

Vitamin D deficiency in Diabetic Peripheral neuropathy : Prevalence, repletion and treatment outcomes

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Entrance



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NAGPUR : HOTTEST CITY



? VITAMIN D DEFICIENCY

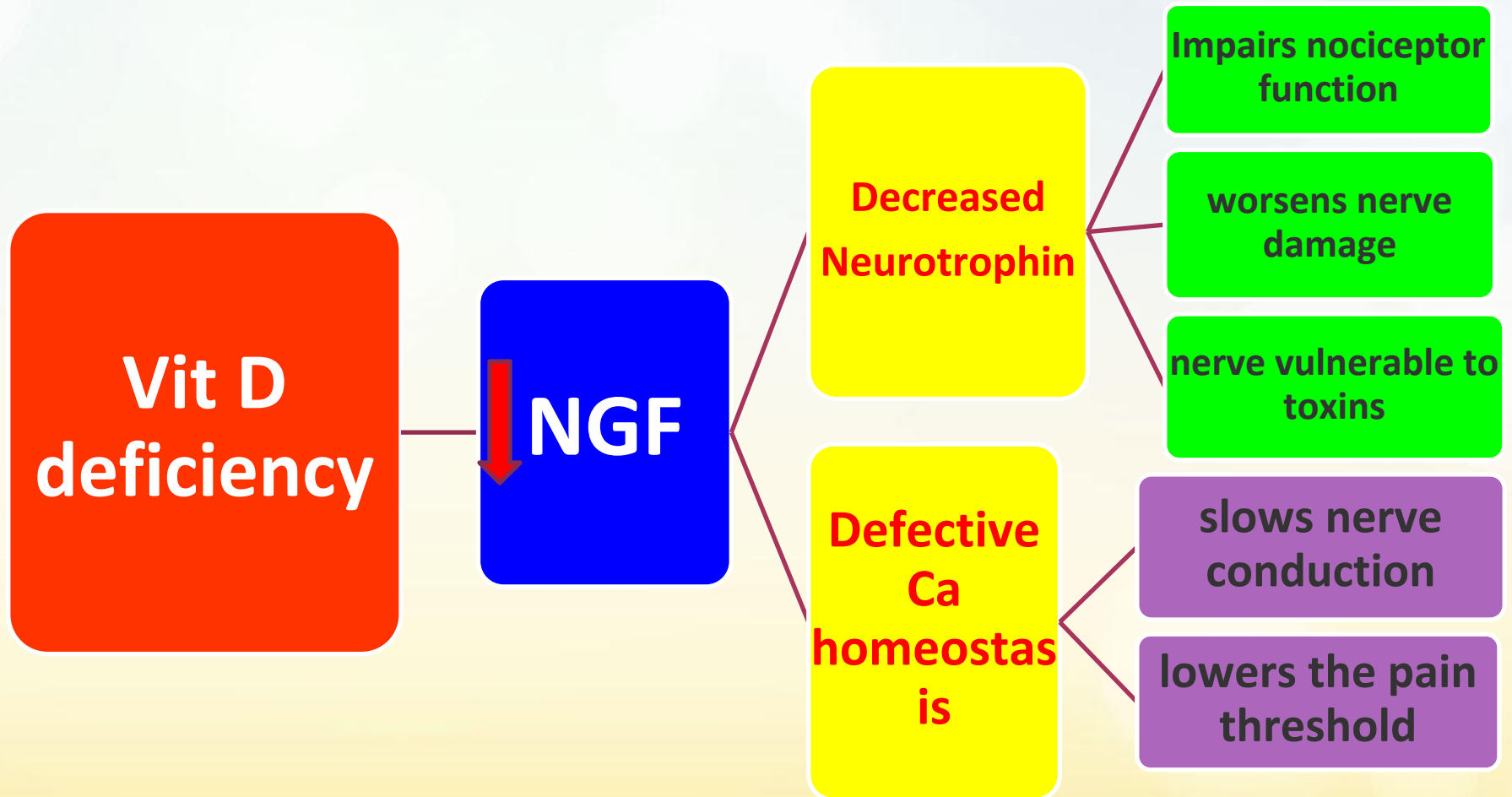
Introduction

- Vitamin D (Vit D) is a multifunctional pro-hormone.
- Effects of vitamin D go beyond its relationship with bone metabolism.
- Vitamin D deficiency : neuropathy and severity of the symptoms in type 2 diabetes.
- Vitamin D deficiency : Increased incidence of plantar ulcers.

