



Impact of gastroesophageal reflux treatment on chronic rhinosinusitis

Mahmoud A Ragae¹; Rehab AbdElAal¹; Ahmed AboElwafa¹; Essam ElDeen Mahran²

1. Otolaryngology department, faculty of medicine, Assiut university, Assiut, Egypt

2. Gastroenterology department, faculty of Medicine, Assiut University, Assiut, Egypt

Abstract:

Background: There is increasing evidence that gastroesophageal reflux induces and aggravates rhinosinusitis. This study aimed to assess the correlation between sinonasal troubles and gastric reflux disease and evaluates the effect of treatment of GERD on improving sinonasal symptoms.

Patients and methods: In this single-arm (pre and post) Quasi-experimental study, thirty-seven patients with GERD who had sinonasal symptoms defined by the European Position Paper on Rhinosinusitis and Nasal Polyps criteria (EPOS) which gather anterior/posterior rhinoscopy results with patient history, and MSCT findings, received medical treatment for GERD only in the form of PPIs. They were reassessed after one and three months for improvement in their symptoms and their effect on the quality of life (QOL) using 22- items sinonasal outcome test (SNOT22), Modified Lund Kennedy (MLK) scoring system to compare findings in the nasal endoscopy and MSCT findings were subjected to Lund-Mackay computed tomography score (LMCTS).

Results: There was a significant improvement in nasal symptoms and signs seen in endoscopic examination and MSCT findings, and the SNOT-22 score was significantly decreased, reflecting patients' satisfaction.

Conclusion: This study suggests a positive correlation between the presence of gastric reflux and an increased incidence of sinonasal symptoms proved by treatment of gastric reflux only without symptomatic treatment of the nose. PPIs are an effective drug for refractory CRS in patients confirmed to have GERD.

Keywords: Chronic rhinosinusitis, Gastroesophageal reflux, Proton pump inhibitors, GERD, Laryngopharyngeal reflux, Refractory chronic rhinosinusitis.

Introduction :

Chronic Rhinosinusitis (CRS) is a common health condition that can be relapsing and remitting, with acute exacerbations. CRS can be defined

clinically based on EPOS criteria requiring both subjectively (smell loss, green/yellow nasal discharge, postnasal drip, facial pain, and/or facial pressure,

nasal congestion/blockage) which presents for more than 12 continuous weeks, and objectively confirmed by CT for the presence of sinonasal mucosal inflammation.¹

Although CRS is a common disorder, little is known yet about its actual etiology. Refractory CRS that does not improve with medical therapy has been associated with an increased risk of gastroesophageal reflux disease (GERD).²

Nowadays GERD is one of the most common diagnoses made by both gastroenterology doctors and general practitioners. It is defined as a gastrointestinal tract (GIT) motility disease which results from the reflux of gastric contents into the esophagus or oral cavity, causing symptoms or complications. The prevalence of GERD in western countries is estimated to be between 10 and 30% in adults.³

Correlation has been found between GERD and certain airway diseases and coexistence with each other's, both asthma and laryngeal disorders can be caused by GERD. Also, pepsin was found in the middle ear of children with middle ear effusion.⁴ Patients with obstructive sleep apnea and snoring are most likely to have a high incidence of nocturnal gastroesophageal reflux (nGER).⁵

Upon Montreal's definition 2006, gastric reflux is defined as GIT motility disease that results from the reflux of gastric contents into the esophagus or oral cavity, causing symptoms or complications.⁶ Manifestations can be divided into typical symptoms which include acid regurgitation and heartburn, atypical symptoms such as epigastric pain, bloating, dyspepsia, nausea, and extra-esophageal symptoms which include chronic cough, laryngeal disorders, asthma, chest pain, dental erosion, and various Ear, Nose and Throat (ENT) symptoms.²

Many authors searched for the possible relation between sinusitis and GERD, reported to occur together more frequently than expected. Group of 20 patients with persistent CRS even after Endoscopic Sinus Surgery (ESS) compared to 20 healthy control patients through dual-channel pH-metry by **Jecker et al.** Reflux events in the distal oesophageal sensor were more in patients with refractory CRS significantly, but not in the hypopharyngeal sensor, which means that there is an association between GERD and CRS, but not with the Laryngopharyngeal reflux (LPR), that would support the nervous vagal response as a mechanism for this interrelation between the two diseases.⁷

