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ORIGINAL ARTICLE

Descriptive Epidemiology of Anorectal Malformations in Chinese Population

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ABSTRACT

Over a twelve year period one hundred and five neonates (30 females) with an anorectal malformation (ARM) were studied at a tertiary referral centre in Hong Kong. A perineal fistula was the most frequent presentation of ARM in males closely followed by rectourethral fistula. Vestibular fistula was the most common anomaly amongst females. An ARM without a fistula was documented in 11 % of patients and dominated by males. Associations and syndromes were present in nearly 30 % of the group with VACTERL association and Down syndrome at the forefront. Isolated anomalies were most frequently seen in the renal tract (23 %), the CNS (20 %) and the heart (18 %). A quarter of the cohort was small for gestational age with syndromes/associations featuring in half of this subgroup. A death rate of 9.5 % was recorded, of which all except one had an underlying syndrome or association. In addition a pre-existing heart condition constituted the most significant factor affecting the mortality in 50 % of this group.

Key words: Anorectal malformation; Perineal fistula; Rectourethral fistula; VACTERL association; Down Syndrome; Krickenbeck classification

INTRODUCTION

ARM manifests itself as an embryological anomaly of the hindgut between the 4th and 8th week of gestation. The pathogenesis is largely unknown, but it is thought the earliest defect leading to the development of an ARM is a deficiency in the dorsal component of the cloacal membrane; the severity of the ARM is related to the extent of this deficit [1]. This study sets out to analyse the various clinical presentations and its associations / syndromes in a Chinese population.

MATERIALS AND METHODS

All neonates with an ARM admitted to this tertiary referral centre between 1. Jan 2002 and 31. Dec 2013 were included into the group. The local clinical research ethical committee approved the study (Ref. No.: CRE-2013.148).

The charts and computer records of all patients with ARM were reviewed analyzing demographics, the details of the ARM, and co-morbidities ranging from syndromes to single organ system anomalies. Furthermore causes for mortality and long-term survival were scrutinized.

The ARMs were categorized according to the Krickenbeck classification with the necessary separation between male and female gender [2,3].

All babies underwent surveillance imaging studies: chest and abdominal radiographs, two-dimensional echocardiography, abdominal and renal sonography. A routine ultrasound of the lumbosacral spine was

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supplemented by an magneto resonance imaging (MRI) scan, if required.

Suspected chromosomal anomalies were confirmed by chromosomal analysis. A VACTERL association, first described in 1965, was considered, if at least three of the possible seven criteria were identified [4-6].

Isolated anomalies were categorised by organ system, e. g., the gastrointestinal tract. Anomalies affecting one organ system were registered once for the individual patient even if an infant had two or more anomalies within the same organ system, e.g., an atrial septum defect (ASD) alongside a ventricular defect (VSD).

The often quoted genitourinary system was divided into renal tract and genital area. Placing genital anomalies together with renal tract aberrations would have distorted the analysis, as genital pathologies (e.g., hypospadias or undescended testis) are mainly seen in boys.

The statistical analysis was conducted with a Fisher's exact test for differences in categorical data. SPSS software (SPSS.22) was utilised. The P-value (P) was set at .05 for significance.

RESULTS

One hundred and five neonates (30 females) were admitted with an ARM. The females were born at a median gestation of 38 (range 31- 42) weeks with a median weight of 2.56 (range 1.12 - 3.69) kg. Eleven female neonates were small for gestational age (SGA) (Figure 1) . The males were born at the same median gestation of 38 (range 30 - 42) weeks with a median weight of 2.84 (range 1.2 - 4) kg; in two boys the weight was not recorded. Fifteen male babies were small for gestational age (Figure 1). In total, 26 (24.8 %) were SGA.

The ARM in both male and female subjects were subclassified in Table 1. Twelve infants presented with an imperforated anus without a fistula. Two had an ARM which could not be verified in detail before their death.

Syndromes and associations accounted for 30 cases (28.6 %) within the cohort. Sixteen (15 %) had a VACTERL association, chromosomal anomalies were seen in 10 (9.5 %), two cases (1.9 %) were part of a genetic syndrome, one presented with the Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome (Müllerian agenesis) and one patient had multiple anomalies not (yet) linked to a specific syndromic complex.

The differences between the gender are illustrated in Table 2. Although it appears the smaller female subgroup is more often affected by associations and syndromes; the difference is not statistically significant (P = .054).