Actions of Vitamin D on glucose metabolism

- Improved insulin exocytosis, direct stimulation of insulin receptor, improved uptake of glucose by peripheral tissues, improving insulin resistance.
- Stimulation of neurotropic factors like nerve growth factor, Glial cell line-derived neurotrophic factor, neurotrophin.
- Vitamin D is implicated in many ways in the pathogenesis of diabetic retinopathy, neuropathy and nephropathy.

Vit D deficiency and Neuropathy



Vit D deficiency : ? Independent risk factor for Neuropathy

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[Does Vitamin D deficiency play a role in peripheral neuropathy in Type 2 diabetes?](#) Shehab D et al. Diabet Med. (2012)

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- [Serum 25-hydroxyvitamin D levels and **peripheral neuropathy** in patients with **type 2 diabetes**: a systematic review and meta-analysis.](#)

1.

Lv WS, Zhao WJ, Gong SL, Fang DD, Wang B, Fu ZJ, Yan SL, Wang YG.

J Endocrinol Invest. 2015 May;38(5):513-8. doi: 10.1007/s40618-014-0210-6. Epub 2014 Dec 21.

PMID: 25527161

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2.

Bajaj S, Singh RP, Dwivedi NC, Singh K, Gupta A, Mathur M.

Indian J Endocrinol Metab. 2014 Jul;18(4):537-41. doi: 10.4103/2230-8210.137512.

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3.

Putz Z, Martos T, Németh N, Körei AE, Vági OE, Kempler MS, Kempler P.

Curr Diab Rep. 2014 Oct;14(10):537. doi: 10.1007/s11892-014-0537-6. Review.

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Abstract ▾

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Arch Intern Med. 2008 Apr 14;168(7):771-2. doi: 10.1001/archinte.168.7.771.

Vitamin D as an analgesic for patients with type 2 diabetes and neuropathic pain.

Lee P, Chen R.

PMID: 18413561 [PubMed - indexed for MEDLINE]



Publication Types, MeSH Terms, Substances



LinkOut - more resources



Research Question

- What is the Prevalence of Vitamin D deficiency in patients with Diabetic Peripheral Neuropathy (DPN) in Type 2 DM in our Diabetes Clinic ?

Hypothesis

- Treatment of Vitamin D deficiency decreases pain in Painful Diabetic Neuropathy.

Aims & Objectives

1. To determine the prevalence of Vitamin D deficiency in patients of T2DM with peripheral neuropathy (DPN).
2. To correlate Vitamin D levels with other risk factors for DPN.
3. To replenish Vitamin D and study the effect on pain in patients with painful DPN as assessed by Visual analogue scale (VAS) before and after treatment.

Material and Methods

STUDY DESIGN : Prospective Interventional cohort study

STUDY SETTING : Diabetes Clinic

STUDY PERIOD: Jan 2015 to March 2015 (3 months).

DATA ANALYSIS : 1 month

SAMPLE SIZE : 340 Screened (300 included)

Methodology

- Cases : Patients with Type 2 DM by WHO criteria with Peripheral neuropathy
- Peripheral neuropathy : Biothesiometry and Toronto clinical neuropathy score
- Vitamin D levels
- Risk Factor evaluation
- Pain quantification by Visual Analogue Scale (VAS) pre and post repletion
- Vit D repletion with continuation of standard care.
- Re-estimation of Vit D levels after 2 months 15 days

Vit D levels in ngm/ml	Interpretation	
0-20	Deficiency	Vit D deficiency
21-30	Insufficiency	
> 30	Sufficiency	
> 50	Excess	
>100	Toxicity	

VISUAL ANALOGUE SCALE FOR PAIN EVALUATION IN DPN



No pain



**Worst pain
ever**

0 1 2 3 4 5 6 7 8 9 10

Analysis

- Prevalence : Comparison of Vit D levels in those with and without DPN
- Comparison of Vit D levels in painful Vs. painless neuropathy
- Correlation with risk factors for DPN and severity
- Comparison of Pain by VAS before and after replenishment of Vit D
- Statistical Analysis : Student t test, Fishers exact test, Mid P test and Chi square test, ANOVA.

