Incidence and spectrum of anorectal malformations in Western Saudi Arabia

Hamdi H. Almaramhy, *FRCS, SBPS.*

ABSTRACT

الأهداف: معرفه معدل حدوث مثل هذه التشوهات ونمط حدوثها وأنواعها في المدينة المنورة، المملكة العربية السعودية، ومعرفة إذا ما كان هذا المعدل مختلف عن بقية أنحاء العالم.

الطريقة: أجريت دراسة رجعية حيث تم جمع ودراسة الملفات الطبية لجميع حالات تشوهات الشرج والمستقيم والتى شخصت فى مستشفى الولادة والاطفال بالمدينة المنورة خلال الفترة من يناير1998م إلى ديسمبر 2010م. تم البحث في قاعدة البيانات للمرضى لتحديد المرضى الذين يعانون من تاريخ عائلي إيجابي لمثل هذه الحالات. واستخدم اختبار كاي لقياس الإختلافات المهمة إحصائيا لدى المعدل السنوي لحدوث مثل هذه التشوهات وتم تعين فترة الثقة 95%.

النتائج: تم الكشف عن 188 حالة حالات تشوهات الشرج والمستقيم من مجموع 189145 ولادة حية بمعدل حدوث 1 لكل 1000 ولادة حية تقريبا و نسبة 1.9:1. ذكر إلى أنثى وأظهرت الدراسة استقرارفي المعدل السنوي. وكان أكثر تشوهات الشرج والمستقيم حدوثا الناسور العجان (32.9%). ووجد أن الفرق فى حدوث هذا النوع بين الجنسين ذا دلالة إحصائية مهمة. أما في الأولاد فكان الأكثر حدوثا هو ناسور مستقيمي إحليلي (47.2%) بينما في الفتيات كان الناسور الدهليزي (46.2%) هو الأكثر، وحصلت تشوهات الشرج والمستقيم بصورة منفرده في 106 (56.3%) من الحالات وحصلت بصورة متكررة في 3عوائل ومجموع 9 حالات (4.7%)، وحصلت مرتبطه مع تشوهات اخرى فى أعضاء الجسم في 73 حالة (38.8%). وكان أكثر التشوهات المصاحبة لتشوهات الشرج والمستقيم هي تشوهات الجهازالبولي (34%)، والقلب (19.2%).

خاتمه: معدل حدوث تشوهات الشرج والمستقيم في المدينة المنورة، المملكة العربية السعودية، أكبر من المعدلات التي ذكرت في كندا وأوروبا والصين وهذا قد يحفز الباحثين للنظر في سبب هذا الاختلاف الكبير فى معدل الحدوث حسب التوزيع الجغرافي. حدوث تشوهات الشرج والمستقيم منفرده هو أكثر شيوعا من حصول تشوهات الشرج والمستقيم المصاحبة بتشوهات أخرى في أعضاء أخرى من الجسم.

Objectives: To present the incidence and spectrum of anorectal malformations (ARMs) and associated anomalies, and to compare the findings with published literature.

Methods: This is a retrospective study conducted during the period January 2011 to December 2011. We reviewed the medical charts of all cases with ARMs admitted to Al-Madinah Maternity and Children Hospital, Madinah, Kingdom of Saudi Arabia during 1998-2010. The incidence and spectrum of ARMs, associated regional anomalies, and those with a positive family history of ARMs were identified. The 95% confidence interval and Chi square trend test were used to quantify the significance of variation in annual incidence.

Results: One hundred and eighty-eight cases of ARMs were detected from 189,145 live births with an incidence of approximately 1/1000 live births with a male-to-female ratio of 1.9:1. The incidence showed yearly stability (p=0.3509). The most common ARMs was perineal fistula (32.9%). There was a statistically significant gender difference (p=0.000). The most common in boys was rectourethral fistula (47.2%) and in girls was vestibular fistula (46.2%). Isolated non-familial ARMs was found in 106 (56.3%), isolated familial 9 (4.7%), and associated ARMs in 73 (38.8%) cases. In terms of associated anomalies, genitourinary (34%), and cardiovascular (19.2%) systems reported a high incidence.

