

Original Research Article

Liquid gastric emptying time 1/2 in infants: establishing reference range and it's co-relation with presence of gastro-esophageal reflux

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ABSTRACT

Background: Gastric emptying time ½ (GET ½) is considered as the half time taken for chyme to pass into the duodenum. Gastric emptying depends upon numerous factors, both endogenous and exogenous. Nerve and hormones along with volume of meal, pH, particle size, composition and viscosity play part in gastric emptying. Aim of the study was to determine liquid gastric emptying Time ½ in infants and to evaluate impact of positive GER on Gastric Emptying Time.

Methods: Total 149 full term babies from 29th day to 1 year of age; underwent Tc-99m labeled with Sulfur colloid GER scintigraphy using age specific formula. Babies with gastro-intestinal anomalies, lactose intolerance and low birth weight babies were excluded. The reference range of GET ½ was estimated from GER negative group and the same was compared with GER positive group.

Results: Out of 149 babies 96 (64%) babies were GER positive and 53 (36%) were negative for GER. The liquid GET ½ values generated for 29th day-3 months, 4-6 months, 7-9 months and 10 months -1year were 62.67 (12.42), 69.84 (13), 63.5 (9.7) and 53.2 (10) minutes respectively. The liquid GET½ was found to be delayed in severe GER positive group.

Conclusions: The reference range for liquid GET½ was estimated from GER negative group utilizing the exclusion criteria thereby avoiding radiation exposure to normal controls. With increasing severity of GER there was consequent prolongation of liquid GET½.

Keywords: Formula liquid meal, GER scintigraphy, Liquid GET½, Reference range

INTRODUCTION

Gastric emptying time ½ (GET ½) is considered as the half time taken for chyme to pass into the duodenum. Gastric emptying depends upon numerous factors, both endogenous and exogenous. Nerve and hormones along with volume of meal, pH, particle size, composition and viscosity play part in gastric emptying.¹ In infant population, gastric emptying also depends upon the maturity at the time of birth. The gastric emptying pattern is different in infants fed with breast milk and formula

feeds and so gastric emptying has to be diligently worked out.²

There have been many studies performed using different radiopharmaceutical meals such as In-111 micro colloid in fixed quantity of milk, Tc-99m sulfur colloid in dextrose, Tc-99m labeled to chicken liver with establishment of various reference standards for liquid and solid emptying times. These studies have included age group varying from infancy till early childhood and age-related dependence was reported.³⁻⁸ The GET ½ or

stomach retention at 1 or 2 hours suggested was variable; depending on the meal selected.³

The comparison of gastric emptying done by scintigraphy method and gastro-esophageal reflux (GER) by manometry has been done in infants; however was found to be invasive and tedious to perform.⁷ The gastric emptying and GER studies have been combined using scintigraphy methods earlier to serve the purpose of obtaining additional information from the same study.^{3,9-11} The gastric motility studies with drugs also have been performed to assess the response to medical management.¹² The relationship between the GER and GET has been studied in the wide age group (infancy to pre-school) by using various protocols, however data specific to infancy is lacking.^{3,7,8,13-17}

It has been noticed that, the establishment of normal range for GET is problematic due to lack of standardization of study technique and the test meal especially in infant group.³ There is lack of reference data for gastric emptying in infants in the existing guidelines.^{3,17-19} The stomach capacity and use of milk or meal preparation varies widely during infancy predominately being liquid. Also the sphincter tone development of infant group is different as compared to the elder children.

Considering the above variables in perspective, the aim of the study was to find out liquid GET $\frac{1}{2}$ in infant group selectively. Due to radiation exposure and ethical issues related to the selection of controls; the controls were selected from the group of babies sent to Nuclear Medicine department for GER scintigraphy by using the exclusion criteria to match the control population. The liquid meal selected was formula milk specific for the age; available worldwide so as to provide the reference range.

METHODS

It was a prospective observational study including 149 babies (84 males and 65 females) between August 2013 to July 2015 referred to Nuclear Medicine department for GER scintigraphy (milk scan) with complaints of recurrent upper or lower respiratory infection, vomiting after feeds were included in the study. The inclusion criteria were babies delivered full term (37 weeks of gestation). The exclusion criteria were neonatal period, gastrointestinal malformations, lactose intolerance and low birth weight.

