*Dissertation on*

# INFECTIONS IN CHILDREN WITH DIABETES MELLITUS

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# CERTIFICATE

Certified that this dissertation entitled "**INFECTIONS IN CHILDREN WITH DIABETES MELLITUS"** is a bonafide work done by **Dr. VIDYA KRISHNA**, Post Graduate, Department of Paediatric Medicine, Institute of Child Health and Hospital for Children, Madras Medical College, Chennai during the academic year 2004-2007.

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# CONTENTS

# Introduction

# 1. INTRODUCTION

Diabetes mellitus comprises of a group of common metabolic disorders that share the phenotype of hyperglycemia. It is the most common endocrine – metabolic disorder affecting both children and adults. The worldwide prevalence of type 1 and type 2 diabetes mellitus is increasing worldwide, with especially type 2 diabetes mellitus rising more rapidly both in children and adults due to the recent epidemic of obesity and also due to lifestyle changes. In 2000, the prevalence of diabetes mellitus was estimated to be 0.19% in people <20years and 8.6% in people >20 years[1].

Type 1 diabetes mellitus, the most common form of diabetes mellitus encountered in childhood, accounts for approximately two thirds of all cases of diabetes mellitus in children[2]. Incidence of the disease varies from as high as 50 per 100,000 population in European countries like Finland to as low as 0.1 per 100,000 population in Asian countries like India[2]. The incidence of the disease is increasing especially in countries with a previous low incidence of autoimmune diseases[3]. It is predicted that the overall incidence of type 1 diabetes will be 40% higher in 2010 than in 1997[3].

**Magnitude of the problem in India:**

Though this disease has a low incidence in our country of only 0.1 per 100,000 population the magnitude of the problem is indeed huge considering the chronicity of the illness, its effect on growth and development and long-term complications on the various organ systems causing considerable morbidity and mortality. The disease also brings about with it a change in lifestyle for the young diabetics with the need for daily exogenous insulin therapy, blood glucose monitoring and dietary changes. Due to the same reasons, diabetes mellitus imposes a great drain on the economy.

In India, Government health expenditure accounts for just 2% of the monetary budget and 0.8% of the Gross Domestic Product (GDP) (World Bank Development indicators). The per capita expenditure on health care is only 6.4% of the average global figure, while India accounts for 23.5% of the world's disability-adjusted life years lost due to diabetes[4]. Given the very limited resources available, the main thrust of health care provision is on the eradication of communicable diseases. There are also services provided by private medical practitioners for those who can afford the cost.

Shobana et al.[5]studied the direct cost of diabetes in patients attending secondary care facilities in Chennai, in the private sector. The median direct cost for patients receiving diabetes care in the private sector was US$107. They have

reported that the median direct cost to the family of an individual with type 1 diabetes is US$310(range US$45 –1936). The percentages of family income spent on diabetes care were 59%, 32%, 18% and 12% in low, middle, upper-middle and upper socio economic groups, respectively. Thus, the disease has its effects not only on the growth, development and emotional aspects of a child; it also carries the risk of long term complications with its associated morbidity and mortality with a significant effect on the economy as well.

**Our experience:**

The Diabetic clinic at the Institute of Child Health and Hospital for Children was started in the year 1999 and has about 300 registered patients. The services provided at the clinic include:

a) Monitoring of blood glucose and insulin therapy
b) Monitoring of glycemic control
c) Growth monitoring
d) Monitoring for complications:
    - Injection site assessment for atrophy / hypertrophy / abscess
    - Annual ophthalmologic review
    - Periodic monitoring of urine microalbuminuria for risk of diabetic nephropathy.
    - Blood pressure monitoring.

- Evaluation of hands, feet and peripheral pulses for signs of neuropathy or peripheral vascular disease.
- Evaluating for associated autoimmune disorder like thyroiditis in suspected cases.

During review at the Clinic it was often seen that these children reported certain infections like furunculosis, candidiasis and urinary tract infections. Literature search did not provide much data on the incidence, type and severity of infections in children with type 1 diabetes. So, this study was conceived to look in the association between infections and type 1 diabetes in children. Infections in diabetic children may be an additional risk factor for morbidity and mortality. Infections may increase the need for hospitalisation, insulin therapy and hence, also increase the health care costs. This study was planned to look into these aspects.

