CHAPTER V

SUMMARY AND CONCLUSIONS

OVERVIEW

The global prevalence of diabetes is expected to double in the next two decades (Danaei et al., 2011) and the greatest contribution will be from Asia and the Indian subcontinent in specific, with more than 130 million individuals likely to be affected by the said metabolic derangement (Zimmet et al., 2001). Of the 72.1 million people who have diabetes in the SEA region, 65.1 million are from India. India also happens to be the largest contributor to regional mortality, with 1.1 million deaths attributable to diabetes in 2013 (IDF, 2013). Diabetics are predisposed to developing a number of disabling and life-threatening health complications (IDF, 2013). Some of the common complications that diabetics develop are; CVD (Morrish et al., 2011), kidney disease (WHO, 2011), eye disease (WHO, 2012), neuropathy (IDF, 2013; WHO 2014), diabetic foot (International Consensus on the Diabetic Foot, 1999). However, a grossly neglected diabetic complication is the NAFLD.

NAFLD is a condition characterised by deposition of triglycerides in the hepatocytes, which exceeds 5% of the liver weight (Ratziu et al., 2010) in the absence of significant alcohol intake (Sanyal, 2002). In the last couple of decades the prevalence of NAFLD has gone up whereas that of the other CLDs has either stabilised or decreased (WGO, 2014). Inspite of being the most common hepatic disease (Mavrogiannaki and Migdalis, 2013), it goes unrecognised (Bhatia et al., 2012). Type 2 diabetes patients are at a higher risk of developing NAFLD and NASH compared to the non-diabetics (Younossi et al., 2004; Neuschwander-Tetri and Caldwell, 2003). Type 2 diabetics with NAFLD have a 22 fold higher risk of liver related mortality and 3.3 relative risk for overall mortality (Younossi et al., 2004).

There are no established evidence based guidelines for the treatment of NAFLD. However, incorporating lifestyle changes is critical for reversing the course of NAFLD and NASH (WGO, 2014). Lifestyle modification is a combination of diet, exercise and positive behaviours (Wadden et al., 2004). Lifestyle modification

through behavioural therapy helps to reduce aminotransferases and improve hepatic steatosis (Sreenivasa et al., 2006; Hickman et al., 2004), reduces hepatic fat, improves glucose control and insulin sensitivity (Conlon et al., 2013; Bhat et al., 2012), liver histology (Bhat et al., 2012) and delays the progression of NAFLD to advanced stages (McCarthy and Rinella, 2012).

Dyslipidemia is commonly reported in patients with NAFLD with a prevalence ranging from 20-92% and hypertriglyceridemia as major abnormality (Angulo, 2002). Correction of dyslipidemia is necessary to reduce CVD risk (Dyson et al., 2014). Tinospora cordifolia remains immensely underutilized as there no human studies to document its ant-diabetic and anti-dyslipidemic potential. It contains; alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoids, phenolics, aliphatic compounds and polysaccharides (Sankhala et al., 2012; Grover and Bansal, 2012; Yadav and Agarwala, 2011) lignans (Grover and Bansal, 2012), proteins, flavonoids, saponins (Yadav and Agarwala, 2011) that serve various physiological functions. In modern medicine Tinospora cordifolia is called 'the magical rejuvenating herb' (Singh et al., 2003) owing to its properties to cure many diseases (Srivastava, 2011).

To conclude, the data on Indian type 2 diabetics with NAFLD is lacking. The cardio-metabolic derangements that occur with NAFLD and its association with MS require elucidation. While social health assessment still awaits inculcation in regular practice, quality of life of a type 2 diabetic NAFLD patient needs to be brought to light. In the absence of evidence based guidelines, delving into the dietary and physical activity profiles of the NAFLD patients may hold scope for introducing lifestyle modification, which has time and again proven to be efficacious in NAFLD management. Tinospora cordifolia has not been studied from the anti-diabetic and anti-dyslipidemic perspective on humans and may hold promise for the management of dyslipidemia in type 2 diabetics.

