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Radionuclide Gastroesophageal Reflux Scan; An Effective Screening Tool For Infants/Children With Repeated Chest Infections

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ABSTRACT

Objective: Unexplained recurrent chest infections are a cause of failure to thrive in infants and young children. Repeated hospital admissions with respiratory symptoms are an extra economic burden on the health budget along with the morbidity. The aim of this study was to analyze the utility of Nuclear Medicine to screen children with clinically significant gastroesophageal reflux. **Design & Place of Study:** This study was descriptive case series and was conducted at Punjab Institute of Nuclear Medicine in collaboration with the department of pediatrics Allied Hospital Faisalabad. **Patients and Methods:** Seventy clinically symptomatic patients underwent Gastroesophageal Reflux (GER) Scan with effective fasting of one to three hours. Four to thirty seven MBq of ^{99m}Tc labeled Colloid was diluted in milk for oral intake. Thirty minutes dynamic study with frame rate of 3 second per frame was acquired in either anterior or posterior projection. Both qualitative and quantitative analysis was done using cine review, time active curves (TAC) and percentage reflux index (%RI). Patients with high grades of reflux were also reviewed after 08 weeks of conventional antireflux treatment. **Results:** Sixty three percent of the patients (44/70) were declared as reflux positive of varying grades on GER scan. Most of the refluxing subjects (26/44) were in grade I/II category while (13/44) of the patient showed moderate degree reflux and only (2/44) of the patients fell into severe reflux category. Chest infection was the chief clinical presentation in each grade of reflux (57%). Of all the refluxing individuals, (9/44) were having no refluxing spikes on TACs while when reflux index (%RI) were calculated (4/44) of the patients showed value below 4%. Eighty percent of selected patients (8/10) showed improvement with conventional antireflux treatment but complete improvement was evident only in (3/10) patients. **Conclusion:** GER scan is a non-invasive and effective way of screening clinically symptomatic babies for reflux of the gastric contents interfering with the respiratory tract. Quantitative assessment of improvement after conventional antireflux treatment offer cost-effective follows up of GERD.

Key Words: Gastroesophageal Reflux Disease (GERD), Gastroesophageal Reflux Scan, Chest infection. Reflux index (RI),

INTRODUCTION

Gastro-esophageal Reflux Disease (GERD), a problem rarely mentioned half a century ago, is now believed to be responsible for a number of morbidities. In the past few years, the rate of GERD diagnosis in hospitalized infants is increased by more than 10 folds. Now it is a common discharge diagnosis in inpediatric patient service[1]. GERD is a potential serious condition that can not only reduce patient's quality of life but is considerable burden on health care system[2,3].

Gastroesophageal reflux disease (GERD) is pathological movement of acid gastric contents into the esophagus[4,5]. It includes any reflux event causing any symptomatic condition or histopatholgic alteration[6]. GERD can result from a transient lower esophageal sphincter relaxation not

associated with swallowing; stress reflux caused by transient increase in intraabdominal pressure, or free reflux across an atonic lower esophageal sphincter[7].

Infants with GERD can present with variety of symptoms including disturbed sleep and feeding, excessive crying, irritability, recurrent vomiting, regurgitation, heartburn, poor weight gain, asthma and recurrent pneumonia, etc. Dysphasia, odynophagia, otolaryngology manifestations, teeth erosion, chronic bronchitis, bronchiectasis, pulmonary fibrosis and emphysema are usual presentation in complicated case with prolonged disease[1,8,9]. Most of the infants with significant reflux are brought to the attention of their primary care provider by 1-2 months of age. The process is benign, self-limiting, and spontaneously resolving with age in the majority of cases[10]. Various diagnostic tests are available for evaluation of the children with GERD. These include barium swallow, endoscopy, pH monitoring and radionuclide reflux scan. Barium swallow is very sensitive in detecting high grades of reflux with high resolution images but significant radiation exposure is a major concern[11]. Endoscopy can view the consequences of the reflux on the esophageal mucosa and allows histological evaluation of the mucosa for inflammatory changes. But the invasive nature of the procedure and need of sedation are hindrance to its common application[12]. The 24 hour pH monitoring technique often is considered the gold standard but the need for hospital admission makes it cumbersome[13].