Ozmen et al. compared 33 patients with refractory CRS who had ESS to 20 patients who would also undergo ESS for concha bullosa or septal deformity, but without CRS confirmed by CT. Results of Dual-channel tube pH-metry were abnormal in 88% of patients with CRS and 55% of controls, being statistically significant. 82% of patients in the study group and in 50% of the control group had pepsin detected in their nasal secretion. LPR was documented by pH-metry in all CRS patients, in whom pepsin was detected in the nasal mucous secretions and was negative in only three patients with LPR. The authors suggested that refractory CRS may be associated with GERD and LPR and pepsin may be an indicator for LPR diagnosis.⁸

Also, **Loehrl et al.** examined 20 patients with refractory CRS, after surgical and medical treatment by pH-metry dual channel esophageal and nasopharyngeal, compared to pepsin in nasal secretions. 95% of the patients had abnormal pH-metry in the nasopharynx, while nasopharyngeal biopsies for pepsin were negative in all patients.

Pepsin was not detected also in nasal lavage samples.⁹

In 2018 Vaezi et al. tried to evaluate the effect of proton pump inhibitors (PPIs), as the treatment of choice for GERD, in 75 patients with CRS complaining of postnasal drip without CT abnormalities in the sinuses. Patients underwent impedance monitoring and pH-metry with an esophageal tube before treatment and followed by validated questionnaires (RSOM-31, QOLRAD, and SNOT-20). Patients who received PPIs improved by 3.12 times after 8 weeks of treatment and 3.5 times compared to controls, with a 50% average improvement after 16 weeks compared to 5% in the placebo group. SNOT-20 and QOLRAD scores significantly improved in the treatment arm (10). Also, Nanda et al. found that PPIs were an effective treatment for post-nasal discharge in patients with refractory CRS and LPR in conjunction with endoscopic sinus surgery (ESS).¹¹

36 middle ears fluid samples from 22 children were collected by Dewan K. et al. and examined by ELISA for pepsinogen and proteolytic activity, who found positivity rates of pepsinogen and proteolytic activity in the samples identified by ELISA assay 73% and 77% respectively.¹²

Nair et al.¹³ found 65-fold higher of pepsinogen levels in the middle ear than in serum, investigating serum and middle ear for pepsinogen levels by electrophoresis, and pepsinogen positivity in 61% of patients' middle ear.

We aimed to study the correlation between sinonasal troubles and gastric reflux disease and assess whether antireflux therapy alone improves the condition of the nose and paranasal sinus in patients complaining of reflux and sinonasal symptoms.

Patients and Methods:

Patients:

This study is considered a single-arm (pre-post) Quasi-experimental study and was conducted between the otorhinolaryngology department and gastroenterology department, Faculty of Medicine, Assiut University Hospital, Egypt, from January 2020 to June 2021 on patients diagnosed to have GERD by either gastroscopy or 24-hour PH-esophageal monitoring at GIT and tropical medicine department.

Using G*Power 3 software, a calculated minimum sample of 40 patients was needed to detect an effect size of 0.3 in the mean VAS-smell score on four repeated occasions, with an error probability of 0.05 and 80% power on a two-tailed test.

Inclusion criteria: Patients above 18 years old were included who were diagnosed to have gastric reflux by upper endoscopy or 24-hours PH-monitoring and they were complaining of sinonasal symptoms.

Exclusion criteria: patients under 18 years old, pregnant females, those with another nasal pathology as severe septal deviation, mass, previous nasal surgery, and patients who refused to participate in the study were excluded.

All patients signed written informed consent before participation. The study was performed according to the guidelines of the Helsinki Declaration of 1975 and its amendments. The study protocol was approved by the Research Ethics Committee at the Faculty of Medicine, Assiut University, Egypt under approval number (IRB no.17101031) and clinical trials approval number (NCT04105894).

Methods

1) Initial assessment and evaluation:

All eligible patients were subjected to

1. Personal History including name, age, sex, occupation, residence, marital status, and special habits.
2. Full history to assess the general condition of the patient.
3. ENT history with special attention to sinonasal symptoms including:
 - Symptoms of chronic rhinosinusitis according to EPOS 2012, these criteria included: two or more symptoms, one of which should be either nasal/obstruction/congestion or nasal discharge either anterior or posterior nasal drip \pm loss or reduction of smell \pm facial pain/pressure for \geq 12 weeks.
 - Symptoms suggestive of GERD include heartburn, regurgitation, sour taste, hoarseness of voice, globus sensation, and throat soreness.