Conclusion: The incidence of ARMs in Madinah Kingdom of Saudi Arabia, is higher than the reported data. Isolated ARMs was more common than the associated category, and the familial one was rarely reported.

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From the Department of Surgery, College of Medicine, Taibah University, Madinah, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Hamdi H. Almaramhy, Department of Surgery, College of Medicine, Taibah University, PO Box 30001, Madinah 41477, Kingdom of Saudi Arabia. Tel. +966 555609298. Fax. +966 (4) 8461407. E-mail: maramhy@hotmail.com

Anorectal malformations (ARMs) are common cause of neonatal intestinal obstruction, which is usually diagnosed by the absence, or ectopic location of the anus. The average reported incidence of the anorectal malformations varies between 1/1500 to 1/5000 live birth.[1-6] However, geographical variations occur in the overall occurrence. Patients with these malformations often have other associated congenital anomalies. The frequency and types of such associated anomalies vary among different reported studies, ranging between 20% and 70%.[5,7-10] Furthermore, there are differences in the published studies regarding which system is most often affected. Previous studies have noted that 16% of the patients with ARMs had facial anomalies,[5] whereas in other study,[7] 34% of patients with ARMs had facial anomalies. The aim of this retrospective study is to find out whether the incidence and spectrum of ARMs and the associated anomalies in Al-Madinah Al-Munawwarah, Saudi Arabia differ from the published literature worldwide.

Methods. This is a retrospective study conducted during the period January 2011 to December 2011. Review of the medical charts was carried out to identify consecutive cases of ARMs cases that were admitted at Al-Madinah Maternity and Children Hospital between 1998 and 2010. This is the only hospital, which provides pediatric surgery services in Madinah region, serving 2 million populations. A capture sheet was constructed to collect data regarding the number of ARMs cases and number of live births each year, patient's characteristics, type of malformation, associated anomalies, and radiological investigations that were carried out. Patient's database with ARMs was searched to identify other family members who had ARMs. In addition, parents were contacted by phone to inquire if they had other children or relatives with ARMs (phone interview). The numbers of live birth newborns were taken from the local hospital registry. The study was approved by Research and Ethics committee at the hospital.

The type of ARMs was determined on the basis of clinical findings and the result of imaging including the lateral cross-table x-ray and the distal colostography in children with a created colostomy according to Krickenbeck classification.[11] In all cases, echocardiogram, abdominal ultrasound, and spine x-ray was carried out, while micturating cystourethogram and MRI spine was carried out by some consultants as a routine, and in only high anomalies by others. The cases then categorized into isolated non-familial ARMs, isolated familial, and associated ARMs (patients with ARMs having other associated anomalies). It was difficult to differentiate between syndromatic and non-syndromatic in the last category.

Statistical analysis was carried out by SPSS software version 19.0 (SPSS Inc, Chicago, Ill). Chi square test was used to compare the frequency of anorectal anomalies among boys and girls where appropriate. Chi-square for trend and confidence intervals were used to detect if there is statistically significant variation in the annual incidence over the span of 13 years. A $p<0.05$ was considered statistically significant.

Results. Over a 13 year-period (1998-2010), 188 cases of ARMs cases were identified from a total of 189,145 live births with an incidence of 1/1000 live births (95% confidence interval 0.86-1.14 per 1000). The average weight was 2.785 Kg and 28 of them were pre-term. One hundred twenty-three were boys and 65 were girls with a boy to girl ratio of 1.9:1. The yearly incidence of ARMs per 1000 live births showed no significant variation (Chi-square 13.25, degrees of freedom 12, and $p=0.3509$) (**Figure 1 & Table 1**).

