ORIGINAL ARTICLE

The effect of serum eosinophilia and lymphocytosis on functional outcomes of Hirschsprung disease patients after Duhamel procedure

Dhira Kumari, MD[1], Hendra Afrila, MD[1], Inna Faradina Putri, MD[1], Achmad Ilham Tohari, MD[1], Dirgantara Fathurrizki Harfanie, MD[1], Zahra Saliha Izzati, MD[1], Lanang Ishanda Aditama, MD[1], Ira Puspitawati, MD[2], Akhmad Makhmudi, PhD[1], Gunadi, PhD[1]

[1]Pediatric Surgery Division, Department of Surgery, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada-Dr. Sardjito Hospital, Yogyakarta, Indonesia, [2]Clinical Pathology and Laboratory Medicine, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada-Dr. Sardjito Hospital, Yogyakarta, Indonesia

ABSTRACT

Introduction: Hirschsprung disease (HSCR) is due to the failure of enteric nervous system precursors to colonize the distal intestine in embryonic development, with surgical treatment like the Duhamel procedure as a definitive intervention. However, complications leading to functional disorders may occur, especially with increased eosinophil levels. No studies have assessed the effect of peripheral blood eosinophil and lymphocyte counts on functional outcomes in HSCR patients post-Duhamel procedure.

Materials and Methods: This observational retrospective study involved 54 patients undergoing Duhamel procedures from January 2014 to June 2020 at Dr. Sardjito Hospital. Patient records were analyzed using the Mann-Whitney U test for continuous variables and the Chi-Square test for categorical variables.

Results: The majority of patients had normal eosinophil levels (78.8%) and normal lymphocyte counts (96.2%). Functional outcomes revealed that 49 patients (94.2%) had no voluntary bowel movements (VBM), 45 patients (86.5%) did not experience constipation, and 48 subjects (92.3%) had no soiling issues. There was no significant association was found between eosinophilia and functional outcomes in Hirschsprung disease patients after Duhamel procedure ($p > 0.05$). Similarly, there was no significant association between lymphocytosis and functional outcomes in these patients following Duhamel procedure ($p > 0.05$)

Conclusion: The functional outcomes of patients with Hirschsprung disease post-Duhamel procedure at our institution are favorable with most having normal eosinophil and lymphocyte counts. Eosinophilia and lymphocytosis might not significantly affect the outcomes of Hirschsprung disease patients after undergoing the Duhamel procedure at Dr. Sardjito Hospital.

KEYWORDS:
Hirschsprung; Duhamel; Eosinophilia; Lymphocytosis; Functional Outcomes (Krickenbeck)

INTRODUCTION

Hirschsprung's Disease (HSCR) is a congenital disorder of the enteric nervous system marked by the absence of ganglion cells in the distal colon, leading to chronic bowel obstruction as affected segments cannot perform normal peristalsis.[1] Originating from disrupted migration of neural crest cells during fetal development, this condition affects around 1 in 5,000 live births worldwide, with higher incidence rates, such as 1 in 3,250, reported in Yogyakarta, Indonesia.[2] Newborns with HSCR commonly show signs of bowel obstruction, including abdominal distention, feeding intolerance, and failure to pass meconium within 48 hours of birth. Diagnosis combines clinical evaluation and imaging, with definitive confirmation through rectal suction biopsy showing absent ganglion cells, leading to the necessity for surgical intervention to remove non-functional bowel segments and restore bowel continuity.[3] The Duhamel procedure is a common surgical approach in HSCR, where the ganglionated segment of the colon is pulled through to connect with the rectum, preserving anal sphincter function and minimizing rectal resection.[4] Although effective, postoperative complications like constipation, soiling, and Hirschsprung-associated enterocolitis (HAEC) may impact recovery.[5] Emerging research highlights that preoperative blood markers, such as elevated eosinophil and lymphocyte counts, may correlate with higher risks of gastrointestinal complications.[6] This study explores the role of these hematological markers in predicting functional outcomes in HSCR patients post-Duhamel surgery, aiming to refine preoperative evaluations and improve postoperative care strategies.