In view of the available literature, the following questions were framed:

1. What is the prevalence of NAFLD among type 2 diabetes patients in the local context?
2. Is there an association between NAFLD and MS among the type 2 diabetics?
3. How is the cardio-metabolic profile of NAFLD patients with type 2 diabetes?

4. Does the diet and physical activity profile differ between NAFLD and normal liver type 2 diabetic subjects?
5. What are the predictor variables for NAFLD among patients with type 2 diabetes?
6. How is the quality of life of type 2 diabetes patients with NAFLD?
7. What are the knowledge attitude and practices of type 2 diabetes patients with NAFLD?
8. Does the propagation of lifestyle modification therapy through inter-personal counselling have scope for the management of NAFLD among type 2 diabetics?
9. What is the impact of inter-personal counselling on the knowledge attitude and practices of type 2 diabetes patients with NAFLD?
10. What is the qualitative phytochemical profile of tinospora cordifolia stem?
11. Does tinospora cordifolia stem have potential to manage diabetic dyslipidemia?

These questions paved the way for strategic construction of the following objectives:

1. To map the prevalence of NAFLD among type 2 diabetes patients.
2. To assess the cardio-metabolic profile of type 2 diabetes patients with NAFLD and normal liver.
3. To map the prevalence of MS among type 2 diabetes patients with NAFLD and normal liver.
4. To study the dietary profile of type 2 diabetes patients with NAFLD and normal liver.
5. To assess the physical activity profile of type 2 diabetes patients with NAFLD and normal liver.
6. To arrive at the predictor variables for NAFLD among type 2 diabetes patients.
7. To determine the quality of life of type 2 diabetes patients with NAFLD.
8. To assess the knowledge attitude and practices of type 2 diabetes patients with NAFLD.
9. To develop lifestyle modification therapy module for the management of NAFLD.
10. To provide interpersonal nutrition counselling to type 2 diabetes patients with NAFLD for lifestyle modification.

11. To assess the impact of interpersonal nutrition counselling in the management of NAFLD.
12. To determine the impact of interpersonal nutrition counselling on knowledge attitude and practices of type 2 diabetes patients with NAFLD.
13. To analyse the phytochemical profile of tinospora cordifolia stem.
14. To assess the impact of tinospora cordifolia stem supplementation in the management of diabetic dyslipidemia.

To achieve the above mentioned goals, the research was divided into three major phases:

Phase I (A): **Prevalence of NAFLD in Association with Cardio-Metabolic Risk Factors in Patients with Type 2 Diabetes Mellitus**

Methods: One hundred and five type 2 diabetics from a clinic were enrolled for the assessment of anthropometric, blood pressure, diet and physical activity profile along with estimations for CBC, hs-CRP, lipid, renal, hepatic, thyroid and glyated hemoglobin estimation. Of them, 95 appeared for abdominal ultrasound for the diagnosis of NAFLD.

Results

- The prevalence of NAFLD was 77.89% in type 2 diabetics. Prevalence of moderate steatosis was 61.05%, followed by 10.52% mild steatosis and 6.31% severe steatosis.
- Overall, 80.76% females and 74.41% males had NAFLD.
- A majority of the NAFLD cases (44.59%) were in the 50-60 years age bracket.
- BMI (28.4 vs. 25.3kg/m^2 P 0.007), WC (98.9 vs. 89.2cm, P 0.0006), WSR (0.62 vs. 0.55, P 0.001), was higher among NAFLD subjects compared to normal liver counterparts.
- The intake of crude fibre (5.4 vs. 6.7g, P 0.0031) and vitamin A (114.1 vs. 175.2 µg, P 0.025) was significantly lower in NAFLD compared to the normal liver subjects.
- NAFLD subjects consumed significantly lower proportion of protein in their diet compared to normal liver subjects (10.9% vs. 12.6%, P 2.84E).
- The intake of crude fibre (P 0.0004), vitamin A (P 0.003) and soluble fibre (P 0.03) differed significantly from normal liver to grade 3 hepatic steatosis.

