

## Research Article

# Metabolic Syndrome Associated with Steatohepatitis Significantly Increases the Risk of Hyperplastic Colonic Polyp

Mahamid M<sup>1,2</sup>, Hana A<sup>1\*</sup> and Nseir W<sup>3,2</sup><sup>1</sup>Department of Internal Medicine, Holy Family Hospital, Nazareth, Israel<sup>2</sup>Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel<sup>3</sup>Divisions of Internal Medicine, EMMS, The Nazareth Hospital, Nazareth, Israel**\*Corresponding author:** Hana Amara, Department of Internal Medicine, Holy Family Hospital, Nazareth, Israel**Received:** February 16, 2018; **Accepted:** March 19, 2018; **Published:** April 03, 2018**Abstract**

**Objective:** This study evaluated whether metabolic syndrome increases the risk of Hyperplastic Polyps (HPs) in patients with Nonalcoholic Steatohepatitis (NASH). In accordance with our previous study, advanced hepatic fibrosis in fatty liver disease is linked to the hyperplastic colonic polyp (ref) to which fatty liver disease is associated with HPs (REF).

**Methods and Materials:** We conducted a retrospective, cohort, observational study between April 2014 and April 2015 on patients who underwent a screening colonoscopy. A total of 123 out of 223 patients had a biopsy-NASH and 100 patients without NASH served as the control group. Extracted data included demographics, anthropometric measurements, vital signs, underlying diseases, medical therapy, laboratory data, endoscopic and pathological data.

**Results:** The results of MS and NASH status with the presence of HP compared with MS negative/NASH negative group, the MS negative/NASH positive group and the MS positive/NASH positive group were significant and exhibited an increase of risk for HPs (OR 1.3; 95% CI, 1.02-2.13 and OR 1.48; 95% CI, 1.05-2.04, respectively).

**Conclusions:** Further analyses supported the conclusion that there is an association between NASH and MS with HPs. Additional efforts are necessary to conduct further research on the importance of the severity of hepatic fibrosis in patients with HPs.

**Keywords:** Hyperplastic polyp; Fatty liver; Metabolic syndrome; Steatohepatitis; Non-alcoholic steatohepatitis

**Introduction**

Hyperplastic Polyps (HPs) of the colon are considered as benign lesions that have little to no malignant potential. However, recent studies have suggested that HPs may either lie in the classic adenoma-carcinoma pathway [1]. Although numerous studies have proposed that Metabolic Syndrome (MS) is a risk factor for Colorectal Cancer (CRC), colonic adenomas, HPs, and nonalcoholic fatty liver disease, there are no current studies that have examined the impact of MS as a risk factor for HPs in NASH. Fatty liver disease may also be represented as a simple hepatic steatosis that has the potential to progress to Non-alcoholic Steatohepatitis (NASH), fibrosis, cirrhosis, and Hepatocellular Carcinoma (HCC) [2,3]. Based on this background, we conducted this study in order to investigate whether MS may increase the risk of HPs in NASH patients [2,3].

**Methods and Materials**

Our data consisted of our previously published articles based on a retrospective, cohort observational study that was conducted at the Division of Internal Medicine at EMMS Nazareth Hospital in Nazareth, Israel between April 2014 and March 2015 on patients who underwent screening colonoscopy within 2 years and liver biopsy in the past 5 years [2,3]. A total of 223 participants consisted of patients

with biopsy proven NASH and are 18 years or older, 100/223 being the control group. The study was approved by the local ethics committee. The data has been coded to keep the anonymity of the patients and the informed consent forms were waived due to the non-interventional study design. The control group consisted of 100 patients, in which the age and sex matched without NASH. The Body Mass Index (BMI) for all patients was calculated in kg/m<sup>2</sup>.

Data was analyzed using SPSS version 19 (IBM SPSS, Chicago, IL, USA). Continuous variables are expressed as the mean  $\pm$  standard deviation. We used Chi-square to test differences in categorical variables between the cases and controls. Analysis of variance (ANOVA) and a t-test was used for comparisons of continuous variables. Spearman rank correlation and univariate regression analysis were used to determine the strength of the relationship between NASH and hyperplastic polyps after adjusting for independent variables. A multiple logistic regression analysis was done to determine the association between the different risk factors for HPs. A significance level of <0.05 was used in this test.

