

Gastroschisis in a developing country: poor resuscitation is a more significant predictor of mortality than postnatal transfer time

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Background: The time from birth to the first paediatric surgical consultation of neonates with gastroschisis is a predictor of mortality in developing countries. This is contrary to findings in the developed world. We set out to document this relationship within our population.

Methods: Neonates with gastroschisis who were transferred to Steve Biko Academic Hospital within the study period were included. The association between mortality and demographic, clinical and biochemical variables was assessed. Significant variables after univariate analysis were subjected to multivariate regression.

Results: Sixty patients were included. The mortality rate was 65%. Mean transfer time and distance were 14.9 hours and 225km. Forty-eight per cent of the neonates were either clinically dehydrated or in hypovolaemic shock on arrival. It was shown through univariate analysis that female sex, appropriate weight for gestational age, hydration status, gestation, transfer time, serum urea, base deficit and serum bicarbonate (HCO₃) were significant predictors of mortality. Only female sex, appropriate weight for gestational age and serum HCO₃ were shown to be significant using multivariate analysis.

Conclusion: Our high mortality rate was not due to lengthy transfer times. The poor clinical condition of the patients on arrival at our hospital, which relates to deficiencies in the neonatal transfer system, had a direct impact on the survival of neonates with gastroschisis.

S Afr J Surg 2016;54(1)

Gastroschisis is the most common congenital anterior abdominal wall defect treated in our hospital. Currently the incidence is 2 to 4.9 per 10 000 live births and increasing throughout the world,^{1,2} with a similar increase reflected in South Africa.³

Mortality of babies born with gastroschisis in developed countries is less than 10%,⁴ whereas mortality in developing countries is between 35 – 80%.^{3,5-8}

One factor which has been shown to result in increased mortality in developing nations is the delay in transfer of these neonates from peripheral hospitals to specialized institutions.^{6,7} However multiple studies in first world countries have shown that the absence of prenatal diagnosis and consequent postnatal transfer does not influence morbidity and mortality.⁹⁻¹² Routine antenatal ultrasound examination is uncommon in the South African public health system and not part of the antenatal workup of uncomplicated pregnancies in all provinces. As a result, the norm is postnatal transfer of neonates diagnosed with gastroschisis at birth to institutions

where specialized paediatric surgical care is available.

Mortality of gastroschisis at our institution was previously shown to be at least 38.7%.³

It was not known whether the mortality of neonates born with gastroschisis within our population catchment area could, similarly to other developing countries, be explained by a delay in transfer or not.

This study of neonates born with gastroschisis within our population catchment area set out to document the relation between the time from their birth to admission in our paediatric surgical unit, their clinical condition on arrival and their mortality.

Method

Setting

Steve Biko Academic Hospital is a public tertiary referral hospital in Tshwane (Pretoria) South Africa, attached to the

University of Pretoria medical campus. The department of paediatric surgery is 1 of 2 paediatric surgical referral centres for the City of Tshwane, and the only referral centre for the adjacent Mpumalanga province. The paediatric surgical department serves a population of approximately 7 million people,¹³ with an average of approximately 124 000 births per year.¹⁴ Six intensive care unit (ICU) beds and five neonatal ward beds, are available for the treatment of all neonatal surgical admissions.

Study Design

This study was conducted prospectively from February 2011 until September 2013.

All neonates born with gastroschisis and transferred to Steve Biko Academic Hospital during this period were eligible for inclusion in the study. Neonates born with gastroschisis at Steve Biko hospital (inborn) were not eligible for inclusion. The study was undertaken with the approval of the University of Pretoria's MMed and Ethics committees and was therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from the parents of all babies included in the study.

Data Collection

Data was collected by the admitting doctor in the paediatric surgical department at the initial admission. Data on demographics, birth history, transfer time and transfer distance were collected. Clinically relevant dates and times of birth and admission were recorded. The clinical condition of the child on arrival, as well as the method of bowel coverage by the referring doctor was also recorded. If any birth information was not available, the transferring hospital was contacted to supply missing information from their birth registers. On admission blood was also taken for analysis of the patient's metabolic status in the form of an arterial blood gas, serum urea (sUrea) and serum creatinine (sCreat). Upon outcome, dates of discharge or mortality were recorded. Data was collected according to definitions in Table 1.

Outcomes

The primary outcome studied was survival to hospital discharge or in hospital mortality.