The type of ARMs with the spectrum of presentations are shown in **Table 2**. The most frequent ARMs defect in the whole group was perineal fistula (n=62 patients). There was statistically significant difference among the male and female patients with these anomalies ($p=0.000$) and the least one was rectovesical fistula, which occur only in boys; found in 2 patient (1.2%). Rectourethral fistula was the most common anomaly in boys whereas vestibular fistula was the most common in girls (**Table 2**). Ectopic anus (anteriorly displaced anus) and imperforate anus without fistula (the no fistula variety in Krickenbeck classification) were more common in girls ($p=0.001$) than boys ($p=0.006$). The clinical pattern of ARMs in this study was the following: isolated non-familial 106 cases (56.4%), isolated familial in 9 cases (4.8%), and associated ARMs in 73 (38.8%).

The associated anomalies and lesions with ARMs are shown in **Table 3**. Among all body systems, the most common affected system was genitourinary, followed by the cardiovascular group of anomalies. A fairly constant association was noted with gastrointestinal anomalies. Other anomalies included those of the vertebral and spinal cord defects, musculoskeletal system, cleft lip and palate, congenital diaphragmatic hernia, and albinism.

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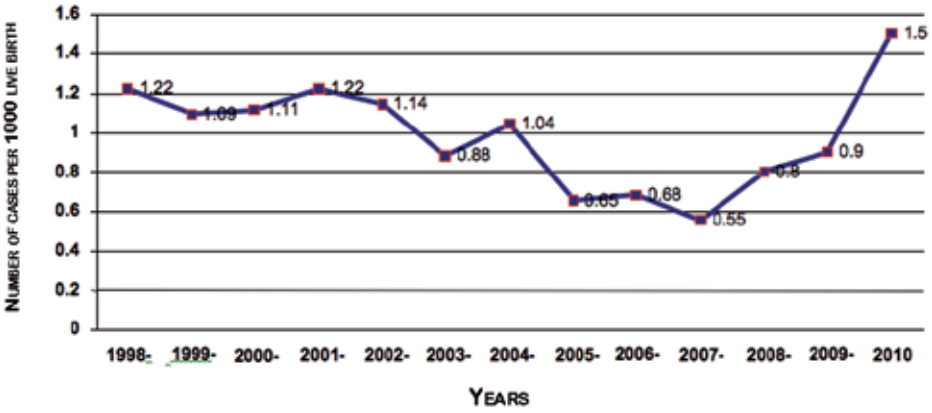

Figure 1 - Incidence trend of anorectal malformations over a 13-year span (p=0.509).

Table 1 - Shows the annual incidence over the 13-year span and the confidence intervals.

Year	No. of live births	Anorectal malformations cases/year	Annual incidence per 1000	95% Confidence intervals
2010	13360	21	1.5	1.0 - 2.36
2009	14294	13	0.9	0.51 - 1.52
2008	14681	12	0.8	0.44 - 1.39
2007	14312	8	0.55	0.26 - 1.06
2006	14656	10	0.68	0.35 - 1.21
2005	13761	9	0.65	0.32 - 1.20
2004	13401	14	1.04	0.59 - 1.71
2003	13633	12	0.88	0.48 - 1.49
2002	14019	16	1.14	0.67 - 1.82
2001	15556	19	1.22	0.76 - 1.87
2000	16200	18	1.11	0.68 - 1.73
1999	15640	17	1.09	0.66 - 1.71
1998	15632	19	1.22	0.75 - 1.86
Total	189145	188	0.98	0.86 - 1.14

Table 2 - Distribution of various types of anorectal malformations by gender (based on Krickenbeck classification with slight modification).

