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RESEARCH ARTICLE

MORBIDITY AND MORTALITY PATTERNS AMONG ADMITTED PATIENTS WITH DIABETES : A HOSPITAL BASED STUDY FROM NORTH INDIA.

Dr. Henna Naqash¹, Prof. Gazanfar Ali², Dr. Mohammad Hayat Bhat³.

1. Senior Resident at Deptt. of General Medicine, GMC, Srinagar.
2. Ex HOD, Deptt. of General Medicine, GMC, Srinagar.
3. Lecturer, Deptt. of General Medicine, GMC, Srinagar.

Study conducted at SMHS Hospital, Associated hospital of GMC, Srinagar, India.

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*Corresponding Author

Dr. Henna Naqash.

Abstract

This study helps us to find the morbidity & mortality patterns in patients with diabetes admitted in a tertiary care hospital in a developing country and confers information about their distribution among males & females of different age groups, their relationship with concurrent diseases, obesity and the effect of various treatment modalities on the morbidity & mortality. The objective is to find the morbidity and mortality patterns in people with diabetes admitted to a tertiary care hospital associated with Government Medical College Srinagar, in India.

Methods: In this prospective study, all patients with diabetes who were admitted to Sri Maharaja Hari Singh hospital [SMHS] (associated hospital of Government Medical College, Srinagar) over a period of 19 months were studied for diabetes-related complications.

Results: The most common morbidity among patients with diabetes admitted in this hospital was infection (47.54%) followed by strokes (9.09%). The most common cause of death in patients with diabetes was again infections (60.34%), followed by strokes (18.96%) and renal failure (17.24%). Among admitted patients with diabetes, type 2 diabetes was the predominant type (95.2%). 6.4% of these patients were obese. Maximum admissions were for infections (47.5%), followed by Diabetic Ketoacidosis (10.64%) and hypoglycaemia (7.87%). Among complications, 52% had neuropathy, 50% had diabetic retinopathy, 27.2% had nephropathy and 4.9% had disease of coronaries. Major metabolic complications were Diabetic Ketoacidosis (3.42%), Hypoglycemia (2.53%) and Hyperglycemic Hyperosmolar state (HHS) (1.93%). 8.64% among admitted patients died. 12.06% died of myocardial infarction and 5.1% died of hypoglycemia.

Conclusions: The most common morbidities in patients admitted with diabetes in this tertiary care hospital in a developing country are infections and strokes and the most common etiology for deaths is again infections followed by strokes and renal failure.

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Introduction:-

Diabetes mellitus is a group of diseases marked by high levels of blood glucose resulting in defects in insulin production, insulin action, or both. Diabetes mellitus has been known to the physicians of ancient times, passing of frequent and large quantity of urine was recorded in Papyrus Ebers, an Egyptian medical journal already old in times of Moses [1]. African Americans, Hispanic/Latino Americans, American Indians, some Asian Americans & native Hawaiians or other Pacific Islanders are at particularly high risk for type 2 diabetes & its complications [2]. Undiagnosed T2DM is common, with an estimated lag of 5 to 7 years between the onset of diabetes & diagnosis [3],[4],[5]. Globally, the number of people with diabetes is expected to rise from the current estimate of 285 million

in 2010 to 438 million in 2030. T2DM has become one of the world's most important public health problems. Type 2 diabetes mellitus is the predominant form of diabetes worldwide, accounting for 90% of cases globally [6],[7]. One of the greatest relative increase in diabetes prevalence over the next 20 years is projected to occur in Africa. As per the National Diabetes Statistics Report, 2014 (the most recent comprehensive assessment of the impact of diabetes in the United States, jointly produced by the CDC, NIH, ADA, and other organizations), in 2012, 29.1 million Americans, or 9.3% of the population, had diabetes. 1.4 million Americans are diagnosed with diabetes every year. Diabetes remains the 7th leading cause of death in the United States in 2010, Diabetes may be underreported as a cause of death. Studies have found that only about 35% to 40% of people with diabetes who died had diabetes listed anywhere on the death certificate and about 10% to 15% had it listed as the underlying cause of death. In 2009–2012, of adults aged 18 years or older with diagnosed diabetes, 71% had blood pressure greater than or equal to 140/90 mmHg or used prescription medications to lower high blood pressure. Diabetes was listed as the primary cause of kidney failure in 44% of all new cases in 2011. About 60% of non-traumatic lower-limb amputations among people aged 20 years or older occur in people with diagnosed diabetes. In India, the prevalence & incidence of diabetes mellitus is also increasing at a very rapid pace & there are reports that the rising incidence of diabetes mellitus in India has given this developing country the dubious distinction of being the “Diabetes Capital of the world” [8]. WHO predicts that developing countries will bear the brunt of this epidemic in the 21st century, with 80% of all new cases of diabetes expected to appear in the developing countries by 2020 [9].

Criteria for the diagnosis of diabetes are shown in table 1.

Classification of diabetes:-

Type 1 diabetes (T1DM) usually strikes children & young adults, or the disease onset can occur at any age. In adults, type 1 diabetes mellitus accounts for approximately 5% of all diagnosed cases of diabetes. An expert committee of the American Diabetes Association, has recommended dividing T1DM into type 1A (immune mediated) & type 1B (other forms of diabetes with severe insulin deficiency) [11].

Type 2 diabetes (T2DM) usually begins as insulin resistance, undiagnosed T2DM is common, with an estimated lag of 5 to 7 years between the onset of diabetes & diagnosis [4],[5],[12]. Genetically, T2DM consists of monogenic & polygenic forms [13],[14].