Statistical Analysis

To determine risk factors for mortality the modelling approach was to consider the associations between mortality and the individual demographic, clinical and biochemical variables. Univariate analysis was done using Fisher's exact test for

Table 1: Definitions with respect to the collection of the study data

Transfer time	Time from the birth to admission at our unit (hours)
Distance of transfer	Distance (kilometres) from the referring hospital to Steve Biko Academic Hospital using the shortest available driving route
Gestation	Obtained from the antenatal card or mother if there was certainty about the dates, or the Ballard score if there was uncertainty
Hydration status	Each neonate was grouped into one of three groups (Table 2), based on the clinical parameters of skin turgor, capillary refill time, the presence of a sunken fontanelle, mucous membrane moisture, pulse rate and blood pressure
Respiratory distress	Regarded as positive in the presence of at least one of the following: <ul style="list-style-type: none"> • Tachypnoea ≥ 60 breaths per minute • Subcostal or intercostals recessions • Nasal flaring
Place of birth	At a referring hospital or clinic (healthcare facility) or at home
ICU admission	The patient was admitted to the ICU if a bed was available, or to the neonatal cubicle of the paediatric surgical ward if not
Weight for gestational age ¹⁵	Small for gestational age less than 10th centile weight for gestation Appropriate for gestational age from 10–90th centile
Birthweight category	<ul style="list-style-type: none"> • Normal birthweight of ≥ 2.5 kg • Low birthweight from 1.5–2.49 kg • Very low birthweight from 1.0–1.49 kg • Extremely low birthweight < 1.0 kg
Sepsis	Regarded as positive at any point during the admission if the patient had clinical features of sepsis, with a positive blood culture result
ICU: intensive care unit	

Table 2: Univariate analysis of the categorical variables as potential predictors of mortality

Categorical variables	<i>n</i>	Mortality rate (%)	<i>p</i> -value
Sex			
Male	24	50.0	0.058
Female	36	75.0	
Weight category			
Normal birthweight	21	71.4	0.471
Low birthweight	37	59.5	
Very low birthweight	2	100.0	
Weight for gestational age			
Appropriate for gestational age	31	80.7	0.014
Small for gestational age	29	48.3	
Place of birth			
Healthcare facility	51	87.2	0.706
At home	9	12.8	
Respiratory distress*			
Present	16	29.0	0.766
Absent	43	71.1	
Clinical hydration status			
Well hydrated	31	51.6	0.074
Dehydrated	20	75.0	
Shock	9	88.9	
Type of dressing applied to viscera			
Modified intravenous bag	36	63.9	0.543
Other form of plastic	14	71.4	
Gauze	9	66.7	
None	1	0.0	
Admission ward on arrival			
Intensive care unit	19	63.16	1.000
Paediatric surgical ward	41	65.85	
Sepsis during admission			
Present	33	57.58	0.277
Absent	27	74.07	

*: Data were not collected for one patient. Therefore, the respiratory status of only 59 patients was analysed

categorical data and Welch's t-test for continuous data. Those factors that were significant at a liberal *p* value of 0.15 were included in a multivariate regression model. A stepwise model was then used to determine the significant factors retained in the final model (*p*<0.05).

Results

Sixty two patients with gastroschisis were admitted from referring hospitals during the study period. Two patients were excluded from the study. One patient was excluded because

the admission data was not recorded adequately and 1 patient was excluded as the patient received specialist paediatric surgical care prior to transfer to our department. During the study period four inborn patients were ineligible for the study. Sixty patients were subjected to statistical analysis.

The mortality rate for the cohort was 65%. Univariate analysis of the categorical variables is shown in Table 2, and of the continuous variables in Table 3.

A male to female ratio of 2:3 was evident. Mean birth weight was 2.4kg and gestation was 36 weeks. Most neonates were born below 2.5kg (65%), while there were similar numbers of

Table 3: Univariate analysis of the continuous variables as potential predictors of mortality

Continuous variables	Range	Mean (95% CI) for the survivor and mortality groups		<i>p</i> -value
		Survive to discharge	Mortality	
Birthweight (kg)	1.00–3.45	2.20 (2.05–2.36)	2.26 (2.08–2.45)	0.611
Gestation (weeks)	32–42	36.70 (35.76–37.67)	35.80 (35.24–36.44)	0.120
Maternal age (years)	15–42	22.00 (19.36–24.64)	20.80 (19.69–21.96)	0.401
Apgar score (1 minute)	4–9	7.53 (6.92–8.13)	7.94 (7.41–8.46)	0.290
Apgar score (5 minutes)	6–10	9.29 (8.72–9.86)	9.38 (8.99–9.78)	0.791
Transfer time (hours)	3.30–104.00	11.20 (6.80–15.49)	17.00 (10.70–23.21)	0.123
Transfer distance (km)	19–439	197.62 (135.50–259.20)	239.20 (193.40–285.00)	0.270
Temperature (°C)	≤ 35.00–39.50*	36.40 (36.10–37.00)	37.30 (35.90–38.80)	0.196
Serum urea (mmol/l)	2.10–14.60	5.33 (4.01–6.66)	7.25 (5.17–9.43)	0.131
Serum creatinine (mmol/l)	39–236	85.45 (64.65–106.25)	90.91 (75.07–106.76)	0.668
pH	6.81–7.60	7.36 (7.32–7.40)	7.32 (7.27–7.63)	0.178
PCO ₂ (mmHg)	10.20–128.00	33.99 (21.66–46.32)	26.74 (24.08–29.40)	0.241
Base deficit (mmol/l)	2.00–29.20	8.71 (7.22–10.20)	10.64 (8.90–12.38)	0.088
Serum HCO ₃ (mmol/l)	8.70–21.50	16.67 (15.46–17.85)	14.61 (13.49–15.73)	0.013