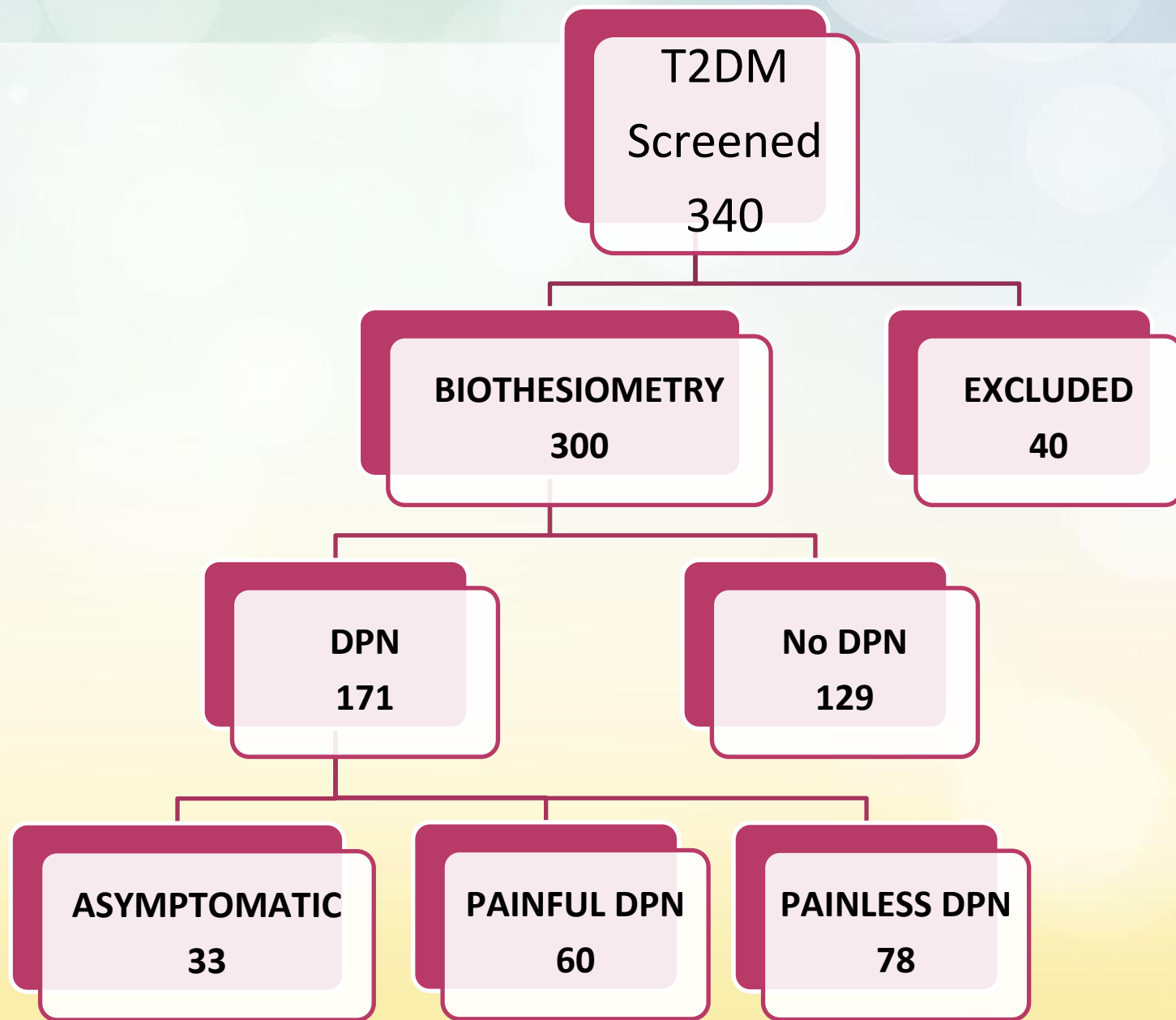
P <0.05 – Statistically Significant, p<0.001, highly significant