Table 1: Krickenbeck Classification of ARM

	Male (n=75)	Female (n=30)	Total (n=105)
Perineal fistula	32	6	**38 (36%)**
Vestibular fistula	**na**	**17**	17
Rectourethral fistula of which *prostatic f. 10* *bulbar f. 12* *ns 3*	25	na	25
Cloaca	na	3	3
Imperforated anus without a fistula	10	2	**12 (11%)**
Rectovesical fistula	6	0	6
Rectovaginal fistula	na	2	2
ARM (ns)	2		2

(f: fistula, na: not applicable, ns: not specified)

Table 2: Associations, chromosomal and genetic anomalies (30/28.6 %,)

Anomaly	Male	Female
Associations		
VACTERL Ass.	9	7
Chromosomal S		
Down S	5	2
Edwards S	1	0
Turner variant	0	1
Cri-du-chat S	1	0
Genetic S		
Kabuki S	0	1
Treacher Collins S	0	1
Others		
Müllerian agenesis	0	1
Multiple cong. A	1	0
Total	**17**	**13**
P = 0.054(ns)		

A: anomalies, Ass: association, cong: congenital, ns: not significant, S: syndrome

Regarding isolated anomalies in organ systems the renal tract system is most often affected [N=24 (23 %)], closely followed by central nervous system (CNS) and vertebra column anomalies [N= 21 (20 %)]. In this subgroup girls were more often affected (P= .032). A tethered cord was seen in only 3 (2.9 %) patients (Table 3).

Cardiac anomalies were noted in 19 infants (18 %) with another preponderance for females in this system (P=.003).

Table 3: Structural anomalies in the renal tract, the CNS and the cardiovascular system

Renal tract anomalies (24/23%)	Male	Female
Vesicoureteric reflux	11	5
Single kidney • Solitary • Dysplastic • MCDK	6 3 2 1	5 2 2 1
Horseshoe kidney	2	0
Vesicoureteric junction obstruction	1	1
Total	20	11
Affected neonates	16	8
p = 0.61(ns)		
CNS and vertebral column anomalies (21/20%)		
Hemivertebra	3	4
Scoliosis	2	2
Absent sacrum	1	0
Extra lumber vertebra	0	1
Teethered cord	1	2
Filum terminale fibrolipoma	1	1
Filum terminale cyst	0	2
Spina bifida occulta	2	0
Syrinx	0	1
Developmental delay	0	1
Microcephaly	1	0
Arnold-Chiari Malformation	1	0
Arachnoid cyst posterior cranial fossa	0	1
Total	12	15
Affected neonates	11	10
p = 0.032		
CVS anomalies (19/18%)		
VSD	1	3
ASD	3	2
Pulmonary stenosis	1	2
PPHN	1	1
Dextrocardia	1	0
PDA	0	1
AVSD	0	1
Teratology of Fallot	1	1
Persistent LSVC	0	1
Total	8	12
Affected neonates	8	11
p = 0.003		

ns= non-significant

Further anomalies in the gastrointestinal, genital, musculoskeletal and craniofacial systems affect 3.8 to 16 % of the cohort with no gender preference (Table 4). Esophageal atresia / tracheo-esophageal fistula (EA/TEF) and duodenal atresia are the most common gastrointestinal conditions associated with ARM.

Overall 10 (9.5 %) patients (5 females) died; five were neonates with SGA. Although the female group was overall smaller, the difference did not reach statistical significance (P = .116). Associated anomalies were seen in 9 of the deaths: four VACTERL associations, one Down syndrome, one Edwards syndrome, one Treacher Collins syndrome, one Turner variant, and one with multiple, non-syndromic anomalies (Table 5).

Table 4: Structural anomalies in the gastrointestinal, genital, musculoskeletal and craniofacial area

GIT anomalies	Male	Female
Esophageal atresia/ trachea-esophageal fistula	4	4
Duodenal atresia	1	3
Malrotation	1	0
Small bowel atresia	1	0
Ileal duplication cyst	1	0
Meckels diverticulum	1	0
Exomphalos major	1	0
Total	10	7
Affected neonates	10	7
p =0.245(ns)		
Genital anomalies		
Hypospadias	10	0
Undescended testis	4	0
Congenital adrenal hyperplasia	0	1
Bifid scrotum	1	0
Micropenis	1	0
Total	16	1
Affected neonates	11	1
p = 0.172 ns		
Musculoskeletal anomalies		
Absent radius	2	0
Polydactyly	4	0
Rib fusion	0	1
Extra pair of ribs	0	1
Total	6	2
Affected neonates	6	2
p=1(ns)		
Craniofacial anomalies		
Cleft palate	1	1
Hearing impairment	0	2
Total	1	3
Affected neonates	1	3
p =0.069(ns)		

ns= non-significant

In four cases death was precipitated by a pre-existing heart condition and cardiac failure was a significant factor in the death of a fifth patient.

