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Research Article

Study On Correlation Of Serum C Reactive Protein (CRP) Levels With Acute Complications OfDiabetes Mellitus In A Tertiary Care Hospital

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Abstract:
Diabetes is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. Patients with diabetes have an increased incidence of atherosclerotic cardiovascular, peripheral arterial and cerebrovascular disease in addition to hypertension and abnormalities of lipoprotein metabolism, which often found co-existing. The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. The inflammatory cytokines, adiponectin (Adp), interleukin-6 (IL-6), high sensitivity C-reactive protein (hsCRP), and tumour necrosis factor-alpha (TNF-a) have been associated with insulin resistance and obesity. CRP has been established as a marker for adverse outcome in acute coronary syndromes, atherosclerosis, and ischemic cerebrovascular accidents. Elevated plasma levels of CRP have been reported to be markers for endothelial cell dysfunction in uncomplicated, well-controlled, type 1 diabetes mellitus (TIDM) and in children with TIDM within the first year after diagnosis. With all this above background the study was planned to determine the relationship between the CRP and Diabetes and its related acute complications. The study focuses to determine the association between serum C-reactive protein among patients with acute complications of Diabetes mellitus, to correlate CRP levels with glycaemic control in Diabetic patients with and without acute complications, and to compare the CRP levels before and after treatment of DKA and HHS among the study participants. In this study, blood sugar values and CRP levels were significantly higher among diabetic patients with acute complication compared to those who do not have acute complication and also there was a strong positive correlation between the CRP levels and glycaemic control both during admission and discharge among the study participants. It was also noted that, there was a significant reduction in CRP level after treatment compared to levels before treatment among the patients with acute complication of diabetes and the reduction was higher in Diabetic Ketoacidosis patients compared to patients with Hyperglycaemic Hyperosmolar State. Hence it can be used as a marker of diabetes with acute complications.

Keywords: Diabetes, C-reactive protein, marker

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INTRODUCTION

International Diabetes Federation in the year 2021, estimated that approximately **537 million adults** (20-79 years) are living with diabetes and **541 million** adults are at increased risk of developing type 2 diabetes. The total number of people living with diabetes is projected to rise to **643 million by 2030** and **783 million by 204**5.

Every **3 in 4** adults with diabetes are found to be **living in low- and middle-income countries** and **almost 1 in 2 (240 million)** adults living with diabetes remain undiagnosed. Apart from the higher global and country prevalence, Diabetes mellitus alone have contributed to around **6.7 million deaths**, which is an alarming situation totackle.[1]

Diabetes is a group of metabolic diseases haracterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the beta cells of the pancreas with consequent insulindeficiency to abnormalities that result in resistance to insulin action. The basis of theabnormalities in arbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from **inadequate insulin secretion** and/or **diminished tissue responses to insulin** at one or more pointsin the complex pathways of hormone action. Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycaemia.

Patients with diabetes have an increased incidence of atherosclerotic cardiovascular, peripheral arterial, and cerebrovascular disease in addition to hypertension and abnormalities of lipoprotein metabolism, which often found co-existing.

The vast majority of cases of diabetes fall into two broad etiopathogenetic categories. This major classification of Diabetes mellitus is based on Insulin dependency and is classified as **Type 1 Diabetes mellitus** and **Type 2 Diabetes mellitus.**

In the type 1 diabetes, the cause is an absolute deficiency of insulin secretion. Individuals at increased risk of developing this type of diabetes can often be identified by serological evidence of an autoimmune pathologic process occurring in the pancreatic islets and by genetic markers. In the other, much more prevalent category, type 2 diabetes, the cause is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response. In the latter category, a degree ofhyperglycemia sufficient to cause pathologic and functional changes in various target tissues, but without clinical symptoms, may be present for a long period of time before diabetes is detected. During this asymptomatic period, it is possible to demonstrate an abnormality in carbohydrate metabolism by measurement of plasma glucose in the fasting state or after a challenge with an oral glucose load. However, Symptoms of marked hyperglycaemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia.[2,3]

Diabetes management targets on maintenance of optimum glucose level and prevention and early diagnosis of complications. According to the American Diabetes Association (ADA) Standards of Medical Care in Diabetes 2017, fasting blood sugar (FBS) measurement can be used for glycaemic control assessment and individuals having FBS ≥152 mg/dl are said to have poorglycaemic control.[4]

Appropriate glycaemic control and management is fundamental to prevent and delay DM complications. Poor glycaemic control is highly correlated with high burden of diabetes complications.[4,5]

Diabetes mellitus as a result of poor glycaemic control can lead to metabolic or micro and macro vascular complications, which could be acute or chronic based on the duration.

The metabolic acute complications are relatively short-term complications, which include **Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycaemic Syndrome (HHS).** The latter is prevalent in the people withT2DM, whereas, the former is mainly associated with the individuals with type 1 diabetes mellitus. However, both of the disorders are correlated with the changing mental state, deficiency of insulin and depletion of volume. The neurological symptoms of the state are seizure, lethargy, changing mental state and obtundation, whereas, the prominent characteristics of the state include orthostatic hypotension and polyuria. Normally, the underlying sources ofHHS include the inadequate fluid intake and deficiency of insulin. The insulin deficiency also significantly contributes to hyperglycaemia. The osmotic dieresis induction by the hyperglycaemia leads to intense depletion of the intravascular volume. Additionally, a study suggests that the adolescents with type2 diabetes are more likely to exhibit several acute complications such as hyperglycaemic hyperosmolar state and diabetic ketoacidosis contributing towards **short-term risks associated with mortality and morbidity**.[6,7]

The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart,and blood vessels.

Interestingly, data on the relevance of systemic inflammation are very scarce in relation to acute complications, although low-grade immune activation represents an important risk factor not only for the development of type 2 diabetes[8] but also for several macrovascular (myocardial infarction and stroke) and microvascular complications (neuropathy and nephropathy).[9] The inflammatory cytokines, adiponectin (Adp), interleukin-6 (IL-6), high sensitivity C-reactive protein (hsCRP), and tumor necrosis factor-alpha (TNF-a) have been associated with insulin resistance and obesity.[10]

C-reactive protein (CRP) is a type I acute phase response protein whose synthesis in the liver is regulated by the pro-inflammatory cytokines IL-6, IL1β, and TNF-α[11,12] CRP has been established as a marker for adverse outcome in acute coronary syndromes, atherosclerosis[13], and ischemic cerebroovascular accidents[14]. Elevated plasma levels of CRP have been reported to be markers for endothelial cell dysfunction in uncomplicated, well-controlled, type 1 diabetes mellitus (TIDM)[15] and in children with TIDM within the first year after diagnosis[16].