Monogenic forms of diabetes:-

Associated with insulin resistance:-

Mutations in insulin receptor gene:-

- ❖ Type A insulin resistance.
- ❖ Leprechaunism.
- ❖ Rabson Mendenhall syndrome.

Lipoatrophic diabetes:-

Mutations in PPAR γ gene:-

Associated with defective insulin secretion:-

- ❖ Mutation in the insulin or proinsulin genes
- ❖ Mitochondrial gene mutations

Maturity onset Diabetes of the Young (MODY):-

- ❖ HNF - 4 α (MODY1)
- ❖ Glucokinase (MODY2)
- ❖ HNF-1 α (MODY3)
- ❖ IPF-1 (MODY4)
- ❖ HNF-1 β (MODY5)
- ❖ NeuroD1/Beta2 (MODY6)

Gestational diabetes is a form of glucose intolerance diagnosed during pregnancy. Pregnancy is normally attended by progressive insulin resistance that begins near mid-pregnancy and progresses through the third trimester to levels that approximate the insulin resistance seen in individuals with type 2 diabetes. The insulin resistance appears to result from a combination of increased maternal adiposity and the insulin-desensitizing effects of hormonal products

of the placenta. Robust plasticity of β cell function in the face of progressive insulin resistance is the hallmark of normal glucose regulation during pregnancy [15].

Other types of diabetes result from specific genetic conditions, surgery, medications, infections, secondary to pancreatic disease, & other illnesses. Such types of diabetes account for 1% to 5% of all diagnosed cases [18].

The association of obesity with T2DM has been recognised for decades. A close association between obesity & insulin resistance is seen in all ethnic groups & is found across the full range of body weights, across all ages & in both sexes [16],[17],[19]. A constellation of metabolic derangements that are often seen in patients with insulin resistance & T2DM are individually associated with an increased risk of cardiovascular disease : hypertension, obesity, non- insulin dependent diabetes mellitus (NIDDM), dyslipidemia, & atherosclerotic cardiovascular disease; or "the deadly quartet"[20],[21]. Hyperglycemia is a primary factor in the development of complications of diabetes, & decreases in average blood glucose have a profound effect to prevent complications in both T1DM & T2DM [22].

There are various complications of diabetes like:-

Heart disease & stroke:- Heart disease death rates in diabetics are about 2 to 4 times higher than non diabetics & the risk for stroke is 2 to 4 times higher in people with diabetes [23],[24]. The Framingham Study showed a twofold to threefold elevation in the risk of clinically evident atherosclerotic disease in patients with T2DM compared to those without diabetes [25].

Hypertension:- Hypertension is very common in population with diabetes as compared to non diabetics [26].

Kidney disease:- Diabetes is the leading cause of kidney failure accounting for 44% of all new cases of kidney failure [27]. In the United Kingdom Prospective Diabetes Study (UKPDS), a reduction in BP from 154 to 144mmHg was associated with a 30% reduction in microalbuminuria [28].

Nervous system disease:- About 60 to 70% of people with diabetes have mild to severe form of nervous system damage including peripheral neuropathies, carpal tunnel syndrome & severe sensorineuropathy resulting in lower extremity amputations & entrapment neuropathies [29],[31].

Blindness & retinopathy:- Diabetes is the leading cause of blindness between ages of 20 to 65 years [30].

Amputations:- More than 60% of lower limb amputations occur in patients with diabetes [32].

Dental diseases:- Periodontal gum disease is more common in people with diabetes. It is twice more common in diabetics than non diabetics. About one-third of people with diabetes have severe periodontal disease consisting of loss of attachment of gums to teeth [33].

Metabolic complications:- like diabetic ketoacidosis, hyperosmolar coma & hypoglycemia are common in diabetics [34]. Diabetic ketoacidosis is a life threatening condition in which severe insulin deficiency leads to hyperglycemia, excessive lipolysis, & unrestrained fatty acid oxidation, producing the ketone bodies acetone, beta-hydroxy butyrate, & acetoacetate. This results in metabolic acidosis, dehydration, & deficits in fluid & electrolytes.

Hypoglycemia is classified as [35]:

- a) Severe..requiring assistance of another person to take corrective actions, with neurologic recovery following glucose administration without documenting low plasma glucose.
- b) Documented symptomatic hypoglycaemia..typical symptoms with plasma glucose < 70 mg/dL.
- c) Asymptomatic hypoglycaemia..blood glucose < 70 mg/dL without typical symptoms.
- d) Probable symptomatic hypoglycaemia..Typical symptoms likely caused by plasma glucose < 70 mg/dL.
- e) Pseudo-hypoglycemia..typical hypoglycaemia symptoms with plasma glucose >70mg/dL.

Others:- Diabetics are more susceptible to many other illnesses, infections & depression [37],[38].

Classification of complications of diabetes:-

Classification of retinopathy [39] is shown in Table 2.

Nephropathy is classified as:-

- ❖ **Stage 1:** Hyperfiltration (glomerular filtration rate >125 mL/min.)
- ❖ **Stage 2:** The Silent Stage
- ❖ **Stage 3:** Microalbuminuria(urinary albumin 30-300 mg/day)
- ❖ **Stage 4:** Macroalbuminuria(urinary albumin > 300mg/day)
- ❖ **Stage 5:** Uraemia

Classification of neuropathy as per San Antonio Convention [40] is as follows:-

Subclinical neuropathy:-

Diffuse clinical neuropathy with distal symmetric sensorimotor & autonomic syndromes.

Focal syndromes:-

Diabetic foot is classified according to Wagner or University of Texas criteria as shown in Tables 3 and 4, respectively.

