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# Investigating The Frequency of Serrated Polyps/Adenomas and Their Subtypes in Colonic Polyp Samples

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## Abstract

**Background:** The purpose of this study was to determine the frequency of Serrated polyps of colonic polyps samples in Hazrat\_e Rasoul\_e Akram Hospital over ten years. **Materials:** The target group in this study was patients with colonic polyps in Hazrat\_e Rasoul\_e Akram Hospital. Pathologic evaluation of these patients was done. Serrated polyps, by location, gender, age and type of polyps were divided and frequency of them were determined separately. **Results:** Of 381 patients studied, 224 (58.79%) and 157(41.20%) were males and females, respectively. Mean age of patients was 59.25 years. In initial diagnosis, frequency of Adenomatous polyp, Hyperplastic polyp and Mixed polyp were 92.44% and 5.33%, and 2.22%, respectively. In final diagnosis (Second evaluation), frequency of Adenomatous polyp, Hyperplastic polyp, Mixed polyp, Sessile Serrated Adenoma/ Polyp, Traditional Serrated Adenoma and SPU (Serrated Polyp Unclassifiable) were 90.44%, 4.88%, 2.44%, 1.11%, 0.66% and 0.44%, respectively. 72.13% and 27.86% of polyps were low grade dysplasia and high grade dysplasia, respectively. According to the results of this study, the incidence of all types of polyps detected was more in men than women. Rectum and sigmoid were most abundant in the area polyp in both initial and final diagnosis. **Conclusion:** Despite the low prevalence of Serrated polyps in patients, early diagnosis is the best action to reduce morbidity and mortality. Probability of the risk of progression from low grade to high grade dysplasia and transforming into Adenocarcinoma is high in Serrated polyps.

**Key words:** Colonic Polyp, Serrated polyp, Rectum, Sigmoid.

## 1. INTRODUCTION

Colorectal cancer is the third lethal cancer in the world and nearly one million people are afflicted with this cancer every year of whom half die (1). In various parts of the world and with different intensities, this cancer has been recognized as one of the most important reasons of death. For example, the second cause of death toll in the US is this cancer (2, 3). This is also the third cause of cancer-related death toll in Iran (4). Based on the studies conducted in Iran, colorectal cancers are the 3<sup>rd</sup> or 4<sup>th</sup> cancer reported among Iranian men, while they are the 2<sup>nd</sup> or 4<sup>th</sup> among Iranian women (except for skin cancer) (5-7). Colon cancer is the most curable type of tumor in the digestive system, thus a quicker diagnosis of the effective

factors which cause such tumors makes a significant contribution to treating the patients (8-10). One of the effective factors in causing colon cancer is background polyp. Of all types of colon polyps, Adenomatous polyps are considered to be background injuries in 60% of colon cancer due to cytological atypia and various studies have been conducted on this class of polyps (11, 12). The results of the studies conducted in recent years have shown that 35% of colon cancer cases were due to the transformation of serrated polyps into Adenocarcinoma. Transformation of Serrated polyps is achieved through methylation of CPG island whose pathway is different from transformation of Adenomatous to Adenocarcinoma.

Although Hyperplastic polyps have been identified as non-dangerous injuries with no potential of becoming malignant, a group of injuries classified as Hyperplastic polyps form a separate group polyps which demonstrate jagged or serrated morphology and possess the potential of becoming malignant. This set of polyps does not just include Hyperplastic polyps, they also include Mixed polyps, Traditional Serrated Adenomas, Sessile Serrated Adenomas/Polyp. Mixed polyps are serrated polyps which show a view of classic adenoma in some parts. In some serrated injuries, classification of the polyps is difficult due to the intermediate morphological view and other factors such as poor orientation and severe artifact cauterization and insufficiency of the tissue. The phrase "Serrated Polyp Unclassifiable" is utilized (13-15). Considering the fact that 35% of the cases of colon cancer are caused by transformation of Serrated polyps to Adenocarcinoma which is often ignored in pathological reports by the pathologists, thus we will study the frequency of serrated polyps in colonic polyp samples and their types based on diagnostic criteria.

