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A Retrospectiveobservational Study on Polycystic Ovarian Syndrome and Its Relation with Metformin and Vitamin B_{12}supplementation

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I. INTRODUCTION:

Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder affecting 4–12% of women (1). In PCOS, hyperinsulinemia has been thought to increase hyperandrogenemia via a central role or by decreasing the circulating levels of sex hormone binding globulin (2). An estimated prevalence of insulin resistance among PCOS patients of 60–70% has been reported (3). Therefore, casting doubt on the role insulin resistance plays in the pathogenesis ofPCOS. In this case, Metformin works by improving the sensitivity of peripheral tissues to insulin (4) which results in a reduction of circulating insulin levels. However, Metformin can also lead to vitamin B12 malabsorption in the distal ileum in approximately 10–30% of patients which is an effect dependent on age, dose and duration of treatment (3). But, Treatment for B_{12} deficiency in PCOS patient is not clearly justified. Moreover, no formal recommendations have been provided by the medical community. Hence the present study planned to observe the symptoms of metformin taking PCOS patient in relation to with or without vitamin B_{12} supplementation, retrospectively.

KEY WORDS: PCOS, Metformin, Vit B_{12}deficiency, Insulin Resistance.

II. AIM & OBJECTIVE:

❖ To observe the symptoms of metformin taking polycystic ovary syndrome patient in relation to with or without vitamin B12 supplementation, retrospectively.

III. METHODOLOGY:

Study Type: Retrospective - observational comparative study

Study Site: This **Retrospective- observational comparative study** was conducted at PSG medical sciences and research institute, Coimbatore. It is a multi-specialty 900 bedded tertiary care hospital located in the south region of Tamil Nadu.

Study Population: Patients were selected based on the statistical significance by using statistical software. 169 patients were selected for this study. In that patients were segregated in to four groups each group is having

Grouping:

- ❖ **Arm 1:** PCOS patient taking metformin with B12 supplement (vegetarian)
- ❖ **Arm 2:** PCOS patient taking metformin with B12 supplement (Non vegetarian)
- ❖ **Arm 3:**PCOS patient taking metformin without B12 supplement (vegetarian)
- ❖ **Arm 4:**PCOS patient taking metformin without B12 supplement (non-vegetarian)

Study Duration:

The study was carried out for seven months from April 2017 to June 2017

Study Approval:

The study was approved by Institutional Human Ethics Committee (IHEC) PSGIMS&R, Coimbatore. Approval number (IHEC- 17/120)

Source of Data:

- Medical record department (MRD)
- Patient Case Report Form (CRF)

Inclusion Criteria:

- ➢ Patient with PCOS taking metformin along with or without vitamin B12 supplementation

Exclusion Criteria:

- ➢ Pregnant women
- ➢ Patient with Severe renal and hepatic diseases
- ➢ Patient with neurological disorders

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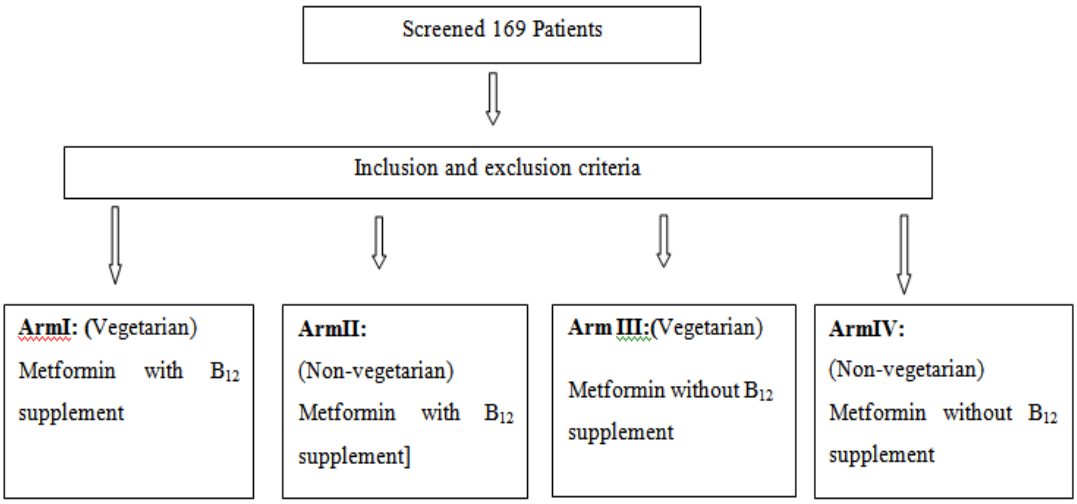
Study Chart:



IV. RESULTS:

PATIENT DEMOGRAPHICAL DATA

	Demographical details	
No of PCOS patients	169	
Age (n)	20-25 (49) 25-39 (74) 30-35 (46)	
BMI(n)	18.5-24.9(13) 24.9-30(86) >30(70)	
	Vegetarian(n) (76)	**Non Vegetarian(n) (93)**
Metformin alone	43	67
Metformin+B_{12} supplement	33	26

PATIENTS AFFECTED BY NEUROLOGICAL SYMPTOMS

Parameters	**Vegetarian**		**Non vegetarian**	
	Metformin alone(n)	Metformin+B_{12} supplement (n)	Metformin alone(n)	Metformin+B_{12} supplement (n)
Neurological symptoms	31	12	42	09

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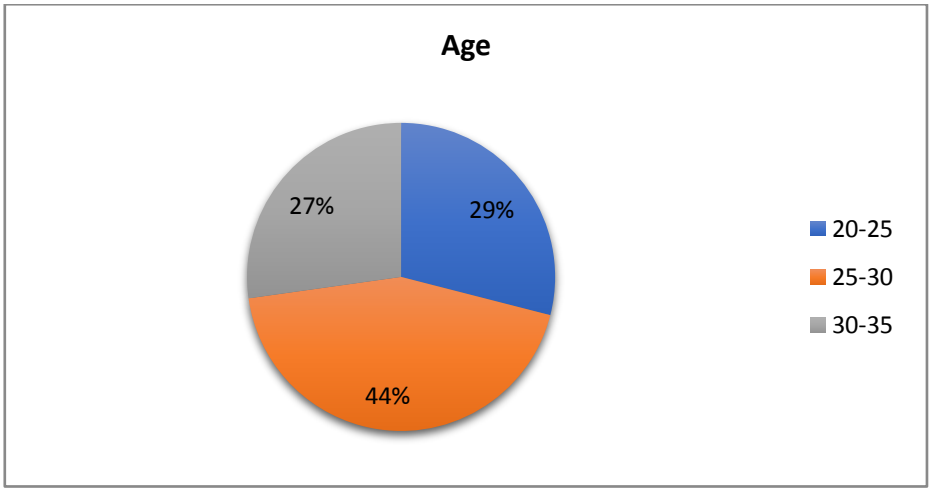
Percentage affected	72.1%	27.9.2%	62.6%	37.4%

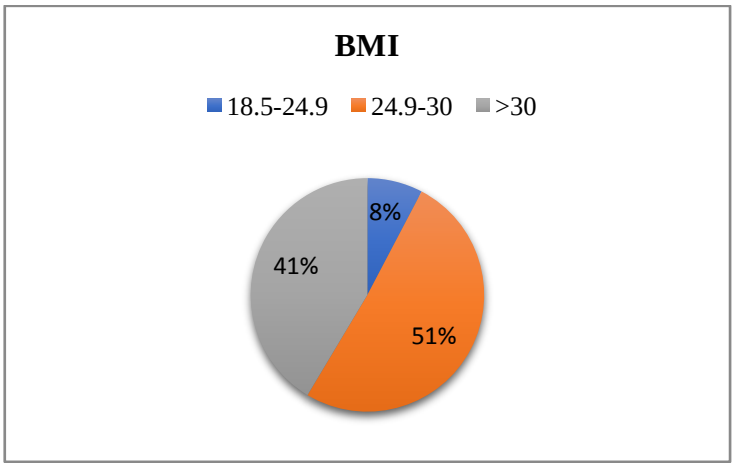
PATIENTS AFFECTED BY NEUROPSYCHOLOGICAL SYMPTOMS

Parameters	**Vegetarian**		**Non vegetarian**	
	Metformin alone(n)	Metformin+B12 supplement (n)	Metformin alone(n)	Metformin+B12 supplement (n)
Neuropsychological symptoms	13	04	09	02
Percentage affected	23%	12%	18%	7%