- The proportion of protein intake differed significantly (P 0.0001) across the various hepatic stages and was significantly higher in the normal liver subjects (12.6%) compared to subjects with grade 1 steatosis (10.7%, P 0.004), grade 2 steatosis (11.07%, 2.5E) and grade 3 steatosis (11.1%, P 0.039).
- Cottonseed oil was consumed more by NAFLD patients (45.94%) than those with a normal liver (45.94% vs. 14.28%, P 0.008, OR: 5.1, CI: 1.26-23.92).
- Obesity was higher (P 0.006) in those with NAFLD (74.32%) than those with a normal liver (74.32% vs. 42.85%, OR: 3.86, CI: 1.26-11.99).
- Abdominal obesity was more prevalent in NAFLD subjects than those with a normal liver (87.83% vs. 57.14%, P 0.0016, OR: 5.42, CI: 1.57-19.09).
- Non-HDL-C (135.9 vs. 119.4mg/dl, P 0.03) was significantly higher amongst the NAFLD patients than the normal liver type 2 diabetics.
- Prevalence of GGT>35U/L was higher in NAFLD subjects than those with a normal liver (28.37% vs. 4.76%, P 0.036, OR: 7.92, CI: 1.01-168.34).
- Hs-CRP was significantly higher among NAFLD subjects than the normal liver subjects (4.8 vs. 2.7mg/l, P 0.017).
- Prevalence of hs-CRP>3mg/l was higher in NAFLD than in normal liver subjects (58.1% vs. 28.57%, P 0.017, OR: 3.47, CI: 1.09-11.41). The Hs-CRP differed (P 0.048) across the various hepatic stages.
- Prevalence of AIP>0.21 was higher in NAFLD than in normal liver subjects (82.43% vs. 57.14%, P 0.015, OR: 3.52, CI: 1.09-11.46).
- The liver span of the type 2 diabetics with NAFLD was above the reference range and was significantly higher than that of the normal liver (168.3 vs. 157.3mm, P 0.019).
- Prevalence of liver span>160mm was higher among NAFLD subjects than the normal liver subjects (64.86% vs. 38.09%, P 0.028, OR: 3, CI: 1.0-9.22).
- The type 2 diabetes patients with a normal liver had significantly higher (P 0.017) total METminutes/week than the type 2 diabetics with NAFLD.
- The total METminutes/week of the normal liver group were significantly higher than that of grade 2 (P 0.01) and grade 3 hepatic steatosis (P 0.00001).
- Prevalence of MS among NAFLD subjects was 72.97% vs. 33.33% in normal liver (P 0.008, OR: 5.4, CI: 1.71-17.54). More features of MS were present amongst the NAFLD patients than those with a normal liver (3.3 vs. 2.7, P 0.036).
- MS was the strongest predictor for NAFLD in type 2 diabetics (P .002, CI: 1.9-15.3).

- The most powerful predictor of severity of NAFLD in type 2 diabetics was WSR (P 0.002).

Conclusions: The prevalence of NAFLD in type 2 diabetics was alarmingly high and had a close association with metabolic syndrome. It calls for selective screening for NAFLD in the said target population. Type 2 diabetics with metabolic syndrome and elevated GGT should be screened for NAFLD.

Phase I (B): Quality of Life of Type 2 Diabetes Patients with NAFLD

Type 2 diabetes patients aged between 30-75 years, with newly confirmed NAFLD were enrolled from the first phase of the study. Quality of life was assessed with the help of Quality of Life Instrument for Indian Diabetes Patients (QOLID).

