

Association of Gastric Residual Volumes With Necrotising Enterocolitis in Extremely Preterm Infants

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Research Article

Keywords: Gastric residuals, Necrotising enterocolitis, Preterm infant

Posted Date: April 5th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-368218/v1>

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Version of Record: A version of this preprint was published at European Journal of Pediatrics on July 17th, 2021. See the published version at <https://doi.org/10.1007/s00431-021-04193-x>.

Abstract

Necrotising enterocolitis (NEC) is a potentially serious illness with significant mortality and morbidity in preterm infants. Previous studies have reported association of volume and colour (bile and blood stained) of gastric residuals (GR) with NEC. We aimed to study this association in our cohort of extremely preterm (EP) infants. In a case-control study using retrospective data (January 2006-December 2011), EP (Gestation <28 weeks) infants with confirmed NEC \geq Stage II (Cases) were compared with infants without NEC (Controls) matched for birth weight (BW) and gestational age (GA). Forty cases of NEC \geq Stage II diagnosed at a median (IQR) age of 16.5 (10.3-23) days were compared with 40 controls matched for gestation (± 3 days), and birth weight (± 680 g). Median maximum GR volume (GRV) from birth to the day of occurrence of NEC was significantly higher in cases vs. controls (5.9 vs. 3.7 ml; p<0.001). Increased maximum GRV was associated with NEC \geq Stage II in adjusted analysis (aOR 1.36, 95%CI 1.06-1.75, p=0.017). There was no significant difference in GRV between cases and controls throughout the clinical course, including 72, 48 and 24 hours before the onset of NEC. However, green (65.0% vs. 27.5%, p=0.001) and haemorrhagic GRs (45.0% vs. 27.5%, p=0.092) were higher 24 hours before the diagnosis of NEC.

Conclusion: GRV was not associated with NEC \geq Stage II. However, green and haemorrhagic GRs were significantly higher 24 hours before the diagnosis of the illness. Adequately powered prospective studies are needed to confirm the significance of our findings.

What Is Known

It is unclear whether large volume, dark coloured and blood stained GRs are associated with NEC.

The value of routine monitoring of gastric residuals in preterm infants is currently being questioned.

What Is New

- Volume of gastric residuals was not associated with significant NEC.
- Green and haemorrhagic GRs were significantly higher 24 hours before diagnosis of NEC.

Introduction

Necrotising enterocolitis (NEC) is a potentially devastating gastrointestinal emergency predominantly affecting preterm infants, with significant health burden [1-3]. Survivors of surgical NEC are at a high risk for complications such as short bowel syndrome, failure to thrive and neurodevelopmental impairment [4-7]. The pathogenesis of NEC is poorly understood [1-3]. Prematurity is the most single most important risk factor for NEC. Other factors that contribute to its pathogenesis include gut dysbiosis, gestation dependent excessive pro-inflammatory response to toxins such as lipopolysaccharides from intestinal gram negative organisms, formula feeding and intestinal ischemia [1-3]. Preventive strategies include

antenatal steroids, exclusive human milk feeding, standardized feeding regimen, prophylactic probiotics, and antimicrobial stewardship [8].

Feeding intolerance is defined as 'the inability to digest feedings presenting as gastric residual volume (GRV) >50%, abdominal distension or emesis or both, disrupting the feeding plan [9]. Preterm infants frequently experience feed intolerance due to gastrointestinal immaturity and decreased intestinal motility [10, 11]. Excessive GRV has been variably defined (e.g. >2 or >5 ml/kg) and its reliability as a predictor of NEC remains unclear [12].

