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Original Research Article

CLINICAL CORRELATION OF ASSOCIATED ANOMALIES IN DIFFERENT VARIANTS OF ANORECTAL MALFORMATION IN CHILDREN

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ABSTRACT

Background: *The routine use of contrast-enhanced computed tomography (CECT) prior to lumbar puncture (LP) in patients with suspected meningitis may delay definitive diagnosis and timely initiation of antimicrobial therapy. Evidence supporting the incremental diagnostic value of CECT over LP in emergency settings, particularly in low- and middle-income countries, remains limited.* ***Objective:*** *To compare the diagnostic significance of contrast-enhanced CT brain and lumbar puncture in adults presenting with suspected meningitis to the emergency department of a tertiary care hospital in Pakistan.* ***Study Design:*** *Prospective observational study.* ***Settings:*** *Department of Paediatric Surgery, Holy Family Hospital, Rawalpindi, Pakistan.* ***Duration of Study:*** *January 2024 to January 2025.* ***Methods:*** *Ninety consecutive adult patients presenting with clinical features suggestive of acute meningitis were enrolled. In accordance with institutional protocol, all patients underwent a contrast-enhanced CT of the brain prior to lumbar puncture. CT findings were evaluated for parenchymal abnormalities and radiological contraindications to LP. Cerebrospinal fluid (CSF) analysis served as the reference standard for confirming and classifying meningitis etiologically. Diagnostic performance indices of CECT were calculated against CSF findings. Post-stratification analysis assessed associations between CT abnormalities, presenting clinical features, and in-hospital outcomes. Statistical analysis was performed using SPSS version 26, with $p < 0.05$ considered statistically significant.* ***Results:*** *The mean age of participants was 34.8 ± 15.6 years, with a male predominance (56.7%). CSF analysis confirmed meningitis in 84.4% of cases. The predominant etiologies were bacterial (41.1%), viral (31.1%), and tuberculous meningitis (12.2%). CECT demonstrated abnormalities in 35.6% of patients and identified radiological contraindications to LP in 8.9%. Using CSF as the reference standard, CECT showed limited sensitivity (42.1%) and moderate specificity (83.3%) for meningitis-related abnormalities. CT abnormalities were significantly associated with altered level of consciousness, seizures, and papilledema ($p < 0.05$). Patients with abnormal CT findings experienced higher rates of intensive care unit admission, mechanical ventilation, neurological sequelae, and in-hospital mortality (all $p < 0.05$). Emergency department length of stay was significantly prolonged among patients undergoing CT prior to LP.* ***Conclusion:*** *Contrast-enhanced CT of the brain demonstrates limited sensitivity for confirming meningitis but remains valuable for identifying contraindications to lumbar puncture and stratifying patients at risk of severe outcomes. Lumbar puncture with CSF analysis remains the definitive diagnostic modality. Selective, guideline-directed use of pre-LP neuroimaging may reduce diagnostic delays and improve outcomes in resource-constrained emergency care settings.*

Keywords: Meningitis, Computed Tomography, Lumbar Puncture, Emergency Department, Cerebrospinal Fluid

INTRODUCTION

Anorectal malformations (ARM) represent a spectrum of congenital defects affecting the anorectal region, with an estimated incidence of approximately 1 in 2,500–5,000 live births (1). These anomalies rarely occur in isolation; rather, they are frequently accompanied by a constellation of additional congenital defects, most notably within the framework of the VACTERL association—a non-random co-occurrence of Vertebral, Anorectal, Cardiac, Tracheo-Esophageal, Renal, and Limb anomalies (2). The diagnosis of VACTERL requires the presence of at least three of these component features, and ARM has been identified as one of the most commonly observed major VACTERL features, occurring in approximately 62% of confirmed VACTERL cases (2).