Limitations of the study

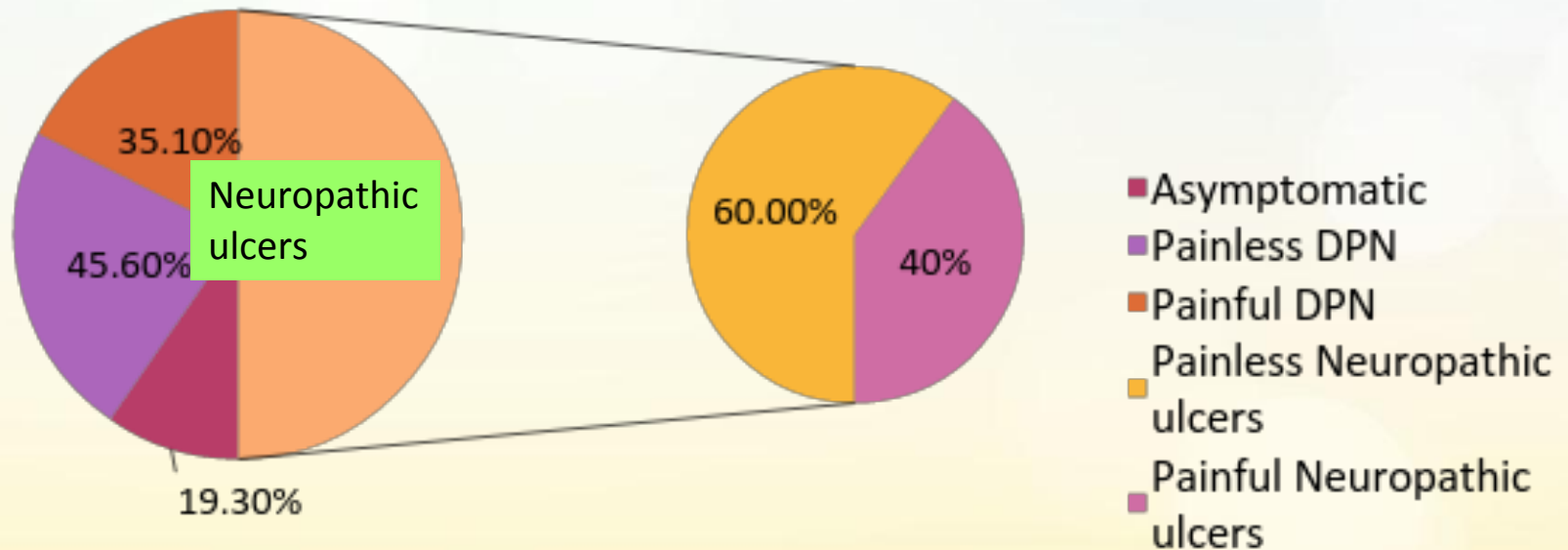
- Short term study
- Not a blinded study
- Possibility of treatment bias
- Investigations like iPTH , Calcium , Phosphorus levels not done

Results

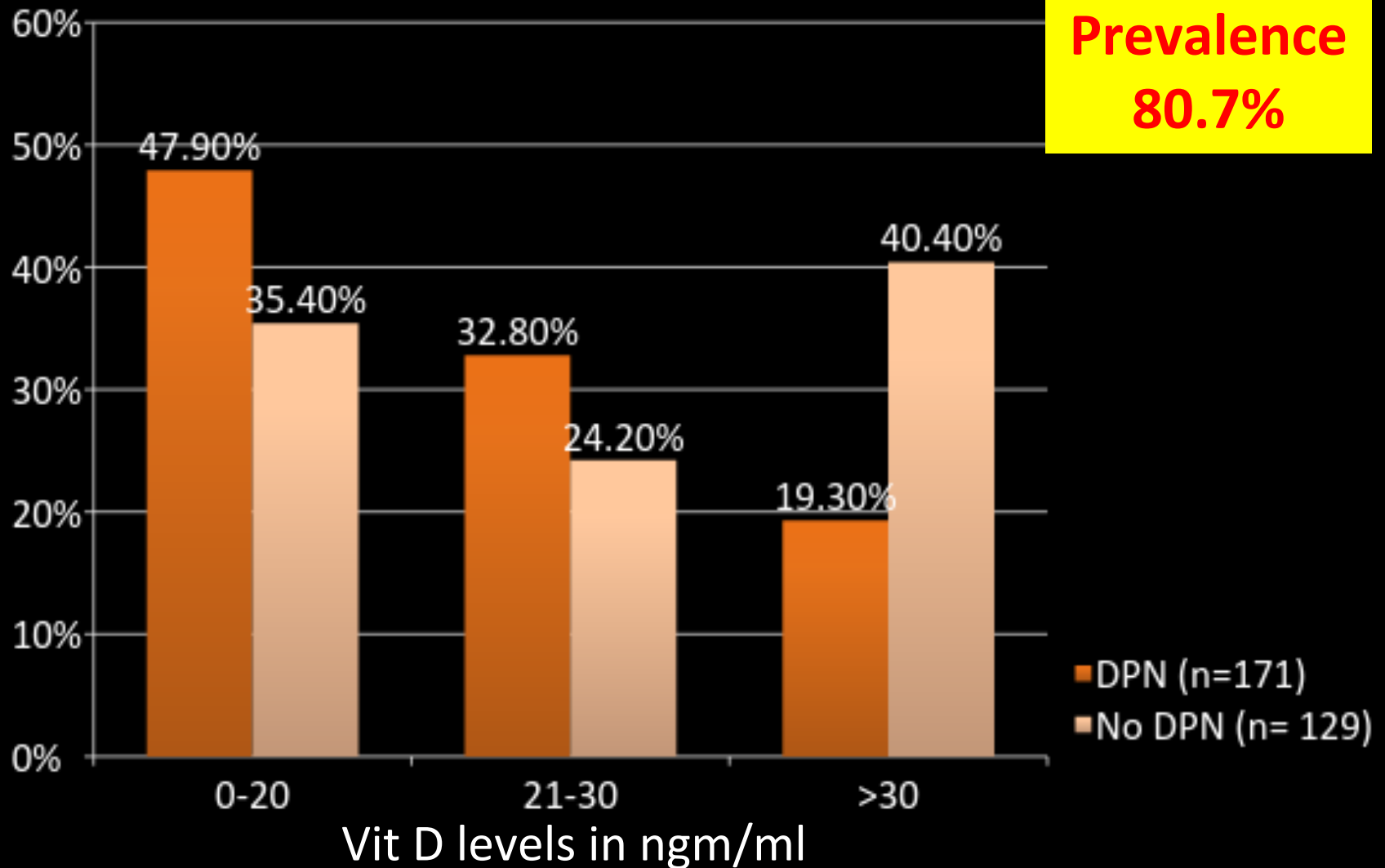
- Total no. of patients with Diabetes screened for Vitamin D deficiency = 340
- Patients excluded due to concomitant deficiencies : 40
- Total No. of patients screened for DPN = 300
- No. of patients without DPN – 129
- No. of patients with DPN – 171