Bertino et al (2009) compared GRV from birth till development of NEC in Very Low Birth Weight (VLBW) infants (Cases=17) with control infants (n=17) matched for GA and BW who did not develop the illness [13]. The mean maximum residual (7.46 ml vs 4 ml; p=0.04) and the mean maximum residual as a percentage of the previous feed (113.24% vs 42.87%; p=0.018) were significantly higher in cases. They concluded that large GRV and haemorrhagic residuals were early markers of NEC [13]. Cobb et al (2004) compared 51 VLBW infants who had proven NEC (Cases) with 102 controls matched for birth weight, gestation, race, and sex who were born in the same period [14]. The median birth weight and gestation was 822 g and 26 weeks in both groups. Feeds were started on day 5, with a planned increase to full feeds over 10 days (median) in both groups. Median time to full feeds (TFF) was 13 days in both groups. Median age of onset of NEC was day 24. Overall, infants who developed NEC had more GRs but there was overlap with data from control infants. Of the various GR parameters assessed, only maximum GR seemed to be the best predictor for later development of NEC [14]. Mihatsch et al assessed the prognostic significance of GRs (volume and colour) in upgrading feeds in preterm extremely low birth weight (Extremely Low Birth Weight/ ELBW: BW <1000g) infants [15]. Regression analysis showed a direct correlation of feeding volume on day 14 with a negative (GRV=0) or milky GR and no significant association with mean GRV or blood or bile-stained aspirates [15]. Shulman et al (2010) prospectively studied the relationship between reaching full feeds and measures such as GRV and abdominal distention and non-invasive gastrointestinal tests in preterm infants (N=50, Gestation: 25–32 weeks) [16]. The mean ± standard deviation (SD) BW and GA was 1200 (± 330) g, and 28.6 (± 2.2) weeks. Overall, there was no correlation between feeding outcomes and GRV (ml/day), GRV >50%, GRV >2 ml/kg. GRV was unreliable in predicting attainment of full feeding [16]. Recent studies have questioned the value of routine monitoring of GRs in preterm VLBW infants [17-19]. Considering the lack of clarity and clinical significance of the issue, we aimed to study the association between GRV and colour with NEC in preterm infants.

Hypothesis: *We hypothesized that volume of GRs will be higher in infants who developed NEC ≥ Stage II compared to controls who did not develop the illness.*

Methods

Design and setting: A case-control study in a tertiary neonatal intensive care unit (NICU).

Ethics approval: Approval from the institutional ethics committee (project number 2015232EW) was obtained prior to commencing the study.

Eligibility: All preterm ELBW infants born <28 weeks of gestation and admitted to the NICU between January 2006 – December 2011 were eligible considering they are at higher risk of NEC [23-31]

Exclusion: Out-born infants, those with congenital gastrointestinal malformations or chromosomal abnormalities.

Cases: Preterm ELBW infants with NEC \geq Stage II as per Bell's criteria [20]. **Controls:** Preterm ELBW infants matched for gestation (± 3 days) and birth weight (± 50 g) who did not develop NEC \geq Stage II, and born within the same year.

Approach to feeding: A standardized protocol for enteral nutrition of preterm infants was followed during the study period [21]. Mom's own milk was preferred for feeding. Pasteurized donor milk was used when mother's own milk was unavailable.

1. Two hourly bolus feeding through an orogastric tube was initiated as soon as possible after clinical stability defined as: (a) No/minimal respiratory assistance (e.g. mean airway pressure: <8 cm H₂O, continuous positive airway pressure (CPAP) support $<5-6$ cm H₂O and oxygen $<30\%$) (b) Normal blood pressure (c) No hemodynamically significant patent ductus arteriosus (d) No sepsis or sepsis treated with antibiotics for at least 48 hours and no respiratory or hemodynamic compromise.
2. **Minimal enteral feeds:** These were started at 5ml/kg/day (Gestation: $<25^{+6}$ weeks) or 10ml/ kg/day (Appropriate for gestational age neonates 26-28 weeks). **Nutritional feeds:** (a) Gestation $<25^{+6}$ weeks: Start feeding at 15ml/kg/day and increase by 7.5ml/kg every 12 h. (b) Gestation 26–28 weeks: Start at 20ml/kg/day and upgrade by 10ml/kg every 12 h. (c) After reaching 100 ml/kg/day feeds, the eight hourly increments were by 7.5ml/kg and 10ml/kg/day for neonates $<25^{+6}$ weeks and 26-28 weeks respectively. (d) Maximum daily total milk volume was 170 ml/kg/day.
3. **Feeding intolerance:** (1) GRs were checked before every feed. Feeding was withheld in presence of pre-feed GRV $>50\%$ of the previous two feedings, dark green or blood stained GRs, or abdominal distension, and during red cell transfusions. (2) Continuous feeding was used for infants with birth weight <750 g with persistent feed intolerance.
4. **Fortification:** This was started when feed volume reached 100ml/kg/day at the discretion of the attending neonatologist.