2) Clinical examination:

1. General examination including:
 - Vital signs (blood pressure, heart rate, temperature, and respiratory rate).
 - Chest, heart, and abdominal examination.
2. Complete ENT examination with special attention to:
 - Nasal examination including nasal endoscopy (Karl Storz, 0 endoscopes, 4ml, Germany) with attention to:
 - State of the nasal mucosa (normal, pale, congested).
 - Hypertrophy or polypoidal changes of the turbinates.
 - Exclusion of anatomical abnormalities as significant septal deviation or presence of pathology as nasal mass or polypi or presence of marks of previous nasal surgery.
 - Oropharyngeal examination:
 - Postnasal discharge.
 - Pharyngeal wall findings.

- Ear examination with special attention to the state of the tympanic membrane (retracted suggesting Eustachian Tube Dysfunction (ETD) or dull suggesting OME).

3) Investigations:

MSCT of nose and PNs axial, coronal, and sagittal cuts without contrast were done on the patients to evaluate the opacity of sinuses, patency of osteomeatal complex, mucosal thickening, and assess the presence of local lesions as hypertrophied turbinates.

4) Follow-up and reassessment:

Patients were asked to come back for follow-up after 1 month and 3 months.

Patients were reevaluated for their response to medical treatment regarding their history and clinical examination. Follow-up MSCT of nose and PNS in the second visit (after 3 months), Comparison was done between the findings before and after treatment. Sinonasal symptoms and their effect on QOL were compared using SNOT-22 (Appendix I), which has 22 questions about general status aspects, and sinonasal symptoms, graded from zero to five; zero means no problem while five is the worst possible problem. The total summation of the questionnaire score indicates the impact of the disease on the QOL of the individual. Modified Lund Kennedy (MLK) scoring system was used to compare findings in the nasal endoscopy with positive findings includes (edema, discharge, crusting, scarring, polyp, scarring, and edematous middle meatus).

MSCT findings were subjected to Lund-Mackay computed tomography score (LMCTS), where each sinus (anterior and posterior ethmoidal, maxillary, frontal, and sphenoidal) is scored for opacification (0, no opacity, 1 partial opacity, 2 total opacity) and

osteomeatal complex is scored 0 for no obstruction, 2 for obstruction. The score of each side of the sinuses was from 0 to 12 and the bilateral score was up to 24.

Statistical analysis:

Data was collected and analyzed by SPSS. Quantitative data were expressed as mean + standard deviation (SD) and compared with student t-tests. Nominal data were given as a number (n) and percentage (%).

Chi2 test, paired T-test, and fisher exact test were implemented on such data. The Level of confidence was kept at 95% and hence, the P value was considered significant if <0.05 .

Results :

A total of 40 patients who presented to our outpatient clinic after being referred from the GIT department diagnosed as GERD patients were included in the study and 3 of them were missed in the follow-up, so thirty-seven patients were included in our study, 19 males, 13 of them were smokers, and 18 females none of them were a smoker. The mean age of included patients was 31.08 ± 7.39 (20.0-48.0) and their mean weight was 86.11 ± 11.74 . Associated comorbidities are shown in Table 1.

There was a statistically significant difference in all of the nasal symptoms except smell dysfunction in most of the patients. Nasal obstruction improved in 20 patients from 29 who had obstruction at the start of the study ($P=0.000$), Both anterior and posterior nasal discharge ($P=0.025$ and 0.000 respectively), and Headache was found in 36 (97.3%) patients in the first visit and only persisted in 8 (21.6%) patients in the third visit with a statistically significant difference ($P<0.05$), also, nasal itching improves significantly in the third visit. While hyposmia shows no statistically

significant difference in the first and second visits of follow-up ($P=0.79$ and 0.259) (Table 2).

Our patients had a mean SNOT-22 score of 18.486 ± 2.468 at the baseline visit, which reached 1.378 ± 1.963 at the end of the follow-up as shown in table 3 ($P<0.000$).

Figure 1 shows the change between the SNOT22 results between the baseline and the end of the study.

We detected a significant statistical improvement in the nasal mucosa condition ($P=0,000$). Hypertrophy of both inferior turbinates was observed in 10 patients (27%) on the third visit while it was in 26 (70.3%) of them on the first visit with a significant statistical difference ($P=0,000$). Middle meatus was discharging in 4 patients (10.8%) on the first visit while it was normal in all patients in the follow-up ($P=0,000$), all patients had postnasal drip (PND) on the first visit and only one had on the third visit, with a statistically significant difference ($P=0,000$). Also, all patients had granular pharyngitis on the first visit which was found in only one patient on the third visit with a statistical significance difference ($P=0,000$). The right tympanic membrane was found dull in 6 (16.2%) patients on the first visit and in 5 (13.5%) patients on the third visit, with no statistically significant difference ($P=0.744$) between the first and third visits. While the left tympanic membrane was dull in 10 (27%) patients on the first visit and in 3 (8.1%) patients on the third visit with a statistically significant difference ($P=0.032$) (Table 4).