## 2. MATERIALS AND METHODS

The target group of this study included all the patients afflicted with colonic polyps who underwent pathological examination over the period of 2002 to 2012 in Hazrat\_e Rasoul\_e Akram Hospital. First, paraffin blocks and the slides in the archive of Hazrat\_e Rasoul\_e Akram Hospital in which colonic polyps were identified over the last 10 years were extracted. Whenever required, recutted and slides were prepared and reviewed after H & E staining. Information was gathered by the computer of pathology department and review of pathological reports and the medical file of the patients and put in a table. If placed in sets of various serrated polyps based on the standard diagnostic criteria of the expert panel of Gastroenterology of German Society of Pathologists, they were classified in terms of location, gender, age and type of polyp. In the present research, left colon refers to Distal to Splenic Flexure and right colon refers to the beginning of the colon to Proximal and to Splenic Flexure. The frequency of each one was measured independently. The slides were then examined by another pathologist and if the results were in line with the first diagnosis, the results would be recorded. If any discrepancies existed between two pathologists in their interpretation of the results, slides observation would be conducted simultaneously and based upon the criteria.

SPSS software edition 21 was used to analyze the information. To describe data, average, standard deviation, mean, range, frequency and percentage were utilized and the corresponding tables and graphs were drawn. Quantitative variables were presented in the form of average and standard deviation, while qualitative variables were represented in the form of number and percentage.

## 3. RESULTS

This study was conducted on 381 patients with colon polyps who had resorted to Hazrat\_e Rasoul\_e Akram Hospital of Tehran over the last 10 years of whom, 224

Location	Left colon and rectum
	Slightly elevated
Size	Usually less than 5 mm
Microscopy	Elongated Crypts Serration in the upper half or one-third of the crypts Small , uniform basally placed nuclei No Cytological atypia or architectural dysplasia

Table 1. Diagnostic criteria for Hyperplastic Polyp

Location	More frequent in left colon and rectum
	Polypoid
Microscopy	Dysplasia / Intra-Epithelial Neoplasia (IEN) Ectopic crypts (ECP) Diffuse Eosinophilic cytoplasm Prominant serration

Table 2. Diagnostic criteria for Traditional Serrated Adenoma (TSA)

Location	Right colon
	Sessile
Size	More than 5 mm
Microscopy	Hyper serration in the lower third of the crypts with or without branching of the crypts L and T shaped crypts above Muscularis mucosa Inverted crypts below Muscularis mucosa Columnar dilatation in the lower third of the crypts Shifting of the proliferation zone to the middle third of the crypts Vesicular nuclei and nucleoli Mature goblet cells at the base of the crypts

Table 3. Diagnostic criteria for Sessile Serrated Adenoma (SSA)

All typs of polyps	Number	Percentage
Adenomatous Polyp	407	90.44
Serrated Polyp	Hyperplastic polyp	22 4.88
	Sessile Serrated Adenoma/Polyp (SSA/P)	5 1.11
	Traditional Serrated Adenoma (TSA)	3 0.66
	SPU	2 0.44
	SSA/AP	1 0.22
	Mixed polyp TSA/AP	1 0.22
	HP/AP	9 2
Total	450	100

Table 4. Frequency of all types of polyps after review

(58.79%) were male and 157 (41.20%) were female. The range of the age of those examined was from 13 to 100 with the average of 59.25 and the standard deviation of 14.12. Of 450 polyps diagnosed in 381 patients with colon polyp, the highest frequency of polyp diagnosis locations were Rectum (21.11%), Sigmoid (16.44%), descending colon (8.67%), and transverse colon (4.89). On the whole, 92.44% of all polyps identified were Adenomatous polyp type, while hyperplastic and mixed polyps made up only 5.33% and 2.22% of polyps respectively. Various types of Adenomas diagnosed can be discussed in terms of their frequency as follows: Adenomatous polyp of tubular type (79.08%), Adenomatous polyp of Tubulovillous type (13.46) and Adenomatous polyp of Villous type (7.45%).

