	1 (25.0%)	1.04 (0.02 - 14.16)
Q2. Always snores	11 (16.7%)	3 (8.6%)	0 27 (0.04 - 1.31)	7 (25.9%)	3.01 (0.67 - 15.82)	1 (25.0%)	1.72 (0.03 - 24.06)
Q3 Snores Loudly	11 (16.7%)	1 (2.9%)	0 06 (0 00 - 0.51)	9 (33 3%)	8.93 (1.61 - 93 35)	1 (25 0%)	1.72 (0 03 - 24.06)
Q4 Heavy breathing	13 (19.7%)	2 (5.7%)	0 11 (0 01 - 0.60)	8 (29 6%)	2.81 (0.70 - 12.61)	3 (75 0%)	14 64 (1 05 - 829.03)
Breathing Problems							
Q5. Trouble breathing	7 (10.6%)	3 (8.6%)	0.63 (0.09 - 4.13)	2 (7.4%)	0.55 (0.05 - 3.69)	2 (50.0%)	10.57 (0.64 - 176.23)
Q6 Observed apneas	2 (3 0%)	1 (2.9%)	0.88 (0.01 - 71 50)	1 (3 7%)	1.45 (0.02 - 117 59)	0 (0 0%)	0 00 (0 00 - 91 88)
Mouth breathing							
Q7. Mouth open during day	29 (43.9%)	10 (28.6%)	0.26 (0.08 - 0.79)	16 (59.3%)	2.86 (0.94 - 9.10)	3 (75.0%)	4.06 (0.31 - 223.70)
Q8. Dry mouth on awakening	36 (54.5%)	14 (40.0%)	0 28 (0 09 - 0.85)	18 (66 7%)	2.30 (0.76 - 7.39)	4 (100 0%)	8 45 (0.43 - 163.53)
Daytime sleepiness							
Q10. Untreshened in the morning	11 (16.7%)	3 (8.6%)	0 27 (0.04 - 1.30)	5 (18 5%)	1.25 (0.27 - 5 59)	3 (75 0%)	18.70 (1.33 - 1073.00)
Q11. Problem with sleepiness	25 (37.9%)	9 (25.7%)	0.33 (0.10 - 1.02)	13 (48 1%)	2.07 (0.67 - 6.51)	3 (75.0%)	5 31 (0.40 - 292.81)
Q12. Sleepy per teacher	6 (9 1%)	3 (8.6%)	0 88 (0 11 - 7.09)	3 (11 1%)	1.49 (0.18 - 12 08)	0 (0 0%)	0 00 (0 00 - 17 28)
Q13. Hard to wake up	19 (28.8%)	6 (17.1%)	0 29 (0 08 - 1.00)	11 (40 7%)	0.80 (0.26 - 2 41)	2 (50 0%)	2 60 (0 18 - 38 59)
Inattention / Hyperactivity							
Q17. Does not listen	22 (33.3%)	6 (17.1%)	0 20 (0.05 - 0.67)	14 (51 9%)	4.07 (1.25 - 14.30)	2 (50.0%)	2.07 (0.14 - 30.56)
Q18. Difficulty organizing	5 (7.6%)	0 (0%)	0 00 (0 00 - 0 00)	5 (18 5%)	19.31 (1.02 - 365 55)	0 (0 0%)	0 00 (0 00 - 21 94)
Q19. Easily distracted	42 (63.6%)	22 (62 9%)	2 59 (0.99 - 7.02)	18 (66 7%)	1.00 (0.31 - 3 26)	2 (50.0%)	0.56 (0.04 - 8.15)
Q20. Fidgets	22 (33.3%)	11 (31.4%)	0.84 (0.26 - 2.63)	11 (40.7%)	1.08 (0.35 - 3 27)	0 (0.0%)	0 00 (0 00 - 3.01)
Q21. On the go	26 (39.4%)	13 (37.1%)	0 82 (0 27 - 2.47)	13 (48 1%)	1.84 (0.60 - 5 71)	0 (0 0%)	0 00 (0 00 - 2 29)
Q22. Interrupts	21 (31.8%)	8 (22.9%)	0 42 (0.12 - 1.34)	12 (44 4%)	2.63 (0.81 - 8.86)	1 (25 0%)	0 70 (0 01 - 9 41)
Other symptoms						•	
Q9 Noctumal enuresis	10 (15.2%)	5 (14.3%)	0.70 (0.14 - 3.48)	5 (18 5%)	1.53 (0.31 - 7.54)	(%0 0) 0	0 00 (0 00 - 8 99)
Q14. Moming headache	11 (16.7%)	4 (11.4%)	0 45 (0 09 - 2.01)	5 (18 5%)	1.24 (0.27 - 5 59)	2 (50 0%)	5 65 (0.37 - 87 65
Q15. Delayed growth	4 (6.1%)	0 (0%)	0 00 (0 00 - 1.28)	4 (14 8%)	15.13 (0.78 - 293.71)	0 (0 0%)	0 00 (0 00 - 29.71)
Q16. Obesity	10 (15.2%)	5 (14.3%)	0.87 (0.18 - 4.24)	3 (11.1%)	0.58 (0.09 - 2 86)	2 (50.0%)	6.44 (0.41 - 100.86)
95% CI - 95% confidence interval based o	on Fisher's exact test						

Table 3. Responses in the pediatric sleep questionnaire

additive, further increasing airway resistance. Thus, the odds of developing OSA or loud snoring in patients with allergic rhinitis becomes higher.[12] This effect was clearly shown in this study, wherein 77.8% of patients with mild persistent allergic rhinitis compared to 5.6% of patients with mild intermittent allergic rhinitis had symptoms of OSA.