Regarding endoscopic nasal examination, findings were compared using Modified Lund Kennedy (MLK) scoring system and there was a statistically significant difference between the first and the last visits MLKS with the mean score changed from 4.38 ± 0.794 at baseline

examination to 0.432 ± 0.834 at the last follow up visit (Table 5).

Radiological findings were compared using the Lund-Mackay score (LMCTS). A higher score indicates more opacification in the sinus and osteomeatal complex, as observed on CT imaging. The mean score at the start was 5.297 ± 3.77 with a significant reduction to 0.0811 ± 2.77 at the end of the follow-up (Table 7). Patients who had mucosal thickening on the first visit were 29 (78.4%) which improved to be in only 3 patients (8.1%) on the third visit, there was a statistically significant difference ($P=0.000$).

There was a significant improvement in both right and left ethmoidal opacity

($P=0.001$ and 0.011). Right maxillary retention cyst was found in 9 (24.3%) patients in the first visit which improved. While left one was in 13 patients (35.1%) and improved to be seen in only one in the follow-up. The opacity of the Osteomeatal complex was detected in 6 patients (16.2%) which became patent in all patients in the follow-up ($P=0.000$). Inferior turbinates hypertrophy was detected in 26 (70.3%) of our patients on the first visit, it was improved in 10 (27%) at the end of the follow-up with a statistically significant difference ($P=0.000$) (Table 6).

Table 1: Demographic distribution of patients

Baseline data	No. (37)	%
Age: (years)		
< 30	17	45.9%
≥ 30	20	54.1%
Mean \pm SD (Range)	31.08 ± 7.39 (20.0-48.0)	
Sex:		
Female	18	48.6%
Male	19	51.4%
Weight:		
Mean \pm SD (Range)	86.11 ± 11.74 (65.0-123.0)	
Smoking:		
Non-smoker	24	64.9%
Smoker	13	35.1%
Associated comorbidities:		
Asthma	1	2.7%
Cardiac	1	2.7%
Chronic Kidney Disease	1	2.7%
HTN	1	2.7%
Systemic lupus erythematosus	1	2.7%
None	32	86.5%

Table 2: Comparison between sinonasal symptoms at the start and the follow-up

Symptoms	First Visit (n= 37)		Second visit (1month) (n= 37)		Third visit (3 months) (n= 37)		P- value ¹	P- Value ²
	No.	%	No.	%	No.	%		
Nasal obstruction	29	78.4	23	62.2	9	24.3	0.127	0.000*
Anterior nasal discharge	6	16.2	0	0.0	0	0.0	0.025*	0.025*
Posterior nasal discharge	37	100.0	12	32.4	1	2.7	0.000*	0.000*
Headache	36	97.3	18	48.6	8	21.6	0.000*	0.000*
Hyposmia	10	27.0	9	24.3	6	16.2	0.790	0.259
Nasal itching	17	45.9	10	27.0	8	21.6	0.091	0.027*

¹: Comparison between First visit and Second visit

²: Comparison between First visit and Third visit

Table 3: Baseline and follow-up SNOT-22 in studied patients

	Baseline	After 3 months	P-value
SNOT-22	18.486 ± 2.468	1.378 ± 1.963	< 0.000

Data expressed as mean (SD). P value was significant if < 0.05.
SNOT-22: 22-item sinonasal outcomes test.