Multiple epidemiologic studies have suggested that there is an association between cardiovascular risk & HbA1c, FPG & 2 hr PP Glucose levels [36]. The various management strategies are lifestyle interventions, education of patients, Medical Nutrition Therapy (MNT), exercise, self monitoring of blood glucose and pharmacotherapy using oral hypoglycemic agents or insulin therapy. The American Diabetes Association (ADA) has advised certain glycemic targets in patients with diabetes. They are shown in Table 5.

Materials And Methods:-

Since the number of patients with diabetes mellitus has increased dramatically, & there are few data on the rates of morbidity, serious complications & mortality from the Government Medical College, Srinagar & associated hospitals. No study has been carried out from this institute. To determine such rates of morbidity & mortality, we have conducted this prospective study on admitted diabetic population. The study is hospital based. All patients with diabetes who were admitted to SMHS hospital, a tertiary care hospital, over a period of 19 months in various wards, both medical/surgical & other wards, were studied for diabetes-related complications like heart disease & stroke, hypertension, blindness & retinopathy, kidney disease, neurologic disease, dermatological disease, diabetic foot/amputations, periodontal (gum) disease & metabolic complications such as diabetic ketoacidosis & hyperosmolar (non-ketotic) coma, hypoglycemia, infections & psychiatric illnesses.

Complete clinical profile of these patients was recorded, which included age, sex, duration of diabetes & treatment, residence, general physical examination, systemic examination.

The primary end-point of this study was to find the morbidity & mortality in diabetics. The secondary end points were observed as differences of morbidity & mortality in males & females and the relationship of morbidity & mortality with age. The patients were divided into three age groups: **A.** < 45 years **B.** 45 to 60 years **C.** > 60 years. The relationship of other concurrent diseases, obesity and various treatment modalities with morbidity & mortality patterns in patients with diabetes was studied. To determine the cause of death, the patients were divided into four groups: Group A: single cause of death; Group B: two causes of death; Group C: three causes of death; Group D: four or more causes of death.

Data analysis:- The data was analysed statistically using Pearson's chi square test of association; wherever needed, Mann-Whitney U-test and Chi Square test with Yates correction was applied. p-value of <0.05 was taken as significant.

Results:-

All patients with diabetes who were admitted to SMHS hospital over a period of 19 months were studied for diabetes-related complications. Among the admitted patients who expired, the most probable cause of death was also studied.

Age distribution of study subjects revealed maximum subjects in 60 – 80 year age group & minimum in upto 20 years of age.

About two-thirds of subjects (60.05%) were females and one-third (39.94%) were males.

As depicted in Table 6, mean age among males was 59.26+13.8 (min14yrs,max 90yrs) which was slightly higher than among females that was 57.56+13.8 (min 8yrs,max 90yrs).

55.89% of total admitted patients were from rural and 44.11% from urban areas as shown in Table 7.

Table 8 shows the percentage of different types of diabetes among studied patients. The bulk of patients were type 2 diabetics (95.23%) and a minority had type 1 diabetes (1.94%), followed by secondary forms of diabetes (1.79%) and gestational diabetes in the rest (1.04%). According to IADPSG (International Association of Diabetes and Pregnancy Study Group) and American Diabetes Association guidelines, gestational diabetes is diagnosed only if the glucose intolerance is identified during pregnancy AND the woman does not qualify for pre-existing (overt) diabetes. Criteria for overt diabetes in pregnancy are HbA1c > 6.5%, fasting blood glucose level > 126 mg/dL, or random glucose level > 200 mg/dL. The diagnostic criteria for gestational diabetes in our patients were a single abnormal value after taking 75 g oral glucose. The values as per ADA are fasting glucose > 92 mg/dL, post 1 hour glucose > 180 mg/dL, and 2-hour post glucose > 153 mg/dL.

About three-fourths of patients were having 1 -10 years duration of diabetes. 15% of the patients had diabetes for more than 10 years. Rest were newly detected or had diabetes for less than 12 months. Results are shown in Table 9.

Maximum number of admissions were for infections, followed by those for glycemic control. 9.09% patients were admitted with strokes. Besides these indications, major admissions were with surgical problems, followed by myocardial infarction, COPD exacerbations and renal failure. The percentage of different reasons for admission of diabetics is shown in Table 10.

As shown in Table 11, maximum number of admitted patients with diabetes were on insulin therapy, followed by OHAs. One-fourth of patients were switched over from one form of therapy to another and only 2.38% patients were on combination therapy of insulin and OHAs.

Table 12 and Figure 1 depicts the distribution of morbidities among diabetic patients. Major morbidities among admitted diabetics were hypertension in 42.62%, and high risk feet in 62% patients. 15% patients had recurrent boils and 13% had non healing ulcers. More than half of admitted females had a history of pruritus vulvae. Hypertension was diagnosed in these patients on the basis of BP > 140/90mmHg or patient already on BP lowering drugs. Patients with high risk feet had cracks, sores in feet with pressure spots, calluses, past ulcers or dirty, infected feet with loss of sensations or proprioception.

23 patients were admitted with diabetic foot and 8 out of those patients underwent amputations.

Psychiatric illness was present in 57 patients (8.49%) in the form of depression, bipolar affective disorder or schizophrenia.

Malignancies were present in 30 (4.47%) patients and involved breast in 5, gall bladder in 4, lung in 3, cecum or colon in 3, larynx in 2, thyroid in 2, stomach in 2, brain (high grade glioma) in 1, blood (chronic lymphocytic leukemia) in 1, urinary bladder in 1, pancreas in 1, esophagus in 1, kidney in 1, prostate plus bladder in 1, and with unknown primary in 1 patient.

Overall, 6.4% among admitted patients and 5.17% among mortalities were obese as shown in Table 13. Obesity was diagnosed by a body mass index greater than or equal to 30 kg/m².

