Variations in the detection of anorectal anomalies at birth amongst European cities

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All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Abstract

Aim: The diagnosis of anorectal malformations (ARM) is made at birth by perineal examination of the newborn, yet small series reported late diagnosis in almost 13%. No large series to date have looked into the magnitude of missed ARM cases in the neonatal period across Europe. This study aimed to define the rate of missed ARM at birth across four UK and EU centers.

Methods: All ARM cases treated at two UK tertiary centers in the past 15 years were compared to two tertiary European centers. Demographic and relevant clinical data were collected. Late diagnosis was defined as any diagnosis made after discharge from the birth unit. Factors associated with late diagnosis were explored with descriptive statistics.

Results: Across the four centers (117/1350, 8.7%) were sent home from the birth unit without recognizing the anorectal anomaly. Missed cases showed a slight female predominance (1.3:1), and the majority (113/117, 96.5%) were of the low anomaly with a fistula to the perineum. The rate of missed ARM cases was significantly higher in the UK centers combined (74/415, 17.8%) compared to those in the EU (43/935, 4.6%), (p<0.00001), and this was independent of individual center and year of birth.

Conclusion: Significant variation exist between the UK and other European countries in the detection of ARM at birth. We recommend raising the awareness of accurate perineal examination at time of newborn physical examination. We feel this highlights an urgent need for a national initiative to assess and address the timely diagnosis of ARM in the UK.

Key words: anorectal malformations, pediatric surgery, postnatal checks, congenital anomaly
Introduction

Anorectal malformations (ARM) constitute a varied group of congenital anomalies with an estimated incidence of one in every 4000 to 5000 newborns. The diagnosis of an anorectal malformation is usually made at birth through an examination of the perineum of the newborn. However, missed diagnosis (i.e. after hospital discharge) has been reported even in adulthood, and accounting in some pediatric series for almost 13% of cases.

UK-based centres have reported that late referral of ARM cases from the birth centres (after 24h of age) accounted for up to 50% of cases, although few of the cases in either series had been discharged from hospital. Delays in diagnosis of ARM are associated with higher morbidity and mortality. It may predispose to bowel perforation when not defunctioned in a timely manner, and prolonged inadequate stooling will result in bowel dilatation, mega-rectum formation and will make further reconstruction challenging and more amenable for failure.

In the UK in 2006, the National Institute For Care and Health Excellence (NICE) introduced a clinical guideline for postnatal care for women and their babies until 8 weeks of life. The guideline recommends a complete physical examination of the newborn baby within 72 hours of birth; it clearly states that “the anus must be checked for completeness and patency”.

However, unlike other European Countries, these guidelines do not specify who is responsible for the neonatal check. Perineal examination in a neonate can be challenging, particularly in females, and anal patency is often usually assumed by presence of meconium in the nappies rather than introduction of a probe in the anus.

To provide a measure of the rate of missed anorectal malformations (ARM) in the newborn period, in this study we review all new cases of anorectal malformation born in the UK and presenting to two pediatric surgery tertiary referral centres over a period of 15 years. The data were compared to 2 tertiary centres in Europe (which have different guidelines on postnatal
checks). We aim here to describe the incidence of late presenting ARM at two large-volume UK tertiary pediatric surgery centres, and to test whether the introduction of the NICE guidelines in 2006 in the UK has improved the rate of detection of ARM in the neonate.
Methods

Four tertiary pediatric surgery centres in four major European cities participated in this study. Two UK centres; Great Ormond Street Hospital (centre A) serves the pediatric population of Central/North London and Royal Manchester Children’s Hospital (centre B) serves the pediatric population of the North West of England; between them, the two centres serve a population of over 9 million people. Each centre had previously independently audited the rate of missed ARM in their referred patient population. This study was registered as a re-audit between the two centres and appropriate approvals were obtained from the audit office in each hospital. Data from the two UK centres were compared to two tertiary referral centres in Europe; Necker Enfants Malades in Paris, France (centre C) and Bambino Gesù in Rome, Italy (centre D).

To determine the rate of missed anorectal malformation in the UK centres, all cases of infants presenting with ARM over a 15-year span between January 2002 and December 2016 (centre A) and 14-year span between January 2003 and December 2016 (centre B) were identified using medical coding and operating theatre records. We defined a missed diagnosis of ARM as a case in which a newborn baby was discharged home from the birth unit or referred to a pediatric surgery unit, having completed all neonatal checks, without identifying the anorectal malformation or being referred to a pediatric surgery unit. We excluded patients born outside the UK, those with cloacal anomalies and cases of anterior or stenotic anus (solitary or in Currarino triad) within a complete sphincter complex defined by sphincter mapping (examination under anaesthetic using Peña stimulator).