With all this above background the study was planned to determine the relationship between the CRP and Diabetes and its related acute complications.

AIMS AND OBJECTIVES

- To determine the association between serum C-reactive protein among patients with acute complications of Diabetes mellitus
- To correlate CRP levels with glycaemic control in Diabetic patients with and without acute complications
- To compare the CRP levels before and after treatment of DKA and HHS among the study participants

MATERIALS AND METHODS

Study Setting:

The present study was carried out at Department of General Medicine of Sri Venkateshwaraa Medical College Hospital and Research centre, Puducherry.

Study Design:

Hospital based Prospective Study design was used.

Study Period:

The study was conducted in between March 2021 to September 2022. Sample size:120 (with p=59.1%[99] (prevalence of elevated CRP among diabetes after 6 months treatment; q=1-p=40.8%, d=9, hence substituting in the formula, $4pq/d^2$, the minimum required sample size came as 119, rounded to 120).

For the study purpose, they are divided in to two groups, as mentioned below

Study Subjects:

The participants were divided in to two groups, as mentioned below

- Group A or Diabetes mellitus without acute complication
- Group B or Diabetes mellitus with acute complication
- For the study purpose, those who have been diagnosed to have DiabeticKetoacidosis or HHS at the time of admission were considered the participants of the group, Diabetes mellitus with acute complication
- Out of 120 participants, participants are divided such that, 60 in Diabetes mellitus without acute complication group and 60 in Diabetes mellitus with acute complication group, of which 30 each for DKA and HHS respectively

Inclusion criteria

***For both the group*:**

- Diabetic patients, aged above 18 years
- willing to participate in the study attending General Medicine OPD during thestudy period.

For Diabetes mellitus with Acute Complication group

- 30 participants of those diagnosed to have Diabetic Ketoacidosis

Exclusion criteria:

- Patients with chronic infection and inflammation
- Patients with gestational diabetes
- Patients with other autoimmune disorders
- Patients with malignancies
- Patients with coronary artery disease
- Those who were unwilling to participate were excluded from the study
- Patient Discharged against medical advice during any course of treatment
- Smokers and alcoholics

Sampling Method: Convenient Sampling method

All the eligible participants, fulfilling the inclusion criteria were included until the desired sample size is reached.

Ethical Consideration:

Institutional Scientific and Ethical Committee clearance was obtained before starting the study. Patient were obtained Informed Consent and also were explained about the freedom of with drawl from taking part in the study.

Study Tool:

Pre – tested and Pre – designed, Semi- structured questionnaire was used as study tool. Content validity was obtained from field experts and by extensive literature review.

Data Collection:

After the informed consent, all the patients fulfilling the inclusion criteria were included. Basic socio demographic details were obtained.

Glycosylated haemoglobin, RBS, CRP measurements was done for all the patients at the time admission (Group B) or OPD (Group A) and FBS, PPBS done wherever appropriate based on time and last meal of patient visit. Parameters like Serum electrolytes, Arterial Ph (Group B), Anion gap calculation, Weight and Height for BMI calculation, other parameters of proforma was assessed

Operational definition and guidelines used for the study purpose

The participants were diagnosed to have Diabetes mellitus based on the below mentioned diagnostic criteria

TABLE 1: Diagnostic criteria for Diabetes mellitus

Fasting Blood Sugar: ≥ 126 mg/dl and/or Post Prandial Blood Sugar: ≥ 200 mg/dl and/or Random Blood Sugar (along with Classic Diabetes symptoms or Hyperglycaemic crisis): ≥ 200 mg/dl and/orHbA_1c : ≥ 6.5 g%

The participants are defined to have Controlled Diabetes based on ICMR GlycosylatedHaemoglobin guidelines *ICMR Guidelines for Classification of Controlled and Uncontrolled Diabetes*

TABLE 2: ICMR Guidelines for Classification of Control and UncontrolledDiabetes

HbA1c	**Diabetes Control**
< 8 g%	Controlled Diabetes
≥ 8 g%	Uncontrolled Diabetes

Level of Physical Activity:
Adequate level of Physical activity: At least engaged ½ hour to 45 minutes per day 5 days a week in moderate intensity activity.
Inadequate level of Physical activity: Anything less than Adequate level of Physicalactivity

OBESITY
Obese: Those who have BMI ≥ 25 (according to Asian cut off guidelines for BMIclassification) Non-obese: Those who have BMI < 25

DIABETIC KETOACIDOSIS
Patients was diagnosed to have Diabetic Ketoacidosis based on the below mentioned criteria apart from the clinical presentation with severe dehydration and signs of Acidosis.

TABLE 3: Parameters levels for Diabetic Ketoacidosis

Parameters	**Levels**
Plasma Glucose	>250 mg/dl
Arterial pHOr Serum Bicarbonate	<7.3Or <15 Meq/L
Moderate to Severe Ketonemia and/or Ketonuria	

Hyperglycaemic Hyperosmolar State (HHS)

TABLE 4: *Parameters levels for Hyperglycaemic Hyperosmolar State*

Parameters	**Levels**
Plasma Glucose	>600 m
Plasma osmolality	>320 mosm

CRP measurement: CRP level was measured using siemens **dimension EXL 200** andquantified results was be obtained and recorded. Based on the below values the CRP levels was considered Normal/High/Low

TABLE 5: *Measurement of CRP levels*

CRP Levels	**Classification**
0-3 mg/L	Normal
< 0 mg/L	Low
>3 mg/L	High

Statistical Analysis:
The data was entered in MS Excel and analysed using SPSS 21. The categorical variables were expressed in terms of Frequency and proportion while continuous variables in terms of mean ± SD.

***TABLE 6:** Objectives and their Statistical Analysis*

Objectives	Statistical analysis
To determine the association between serum C-reactive protein among patients with Diabetes mellitus having acute complications and those without acute complications	Chi square test
To correlate CRP levels with glycaemic control in Diabetic patients with andwithout acute complications	Pearson correlation
To compare the CRP levels before and after treatment of DKA and HHS among the study participants	Paired t test

The association is considered statistically significant, if the p value is < 0.05, thus rejecting null hypothesis.
Age, gender association with glycaemic control was assessed using Chi square test, while mean CRP difference among Hypertensive and non-hypertensive was assessed using Paired t Test, p value of < 0.05 is considered statistically significant.