Figure 2 shows that half of all patients had diabetic retinopathy, more than half had neuropathy (either clinical or nerve conduction study based). Nephropathy was found in about one – fourth of all patients and 4.9% had disease of coronaries. Coronary Artery Disease (CAD) was diagnosed in patients who were presently admitted with myocardial infarction or ischemia, already diagnosed as ischemic heart disease in past (clinical or angiographic).

As the level of HbA1c increases, the proportion of retinopathy subjects also increases. Notice that the Pearson's Chi Square test is highly significant for this relation with p-value of <0.001. It tests the hypothesis that the percentage of subjects with retinopathy shows marked increase with the increase in HbA1c. Similarly, it was found that there is a significant relation between rising levels of HbA1c and neuropathy as well as nephropathy. The relation between

rising HbA1c levels and CAD was found to be insignificant. HbA1c was determined in protocol with the assays calibrated against the DCCT (Diabetes Control and Complications Trial) A1c assay. Results are shown in Figure 3.

There was found to be a highly significant association between increasing duration of diabetes and retinopathy, neuropathy and nephropathy. However, coronary heart disease had an insignificant association with the duration of diabetes. Results are revealed in Figure 4.

There is a significant association between treatment modality used and development of diabetic ketoacidosis. However no significant association was found between treatment type and HHS or hypoglycemia. See Table 14.

More than half of patients died because of infections. Next major cause was strokes followed by renal failure and myocardial infarction (See Figure 5). Mean age of men who died was 60.8 years and among females, it was 66.5 years. Maximum number of patients died of a single cause. See Table 15 and Figure 6.

Mean HbA1c level was highest in patients who died of infections (8.47) and lowest in those who died of hypoglycaemia (6.67). Hypoglycemia in our studied patients was documented symptomatic class. See Table 16 and Figure 7.

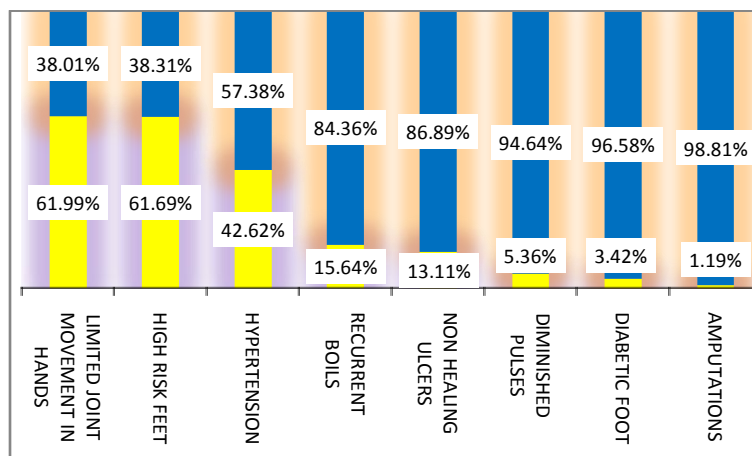


Figure 1:- Distribution of morbidities among study subjects.

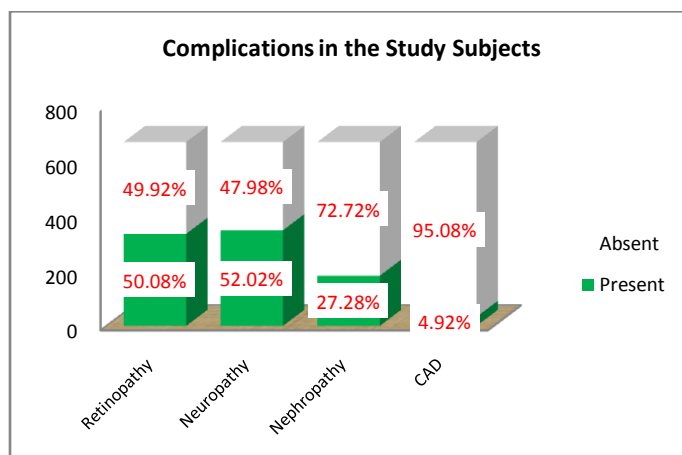


Figure 2:- Complications among study subjects.

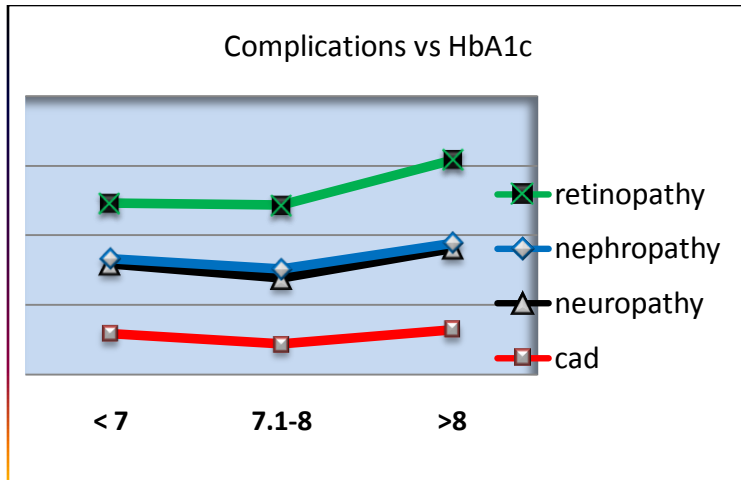


Figure 3:- Relation of complications with HbA1c level.