# Immunopathology of infections in diabetes mellitus

# 2. IMMUNOPATHOLOGY OF INFECTIONS IN DIABETES MELLITUS

Diabetes Mellitus is a common chronic metabolic disorder affecting both children and adults. It is characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin action or insulin secretion or both. It can have long-term effects on the various organs of the body like the eye, kidneys, heart, peripheral vessels and nerves.

The disease was first mentioned in the Eber's papyrus as early as 1500 B.C The discovery of insulin by Banting et al. was a significant breakthrough in the history of diabetes. They were followed by many such researchers, who have helped us to understand this disease better. And hence there has been a shift of terms from the older 'Non insulin dependent diabetes mellitus' and 'Insulin dependent mellitus' to the newer 'type 1 diabetes mellitus' and 'type 2 diabetes mellitus'.

**Type 1 Diabetes Mellitus:**

Type 1 Diabetes Mellitus is a T cell mediated autoimmune disease involving β cell damage from inflammatory cytokines and auto-aggressive T-lymphocytes. In Type 1 DM, there is absolute insulin deficiency leading on to symptomatic hyperglycemia and immediate need for exogenous insulin replacement.

## Epidemiology:

Type 1 diabetes mellitus, the most common form of diabetes mellitus encountered in childhood, accounts for approximately two thirds of all cases of diabetes mellitus in children[2].

The incidence and prevalence of Type 1 DM varies dramatically around the world, with more than 400 fold variation in the incidence in reporting countries[2]. Type 1 DM is uncommon in India, China with an incidence of only 0.1 / 100,000[2]. It is more common in Finland & Sardinia with an incidence of 50 cases per 100,000 population per year[2]. The incidence of Type 1 DM is increasing throughout the world especially in nations with a previous low incidence of autoimmune diabetes. It is predicted that the overall incidence of Type 1 DM will be 40% higher in 2010 than in 1997[3]. Also the disease has a younger age of onset now than earlier[3].

## Complications of Diabetes Mellitus:

Diabetes Mellitus is a chronic metabolic disorder characterised by both acute and chronic complications.

## Acute complications of Diabetes Mellitus:

These include DKA, hyperglycemia and hypoglycemia, which occur due to the imbalance between insulin therapy and dietary intake or exercise. These are often encountered in Type 1 DM.

**Diabetic Ketoacidosis:**

It is an important complication of childhood diabetes mellitus and the most frequent diabetes – related cause of death in children. It is a syndrome characterised by hyperglycemia, ketosis and acidemia. Diabetic Ketoacidosis (DKA) in diabetes mellitus can be the initial presentation, an acute metabolic compensation or the cause of mortality. In established diabetics, it can be precipitated by infections, intercurrent illness or by omission of insulin.

**Chronic complications of Diabetes Mellitus:**

These include retinopathy, cataracts, hypertension, nephropathy, neuropathy, coronary artery disease, peripheral vascular disease etc., These occur due to the effects of hyperglycemia or insulinopenia on the various tissues and can be prevented by proper glycemic control as was established by the Diabetes Control and Complications Trial (DCCT) [6].

Infections are an important complication of Diabetes Mellitus and they can be commonly encountered in children, whereas the other complications may be delayed in their presentation till adolescence or early adulthood.

**Associated complications:**

These include other autoimmune diseases like thyroiditis, Addison's disease, Celiac disease and Multiple Sclerosis[3].

**Infections and Diabetes Mellitus:**

It has been a time-honoured concept that the incidence of infections is higher in persons with diabetes mellitus and that such infections in the diabetic person result in complications and death more frequently than would be anticipated in otherwise healthy individuals[7, 8].

Older studies, upon which much of this information is based, focus particularly on infections of the urinary tract, respiratory tree and the extremities and derive their data from autopsy cases. However, in these studies, the degree to which infection at these sites actually contributed to the cause of death is frequently not clear, and control groups were typical lacking[9].