RESULTS

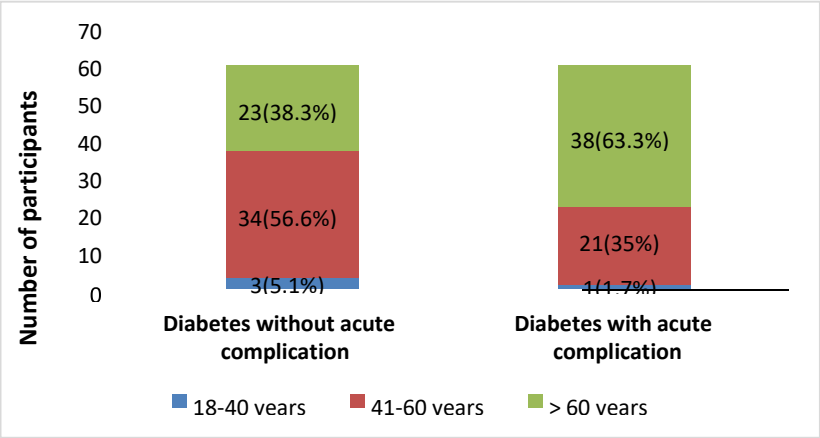


Figure 5: Distribution of participants based on Age category (n=120)

Proportion of participants aged between 18-40 years(5.1%) and 41-60 (56.6 %) years was higher among those who had Diabetes without any acute complication compared to those with acute complication whereas, the proportion of participants aged above 60years(63.3%) was higher among those who had Diabetes with acute complication compared to those without complication.

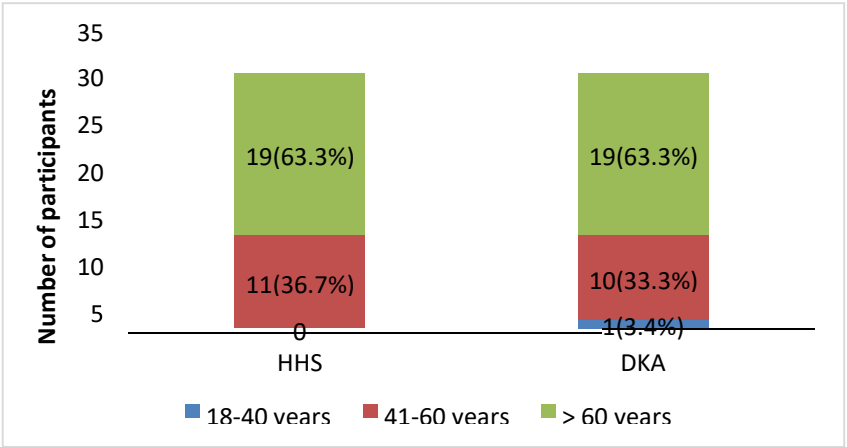


***Figure 6:** Distribution based on Age category among participants with acutecomplication of Diabetes mellitus (n=60)*
Both the participants with either HHS or DKA had higher number of those aged above 60 years, 63.3% each respectively, while those aged between 41-60 years (36.7%) were higher among HHS patients, while proportion of 18-40 years (3.4%) was higher amongDKA patients.

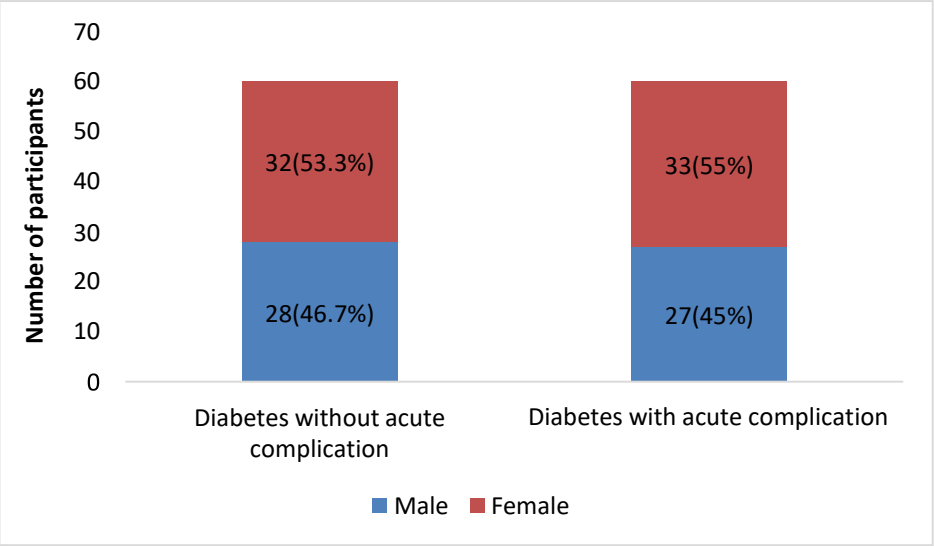


Figure 7: *Distribution based on Gender among the study participants (n=120)*

Proportion of females were higher (55%) among those who had Diabetes with acute complication compared to Diabetes without acute complication (53.3%), whereasproportion of males were higher (46.7%) among those who had Diabetes without acutecomplication compared to Diabetes with acute complication (45%).

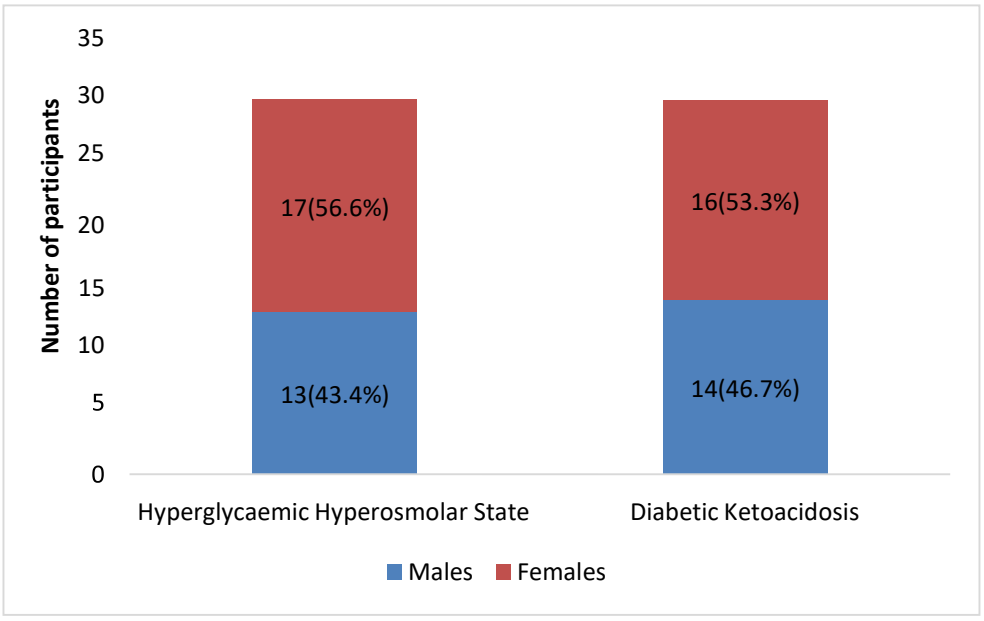


Figure 8: *Distribution based on Gender among the participants having Diabeteswith acute complication (n=60)*