Results

- The type 2 diabetic males with NAFLD had significantly higher mean scores were better than the female NAFLD patients on the following domains of quality of life; role limitation due to physical health (P 1.49E), physical endurance (P 1.62E), symptom botherness (P 1.72E), perceptions regarding general health (P 2.12E), treatment satisfaction (P 3.09E), financial worries (P 2.91E), emotional and mental health (P 4.05E).
- A significant reduction (P 0.009) in mean likert score in role limitation due to physical health in terms of grade of hepatic steatosis was observed. The grade 3 hepatic steatosis subjects had significantly lower scores than grade 1 hepatic steatosis subjects (P 0.0024) and grade 2 hepatic steatosis patients (P 0.0024) in the domain of role limitation due to physical health.
- The grade 3 hepatic steatosis scores of physical endurance were significantly lower than that of the grade 1 hepatic steatosis (P 0.0005) scores and grade 2 hepatic steatosis (P 0.0001) scores.
- The mean scores of treatment satisfaction reflected that grade 1 hepatic steatosis patients scored better than the grade 2 hepatic steatosis patients and grade 3 hepatic steatosis patients scored the worst amongst them (P 0.016). The grade 3 hepatic steatosis had significantly lower scores of treatment satisfaction as compared to grade 1 hepatic steatosis patients (P 0.002) and grade 2 hepatic steatosis patients (P 0.0067).
- Diet satisfaction was the least scoring domain.

Conclusions: The type 2 diabetics with newly diagnosed NAFLD had a poor QoL in terms of physical endurance and diet satisfaction, both of which are lifestyle related and hence can be modulated. Females had a compromised QoL than the males.

Phase II (B): Impact of Inter-Personal Counselling On the Knowledge Attitude and Practices of Type 2 Diabetes Patients with NAFLD

Methods: Sixty type 2 diabetic NAFLD subjects from the first phase of the study were enrolled and randomly allocated into the intervention arm to receive nutrition counselling propagating lifestyle modification for a period of four months in addition to standard care and either into the control arm to receive standard care alone. They were evaluated for their knowledge attitude and practices regarding type 2 diabetes and NAFLD.

Results

- The intervention increased the scores significantly (9.56 to 20.1, P 4.3E). The controls also had an increase (9.03 to 10.5, P 2.51E), however, the intervention arm subjects had significantly higher knowledge score than controls (20.1 vs. 10.5, P 2.39E).
- The prevalence of low knowledge score about type 2 diabetes reduced from 73.3% and became nil (P 0.000) and therefore the prevalence of low score was only evident among controls (70% vs. 0%, P 0.000). Consequently the prevalence of average score increased from 26.6% to 90% with the intervention (P 0.000) and was also significantly higher from controls (P 0.000).
- The knowledge score on NAFLD improved significantly with the intervention from 0.3 to 13.7 (P 1.08E) and improved among controls from 0.6 to 5.4 (P 9.84E). But, the scores of the intervention arm was significantly higher from the controls (13.7 vs. 5.4, P 1.18E).
- The prevalence of low knowledge scores on NAFLD came down from 96.6% to 6.6% (P 0.000) in the intervention arm and was also significantly lower from controls who had a prevalence of 86.6% of low score in NAFLD (P 0.000). The prevalence of average score on NAFLD increased from 3.3% to 90% (P 0.000) and was significantly higher from controls who had a 13.3% prevalence (P 0.000).
- The attitude and practice score on type 2 diabetes and NAFLD improved significantly with the intervention from 6.8 to 10.2 (P 5.99E) and improved among controls (P

0.006). But, the score of intervention subjects remained significantly higher from controls (10.2 vs. 7.7, P 5.59E). The prevalence of average score decreased from 53.3% to 23.3% (P 0.017) as the prevalence of good score increased from 36.6% to 76.6% (P 0.0019). The prevalence of average (P 0.033) as well as good (P 0.033) score remained significantly higher from controls (50%).

- The KAP score improved from 16.6 to 44.03 (P 1.8E) with the intervention and among controls improved from 16.5 to 23.7 (P 1.05E). However, the score of the intervention subjects was significantly higher from controls (44.03 vs. 23.7, P 8.72E).
- The prevalence of low KAP score reduced from 93.3% to become nil among intervention arm subjects (P 0.000) and among controls from 96.6% to 70% (P 0.005), hence the former had a lower prevalence than the latter (P 0.000). The prevalence of average KAP score increased from 6.6% to 80% (P 0.000) among intervention subjects and increased from 3.3% to 30% among controls (P 0.005) because of which the intervention subjects had a higher prevalence than the controls (P 0.0001). Prevalence of good KAP score became 20% from nil at baseline among the intervention subjects (P 0.023) and remained nil among controls because of which only the former had good KAP score (P 0.023).