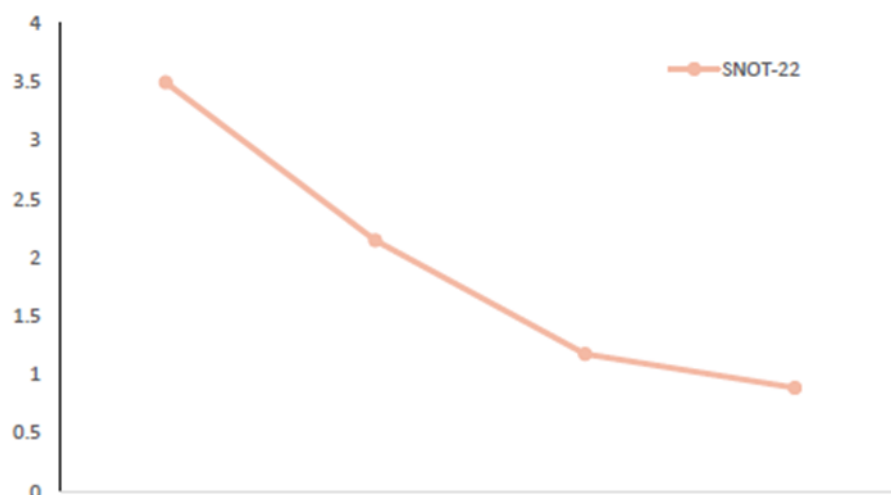


Figure 1: Baseline and follow-up nasal symptoms score in studied patients

Table 4: Comparison between findings of endoscopic examination of the nose at the start and the follow-up

	First Visit (n= 37)		Second visit (n= 37)		Follow-up (n= 37)		P- value ¹	P- Value ²
	No.	%	No.	%	No.	%		
Mucosa:								
Pale	16	43.2	11	29.7	9	24.3	0.000*	0.000*
Congested	19	51.4	3	8.1	0	0.0		
Hypertrophied Inferior turbinate:	26	70.3	19	51.4	10	27.0	0,096	0,000*
Discharging middle meatus:	4	10.8	2	5.4	0	0.0	0.674	0.000*
Post-nasal discharge:	37	100.0	11	29.7	1	2.7	0.000*	0.000*
Granular pharyngitis:	37	100.0	11	29.7	1	2.7	0.000*	0.000*
Dull tympanic membrane:								
Right	6	16,2	6	16,2	5	13,5	1.000	0.744
Left	10	27	8	21,6	3	8,1	0,588	0,032*

Table 5: Comparison between MLKS at the start and the follow-up

	Baseline	After 3 months	P-value
MLKS	4.38 ± 0.794	0.432 ± 0.834	< 0.000

Data expressed as mean (SD). P value was significant if < 0.05.

Table 6: Comparison between MSCT findings at the start and the follow-up:

Radiology	First Visit (n= 37)		Follow-up (n= 37)		P-value
	No.	%	No.	%	
Mucosal thickening:					
Yes	29	78.4	3	8.1	0.000*
No	8	21.6	34	91.9	
Ethmoidal opacity:					
Right	10	27.0	0	0.0	0.001*
Left	7	18.9	0	0.0	0.011*
Maxillary retention cyst:					
Right	9	24.3	0	0.0	0.002*
Left	13	35.1	1	2.7	0.000*
Patency of osteomeatal complex:					
Normal	31	83.8	37	100.0	0.025*
Opacity	6	16.2	0	0.0	
Hypertrophied inferior turbinates:					
Yes	26	70.3	10	27.0	0.000*
No	11	29.7	27	73.0	0.000*

Table 7: Comparison between LMCTS at the start and the follow-up

	Baseline	After 3 months	P-value
LMCTS	5.297 ± 3.77	0.0811 ± 2.77	< 0.000

Data expressed as mean (SD). P value was significant if < 0.05.

Discussion :

CRS is defined as a persistent inflammatory disease of the sinonasal mucosa. It is believed to develop because of defects in the immune system of the host or less commonly exposure to exogenous bacteria (leads to abnormal microbiome), excessive compensatory immune responses, and increased exposure to allergens. The reflux of stomach contents is assumed to cause potentiation and/or induction of the CRS disease process.¹⁴

CRS and GERD are prevalent disorders and their coexistence by chance in several patients can be expected, controversially their coexistence is due to the same pathogenic mechanisms. There is evidence that the association between impaired sinonasal functions and GERD may predispose patients to develop CRS regardless of the precise mechanism.¹⁵ The present study aimed to explore

more the impact of GERD on CRS. In this study, we compared the sinonasal symptoms before and after medical treatment of GERD only in patients with CRS and GERD.

In our study GERD was diagnosed based on clinical symptoms and diagnosis was strengthened by upper gastroscopy findings and/or results of 24-hour PH manometry. Patients with GERD who had sinonasal symptoms were examined endoscopically and radiological evaluation was done to confirm the diagnosis of CRS upon EPOS criteria and to exclude any other etiologies that may be the cause of their sinonasal symptoms. Our patients were maintained on PPIs in the form of omeprazole 40 mg twice daily for 3 months.