Radionuclide gastroesophageal reflux scan is sensitive, physiological, easily performed, well tolerated and quantitative. Its sensitivity ranges from 70 to 80% and specificity of 93 to 100%[7,14,15]. Additionally, the study permits quantitation of the reflux into esophagus and it also can be extended to detect pulmonary aspiration of gastric contents[16]. The best results are achieved by using the combination of radionuclide scan, pH monitoring, and manometery.

The rationale of this work is to look for the utility of GER scan as simple, noninvasive and easily performable procedure in children and infants; not only to rule out gastroesophageal reflux but also to be utilized in follow-up cases with low radiation burden.

AIMS AND OBJECTIVE:

The study aimed to analyze the utility of Nuclear Medicine to screen children with repeated respiratory problems for clinically significant gastroesophageal reflux.

METHODS

The Research Ethics Committee approved the study with descriptive case series design. A Performa was designed for clinical and scintigraphic evaluation of the subjects included in the study and a written informed consent was taken from parent/guardians.

Seventy patients were included using non-probability purposive sampling; 41 males and 29 females, aged between 3 and 180 months (mean age 29.9 month). All patients were referred to Nuclear Medicine department of PINUM from Department of Pediatrics Allied Hospital for GER scan.

All patients above the age of 03 months with clinical evidence of repeated chest infections, vomiting, gagging or late night symptoms of cough and dyspnoea (older children) were included in study.

Patients below age of three months and in whom GER study was not technically feasible due to uncontrolled motion or who were clinically unstable were excluded from study.

Attendants were asked not to feed their children 1-3 hours before the study. Test procedure was fully explained to the parent/guardian. All the subjects were given 4 -37 MBq of ^{99m}Tc-labbeld colloid mixed with 200 milliliter of milk with effective dose of 185 KBq / mL in 2-5 minutes per orum. After completion of the meal a small amount of feeding was done with plain amount of milk to clear the residual activity in the esophagus. Small infants were burped before starting the scan.

Later the patients were placed supine on the imaging table of (Siemens ECAM) Gamma Camera and dynamic study of 30 minutes with frame rate of 03 seconds per frame was acquired in either anterior or posterior projection. Study was acquired with a large field of view detector, low energy all purpose collimator, 20% window around 140 Kev and 64 x 64 matrix.

Computer analysis was done by generating time activity curve (TACs) and visual interpretation of raw data in cine mode. Region of interests (ROIs) were drawn over the entire esophagus and over the upper and lower halves of the esophagus. Time activity curves were generated from these regions. Number of the episodes of reflux was noted. Percentage reflux index (%RI) [7], which is ratio of reflux activity to the corrected activity of stomach, was also calculated in all studies using formula **RI (%)= E(t) –E(b) x100/G_o** where **E (t)** is esophageal counts at time t; **E(b),** esophageal background counts; and **G_o**, the gastric counts at the start of study. A cutoff of ≥4% was used to declare the subject as reflux positive.

When interpreting the results, one or two episodes of reflux in the first five minutes study were ignored as physiological. Repeated episodes and those occurring in the later half of the study was considered as abnormal. Reflux were graded arbitrarily in 03 grades;, Grade I (mild) involving the lower third of esophagus, Grade II (moderate) extending to lower 2/3rd and the reflux involving the entire esophagus was graded as III (severe). While joining two grades, like I/II and II/III, intermediate categories were also generated when exact definition of reflux was not possible.

Statistical analysis

Statistical analysis of the compiled data was purely based on descriptive statistics portraying frequencies and percentages for qualitative variables and Mean ± Standard Deviation for quantitative variables.

RESULTS

After calculation of percentage of reflux positive patients, results of the study were summarized in four different groups. These were categorized as clinical presentation of refluxing subjects, severity of reflux (according to grading system already mentioned), correlation of positively reflux group with TACs and percentage reflux index (%RI) and finally reflux status of the patients after antireflux treatment follow-up.

Of the seventy selected subjects for GER scan 41 were male patients while rest were female patients. Sixty three percent (44/70) of the selected population were declared as having reflux of varying grades on qualitative analysis. This was based on static image analysis and review in cine mode. Most of the refluxing subjects (34%) showed mild to moderate degree reflux, which was accorded with grade I/II of the grading system. Moderate reflux was seen in 29 % (13/44) of patients. While 9% patients showed reflux more than grade II with only 2% patients falling in category of severe or grade III reflux as shown in Table 1.

