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RESEARCH ARTICLE

EFFECT OF 12 WEEKS OF INTENSIVE LIFESTYLE INTERVENTION ON TYPE 2 DIABETES MELLITUS COMPLICATIONS

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Abstract

India is known as diabetic capital of the world and growing in age group between 20 and 70 years.The reason for rising prevalence of diabetes and other noncommunicable diseases are due to various factors like rapid urbanization, sedentary lifestyles, unhealthy diet and stress. Diabetes mellitus is a chronic, metabolic disease characterized by elevated levels of blood glucose, which leads to serious damage to the heart, blood vessels, eyes, kidneys and nerves**.** Symptoms of DM include increased thirst, frequent urination and increased appetite and complications includes microvascular, macrovascular, and neuropathic issues. Lifestyle Medicine is a medical specialty that uses lifestyle interventions as a primary modality to treat chronic conditions including, cardiovascular diseases, type 2 DM, and obesity. Lifestyle medicine clinician are the certified clinicians who are trained to apply evidence-based, prescriptive lifestyle changes to treat and, to reverse such chronic conditions. By applying the pillars of lifestyle medicine that are a whole plant-based food, physical activity, restorative sleep, stress management, and positive social connection provides effective prevention for these chronic diseases. Hence this study was undertaken to assess the effect of 12 weeks structured lifestyle intervention programmed on complications in chronic type 2 DM.

Introduction:-

India is known as the diabetic capital of the world and a growing incidence of DM in the age group between 20 and 70 years. The reason for rising prevalence of diabetes and other noncommunicable diseases are due to various factors like rapid urbanization, sedentary lifestyles, unhealthy diet and stress. In India, prevalence of diabetes mellitus is 9.3% among 18-69 yrs.(1) Diabetes mellitus is a chronic, metabolic disease characterized by elevated levels of blood glucose, which leads to serious damage to the heart, blood vessels, eyes, kidneys and nerves.(1)Symptoms of DM includeincreased thirst,frequent urination, andincreased appetiteand complications includes microvascular, macrovascular, and neuropathic issues. Acutecomplications arediabetic ketoacidosis,hyperosmolar hyperglycemia state, or even death. Chronic complications like cardiovascular disease,stroke,chronic kidney disease,foot ulcers,damage to the nerves,damage to the eyesandcognitive impairment. Depend on the duration of poorly controlled diabetes there are microvascular and macrovascular complications (include nephropathy, retinopathy, neuropathy, and ASCVD events). By diet modifications, regular exercise, proper sleep schedule and monitoring glucose level, better outcomes are seen. For controlling blood glucose and early detection of complications, regular screening is required. The treatment of diabetes is complex and successful management of disease requires a multitude of interventions. Patient education and engagement play most important

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role in management. Lifestyle Medicine is a medical specialty that uses lifestyle interventions as a primary modality to treat chronic conditions including, cardiovascular diseases, type 2 DM, and obesity. Lifestyle medicine clinician are the certified clinicians who are trained to apply evidence-based, prescriptive lifestyle changes to treat and, to reverse such chronic conditions. By applying the pillars of lifestyle medicine that are a whole plant-based food, physical activity, restorative sleep, stress management, and positive social connection provides effective prevention for these chronic diseases. Standard treatment protocols are insufficient to manage long standing DM and its complications. Incorporating lifestyle modifications along with standard treatment protocol increases the chances of better control over blood glucose and reduces the effects of hyperglycemia on other organ systems causing relapse of DM further leading to remission. Hence this study was undertaken to assess the effect of 12 weeks structured lifestyle intervention programmed on complications in chronic type 2 DM. (2)

Material and Methods:-

This is a Quasi-Experimental study (pre and post comparison without control) of 1 year duration conducted in D/o Physiology (Lifestyle intervention clinic) collaboration with D/o Ophthalmology at AIIMS Nagpur recruited 75 Patients with type 2 diabetes mellitus of >5yrs duration under following criteria.