Three death could be attributed to an (associated) surgical condition: one had a rectal perforation of his ARM prior to stoma formation leading to sepsis, one died of the sepsis following perforation of an associated malrotation volvulus and the third had an aspiration pneumonia in conjunction with a tracheomalacia post EA/TEF repair.

Only two individuals died of factors unrelated to their underlying anomalies: one had total parenteral nutrition (TPN) related liver failure and one suffered with pneumonia.

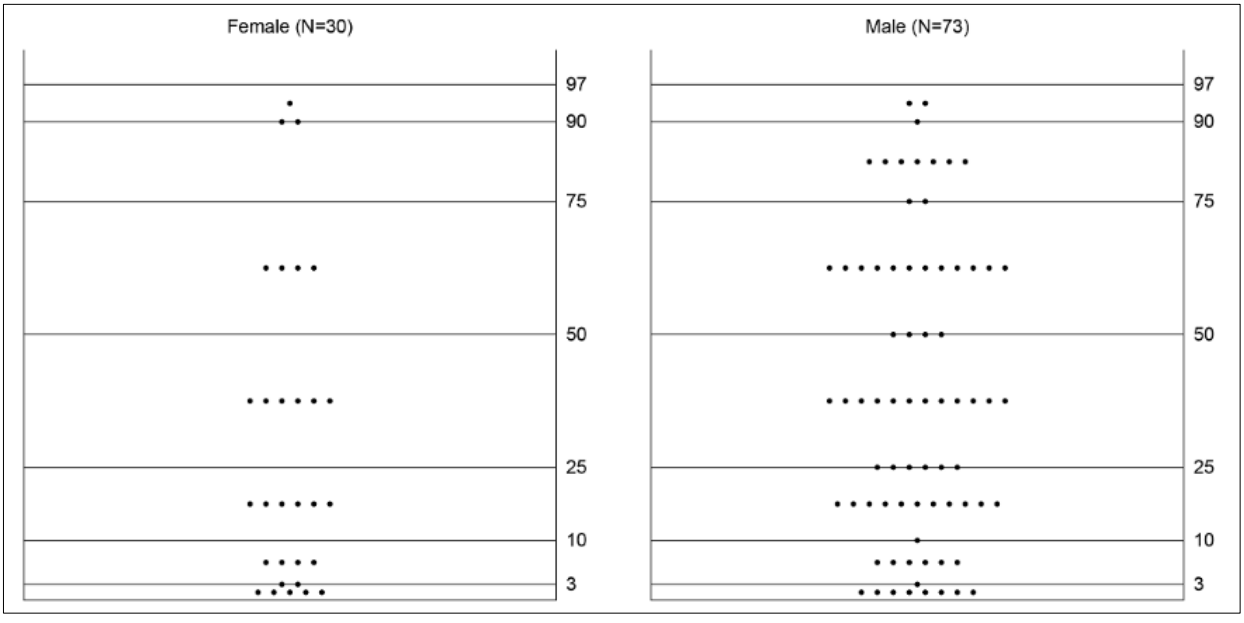

Figure 1: Percentile weight distribution of infants with ARM; all babies with weight less than 10th percentile considered SGA. (Note that no infants had intrauterine growth retardation).

Table 5: Mortality Analysis (n=10)

No	Anorectal malformation	Sex	Cause of death	Age at death	Underlying condition	Association/ Syndrome
1	ns	M	Sepsis MSOF	2 d	Rectal perforation	VACTERL
2	Vestibular fistula	F	Cardiac arrest	3 d	PPHN	---
3	ns	M	Cardiac arrest	5 d	PPHN	Edward Syndrome
4	Perineal fistula	M	Aspiration pneumonia	2m	hypertrophic cardiomyopathy	VACTERL
5	Imperforated anus without fistula	F	Cardiac arrest	2m	Teratology of Fallot	VACTERL
6	Perineal fistula	F	Sepsis MSOF	3m	Perforation 2nd degree malrotation volvulus	Turner variant
7	Rectourethral fistula	M	Liver failure	4m	TPN related cholestasis	VACTERL
8	Vestibular fistula	F	Aspiration pneumonia	10.5m	Tracheostomy, Tracheomalacia	Treacher-Collins Syndrome
9	Rectourethral fistula (bulbar)	M	ARDS, Pneumonia	16 m	ns	Multiple, non-syndromic anomalies (microcephaly etc.)
10	Rectovaginal fistula	F	Sepsis, DIC, MSOF	18 m	PPHN, gastroenteritis	Down Syndrome

ns: not specified, DIC: disseminated intravascular coagulation, MSOF: multi system organ failure, PPHN: persistent pulmonary hypertension of the newborn, TPN: total parenteral nutrition