The proportion of females were higher (56.6%) among those who had HyperglycaemicHyperosmolar State compared to Diabetic Ketoacidosis (53.3%), whereas proportion of males were higher (46.7%) among those who had Diabetic Ketoacidosis compared to Hyperglycaemic Hyperosmolar State (43.4%).

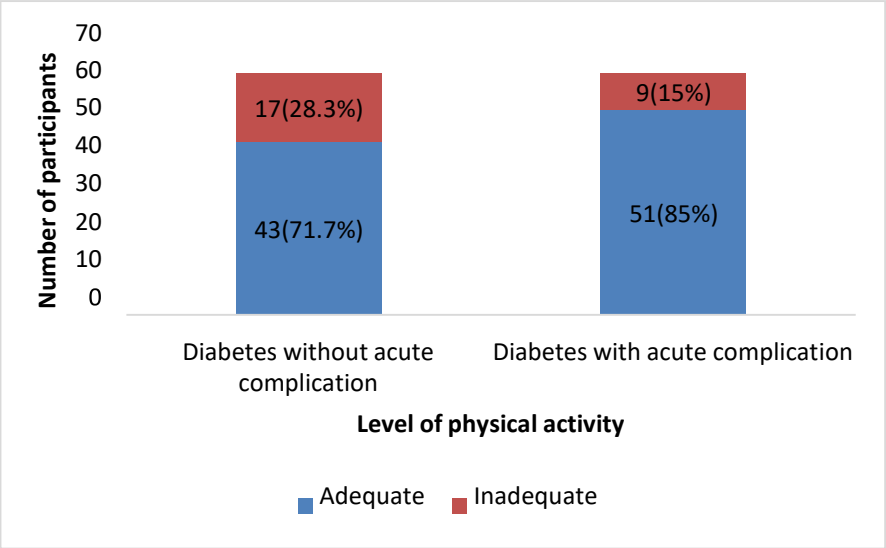


Figure 9: Distribution *based on level of physical activity among the studyparticipants (n=120)*

The proportion of participants with inadequate physical activity was more among Diabetes without acute complication (28.3%) compared to Diabetes with acute complication (15%).

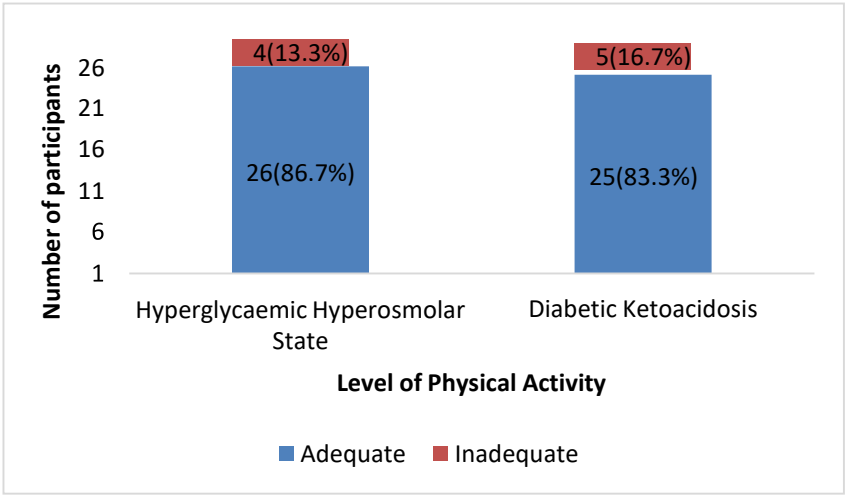


Figure 10: Distribution based on level of physical activity among the participantshaving Diabetes with acute complication (n=60)

The proportion of Inadequate physical activity was higher in Diabetic Ketoacidosis (16.7%) compared to Hyperglycaemic Hyperosmolar State (13.3%).

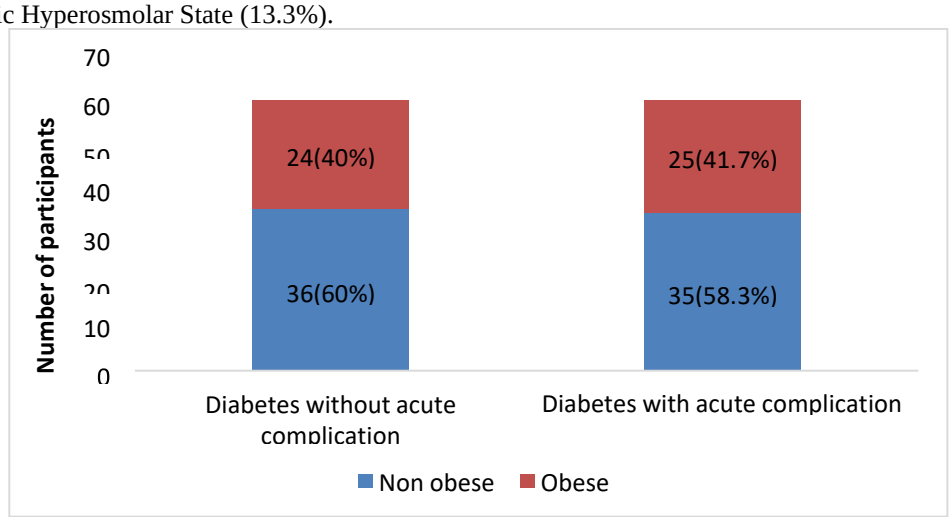


Figure 11: *Distribution based on presence of obesity among the studyparticipants (n=120)*

The proportion of Obese participants were higher in Diabetes with acute complication(41.7%) compared to Diabetes without acute complication (40%)