Type Of Diabetic Neuropathy



Prevalence Of Vit D Deficiency In DPN



Vitamin D levels in T2DM

S.N.	Vit D levels ngm/ml	DPN (n=171)	No DPN (n=129)	p-value
1	0-20	82 (47.95%)	42 (35.35%)	0.003
2	21 -30	56 (32.75%)	31 (24.24%)	0.040
3	>30	33 (19.30%)	56 (40.41%)	0.001
4	Mean	17.99 ± 4.6	26.19 ± 6.3	<0.001

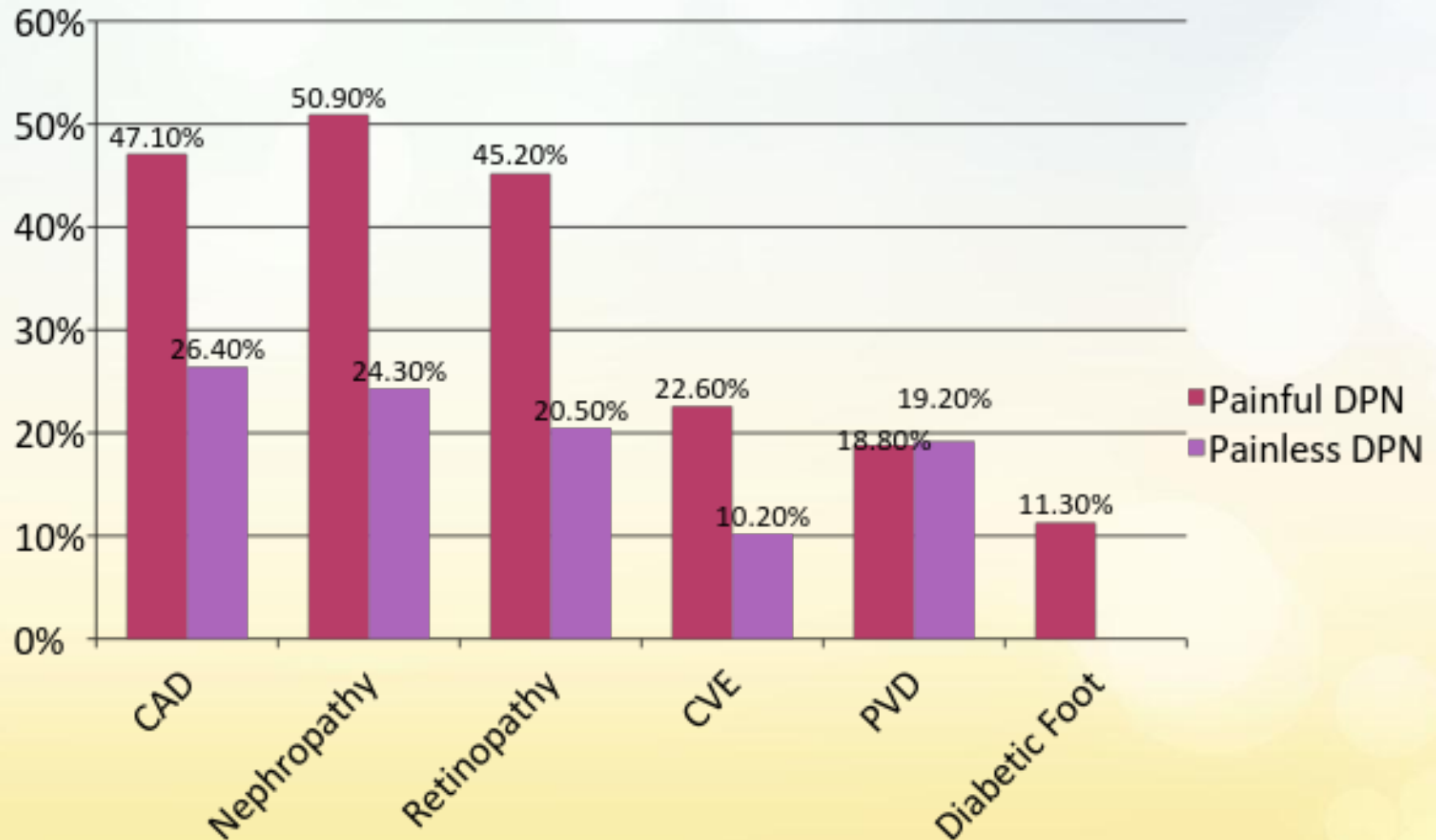
Baseline Characteristics

S.N.	Clinical Feature	Painful DPN (n=60)	Painless DPN (n=111)	p-value
1	Age	64.65 \pm 9.45	58.25 \pm 9.89	NS
2	M : F	1 : 1.5	1 : 1.03	p<0.05
3	BMI	25.82 \pm 3.38	24.76 \pm 1.12	NS
4	Smoking	28.3%	30.7%	NS
5	Alcoholism	37.7%	37.1%	NS
6	Hypertension	71.6%	64.1%	p<0.05
7	Dyslipidemia	63.6%	58.5%	p<0.05

Diabetic Status

S.N.	Parameter	Painful DPN (n=60)	Painless DPN (n=111)	p-value
1	Duration of Diabetes	8.46 ± 4.9	4.51 ± 2.8	<0.001
2	Treatment			
	OAD s alone	52.8%	79.4%	
	Insulin + OAD	30.1%	12.8%	
	Insulin alone	16.9%	7.6%	
3	Glycemic status			
	Fasting PG	156.71 ± 40.3	117.36 ± 19.1	<0.05
	Post prandial PG	256.35 ± 61.6	223.18 ± 41.72	NS
	HbA1C	9.6 ± 1.04	8.73 ± 1.51	NS