Conclusions: The KAP score improved significantly with the nutrition counselling intervention.

Phase II (C): Impact of Lifestyle Modification Therapy in the Management of NAFLD among Type 2 Diabetes Patients

Methods: Sixty type 2 diabetic NAFLD subjects from the first phase of the study were enrolled and randomly allocated into the intervention arm to receive nutrition counselling propagating lifestyle modification for a period of four months in addition to standard care and either into the control arm to receive standard care alone. They were evaluated for anthropometric, blood pressure, physical activity, dietary, biochemical and abdominal ultrasound assessment.

Results:

- Subjects of both the arms had a similar drug profile.

- The prevalence of NAFLD declined significantly in the experimental arm from 100% to 63.3% (P 0.0002) and was also significantly lower from controls at the end of the study, who only had 3.3% subjects with reversal of NAFLD (63.3% vs. 96.7%, P 0.0013).
- The severity of steatosis declined with the intervention (1.86 to 1.2, P 0.00016) and remained unaltered in controls because of which the former had a significantly lower grade of hepatic steatosis than the latter (1.2 vs. 1.93, P 0.0003).
- Weight of the experimental arm was significantly lower than the control arm at the end of the study (65.8 vs. 72.1kg, P 0.05).
- The SBP declined from 145.2 to 128.1mmHg (P 3.23E) during the tenure of the study.
- Fat intake was significantly lower in intervention arm subjects than the controls at the 1st month (45.8g vs. 52.6g, P 0.029).
- The soluble fibre intake increased significantly with the intervention (P 0.041). It was significantly higher in the 3rd month compared to baseline (3.7g vs. 2.9g, P 0.042) and 2nd month (3.3g vs. 2.9g, P 0.020). However, the soluble fibre content was the highest in the 4th month which was significantly higher from the soluble fibre content of the 2nd month (3.8g vs. 2.9g, P 0.028).
- The proportion of fat was significantly lower in the intervention arm compared to controls at baseline (32.8% vs. 35.4%, P 0.011) and at 1st month (29.05% vs. 33.1%, P 0.028).
- The HDL-C increased (47.2 to 52.2mg/dl, P 3.6E) in the experimental arm and was also significantly higher from the control arm (52.2 vs. 46.7mg/dl, P 0.049).
- Triglycerides (138.7 to 121.5mg/dl, P 0.031), VLDL-C (27.7 to 23.9mg/dl, P 0.021) and hs-CRP (4.6 to 3.4mg/l, P 0.024) declined significantly only in the experimental arm.
- At the termination of the study the HbA1c in the experimental arm (8.1 to 7.6%) declined more than the control arm (8.06 to 7.8%) within the group.
- SGPT declined significantly (26.05 to 20.7U/L, P 0.03) in the experimental arm and was also significantly lower than the control arm (20.7 vs. 27.8U/L, P 0.014).
- MS was prevalent in 76.66% of the experimental subjects which declined to 53.33% and 73.33% of the controls had MS which declined to 70%.

- The numbers of features of MS were significantly higher in the experimental arm than the control arm at baseline (3.66 vs. 3.1, P 0.037). It declined significantly in the experimental arm (3.66 to 3.03, P 0.0008) after the intervention.
- At the end of the study, the experimental arm (1301.08 total METminutes/week) had non-significantly higher total MET minutes/week than the control arm (941.7 total METminutes/week).
- A reduction in the liver span in the experimental arm also occurred (173.5 to 166.4mm, P 0.037).