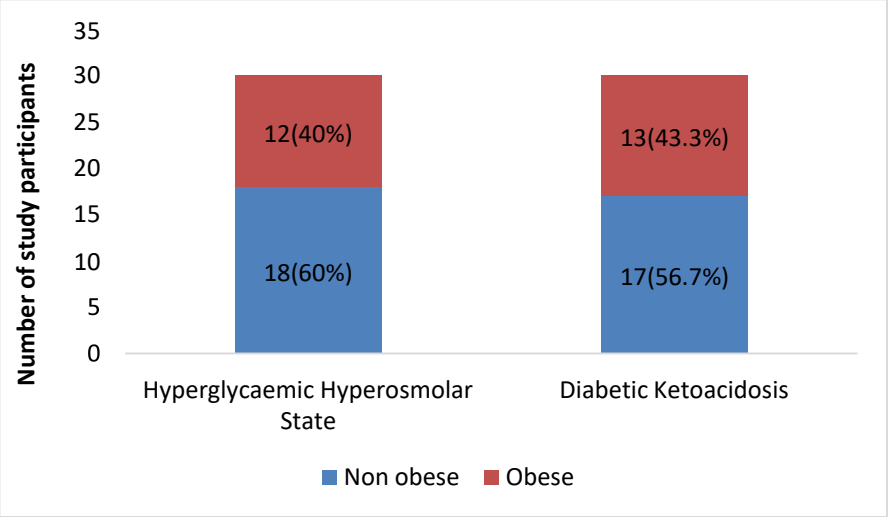


Figure12: Distribution based on presence of obesity among the participantshaving Diabetes with acute complication (n=60)

The proportion of obese participants were higher in Diabetic Ketoacidosis (43.3%)compared to Hyperglycaemic Hyperosmolar State (40%).

Table 7: *Distribution of participants having Diabetes without acute complicationbased on admission Glycaemic parameters and CRP level (n=60)*

Parameters	**Mean ±SD**
Random Blood glucose (mg/dl)	192.12±37.9
HbA1c (g%)	7.8±1.01
CRP(mg/L)	3.7±0.92

The mean admission Random Blood glucose (mg/dl), HbA1c (g%) and CRP(mg/L) ofpatients having Diabetes mellitus without acute complications was 192.12±37.9, 7.8±1.01 and 3.7±0.92 respectively.

Table 8*: Distribution based on admission Glycaemic parameters and CRP levelamong participants with Hyperglycaemic Hyperosmolar State (n=30)*

Parameters	**Mean ±SD**
Random Blood glucose (mg/dl)	637.5±19.4
HbA1c (g%)	8.7±1.8
CRP(mg/L)	7.07±1.31

The admission mean Random Blood glucose (mg/dl), HbA1c (g%) and CRP(mg/L) was637.5±19.4, 8.7±1.8, 7.07±1.31 respectively.

Table 9: *Distribution based on admission Glycaemic parameters and CRP levelamong participants with Diabetic Ketoacidosis (n=30)*

Parameters	**Mean ±SD**
Random Blood glucose (mg/dl)	363.7±50.4
HbA1c (g%)	8.5±1.6
CRP(mg/L)	13.6±1.24

The admission mean Random Blood glucose (mg/dl), HbA1c (g%) and CRP(mg/L) was 363.7±50.4,8.5±1.6 and 13.6±1.24 respectively.

Table 10: *Distribution based on discharge Glycaemic parameters and CRP levelamong participants with Hyperglycaemic Hyperosmolar State (n=30)*

Parameters	**Mean ±SD**
Random Blood glucose (mg/dl)	211.6±10.5
CRP(mg/L)	4.74±1.71

The discharge mean Random Blood glucose (mg/dl) and CRP (mg/L) was respectively 211.6±10.5 and 4.74±1.71 respectively.

Table 11: *Distribution based on discharge Glycaemic parameters and CRP levelamong participants with Diabetic Ketoacidosis (n=30)*

Parameters	**Mean ±SD**
Random Blood glucose (mg/dl)	237.7±9.4
CRP(mg/L)	4.31±1.22

The discharge mean Random Blood glucose (mg/dl) and CRP (mg/L) was 237.7±9.4 and 4.31±1.22 respectively.

Table 12: *Comparison of CRP level in Hyperglycaemic Hyperosmolar State andDiabetic Ketoacidosis during admission and discharge (n=60)*

	CRP level on Admission		**CRP level on Discharge**	
	Normal	*High*	*Normal*	*High*
Hyperglycaemic Hyperosmolar State	0	30(100%)	24(80%)	6(20%)
Diabetic Ketoacidosis	0	30(100%)	20(66.7%)	10(33.3%)

Compared to CRP level during admission the proportion of participants who were normal was high during discharge in both Hyperglycaemic Hyperosmolar State (0 vs 80%) and Diabetic Ketoacidosis patients (0 vs 66.7%).

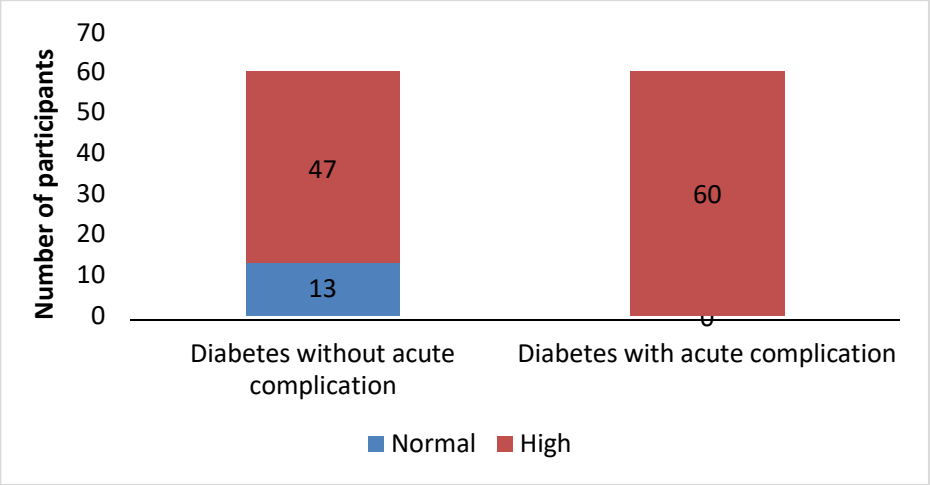
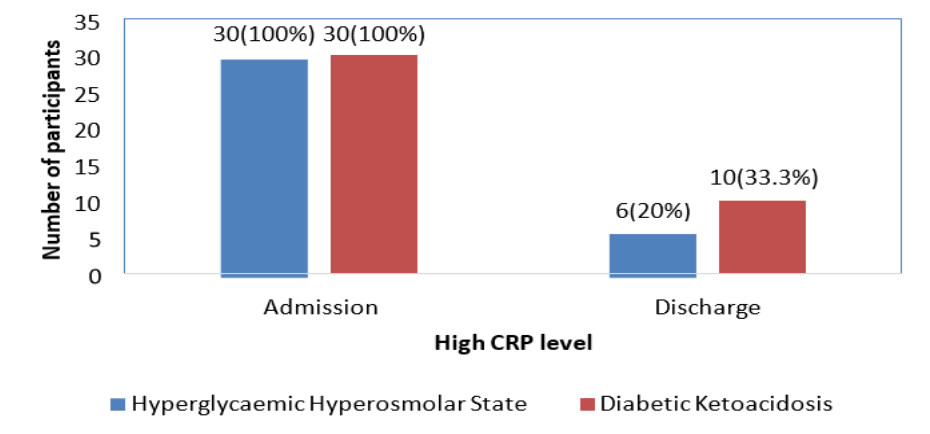