MATERIALS AND METHODS

This retrospective observational study aims to evaluate the association between eosinophilia and lymphocytosis on functional outcomes in Hirschsprung's disease patients following Duhamel surgery. The study was carried out in the Pediatric Surgery Department at Dr. Sardjito General Hospital, gathering data from the medical records of patients who underwent the Duhamel procedure. The target population includes Hirschsprung's disease patients in

This article was accepted: 20 November 2025
Corresponding Author: Gunadi
Email: drgunadi@ugm.ac.id

Table I: Clinical Characteristics, Hematological Findings, and Postoperative Functional Outcomes of Study Subjects

Parameter	Subjects (n = 52)	Percentage
Characteristics of Study Subjects		
Gender		
- Male	38	73.1%
- Female	14	26.9%
Eosinophil and Lymphocyte Count in Peripheral Blood		
Eosinophil		
- Normal	41	78.8%
- Eosinophilia	11	21.2%
Lymphocyte		
- Normal	50	96.2%
- Lymphocytosis	2	3.8%
Functional Outcomes After Surgery		
Voluntary Bowel Movement		
- Present	49	94.2%
- Absent	3	5.8%
Soiling		
- Present	4	7.7%
- Absent	48	92.3%
Constipation		
- Present	7	13.5%
- Absent	45	86.5%

Table II: The correlation between eosinophil and lymphocyte counts in the peripheral blood and Voluntary Bowel Movement (VBM)

Variable		Presence of VBM		Absence of VBM		p-value	Odds Ratio (95% CI)
		Subjects	%	Subjects	%		
Eosinophils	Normal	38	92.7	3	7.3	1	0.78
	Eosinophilia	11	100	0	0		(0.67-0.9)
Lymphocytes	Normal	47	94	3	6	1	0.96
	Lymphocytosis	2	100	0	0		(0.9-1.02)

Table III: The correlation between eosinophil and lymphocyte counts in the peripheral blood and Soiling

Variable		Presence		Absence		p-value	Odds Ratio (95% CI)
		Subjects	%	Subjects	%		
Eosinophils	Normal	4	9.8	37	90.2	0.57	1.3
	Eosinophilia	0	0	11	100		(1.11-1.51)
Lymphocytes	Normal	4	8	46	92	1	1.04
	Lymphocytosis	0	0	2	100		(0.98-1.11)

Table IV: The correlation between eosinophil and lymphocyte counts in the peripheral blood and Constipation

Variable		Presence		Absence		p-value	Odds Ratio (95% CI)
		Subjects	%	Subjects	%		
Eosinophils	Normal	6	14.6	35	85.4	1	1.71
	Eosinophilia	1	9.1	10	90.9		(0.184-15.95)
Lymphocytes	Normal	7	14	43	86	1	1.05
	Lymphocytosis	0	0	2	100		(0.98-1.12)

Yogyakarta who had Duhamel surgery at Dr. Sardjito General Hospital between January 2014 and June 2020, under the age of 18, and with complete medical records. Patient records were analyzed using the Mann-Whitney U test for continuous variables and the Chi-Square test for categorical variables.[7]

All patients underwent a standardized Duhamel procedure in which the posterior rectal wall and the anterior wall of ganglionated bowel were aligned and stapled using a gastrointestinal stapler. This approach minimizes the formation of a long rectal spur and preserves rectal sensation, as approximately half of the pulled-through segment remains ganglionated. These technical considerations are essential to achieving satisfactory postoperative continence and preventing residual fecal stasis.

Ethics Approval

This study received approval from the Medical and Health Research Ethics Committee (MHREC) at the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada (KE/FK/0124/EC/2020).

RESULTS

This study included 52 patients with Hirschsprung's disease who underwent the Duhamel procedure. The majority of patients were male, with 38 males (73.1%) and 14 females (26.9%) (Table I).