Source	Frequency
Barirol et al., 2003 (32)	255 polyps (72 HPs, 9 SAs, 4 MPs, 170 conventional adenomas)
Sandmir et al., 2007 (33)	102 SPs (58 HPs, 7 SSAs, 5 TSAs, 3 MPs, 29 UCPs)
Glatz et al., 2007 (34)	20 SPs (8HPs, 4 TSAs, 4 SSAs, 4 tubulovillous adenomas)
Farires et al., 2008 (35)	185 SPs (92 HPs, 74 SSAs, 19 TSAs)
Boustament-Balen et al., 2009 (36)	195 SPs (187 HPs, 8 SAs)
Vang et al., 2009 (37)	60 polyps (26 SAs, 11 HPs, 6 MPs, 12 conventional adenomas, 5 other polyps)
Khalid et al., 2009 (38)	40 SPs (comprised of HPs and SSAs and all originally diagnosed HPs)
Gonia et al., 2011 (39)	19 SPs (8 SSAs, 3 TSAs, 8 inflammatory polyps)

Table 5. A summary of the reported frequencies of SPs in various researches. SPs: Serrated Polyps, HPs: Hyperplastic Polyps, SAs: Serrated Adenomas, MPs: Mixed Polyps, SSAs: Sessile Serrated Adenomas, TSAs: Traditional Serrated Adenomas, UCPs: Unclassified Colonic Polyps

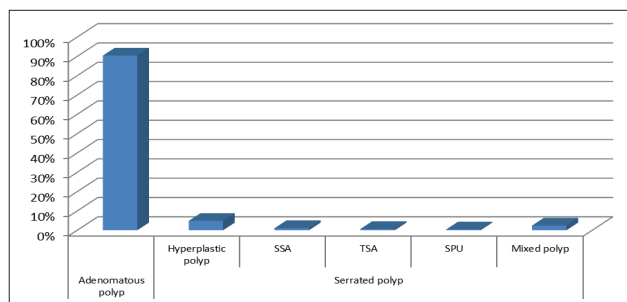


Chart 1. Frequency chart of all types of polyps after review

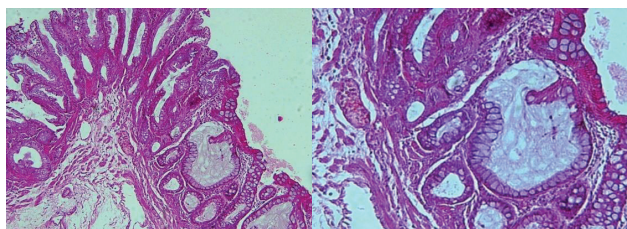


Figure 1. Sessile Serrated Adenoma (SSA)

The highest age average (71.50 years) was observed in female patients afflicted with Tubulovillous type and the lowest age average (53.50 years) was witnessed in male patients afflicted with the mixed type. Rectum, sigmoid and descending colon were the most common areas identified with various types of colons.

Among 122 polyps whose degree of dysplasia was diagnosed, 72.13% had low grade dysplasia and the remaining 27.86% had high grade dysplasia. As of low grade dysplasia, the highest frequency is for the Adenomatous polyp of tubular type while Adenomatous polyp of Tubulovillous type displayed the highest level of frequency in high grade dysplasia. Based on the results achieved in the present study, 51.11% of the polyps were located in the left colon, while 9.77% of them were recorded to be in the right colon. After reviewing the results, the highest frequencies were for Adenomatous polyp (90.44%) and Hyperplastic polyp (4.88%) respectively. The frequency of other polyps were as follows: Mixed type (2.44%), Sessile

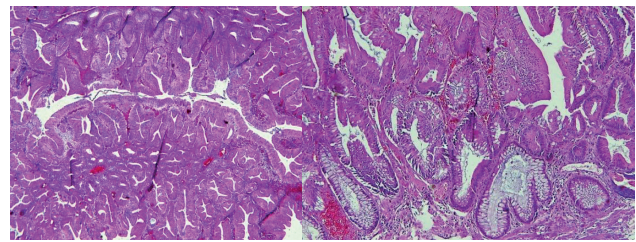


Figure 2: Traditional Sessile Adenoma (TSA)

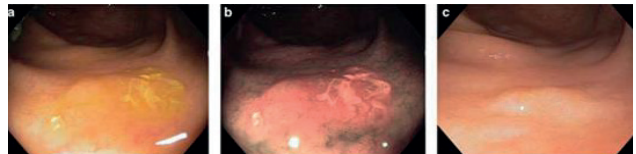


Figure 3: a, b, c Colonoscopic view of Serrated Polyp (Mucus cap)

Serrated Adenoma/Polyp (1.11%) (Figure 1), Traditional Serrated Adenoma (0.66%) (Figure 2) and Serrated Polyp Unclassified (0.44%) (Chart 1, Table 4).