Apgar: appearance, pulse, grimace, activity and respiration, CI: confidence interval, PCO₂: partial pressure of carbon dioxide in arterial blood, HCO₃: bicarbonate

*: The minimum recordable temperature was indicated as ≤ 35 °C on the digital thermometer used on all patients

small for gestational age and appropriate for gestational age neonates. The mean maternal age was 21 years. The minority of births occurred outside a healthcare facility (17%).

Mean transfer time was 14.9 hours (Median 9hrs, Range 3.3–106.4hrs.) and transfer distance was 225km (19–439km).

The hydration status of 48% of neonates was assessed as either dehydrated or in hypovolemic shock. Only 1 patient arrived without any coverage of the viscera, while 68% of neonates had their exposed viscera covered with a modified intravenous fluid bag. Eight patients arrived with a temperature of less than 36°C, five of whom had a temperature of less than or equal to 35°C. The majority of neonates were admitted to the paediatric surgical ward (68%) and not ICU. Two patients had complete midgut necrosis on admission, were not actively managed further and were transferred back to the referring hospitals for palliative care after counselling the parents. Both were included in the mortality group.

The mean blood gas analysed serum bicarbonate (sHCO₃) for those that survived was 16.67mmol/l while the mean sHCO₃ on admission of neonates who died was 14.61mmol/l, pH was 7.32 and pCO₂ was 26.74mmHg.

Univariate analysis revealed that variables associated with mortality at a liberal *p* value of 0.15 included: female sex, appropriate weight for gestational age, hydration status of dehydrated or in hypovolemic shock, gestation, transfer time, sUrea, arterial base deficit and arterial serum bicarbonate (sHCO₃).

Table 4: Logistic regression analysis of factors associated with mortality

Factors	Odds ratio	95% CI	<i>p</i> -value
Female sex	5.80	1.31–25.66	0.020
Appropriate weight for gestational age	6.86	1.60–29.34	0.009
Serum HCO ₃	1.37	1.08–1.74	0.009

CI: confidence interval, HCO₃: bicarbonate

Logistic regression analysis (Table 4) found only female sex, appropriate weight for gestational age and sHCO₃ on admission to be significantly associated with mortality (*p*<0.05). The odds of mortality in a female neonate with gastroschisis were 5.8 times that of a male neonate (*p*=0.02). Neonates with gastroschisis and appropriate weight for gestational age had a 6.8 fold greater odds of mortality during their admission than those who were small for gestational age (*p*=0.009). A decrease of 1 mmol/l in sHCO₃ measured on admission, resulted in a 1.37 fold increase in odds of mortality (*p*=0.009).

Discussion

The mortality rate for this study of 65% was far greater than our previously reported mortality of 38.7% for neonates with gastroschisis.³ The previous study's inclusion of inborn patients from both Steve Biko and Kalafong hospitals, as well as a 16 month deficiency in their data collection would have influenced this comparison. This is however unlikely to explain the large difference in mortalities between studies. Of note in our current study was that gastroschisis was the underlying cause of death in 33% of all mortalities in our unit over the study period.

The previous study identified 48 cases of gastroschisis over a 20 year period (1981-2001),³ whereas our 60 patients were admitted over a 32 month period. This is in keeping with the rise in the incidence of gastroschisis worldwide,² as well as reflecting the likely increase in the population within our drainage area. Our cohort is far greater than the 19 neonates with gastroschisis reported over a 4 year period in Cape Town,¹ and similar to the cohort of approximately 17 patients per year reported in Durban.¹⁷ Further epidemiological studies are required to accurately assess the incidence of this disease across the South African paediatric surgical centres.

A mean maternal age of 21 years is in keeping with reported data of a higher incidence of gastroschisis amongst babies of young mothers.¹⁸

Lower gestational age did not result in greater odds of mortality in our study despite the mean gestation being preterm, 36 weeks. Spontaneous preterm labour is more common in pregnancies complicated by foetal gastroschisis,¹⁹ and our results are in keeping with these findings.