Pre-planned subgroups: These were planned for surgical vs. medical NEC, and surgical NEC vs. matched controls.

Data collection: Neonatal demographic and clinical data until the time of NEC in each matched pair were extracted from the neonatal electronic database. Maternal demographic and risk factors (e.g. pregnancy

induced hypertension, prolonged rupture of membranes, chorioamnionitis, and antenatal glucocorticoids) were recorded.

Data collection for each control was up to the postnatal day on which NEC \geq Stage II was confirmed in the matched 'case'. Data specific to the study included the type and volume of feeds, the volume and colour of GRs from day one of life till development of NEC, including in the 72, 48 and 24 hours prior to the diagnosis of the illness, postnatal age at first and maximum feeding, and maximum residual volume.

Data Analysis: Continuous data were summarised using median, interquartile range (IQR) and range and categorical data using frequency distributions. Univariable comparisons between case-control pairs were made using the Wilcoxon signed-rank test for continuous outcomes and the McNemar test for categorical data. Conditional logistic regression analysis was conducted to assess the influence of GRV characteristics on NEC cases and controls while adjusting for sex and assessing other characteristics known to influence NEC such as intrauterine growth restriction, CRIB score, chorioamnionitis and antenatal steroid coverage. Time until enteral feeds commenced was analysed using survival methods with infants censored at time of NEC in the matched case-control pair if feeds had not started. Results were presented as unadjusted and adjusted odds ratios or hazard ratios (OR, aOR, HR, aHR) and corresponding 95% confidence intervals (CI). IBM SPSS 20.0 statistical software (IBM Corp, Armonk, NY) and Stata 12 statistical software (StataCorp. 2011, College Station, TX) were used for data analysis. P-values <0.05 were considered statistically significant.

Results

Forty cases of NEC \geq Stage II diagnosed at a median age of 16.5 days (IQR: 10.3-23.8; range 5-54 days) were matched with 40 controls for GA (± 0.7 weeks), BW (± 680 grams) and birth year (2006-2011). There was no change in antenatal management obstetric guidelines during this period. The median GA of the cases and controls were 24.9 (24.0-26.3; 23.0-27.7) and 24.6 (24.0-26.4; 23.1-27.7) weeks with median BW of 698 (567-829; 455-1505) and 693 (603-823; 455-1015) grams respectively.

The cases and controls were compared on many antenatal and postnatal risk factors for NEC as shown in **Table 1**. The case-control pairs were comparable for most pregnancy, labour and neonatal characteristics including median CRIB score. The proportion of infants exposed to antenatal steroids (70% vs 50%, p=0.039) and infants with male gender (75% vs 42.5%, p=0.007) was higher in cases who developed NEC compared to controls.

Primary outcomes (Table 2)

The median maximum GRV from birth to the day of occurrence of NEC was significantly higher in cases vs. controls (5.9 vs.3.7 ml; p<0.001) and increased maximum GRV was associated with NEC \geq Stage II (aOR 1.36, 95%CI 1.06-1.75, p=0.017) in univariable analysis and with adjustment for sex of infant and completed antenatal steroids. There were no significant differences in the day of maximum GRV, feeding volume (FV) at maximum GRV, maximum GRV as percentage of FV, and 24 hr GRV as % of FV in infants

on feeds. A total of 25% of cases developed NEC \geq Stage II without being commenced on enteral feeds. Feeds were commenced late in cases compared to controls (median 8 vs. 6 days, $p=0.025$; aHR 0.63, 95%CI 0.39-1.00, $p=0.050$) (**Table 2**).

Secondary outcomes (Table 3)

Overall, the frequency of haemorrhagic GRVs and the age at first haemorrhagic residual was comparable in cases vs. control infants. GRVs were comparable at 72, 48, and 24 hours prior to NEC diagnosis in cases and controls (Table 3 and Fig 1). Coloured aspirates were significantly more frequent among NEC cases at 48 hours (47.5% vs 25.0%, $p=0.049$) and at 24 hours prior to development of NEC (65.0% vs 27.5%, $p=0.001$) compared with controls. Coloured aspirates were classified into *pale green* (Lime, Wasabi) and *dark green* (Avocado and Spinach) shades however these were not individually statistically tested. Haemorrhagic aspirates were more common in cases at 24 hours prior to NEC diagnosis as compared to controls but not statistically significant.