Even after the review, the frequency of all types of polyps among men was much more than women. The lowest age average (45.75 years) was witnessed among men afflicted with Sessile Serrated Adenoma/Polyp, while the highest age average (74 years) was seen among men afflicted with mixed polyp (SSA/AP). Rectum and sigmoid had the highest frequency in terms of polyp location. Hyperplastic polyp (53.84%) and Traditional Serrated Adenoma/Polyps (37.5%) had the highest frequencies in rectum and sigmoid, respectively.

#### 4. DISCUSSION AND CONCLUSION

This study was conducted on 381 patients with colon polyps who had resorted to Hazrat\_e Rasoul\_e Akram Hospital of Tehran over the last 10 years of whom, 224 (58.79%) were male and 157 (41.20%) were female. In the studies conducted by Zare\_Mirzaie et al. (5) and Buda et al. (17), men made up 58.8 and 38 percent of the patients respectively. Of 60 patients afflicted with colorectal polyp who were studied by Nourmohammadi et al. (18), 40 of them (66.7%) were men. There is an assumption which says hormonal and immune factors are responsible for different levels of colorectal cancer among men and women. Women are more immune against this cancer due to high levels of steroid secretion. Furthermore, they will have a higher chance of survival if they get afflicted (18). The age of the people who participated in this study ranged from 13 to 100 with the average of 59.25 and the standard deviation of 14.12. The average age of men was 59.88±14.75, while the average age for women was 60.17±13.09. The youngest (13 years) and the oldest (100 years) patients were witnessed among male patients. The average age of patients in the study conducted by Moulai'e et al. (18) was 60.17 years, while the average age in the studies conducted by Buda et al. (17) and Nourmohammadi et al. (18) was 53 and 62.2 years respectively. In a study conducted on patients with colorectal cancer who had resorted to Shari'ati Hospital of Isfahan, Rafi'ee et al. (20) came to the conclusion that one's age alone can not increase the chances of colon polyps. They reported that a set of dangerous factors increase the chance of col-



orectal polyps. Zare\_Mirzaie et al. (5), however, reported that 17% of colorectal cancers in Iran are observed among people below 40.

Based on the initial diagnosis in the present study, 92.44% of the polyps diagnosed were Adenomatous, 5.33% of them was hyperplastic and 2.22% was mixed. Different types of Adenomas diagnosed had the following frequencies: Tubular (79.08%), Tubulovillous (13.46%) and Villous (7.45%). After review, the highest frequencies were for Adenomatous polyp (90.44%) and Hyperplastic polyp (4.88%) respectively. The frequency of other polyps was as follows: Mixed type (2.44%), Sessile Serrated Adenoma/Polyp (1/11%), Traditional Serrated Adenoma (TSA) (0.66%) and SPU (0.44%). The frequency of Tubular, Tubulovillous and Villous polyp types in the study conducted by Dr. Zare Mirzaie et al. (5) is 73.3, 16.2 and 10.5 percent respectively. In their study of 7192 cases of colorectal polyp, Hetzek et al. reported the frequency of HP, SSA and TSA polyps as 7.7-31 %, 0-2.2 %, 0-0.5 % respectively. In a cross-sectional study, Bettington et al. (23) reported the prevalence of Serrated polyp in 6340 colorectal polyps to be 12.1%. Kim et al. (24) reported the frequency of HP and SSA polyp to be 14.7 and 0.5% respectively. The prevalence of serrated polyps in patients above 50 is 15.3, while the prevalence for all patients is reported to be 15.1%. In the study conducted by Buda et al, Serrated polyps were reported to make up 40% (102 polyps) of all the polyps (263 polyps) diagnosed (17). In the study conducted by Kahi et al. (25), the prevalence of serrated polyps in 6681 colonoscopy samples ranges from 1 to 18 percent.