The prevalence of associated anomalies in ARM patients is substantial. Cardiovascular anomalies have been reported in up to 67.1% of patients with anal atresia, renal anomalies in 27.1%, vertebral anomalies in 9.7%, and limb anomalies in 2.6% (3). Veras et al. reported that up to 66% of ARM patients harbor at least one associated anomaly, with the rate of VACTERL-associated anomalies reaching 71% in some series (4). Importantly, higher-grade ARM lesions have consistently demonstrated a greater burden of associated anomalies than lower-grade lesions (4). Beyond the classical VACTERL components, emerging evidence has expanded the phenotypic spectrum to include genital anomalies—present in 34% of VACTERL patients—the majority of which are functionally significant and often require surgical intervention (5). Bladder dysfunction has similarly been recognized as an additional phenotypic component, particularly prevalent among patients with anorectal malformations, sacral dysplasia, and renal anomalies (6).

The etiology of ARM and VACTERL association remains incompletely understood and is considered multifactorial. Pathogenic or likely pathogenic variants have been identified in genes such as SALL1, SALL4, and MID1 in a subset of patients, underscoring the importance of a genetics-first diagnostic approach (7). Disruption of Sonic Hedgehog (Shh) and Wnt signaling pathways, as well as structural cilia defects, have been implicated in the pathogenesis of VACTERL (8). Candidate genes, including FOXF1, HSPA6, HAAO, and KYNU, have been investigated, though large-scale re-sequencing studies have not confirmed their major roles (9). Exome sequencing in patients with renal VACTERL phenotypes has further identified potentially pathogenic variants in B9D1, FREM1, and ZNF157,

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among others (10), highlighting the genetic heterogeneity of this condition.

The clinical implications of associated anomalies in ARM extend well beyond the neonatal period. Kassa and Lilja et al. demonstrated that individuals with VACTERL association carry a significantly elevated risk of neurodevelopmental disorders, including ADHD (HR 2.25), autism spectrum disorder (HR 5.15), and intellectual disability (HR 8.13), compared to matched controls (11). Furthermore, children with VACTERL association have been shown to have a 3.9-fold higher risk of developing pediatric cancer compared to unaffected children, with particularly elevated risk for embryonal tumors (12). These findings underscore the necessity of comprehensive, systematic screening for associated anomalies across all ARM variants.

Despite the well-established global burden of ARM and its associated anomalies, data from low- and middle-income countries, including Pakistan, remain limited. Pakistan faces several contextual challenges, including a high birth rate, consanguineous marriage practices that may increase the expression of recessive genetic variants (10), and limited access to multidisciplinary neonatal care. Systematic screening for VACTERL-associated anomalies—including cardiac, renal, vertebral, and increasingly recognized features such as genital anomalies (5) and bladder dysfunction (6)—is inconsistently performed in many tertiary care centers. The absence of local prevalence data limits the development of evidence-based clinical protocols and optimal resource allocation. This study, therefore, aims to characterize the patterns and clinical associations of associated anomalies across different ARM variants in Pakistani children, providing foundational epidemiological data to guide screening protocols, improve surgical planning, and inform multidisciplinary follow-up strategies in a resource-constrained setting.

METHODOLOGY

This analytical cross-sectional study was conducted at the Department of Paediatric Surgery, Holy Family Hospital, Rawalpindi, Pakistan, from January 2025 to December 2025. A total of 90 consecutive pediatric patients diagnosed with anorectal malformation were enrolled using non-probability consecutive sampling. Sample size was calculated using the WHO sample size calculator, assuming a prevalence of associated anomalies of 50%, a 95% confidence level, and a 10% margin of error.

Children aged ≤12 months with a confirmed diagnosis of anorectal malformation based on clinical examination and radiological assessment were included. Patients with previous corrective surgery elsewhere, incomplete records, or syndromic conditions already diagnosed prenatally were excluded. Written informed consent was obtained from parents or legal guardians prior to enrollment. Ethical approval was obtained from the hospital's Institutional Review Board.