Comparsion between ≥7% weight loss and <7% weight loss subjects

- All of the subjects who had ≥7% weight loss were on OHAs.
- Subjects with ≥7% weight loss had more profound reduction in BMI (9.9% vs. 4.8%), WC (6.4% vs. 3.4%), WSR (6.3% vs. 3.2%), SBP (12.7% vs. 10.5%) and had significantly lower frequencies of eating out than the subjects who lost <7% weight.
- Subjects with ≥7% weight loss had a significant increase in soluble fibre intake (P 0.017). The soluble fibre intake in the 3rd (4.1g vs. 3.3g, P 0.039) and the 4th month (4.3g vs. 3.3g, P 0.031) was significantly from baseline in subjects with ≥7% weight loss and soluble fibre intake in the 3rd month (4.1g vs. 3.1g, P 0.011) and the 4th month (4.3g vs. 3.1g, P 0.011) was also significantly higher from the soluble fibre intake in the 2nd month in subjects with ≥7% weight loss.
- In subjects who had ≥7% weight loss, their proportion of protein intake increased significantly (P 0.034). It was significantly higher at the 3rd month (12.4% vs. 11.04%, P 0.040) and 4th month (13% vs. 11.04%, P 0.0017) compared to baseline proportion of protein intake.
- Subjects with ≥7% weight loss (P 0.0007) had a significant increase in HDL-C compared to subjects with <7% weight loss.
- Prevalence of hypertriglyceridemia became significantly lower in subjects who lost ≥7% weight compared to those who lost <7% weight (16.7% vs. 58.3%, P 0.045).
- Prevalence of AIP>0.21 reduced significantly from 94.4% to 61.1% in subjects with ≥7% weight loss (P 0.040).
- GGT reduced significantly (28 to 22.4U/L, P 0.007) in subjects with ≥7% weight loss and became significantly lower from subjects who had <7% weight loss (22.4 vs. 32.3U/L, P 0.033).

- Subjects with ≥7% weight loss had a significant increase in total METminutes/week (1063 to 1622, P 0.012) and had better profile than subjects who lost <7% weight (1622 vs. 819, P 0.032).
- Liver span reduced (179.1 to 167.3mm, P 0.004) in subjects with ≥7% weight loss.
- Prevalence of MS came down from 77.7% to 44.4% (P 0.043) in subjects who lost ≥7% weight as the number of features reduced significantly (3.6 to 2.72, P 0.0006).
- Prevalence of NAFLD reduced significantly from 100% to 61.1% (P 0.007) in subjects who lost ≥7% weight.

Conclusions: Four months of nutrition counselling propagating lifestyle modification brought about reversal of NAFLD in 36.7% of the type 2 diabetics. It implies that nutrition counselling can be an effective strategy to ameliorate and manage NAFLD in type 2 diabetics. It also brought about improvement in anthropometric, biochemical, dietary and physical activity profile.

Phase III (A): Qualitative Phytochemical Analysis of Tinospora Cordifolia Stem

Method: Mature stem of tinospora cordifolia was analysed for qualitative phytochemical profile estimation.

Result: The phytochemicals present in tinospora cordifolia stem were tannins, alkaloids, flavanoids, terpenoids, cardiac glycosides and saponins and steroids were absent.

Phase III (A): Impact of Tinospora Cordifolia Stem Supplementation in the Management of Diabetic Dyslipidemia

Type 2 diabetics with dyslipidemia on OHAs and statins were enrolled; those with secondary complications, gestational diabetes and type 1 diabetes were excluded. The participants were randomly allocated into two groups; intervention group (n=29) to receive 250mg of encapsulated mature stem of tinospora cordifolia pre meal twice a day along with prescribed OHA and statin and control group (n=30) only on OHAs and statin for a period of 60 days. Baseline data on medical history, family history of lifestyle diseases, duration of diabetes, drug and disease profile and was obtained with the help of a pre-tested questionnaire. Data on physical activity was obtained with the help of IPAQ short form (IPAQ, 2005). Anthropometric, blood pressure data and 24

hour dietary recall data were also obtained. A 12 hours fasting blood sample was obtained for estimating hs-CRP, hepatic, renal, thyroid, lipid profile and glycated hemoglobin through standard laboratory procedures. Diabetic dyslipidemia was defined according to the NCEP ATP IV criteria. After 60 days all the parameters were re-assessed to analyse the impact of the intervention.