Based on the initial diagnosis in the present study, rectum (21.11%), sigmoid (16.44%) and descending colon (8.67%) were the most frequent areas diagnosed for polyps. After the review, it turned out that rectum and sigmoid had the highest frequency in terms of polyp area. The highest frequencies in rectum and sigmoid were for Hyperplastic (53.84%) and TSA (37.5%) respectively. In the study conducted by Rahbar et al. (26), the distribution of colorectal polyps was as follows: descending colon (36.2%), rectum (34.6%), cecum and ascending colon (27.7) and Transverse colon (1.5%). Based on the results achieved in the present study, 72.13% of 122 polyps whose dysplasia degree was determined had a low grade dysplasia, while 27.86% had high grade dysplasia. Adenomatous polyp of Tubular type and Tubulovillous type had the highest levels of frequency in low and high grade dysplasia respectively. In the study conducted by Moulai'e et al. (19), 324 (81%) cases of polyps with low grade dysplasia were observed, while 76 (19%) cases of polyps with high grade dysplasia were recorded. In the study conducted by Zare\_Mirzaie et al. (5) on 240 colorectal Adenomatous polyps, 16.2% of polyps had a high grade dysplasia.

Based on the results achieved from the present study, polyps are more common in left colon than the right colon. In the research conducted by Moulai'e et al (19), polyp was located in the right colon in 136 (34.1%) cases, while 201 (50.4) polyps were located on the left side and 62 (15.5%) cases were reported to be located in rectum.

In the study conducted by Gesvantler et al. (26) on 7590 Adenomatous polyps, 5810 (76.5%) polyps were in the left colon while 1780 (23.5%) of them were located in the right colon. The majority of polyps in the study of Patel et al. (27) were reported to be located in the left colon. 92% of all polyps were in the left colon in the study of Toni et al. (28). Contrary to the reports presented in other papers, the researches conducted in Taiwan showed a higher frequency of Adenomatous polyps distribution in the Right colon (29). In the previous studies conducted on the Iranian population by Khodadoust et al. (30) and Bafandeh et al. (31), polyps were more common in the left colon. In the previous studies just mentioned (Table 5), serrated polyps made up around one-third of intestine polyps. Two-third of the polyps were hyperplastic and one-third was serrated adenoma.

However, the small number of Hyperplastic and serrated polyps in our research raises questions and is one of the limitations of this study. As we know, the majority of serrated polyps are located in proximal parts of the intestine and have a flat view which makes them difficult to identify in endoscopy. In fact, one of the reasons of seeing less polyps in this research is that they were not discerned during the endoscopy, in which case certain clinical symptoms are witnessed (for example, in a significant number of colon carcinoma in people who undertake colonoscopy regularly). Considering the fact that the majority of the serrated polyps diagnosed in this study were in the sample of previous years and bearing in mind the significance difference in their prevalence in recent years and higher level of colonoscopists' knowledge of this set of polyps and routine colonoscopy of colon might, somehow, explain the discrepancy. Considering the training-treatment nature of this center and acceptance of new gastrointestinal fellowship every year, incomplete or incorrect colonoscopy is a serious issue and attention must be paid to the existence of such polyps. SSA/P and hyperplastic polyps have a clear endoscopic appearance in proximal colon which includes Mucus Cap and being isochromatic with natural mucosa with unclear edges (Figure 3).

As one third of colon cancers take place through the serrated path, all colonoscopists must be able to identify such polyps so as to perform effective colonoscopy. There is a strong relationship between the diagnosis of serrated polyps and Adenomatous polyps and colonoscopists are required to calculate this relationship so that they can effectively diagnose serrated devastations. It is recommended to take out all proximal serrated polyps to sigmoid colon and those serrated polyps larger than 5 mm rectosigmoid while conducting colonoscopy(40). Another limitation in this research was that the frequency of polyps was studied only in one center. We may need to conduct wider studies in multiple centers, especially centers with a lot of samples, so that we may be assured about the validity of the results achieved in this study.

- Conflict of interest: None declared.

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