Eosinophilia, defined as eosinophil counts >5%, >500 cells/mm³, or >0.5 x 10^9/L, was identified in 11 patients (21.2%), while the remaining 42 patients (78.8%) had normal eosinophil levels. Lymphocytosis, defined as lymphocyte counts >9,000/mm³ or >9.0 x 10^9/L, was present in 2 patients (3.8%), whereas 50 patients (96.2%) had normal lymphocyte levels. (Table I)

Postoperative outcomes were classified into three categories based on the Krickenbeck classification: voluntary bowel movement (VBM), soiling, and constipation. Among the patients, 3 (5.8%) experienced VBM disturbances, while 49 (94.2%) had normal VBM. Regarding soiling, 4 patients (7.7%) reported soiling complaints, whereas 48 patients (92.3%) had no complaints. Constipation was observed in 7 patients (13.5%), while 45 patients (86.5%) did not report constipation issues. (Table I)

Based on eosinophil counts, 38 out of 41 patients with normal eosinophil levels (92.68%) and all 11 patients with eosinophilia (100%) had normal VBM. Three patients with normal eosinophil levels reported VBM disturbances. This difference was not statistically significant (p=1.000).

Regarding lymphocyte counts, 47 out of 50 patients with normal lymphocyte levels and both patients with lymphocytosis (100%) had normal VBM. Three patients with normal lymphocyte levels reported VBM disturbances. This finding was also not statistically significant (p=1.000). (Table II)

For soiling outcomes, 4 out of 41 patients with normal eosinophil levels reported soiling complaints, while no patients with eosinophilia or 37 patients with normal eosinophil counts reported soiling. This result was not statistically significant (p=0.57). In terms of lymphocyte counts, 4 out of 50 patients with normal lymphocyte levels reported soiling complaints, while none of the patients with lymphocytosis experienced soiling. This finding was not statistically significant (p=1.000). (Table III)

Regarding constipation, 6 out of 41 patients with normal eosinophil levels and 1 out of 11 patients with eosinophilia, experienced constipation. This result was not statistically significant (p=1.000). Similarly, 7 out of 50 patients with normal lymphocyte levels experienced constipation, while none of the patients with lymphocytosis reported constipation. This finding was also not statistically significant (p=1.000). (Table IV)

DISCUSSION

The characteristics of the subjects evaluated include gender, type of aganglionosis, age at the time of Duhamel surgery, nutritional status, and the presence or absence of complications during and after surgery. Previous research has found that there is a higher proportion of male subjects compared to females, as Hirschsprung disease is more commonly seen in males than in females.[8-10] It has also been suggested that female patients may be more prone to constipation, possibly due to hormonal influences.[11-12] A previous study demonstrated that male patients were more likely to experience abnormal defecation frequency compared to females, despite having comparable overall bowel function scores between the two groups.[13] Another study reported that male patients generally exhibited less favorable postoperative outcomes.[14] Notably, several other studies have supported the notion that sex may influence outcomes in pediatric patients with various conditions.[14-16] These variations may be attributed to anatomical distinctions between males and females, particularly in pelvic structure and pelvic floor configuration.[13,17]

Regarding the length of the aganglionic segment, more subjects had short-segment aganglionosis compared to long-segment types. This finding aligns with Nelson's study, which found that 60-85% of HSCR cases have short-segment aganglionosis.[8] Furthermore, postoperative functional disturbances can partly result from the absence of coordinated motility in the aganglionic colon. A longer aganglionic segment corresponds to a more proximal obstruction site, which raises intraluminal pressure and worsens dysmotility. Evidence regarding the association between long-segment Hirschsprung disease (HSCR) and poorer functional outcomes remains inconclusive. Some studies have reported higher rates of soiling and incontinence among long-segment HSCR patients, whereas others found no significant correlation.[18-19]