Table 1: Data from different modes of GER scan analysis

Total Patients (n=70)	Male		41/70
	Female		29/70
Reflux Status	GER Positive	44/70 (63%)	Male 26/44 Female 18/44
Time Activity Curve	Positive	35/44	(80%)
	Negative	9/44	(20%)
% Reflux Index (RI)	>4% RI	40/44	(91%)
	<4% RI	4/44	(9%)

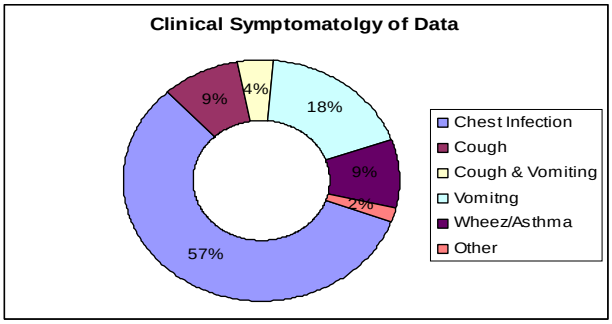


Fig. 1: Frequency distribution of clinical presentation

Chest infection was the chief presenting complaint of the refluxing subjects in nearly all grades of reflux as shown in Figure 1. Overall 57% patients with positive reflux were presented with repeated chest infections. When clinical presentation was further analyzed, 72% of grade I had presented with repeated chest infection. While 38% of grade II and 100% of grade III presented with chest symptomatology. As a whole Chest infection was the leading symptom in the refluxing individuals followed by repeated vomiting and only cough.

Of all the subjects with positive reflux, 20 %

patients had no evidence of reflux on time activity curves (TACs). Of these TAC negative, 9% with no refluxing spike on TAC were of grade I category; while remaining 11% showed curves which were not interpretable due to significant motion of the child during scanning procedure.

When percentage reflux index (%RI) was calculated for all the positive subjects, 9% (4/44) of the refluxing patient of mild severity group showed reflux index below 4% while on qualitative analysis they were declared as positive as shown in Table 1. Please note that 4% of RI was set as cutoff for declaring reflux.

Nine percent of the GER positive patient did not show quantitative evidence of the reflux including both the %RI and TAC. While another 4% (2/44) had equivocal results with absolute value of 4% RI and negative TAC as shown in Table 1.

Table 2: GER severity frequency distribution

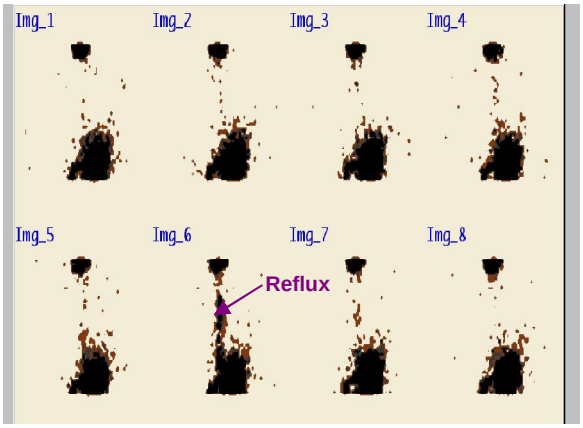
	Reflux grade (n=40)
Grade I	11/44 (25%)
Grade I/II	15/44 (34%)
Grade II	13/44 (30%)
Grade II/III	4/44 (9%)
Grade IIII	1/44 (2%)

Table 3: Reflux treatment response analysis

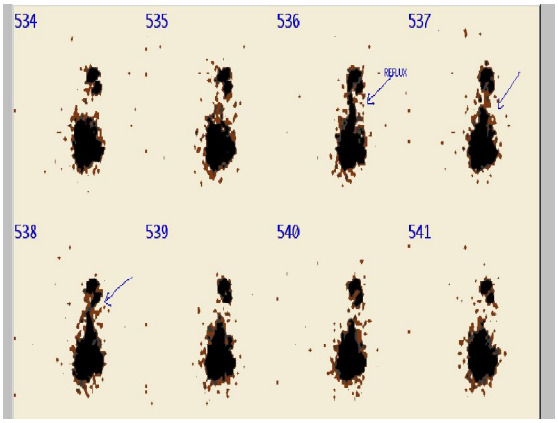
Anti Reflux Treatment Follow up Data n=10	Improved Completely	3/10 (30%)
	Improve Partially	5/10 (50%)
	No Change	2/10 (20%)

Ten patients (23%) with reflux of grade II or more falling in moderate severity were followed after anti reflux treatment of 08 weeks. Eighty percent of the followed patients showed improvement with only 30% showing complete improvement with no evidence of reflux after treatment. While 50% of the patients with follow-up; showed decrease in grade/severity of the reflux. Hundred percent falling in grade III category showed significant improvement of scan presentation and clinical symptoms. This improvement was read as change in the reflux index and decrease in number of spikes on TAC along visual analysis.