Type of anomaly	Male n=123		Female n=65		Total n-188		*P*-value*
	n	(%)	n	(%)	n	(%)	
Perineal fistula	53	(43.1)	9	(13.8)	**62**	**(30.0)**	0.000*
Ectopic anus	3	(2.4)	10	(15.4)	**13**	**(6.9)**	0.001*
No fistula (Imperforated anus without fistula)	5	(4.1)	10	(15.4)	**15**	**(8.0)**	0.006*
Rectal atresia	2	(1.6)	1	(1.5)	**3**	**(1.6)**	0.964
Cloaca	0	(0.0)	5	(7.7)	5	(2.7)	NA†
Rectovesical fistula	2	(1.6)	0	(0.0)	**2**	**(1.1)**	NA†
Vestibular fistula	0	(0.0)	30	(46.2)	**30**	**(16.0)**	NA†
Rectorethral fistula	58	(47.2)	0	(0.0)	**58**	**(30.9)**	NA†

*p-value is significant at <0.05 level. NA - not available. †Comparison was not possible as there were no corresponding male and female cases

A family history of ARMs was found in 9 cases (4.8%), where ARMs was the only abnormality in the affected family member without any other associated anomalies. The analysis of the families regarding the number of children, types of anomaly other relative affection, and relation between the father and mother are shown in **Table 4**.

Discussion. Geographical difference in the incidence of ARMs has been found in the reported studies. In a study from Alberta, Canada, the documented incidence was 1/2162 (4/10,000 total birth).[12] In Europe, the incidence ranges between 1.14 in 10,000 to 5.96 in 10,000.[13] In China, the incidence is 0.4/1000 live births.[14] In this study, the incidence was greater compared with the existing literature, approximately 1/1000 (9.9 in 10,000). However, there is no previous published study from other pediatric centers in Saudi Arabia on the incidence to compare with. It may vary from one area to another, and this need further studies from other part of the country, as environmental factors have been claimed to have a role in the incidence variation.[15,16] The incidence over the period of the study showed stability approximately 1/1000. This stability in the rate per year was also found in other study, although there was an insignificant fluctuation in the yearly rate.[11,15] This study is in keeping with the findings of other workers that low ARMs is more common than high ARMs, and boys are affected more than girls.[3-5] The study demonstrated low ARMs in 103 children while high variety in 85, with a male to female ratio of 1.9;1. This gender ratio is slightly higher than the reported range of 1.2:1 to 1.8:1,[3-5] but less than the ratio of 2:1 reported by Cho et al.[7] Ectopic anus (anteriorly placed anus) was detected

only in 13 cases. This represent only cases proved by examination under anesthesia and underwent surgical correction, which is not reflecting the true incidence. This is because the diagnosis is usually subjective during clinical examination and need good attention to the position of the anus, followed by, examination under anesthesia using Penna stimulator. Nevertheless, some reports claimed that the API measurement is a prize tool to diagnose anterior anus.[17,18] The presence of concomitant anomalies with ARMs is not rare. The frequency of such occurrence ranges between 20-70%.[7-10] In this series, associated anomalies were found in 38.8%, which sets in the reported range. The genitourinary tract was the most affected system with anomalies (34%), which is not different from what have been reported.[1,19,20] The cardiovascular anomalies are being the second in these associations. They observed in 19.5% of patients, which is less than that observed by Stoll et al[10] and Cho et al.[7] However, it is in the range reported by others.[5,9] The most common cardiac anomaly in this series was patent ductus arteriosus, followed by atrial septal defect, and ventricular septal defect. The involvement of gastrointestinal tract (GIT) is less common. In 188 cases, only 12 cases (6.4%) with GIT anomalies were demonstrated. The trache-esophageal fistula was the most frequent GIT anomalies detected, as found in other study.[7] The variability in the reported frequencies of the associated anomalies may be related to population characters, the meticulousness in searching for associated anomalies, and the absence of agreed protocol among pediatric surgeons for investigating ARMs cases, as well as the difference in the method of calculating the percentage of the anomalies. Some authors calculate the percentage of anomalies from the total number of ARMs cases,[5,7] while others calculate it from the cases of associated and non-syndromatic ARMs.[8,10] Recent studies on animals and human point out the genetic component of ARMs.[21-25] Moreover, the presence of multiple affected members in the same family[26-31] and the reports of familial, isolated, and non-syndromatic ARMs cases,[32,33] raise the probability of a responsible gene for ARMs. Yet, in human being, it has not been identified. Nevertheless, different modes of inheritance have been suggested including x-linked, autosomal dominant, and autosomal recessive.[28-31] Kubiak et al[33] studied the relation between twins/siblings and ARMs and reported 19 families with 2 or more siblings with isolated ARMs, but only 5 families had ARMs in monozygotic twins. In