At the time of surgery, age was categorized into one year or less and over one year. More subjects were older than one year compared to those one year and younger. In another study, neonates comprised the majority of HSCR patients undergoing definitive therapy (84%), followed by infants (5%), toddlers (4%), children (3%), and adolescents (1%).[5] Older patients with HSCR tend to present with more severe intestinal obstruction.[20] A recent study reported that while postoperative functional impairments are frequent, intestinal function tends to improve as patients grow older.[21] Conversely, other studies have found that bowel dysfunction remains unchanged with advancing age.[22-23] Motivation and training to help control and distinguish stool types, along with social awareness with age, may reduce soiling and help achieve normal VBM.[6,12]

Nutritional status in children with Hirschsprung disease was generally good. This contrasts with common signs and symptoms of Hirschsprung disease, such as abdominal distention and bowel obstruction, which can lead to difficulty eating and green-colored vomiting.[4]

Postoperative complications are often related to obstructive issues such as anastomotic stricture, anemia, and surgical wound infections, which can impact functional outcomes such as constipation and soiling.[4,24] Newborns with eosinophilia on rectal biopsy but without HSCR showed a higher percentage of gastrointestinal symptoms compared to

those without eosinophilia. However, in studies involving HSCR patients with mucosal eosinophilia, this finding did not increase postoperative complications or affect feeding management.[25-26]

Subjects with eosinophilia were fewer in number compared to normal patients. Eosinophil levels in HSCR patients did not impact outcomes or affect postoperative complications. Although some studies excluding HSCR patients found that those with mucosal eosinophilia reported a high percentage of constipation complaints.[12]

More subjects had normal lymphocyte counts compared to those with lymphocytosis. However, no studies have specifically investigated lymphocytosis in HSCR patients. Voluntary Bowel Movement (VBM), soiling, and constipation are functional outcomes assessed using the Krickenbeck classification. These issues are commonly observed and significant following definitive surgery in HSCR patients.[10]

Postoperatively, HSCR patients often struggle to maintain continence and lack the reflex and sensation to control bowel movements and sphincters, making it challenging to differentiate rectal contents as solid, liquid, or gas.[6,12] Our previous study indicated that the type of definitive surgical procedure could influence long-term bowel function outcomes. Patients who underwent transabdominal Duhamel procedures tended to experience less favorable functional bowel results.[27]

Constipation is a functional bowel disorder that remains a concern in postoperative HSCR patients. In the Duhamel procedure, the incidence of postoperative constipation is 17.2%. Reducing the risk of constipation involves leaving a short native rectum; however, constipation may improve over time.[28] Additionally, increasing fiber intake or using loperamide may be effective.[4]

In this study, 92.68% of patients with normal eosinophil levels and 100% of patients with eosinophilia had normal VBM. The calculated OR value was 0.78, indicating that HSCR patients with normal eosinophil levels are more likely to have normal VBM than those with eosinophilia. However, this study had a p-value >0.05, indicating that the eosinophil level did not significantly impact VBM outcomes. Meanwhile, patients with normal lymphocyte levels were more likely to have normal VBM compared to those with lymphocytosis, with an OR value of 0.96. This data also lacked statistical significance due to a p-value >0.05.

For soiling, the OR was 1.3 for eosinophilia and 1.04 for lymphocytosis, suggesting that patients with eosinophilia are more likely to experience soiling compared to those with normal eosinophil levels, while patients with lymphocytosis are also more likely to experience soiling than those with normal lymphocyte levels. However, both findings lacked statistical significance due to p-values >0.05, indicating no effect on soiling outcomes.