Houser, et al. [12] used acoustic rhinometry to evaluate nasal patency and nasal congestion in patients with allergic rhinitis with or without OSA. The results showed that the mean congestion factors were significantly higher in allergic rhinitis patients with OSA compared to the non-OSA group showing the correlation between nasal obstruction and presence of sleep-disordered breathing.

Nasal congestion and obstruction can also lead to sleep disruptions or microarousals resulting in sleep fragmentation and unsatisfactory sleep. Sleep loss can cause daytime somnolence and fatigue, mood changes, inattentiveness or compromised alertness, poor school performance, and increased risk of accidents, all of which can adversely affect the quality of life of allergic rhinitis patients.[12,13] Our study showed that 18.5% of patients with mild persistent allergic rhinitis feel unrefreshed in the morning, which may suggest daytime fatigue. It was speculated that if nasal congestion can be reduced, symptoms of OSA, sleep quality, and associated symptoms of daytime fatigue may improve. Topical corticosteroid, an anti-inflammatory agent, relieves nasal congestion, thereby increasing nasal patency, decreasing nasal resistance, increasing nasal airflow, and consequently improving sleep quality, and reducing associated daytime fatigue and somnolence. This hypothesis was supported by Craig, et al. wherein the application of topical nasal corticosteroids over an 8-week period significantly reduced nasal stuffiness and improved sleep, daytime fatigue, and quality of life of patients with allergic rhinitis.[13]

CONCLUSION

There is an association between allergic rhinitis and SRBD using the validated Filipino version of the PSQ. The demographic profile of participants in both the study groups were comparable. OSA has a greater likelihood to be observed among patients with mild persistent allergic rhinitis compared to those with mild intermittent allergic rhinitis. A larger scale research is recommended to strengthen the association of allergic rhinitis and SRBD.

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APPENDIX A

Filipino Version of the Sleep-Disordered Breathing Subscale Within the Pediatric Sleep Questionnaire

PALATANUNGAN UKOL SA PAGTULOG NG MGA BATA: SUBSCALE SA KARAMDAMAN SA PAGHINGA HABANG NATUTULOG

(Filipino version of the Sleep-disordered breathing subscale within the pediatric sleep questionnaire)

Pangalan ng bata:	ID#:

Pangalan ng sumasagot sa palatanungan: ______ Petsa: _____

Pakisagutan ang mga tanong ukol sa kilos/gawi ng bata sa pagtulog at sa pagkagising. Ang mga tanong na ito ay tumutukoy sa karaniwang ikinikilos ng bata sa nakaraang buwan, at hindi lamang ng mga nakaraang araw dahil ang mga kilos na ito ay maaring hindi pangkaraniwan lalo na kung ang bata ay may karamdaman. Bilugan ang tamang kasagutan o isulat ng malinaw sa patlang na nararapat. Ang "O" ay nangangahulugang "oo", ang "H" ay nangagahulugang "hindi" at ang "HA" ay nangangahulugang "hindi alam/angkop."

HABANG NATUTULOG, ANG BATA BA AY:			
humihilik nang higit sa kalahati ng oras ng pagtulog?	0	н	HA
parating humihilk?	0	н	HA
humihlik nang malakas?	0	н	HA
may "mabigat" or malakas na paghinga?	0	н	HA
may hirap sa paghinga o nagpupumilit makahinga?	0	н	HA
NAKITA MO BA ANG BATA NA HUMINTO SA PAGHINGA SA GABI?	0	н	HA
ANG BATA BA AY:			
madalas huminga sa pamamagitan ng bibig sa umaga	0	н	HA
natutuyo ang bibig sa paggising sa umaga?	0	н	HA
paminsan-minsang na@hi sa kama?	0	н	HA
ANG BATA BA AY:			
pagod ang pakiramdam pagkagising sa umaga?	0	н	НА
Inaantok sa umaga?	0	н	HA
	-		
MAY GURO O TAGAPANGALAGA BA ANG NAKAPAG\$ABI			
NA ANG BATA AY PARANG INAANTOK MAGHAPON?	0	н	HA
MAHIRAP BANG GISINGIN ANG BATA SA UMAGA?	0	н	на
MA\$AKIT BA ANG ULO NG BATA PAG GUMIGISING			
SA UMAGA?	0	н	HA
HUMINTO BA SA PAGLAKI SA NORMAL NA BILIS SA ANUMANG			
ORAS MULA SA PAGKASILANG NG BATA?	0	н	HA
ANG TIMBANG BA NG BATA AY HIGIT \$A NORMAL?	0	н	на
ANG BATA NA ITO AY MADALAS NA:			
narang bindi nakikinin kabit siya mismo ang kinakausan mo	0	н	нΔ
nabibiranan manaragisa no mga gawain	ŏ	H	HA
madaling matawag ang nancin (o magambala ang atencyon)	~	.,	
ng mga kaguluhan o ingay na nagmumula sa labas	0	н	HA
hindi mapakali ang kamay o paa o di mapakali sa upuan	õ	H	HA
narating gumagalaw o parang "sinusiang motor"	õ	н	HA
sumasabat sa usapan o nangugulo sa Iba (sa mga usapan	Ŭ		101
o sa laro)	0	н	на

Maraming salamat pol