DISCUSSION

The first attempt to classify ARMs dates back to 1835 when Amussat described several groups of ARMs [7]. This study is based on a consensus classification system agreed upon at the Krickenberg conference [2]. It was developed because of dissatisfaction with previous classification systems; the relatively arbitrary definitions of 'high', 'intermediate' and 'low' ARMs were difficult to translate into clinical practice [8].

The Krickenberg classification reflects the anatomical findings of ARMs, as they were identified through the experience with the posterior sagittal anorectoplasty and the radiological studies of the relationship between the renal tract, the genital area and the hindgut structures (e.g. fistula) [3].

The classification identifies major clinical groups of ARM whilst making allowances for rare conditions and regional variants [2].

In this study perineal fistula is overall the most common ARM affecting more than a third of the group. Separating the cohort along gender lines the perianal fistula continues to be the most frequent ARM in boys followed by rectourethral fistula, but in girls the most dominant ARM is a rectovestibular fistula (Table 1). These results are confirmed by the findings of Nah et al. [9] , but partially contradicted by Levitt's and Chen's assertion that rectourethral fistula dominates the ARM in boys [10,11].

ARM without a fistula is considered a relatively uncommon condition. Large scale studies from the US and Japan identified imperforated anus without a fistula ranging from just 4 % to 5 % respectively [12,13]. However in our cohort this condition was twice more common [N=12 (11.4 %)] with only 2 affected females. One-third had Down syndrome. Nah et al. reported a similar rate of 13 % patients with ARM without a fistula in a Singaporean population, albeit they did not specify the frequency of Down syndrome within this subgroup [9]. Likewise Cho et al. identified an ARM without a fistula at a rate of 15.5 % within their cohort of predominantly Caucasian infants [14].

Moore asserts in his monograph on the epidemiology of ARM a near equal ratio between male and female ARMs; we were unable to confirm this finding [15]. We found a clear male preponderance resulting in a male to female ratio of 2.5 : 1. Our observation was confirmed by other authors with male to female ratios ranging from 1.46 : 1 to 2.4 : 1 [9,13,14,16].

The gestational age was a median of 38 weeks for both boys and girls being similar to other studies [17].We noted a quarter of the neonates were SGA. Just over half of these small-for-date babies had a syndrome or VACTERL association; this finding was confirmed in the series by Stoll et al. [16].

Syndromes and associations accounted for 28.6 % (30 infants) in this cohort. Chromosomal anomalies alone were seen in 10 (9.5 %); this is in line with other series [9,14,18]. Down syndrome is the most common chromosomal anomaly associated with ARM present in 6.7 % of the cohort and similar to the 2 to 9 % observed by other authors [11,18].

VACTERL association was the most frequent association seen in 16 infants (15 %); other investigators noted VACTERL association in 5 - 15 % of their respective cohorts [9,14,18].

The three most frequently affected organ systems were the renal system (23 %) followed by the CNS (20 %) and the heart (18 %).

Within the subgroup of CNS and vertebra anomalies a tethered cord was seen in only 3 patients (2.8 %). Nah et al. reported 20 infants (20 %) with tethered cord in their cohort [9]. We have no explanation for this discrepancy in particular as all our patients underwent spinal ultrasound screening followed by an MRI scan, if required. Notably, Stoll et al. identified just one tethered cord in their series of 174 ARMs, and other authors reported no tethered cord at all [11,16].

Cardiac anomalies [N=19 (18%)] were only considered, if clinically relevant, e.g., a spontaneously closing patent ductus arteriosus (PDA) was not included. Godse et al. reported a similar rate of cardiac anomalies [17]. We noted a predilection for girls with cardiac anomalies (p = .003); a finding not reported previously.

The mortality in our cohort is overall 9.5 % (10 individuals); the seemingly higher proportion of deaths in the smaller female group (5/30,16.7 %) is not statistically significant (P = .116). Half of all mortality cases were small for gestational age (SGA) babies.