The results of this study reveal a significant improvement in sinonasal symptoms after treatment of gastric reflux using proton pump inhibitors. All our patients had PND and subsequent

granular pharyngitis which improved at the end of the follow-up with a significant P-value (0,000), which was in line with vaezi et al.¹⁰ who evaluated the effect of PPIs in 75 patients complaining of postnasal drip, Patients received PPIs improved by 3.12 times after 8 weeks of treatment and 3.5 times after 16 weeks compared to 75 controls. While these results were opposed by Flook and Kumar who found no causal link or evidence that refractory CRS can be caused or induced by GERD. Furthermore, they stated that there is no evidence that refractory CRS can be improved or resolved by anti-reflux therapy.¹⁶

Nasal obstruction was found in most of our patients (78.4%). With statistically significant improvement after treatment (P-value 0,000). This was compatible with the endoscopic nasal examination that showed 51.4% of our patients had nasal congestion and 70.3% of them had hypertrophied inferior turbinates which was evident also by radiological evaluation, these findings show significant improvement in the follow-up (Tables 1, 3, 5).

These results matched with Dagli et al. results who conducted a study in which 50 patients with confirmed esophagitis and symptoms of laryngopharyngeal reflux were treated for 12 consecutive weeks with PPIs with no other symptomatic treatment, compared with a control group and there was a significant improvement in nasal obstruction.¹⁷ Thirty-six of our patients (97.3%) were complaining of headache, and only eight of them were still complaining at the end of our study with statistically significant improvement (P-value 0,000), which could be attributed to nasal congestion, mucosal edema, occlusion of the osteomeatal complex that was evident by endoscopic examination in most of our patients and confirmed by radiological findings of

opacification of paranasal sinuses and osteomeatal complex that showed significant improvement at the end of our study (Table 1,3,5).

Six of our patients had anterior nasal discharge that disappeared in the first follow-up (after 1 month). A retrospective chart by Nation et al. reviewed 63 children, aged from 6 months to 10 years old with nasal congestion, rhinorrhea, and chronic cough who had distal third esophageal biopsies, adenoidectomy, and maxillary cultures. GERD played an important role in all patients, as over 40% of patients had positive biopsies.¹⁸

Nasal itching was found in about one-third (17 patients) with statistically significant improvement. These results matched with Finocchio et al. who conducted a study to investigate more than 2 thousand patients aged 20–84 years who underwent a clinical visit in seven Italian centers and found that there is a four-fold increase in the risk of non-allergic rhinitis with symptoms of nasal congestion, rhinorrhea, nasal itching, and nasal obstruction with gastritis and GERD.¹⁹

It was noticed that hyposmia was detected in about one-fourth (10 patients) but had no statistically significant improvement at the end of our study. A study of 76 subjects, 13 healthy controls, 30 patients of gastroparesis alone, 10 patients with GERD alone, and 23 with both gastroparesis and GERD that was conducted by Kabadi et al. found that disturbances in smell and taste were higher in patients with GERD, gastroparesis, and both gastroparesis and GERD compared to controls. Increasing symptoms and severity of GERD were associated with taste and smell abnormalities which may contribute to the food intolerance that most of these patients experienced. There was a dramatic improvement in

smell and taste senses after treatment of GERD, but this study did not find the relationship between these two parameters and recommends further investigations.²⁰

Regarding endoscopic nasal examination and multislice computed tomography (MSCT) evaluation of our patients, we found that a large number of our patients had mucosal congestion, ethmoidal opacity, maxillary opacity in the form of maxillary mucosal thickening or maxillary retention cyst, bilateral hypertrophied inferior turbinates and osteomeatal complex occlusion, with significant improvement at the end of our study (Tables 3,5) these findings follow other studies that support the relationship between GERD and sinonasal symptoms. For example, Delgaudio JM studied nasopharyngeal reflux with 24-hour pH monitoring of patients with refractory CRS and suggested that direct contact between sinonasal tissues and stomach contents from GERD may initiate or induce the mucosal inflammation of CRS. Patients with refractory CRS had significantly more nasopharyngeal reflux events compared to control groups.²¹

Another study by Katle et al. 2013 revealed an increase in the total number of reflux events in patients with CRS in comparison to healthy controls.²²

Also, it was found that ten of our patients (27%) had left and six (16.2%) had right dull tympanic membrane either due to middle ear effusion or Eustachian tube dysfunction which was confirmed by tympanogram evaluation, there was a significant improvement in the follow-up of patients with the dull left tympanic membrane but interestingly not in those with dull right one with no definite explanation in our opinion, further studies are recommended with more focus on this point. Eustachian tube dysfunction is defined by symptoms and signs of

middle ear pressure dysregulation in the 2015 Eustachian Tube Dysfunction (ETD) Consensus Statement. The Consensus Statement panel stated that if the Eustachian tubes function normally, they will protect the middle ear against inflammation, infection, and GERD. They agreed that gastric juice can affect the Eustachian tube and can cause ETD and otitis media.²³