All patients underwent detailed clinical evaluation, including perineal examination, to classify ARM as high, intermediate, or low according to standard international classification systems. Radiological investigations included invertogram or cross-table lateral radiographs. Screening for associated anomalies was systematically performed in all patients using echocardiography, abdominal ultrasonography, spinal radiographs, renal ultrasound, and other investigations as clinically indicated.

Data were collected using a structured pro forma that included demographic variables, ARM type, associated anomalies, operative details, duration of hospital stay, and postoperative complications. Data were entered and analyzed using SPSS version 26. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were presented as frequencies and percentages. Chi-square test was applied to determine associations between categorical variables. Independent sample t-test and ANOVA were used for comparison of means. Multivariate logistic regression analysis was performed to identify independent predictors of associated anomalies. A p-value ≤0.05 was considered statistically significant.

RESULTS

A total of 90 pediatric patients diagnosed with anorectal malformation (ARM) were included in the final analysis. The mean age at presentation was 3.8 ± 2.6 months (range: 1 day–12 months). The majority were neonates presenting within the first month of life (62.2%). There was a male predominance, with 56 (62.2%) males and 34 (37.8%) females, yielding a male-to-female ratio of 1.6:1. Most participants were from rural areas (58.9%), reflecting referral patterns to tertiary care centers in Pakistan. The demographic characteristics are summarized in Table 1.

Table 1: Baseline Demographic Characteristics of Children with Anorectal Malformation (n = 90)

Variable	Frequency (n)	(%)
Age at Presentation		
Neonates (≤28 days)	56	62.2
1–6 months	22	24.4
6–12 months	12	13.3
Gender		
Male	56	62.2
Female	34	37.8
Residence		
Rural	53	58.9
Urban	37	41.1
Birth Weight		
<2.5 kg	21	23.3
≥2.5 kg	69	76.7

High-type ARM was observed in 38 (42.2%) patients, intermediate-type in 21 (23.3%), and low-type in 31 (34.4%). High variants were more frequent among males, whereas low variants were relatively more common in females. The distribution of ARM types by gender is shown in Table 2.

Table 2: Distribution of ARM Variants According to Gender (n = 90)

ARM Variant	Male (n=56)	Female (n=34)	Total n (%)
High type	26	12	38 (42.2)
Intermediate type	13	8	21 (23.3)
Low type	17	14	31 (34.4)

Chi-square analysis showed no statistically significant association between gender and ARM variant ($\chi^2 = 1.84$, $p = 0.398$).

Associated congenital anomalies were identified in 49 (54.4%) children. Cardiovascular anomalies were the most common (28.9%), followed by genitourinary (24.4%), vertebral (20.0%), gastrointestinal (15.6%), and limb (8.9%) anomalies. The distribution is presented in Table 3.

Table 3: Spectrum of Associated Anomalies in Children with ARM (n = 90)

Associated Anomaly	Frequency (n)	(%)
Cardiovascular anomalies	26	28.9
Genitourinary anomalies	22	24.4
Vertebral anomalies	18	20.0
Gastrointestinal anomalies	14	15.6

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Limb anomalies	8	8.9
No associated anomaly	41	45.6

Among cardiac defects, the most frequent was a ventricular septal defect.

Children with high-type ARM demonstrated the highest frequency of associated anomalies (73.7%), followed by intermediate (57.1%) and low-type variants (29.0%). The association between ARM type and the presence of anomalies was statistically significant ($\chi^2 = 12.96$, $p = 0.002$). Detailed correlation is shown in Table 4.

Table 4: Correlation of ARM Variant with Presence of Associated Anomalies (n = 90)

ARM Variant	With Anomalies n (%)	Without Anomalies n (%)	p-value
High type (n=38)	28 (73.7)	10 (26.3)	
Intermediate (n=21)	12 (57.1)	9 (42.9)	
Low type (n=31)	9 (29.0)	22 (71.0)	
Total	49 (54.4)	41 (45.6)	0.002

Multivariate logistic regression analysis demonstrated that high-type ARM independently predicted the presence of associated anomalies (Adjusted OR: 3.84; 95% CI: 1.52–9.71; $p = 0.004$).