DEMOGRAPHICAL DETAILS
BASED ON THE AGE



BASED ON THE BMI



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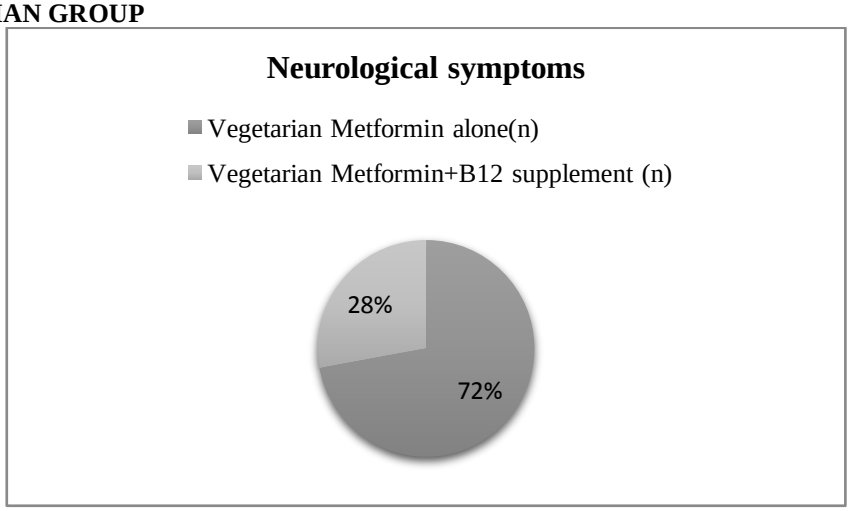
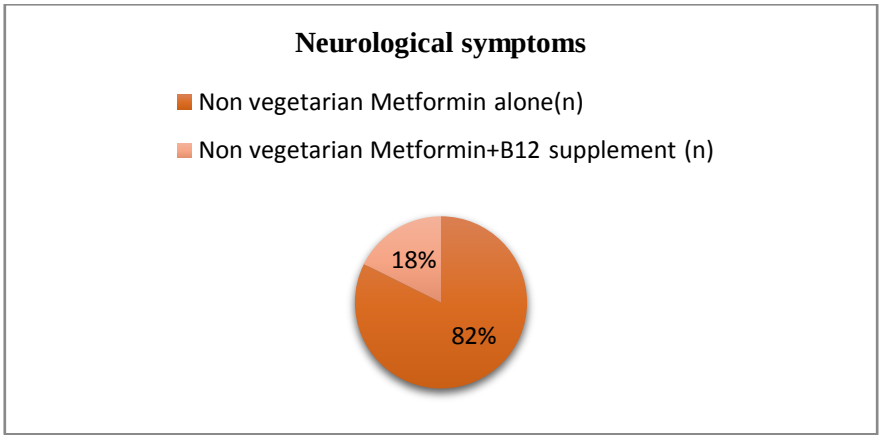
PERCENTAGE OF POLYCYSTIC OVARY SYNDROME AFFECTED BY NEUROLOGICAL SYMPTOMS