Later studies, while documenting excess mortality among patients with diabetes, ascribed it largely to cardiovascular diseases rather than to uncontrolled infection[10, 11]. For example, pneumonia did not cause an increase in mortality rate over that in age and sex matched controls[10, 11].

Though the associations of diabetes with an increased propensity of infection has in general, been well recognised, a more critical re-evaluation of this association has received more attention lately. Clearly, some infections occur almost exclusively in the diabetic population[12]. Others are more common in the diabetic population[12]. Still others have a different and more aggressive clinical course in the diabetic host[12].

The increased frequency and severity of infection in diabetes mellitus have been ascribed to the incompletely defined abnormalities in cell-mediated immunity and phagocyte function, hyperglycemia and diminished vascularisation. Hyperglycemia is proposed to aid the colonisation and growth of a variety of organisms like Candida and other fungal species[1].

**Diabetes Mellitus and Host Defence:**

Application of immunological techniques in the laboratory has facilitated early diagnosis of functional defects in the immune system. The World Health Organisation (WHO) has included diabetes in its classification of secondary immunodeficiency diseases[13]. These secondary immunodeficiencies, unlike primary immunodeficiencies, can be resolved if their underlying cause (e.g. a tumour or steroid treatment) is eliminated.

The immune system is a system designed to fight infections while maintaining homeostasis, thus avoiding chronic inflammatory processes and autoimmune disease. It comprises two arms, one recognising molecular patterns and the other recognising variable molecular details. These two components of the immune system are called innate and adaptive, respectively.

The innate and adaptive immune systems differ both in their mode of immune recognition of triggering factors and in their ability to respond to further signals. The adaptive response is generated in such a way as to retain memory, the

basis for vaccine design. The innate response on the other hand does not have the ability to remember a previous challenge and therefore has no immunological memory. There is a close relationship between innate and adaptive immunity, and changes in the former could provoke inappropriate responses in the latter. Since changes in innate immunity have been reported in type 1 diabetes, it is possible that these changes predispose not only to the disease but also to infections[14]. There is no evidence that the immune response to infections is altered in subjects at risk of type 1 or type 2 diabetes. The evidence supports the concept that hyperglycemia per se or the metabolic abnormality of diabetes is sufficient to explain the impaired immune response in patients responding to infections[15].

**Polymorphonuclear Cells:**

Polymorphonuclear (PMN) granulocytes represent the host's first defence against bacterial agents. In diabetic patients these cells show functional alterations in chemotaxy and under some circumstances also in phagocytosis[15,16.]

**Chemotaxy:**

This process involves the migration of WBCs. PMN cells are attracted to the site of infection by various chemotactic substances secreted by microorganisms. In addition complement activation and factors induced locally by PMN cells also play a role in this process. The energy required for this is supplied by anaerobic glycolysis and by HMP shunt.

Cells from diabetic patients have a reduced chemotaxy especially when the diabetes is poorly controlled[15]. Monocytes in diabetic patients show a decreased cellular response to a chemokine, vascular endothelial growth factor α, because of a downstream signal transduction defect[17].

**Phagocytosis:**

There are two phases of phagocytosis 1) Adhesion 2) Ingestion of foreign particles into intra cytoplasmic vacuoles. The energy required for this process is supplied by ATP produced during anaerobic glycolysis. Phagocytosis may be impaired in patients with long standing diabetes[16,18] and there is evidence for PMN functional impairment[19, 20]. In general terms the metabolic disturbances associated with diabetes are probably important in impairing the function of immune effector cells.

**Killing Activity:**

Once phagosome and lysosome fusion has taken place, killing is carried out by lysosomal enzymes. This process is dependent on the integration of oxidative and non-oxidative metabolism. Killing activity is usually measured by 1) Nitro blue tetrazolium test. 2) Chemiluminescence. Both tests show a decrease in the killing activity of PMN granulocytes associated with high blood glucose. Its normalization following intensive insulin therapy augments killing activity within 48 hours[21].