Preparation of liquid meal

The age specific liquid formula meal was used for the study. The meal was prepared from the formula available as Similac 1 and 2 (Abbott Pharmaceuticals, India). The nutritional constitution of the formula feed for infants <6 (Similac 1) months had protein: 14.58g, fat: 28.2g, carbohydrate: 49.4g providing 511Kcal/100gm and for

>6 months (Similac 2) had protein: 14.7g, carbohydrate: 56.81g, providing 466 Kcal/100gm. The reference standard provided in the information leaflet with the formula preparation was used to calculate the volume of feed for the age and weight of baby. The one scoop measure provided with formula was mixed per 30ml of water by taking aseptic precautions. The feed was thoroughly mixed to ensure its uniform distribution. 16 MBq to 37 MBq of Tc-99m Sulfur colloid was added to mixture and mixed thoroughly.

Scintigraphy acquisition parameters

The study was performed considering the feeding time of babies with minimum time gap of 2 hours from the last feed of the baby. These babies underwent Gastro-oesophageal reflux scintigraphy by including mouth to pubic symphysis of baby under the gamma camera. The babies were administered with 16 MBq to 37MBq of Tc-99m labeled sulphur colloid mixed in the age specific formula feed prepared just before the scan; through the infant feeding tube secured before. The infant feeding tube was removed under the gamma camera after giving the feed. Dynamic anterior and posterior acquisition in supine position (15 seconds/frame), later merged to get 1min/frame, (64X64 matrix) for 60 minutes followed by static acquisition in anterior and posterior projection for 60 seconds (128x128 matrix) at the end of 1hr. Another static image was acquired (128x128matrix) in anterior and posterior projections for 60 seconds at 2 hour to look for aspiration into the lung and gastric content.²⁰

Review and processing of study

The dynamic and static images were studied visually by Nuclear Medicine Physicians to assess the GER. A reflux, if present was visualized as a distinct spike of activity into the esophagus. The grading of reflux was done based on frequency. The single episode of reflux during the 60 min study was graded as mild whereas more than one (>1) episode of reflux was graded as severe. The GER positive group was divided in the mild and severe grade of reflux.

For estimation of liquid GET $\frac{1}{2}$, Region of Interest (ROI) was drawn over the stomach and also a background ROI to eliminate background counts on the dynamic and static images. A decay and background corrected Time Activity Curve (TAC) was obtained to calculate the time by which activity present into the stomach reduces to half ($T_{\frac{1}{2}}$) of its initial value. The study sample was divided into gastro-esophageal reflux positive and negative groups. This each group was further divided into four categories as per age into 29th day-3 months, 4-6 months, 7-9 months and 10 months -1year; considering rapid anatomic-physiological changes of the babies during infancy. The liquid GET mean, average and SD for $T_{\frac{1}{2}}$ values for each subgroup was calculated. The GET $T_{\frac{1}{2}}$ GER negative group was considered as control. The delayed GET $\frac{1}{2}$ for an age group mentioned was defined

as GET½ more than the mean (SD). The age matched comparison of T½ values for liquid GET was done between the GER negative and GER positive groups to look for delayed and normal GET½ during each quarter of the infancy period. The GET½ of mild GER and severe GER were also compared. Significance between the above mentioned age matched groups was assessed at 5% level of significance (chi square test, two tiled).

RESULTS

Out of 149 babies 96 (64%) babies showed presence of GER and 53(36%) did not show presence of GER. The liquid GET ½ in GER negative group for 29th day-3 months, 4-6 months, 7- 9 months and 10 months -1year was 62.67 (12.42), 69.84(13), 63.5(9.7) and 53.2(10) minutes respectively (Table 1).

Table 1: T½ for liquid GET (min) for GER negative group (controls for establishing reference range).

Age group	n	Mean T ½ for GET in min	SD	SE of mean
29 th days to 3 month	15	62.67	12.42	3.3
4-6 months	13	69.84	12.9	3.7
7-9 months	12	63.5	9.7	2.9
10months to 1 year	13	53.2	10	2.8

n- Total number, GET-Gastric Emptying Time, SD-Standard Deviation, SE-Standard Error of Mean, GER- Gastro-Esophageal Reflux.

Table 2: Correlation of T½ of GET in GER positive group.

Age group with n	Delayed GET ½	Normal GET ½	GET ½ in min with SD (amrr*)	p value#	SS\$ for GET½ with amrr*
29 th day to 3 months (n=29)	11 (38%)	18 (62%)	62.67 (12.42)	0.005	significant
4-6 months (n=23)	2 (9%)	21 (91%)	69.84 (12.9)	0.230	not significant
7-9 months (n=22)	9 (41%)	13 (59%)	63.5 (9.7)	0.353	not significant
10 months to 1 year (n=22)	12 (55%)	10 (45%)	53.2 (10)	0.017	significant

n- Total number of subject in the age group, GET T½- time to half for Gastric Emptying Time, SD- Standard Deviation; *: age matched reference range, #:p value using chi square test, two tiled (5% level), \$: statistical significance.