Our results supported that regardless of the precise mechanism, GERD has a significant role in the development of many sinonasal symptoms medical treatment of GERD only can be sufficient to relieve most of these symptoms. This matched with other studies as DiBaise et al. who compared 11 patients who had no improvement in their symptoms after medical and surgical treatment of CRS, treatment with PPIs twice daily for 12 weeks was instituted, and they were reassessed monthly. The authors noted mild improvement in symptoms and overall satisfaction with the treatment.²⁴

Durmus et al. 2010 on the other hand studied 50 patients with GERD and nasopharyngeal reflux and compared them to 30 controls based on endoscopic and clinical diagnosis. All patients were treated with PPIs twice daily for 12 weeks and there was no statistical difference between the study groups and the controls before and after treatment, which leads the authors to conclude that nasal mucociliary transport was not affected by GERD and nasopharyngeal reflux.²⁵

We used three known scoring systems to evaluate and support our results: SNOT22 in history, MLKS for endoscopic examination of the nose, and LMCTS for evaluation of Computed tomography. In all these scoring systems we had highly significant improvement which supports our belief that GERD can induce or aggravates inflammation of the nasal mucosa.

The limitations of the study included a small sample size due to the high cost of radiology both pre and post-treatment upper endoscopy and/or 24-hours PH-monitoring and MSCT and we couldn't find multichannel PH-metry to determine acidic reflux in the nasopharynx.

Conclusion:

At the end of our study, we concluded that many sinonasal symptoms improved with medical treatment of gastric reflux only in the form of PPIs especially PND, nasal obstruction, nasal itching, and headache. GERD might be a possible cause and aggravating factor of CRS.

Authorship Contribution

1. Ahmed AbolEwafa: supervision.
2. Mahmoud A. Ragaee: Conception and design, Acquisition of data, Analysis and interpretation of data, Critical revision of the submitted protocol for important intellectual content.
3. Rehab A. Mohammed: Data collection.
4. Essam ElDeen M.O. Mahran: Examination of patients at gastroenterology department and diagnosis and treatment of GERD.

Conflict Of Interest: No conflict of interest exists.

Funding: No funds were received for this study.

Reference:

1. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinol Suppl.* 2012;23:1---298
2. Badillo R, Francis D. Diagnosis and treatment of gastroesophageal reflux disease. *World journal of gastrointestinal pharmacology and therapeutics.* 2014;5(3):105.
3. Hait EJ, McDonald DRJ. Impact of immunology. *Impact of gastroesophageal reflux disease on mucosal immunity and atopic disorders.* 2019;57(2):213-25.
4. Messerklinger W. Über den Recessus frontalis und seine Klinik. *Laryngologie, Rhinologie, Otologie und ihre Grenzgebiete.* 1982;61(05):217-23.
5. Elhennawi D, Ahmed M, Abou-Halawa A. Correlation of obstructive sleep apnoea and laryngopharyngeal reflux: phmetry study. *Clinical Otolaryngology.* 2016;41(6):758-61.
6. Vakil, N., Van Zanten, S.V., Kahrilas, P., Dent, J. and Jones, R., 2006. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Official journal of the American College of Gastroenterology| ACG*, 101(8), pp.1900-1920.
7. Jecker P, Orloff LA, Wohlfeil M, Mann WJ. Gastroesophageal reflux disease (GERD), extraesophageal reflux (EER) and recurrent chronic rhinosinusitis. *European Archives of Oto-Rhino-Laryngology and Head & Neck.* 2006;263(7):664-7.
8. Ozmen S, Yücel OT, Sinici I, Ozmen OA, Süslü AE, Öğretmenoğlu O, et al. Nasal pepsin assay and pH monitoring in chronic rhinosinusitis. *The Laryngoscope.* 2008;118(5):890-4.
9. Loehrl TA, Samuels TL, Poetker DM, Toohill RJ, Blumin JH, Johnston N. The role of extraesophageal reflux in medically and surgically refractory rhinosinusitis. *The Laryngoscope.* 2012;122(7):1425-30.
10. Vaezi MF, Katzka D, Zerbib F. Extraesophageal symptoms and diseases attributed to GERD: where is the pendulum swinging now?