Inclusion criteria

1. Age between 18-60 years of either gender
2. Known case of type 2 diabetes mellitus of >5yrs duration
3. HbA1C between 6.5% to 9.9%
4. Patient should be on a stable dose of oral antidiabetic medications during study period
5. Non hypertensive, non-smoker, non-alcoholic

Exclusion criteria

1. Recently diagnosed diabetes mellitus
2. HbA1C >10%
3. Pregnant and lactating women
4. Presence of associated psychiatric illness
5. Undergone recent surgery
6. Patients taking steroids
7. Failure to give informed consent.

After taking clinical history and anthropometry parameters, visual evoked potential and Optical coherence tomography done. Then lifestyle intervention session of 1.5hrs conducted. Followed by follow up on 15th day, 30days and 45 days done with biweekly follow up in between through telephonic/ WhatsApp group.

Statistical analysis plan:

The collected data entered into Microsoft excel spreadsheet. Jomovi 2.3.28 used for data analysis. Depending on the normality tests, parametric and non-parametric paired t test applied, that is student's t-test and Wilcoxon signed - rank test respectively for comparing pre(baseline) and post intervention parameters. P value <0.05 will be considered as statistically significant.

Result and Analysis:-

Table 1: - Nerve conduction studies.

Upper limbs	**Pre-I**	**Post-I**	**Pre-I**	**Post-I**	**Pre-I**	**Post-I**	**Pre-I**	**Post-I**
Variables	RIGHT LIMB (Median Nerve)		LEFT LIMB (Median nerve)		RIGHT LIMB (Ulnar nerve)		LEFT LIMB (Ulnar nerve)	
Latencies(ms)	2.95+0.953	2.83+ 1.01	2.92+ 0.862	2.63+ 0.85	2.51+1.02	2.75+ 1.09	2.5+ 0.685	2.31+ 0.559
Conduction velocity(m/s)	43.7+12.9	43.1+ 13.5	44+ 10.9	43+ 11.9	43+13.1	52.7+ 17.4*	46.1+ 10.2	45.8+ 11.1

Lower limbs	Pre-I	Post-I	Pre-I	Post-I	Pre-I	Post-I	Pre-I	Post-I
Variables	RIGHT LIMB (Peroneal nerve)		LEFT LIMB (Peroneal nerve)		RIGHT LIMB (Tibial nerve)		LEFT LIMB (Tibial nerve)	
Latencies(ms)	3.62+1.45	3.51+ 1.34	3.91+ 0.911	3.72+ 0.99	4.94+2.05	4.59+ 1.48	5.08+ 2.05	4.73+ 1.83*
Amplitude(ms)	5.97+3.99	5.97+ 3.45	6.68+ 2.84	6.33+ 2.52	11+5.53	10.1+ 4.56*	12.6+ 6.14	11.7+ 5.76*
Conduction velocity(m/s)	42.5+14.1	41.3+ 13.3	43.9+ 7.44	42.9+ 7.11	42.9+5.38	41.8+5.53	43.5+ 6.26	42.6+6.08

Pre-I=Preintervention, Post-I=Postintervention
*Statistically significant (<0.05)

Table 2: -Heart rate variability

(1) Time domain

Variables	Pre-I	Post-I
SDNN (ms)	30.1+39.7	23+12.4
RMSSD (ms)	27+63.1	16.7+10.3
pNN50(%)	3.83+9.29	1.54+4.46 *

Pre-I=Preintervention, Post-I=Postintervention, SDNN-Standard deviation of all NN intervals, RMSSD-Square root of the mean of the sum of the square of the differences between adjacent NN interval
*Statistically significant (<0.05)

(2) Frequency domain

Variables	Pre-I	Post-I
VLF (%)	47.6+18.5	51.1+17.9
LF (%)	28+13.7	25.6+12.6
HF (%)	23.2+14.7	20.7+13.8 *
LF/HF ratio	2.05+2.02	2.16+2.25

Pre-I=Preintervention, Post-I=Postintervention, VLF- very low frequency, LF- low frequency, HF-High frequency
*Statistically significant (<0.05)

Table 3: -Renal blood parameters

Variables	Pre-I Mdn (IQR)	Post-I Mdn (IQR)	Mean difference
Blood urea(mg/dl)	19.1(13.1)	19.3(12.6) *	1.25
Serum creatinine(mg/dl)	0.8(0.21)	0.9(0.29)	-0.04
ACR	25(17)	27(16)	-0.5

Pre-I=Preintervention, Post-I=Postintervention, ACR- Albumin creatinine ratio
*Statistically significant (<0.05)

Table 4: -Visual evoked potential and Optical coherence tomography

Table A**:** Visual evoked potential (Pattern).