Figures 2 and 3 are typical images showing visual analysis and TAC produced spikes of gastroesophageal reflux.



Patient 1



Patient 2

Fig. 2: Gastroesophageal reflux involving entire esophagus

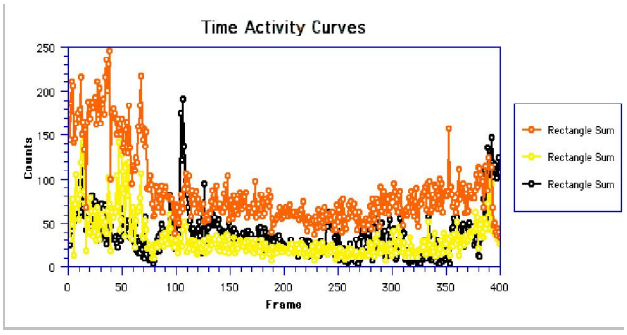


Fig. 3: Time activity curve showing spikes of gastroesophageal reflux.

DISSCUSSION

Seventy patients above the age of 03 months and with known repeated clinical presentations of chest infection were included in this study. All subjects underwent GER scan and selected patients with high grades of reflux were followed after reflux treatment. Both qualitative and quantitative analysis was done as already mentioned.

Reflux is common in infants below the age of 03 months, reducing the utility of any screening test in this age group[17]. Chest symptomatology was the primary inclusion criteria because several reports have shown an association between respiratory tract disturbances and acid reflux. Most of our patients had with repeated hospital admissions because published data shows that GER is very common in this group[18, 19].

Use of the isotope labeled colloid with milk is safe and delivered radiation dose is within the permitted limits[20]. High frame rate is recommended by most of the authors to avoid missing of the reflux episodes[21]. All three methods including cine review, TACs and %RI was used to diagnose and grade the reflux[22].

GER scan is highly sensitive to screen the gastroesophageal reflux as 63% of the patients with variety of respiratory and gastroesophageal symptoms were test positive in our study. This was in good correlation with previously published clinical data of 60 to 80% by various authors under different clinical scenarios and selected populations [15, 23]. Specificity was not calculated due lack of availability of 24 hour pH metry.

All the GER positive subjects showed spontaneous reflux as we have not used abdominal pressure as there is lack of agreement on this by different authors[7].

We have found various grades of reflux in different clinical presentation, so it is not possible to make any correlation between the severity of reflux and clinical presentation. This finding is in accordance with published data by many researchers[14].

Correlation of the time activity curve and %reflux index parameters show that 20% of mild/grade I reflux has no evidence of reflux on TAC and 9% of the patients were having reflux index of below 4%. Major factor involved in these cases was uncontrolled patient motion. Whereas the problem with calculation of reflux indices was interference by the stomach activity in mentioned case due to improper region of interest placement. So all three i.e., visual analysis, TAC, and %RI are necessary to comment on the reflux involving the lower third of esophagus[22].

Selected patients with high grades of reflux were followed with 8 weeks of conventional antireflux treatment. Most of these patients showed improvement of reflux grades with few showing complete recovery as depicted on GER scan. Patients who showed partial improvement should be followed for another 8 week of treatment as accepted by most of the clinicians[23]. Previously too little data regarding treatment follow up using GER scan as investigation tool is published[24]. Detection of improvement in quantitative terms i.e., changes in the reflux index and number of spikes on time activity curve is one of the major utility of this scan. Considering the cost analysis with other modalities, GER scan is the most acceptable[25].

STUDY LIMITATIONS

Most of the authors recommend 60 minute GER scan but we used 30 minutes due to imaging time constraints because of heavy patient load. Multi diagnostic modality comparison was not done due to lack of facilities and also the radiation dose. Number of followed up cases were smaller for adequate statistical analysis.

CONCLUSIONS

We conclude that GER scan is non-invasive, sensitive and effective way of screening clinically symptomatic babies for reflux of gastric contents. Assessment of improvement after conventional antireflux treatment offers an objective and cost effective follow-up.

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