**Lymphocytes Population and their Functions:**

Type 1 DM is associated with alterations in some lymphocyte sub population. Several studies have reported a reduction in total number of T-lymphocytes and more specifically the number of CD4 T cells causing a subsequent reduction in CD4/CD8 ratio[22,23,24]. This defect could due to either decreased insulin levels or decreased insulin activity or both[25]. However, optimisation of metabolic control is accompanied by normal lymphocyte transformation and normalization of levels of T lymphocytes sub populations[26].

**Immunoglobulins:**

Serum Immunoglobulins levels (IgG and IgA) have been reported to be reduced diabetic patients compared to normal subjects[27,28]. However the antibody response in the diabetic population for example to pneumococcal polysaccharide is normal[29].

**Complement:**

It is only recently that attention has been paid to the possibility that a significant reduction in the quantity and functional activity of complement components may occur in diabetic patients. Low C4 levels, often associated with the possession of the C4A null gene, are present in approximately 25% of the patients with type 1 diabetes[30] and abnormalities of other components, e.g., C1q and C3 have also been documented[31].

**Table 1: Predisposing factors for infections in diabetes mellitus[12].**

| |
|---|
| **Primary Factors** |
| Granulocyte adherence, chemo taxis and phagocytic dysfunction |
| Myeloperoxidase deficiency |
| Complement pathway defects |
| Cytokine-mediated (e.g. interleukin-1, tumour necrosis factor) |
| **Secondary Factors** |
| Ketoacidosis |
| Use of intra vascular access lines |
| Antibiotic misuse / resistance |
| Frequent hospitalisation |
| Peripheral vascular disease |
| Neuropathy |
| Gastro paresis, reflux and aspiration |
| Indwelling urinary catheters |
| Chronic renal failure and dialysis |

A number of factors make certain tissues in diabetic patients particularly prone to infections. The four most important elements are an underlying susceptibility to infections, vascular disease, nerve damage and hyperglycemia[14]. Hyperglycemia may predispose the diabetic patient to bacterial and fungal infections. Neuropathy can 1) alter the pressure distributions contributing to ulceration and as a result infection of the feet[32] and 2) lead to autonomic involvement of the bladder with urine retention which predisposes to bacteriuria[32]. Vascular insufficiency and tissue hypoxia allow the growth of anaerobic organisms and limit host defense mechanisms[14].

The complex deterioration of both large and small blood vessels in diabetes can result in reduced peripheral circulation, relative hypoxia and as a result a predisposition to proliferation of anaerobic bacteria[33]. Furthermore hypoxia can modify the oxygen dependent function of PMN granulocytes[34]. Finally, reduction in antibiotic absorption in diabetic patients with microangiopathy might lead to persistence of infections[14].

**Diabetes Mellitus and Specific Infections:**

Some infections occur almost exclusively in the diabetic population. Others are more common in the diabetic population. They are also predisposed to infections with specific micro-organisms and at risk of infections from iatrogenic causes.

**Table 2:Classifications of Infections in Diabetes**

A) Common infections with increased incidence in diabetic patients

1) Urinary tract infections
2) Respiratory tract infections
3) Soft tissue infections

B) Infections predominantly occurring in diabetic patients

1) Malignant otitis externa
2) Rhinocerebral mucormycosis
3) Necrotizing fasciitis
4) Fournier's gangrene
5) Emphysematous cholecystitis and pyelonephritis
6) Infections in diabetic foot

C) Micro-organisms strongly associated with infections in diabetic patients

1) Candida species
2) Group B streptococcus
3) Klebsiella species
4) Hepatitis C

D) Infections resulting from Iatrogenic causes

1) Insulin injection
2) Dialysis

Infections of the urinary tract, respiratory tract and soft tissues occur with increased frequency in the diabetic population[12].

**1. <u>Urinary Tract Infections:</u>**

Urinary tract infection (UTI) is a frequently encountered problem in diabetic patients. The probable causes for increased risk of UTI in diabetic patients include:

a) Increased use of urinary catheters[35]

b) Presence of diabetic autonomic neuropathy, which causes increased residual urine volume, vesicoureteric reflux and recurrent upper UTIs[36, 37]

c) Coexistent vaginitis, cystocoele and rectocoele[12].

