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List of Abbreviations

AchE.....Acetylcholinesterase
AD .....Autosomal dominant
AR .....Autosomal recessive
BMI.....Body Mass Index
CI.....Confidence interval
CNS .....Central nervous system
DNA .....Deoxyribonucleic acid
DS.....Down syndrome
ECE-1 .....Endothelin converting enzyme 1
EDN3 .....Endothelin 3
EDNRB .....Endothelin receptor type B
ENS .....Enteric nervous system
GDNF.....Glial cell-derived neurotrophic factor
GLU .....Glucose transporter
H/E .....Hematoxylin and Eosin
HAEC.....Hirschsprung-associated enterocolitis
HD .....Hirschsprung's Disease
IBD .....Inflammatory Bowel Disease
ICC .....Interstitial cells of Cajal
MEN 2.....Multiple Endocrine Neoplasia 2
OR .....Odds Ratio
PHOX2B .....Paired-like homeobox 2b
QoL.....Quality of Life
SOX10 .....Sex determining region Y box 10
SRY .....Sex determining region Y
TCA .....Total colonic aganglionosis

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TZ .....Transitional Zone

WHO .....World Health Organization

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Abstract

Background: Despite the increased knowledge of Hirschsprung's Disease (HD) by advances in the understanding of the embryogenesis and surgical care, still, significant complications continue to be associated with the different procedures. However the most annoying complications are the persistent constipation and the recurrent enterocolitis induced by transitional zone pull-through or residual aganglionosis. Nevertheless in literature review both were mentioned as the major cause of redo-pullthrough[(1)].

Aim of the Work: The aim of this study is to define the characteristic histopathological features of the transitional zone in patients with HD, and it is impact on the clinical outcome.

Methodology:

Study: Retrospective and prospective cohort study was conducted to study the histopathological features (regarding ganglion cells and nerve bundle) of the transitional zone in patients with HD from 2010-2016, and its impact on the clinical outcome. Was performed in Pediatric surgery department in Ain Shams university hospitals in the period between 2015-2016.

Results Clinical outcome postoperatively among the 35 studied cases 71.4% were of good outcome (group A) they have normal or semi normal bowel habits after surgery; while (group B) 28.6% had recurrent bowel symptoms. The two groups were compared with their histopathologicaly findings. The significant findings were found in group B: the histopathological findings in the proximal wide assumed to be healthy part Ganglion cells are present in all cases and are classic, inspite of that Aurbach's nerve bundle show focal disarray in 28.6% and are unmylinated in 65.7% ,moreover their mean diameter 65.8±16.2 (µm) with range of 40.5–117.2 (µm). Meissner's nerve bundle in the same specimens show mean diameter 36.0±10.4 (µm) with range 11.5–62.8 (µm). Cases with postoperative group B had significantly more frequent focal disarray of nerve bundles, acute& mixed inflammatory cells and larger nerve bundles diameter.

Conclusion: Wide zone Auerbach'e nerve bundles mean diameter ≥68.0 µm had high sensitivity & (**Negative Predictive value**) NPV and other diagnostic characteristics moderate in prediction of abnormal bowel.

Keywords: Hirschsprung’s disease postoperative outcome, histopathological features Transition-zone pull-through Residual aganglionosis Redo pull-through operation.

INTRODUCTION

Hirschsprung's disease HD is a congenital megacolon characterized by the absence of ganglion cells in the myenteric and submucosal plexuses of the intestine ***(Jacob, 2014).*** HD incidence approximately 1:5,000 live births ***(Jeffrey and Levitt, 2017), (Matthew et al, 2017), (Jacob, 2014), (Lake and Heuckeroth, 2013).*** Moreover HD is relatively the most common cause of intestinal obstruction in the newborn ***(Jacob, 2014), (Pure, 2011).*** The first description in the modern medical literature of Hirschsprung's disease was in 1886 by a pediatrician Harald Hirschsprung, from Copenhagen, who described two cases. However the first description of a reconstructive operation for HD was in 1949 by Swenson, but still there were technical difficulties in small infants and many children who presented with debilitated and malnourished state ***(Jacob, 2014).*** Nevertheless the staged surgical approach has changed dramatically over the past three decades, and transition to primary pull-through is now the predominant. As the transanal pull-through is now used by a large proportion of pediatric surgeons. Moreover the minimal invasive surgery is used to facilitate both the diagnosis of HD and the pull-through procedure, therefore, also become one of the common pull-through procedure ***(Teitelbaum and Coran, 2013).***

The diagnoses of HD is usually based on clinical history, radiological studies, anorectal manometry and in particular rely on histopathological examination of rectal wall biopsy ***(Pure, 2011).*** The gold standard for the diagnosis is the absence of ganglion cells in the submucosal and myenteric plexuses on histological examination. Most of patients will also have evidence of hypertrophied nerve trunks, although this finding is not always present, particularly in children with total colonic HD or a very short aganglionic segment HD ***(Jacob, 2014).***

Despite the increased knowledge of HD by advances in the understanding of the embryogenesis and surgical care, significant complications continue to be associated with the different procedures ***(Teitelbaum and Coran, 2013).*** However the most annoying ones are the late complications include conistipation, enterocolitis, incotenance anastomatic problems, adhesive bowel obstruction and urogenital complications ***(Pure, 2011).*** However these long-term problems mandate close follow up of these patients ; at least until they are through the toilet training process, in order to identify and provide timely treatment for these problems ***(Jacob, 2012).***

Aim of the Work

The aim of this study is to define the characteristic histopathological features of the transitional zone in patients with HD, and it is impact on the clinical outcome.