The mean hospital stay was significantly longer in children with associated anomalies (11.6 ± 4.2 days) than in those without (7.3 ± 3.1 days), $p < 0.001$. Postoperative complications occurred in 18.9% of patients, with higher rates observed among high-type ARM ($p = 0.021$). Details are summarized in Table 5.

Table 5: Clinical Outcomes According to ARM Variant (n = 90)

Outcome	High Type	Intermediate	Low Type	p-value
Mean Hospital Stay (days)	12.8 ± 4.1	10.2 ± 3.7	7.1 ± 2.8	0.001
Postoperative Complications n (%)	11 (28.9)	4 (19.0)	2 (6.5)	0.021

DISCUSSION

The present study evaluated the pattern and clinical correlation of associated congenital anomalies across different variants of anorectal malformation (ARM) in 90 pediatric patients at a Pakistani tertiary care center. Associated anomalies were identified in 54.4% of patients, with cardiovascular anomalies being the most prevalent (28.9%), followed by genitourinary (24.4%), vertebral (20.0%), gastrointestinal (15.6%), and limb anomalies (8.9%). These findings are broadly consistent with, yet contextually distinct from, the existing international literature, and warrant careful comparative analysis.

The overall prevalence of associated anomalies in our cohort (54.4%) aligns closely with figures reported in the global literature. Veras et al. demonstrated that up to 68% of ARM patients had at least one screening test for VACTERL-associated anomalies, with a substantial proportion harboring confirmed defects (4). Similarly, Ahn and Choi et al. reported cardiovascular anomalies in 67.1% and renal anomalies in 27.1% of patients with anal atresia, figures somewhat higher than those observed in our cohort (28.9% and 24.4%, respectively) (3). This discrepancy may reflect differences in screening completeness, referral patterns, and diagnostic resource availability in a resource-constrained Pakistani setting, where systematic echocardiographic and renal ultrasonographic screening is not uniformly performed. Pijpers et al. similarly reported that associated anomalies were present in approximately 47% of neonates with congenital duodenal obstruction, with cardiac anomalies occurring in 31%, underscoring the broader principle that congenital gastrointestinal anomalies frequently co-occur with cardiovascular defects and that preoperative echocardiography should be considered standard of care (16). In our series, ventricular septal defect was the most frequently identified cardiac lesion, a finding consistent with the broader VACTERL literature (2).

A central and clinically significant finding of this study is the statistically significant gradient of associated anomaly burden across ARM variants: high-type ARM was associated with anomalies in 73.7% of cases, intermediate-type in 57.1%, and low-type in only 29.0% ($\chi^2 = 12.96$, $p = 0.002$). Multivariate logistic regression confirmed that high-type ARM independently predicted the presence of associated anomalies (Adjusted OR: 3.84; 95% CI: 1.52–9.71; $p = 0.004$). This finding is corroborated by Veras et al., who similarly reported that higher-type ARM lesions carry a greater burden of associated anomalies (4). Minneci et al. further demonstrated that ARM subtype was the only independent predictor of fecal continence outcomes, reinforcing the clinical primacy of ARM variant classification in prognostication (17). The male predominance observed in our cohort (62.2%) and the higher frequency of high-type ARM in males are consistent with the findings of Ahn and Choi et al., who reported a significantly higher proportion of male patients in the VACTERL-positive subgroup (58.3% vs. 37.0%, $p = 0.033$) (3).

Genitourinary anomalies constituted the second most common associated defect in our cohort (24.4%). Wu et al. reported that 45.7% of ARM patients had concomitant genitourinary tract anomalies, with male gender being the only independent predictor of urinary tract infection prior to anorectoplasty (OR = 7.306, $p = 0.001$) (18). The relatively lower genitourinary anomaly rate in our series may reflect incomplete urological workup in a resource-limited environment. Vertebral anomalies were identified in 20.0% of our patients, a figure higher than the 9.7% reported by Ahn and Choi et al. (3) but lower than rates approaching 40% reported in series with multiple atresias (16). Lim et al. reported that among patients undergoing surgery for fibrofatty filum terminale, 11.6% had VACTERL association, with anorectal anomaly being the most common associated malformation (n = 37), further emphasizing the importance of spinal screening in ARM patients (19).