VEP(Pattern)	Latencies(ms)		Amplitudes(mv)		Normal		Abnormal	
	Pre-I	Post-I	Pre-I	Post-I	Pre-I	Post-I	Pre-I	Post-I
RIGHT EYE	113.19+33.75	114.25+35.27	6.14+4.24	5.88+3.24	21(28%)	22(29%)	54(72%)	53(71%)
LEFT EYE	114.15+ 34.14	112.64+35.56*	5.33+3.23	5.21+2.65	20(27%)	20(27%)	55(73%)	55(73%)

Pre-I=Preintervention, Post-I=Postintervention
*Statistically significant (<0.05)

Table:Visual evoked potential (Flash).

VEP(Pattern)	Latencies(ms)		Amplitudes(mv)		Normal		Abnormal	
	Pre-I	Post-I	Pre-I	Post-I	Pre-I	Post-I	Pre-I	Post-I
RIGHT EYE	123+32.18	123.51+28.52	7.17+3.61	7.69+3.77*	45(60%)	47(63%)	30(40%)	28(37%)
LEFT EYE	123.07+36.84	119.59+33.89*	7.34+3.55	6.99+3.66*	47(63%)	44(59%)	28(37%)	31(41%)

Pre-I=Preintervention, Post-I=Postintervention
*Statistically significant (<0.05)

TableB**: -** Optical coherence tomography (OCT).
(1) Retinal nerve fiber layer (RNFL)

Variables	RIGHT EYE(RNFL)		LEFT EYE (RNFL)	
	Pre-intervention	Post-intervention	Preintervention	Postintervention
Normal	49(65.33%)	54(72%)	53(70.67%)	57(76.00%)
Thinning	13(17.33%)	16(21.33%)	10(13.33%)	8(10.67%)
Thickening	13(17.33%)	5(6.67%)	10(13.33%)	8(10.67%)
Cataract	0(0.00%)	0(0.00%)	2(2.67%)	2(2.67%)

(2) Central macula thickness(μm)

Variables	Pre intervention Mdn (IQR)	Post intervention Mdn (IQR)	Mean difference
RIGHT EYE	262(36)	261(30) *	1.5
LEFT EYE	261(33)	261(33.5)	1.5

*Statistically significant (<0.05)

Discussion:-

Diabetes is a chronic metabolic disease that leads to elevated levels of blood glucose that results in serious complications of the heart, blood vessels, eyes, kidneys and nerves. The pathologic hallmark of DM involves the vasculature leading to both microvascular and macrovascular complications. Diabetic neuropathy (DN) - most common complication of T2DM, can lead to axonopathy. (3)Diabetic retinopathy (DR)- most common causes of severe vision loss in adults with diabetes. T2DM leads to microvascular alterations in the retinal capillary network, microaneurysms, intraretinal microvascular abnormalities, and neovascularization. (4)Diabetic nephropathy- One of the most feared diabetic chronic microvascular complications and the major cause of end stage renal disease (ESRD). T2DM affects kidney by hyperfiltration and albuminuria in the early phases which is then followed by a progressive renal function decline. Blood urea nitrogen, serum creatinine are elevated in nephropathy.(5) Cardiac autonomic neuropathy, a macrovascular complication of Diabetes. Altered glucose metabolism leads to affect both sympathetic and parasympathetic activities, leading to cardiac autonomic neuropathy.(6)

Microvascular complications of diabetes are those long-term complications affecting small blood vessels. These typically include neuropathy, retinopathy, nephropathy.