The variables collected for analysis included: patient demographics, mode of presentation, anatomical type of the ARM anomaly, timing of the first surgical intervention (as a surrogate for date of diagnosis which was not reliably recorded in this retrospective study), type of
surgical repair and presence of other VACTERL (vertebral defects, anal atresia, cardiac
defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities) anomalies.

Binary logistic regression analysis (outcome variable = missed diagnosis) was performed on
data from 2009-2016 using SPSS v24.0 and the following co-variates: gender, years from
2009, VACTERL (y/n), hospital (centre A/B) and high anomaly/low anomaly. Fisher’s exact
test was used to compare proportions. Data are presented as median and interquartile ranges
or as numbers with proportion. A p value of p<0.05 was considered significant, except for the
comparison of UK with European centres, where the Bonferroni corrected p value cut-off of
p<0.017 (0.05/3) was used.
Results

Over the study period, 415 new cases of ARM were admitted to the two UK centres of which 74 (17.8%) overall (centre A: 26/192 [13.5%]; centre B: 48/223 [21.5%]) were missed at postnatal checks and discharged home. These patients had their first surgery at a median age of 159 days (range 2 days to 2.65 years of age, IQR 19.5-234 days). The number of missed cases and total cases year by year is shown in Figure 1A. Seventeen out of 141 cases (12.1%) were missed between 2002-2006 whereas 57/274 (20.8%) were missed between 2007-2016; thus, the incidence of missing ARM at birth has significantly increased across the two centres (p=0.03) despite the introduction of the NICE guidelines in 2006 (Figure 1B).

The male: female ratio in the missed group was 2:3 (29 boys and 45 girls); 72 (97%) had an external fistula (56 [76%] perineal fistula, 16 [22%] vestibular fistula) while 2 cases had an imperforate anus with recto-urethral fistula. In addition, 22 cases (30%) had at least one additional VACTERL association anomaly.

Data for the ARM patients who were diagnosed before hospital discharge was unavailable for the study cohort prior to 2009; we describe all 213 patients with ARM between 2009-2016 in Table 1. Of note, 44% of all perineal fistula patients were missed in this period. There was a significant difference in the proportion of missed cases when comparing low anomalies (vestibular + perineal) (47/138 [34%]) with high anomalies (bladder, prostatic, urethral, vaginal + no fistula) (2/75 [3%]) (p<0.0001) (Figure 2A). Patients with a further VACTERL anomaly (14/108 [13%]) were significantly less likely to be missed than those with isolated ARM (35/105 [33.3%]) (p=0.0006) (Fig. 2B), this likely reflects the anatomy of the missed cases as VACTERL is more associated with high than low ARM anomalies as previously reported.14

In order to examine factors associated with having a missed diagnosis, we performed a binary logistic regression analysis. The only factors associated with missed diagnosis were: low
anomaly (OR 37.0 [4.8-283.2]; p=0.001) and non-VACTERL (OR 3.2 [1.5-7.0]; p=0.003).

There was no significant association between having a missed ARM and time (year of birth) (p=0.13), suggesting no improvement in detection of ARM over time from 2009-2016, noting the limited power of this analysis.

The operative management of the 2009-2016 patient cohort is displayed in Table 2. Those patients who had a missed diagnosis were more likely to be managed with a single stage surgery (primary anoplasty, trans-anal proctoplasty [TAP] and posterior sagittal anorectoplasty [PSARP]) than those whose anorectal malformation was diagnosed before discharge (38/49 vs. 93/213, p<0.0001). However, this probably reflects the anatomy of the defect rather than a different attitude towards surgical management of late diagnosed ARM cases. This is supported by the observation that in the low anomaly group (perineal and vestibular fistula), there was no difference in the proportion of single stage repair whether the diagnosis was made or missed prior to discharge from the birth centre (25/48 [52%] vs. 36/91 [40%], p=0.15).

In the two European centres, there were 935 new cases of ARM treated over the last 15 years; 43/935 (4.6%) were missed at birth (centre C: 34/696 [4.9%]; centre D: 9/239 [3.8%]). The age at presentation of those with missed diagnosis ranged between 6 days and 8.4 years and all except for two cases (41/43, 95%) were low anomalies with a fistula to the perineum; over half (23/43) of these cases were in males. During the study period the two UK centres had a significantly higher rate of missed anorectal anomalies compared to the two EU centres individually (74/415 [17.8%], 34/696 [4.9%), 9/239 [3.8%] p<0.0001) and as a whole (74/415 [17.8%], 43/935 [4.6%] p<0.00001) (Figure 3 A, B).
**Discussion:**

Delayed presentation of anorectal malformation remains significant in the NHS. Despite the introduction of a standardised postnatal care guideline by NICE in 2006\(^\text{11}\), we demonstrate here a significant increase in missed diagnosis of anorectal malformation in recent years. Two equivalent European centres are referred a much lower proportion of missed diagnosis, suggesting more effective detection within the immediate postnatal period.