Complications vs Duration of diabetes

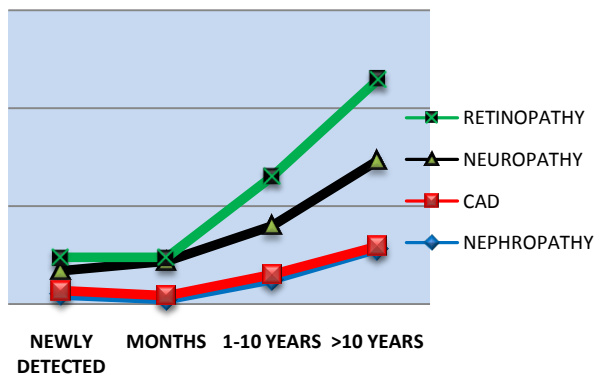


Figure 4:- Relation of complications with the duration of diabetes.

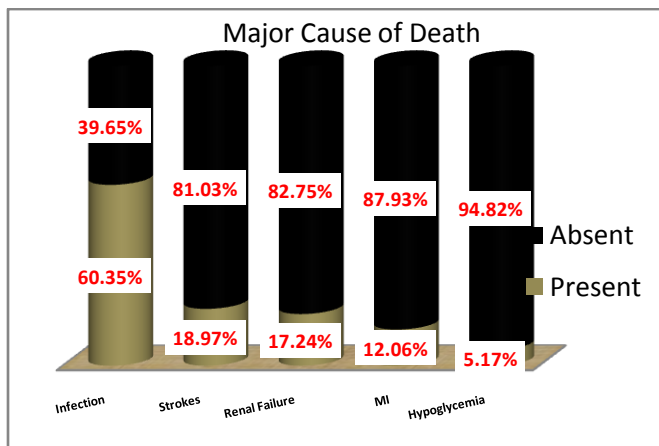


Figure 5:- Causes of mortality among diabetics.

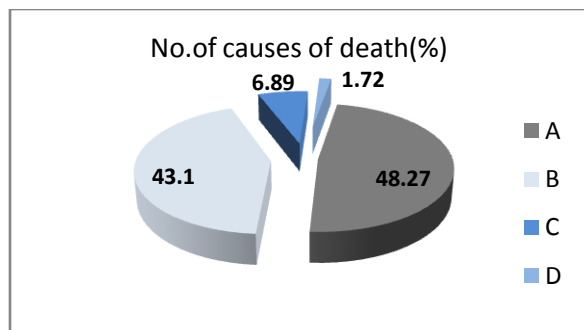


Figure 6:- Number of causes of death.

A :Single cause of death.

B : Two causes of death.

C: Three causes of death.

D: Four or more causes of death.

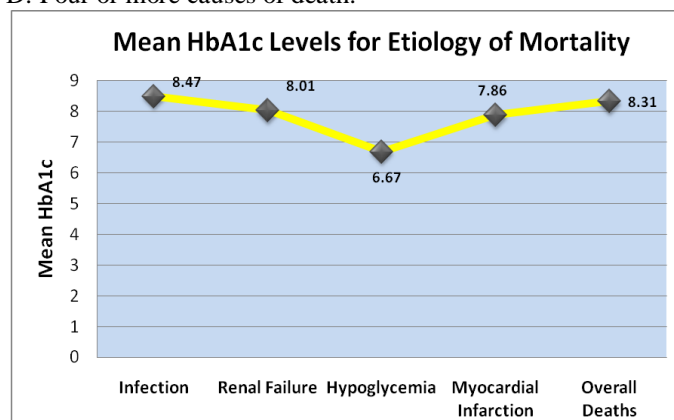


Figure 7:- Mean HbA1c level among mortalities.

Table 1:- Criteria for diagnosis of diabetes.

| Test | Normoglycemia (mg/dl) | IFG (mg/dl) | IGT (mg/dl) | Diabetes |
|-----------------------|-----------------------|-------------|-------------|--|
| FPG | <100 | 100-125 | | ≥126mg/dl |
| 2-hr PG | <140 | | 140-199 | ≥200mg/dl |
| HbA1c | <5.6% | | | >6.5 % |
| Casual plasma glucose | | | | ≥200mg/dl plus symptoms of diabetes; or hyperglycaemic crisis. |

IFG : Impaired fasting glucose; IGT: impaired glucose tolerance.

Fasting is defined as no caloric intake for at least 8 hours.

Symptoms of diabetes include polyuria , polydipsia , polyphagia, weight loss.

Table 2:- Classification of retinopathy.

| International Classification Level | ETDRS Level |
|------------------------------------|--|
| No apparent retinopathy | Level 10:DR absent |
| Mild NPDR | Level 20:very mild NPDR |
| Moderate NPDR | Levels 35, 43, 47;moderate NPDR |
| Severe NPDR | Levels 53A-E;severe to very severe NPDR |
| PDR | Levels 61, 65, 71, 75,81, 85;PDR,high risk PDR,very severe or advanced PDR |

ETDRS : Early Treatment Diabetic Retinopathy Study; NPDR : Non proliferative diabetic retinopathy; PDR Proliferative diabetic retinopathy.

Non proliferative diabetic retinopathy is characterised by retinal microaneurysms, occasional blot haemorrhages, hard exudates and one or two soft exudates.

Proliferative diabetic retinopathy is characterised by new vessels on the optic disc or elsewhere on the retina, preretinal or vitreous haemorrhage or fibrous tissue proliferation.