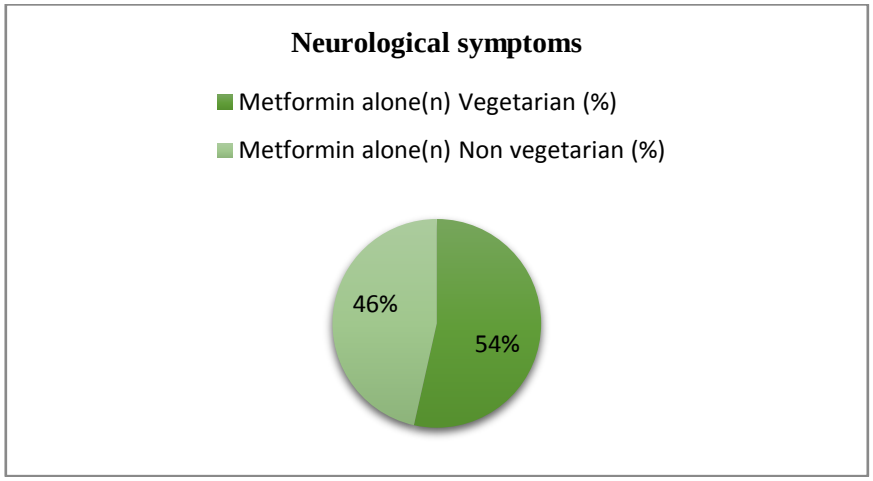
IN VEGETARIAN GROUP



IN NON-VEGETARIAN GROUP



IN METFORMIN GROUP



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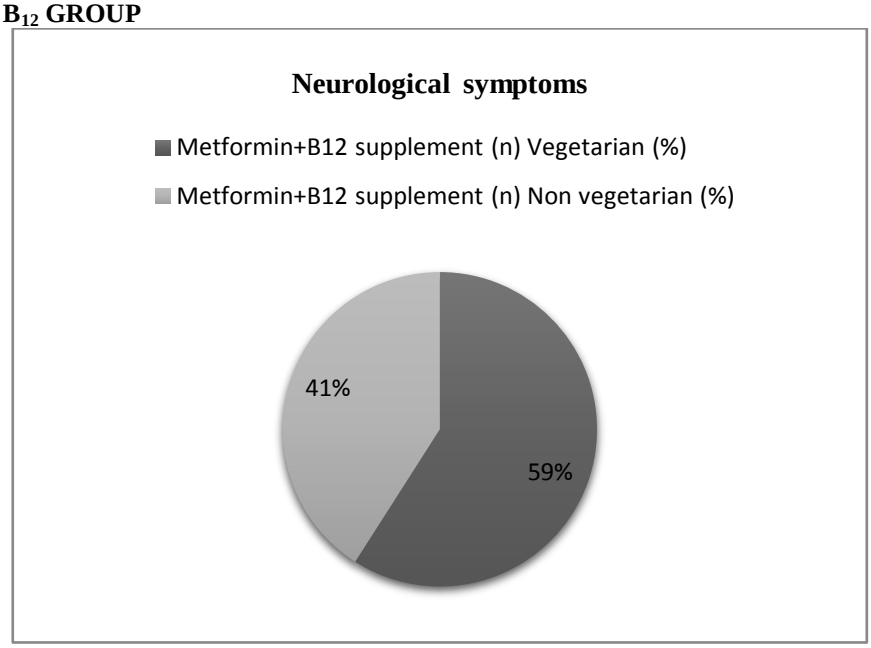
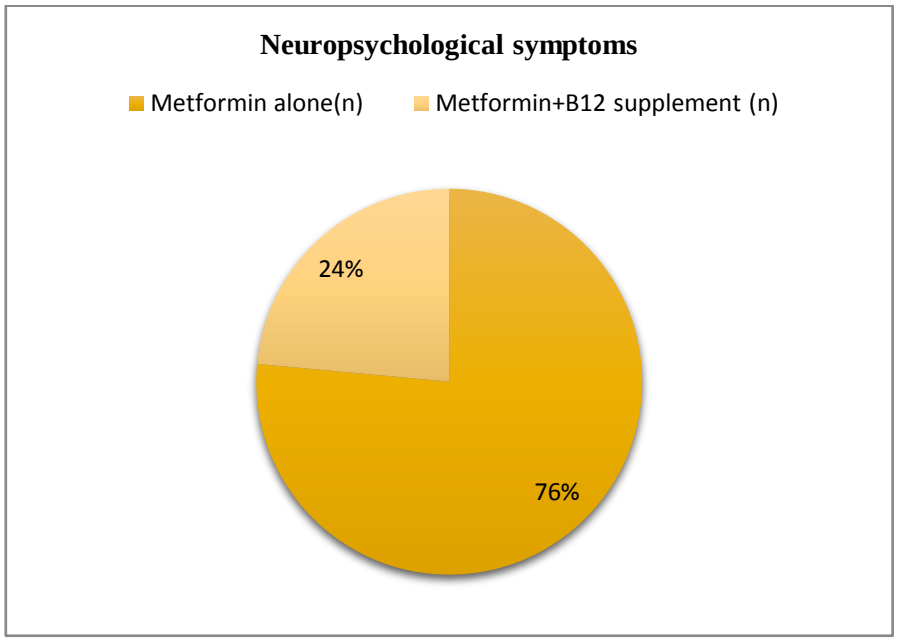
IN VITAMIN B_{12} GROUP



PERCENTAGE OF POLYCYSTIC OVARY SYNDROME AFFECTED BY NEURO-PSYCHOLOGICAL SYMPTOMS

IN VEGETARIAN GROUP



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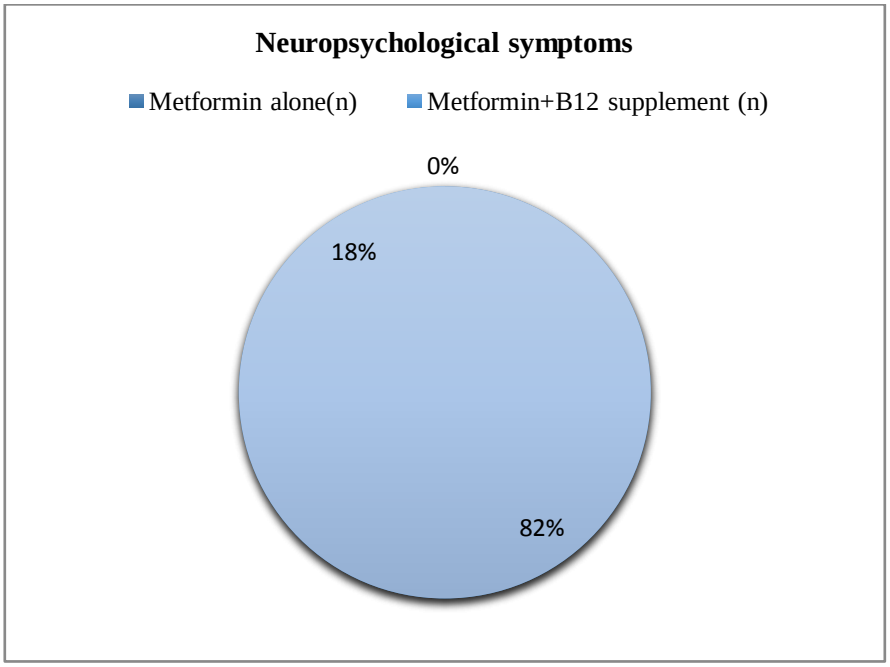
IN NON-VEGETARIAN GROUP