In constipation tests, eosinophil levels had an OR of 1.714, while lymphocyte levels had an OR of 1.05. This indicates that patients with eosinophilia are more likely to experience constipation than those with normal eosinophil levels. Likewise, patients with lymphocytosis are also more likely to experience constipation than those with normal levels. However, neither result was statistically significant due to p-values >0.05, indicating no effect on constipation outcomes. Studies have suggested that while there may be concerns that HSCR patients with mucosal eosinophilia could have worse outcomes than HSCR patients without eosinophilia, especially concerning feeding and defecation, findings indicate similar outcomes between patients with or without mucosal eosinophilia.[25]

CONCLUSIONS

The functional outcomes of patients with Hirschsprung disease post-Duhamel procedure at our institution are favorable with most having normal eosinophil and lymphocyte counts. Eosinophilia and lymphocytosis might not significantly affect the outcomes of Hirschsprung disease patients after undergoing the Duhamel procedure at Dr. Sardjito Hospital.

This study has several limitations. First, as a retrospective single-center review, the data were limited to available records (small sample size) and may be subject to selection bias. Second, we did not include certain potentially confounding factors in the multivariate analysis, which may have affected the statistical associations observed. Third, anal manometry, histopathological confirmation of ganglion cells, and long-term quality-of-life assessments were not routinely performed and could provide more objective evaluation of functional outcomes. Future multicenter, prospective studies incorporating these variables are warranted to better delineate the complex determinants of postoperative function in Hirschsprung disease.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the great support received from Big Data Universitas Gadjah Mada Academic Health System for technical assistance and for preparation of the manuscript. The authors also acknowledge the major contribution from the scholars whose articles are cited and included in this manuscript.

FUNDING

There was no funding for this study.

REFERENCES

1. Chhabra S, Kenny SE. Hirschsprung's disease. Surgery (Oxford). 2016; 34(12): 628–32.
2. Feng J, Li T, Li N. Laparoscopically Assisted Pull-Through Operation for Hirschsprung's Disease. In: Puri P, editor. Hirschsprung's Disease and Allied Disorders. Dublin: Springer; 2019. p. 357-71.
3. Fischbach F, Dunning MB III. A Manual of Laboratory and Diagnostic Tests. Philadelphia: Wolters Kluwer Health; 2015.

