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Non-alcoholic fatty liver disease in women with polycystic ovary syndrome: systematic review and meta-analysis – An update

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a pathologic condition that develops in four stages, expressing itself from simple fatty liver (steatosis) to non-alcoholic steatohepatitis (NASH), in which inflammation of the liver takes place. Fibrosis and cirrhosis may occur in extreme cases [1][2]. Polycystic ovary syndrome (PCOS) is characterized by altered hormone patterns, irregular menstruation and polycystic ovaries [3]. An increased risk for NAFLD has been demonstrated in PCOS women, although no specific cause has been determined [2]. A systematic review and meta-analysis was performed to evaluate the association between PCOS and NAFLD. Comparing PCOS women with NAFLD vs. PCOS women without NAFLD, total testosterone (nmol / L) and free androgen index (FAI) were meta-analyzed. The objective is to update the previous systematic review and meta-analysis- “Non-alcoholic fatty liver disease in women with polycystic ovary syndrome: systematic review and meta-analysis”, Rocha, A. L. L. et al., 2017.

Methods

An electronic search of databases including PubMed, Scopus, SciELO and Google Scholar was performed. Articles were screened and extracted according to the inclusion and exclusion criteria defined by the researchers and 23 studies published between May 2007 and December 2019 were selected, being 6 of them a result of the update. 66 806 women diagnosed with PCOS were compared with 123 928 healthy control women, matched in age and BMI.

Meta-analysis employed a random-effects model (inverse variance), and was made using RStudio Software. The heterogeneity was assessed by χ^2 and I² methods and a sensitivity analysis was performed to identify the potential sources of heterogeneity. Publication bias was also assessed by visual inspections of Funnel Plot and Begg’s test.

Furthermore, to complement the original meta-analysis, a subgroup analysis and a meta-regression were made to evaluate the influence of age and BMI in the development of NAFLD and the studies were also analyzed by publication date.

To evaluate the relationship between free androgen index (FAI) and serum total testosterone in women with PCOS and the coexistence of NAFLD, two meta-analyses of continuous outcome data (Mean Difference) were made in RStudio Software, where 7 and 9 studies were considered, respectively.

Results

Heterogeneity was tested and identified with χ^2 and I² (I²=51.3%; χ^2 = 45.18, p=0.0025). PCOS patients have an increased prevalence of NAFLD (OR 2.62, 95% CI 2.18 – 3.15). Moreover, publication bias was identified with the Funnel Plot Method and Begg’s Test (p-value=0.020). Trim and Fill Method was made to correct publication bias and 5 studies were added. The results of the Trim and Fill method report that there is consistency with the main results associated with true studies (OR 2.31, 95% CI 1.87 – 2.85).

The subgroup analysis showed that age (less than 20 - OR 3.41, 95% CI 1.48 – 7.83; between 20 and 29 - OR 2.58, 95% CI 1.92 – 3.47; 30 or more - OR 2.61, 95% CI 2.13 – 3.19) and BMI (normal - OR 2.61, 95% CI 1.91 – 3.56; overweight - OR 3.06, 95% CI 2.08 – 4.52; obese – OR 3.44, 95% CI 1.84- 6.44) do not influence the development of NAFLD, and no differences were identified when the studies were analyzed by

Keywords:
Non-alcoholic fatty liver disease;
Polycystic ovary syndrome;
Cirrhosis; Steatosis; Non-
alcoholic steatohepatitis; Free
androgen index; Serum total
testosterone.

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First published: 23 OCT 2020



Open Access Publication

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publication date (May 2007 to May 2017 - OR 2.67, 95% CI 2.07 – 3.44; April 2017 to December 2019 - OR 2.61, 95% CI 1.99 – 3.41).

The results of the meta-regression corroborate the results of the analysis by subgroups, either by Age (coefficient 0.0106, p value=0.698) and BMI (coefficient 0.0091, p value= 0.737).

The secondary meta-analysis showed that among women with PCOS, those with NAFLD have higher serum total testosterone (MD 0.33, 95% CI -0.10 – 0.76) and FAI (MD 5.12, 95% CI 2.25 – 7.99). However, unlike the original meta-analysis, the serum total testosterone is not statistically significant.

Conclusion

Women with PCOS have an higher risk (2,62 times increase) of developing NAFLD than healthy women. NAFLD is not related to age or BMI, however, increased values of FAI contribute to the development of NAFLD. Regarding the analysis considering the year of publication, it is possible to observe the same tendency in both periods, May 2007-May 2017 and May 2017-December 2019. Therefore, this update reaches the same conclusion as the original meta-analysis.

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