Figure 13: *Comparison of CRP level during admission among diabetic patientswith and without acute complication (n=120)*

During admission, All (100%) the diabetic patients with acute complication had high CRP level whereas, among those who did not have acute complication, 78% of the participants had high CRP level.

Figure 14: *Comparison of patients with acute complication of diabetes based onpresence of high CRP level during admission and discharge (n=60)*



The proportion of patients with high CRP level have reduced from 100% on admission to 20% for Hyperglycaemic Hyperosmolar State, whereas from 100% to 33.3% for Diabetic Ketoacidosis patients.

Table 13: *Association between Age category and glycaemic control (n=120)*

Age category	**Glycaemic Control**		**Significance**
	Controlled HbA1 c (< 8 g%)	Uncontrolled HbA1 c (≥ 8 g%)	
18-40 years	2(50%)	2(50%)	0.575
41-60 years	34(61.8%)	21(38.2%)	
>60 years	32(52.5%)	29(47.5%)	

Though the proportion of participants with poor glycaemic control/Uncontrolled Diabetes was higher among those aged between 18-40 years compared to those aged >60 years and those aged between 41-60 years, the association is statisticallyinsignificant with a p value of 0.575.

Table 14: *Association between gender and glycaemic control (n=120)*

Gender	**Glycaemic Control**		**Significance**
	Controlled HbA1 c (< 8 g%)	Uncontrolled HbA1 c (≥ 8 g%)	
Females	35(53.8%)	30(46.2%)	0.498
Males	33(60.0%)	22(40.0%)	

Though the proportion of participants with poor glycaemic control/Uncontrolled Diabetes among females were higher compared to males, the association is statisticallyinsignificant with a p value of 0.498.

Table 15: *Association between level of physical activity and glycaemic control(n=120)*

Level of physicalactivity	**Glycaemic Control**		**Significance**
	Controlled HbA1 c (< 8 g%)	Uncontrolled HbA1 c (≥ 8 g%)	
Adequate	59(62.8%)	35(37.2%)	0.010
Inadequate	9(34.6%)	17(65.4%)	

The proportion of participants with poor glycaemic control/Uncontrolled Diabetes was higher among those who had inadequate physical activity compared to those who weredoing adequate level of physical activity and this was found, statistically significant with a p value of 0.010 (<0.05).

Table 16: *Association between Obesity and glycaemic control (n=120)*

BMI	**Glycaemic Control**		**Significance**
	Controlled HbA1 c (< 8 g%)	Uncontrolled HbA1 c (≥ 8 g%)	
Non obese	38(53.5%)	33(46.5%)	0.402
Obese	30(61.2%)	19(38.8%)	

Though the proportion of participants with poor glycaemic control/Uncontrolled Diabetes among non-obese participants were high compared to obese individuals, however the association is statistically insignificant with a p value of 0.402.

Table 17: *Association between Hypertension and mean CRP level(n=120)*

Hypertension	**Mean CRP level**	**Significance**
Present	9.92 ± 4.4 mg/L	0.0001
Absent	6.02 ± 3.6 mg/L	

The mean CRP level of hypertensive patients was higher than mean CRP level of non-hypertensive patients 9.92 ± 4.4 mg/L and 6.02 ± 3.6 mg/L respectively and it was statistically significant with p value of 0.0001

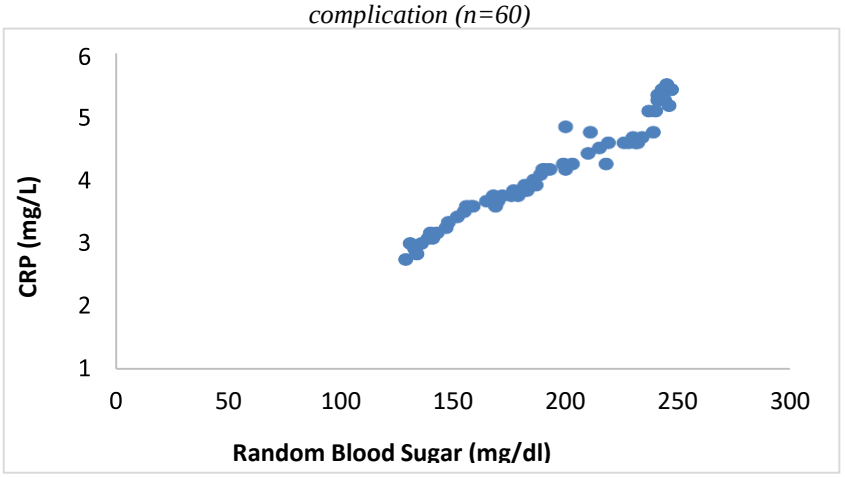
Table 18: *Association between CRP level and Acute complication of Diabetes(n=120)*

Diabetes mellitus	**CRP level**		**Significance**
	Normal	**High**	
Without acute complication	12	48	0.0001*
With acute complication	0	60	

*p value is computed using Fischer Exact test instead of chisquare, as minimal cell value is <5 in one cell.

The proportion of participants with High CRP level is more among diabetes patients with acute complication, compared to those without acute complication and it was found statistically significant, with a p value of 0.0001(<0.05).

Figure 15: *Correlation between admission Random blood sugar and CRP amongthose having Diabetes without acute complication (n=60)*



The above figure 15, shows a positive relationship between admission Random blood sugar and CRP among those having Diabetes without acute complication.