4. Green HL, Rizzolo D, Austin M. Surgical management for Hirschsprung disease. J Am Acad Physician Assist. 2016; 29(4): 249.
5. Gunadi, Karina SM, Dwihantoro A. Outcomes in patients with Hirschsprung disease following definitive surgery. BMC Res Notes 2018; 11(1): 644.
6. Aworanti O, McDowell D, Martin I, Quinn F. Does Functional Outcome Improve with Time Postsurgery for Hirschsprung Disease? European Journal of Pediatric Surgery 2015; 26(02): 192-9.
7. Puspitawati DK, Akhmad M, Gunadi. Pengaruh Eosinofilia dan Limfositosis terhadap Luaran Pasien Hirschsprung Pasca Operasi Duhamel di RSUP Dr Sardjito (Bahasa). [Yogyakarta]: Universitas Gadjah Mada; 2021.
8. Nelson W, Marcdante K, Kliegman R. Nelson essentials of pediatrics. United States: Elsevier Saunders; 2015. 440 p.
9. Puri P, Nakamura H. Epidemiology and Clinical Characteristics of Hirschsprung's Disease. In: Puri P, editor. Hirschsprung's Disease and Allied Disorders. Dublin: Springer; 2019. p. 167-74.
10. Stensrud KJ, Emblem R, Bjørnland K. Functional outcome after operation for Hirschsprung disease—transanal vs transabdominal approach. J Pediatr Surg. 2010 Aug; 45(8): 1640-4.
11. Zakiyah AN, Prasetyo KR, Puspitawati I, Makhmudi A, Gunadi. Association between eosinophilia and lymphocytosis with functional outcomes of patients with Hirschsprung disease following transabdominal Yancey-Soave pull-through. Med J Malaysia. 2024; 79(Suppl 4): 6-11.
12. Widyasari A, Pavitasari WA, Dwihantoro A, Gunadi. Functional outcomes in Hirschsprung disease patients after transabdominal Soave and Duhamel procedures. BMC Gastroenterol. 2018; 18(1): 56.
13. Granéli C, Dahlin E, Börjesson A, Arnbjörnsson E, Stenström P. Diagnosis, Symptoms, and Outcomes of Hirschsprung's Disease from the Perspective of Gender. Surg Res Pract 2017; 2017: 9274940.
14. Prato AP, Gentilino V, Giunta C, Avanzini S, Mattioli G, Parodi S, et al. Hirschsprung disease: do risk factors of poor surgical outcome exist? J Pediatr Surg. 2008; 43(4): 612-9.
15. Kent AL, Wright IMR, Abdel-Latif ME. Mortality and Adverse Neurologic Outcomes Are Greater in Preterm Male Infants. Pediatrics 2012; 129(1): 124-31.
16. Stone ML, Lapar DJ, Kane BJ, Rasmussen SK, McGahren ED, Rodgers BM. The effect of race and gender on pediatric surgical outcomes within the United States. J Pediatr Surg 2013; 48(8): 1650-6.
17. Gunadi, Ivana G, Mursalin DA, Pitaka RT, Zain MW, Puspitarani DA, et al. Functional outcomes of patients with short-segment Hirschsprung disease after transanal endorectal pull-through. BMC Gastroenterol 2021; 21(1): 85.
18. Wardhani AK, Dwiantama K, Iskandar K, Yunus J, Gunadi. Outcomes of children with long-segment and total colon Hirschsprung disease following pull-through. Med J Malaysia 2024; 79(Suppl 4): 1-5.
19. Verkuijl SJ, Meinds RJ, van der Steeg AFW, van Gemert WG, de Blaauw I, Witvliet MJ, et al. Functional Outcomes After Surgery for Total Colonic, Long-Segment, Versus Rectosigmoid Segment Hirschsprung Disease. J Pediatr Gastroenterol Nutr 2022; 74(3): 348-54.
20. Ademuyiwa AO, Bode CO, Lawal OA, Seyi-Olajide J. Swenson's pull-through in older children and adults: Peculiar peri-operative challenges of surgery. International Journal of Surgery 2011; 9(8): 652-4.
21. Davidson JR, Kyrklund K, Eaton S, Pakarinen MP, Thompson DS, Cross K, et al. Long-term surgical and patient-reported outcomes of Hirschsprung Disease. J Pediatr Surg 2021; 56(9): 1502–11.
22. Fosby M V., Stensrud KJ, Bjørnland K. Bowel function after transanal endorectal pull-through for Hirschsprung disease – does outcome improve over time? J Pediatr Surg 2020; 55(11): 2375–8.
23. Meinds RJ, van der Steeg AFW, Sloots CEJ, Witvliet MJ, de Blaauw I, van Gemert WG, et al. Long-term functional outcomes and quality of life in patients with Hirschsprung's disease. British Journal of Surgery 2019; 106(4): 499-507.
24. Parahita IG, Makhmudi A, Gunadi. Comparison of Hirschsprung-associated enterocolitis following Soave and Duhamel procedures. J Pediatr Surg 2018; 53(7): 1351-4.
25. Sola R, Poola AS, Memon R, Singh V, Hendrickson RJ, St. Peter SD, et al. The relationship of eosinophilia with outcomes of Hirschsprung disease in children. Pediatr Surg Int 2019; 35(4): 425-9.
26. Ure B, Metzelder M. Duhamel's Procedure. In: Puri P, Holschneider A, editors. Hirschsprung´s Disease and Allied Disorders. Berlin: Springer; 2008. p. 365-73.
27. Gunadi, Monica Carissa T, Stevie, Daulay EF, Yulianda D, Iskandar K, et al. Long-term functional outcomes of patients with Hirschsprung disease following pull-through. BMC Pediatr 2022; 22(1): 246.
28. Seo S, Miyake H, Hock A, Koike Y, Yong C, Lee C, et al. Duhamel and Transanal Endorectal Pull-throughs for Hirschsprung' Disease: A Systematic Review and Meta-analysis. European Journal of Pediatric Surgery 2018; 28(01): 081–8.