Table 3 - Associated anomalies with anorectal malformation affecting different body systems (some patients have more than one anomaly).

Associated anomaly	Number of anomalies	Percentage of total patients (n=188)	Percentage of total Anomalies (n=131)
Cardiovascular system (n=36)		19.2	27.5
Ventricular septal defect	6	3.2	16.7
Atrial septal defect	6	3.2	16.7
Patent ductus arterioris	18	9.6	50.0
Bicuspid aortic valve	1	0.5	2.8
Pulmonary stenosis	3	1.6	8.3
Single ventricle	2	1.1	5.6
Genitourinary (n=64)		34.0	48.9
Vesicoureeteric reflux	18	9.6	28.1
Hydronephrosis	10	5.3	15.6
Absent kidney	12	6.4	18.8
Undesended testis	8	4.3	12.5
Hypospadias	14	7.5	21.9
Penoscrotal transposition	2	1.1	3.1
Gastrointestinal tract (n=12)		6.4	9.16
Tracheoesophageal fistula	8	4.3	66.7
Duodenal atresia	3	1.6	25.0
Ilial atresia	1	0.5	8.3
Others (n=19)		9.6	14.5
Vertebral & spinal cord	7	3.7	36.8
Musculoskeletal	4	2.1	21.1
Cleft lip and palate	5	2.7	26.3
Congenital diaphragmatic hernia	2	1.1	10.5
Albinism	1	0.5	5.3

Table 4 - Cases of isolated familial anorectal malformations among subjects included in a study at Al-Madinah Maternity and Children Hospital, Madinah, Kingdom of Saudi Arabia.

Family number	No. of children in the family	No. of children affected	Type of anomaly	Other relative with anorectal malformations	Relation between mother and father
1	6	5	First was boy with perineal fistula Second was girl with ectopic anus Third was boy with perineal fistula Fourth was girl with vestibular fistula Fifth was boy with perineal fistula	No	Cousin
2	4	2	Girl with vestibular fistula* Girl with ectopic anus*	No	Cousin
3	2	2	Girl with vestibular fistula Girl with vestibular fistula	Maternal aunt	No relation between parents

*The girls were twins

this study, 3 families had isolated familial ARMs; and only one had ARMs in monozygotic twins were found. All were of low type anomaly. This is in line with the findings of Falcone et al.[34] They stated that the risk of isolated familial ARMs was higher in low types ARMs. This may raise the question why the familial isolated ARMs cases are of low type. The male to female ratio in the familial subgroup in this series was 1:2, which is slightly lower than 1:2.4, as reported by Falcone et al.

One limitation of this study is that it was difficult to classify the associated anomalies into syndromatic and non-syndromatic as there are no facilities for karyotyping in our hospital. Other limitation of this study is that the findings of this study apply only to Al Madinah population, and cannot be generalized to the whole Kingdom of Saudi Arabia (KSA) population. However, the study findings could serve as baseline for future in-depth studies in KSA in the area of anorectal malformations and help the health officials to manage and plan health services for future cases of ARMs.

In conclusion, the incidence of ARMs in Almadinah, Saudi Arabia, is greater than that reported in Canada, Europe, and China and this may stimulate researchers to look in the reason for this substantial variation in geographical distribution. In spite, there are yearly fluctuations in the incidence, this variation is statistically insignificant. Isolated ARMs in this series is more common than the associated category, and the familial one is rarely occurred.

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