Subgroup analysis: Surgical NEC vs. Medical NEC

Out of the 40 NEC cases, 50% ($n=20$) had surgical NEC and the remaining received conservative management (medical NEC). There was no difference in GRV (OR: 0.73; 95% CI: 0.46-1.16, $p=0.189$), coloured (OR 1.03; 95% CI: 0.24-4.35, $p=0.96$) and haemorrhagic aspirates (OR 1; 95% CI: 0.23-4.27, $p=1$) between surgical ($n=20$) and medical NEC ($n=20$) cases.

Subgroup analysis: Surgical NEC vs. Controls

No differences were found between surgical NEC cases and controls ($n=20$ pairs). However, the analyses were underpowered due to the small sample size. The high ORs and wide CIs are indicative of this, especially for the analysis of shade of aspirate colour (OR: 3.45; 95% CI: 0.59-20.04, $p=0.168$) and presence of haemorrhagic aspirate (OR: 6.43; 95% CI: 0.61-68.08, $p=0.122$).

Discussion

Our results showed that the mean maximum GRV from birth to the day of occurrence of NEC was significantly higher in cases than controls. The GRV did not differ significantly between cases and controls throughout the clinical course, including 72, 48 and 24 hours before the onset of NEC. However, green and haemorrhagic GRVs were higher 24 hours before the diagnosis of NEC in cases. There was no significant difference in other GRV variables in cases vs controls (e.g. day of maximum GRV, volume of feeds at maximum GRV, maximum GRV as percentage of feeding volume).

Comparing our results with previous studies is difficult due to the differences in participant characteristics, methodology (e.g. feeding protocol, GRV monitoring), and the time periods. Compared to our study, the mean (SD) GA and BW of infants were higher in Bertino et al [13], and comparable in Cobb et al [14]. Limitations of the study design, the long list of factors influencing GRs (e.g. degree of prematurity, infant and feeding tube position, frequency, type and osmolality of feeds, medications,

fortifiers), and changes in clinical practice over time make comparison with old studies difficult [22]. Commenting on haemorrhagic residuals as a predictor of NEC is difficult considering they may relate to gastric mucosal injury by frequent aspirations to check GRs, stress-induced gastritis, or airway injury during endotracheal intubation [22, 23].

Recent studies have questioned the utility of routine monitoring of GRVs – a practice lacking robust evidence [17-19]. They show that the fear of NEC based on signs of ‘feed intolerance’ on routine monitoring of GRs is probably causing more harm (suboptimal nutrition due to frequent stopping of feedings) than benefit.

Riskin et al (2017) evaluated the effect of change in practice from ‘routine’ to ‘selective’ evaluation of pre-feed GRV on time to full feeds (TFF: 150 ml/kg/day) and incidence of NEC in preterm infants [17]. Data was collected from 2 years before (n=239) and 2 years after the change (n=233). The median (IQR) gestation of infants after the change was higher (before vs. after: 32.0 (29.7-33.0) vs. 32.4 (30.4-33.4) weeks, p=.02). Compared with historic controls, infants with selective evaluations of GRV were weaned from parenteral nutrition 1 day earlier (p<.001) and achieved full feeds 1 day earlier (p=0.002). The incidence of NEC Stage \geq II was not significantly different between the two groups (Selective GRV: 1.7 vs. Historical controls: 3.3%, p=0.4). Gestation was the strongest predictor of TFF on regression analysis. Routine monitoring of GRV and increasing time on non-invasive ventilation prolonged the TFF. Findings were consistent in VLBW infants (BW <1500 g). Not monitoring GRV routinely significantly contributed to higher weight at discharge [17].