Table 3:- Grading of diabetic foot as per Wagner classification.

| Grade | Description |
|-------|--|
| 0 | No ulcer, but high risk foot(e.g., deformity, callus, insensitivity) |
| 1 | Superficial full thickness ulcer |
| 2 | Deeper ulcer, penetrating tendons, no bone involvement |
| 3 | Deeper ulcer with bone involvement, osteitis |
| 4 | Partial gangrene(e.g., toes, forefoot) |
| 5 | Gangrene of whole foot |

Table 4:- University of Texas classification of diabetic foot.

| Stage | Grade 0 | Grade 1 | Grade 2 | Grade3 |
|-------|--|-----------------------|---------------------------------|---------------------------------|
| A | Preulcer or postulcer lesion.No skin break | Superficial ulcer | Deep ulcer to tendon or capsule | Wound penetrating bone or joint |
| B | +Infection | +Infection | +Infection | +Infection |
| C | +Ischemia | +Ischemia | +Ischemia | +Ischemia |
| D | +Infection & Ischemia | +Infection & Ischemia | +Infection & Ischemia | +Infection & Ischemia |

Table 5:- Glycemic targets in patients with diabetes.

| Parameter | Normal | ADA |
|-------------------------------------|--------|--------|
| Premeal plasma glucose (mg/dl) | <100 | 70-130 |
| Postprandial plasma glucose (mg/dl) | <140 | <180 |
| HbA1c | 4-6% | <7% |

Table 6:- Age and Gender Distribution of Study Subjects.

| Age (Years) | Males | | Females | | Total | |
|---------------------|--------------------|----------|-------------------|----------|-------------------|-------|
| | n (268) | %(39.94) | n (403) | %(60.05) | n (671) | % |
| ≤20 | 4 | 1.49 | 8 | 1.98 | 12 | 1.78 |
| 21-40 | 24 | 8.95 | 43 | 10.66 | 67 | 9.98 |
| 41-60 | 117 | 43.65 | 192 | 47.64 | 309 | 46.05 |
| 61-80 | 118 | 44.02 | 153 | 37.96 | 271 | 40.38 |
| >80 | 5 | 1.86 | 7 | 1.73 | 12 | 1.78 |
| Mean + SD (Min;Max) | 59.26+13.8 (14,90) | | 57.56+13.8 (8,90) | | 58.24+13.8 (8,90) | |

Table 7:- Dwelling of the Study Subjects.

| Dwelling | No. of Patients | % age |
|----------|-----------------|-------|
| Rural | 375 | 55.89 |
| Urban | 296 | 44.11 |
| Total | 671 | 100.0 |

Table 8:- Type of diabetes in study subjects.

| Type of Diabetes | n | % age |
|------------------|-----|-------|
| Type-2 | 639 | 95.23 |
| Type-1 | 13 | 1.94 |
| Secondary | 12 | 1.79 |
| Gestational | 07 | 1.04 |
| Total | 671 | 100.0 |

Table 9:- Duration of diabetes in patients.

| Duration | No. of patients | %age |
|-------------|-----------------|-------|
| Upto 1 year | 88 | 13.11 |
| 1- 10 years | 481 | 71.68 |
| >10years | 102 | 15.20 |

Table 10:- Reasons for admission.

| | n | %age |
|------------------------|-----|-------|
| Infections | 319 | 47.54 |
| DKA | 23 | 10.64 |
| Strokes | 61 | 9.09 |
| Surgical problems | 56 | 8.34 |
| Hypoglycemia | 17 | 7.87 |
| Myocardial Infarction | 38 | 5.66 |
| Exacerbation of COPD | 38 | 5.66 |
| Renal failure | 28 | 4.17 |
| Cataract extraction | 23 | 3.42 |
| Skin disease | 21 | 3.12 |
| Hepatic encephalopathy | 13 | 1.93 |

Table 11:- Treatment modalities among study subjects.

| DRUGS | n | % |
|----------------|-----|-------|
| Insulin | 284 | 42.33 |
| OHAs | 200 | 29.81 |
| OHAs → Insulin | 171 | 25.48 |
| OHAs + Insulin | 16 | 2.38 |
| Total | 671 | 100.0 |

Table 12:- Distribution of morbidities among study subjects.

| Morbidities | n | % age |
|---------------------------------|-----|-------|
| Osmotic Symptoms at onset | 586 | 87.33 |
| Limited Joint Movement in hands | 416 | 61.99 |
| High Risk Feet | 414 | 61.69 |
| Pruritus Vulvae | 230 | 57.07 |
| Hypertension | 286 | 42.62 |
| Cataracts | 148 | 22.05 |
| Recurrent Boils | 105 | 15.64 |
| Gum disease | 94 | 14% |
| Non Healing Ulcer | 88 | 13.11 |
| Diminished Peripheral Pulses | 36 | 5.36 |
| Asymptomatic | 23 | 3.42 |
| Diabetic foot | 23 | 3.42 |
| Amputations | 8 | 1.19 |

Table 13:- Obesity among admitted patients with diabetes.

| | n | %age |
|------------------|-----|-------|
| Overall | | |
| Obese | 43 | 6.40 |
| Non obese | 628 | 93.60 |
| Mortality | | |
| Obese | 3 | 5.17 |
| Non obese | 55 | 94.83 |

Table 14:- Metabolic complications among study subjects.

| Complications | | Drugs | | | OHAs to Insulin | P - value |
|---------------|---------|-------|---------|----------------|-----------------|------------|
| | | OHAs | Insulin | OHAs + Insulin | | |
| DKA | Present | 1 | 15 | 2 | 5 | 0.007(Sig) |
| | Absent | 199 | 269 | 14 | 166 | |
| HHS | Present | 0 | 7 | 1 | 5 | 0.078(ns) |
| | Absent | 200 | 277 | 15 | 166 | |
| Hypoglycemia | Present | 6 | 7 | 0 | 4 | 0.891(ns) |
| | Absent | 194 | 277 | 16 | 167 | |

OHA :Oral hypoglycaemic agent; DKA: diabetic ketoacidosis; HHS :Hyperglycemic hyperosmolar state.