Results

- About 51.7% in the intervention arm and 56.7% controls were in 50 to 60 years age bracket.
- Subjects had a similar diet and physical activity profile at baseline as well as after the intervention.
- After the intervention, the WC (94.7 cms to 94.2 cms, P 0.004) and WSR (0.594 to 0.591, P 0.004) declined significantly in the experimental arm.
- The prevalence of normal BMI increased 13.79% to 17.2%, prevalence of overweight declined from 24.13% to 20.6% in the experimental arm.
- Prevalence of increased WC declined from 86.2% to 82.7% and that of increased WSR from 79.3% to 72.4% in the experimental arm.
- Total cholesterol declined from 208.3 to 178 mg/dl (P 0.0008), LDL-C from 122.4 to 105.8mg/dl (P 0.0028), triglycerides from 146.1 to 124.3mg/dl (P 0.036), VLDL-C from 28.9 to 23.6mg/dl (P 0.003), non-HDL-C from 161.6 to 132.6 (P 0.0004) and hs-CRP from 4.6 to 2.8mg/l (P 0.0007) in the experimental arm.
- In controls total cholesterol declined from 188.2 to 175.4mg/dl (P 0.009), LDL-C from 112.6 to 97.5mg/dl (P 0.0012), triglycerides from 154.6 to 129.9mg/dl (P 0.0017), VLDL-C from 30.4 to 25.1mg/dl (P 0.010) and non-HDL-C from 142.7 to 128.7mg/dl (P 0.005).
- The average number of dyslipidemic features reduced more profoundly in the intervention subjects from 2.27 to 1.62 (P 0.0036) and in controls from 2.06 to 1.66 (P 0.020).
- The prevalence of hs-CRP >3mg/l declined by 13.4% from 50 to 36.6% in the control arm and by 27.61% from 65.5 to 37.9% in the experimental arm after the intervention.
- A non-significant decline in HbA1c was observed in both the arms, but the decline was more evident in the experimental arm from 7.7 to 7.5% (P 0.09).

- The prevalence of MS decreased from 68.9% to 55.17% with the intervention as the number of features of MS declined from 3.2 to 2.86.

  Conclusions: A dosage of 500mg of tinospora cordifolia stem had a significant impact on lipemic and anti-inflammatory profile and brought about favourable changes in the glycemic profile as well in a period of 60 days.

RECOMMENDATIONS

1. Screening for NAFLD should be made mandatory based on the below proposed algorithm; type 2 diabetics should be annually screened for the presence of metabolic syndrome according to the IDF classification. Should metabolic syndrome be present, the type 2 diabetic should be assessed for the presence of GGT >35U/L. If GGT is >35U/L, the type 2 diabetic should be screened for NAFLD by ultrasonography.
2. The algorithm will aid in identifying the type 2 diabetics with NAFLD so as to prevent the occurrence of cardiovascular disease and end stage liver disease.
3. The protein intake by a type 2 diabetic patient needs to be closely monitored and modified so as to prevent the occurrence of NAFLD.
4. Quality of life assessment should be included as a part of standard care to identify the modifiable factors that, if corrected, can aid in holistic treatment of NAFLD.
5. Nutrition education for the prevention and management of NAFLD should be given to all the type 2 diabetics, if not through one to one communication, at least through ready leaflets.
6. Lifestyle modification therapy should be propagated as a prophylactic measure amongst all the type 2 diabetics with NAFLD to prevent progression of the disease and also among the non-diseased ones to avert the occurrence of NAFLD.
7. To check on the sustainability aspect of lifestyle modification, future research should be planned with a wash out effect.
8. Tinospora cordifolia can be used as a complementary therapy for cholesterol management.
9. Future studies can be conducted on subjects with borderline dyslipidemia to better observe the impact of tinospora cordifolia supplementation.