Currently, all babies born in the UK will, ideally, have a systematic examination prior to discharge home or within 72 hours of birth. This newborn physical examination is commonly known as the “baby check” and is performed by trainee pediatricians or by midwives who completed an Examination of the Newborn accredited course. Historically, the effectiveness of neonatal examinations in detecting birth defects has been questioned in both the UK\(^\text{15}\) and overseas\(^\text{16}\), and specific data on cataracts has highlighted that a substantial proportion of children with congenital and infantile cataract are not diagnosed by 3 months of age\(^\text{17}\).

In this series from two UK centres, we encountered 74 cases of missed ARM, defined as diagnosis after discharge from the birth center. Clinical examination was sufficient to diagnose the anomaly in all missed cases. Delays in diagnosis resulted in surgery being performed outside the neonatal period in a significant proportion of patients, even in childhood in some cases. As one might expect, the missed cases were mostly low-type ARM where an external fistula allows passage of meconium, perhaps suggesting anal patency to the examining professional. We observed milder phenotype in those patients that were diagnosed late, evidenced by the fact that most late diagnoses were amenable to single stage surgery as opposed to requiring a colostomy while awaiting definitive repair.

In order to provide a subjective estimate of the truly missed anorectal anomalies at birth, we excluded in this study cases of anterior anus and anal stenosis which are challenging to diagnose especially in the early neonatal period. In addition, we did not observe any increase
in the total numbers of ARM cases treated at the two UK centres overtime to suggest over
treatment of milder cases of ARM anomalies.

Our study represents the largest reported series of late diagnosed ARM cases; and, including
only UK-born patients, it is indicative of the delivery of newborn care within the NHS over
the past 15 years. This longitudinal data set spans a period where routine baby checks were
initially guided by the 1989 RCPCH report “Health for All Children”, its 2003 revision
(commonly referred to as Hall 4) \(^{18}\), as well as the 2006 NICE guidelines. More recently, the
NHS Newborn and Infant Physical Examination Screening Programme (NIPE) is replacing
previous recommendations to ensure a consistence service across all health care providers in
England \(^{19}\), and how this change will affect the detection of ARM at birth is still to be seen.

One of the limitations of this study is that differences in the health care systems and referral
patterns exist between the UK and the studied EU centers. This might have partially
influenced the rate of missed cases amongst the centers making the comparison more
complex to interpret. In addition, as a retrospective review of referred patients, this study is
unable to give as much information as a full epidemiological study. The awaited report from
BAPS-CASS (British Association of Paediatric Surgeons – Clinical Anomalies Surveillance
System) describing UK nationwide incidence and spectrum of anorectal malformation cases
in a calendar year will provide more insight into the nationwide incidence of ARM and the
associated missed diagnosis rate as well as delineating those delays due to diagnosis, referral
or access.

Although we do not report any serious morbidity or mortality associated with delayed
diagnosis in our cohort, other centres report delayed diagnosis to be associated with
perforation in 10% of cases \(^{9}\), and a mortality of approximately 4% \(^{5,6,10}\). Moreover, this study
was not designed to look at the long-term morbidities such as constipation, incontinence,
urinary problems which can be associated with ARM and could potentially increase in the

Our data presented here indicate that there are 2 possible levels of problems. The first relates
to the postnatal care of infants and guidelines on baby checks; contrary to our studied
European Countries, babies are often discharged very early after birth (hours), and the
newborn examination is therefore rarely performed by a neonatologist. In fact, according to
NHS guidelines “The health professional doing the examination could be a doctor, midwife,
nurse or health visitor who has been trained to do the examination” 20. Nevertheless, the
perineal examination of a newborn is challenging, even in experienced hands, and our data
suggest that the current training pathway for the health professionals currently performing
neonatal discharge examination maybe inadequate. One interim solution to overcome this
problem is to provide photographic documentation as part of the infant newborn examination.
This could be accessed remotely by a paediatric surgeon if required and would prevent
unnecessary travel and displacement of families to see a paediatric surgeon. Secondly, in
France and Italy, as elsewhere in Europe, primary care for infants and children is performed
by a pediatrician rather than a general practitioner. Our data indicate that a third of children
with missed diagnosis of ARM may present after 6 months of age, suggesting potential
difficulties in forming a diagnosis in the constipated child within the UK primary care setting,
where broadly trained general practitioners may lack awareness of rare congenital anomalies
to detect the more subtle variants, further delaying a definitive diagnosis.
We believe action is needed to improve the rate of neonatal detection of ARM, similarly to
actions improving the quality of hip examination which have improved DDH (developmental
dysplasia of the Hip) detection in the UK 21,22. There is a need to focus on improving the
quality of training provided to health care professionals performing routine newborn
examinations to avoid the consequences of missing a major congenital anomaly.
Conclusion:

This study of two UK centres highlights a significant issue in the timely diagnosis of anorectal anomalies. Two comparable European centres have a significantly lower rate of missed diagnosis, thus there is a need to improve the newborn detection rate in the UK in order to avoid morbidity and mortality.
Figure Legends:

**Figure 1.** A: Cases year by year. B: Percentage of cases that were missed before (2002-2006) and after (2007-2016) the NICE guidelines, compared using Fisher’s Exact test.

**Figure 2.** A: Distribution of missed cases between high and low ARM. B: Distribution of missed cases in isolated ARM and VACTERL ARM.

**Figure 3.** Percentage of cases study period in the two UK centers compared to the two EU centers individually (A) or as a whole (B).

**Table 1.** 2009-2016 ARM missed cases by anatomical type of malformation

**Table 2.** 2009-2016 Operative management by type of malformation, missed cases vs. not missed. (Single Stage included patients in whom a covering stoma was formed during the definitive surgery)

**Supplementary Table 1**

Binary logistic regression analysis examining the association between missed diagnosis (dependent variable) and gender, year, VACTERL anomaly, hospital and high anomaly.
References


Figure 1.
Figure 2.

A

Low
High

\[ p < 0.0001 \]

Number of patients

Missed
Non-missed

B

Isolated ARM
VACTERL

\[ p = 0.0006 \]

Number of patients

Missed
Non-missed
Figure 3.
<table>
<thead>
<tr>
<th>Location</th>
<th>Total</th>
<th>Missed</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fistula</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bladder</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Perineal</td>
<td>94</td>
<td>41</td>
<td>43.6%</td>
</tr>
<tr>
<td>Prostatic urethra</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vaginal</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urethral</td>
<td>33</td>
<td>1</td>
<td>3.0%</td>
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<tr>
<td>Vestibular</td>
<td>44</td>
<td>7</td>
<td>15.9%</td>
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<tr>
<td><strong>Total</strong></td>
<td>213</td>
<td>49</td>
<td>23.0%</td>
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### Table 2.

<table>
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<tr>
<th>ARM Type</th>
<th>Stoma total</th>
<th>missed</th>
<th>%</th>
<th>Primary Repair total</th>
<th>missed</th>
<th>%</th>
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<tr>
<td>No fistula</td>
<td>12</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>0</td>
<td>0.0</td>
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<tr>
<td>Bladder</td>
<td>12</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
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<td>0.0</td>
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<tr>
<td>Perineal</td>
<td>32</td>
<td>8</td>
<td>25.0</td>
<td>62</td>
<td>33</td>
<td>53.2</td>
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<tr>
<td>Prostatic urethra</td>
<td>5</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
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<td>5</td>
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<td>0.0</td>
<td>4</td>
<td>0</td>
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<tr>
<td>Urethral</td>
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<td>1</td>
<td>3.1</td>
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<td>0</td>
<td>-</td>
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<tr>
<td>Vestibular</td>
<td>21</td>
<td>2</td>
<td>9.5</td>
<td>23</td>
<td>5</td>
<td>21.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>120</strong></td>
<td><strong>11</strong></td>
<td><strong>91.6</strong></td>
<td><strong>93</strong></td>
<td><strong>38</strong></td>
<td><strong>40.9</strong></td>
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## Supplementary Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exp B (95% CI)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Gender</td>
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<td>0.875</td>
</tr>
<tr>
<td>Year</td>
<td>1.1 (1.0-1.3)</td>
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<tr>
<td>VACTERL Y/N</td>
<td>3.2 (1.5-7.0)</td>
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<tr>
<td>Hospital</td>
<td>0.7 (0.3-1.6)</td>
<td>0.444</td>
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<tr>
<td>High anomaly</td>
<td>37.0 (4.8-283.2)</td>
<td>0.001</td>
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