The finding that small for gestational age neonates in our cohort had a lower odds of mortality than their appropriate for gestational age counterparts is counter intuitive. It is accepted that small for gestational age neonates have a greater mortality when compared to those with appropriate weight, especially in the preterm neonate.²⁰ With a mean gestation of 36 weeks for our cohort, it is difficult to explain the significant difference in mortality (48.3% vs. 80.7%), between the small- and appropriate for gestational age groups, that remains consistent after multivariate analysis. Controlling for prematurity also does not change the findings as equal numbers of small- and appropriate for gestational age births were preterm.

It is our policy to admit all neonates with gastroschisis to the ICU facility if a bed is available. As only 32% of the cohort was admitted initially to ICU, it is evident that we, as with most developing countries, have significant difficulty in caring for these patients in an appropriate ICU setting due to lack of available facilities.

The type of material used to cover the viscera by the transferring medical practitioner was not shown to influence mortality. Two patients who had their exposed viscera directly covered with gauze arrived with acute haemorrhage from their livers due to erosion by the dried out gauze, neither survived. We therefore advocate the use of a soft plastic covering of the viscera, in keeping with published guidelines.^{9,21} Female sex resulted in significantly greater odds of mortality in our

cohort. This contradicts previous results that indicated a higher risk of mortality in males.²²

Our chief aim was to evaluate if transfer time was a significant predictor of mortality amongst neonates born with gastroschisis in our drainage population. We showed, that contrary to previous studies in developing countries,^{6,7} transfer time itself does not seem to be a predictor of mortality. We, however, need to factor in the role a prolonged transfer time plays in the on-going dehydration of these neonates and its influence on their SHCO_3 , which was shown to be a significantly associated with mortality. The metabolic findings on admission indicated a state of compensated metabolic acidosis in those neonates who eventually died, likely resulting from fluid and heat losses that these neonates experience if not appropriately managed. None of the clinical variables withstood logistic regression as significant. Mills et al showed that clinical variables in the form of the score for neonatal acute physiology-II (SNAP-II) to be a significant predictor of mortality and survival outcomes in gastroschisis.²³ Review of our data and inclusion of a SNAP-II on admission would have allowed us to compare our cohort with this study directly. Using the SNAP-II would have allowed us to gain a structured overall clinical impression for comparison, rather than using individual clinical factors. Unfortunately the data required for completing the SNAP-II was not completely recorded to allow its utilization in retrospect.

Despite advice to referring doctors it is not uncommon for patients to arrive from the transferring hospital without a functional intravenous line, a finding similar to Hadley and Mars.²⁴ While we can only speculate as to whether these were functioning prior to transfer or not, the management of the neonates prior to, and during transfer is brought into question by their poor clinical state on arrival. Poor neonatal transfer systems in South Africa have been shown to contribute to poorer outcomes.^{24,25} Transfer times and poor clinical state of the patients on arrival at our hospital is further testament to the deficiencies in neonatal transfer within our healthcare system.

It must be noted that some patients were not able to be transferred timeously due to the lack of available beds in our hospital. These patients were diverted to other paediatric surgical centres or were transferred to the nearest hospital with the highest available level of care while awaiting a bed in our unit. Reasons for the lengthy transfer time and poor condition of the child on arrival were not included in this study, opportunity therefore exists for further research to accurately identify these causes and aid in addressing the high mortality of gastroschisis in our unit, and elsewhere in South Africa.¹⁷ Likely areas of concern include: delay in initial consultation from the peripheral hospital, delay in ambulance transport to collect the patient, inadequate initial resuscitation prior to transport, failure of the referring doctor to adhere to telephonically communicated management as well as equipment and medication shortages at the peripheral hospitals and during ambulance transport.

We did not include the influence of varying methods of definitive surgical treatment of gastroschisis on the outcomes.

Due to the long transfer times and poor clinical condition of our cohort on arrival, the majority of patients were initially stabilised with application of a preformed silo bag, with delayed closure of the abdomen. Some patients however were closed primarily. This decision was made by the treating surgeon based on the appearance of the bowel, the clinical condition of the patient and the availability of a postoperative ICU bed. The relationship of treatment method and outcome at our institution therefore remains to be studied, but the cohort would have to be far larger to show any significant difference in outcomes as very few patients are closed primarily. As the state of the bowel and condition of the patient at initial presentation determine the method of surgical treatment employed, findings of the relationship between treatment used and outcomes would not be independent of the clinical condition of the patient on arrival in our unit.

In conclusion, while we have shown that our high mortality rate does not seem to be directly due to lengthy transfer times, the poor clinical condition of the patients on arrival at our hospital, likely related to the deficiencies in our neonatal referral and transfer system, has a direct impact on the survival of neonates with gastroschisis. If these patients are adequately resuscitated prior to, and during transfer, we may see a decline in the high mortality rate of gastroschisis within our population.

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