**Results**

Using the data from our previously published articles [2,3] a total of 223 patients were included in the study: 123 patients with biopsy-

proven Non-alcoholic Steatohepatitis (NASH) and 100 patients without NASH who served as the control. Fourteen colonic adenomas (11% of patients) were found in the NASH group vs. 16 (16%) in the control group ( $P=0.9$ ); 28 HPs were found in the NASH group (22.7%) vs. 8 in the control group (8%) ( $P < 0.05$ ) [2,3]. No significant increase for risk of colonic adenomas were found when compared to individual component for MS and MS adenoma [2,3]. The location, size, number, morphology, and degree of dysplasia of the adenomas were similar between the two groups [2,3]. The multivariate analysis, after adjusting for, age, C-reactive protein and smoking, showed that the presence of NASH (OR 1.69, 95%CI 1.36-1.98,  $P < 0.01$ ) was associated with increased risk for HP [2,3].

Among the NASH participants the mean age was 41+13years vs. 42+12years in control group, 72/123 patients (86%) were males vs. 43/100 (43%) in control group; the mean BMI was 29+4.7Kg/m<sup>2</sup> vs. 27.7+3.2Kg/m<sup>2</sup>. The patients who met the criteria for MS were 88/123 patients (72%) vs. 57 (57%), and the mean C - reactive protein (CRP) levels was 1.1+0.7mg/dl. The only significant differences between the two groups were in male gender and CRP levels,  $P<0.05$  of each one. All HPs in the NASH-group were located in the left colon where (25%) of HPs in the control group were located in the right colon. The degree of liver fibrosis among the NASH group, according to the liver biopsy, are the following: Stage 0 fibrosis, on 18 patients (15%), Stage 1 fibrosis, 29 patients (23%), Stage 2 fibrosis, 32 patients (26%), Stage 3 fibrosis, 37 patients (30%), and Stage 4 fibrosis, 7 patients (6%). Results showed a significant correlation between the degrees of fibrosis with a prevalence of 75% of HPS. More sig. HPs diagnosed in the NASH-group were observed in the high degree fibrosis patients (Fibrosis Stage 3,4), 6 HPs (21 %) were associated with Fibrosis stages 1 through 2 and single HP (4%) was associated with Fibrosis Stage 0 { $P<0.05$ } [2,3].

The logistic regression analysis showed that those older aged (>50), male sex, current smoking, high CRP levels, low vitamin D levels, NASH, and advance fibrosis were associated with increased risk for HP. The results of MS and NASH status with the presence of HP, compared with MS negative/NASH negative group, MS negative/NASH positive group and the MS positive/NASH positive group were significant and exhibited an increase of risk for HPs (OR 1.3; 95% CI, 1.02-2.13 and OR 1.48; 95% CI, 1.05-2.04, respectively).

## Discussion

In accordance to our previous studies [2,3], this study examines the relationship between biopsy-proven steatohepatitis and colonic hyperplastic polyps. The results of this study demonstrate that

NASH was significantly associated with an increase frequency of colonic hyperplastic polyps [3]. Furthermore, the frequency of HPs is correlated with the degree of liver fibrosis, in patients with advance fibrosis. The frequency of HPs was more common compared with patients with early or no hepatic fibrosis [2].

Patients with MS are shown to have a higher risk of colorectal HPs, as illustrated by several studies. The mechanism that joins the two entities is most likely linked to insulin resistance, or perhaps a mechanism that leads to a metabolic syndrome also plays a distinct role in the development of HPs [4]. According to our findings, the combination of both NASH and MS has increased the frequency of HPs due to the involvement of all the previously suggested factors [3]. Recent published data claims HPs are more common in advance hepatic fibrosis and cirrhotic patients compared to early or no hepatic fibrosis [2]. Further studies are required to confirm this hypothesis and to elucidate possible mechanism responsible for the phenomena.

Our study consisted of several limitations; the retrospective design of the study proved difficult to infer causality between NASH and risk for HPs. Secondly, our study accounts for selection bias, as our subjects were recruited from patients who visit the hospital our liver unit at EMMS Nazareth Hospital for health examination. Thus, participants were more concerned about their health status. In addition, the population size used was too small to accurately reflect known lifestyle and dietary risk factors that could be associated with HP such as, ethnicity and family history.

## Conclusion

Our study is the first to show that the association between biopsy proven NASH and metabolic syndrome significantly increases the risk of hyperplastic polyp and the severity of hepatic fibrosis may play an important role in the increasing frequency of HP in those patients.

## References

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