V. DISCUSSION:

That malabsorption of vitamin B12 occurs with metformin in 30% of diabetic subjects has been recognized for many years. This potentially debilitating side-effect of metformin was not well recognized in the United States when metformin was first approved in 1994. It was not until 2006 that the increased risk of vitamin B12 deficiency with metformin was rediscovered through a case-control study of Chinese patients which showed a correlation between the dose and duration of metformin use with vitamin B12 deficiency.

While vitamin B12 deficiency is associated with a macrocytic and megaloblastic anemia, the anemia is often preceded by the development of neuropathy. While the anemia of vitamin B12 deficiency is reversible, the progress of the neuropathy is only arrested and not reversed with initiation of vitamin B12 therapy. In the nervous system, vitamin B12 deficiency causes demyelination followed by axonal degeneration and neuronal death not only in peripheral nerves but also in the posterior and lateral columns of the spinal cord and the cerebrum. Clinically, the earliest manifestations are numbness and paraesthesia in the feet, which, unless the vitamin B12 deficiency is corrected, can be followed by weakness, ataxia, sphincter disturbance, and changes in mental status.

The mechanism of vitamin B12 deficiency with metformin is undoubtedly due to malabsorption of vitamin B12 at its absorption site in the terminal ileum. Initially, it was believed that metformin caused proliferation of bacteria in the small bowel either due to an effect on intestinal motility or an increased intestinal glucose level.However, the current and more likely explanation for metformin induced vitamin B12 malabsorption and deficiency is that metformin has an effect on calcium-dependent membrane action in the terminal ileum.Absorption of the vitamin B12-intrinsic factor complex is calcium dependent and metformin interferes with this absorption. In support of this hypothesis is evidence that dietary calcium supplementation reverses metformin induced vitamin B12 malabsorption.

The risk of adverse effects from metformin-induced vitamin B12 malabsorption will increase with the time of exposure to metformin since, after partial gastrectomy and removal of intrinsic factor, it takes twelve to fifteen years for vitamin B12 levels to become deficient.Therefore, in those patients who have been on long-term metformin, an annual vitamin B12 level should be obtained. Perhaps a more practical and cost-effective approach would be to give every patient on metformin an annual 1000 microgram injection of vitamin B12 which is sufficient to cover vitamin B12 needs for at least a year. An alternative therapy would be to prophylactically administer calcium carbonate (1.2 grams daily) which may also correct

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the "loose stools" associated with metformin therapy.

Rapid development of neuropathy due to vitamin B12 deficiency. The first case described of metformin-induced neuropathy due to metformin-induced vitamin B12 malabsorption.In conclusion, vitamin B12 malabsorption is a chronic complication of metformin therapy which can present with irreversible neuronal damage. On metformin therapy vitamin B12 levels should be checked on an annual basis. An alternative and a more practical and cost-effective method to avoid vitamin B12 deficiency would be an annual vitamin B12 injection that would provide more than the annual vitamin B12 needs for every patient on chronic metformin therapy**.**

VI. CONCLUSION:

In this study, non-vegetarian group has decreased neuropathic pain syndrome than vegetarian group. Since non vegetarian people have ability to synthesis the Vit B_{12} in their own. Also, neuropsychiatric symptoms have been increased in vegetarian group than non-vegetarian group which was reflection with deficiency of vitamin B_{12} in patients with PCOS taking Metformin.

SUMMARY:

From the study the following details were obtained

- Most of the patients having **PCOS** are also suffering from**HYPOTHYROIDISM.**
- The **PCOS** patients taking **Metformin** for a prolonged period of time are subjected to get **muscle pain & anemia** which is a result of Vitamin B12 deficiency.

It is important to prescribe **Vitamin B12 Supplementation** along with **Metformin** for **PCOS** patients in order to minimize the vitamin B12 deficiency symptoms.

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