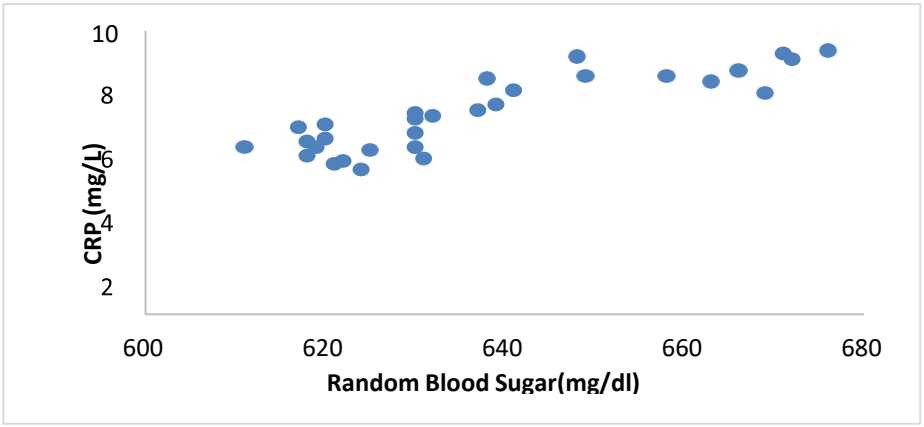


Figure 16: Correlation between admission Random blood sugar and CRP amongpatients with Hyperglycaemic Hyperosmolar State (n=30)

The above figure 16, shows a positive relationship between admission Random bloodsugar and CRP among those with Hyperglycaemic Hyperosmolar State.

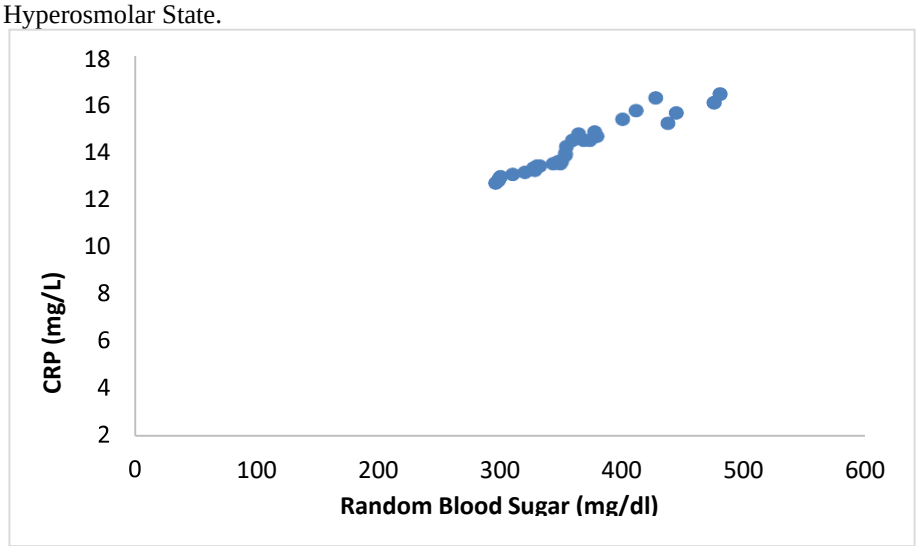


Figure 17: *Correlation between admission Random blood sugar and CRP amongpatients with Diabetic Ketoacidosis (n=30)*

The above figure 17, shows a positive relationship between admission Random blood sugar and CRP among those with Diabetic Ketoacidosis.

Table 19: *Correlation between Random Blood glucose and CRP level duringadmission (n=120)*

Participants	**Pearson Correlation**	**Significance (p value)**
Diabetes without acute complication	0.975	0.0001
Hyperglycaemic Hyperosmolar State	0.868	0.0001
Diabetic Ketoacidosis	0.960	0.0001

The Correlation between Random Blood glucose and CRP level during admission wasfound to be strongly positive and highly significant for participants having Diabetes without acute complication, Hyperglycaemic Hyperosmolar State and Diabetic Ketoacidosis having obtained the r value of 0.975,0.868 and 0.960 respectively and it was statistically significant with p value of 0.0001 (<0.05).

Table 20: *Correlation between Blood glucose and CRP level during dischargeamong diabetic patients with acute complication (n=60)*

Participants	**Pearson Correlation**	**Significance (p value)**
Hyperglycaemic Hyperosmolar State	0.902	0.0001
Diabetic Ketoacidosis	0.754	0.0001

The Correlation between Random Blood glucose and CRP level during discharge among patients with Hyperglycaemic Hyperosmolar State and Diabetic Ketoacidosis was found to be strongly positive and highly significant having obtained the r value of0.902,0.754 respectively and it was statistically significant with p value of 0.0001 (<0.05).

Table 21: Comparison of CRP levels during admission and discharge ofHyperglycaemic Hyperosmolar State patients (n=30)

Hyperglycaemic Hyperosmolar State	**CRP (mg/L)**	**Significance**
Admission	7.07 ± 1.31	**0.0001**
Discharge	4.74 ± 1.71	

Among the Hyperglycaemic Hyperosmolar State patients, compared to admission, there is a significant reduction in CRP level during discharge following the treatment and this difference was found statistically significant with t statistic of and p value of 0.0001 (<0.05).

Table 22: Comparison of CRP levels during admission and discharge of DiabeticKetoacidosis patients (n=30)

Diabetic Ketoacidosis	**CRP (mg/L)**	**Significance**
Admission	13.6±1.24	0.0001
Discharge	4.03±1.23	

Among the Diabetic Ketoacidosis patients, compared to admission, there is a significantreduction in CRP level during discharge following the treatment and this difference wasfound statistically significant with t statistic of and p value of 0.0001 (<0.05).

Table 23: Correlation between Glycaemic control and CRP level based onadmission values (n=120)

Parameters	**Pearson correlation (r)**	**Significance (p value)**
Diabetes without acute complication	0.809	0.001
Hyperglycaemic Hyperosmolar State	0.624	0.001
Diabetic Ketoacidosis	0.663	0.001

Glycaemic control was positively correlated with CRP, higher the HbA1c higher was the CRP values and this was found statistically significant with a p value of < 0.05, the correlation was strong between Diabetes without acute complication followed by Diabetic Ketoacidosis and Hyperglycaemic Hyperosmolar State.