Table 15:- Mean ages among mortalities.

| | Mean+SD |
|-----------------------|----------------|
| Overall | 63.79+ 12.02SD |
| Males | 60.85+ 13.0 |
| Females | 66.53+ 10.51 |
| Death due to: | |
| Infections | 63.47+ 12.54 |
| Strokes | 58.14+ 13.92 |
| Renal failure | 69.80+ 9.46 |
| Hypoglycemia | 65.0+ 13.22 |
| Myocardial infarction | 64.57+ 5.12 |

Table 16:- Mean HbA1c levels in studied patients.

| Characteristics | n | Min ; Max | Mean + SD |
|---------------------------|-----|---------------|--------------|
| Overall | 671 | (5.6 ; 18.0) | 8 .07 + 1.36 |
| Cause of Mortality | | | |
| Infection | 35 | (6.1 ; 15.0) | 8.47 + 1.69 |
| Renal Failure | 10 | (6.2 ; 10.2) | 8.01 + 1.36 |
| Myocardial Infarction | 07 | (6.8 ; 9.5) | 7.86 + 0.89 |
| Hypoglycemia | 03 | (6.1 ; 7.1) | 6.67 + 0.51 |
| Overall Deaths | 58 | (6.1 ; 15.0) | 8.31 + 1.53 |

Discussion:-

This study is hospital based carried out in SMHS Hospital on admitted patients with diabetes over a period of 19 months. The study was carried on a total of 671 patients out of whom 268 (39.9%) were males and 403 (60%) were females. The main findings of the study are:

1. the most common morbidity among diabetics admitted in this hospital is infection followed by strokes.
2. the most common cause of death in diabetics is again infections, followed by strokes and renal failure.

About 40% of patients were males and 60 % were females. The mean age of admitted patients was 58.2 years (59.2 years in males and 57.5 years in females).Maximum number of subjects were in 60 – 80 year age group & minimum in upto 20 years of age. Minimum age among study subjects was 8 years and maximum was 90 years. These results are consistent with other published reports [41],[42],[43],[44],[45],[46],[47]. There was a predominance of diabetics from rural areas (55.89%) as compared to urban areas (44.11%).Similar findings have been reported by JCN Mbanya *et al* [44] but are in contrast to findings of Daina Lucia *et al* [41] and B.B.Tripathy [48] who showed a predominance of diabetics from urban areas. The bulk of patients were type 2 diabetics (95.2%) and a minority had type 1 diabetes (1.9%), followed by secondary forms of diabetes (1.7%) and gestational diabetes (1%) in the rest, these observations are similar with other published studies [41],[48]. Overall 6.4% admitted patients were obese. Similar results were reported by Raoul M Kamadjeu *et al* [49]. Maximum number of patients (about three-fourths) were having 1 -10 years duration of diabetes.15% of the patients had diabetes for more than 10 years. Rest were newly detected or had diabetes for less than 12 months.

Maximum number of admissions were for infections (47.5%). Mortality and morbidity in our diabetic population is higher from both pyogenic and tubercular infections as reported previously also [48]. Commonest infections found in our patients were those involving the urinary tract (23.5%) followed by pneumonias (17.5%). 10.64 % admissions were because of Diabetic Ketoacidosis. In the least developed countries, diabetic ketoacidosis continues to be the commonest emergency in diabetes, often precipitated by infections, and its contribution to mortality rate is 3.4% in India [50],[51]. 9.09 % patients were admitted with strokes (36% ischemic and 64% haemorrhagic). Besides these indications, major admissions were with surgical problems (8.34%), followed by myocardial infarction (5.6%), COPD exacerbations (5.6%) and renal failure (4.1%). These observations are not consistent with findings reported by Alain G Bertoni *et al* [52] who reported that the incidence of ischemic heart disease & stroke was higher than the incidence of all other diabetes related morbidities. Cardiovascular complications were a leading cause for morbidity as shown by M. Angelyn Bethel *et al* [53] and other studies [47],[54],[55], however, these were seen only in 53.28% of patients in the present study. Majority of admitted diabetics were on insulin therapy (42.3%), followed by OHAs (29.8%). One-fourth of patients were switched over from one form of therapy to another and only 2.38% patients were on combination therapy of insulin and OHAs. Type of treatment correlates with micro-angiopathic complications as shown by MMS Ahuja *et al* [56]. Major morbidities among admitted diabetics were hypertension in 42.62 %, and high risk feet in 62% patients. 15 % patients had recurrent boils and 13% had non healing ulcers among others as shown in Table 12 .