Children with associated anomalies in our cohort had significantly longer hospital stays (11.6 ± 4.2 vs. 7.3 ± 3.1 days, $p < 0.001$), and postoperative complications were more frequent in high-type ARM (28.9%, $p = 0.021$). Riley et al., utilizing the Kids' Inpatient Database, demonstrated that cardiac defects (IRR 1.47), vertebral anomalies (IRR 1.10), and anorectal malformation itself (IRR 1.12) were all independently associated with increased length of stay in VACTERL neonates, with a median hospital stay of 14 days (20). Zeng et al. reported that the presence of an associated malformation was an independent predictor of mortality in congenital gastrointestinal malformations (OR = 13.299; 95% CI: 1.370–129.137), underscoring the prognostic weight of co-existing anomalies (21). Tagesse et al. similarly reported a mean hospital stay of 10 days and an overall neonatal surgical mortality of 26.8% in an Ethiopian tertiary center, with sepsis as the leading cause of death, highlighting the shared challenges of neonatal surgical care in low-resource settings (22).

Saeed et al., in a Pakistani tertiary care hospital study, reported an ARM prevalence of 6.5% among pediatric ward admissions, with female gender, neonatal age, and delayed presentation identified as predictors of higher mortality (23). The predominance of rural patients in our cohort (58.9%) mirrors the referral dynamics described by Saeed et al.. It reflects the systemic barriers to early diagnosis and timely surgical intervention that characterize healthcare delivery in Pakistan (23). Jerry et al. reported that one-fifth of neonates with gastrointestinal malformations had associated anomalies, and that modifiable factors such as in-utero referral of antenatally diagnosed

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anomalies required urgent attention (24). This recommendation remains highly relevant in the Pakistani context, where antenatal screening infrastructure remains underdeveloped.

Collectively, the findings of this study confirm that associated congenital anomalies are prevalent across all ARM variants in Pakistani children, with a significantly higher burden in high-type lesions. The results are broadly concordant with international literature while highlighting unique epidemiological and healthcare delivery challenges in Pakistan. Systematic, protocol-driven screening for cardiovascular, genitourinary, vertebral, and other associated anomalies is imperative across all ARM variants, and multidisciplinary care pathways should be strengthened in tertiary centers serving resource-limited populations.

CONCLUSION

More than half of children with anorectal malformations in this tertiary care cohort had associated congenital anomalies, with a clear gradient of increasing burden from low- to high-type variants. High-type anorectal malformation emerged as an independent predictor of coexisting anomalies and was associated with prolonged hospitalization and higher postoperative complication rates. These findings support the implementation of standardized, multisystem screening protocols for all children with anorectal malformations in Pakistan, with prioritization of high-risk variants to improve early detection, surgical planning, and clinical outcomes.

DECLARATIONS

Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned. (IRBEC-HFHISB-0343C/24)

Consent for publication

Approved

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

NIDA ZARQOON (Resident)
Conceived the study, collected data, performed initial analysis and prepared the first draft of the manuscript
MUDASSIR FIAZ GONDAL (Associate Professor)
Supervised the research, provided expert guidance, critically reviewed the manuscript and approved the final version
ZUNAIRA AZAM (Resident)
Assisted in data collection, literature review and manuscript editing
HIBA FAROOQ (Resident)
Contributed to data organization, interpretation of findings and preparation of tables
ISHAA NASEER (Forensic Scientist)
Provided technical input, assisted in data validation and contributed to interpretation of results
MUHAMMAD FAHAD NASEER (Physiotherapist Intern)
Assisted in data entry, literature search and proofreading of the manuscript

All authors read and approved the final version of the manuscript

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