DISCUSSION

In the present study conducted among diabetic patients, Out of 120 study participants, the proportion of participants aged above 60 years (63.3%) was higher among those who had Diabetes with acute complication compared to those without complication, this finding was similar to the finding of **Krulijac I et al**[17] which reported more numberof patients being older having Hyperglycaemic Hyperosmolar state.

The current study showed that there was equal high proportion of participants who areaged above 60 years presented with Diabetic ketoacidosis and Hyperglycaemic Hyperosmolar state (63.3% each). This was contrast to the study finding of **Wu XY et al**[18] in their study titled "Clinical profiles, outcomes

and risk factors among type 2 diabetic inpatients with diabetic ketoacidosis and hyperglycaemic hyperosmolar state: a hospital-based analysis over a 6-year period", which stated based on their findings that there was statistically higher number patients who are older in Hyperglycaemic Hyperosmolar state compared to Diabetic ketoacidosis (75.4 ± 11.6 vs 53.4 ± 16.5 years, P < 0.001).[18]

In the current study we had 89% of the participants with high crp levels, whereas the prevalence of high CRP level was 51.5%, in the study conducted by **King DE et al.**[19] This high proportion of particiants in the present study with high CRP level could be because of the 50 % of our study participants being those with acute complication of diabetes mellitus which could have exaggerated the overall prevalenceof high CRP level.

In the current study, among the participants with acute complication of diabetes, the proportion of obese participants were higher in Diabetic Ketoacidosis (43.3%) compared to Hyperglycaemic Hyperosmolar State (40%), this was similar to the finding of **Krulijac I et al**[17] who also reported lesser number of obese patients among patients with Hyperglycaemic Hyperosmolar State.

The current study showed higher mean CRP level among hypertensive patients (9.92± 4.4) compared to non-hypertensive patients (6.02±3.6) and it was statistically significant with a p value of 0.0001.

The current study finding in association with hypertension and CRP, was also supported by the findings of **Shafidar M et al**[20] in their study titled "hs-CRP: A potential marker for hypertension in Kashmiri population" reported that the mean serum hs-CRP level in hypertensive patients was 3.26 mg/L compared with 1.36 mg/L among normotensive control subjects and it was statistically significant with a p value of <0.001.

Another study by **Abbas MS et al**[21] also supported the current study by showing highermean CRP level among Hypertensive patients (3.23±0.83mg/L) compared to non- hypertensive, p value 0.00001.

Compared to the study finding of **Shafidar M et al**[20] and **Abbas MS et al**[21] the mean values of CRP in the current study finding was higher because all the patients of the present study were Diabetic and 50% of the participants were presented with acute complication of diabetes.

The mean HbA1c of the 120 participants in the present study was 8.2 ± 1.49 g%, this was less compared to the study conducted by **Rajagopal L et al**[22] which have showed increased HbA1C value of 10.82±0.19 this could be due to the difference in geographic setting and also the study was carried out considering anaemia as a main confounding factor.

In the present study, on determining the Correlation between Random Blood glucose and CRP level during admission it was found to be strongly positive and highly significant for participants having Diabetes without acute complication, Hyperglycaemic Hyperosmolar State and Diabetic Ketoacidosis having obtained ther value of 0.975, 0.868 and 0.960 respectively and it was statistically significant with p value of 0.0001 (<0.05): **Petchiappan V et al** also reported positive correlation between the level of glycaemic parameters and CRP levels and also concluded that, better glycaemic control will results in significant reduction in the hsCRP levels.[23]

In the current study, Glycaemic control was positively correlated with CRP, higher theHbA1c higher was the CRP values and this was found statistically significant with ap value of < 0.05, the correlation was strong between Diabetes without acute complication followed by Diabetic Ketoacidosis and Hyperglycaemic Hyperosmolar State.

King et al also found a strong correlation between HbA1c levels and CRP, he concluded it also by analysing the association of HbA1c at various levels with the CRPlevel and found out, that at HbA1c level of 7, the proportion of participants with high CRP was 48.9%, whereas at a HbA1c value of 11 g%, the proportion of participants with elevated CRP was 70.6% and that was found statistically significant with p valueof < 0.05.[19]

In other study titled "**Study of Highly Sensitive C - Reactive Protein (hs-CRP) In Type 2 Diabetes Mellitus and Its Correlation with Glycosylated Hemoglobin", it was noted that** the proportion of participants with high CRP level increase with increase in HbA1c value, for HbA1c of 6.5 g% (5%), whereas, with HbA1c of >8.6 g% the proportion of participants with Higher CRP was 67% .[24]

Though the proportion of participants with poor glycaemic control/Uncontrolled Diabetes was higher among those aged between 25-40 years compared to those aged > 60 years and those aged between 41-60 years. This was similar to the findings of various other studies[20] which also reported poor glycaemic control among Younger patientscompared to Older patients.

There was a significant reduction in the level of CRP among Diabetes ketoacidosis patients compared to admission Vs Discharge 13.6±1.24 mg/L Vs 4.31 ± 1.22, this wassimilar to the findings of **Kitabchi AE**[25] in their study titled" Thirty years of personal experience in hyperglycemic crises: diabetic ketoacidosis and hyperglycemic hyperosmolar state" which reported a significant reduction in CRP level compared to admission to discharge 59 ± 13 vs 34 ± 9 p value / 0.05.[33]

Similarly **Dalton RR**[26] also reported a decrease in CRP value in acute complication ofdiabetes from admission baseline compared to discharge. The median pre-treatment CRP value was 1.91 µg/dl (range 0.45-5.42); at 6-8 hr, 3.41 µg/dl (range 0.5-6.8); at 24 hr, 2.09 µg/dl (range 0.78-13.11); and at 120 hr, 0.63 µg/dl (range 0.46-1.63).[26]

CONCLUSION

The present study findings conclude that, both the Blood sugar values and CRP levels were significantly higher among diabetic patients with acute complication compared to those who do not have acute complication and also there was a strong positive correlation between the CRP levels and glycaemic control both during admission and discharge among the study

participants and it was statistically significant with p value of < 0.05.It was also noted that, there was a significant reduction in CRP level after treatment compared to levels before treatment among the patients with acute complication of diabetes and the reduction was higher in Diabetic Ketoacidosis patients compared to patients with Hyperglycaemic Hyperosmolar State. Hence it can be used as a marker of diabetes with acute complications.

LIMITATION

Though the study have significant findings on relationship with CRP level and Diabetes mellitus, the details of precipitator cause of CRP level if could have included have beenmore valid

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