Half of all patients (50%) had diabetic retinopathy in the present study, which is not same as findings of Jean Claude Mbanya *et al* [46] who reported only 18% diabetics with retinopathy and Eugene Sobngwi *et al* [46] also observed background retinopathy in only 18% and cataract in 14% and these were the most common eye complications in diabetics as reported in other studies [30],[45],[57] also. In our study, 20% of patients had cataract. In the present study, more than half (52%) had neuropathy, that was consistent with the study of Jean Claude Mbanya *et al* [46] who reported neuropathy in 48% and the study by Upinder K Dhand [58] who showed that 60% of peripheral neuropathy was due to diabetes, however, the results were not same as reported by Pradeepa R *et al* [59] where only 26.1% had diabetic neuropathy. Symptomatic polyneuropathy appears to be more common and autonomic neuropathy less dangerous among our patients compared to those in the West as reported by P L Wahi [60]. Nephropathy in the form of albuminuria was found in about one – fourth of all patients (27.2%). In the European Diabetes Prospective Complications Study, the cumulative incidence of microalbuminuria in patients with type 1 diabetes was ~ 12% during a period of 7 years [61],[62]. In the UKPDS, the incidence of microalbuminuria was 2% per year in patients with type 2 diabetes, and the 10-year prevalence after diagnosis was 25% [10],[61]. As per the National Diabetes Fact Sheet, 2011 [63], diabetes is the leading cause of kidney failure, accounting for 44% of all new cases of kidney failure in 2008. A recent population based study by Mohan *et al* [64] reported that the prevalence of overt nephropathy was 2.2 per cent in Indians while microalbuminuria was present in 26.9 percent. Nearly 30% of patients have proteinuria after 20 years of type 2 diabetes as observed by Krolewski AS and Warram JH [65]. 4.9 % had disease of coronaries (patient either already diagnosed or presently admitted with myocardial ischemic insult) in the present study which is in confirmity with other studies. PL Wahiet *et al* [60] reported IHD to be present in 15% of diabetic population. Andre Pascal Kengne *et al* [66] showed that coronary heart disease may affect 5 – 8 % of type 2 diabetic patients. The increased vulnerability of South Asians to coronary artery disease has also been reported by Rajendra Pradeepa *et al* [67] and others [47],[54],[55]. The INTERHEART study conducted in 52 countries demonstrated that over 90% of the population-attributable risk of acute myocardial infarction were accounted for by nine modifiable risk factors, which included diabetes [50].

Mean HbA1c level in study population was 8.07+ 1.36. A significant relation between increasing HbA1c levels and risk of complications namely retinopathy (p-value <0.001) , neuropathy (p-value=0.038) and nephropathy (p-value=0.024) was observed in the present study. Similar results were observed by Mutou E [68]. Samathia P *et al* showed that HbA1c can predict the microvascular complications in patients with type 2 diabetes mellitus [69]. A 10% lower HbA1c is associated with a 43% lower risk of retinopathy [70] . Another study by Kamran Mehmood [71] showed an association between higher HbA1c and progression of retinopathy. The relation between rising HbA1c levels and coronary artery disease was found to be insignificant (p-value 0.34). As compared with standard therapy, the use of intensive therapy to target normal glycated hemoglobin levels for 3.5 years increased mortality and did not significantly reduce major cardiovascular events in the ACCORD trial [70]. There was a highly significant association between increasing duration of diabetes and retinopathy, neuropathy and nephropathy (p-value <0.001). This was consistent with findings of O.P. Ahuja *et al* [72] and M. Angelyn Bethel *et al* [53]. However, coronary heart disease had an insignificant association with the duration of diabetes (p-value 0.77) in the present study.

There is a significant association between treatment modality used and development of diabetic ketoacidosis (p-value 0.007). However no significant association was found between treatment type and Hyperglycemic Hyperosmolar State (p-value 0.078) or Hypoglycemia (p-value 0.891). In the studied population, most common metabolic complications were Diabetic Ketoacidosis (3.42%), Hypoglycemia (2.53%) and Hyperglycemic Hyperosmolar state (1.93%). Gullermo E Umpierrez et al [73] and Nugent BW [74] showed that the incidence of HHS is lower than DKA and accounts for <1% of all primary diabetic admissions.

Out of total admitted patients with diabetes, 8.64% died (28 males and 30 females). This was in contrast to the findings of Chin Hsiao Tseng [45] where diabetic men have higher risk of dying than women. However similar findings have been reported by JH Fuller et al [75]. Mean age at death was 63.7 years (60.8 years in males and 66.5 years in females) in our study, consistent with the finding of AH Zargar et al [8] and Chin Hsiao Tseng [45] for males but higher age at death in females was seen in their study. Mean HbA1c level among mortalities was 8.31 + 1.53. It was highest in patients who died of infections (8.47) and lowest in those who died of hypoglycaemia (6.67). More than half of patients died because of infections (60.3%). This has also been reported by AH Zargar et al [8], Wei et al [76] and BB Tripathy et al [48]. However, the results are not in conformity with the studies of Toshihiko Mihara et al [77] where acute cardiac failure was the leading cause of death and Shelagh I Dawson et al [78] reported same about cardiovascular disease in diabetics. Naveen Krishan Goel et al [79] also observed circulatory diseases as a leading cause of death. Next major cause of death in the present study was strokes (18.9%). These observations have been reported by AH Zargar et al [8] (13.2%) also. Renal failure (17.2%) and myocardial infarction (12%) in our study were other causes of mortality. Chronic renal failure contributed to 33.6% deaths in the study of AH Zargar et al. In his study, coronary artery disease and cerebrovascular disease were responsible for 16.9% and 13.2% of deaths respectively [8]. Hypoglycemia was responsible for death in 5.1% patients in the present study. In the study by AH Zargar et al [8], hypoglycaemia was the cause of death in 3.5% patients. In the developed world, coronary artery disease and cerebrovascular disease (CVD) are the principal causes of death in diabetics. According to WHO data, CVD and their risk factors are major contributors to global morbidity and mortality [51]. Stroke is reported as a leading cause of disability, second only to dementia [80].

Mean age at death in present study was 63.79 years (60.85 years in males and 66.53 years in females) which is in conformity with the study by AH Zargar et al [8] in which the mean age of death was 58.76 years, being significantly lower in women than men (57.4 vs 60.1 years, respectively). In a study by Das et al [81] the age at the time of death for people with diabetes was reported to be 55–61 years. Maximum number of patients died of a single cause (48.2%), 43.1% died of two causes, 6.8% of three causes and 1.7% of four or more causes of death. This was consistent with the results by AH Zargar et al [8] showing that death was attributed to a single cause in 392 (52.9%), two causes in 269 (36.3%), and three or more causes in 59 (8.0%) cases.

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