Upper urinary tract is more commonly involved in diabetic patient. A poor response to therapy may be due to complications, which may include, papillary necrosis or perinephric abscess. Emphysematous pyelonephritis is rare, necrotising infection of the renal parenchyma and perirenal tissue with gas formation, mostly caused by E.coli[12].

**2. <u>Respiratory Tract Infections:</u>**

Diabetic population has an increased propensity to develop infections, in particular, Tuberculosis and Pulmonary fungal infections (Coccidiomycosis, Aspergillosis and Mucormycosis)[38]. The frequency of occurrence of tuberculosis is

four times more in diabetics than in non – diabetics[38]. There is a predilection for lower lobes and the disease is more aggressive in poorly controlled diabetes[38]. The lungs in patients with diabetes show histopathologic alterations due to accumulation of non- enzymatic glycosylation end products (NGEs) of tissue proteins in the connective tissue and this manifests as functional abnormalities: reduced lung volumes, reduced pulmonary diffusion capacity and elastic recoil[38]. Again, the alteration in chemo tactic, phagocytic and bactericidal activity of PMNs predisposes to infections.

**3. <u>Skin and Soft Tissue Infections:</u>**

Skin is the body's largest and thinnest organ and is protected from infections by virtue of many factors:

- Intact stratum corneum
- Dry and acidic microenvironment
- Antibacterial effects of lipids, free fatty acids and IgA
- Endogenous micro flora and
- Mast cells

Diabetics are more prone to infections of skin and soft tissue due to:

- PMNL dysfunction
- Increased rates of skin colonization with Staphylococcus aureus[39]
- Insulin therapy

They are especially prone to specific infections like necrotising fasciitis, Fournier's gangrene, Rhinocerebral Mucormycosis, malignant otitis externa etc[12]. Infections of the foot are seen in adults due to neuropathy, peripheral vascular disease and hyperglycemia.

**Micro-organisms Strongly Associated with Infections in Diabetes:**

Certain micro-organisms appear to cause infections in patients with diabetes at a disproportionately high rate. A higher incidence of underlying diabetes has been noted in patients with Klebsiella infections such as bacteremia, liver abscess, thyroid disease and endophthalmitis[40-43]. Although an increased incidence of Staphylococcal infections has been noted, a careful recent review did not confirm the same[39].Among enteric pathogens, Campylobacter and Salmonella enteritidis have been reported with increased frequency in patients with diabetes[44,45].There is a strong association of diabetes with chronic Hepatitis C virus (HCV)[46].

The association of Candidal infection with diabetes has been well recognized. Candidiasis in diabetes is generally localized rather than truly invasive or disseminated disease[12]. Intertriginous candidiasis involves moist skin folds of inframammary, inguinal and intergluteal areas and webs of fingers and toes in obese individuals. Candida paronychia leads to chronic infection of the proximal nail fold. Candida vulvovaginitis is common in women with diabetes mellitus[47].

Oropharyngeal candidiasis is a well-documented complication of uncontrolled diabetes mellitus[12].

**Iatrogenic infections:**

Infection occurring from self-injection of insulin is quite uncommon, despite lack of practices like cleaning the skin or vial[48]. More recently it has been documented that it is not only therapeutically effective to administer insulin through clothing, but such practice is not associated with an increased incidence of infection. However, needle-site abscesses can occur in patients receiving subcutaneous insulin infusion (CSII)[49]. Infection rates in those receiving Continuous Ambulatory Peritoneal Dialysis (CAPD) are comparable to those in non- diabetic subjects[50].

# Literature Review

# 3. LITERATURE REVIEW

Infections have all along been considered to occur with greater frequency and severity in patients with diabetes mellitus[51]. This was because at the turn of the century, many diabetic patients died of overwhelming infections. However, subsequently the introduction of insulin dramatically altered the status and today non – communicable diseases like cardiovascular diseases are the leading cause of death in diabetic patients as was found by Sasaki et al.[10] and Kessler II.[11] in two independent studies on mortality in diabetic patients. So, it is considered that the association between infections and diabetes mellitus needs a more critical re-evaluation.