Complications of Diabetes



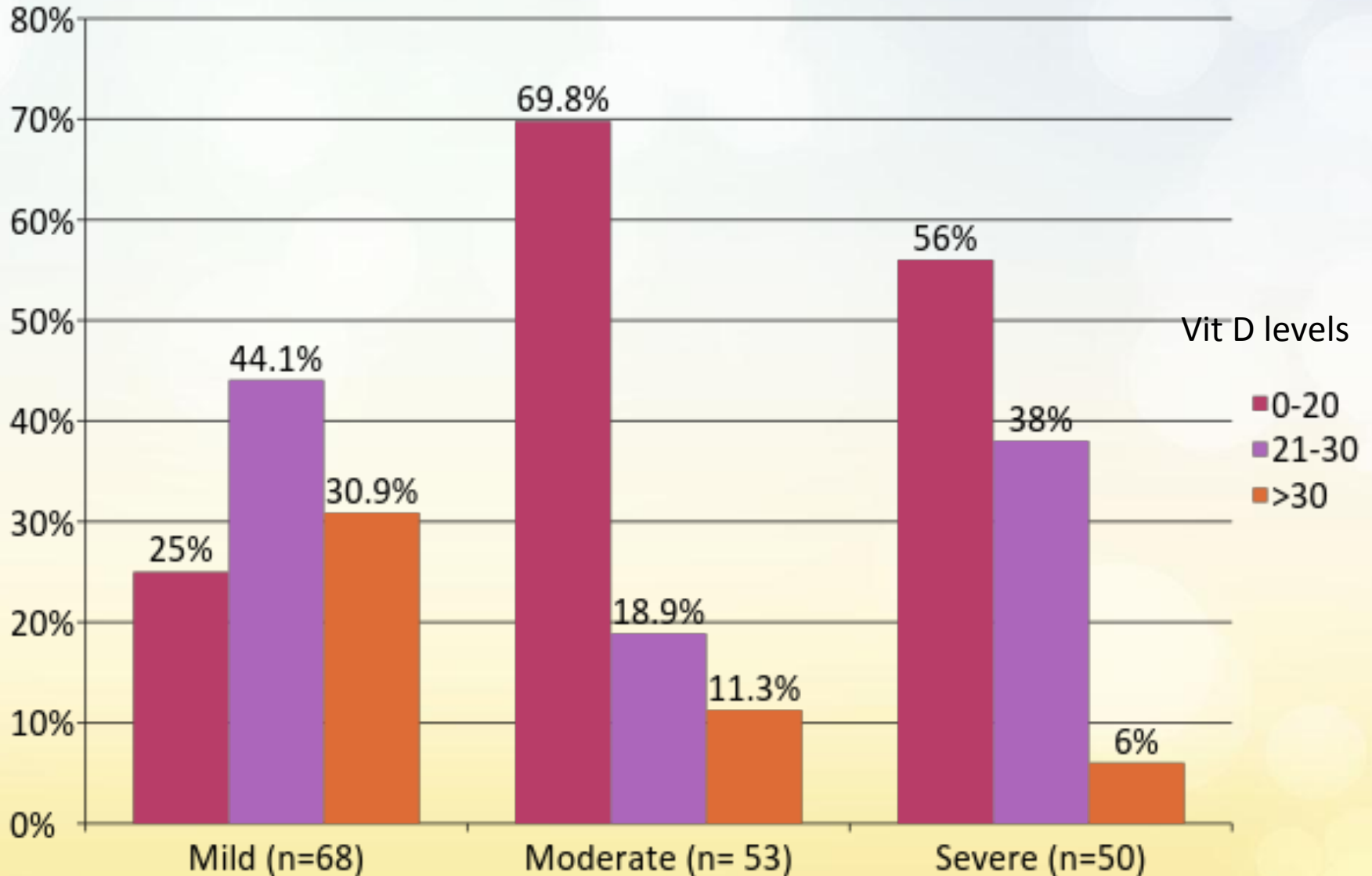
Vitamin D levels in Painless vs. Painful Neuropathy

Vit D levels ngm/ml	Asympt. (n= 33)	Painless DPN (n=78)	Painful DPN (n=60)	Total (n=171)	p-value
0-20	6 (18.2%)	40 (51.3%)	36 (60%)	82	<0.001
21 -30	8 (24.2%)	31 (39.7%)	17 (28.3%)	56	0.18, NS
>30	19 (57.6%)	7 (10.0%)	7 (11.7%)	33	<0.0001
Mean	31.96 + 7.4	18.01 + 5.3	13.88 + 2.6	171	<0.001

Vitamin D levels and Severity of DPN

S.N.	Vit D levels ngm/ml	Mild (n=68)	Moderate (n=53)	Severe (n=50)	p-value
1	0-20	17 (25%)	37 (69.8%)	28 (56%)	<0.001
2	21 -30	30 (44.1%)	10 (18.9%)	19 (38%)	0.012 <0.05
3	>30	21 (30.9%)	6 (11.3%)	3 (6%)	0.002 <0.05
4	Mean	26.02 ± 3.9	17.30 ± 5.1	14.76 ± 4.8	<0.001 ANOVA

Vit D levels and Severity of DPN



Correlation of Vit D deficiency with Risk factors for Neuropathy

S. N.	Risk Factor	Vit D Deficiency	Vit D Sufficiency	p-Value
1	Mean Age	67 ± 7.5	56 ± 11.8	<0.05
2	M : F	1 : 1.3	1 : 0.8	< 0.05
3	BMI	26.01 ± 2.14	24.32 ± 1.67	NS
4	Smoking	20.2%	18.1%	NS
5	Alcoholism	34.7%	24.2%	<0.05
6	Hypertension	68.1%	60.6%	NS
7	Non HDL	141.6 ± 14.8	137.81 ± 18.55	NS
8	HDL	38. 03 ± 5.45	41.24 ± 7.81	NS
9	Family History DPN	32%	27.7%	NS