A Cochrane systematic review (2019) has assessed the effects of routine GRV monitoring in preterm infants [18]. Two Randomised Controlled Trials (RCTs) (n=141 preterm VLBW infants) were included in the meta-analysis. The effect of routine GRV monitoring on NEC was uncertain (RR: 3.07, 95% CI: 0.50 to 18.77; Quality of evidence: Low), and such practice may increase the risk of feeding interruptions (RR: 2.07, 95% CI 1.39 to 3.07), the TFF (MD: 3.92, 95% CI: 2.06 to 5.77 days] and duration of parenteral nutrition (PN) (MD 3.29, 95% CI 1.66 to 4.92 days). It may also increase the time to regain birth weight (MD: 1.70, 95% CI 0.01 to 3.39 days; n=80; One study). Only one trial (n=87, BW: 1500-2000g) allowed comparison of two different GRV criteria to stop feeds. The effect of such a policy on various outcomes including NEC, TFF and time to regain birth weight was uncertain. Given the inadequate data further RCTs were recommended [18].

Parker et al (2019) evaluated the effect of avoiding routine assessment of pre-feed GRs on nutritional outcomes in preterm infants in a RCT [19]. Infants (GA \leq 32 weeks, BW \leq 1250 g) were enrolled within 72 hours after birth and within 24 hours after starting feeds, and followed for 6 weeks. Feeding decisions were based on nutritional guidelines. All infants received only human milk. Weekly milk intake (ml/kg) for 6 weeks after birth was the primary outcome. Enrolled infants were randomized to ‘routine’ (n=74) or ‘no GRV’ (n=69) evaluation groups. The median (SD) GA and BW of infants in these groups was 27.1 (2.4) weeks and 888.8 (206.6) grams vs. 27 (1.2) weeks, and 915.2 (180) grams respectively. Feeding was advanced quicker (mean weekly increase, 20.7 mL/kg/d vs 17.9 mL/kg/d; p=.02), and consumption of

feeds was more at 5 weeks [137.2 (95% CI: 128.6-145.8); p=.03] and 6 weeks [141.6 (95% CI: 133.2-150.0); p=.03] in the 'no' vs 'routine' GRV evaluation group respectively. The no GRV evaluation group had higher mean estimated log weights (p=.03), and lesser frequency of abdominal distention (p=.001), and were discharged 8 days earlier (p=.01). The odds for NEC, death, late-onset sepsis, and ventilator-associated pneumonia were comparable [19].

Akar et al (2020) recently assessed the impact of avoiding routine monitoring of GRV on TFF and incidence of NEC in preterm (GA ≤ 33 weeks) infants [24]. Their observational study compared infants in the historical (Epoch 1: 169, routine GRV monitoring) vs. prospective cohort (Epoch 2: n=122, no routine GRV monitoring). BW, male gender, and mode of delivery were comparable but mean (\pm SD) gestation was lower in epoch 2 [Epoch 1: 30.37 (\pm 2.58) weeks vs. Epoch 2: 29.31 (\pm 3.37) weeks, p<0.05]. The TFF was significantly shorter in epoch 2 (p<0.05) but NEC ≥ Stage II, duration of parenteral nutrition and hospital stay, and weight at discharge were comparable. Duration of invasive mechanical ventilator support was shorter in epoch 2. [24].

The limitations of our study include the case control design and small numbers. We could not get 2 controls per case due to difficulties in matching. However, we believe that despite these limitations it adds useful contemporary data on EP infants exclusively fed breast milk.

In summary, GRV was not associated with NEC ≥Stage II in EP infants in our study. However, green and haemorrhagic GRs were significantly higher 24 hours before the occurrence of NEC. Adequately powered and well-designed RCTs are needed to confirm the significance of our findings in EP infants. The need for such a trial is further supported by a recent study in EP infants which showed that discarding dark green/yellow GRs may represent loss of beneficial nutrients including bile, which has an important role in nutrition [25]. The primary outcome should preferably be optimisation of enteral nutrition without increasing the risk of NEC. Masking of investigators and standardising the protocol for monitoring GRV will be important issues in designing such trials [26]. Results of current trials (NCT03111329, NCT04062851, and NCT04064398) will provide important data in this context.