1. Diabetic neuropathy (DN) is a common peripheral nerve dysfunction disorder and one of the commonest causes of peripheral neuropathy. This complication of DM can lead to more frequent hospital visit than other complications of diabetes and also is the most frequent cause of non-traumatic amputation. (3) Median, ulnar, and peroneal are most commonly affected nerves. Nerve conduction studies (NCS) are important methods of documentation and follow up of nerve functions in DN. The commonest abnormality in diabetes seen in NCS is reduction in the amplitudes of motor or sensory action potentials because of axonopathy. Demyelinating neuropathy, a pronounced slowing of NCV, is rarely associated with diabetes; therefore, should prompt investigations for an alternative diagnosis. (3)
2. Diabetic retinopathy (DR) is a microvascular disorder occurring due to the long-term effects of diabetes mellitus and most common cause of severe vision loss in adults. Diabetic retinopathy may lead to vision-threatening damage to the retina, eventually leading to blindness. (7) The neurophysiological techniques help to assess retinal and nervous (optic tract) function. In visual evoked potential (VEP), the changes in latency of waves and the amplitude of the P100 wave have been observed in patients with diabetic retinopathy, which proved the importance of this study with the possibility to examine the prognosis of this disabling disease. (8) Diabetic macular oedema (DME) is a major cause of decreased visual acuity in patients with diabetic

retinopathy. Optical coherence tomography angiography (OCTA) has been developed to visualize the retinal microvasculature and choriocapillaris based on the motion contrast of circulating blood cells. This enables quantification of microvascular alterations in the retinal capillary network, with the detection of classical features associated with DR, includes microaneurysms, intraretinal microvascular abnormalities, and neovascularization. (4)

3. Diabetic nephropathy is the most feared of the diabetic chronic microvascular complications and the major cause of end-stage renal disease (ESRD). The classical presentation of diabetic nephropathy is characterized by hyperfiltration and albuminuria in the early phases which is then followed by a progressive renal function decline. Blood urea nitrogen (BUN)- A waste product of thedigestionof protein produces urea. Normal human adultbloodshould contain 7 to 18 mg/dL (0.388 to 1 mmol/L) of urea nitrogen. The test is used to detectkidneyproblems .Serum creatinine- An important indicator ofkidneyhealth, because it is measured byproduct of muscle metabolism that is excreted unchanged by the kidneys. The reference interval is 0.6–1.3 mg/dL (53–115 μmol/L). Albumin to creatinine ratio (ACR)- also called as urine microalbumin, albumin detected in the urine may represent a sign of kidney disease. Urine albumin-to-creatinine ratio (UACR) is most frequently applied to diagnose albuminuria. Normal level of UACR is below 30 mg/g.(5)

Macrovascular complications- Cardiac autonomic neuropathy, a macrovascular complication of Diabetes can be studied by one of the parameters of autonomic function tests that is heart rate variability (HRV), a reliable reflection of many physiological factors modulating the normal rhythm of the heart and gives information of the sympathetic and parasympathetic nervous systems. (26) In T2DM, an overall decrease in the HRV parameters (time domain and frequency domain). Altered glucose metabolism affects both sympathetic and parasympathetic activities, leads to cardiac autonomic neuropathy. (6)

Lifestyle Medicine is a medical speciality that uses therapeutic lifestyle interventions as a primary modality to treat chronic conditions including, cardiovascular diseases, type 2 DM, and obesity. Lifestyle medicine physician are certified clinicians who are trained to apply evidence-based, whole-plant based, prescriptive lifestyle changes to treat and, when used intensively, reverse such conditions. Applying the pillars of lifestyle medicine—a whole plant-based food, regular physical activity, restorative sleep pattern, stress management, and having positive social connections—provides effective prevention for these conditions. (2) Diabetes-protective lifestyle' is the keys for diabetes prevention and control. Getting blood glucose level under control can't just reverse the complications of diabetes mellitus but also can prevent further damage from occurring. With change in Lifestyle (lifestyle modification) and on metformin medication, both reduced the incidence of high risk of diabetes but the lifestyle intervention was more effective than metformin. (9)The available evidence from RCTs shows that lifestyle intervention is more effective than the standard care regarding the glycaemic control of type 2 diabetic patients. (10)

We aimed to assess "the effect of intensive lifestyle intervention program on T2DM complications". Our study was a quasi- experimental study. A total 75 patients of DM of>5yrs durations were included. This study was conducted from January 2023 to June 2024 in Department of Physiology in collaboration with Department of Medicine and Department of Ophthalmology at AIIMS Nagpur.