Table 3: Correlation between GET½ with mild and severe grade of GER.

Grade of GER	Normal GET ½	Delayed GET ½	Total
Mild	52 (86%)	8 (14%)	60
Severe	11 (30%)	25 (70%)	36

Chi square test (two tiled) shows p < 0.01 suggesting significant difference between the two groups.

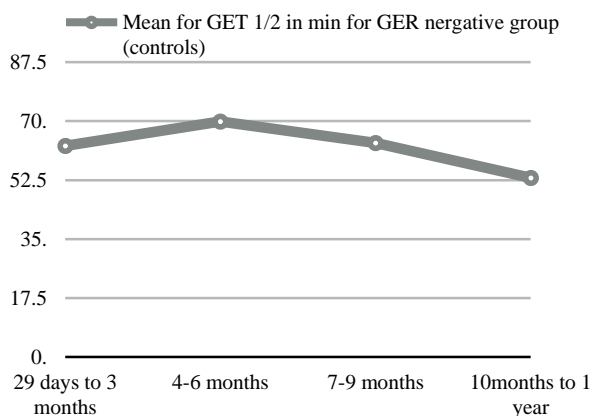


Figure 1: Mean for GET 1/2 in minutes for GER negative group (controls) across the age groups during infancy period.

The liquid GET ½ (in minutes) was noted to be gradually decreasing over age during the infancy period (Figure 1). These values were considered as controls (reference range) to compare with the age matched groups.

The delayed liquid GET ½ was observed in 11 (38%), 2 (9%), 9 (41%) and 12 (55%) babies in 29th day-3 months, 4-6 months, 7-9 months and 10 months -1year respectively (Table 2). The difference between the age matched liquid GET ½ of two groups (GER positive compared with age matched reference range) was found to be significant (p<0.05) in the age groups of 29 days to 3 months and 10 months to 1 year.

The 4-6 months and 7-9 months groups (GER positive group compared with age matched reference range) did not show statistically significant difference in liquid GET

½ values (Table 2). There were 61 (63%) babies with mild grade of GER and 35 (37%) babies with severe grade of GER in GER positive group. There was statically significant difference ($p < 0.001$) noted between the above two groups for liquid GET ½ (Table 3).

DISCUSSION

The selection of liquid meal was standard, widely available with predominantly fixed nutrient and calorie content. However, minor variations in the nutrient and calorie content may be noted based on the country of production of formula milk.

The preparation of the liquid meal was easy and reproducible for all age groups of babies. The selection of controls from the GER negative groups avoided the unnecessary exposure of normal babies to radiation. The inclusion and exclusion criteria used specified the GER negative group close to the control population criteria. Thus the reference value generated (Mean T½ and SD) can be considered appropriate as reference range.

The liquid GET ½ values generated for 29th day-3 months, 4-6 months, 7-9 months and 10 months -1 year were 62.67 (12.42), 69.84 (13), 63.5 (9.7) and 53.2 (10) minutes respectively. A declining pattern of liquid GET ½ was observed in the latter half of infancy with reduction in the time for gastric emptying as the age matures. The determination of liquid GET ½ in age specific group during infancy was done in our study when compared to the previous studies where predominantly children age groups of infancy were compared with older children.²⁻⁸

The radiopharmaceutical used in this study gave less radiation to the infants as opposed to the radiopharmaceutical used earlier.⁴ There was significant difference found for liquid GET ½ in 29 days to 3 months and 10 months to 1 year groups; whereas Argon et al did not find significant difference in GET ½ between GER positive and GER negative groups.⁸

There was statistically significant difference for liquid GET ½ found between the mild GER and severe GER in our study, that supports the finding of association delayed gastric emptying and presence of severe degree of gastroesophageal reflux.^{7,8,16} The association of all age groups with delayed emptying could not be established due to strict exclusion criteria applied for selection of reference range. The delayed liquid GET ½ was studied whereas the early emptying was not taken into consideration, as it may not influence the GER.²¹

CONCLUSION

The study has provided reference range for liquid GET ½ for subgroups during infancy period. The use of age specific formula preparation is easy, reproducible and reliable to be used. The time required for liquid gastric

emptying was found to be reducing as the age progresses during infancy.

There was correlation established between delayed liquid GET ½ with presence of GER during early and late quarters of infancy (29 days to 3 months and 10 months to 1 year). Also there was strong association between presences of severe grade of GER with delayed liquid gastric emptying.

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