- Clinical Gastroenterology and Hepatology. 2018;16(7):1018-29.
11. Nanda MS, Kaur M, Gupta V. Correlation between chronic rhinosinusitis and laryngopharyngeal reflux. National Journal of Physiology, Pharmacy and Pharmacology. 2018;8(4):544-9.
 12. Dewan K, Lieu J. A clinical trial of proton pump inhibitors to treat children with chronic otitis media with effusion. The journal of international advanced otology. 2018;14(2):245.
 13. Nair S, Kumar M, Nair P. Role of GERD in children with otitis media with effusion. The Indian Journal of Pediatrics. 2012;79(10):1328-32.
 14. Bohnhorst I, Jawad S, Lange B, Kjeldsen J, Hansen JM, Kjeldsen ADJA, et al. Prevalence of chronic rhinosinusitis in a population of patients with gastroesophageal reflux disease. 2015;29(3):e70-e4.
 15. Brown HJ, Kuhar HN, Plitt MA, Husain I, Batra PS, Tajudeen BA. The impact of laryngopharyngeal reflux on patient-reported measures of chronic rhinosinusitis. Annals of Otolaryngology, Rhinology & Laryngology. 2020;129(9):886-93.
 16. Flook E, Kumar B. Is there evidence to link acid reflux with chronic sinusitis or any nasal symptoms? A review of the evidence. Rhinology. 2011;49(1):11.
 17. Dagli E, Yüksel A, Kaya M, Ugur KS, Turkay FC. Association of oral antireflux medication with laryngopharyngeal reflux and nasal resistance. JAMA Otolaryngology–Head & Neck Surgery. 2017;143(5):478-83.
 18. Nation J, Kaufman M, Allen M, Sheyn A, Cotichia J. Incidence of gastroesophageal reflux disease and positive maxillary antral cultures in children with symptoms of chronic rhinosinusitis. International journal of pediatric otorhinolaryngology. 2014;78(2):218-22.
 19. Finocchio E, Locatelli F, Sanna F, Vesentini R, Marchetti P, Spiteri G, et al. Gastritis and gastroesophageal reflux disease are strongly associated with non-allergic nasal disorders. BMC Pulmonary Medicine. 2021;21(1):1-9.
 20. Kabadi A, Saadi M, Schey R, Parkman HP. Taste and smell disturbances in patients with gastroparesis and gastroesophageal reflux disease. Journal of neurogastroenterology and motility. 2017;23(3):370.
 21. DelGaudio JM. Direct nasopharyngeal reflux of gastric acid is a contributing factor in refractory chronic rhinosinusitis. The Laryngoscope. 2005;115(6):946-57.
 22. Katle E-J, Hatlebakk JG, Steinsvåg S. Gastroesophageal reflux and rhinosinusitis. Current allergy and asthma reports. 2013;13(2):218-23.
 23. Tysome, J.R., 2015. Eustachian tube dysfunction consensus. Clinical Otolaryngology, 5(40), pp.406-406.
 24. DiBaise JK, Olusola BF, Huerter JV, Quigley EM. Role of GERD in chronic resistant sinusitis: a prospective, open label, pilot trial. The American journal of gastroenterology. 2002;97(4):843-50.
 25. Durmus R, Naiboglu B, Tek A, Sezikli M, Cetinkaya ZA, Toros SZ, et al. Does reflux have an effect on nasal mucociliary transport? Acta oto-laryngologica. 2010;130(9):1053-7.

Appendix I: SNOT-22 scoring system

SNOT-22 SCORE						
	No problem	Very mild problem	Mild	Moderate	Severe	The problem as bad as it can be
Need to blow	0	1	2	3	4	5
sneezing	0	1	2	3	4	5
Runny nose	0	1	2	3	4	5
Cough	0	1	2	3	4	5
Post. nasal discharge	0	1	2	3	4	5
Thick nasal discharge	0	1	2	3	4	5
Ear fullness	0	1	2	3	4	5
dizziness	0	1	2	3	4	5
Ear pain	0	1	2	3	4	5
Facial pain	0	1	2	3	4	5
Difficulty falling asleep	0	1	2	3	4	5
Waking up tired	0	1	2	3	4	5
Lacking a good night's sleep	0	1	2	3	4	5
Waking at night	0	1	2	3	4	5
Fatigue during day	0	1	2	3	4	5
Reduced productivity	0	1	2	3	4	5
Reduced concentration	0	1	2	3	4	5
Restless/irritable	0	1	2	3	4	5
Sad	0	1	2	3	4	5
embraced	0	1	2	3	4	5
Decreased sense of taste/smell	0	1	2	3	4	5
Nasal blockage	0	1	2	3	4	5