Most common complication of diabetes is diabetic neuropathy (DN). Lifestyle modifications like regular exercise, maintaining a healthy weight through diet, and managing blood sugar levels can improve diabetic neuropathy by reducing oxidative stress, improving blood flow to the nerves, promoting nerve regeneration, and mitigating the damage caused by high glucose levels, ultimately leading to a decrease in neuropathic pain and improved nerve function.In our study, for diagnosis of neuropathy, nerve conduction studies of sensory median and ulnar nerves and motor peroneal and tibial nerves were done. Comparing difference of peripheral neuropathy severity, mild changes were seen in latencies, amplitudes and conduction velocities of different nerves but overall mixed (axonal and demyelinating) neuropathy incidence increased. The study by Haleh Ghavamiet al. (2018) did the same study with control and intervention group for 12 weeks and demonstrated significant change in intervention group with neuropathy.(3) More adherence to whole food plant-based diet with regular exercise required to see a significant changes in DN.Diabetic nephropathy is a potentially fatal microvascular complication of diabetes. Lifestyle modifications like weight loss, regular exercise, a healthy diet low in sodium, low protein diet and saturated fat can improve diabetic nephropathy by helping to control blood pressure, blood sugar levels, and inflammation, which are key factors in the progression of kidney damage associated with diabetes and ultimately slowing down the deterioration of kidney function in patients with diabetic nephropathy. Abnormalities in renal structure and function

have been noted in obese individuals. The most commonly structural abnormalities are glomerulomegaly, mesangial expansion and sclerosis, and podocyte abnormalities, including a specific form of focal segmental glomerulosclerosis (FSGS) known as obesity-associated FSGS.Functional abnormalities include glomerular hyperfiltration and proteinuria. Long term regular exercise has been shown to improve proteinuria in diabetes.(11) In our study renal function was assess by blood urea ,serum creatinine and ACR of which blood urea showed the significant results .The study by Li Donget al.(2019) ,did a follow up study of 3 and 6months between intervention and control group and a study by Elizabeth P Nealeet al. (2023) analysed the records of different studies based on diabetes nephropathy and lifestyle modification demonstrated significant reductions in urine ACR, serum/urine , serum creatinine. (12) Lifestyle modification been a promising cost-effective therapeutic adjunct to pharmacologic treatment of kidney disease incidence and progression.Diabetic retinopathy (DR) is a devastating complication of individuals with type 2 diabetes mellitus and can lead to blindness due to microangiopathy and neuropathy because of metabolic abnormalities and intraneural blood flow disorders. Assessment of diabetic visual pathway impairment and fundus examination was done by VEP and OCT. (13) In our study with the lifestyle modification in dietary pattern, regular exercise, healthy sleep schedule and stress management showed mild improvement in PRVEP and FVEP with no major changes in retinal nerve fibre layer and central macula thickness. From this we can infer that lifestyle modifications play a crucial role in improvement of retinopathy.The study by Aleix Sala-Vila el al. (2016) and A. Aro el al.(2019) reported that dietary involvement of LCω3PUFA , lifestyle changes with involvement of exercise and healthy diet is associated with a reduced incidence of severe DR in individuals with type 2 diabetes and can lead to significant reduction of retinal microaneurysm , macular oedema.(14)Dietary changes like including nitrates, a dietary source found in dark leafy greens (represents 80% of nitrate intake), are converted to nitric oxide once ingested. Nitric oxide has a protective action against DR as it causes vasodilation and increased blood flows to eye vessel. Omega-3 fatty acids in diet also improve systemic microcirculation and ocular blood flow which leads to improve ocular health. Another study by María el al. (2015) , Yaun et al. reported that oxidative stress causes optic nerve injury so the fruits and vegetables with high antioxidants act as neuroprotection from oxidative stress, affecting the cell and tissue morphology and its functions, leads to cell death, which has an important role in the pathogenesis of retinal diseases .The study by Soleimani et al. (2023) and Pan et al. (2020) each reported that 5000 steps daily or two and half hours of non-sedentary life reduced the visual field progression significantly by 10%.(15)Every additional 10 minutes of evening activity per day, leads to a slowing the rate of ganglion cell-inner plexiform layer thinning.(16) And exercise also improves blood flow throughout the body including the eyes, which helps in deliver nutrients for collagen production. Stress reduction techniques like yoga and meditation have a positive impact on eye health as because of high stress, hormones like cortisol and adrenaline that cause insulin resistance, which can raise your blood sugar and increase risk of diabetes retinopathy.(17) So, Relaxation techniques, such as meditation, yoga, deep breathing and mindfulness along with positive social connection with family and friends and good sleep can help individuals to relax the body and manage their pain in a better way.But, a 12 week-long intervention might not be a sufficient time period to see any significant changes in diabetic retinopathy, hence more follow up is warranted.