Abbreviations

BW: birth weight, **CI:** confidence interval, **CRIB:** clinical risk index for babies, **EP:** extremely preterm, **FV:** feeding volume, **GA:** gestational age, **GRV:** gastric residual volume, **NEC:** Necrotising enterocolitis, **NICU:** neonatal intensive care units, **PN:** parenteral nutrition, **RCT:** randomised controlled trial, **SD:** standard deviation, **VLBW:** very low birth weight

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Tables

Table 1: Pregnancy, labour and neonatal characteristics

	Cases (NEC) N=40	Controls (No NEC) N=40	p-value
Pregnancy and labour			
APH@	8 (20.0%)	9 (22.5%)	1.000
PIH@	5 (12.5%)	5 (12.5%)	1.000
PROM@	11 (27.5%)	15 (37.5%)	0.481
CA@	8 (20.0%)	8 (20.0%)	1.000
Steroids complete@	28 (70.0%)	20 (50.0%)	0.039
Antibiotics@	27 (67.5%)	31 (77.5%)	0.388
Labour@	29 (72.5%)	28 (70.0%)	1.000
Caesarean section@	15 (37.5%)	22 (55.0%)	0.167
Inborn@	37 (92.5%)	40 (100%)	0.250
Neonatal characteristics			
Gestational age (weeks)*	24.9 (24.0-26.3)	24.6 (24.0-26.4)	0.538
Male@	30 (75.0%)	17 (42.5%)	0.007
Birthweight (grams)*	698 (567-829)	693 (603-823)	0.814
Length (cm)*	32 (30-34)	32 (30-34)	0.838
Head circumference (cm)*	23 (21-24)	23 (21-24)	0.505
IUGR@	7 (17.5%)	7 (17.5%)	1.000
Apgar at 1 min <7@	36 (90.0%)	30 (75.0%)	0.146
Apgar at 5 mins <7@	13 (32.5%)	13 (32.5%)	1.000
CRIB*	13 (11-15)	13 (11-14)	0.711

Data represents - *median and interquartile range, @range or number (%)

Abbreviations: APH: Antepartum haemorrhage, CRIB: Clinical Risk Index for Babies, IUGR: Intrauterine growth restriction PIH: Pregnancy induced hypertension, PROM: Prolonged rupture of membranes

Table 2: Association of gastric residual characteristics on infants with and without NEC

	Cases (NEC) N=40	Controls (No NEC) N=40	p-value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted p-value
Maximum residual volume	5.9 (2.6-10.9)	3.7 (2.3-5.1)	<0.001	1.47 (1.09-1.99)	1.36 (1.06-1.75)	0.017
Day of maximum residual	12 (8-22)	13 (8-18)	0.182	1.08 (0.97-1.21)	1.06 (0.94-1.19)	0.367
FV at maximum residual#	2.5 (0-50)	9 (1-88)	0.326	0.84 (0.67-1.06)	1.03 (0.77-1.35)	0.861
Maximum residual as % of FV# (n=22 pairs on feeds)	36 (13-108)	15 (6-77)	0.277	1.20 (0.85-1.71)	0.99 (0.63-1.53)	0.949
24hr GRV as % of FV# (n=16 pairs on feeds)	13 (2-31)	2 (0.3-19)	0.382	1.55 (0.93-2.58)	1.46 (0.85-2.50)	0.170
Commenced on enteral feeds	30 (75%)	35 (88%)	0.180	0.29 (0.06-1.38)	0.23 (0.04-1.27)	0.091
Days until enteral feeds started##	8 (5-10)	6 (4-8)	0.025	0.59 (0.38-0.91)	0.63 (0.39-1.00)	0.050

Abbrev: FV: Feeding volume, GRV: Gastric residual volume.

Data represent median, interquartile range and range or Number (%), and unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI), unless otherwise stated.

variable transformed to the base-2 logarithm in regression analysis, ## summaries represent median (25th-75th percentile) Kaplan-Meier survival estimates, and hazard ratios and 95% confidence intervals from Cox proportional hazards regression model adjusted for completed antenatal steroids and sex of infant.

P-value represents the univariate comparison between cases and controls and the adjusted p-value represents the effect of the gastric residual variable on NEC in a conditional logistic regression model adjusted for completed antenatal steroids and sex of infant.