MLR = NS

Outcome after Vit D Repletion

Painful DPN : n = 60, Vit D deficiency = 53 , Vit D sufficiency = 7

S.N.	Parameter	Pre intervention (n=53)	Post intervention (Relief)	p-value
1.	Neuritic pain	53 (100%)	21(39.6%)	<0.05
2.	Tingling	53 (100%)	13 (24.5%)	NS
3.	Hyperaesthesia	44 (83.01%)	16 (36.6%)	<0.001
4.	Muscle pain	53 (100%)	38 (71.6%)	<0.0001
5.	Bony pain	40 (75.47%)	22 (55%)	<0.0001
6.	Hypoaesthesia	12 (22.64%)	04 (33.3%)	NS
7.	Vibration impairment	53 (100%)	02 (3.7%)	NS
8.	Neurotropic ulcers	14 (26.4%)	04 (28.5%)	NS

Type of pain and Outcome after Vit D repletion



No pain



Worst pain ever

S.N.	Pain Type	Pre-intervention Mean VAS	Post-intervention Mean VAS	p-value
1	Neuritic pain	4.6	2.7 (-41.3%)	<0.05
2	Bony pain	7	1.8 (-74.2%)	<0.001
3	Muscle pain	7.8	4 (-48.7%)	<0.001
4	Paraesthesias	6.5	4.6 (-29.2%)	0.068

Effect of Vit D on Biochemical Parameters

S.N.	Biochemical Parameter	Pre intervention	Postintervention	p-value
1.	Fasting plasma glucose	145.16 \pm 41.94	138 \pm 39.97	0.729
2.	Postprandial plasma glucose	268 \pm 72.40	232.56 \pm 57.67	0.064
3.	HbA1C	9.01 \pm 2.33	7.9 \pm 1.04	< 0.05
4.	Vit D levels	11.49 \pm 3.5	29.07 \pm 5.5	<0.001

Discussion

- Prevalence in our study : 80.7% in DPN and 30.9% in Painful DPN.
- Lv WS et al. : meta analysis of 6 studies – Vit D def. in DPN and Increased risk of DPN in T2DM
- Shehab D et al. : Mean vitamin D significantly lower in those with neuropathy [36.9 (39.9) nmol/l] compared with those without [58.32 (58.9) nmol/l] and 81.5% of patients with neuropathy had vitamin D deficiency compared with 60.4% of those without.

- NHANES 2001-2004: vitamin D deficiency associated with the symptoms of diabetic neuropathy after statistical correction for the HbA1c level.

Vit D deficiency & complications

- ❖ Neuropathy alone = 19.94 ± 5.2 ngm/ml
- ❖ Neuropathy with
Retinopathy/ Nephropathy = 16.64 ± 6.2 ;
 17.12 ± 4.4 ngm/ml
- ❖ Triopathy = 14.63 ± 4.4 ngm/ml, $p= 0.0001$

Conclusion : vitamin D deficiency in T2DM :
significantly associated with any of the individual
and/or combination of microvascular complications.

Bajaj S, et al. Indian J Endocr Metab 2014;18:537-41

Effect of Vit D repletion on Pain in DPN

Parameter	Lee et al. 2008	Our study
No. of Subjects	51	300 (53)
M: F	1: 2.6	1: 1.5
Mean age	62 \pm 13	64.65 \pm 9.45
BMI	30 \pm 2.3	25.82 \pm 3.38
Vit D at baseline	18 \pm 3	11.49 \pm 3.5
Vit D at 3 mon	30 \pm 5	29.07 \pm 5.5
VAS at baseline	3.3	4.6
VAS at 3 mon	1.7	2.7
Change in VAS	-48.5%	-41.3%

Conclusions

1. Vitamin D deficiency is highly prevalent in T2DM with Peripheral neuropathy (80.7%).
2. Vit D deficiency is more prevalent in elderly patients, in females, in severe DPN and Painful DPN.
3. Vit D deficiency correlates with increased age, increased duration of Diabetes and Alcoholism but is not an independent risk factor for DPN.
4. Vit D repletion improves neuritic pain, paraesthesias, muscle pain and bony pain but has little effect on glycaemic control parameters.

Implication

- Estimation of Vit D levels in patients with DPN, especially painful DPN and Correction of Vit D deficiency may decrease neuropathic symptoms and prevent further nerve damage.



Vitamin D

The body makes vitamin D when it is exposed to Ultraviolet (UV) rays from the sun.

FOOD SOURCES:

Cheese

Margarine

Butter

Fortified Milk

Healthy Cereals

Fatty Fish





THANK YOU



NAGPUR, INDIA