Cardiac autonomic neuropathy (CAN) is a result of impaired autonomic function and subsequent nervous system imbalance of the cardiovascular system that occurs as a result of diabetes. Diabetes is the most common cause of CAN globally. Alterations in autonomic function result in an increased risk of cardiac arrhythmias and cardiovascular events, including acute myocardial infarction.This risk can be observed through abnormal surface measures of cardiac repolarization, including an increase in the corrected QT interval. Increases in QT interval in progressive CAN have been correlated to an increased risk for sudden cardiac death. Indeed, intraoperative instability and silent myocardial ischemia and infarction are all associated with CAN.A reduction in parasympathetic autonomic tone is primarily observed in early CAN as measured through CARTs and indicated by a blunted heart rate variability (HRV). As a result, there is a sympathetic predominance, reflected by a higher resting heart rate. Imbalance of the autonomic nervous system develops early in CAN pathogenesis and is associated with increased cardiovascular risk prior to definitive CAN development. Sympathetic predominance is exacerbated by insulin resistance, a feature of type 2 diabetes. (18)In our study, we analyzed the CAN on basis of time and frequency domain. There is reduced HRV (decreased LF and HF) and sympathetic dominance was seen based on LF/HF ratio. The study by Thomas Benichouel al. (2018) did a systematic review and meta-analysis of total twenty-five case-control studies and found similar results as lower RR-intervals, lower SDNN, lower RMSSD, lower pNN50, lower total power, lower LF and lower HF but there LF/HF did not differ between groups. Overall, from our study we concluded that, both sympathetic and parasympathetic activity were altered with decrease in the HRV parameters, reasons for altered sympathetic and parasympathetic activity due to altered glucose metabolism

leading to cardiac autonomic neuropathy. More adherence and follow up required to improve HRV parameters and parasympathetic activity as 12 weeks is not a sufficient time period.

Overall, we concluded that diet and lifestyle modification (regular physical exercise, restorative sleep pattern, stress management and positive social connection) remain the cornerstone of the management of diabetes. Consuming foods with low glycaemic index, high in fibre and fruits, less sodium, lots of veggies, lean protein, long-chain ω-3 polyunsaturated fatty acids (LCω3PUFAs), which has anti-inflammatory and antiangiogenic properties, low fat dairy, low in saturated fat, trans fat is digested more slowly and gradually rise sugar spike. Regular exercises and being physically active help body to use insulin more efficiently by muscles and makes the body more sensitive to insulin which helps to burn glucose and improves insulin sensitivity. Exercise also improves circulation which relieves pain, improves muscle strength and controls blood sugar levels, that prevent muscle loss and helps with good quality of sleep. Relaxation techniques, such as meditation, yoga, deep breathing and mindfulness can help individuals manage their pain in a better way and help to relax the body and mind along with positive social connection with family and friends. Including all the lifestyle modifications not only helps in getting blood glucose level, lipid profile or inflammation under control but also has a positive impact with better quality of life and reduced risk in complications of diabetes.

In our study, improvement in quality of life was seen when pre and post intervention groups were compared. Dosage of medications were reduced with decrease in economic burden related to treated for diabetes. Patients experienced more positivity and good mood to do day-to-day activity. Through this study, in many patients who were asymptomatic of complications, early detection of complications was possible so that further precautions can be taken. But, a 12 week-long intervention might not be a sufficient time period to see any significant changes in diabetic complications, hence more follow up and more adherence is warrantedfor significant changes.

Authentication
The study conducted after the Institutional ethics committee approval.

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Any cost incurred by the patients for additional investigations during the study was given by the principal investigator.

Conflicts of interest
There are no conflicts of interest.

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