Other series report similar or higher mortality rates: Godse et al. had a 12.6 % mortality in a Caucasian cohort and an Indian series reported a 16 % death rate [17,19].

Looking at the underlying causes it is noteworthy all deaths except one were seen in babies with a syndrome or an association (Table 5). Five infants (50%)

died of their respective heart condition, of which four within the first 3 months.

REFERENCES

1. H Hutson JM, van der Putte SCJ, Penington E, Kluth D, Fiegel H. The embryology of anorectal malformations. (Chap 4) In: Holschneider AM, Hutson JM (eds) Anorectal malformations in children. Berlin Heidelberg New York, Springer, 2006, pp 49-63.

2. Holschneider AM, Hutson JM, Peña A, Bekhit E, Chatterjee S, Coran A, et al. Preliminary report on the international conference for the development of standards for the treatment of anorectal malformation. J Ped Surg 2005; 40: 1521-6.

3. Peña A, Levitt MA: Anorectal malformations: experience with posterior sagittal approach. (Chap 31) In: Stringer M, Oldham K, Mouriquand P (eds) Pediatric Surgery and Urology: Long-term Outcomes. Cambridge, Cambridge University Press, 2nd edn, 2006, pp 401-15.

4. Czeizel A, Ludányi I. An aetiological study of the VACTERL-association. Eur J Pediatr 1985; 144: 331-7.

5. Wheeler PG, Weaver DD. Adults with VATER association: long-term prognosis. Am J Hum Genet A 2005; 138A: 212-7.

6. Kirkpatrick JA, Wagner ML, Pilling GP. A complex of anomalies associated with tracheo-esophageal fistula and esophageal atresia. Am J Roentgenol 1965; 95: 208 -12.

7. Amussat JZ. Histoire d'une opération d'anus artificial practiqué avec succèss par un nouveau procédé. Gaz Med Paris 1835; 3:753-8.

8. Murphy F, Puri P, Hutson JM, Holschneider AM. Incidence and frequency of different types, and classification of anorectal malformations. (Chap 8) In: Holschneider AM, Hutson JM (eds) Anorectal malformations in children. Berlin Heidelberg New York, Springer, 2006, pp 163-84.

9. Nah SA, Ong CCP, Lakshmi NK, Yap T-L, Jacobsen AS, Low Y. Anomalies associated with anorectal malformations according to the Krickenbeck anatomical classification. J Ped Surg 2012; 47: 2273-8.

10. Levitt MA, Peña A : Anorectal malformations. (Chap 53) In: Ziegler MM, Azizkhan RG, von Allmen D, Weber TR (eds) Operative Pediatric Surgery. New York, McGraw-Hill Education Medical, 2nd edn, 2014, pp 669-93.

11. Chen C-J. The treatment of imperforate anus: experience with 108 patients. J Ped Surg 1999; 34: 1728-32.

12. Bischoff A, Frischer J, Dickie BH, Peña A. Anorectal malformation without fistula: a defect with unique characteristics. Ped Surg Int 2014; 30: 763-6.

13. Endo M, Hayashi A, Ishihara M, Maie M, Nagasaki A, Nishi T, et al. Analysis of 1992 patients with anorectal malformations over the past two decades in Japan. Steering committee of Japanese study group of anorectal anomalies. J Ped Surg 1999; 34: 435-41.

14. Cho S, Moore SP, Fangman T. One hundred three consecutive patients with anorectal malformations and their associated anomalies. Arch Pediatr Adolesc Med 2001; 155: 587-91.

15. Moore SWM. Genetics, pathogenesis and epidemiology of anorectal malformations and caudal regression syndrome. (Chap 3) In: Holschneider AM, Hutson JM (eds) Anorectal malformations in children. Berlin Heidelberg New York, Springer, 2006, pp 163-84.

16. Stoll C, Alembik Y, Dott B, Roth MP. Associated malformations in patients with anorectal anomalies. Eur J Med Genet 2007; 50: 281-90.

17. Godse AS, Best KE, Lawson A, Rosby L, Rankin J. Register based study of anorectal anomalies over 26 years: Associated anomalies, prevalence, and trends. Birth Def Res (Part A) 2015; 103:597-602.

18. Cuschieri A and EUROCAT Working Group. Anorectal anomalies with or as part of other anomalies. Am J Med Genet 2002; 110: 122-30.

19. Kumar A, Agarwala S, Srinivas M, Bajpai M, Bhatnagar V, Gupta DK, et al. Anorectal malformations and their impact on survival. Indian J Pediatr 2005; 72: 1039-42..