Table 3: Gastric residual characteristics 72, 48 and 24 hours before the diagnosis of NEC

	Cases (NEC) N=40	Controls (No NEC) N=40	p-value
Haemorrhagic residual@	38 (95%)	36 (90%)	0.500
Day of haemorrhagic residual (n=36 pairs)*	4 (2-8)	3 (2-5)	0.061
72 hours prior:			
GR volume*	0.6 (0.2-1.7)	1.2 (0.4-2.5)	0.077
FV*	0.3 (0-84)	12 (1-90)	0.570
% GR volume (n=19 pairs on feeds)*	2.5 (0.7-5.9)	3 (0.5-74)	0.151
Blood@	7 (17.5%)	14 (35.0%)	0.118
Colour@	15 (37.5%)	15 (37.5%)	1.000
<i>Colour type</i>			
Lime	7	6	NT
Wasabi	7	8	
Avocado	1	0	
Spinach	0	1	
48 hours prior:			
GR volume*	0.9 (0.3-2.0)	0.9 (0.3-2.1)	0.326
FV*	1 (0-89.4)	22 (0.3-95)	0.304
% GR volume (n=19 pairs on feeds)*	1.5 (0.5-1)	3.3 (0.4-10)	0.509
Blood@	10 (25.0%)	6 (15.0%)	0.388
Colour@	19 (47.5%)	10 (25.0%)	0.049
<i>Colour type</i>			
Lime	9	3	NT
Wasabi	10	6	
Avocado	0	0	
Spinach	0	1	
24 hours prior:			
GR volume*	1.8 (0.3-6.1)	1.1 (0.3-3.0)	0.159

FV*	0 (0-56.0)	21.9 (1.3-99.6)	0.002
% GR volume (n=16 pairs on feeds)*	13 (2-31)	2 (0.3-19)	0.382
Blood@	18 (45.0%)	11 (27.5%)	0.092
Colour@	26 (65.0%)	11 (27.5%)	0.001
<i>Colour type</i>			
Lime	9	5	NT
Wasabi	15	5	
Avocado	2	0	
Spinach	0	1	

Abbrev: FV: Feeding volume, GR: Gastric residual, NT: Not statistically tested

*median and IQR, @number and percentage

Figures

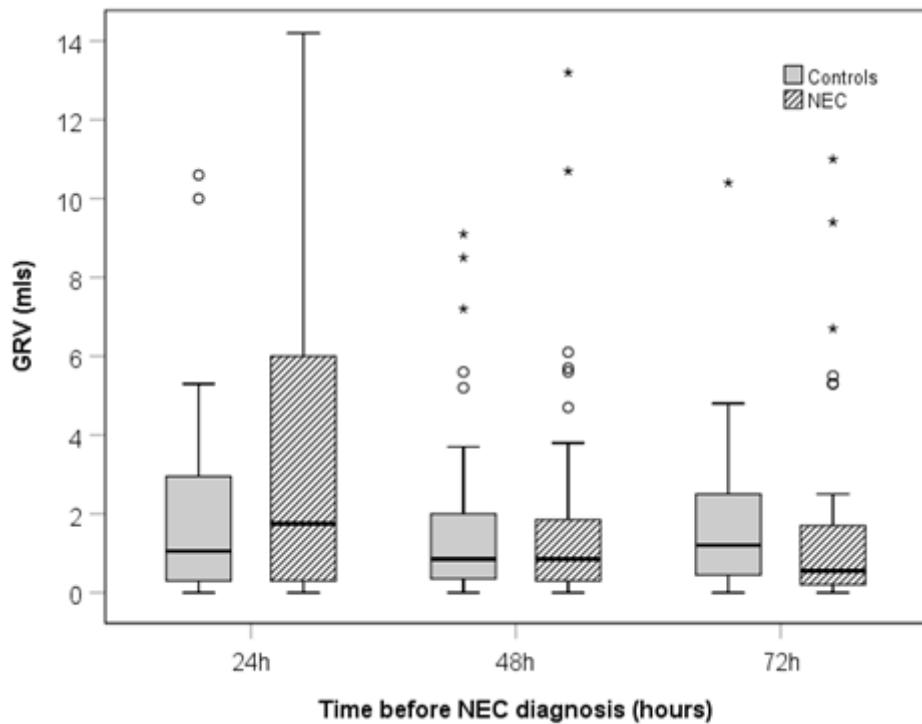


Figure 1

Boxplots showing gastric residual volumes 24, 48 and 72 hours before NEC diagnosis GRV: Gastric residual volume, NEC : Necrotising enterocolitis