The earliest studies in diabetes and infection were done in 1920s when Greenwood et al[52] in 1927 studied 400 cases of diabetes mellitus and found an increased frequency of skin infections, notably, furunculosis, erysipelas, and carbuncle. Very recently a cohort study compared all patients with diabetes in Ontario, Canada, to matched non- diabetic subjects[53]. The risk ratio of suffering from an infectious disease or death caused by an infectious disease in diabetic and non diabetic patients showed that risk ratio was up to 1.92(1.79-2.05). Several infections occur more frequently in diabetes, especially severe bacterial infections. Diabetes therefore appears to increase the risk of developing an infectious disease and dying from an infectious disease.

**Urinary Tract Infections and Diabetes Mellitus:**

Urinary tract infections (UTI) are a common problem in diabetes. Asymptomatic bacteriuria occurs with a higher frequency in diabetics: a study by Geerlings et al[54] demonstrated 26% prevalence in diabetic women, compared to 6% in controls. Studies have failed to demonstrate significant differences in epidemiological, clinical and microbiological features of UTI in patients with or without diabetes mellitus except for a higher frequency of catheterization and difficulty in eradicating infection in the former group[55].

Upper urinary tract involvement may be up to five times more frequent tin diabetics than non-diabetics[12]. Bilateral kidney disease is also more frequent[56]. Complications like pyelonephritis, renal abscess and papillary necrosis are more common. Cortical and peri-renal cysts are more frequent in the diabetic population and 25% are caused by staphylococcal septicemia.

E.coli is the most common bacterial pathogen causing urinary infection in patients with diabetes, other organisms being Klebsiella pneumoniae and Proteus mirabilis[12]. Pseudomonas aeruginosa should be suspected if there is a history of recent instrumentation or hospitalization[12].

In a study by Lye et al.[57]comparing 287 diabetic patients with both community and hospital acquired UTI and 265 patients with UTI no known risk factors, it was found that, E.coli was the most common pathogen causing UTI in

diabetic patients but the number was significantly less than in the control group. The number of diabetic patients with Klebsiella as community-acquired infection was significantly more than in the control group. In nosocomial UTI in the diabetics, Klebsiella preponderance was noted. They concluded that patients with diabetes had increased susceptibility to Klebsiella as a pathogen in both community acquired and nosocomial UTI.

**Respiratory Infections and Diabetes Mellitus:**

It is unclear whether diabetes constitutes an independent risk factor for an increased incidence and severity of common upper and lower respiratory tract infections[12]. In a prospective study on pneumonia in the community by Woodhead et al.[58], it was found that compared to patients without diabetes, the overall incidence of community – acquired pneumonia may not be higher in patients with diabetes. In a large meta- analysis of community-acquired pneumonia by Fine MJ et al[59], the odds ratio for death associated with diabetes was only 1.3(95% confidence interval, 1.1- 1.5). However, the incidence of bacteremia, delayed resolution and recurrence may indeed be higher. In addition, infection due to certain specific organisms clearly occurs with an increased frequency in diabetes. These include Staphylococcus aureus, Gram-negative bacteria, Mycobacterium tuberculosis and Mucor.Another group of infections associated with increased morbidity and mortality, though not an increased frequency include infections by

streptococci, Legionella and Influenza[60]. These were observed by Koziel et al[60]. in their study on pulmonary complications of diabetes mellitus: pneumonia. Lipsky et al[61] observed in Type 2 diabetics that up to 30% of diabetics are nasal carriers of Staphylococcus aureus compared to 11% of the healthy individuals. This is a major organism in both community-acquired and nosocomial pneumonia. Gram-negative organisms are acquired by aspiration, hematogenous spread or contaminated equipment. Aspergillus species, Coccidiodes immitis and Cryptococcus neoformans can cause primary pneumonia in the diabetic host.

Studies by Marrie et al[62]. on pneumococcal pneumonia and Bouter et al[63]. on ketoacidosis and pneumonia show that patients with diabetes who develop pneumococcal pneumonia are at increased risk of bacteremia as well as a higher mortality. During epidemics of influenza, there is an increased mortality and an increased incidence of bacterial pneumonia and ketoacidosis in diabetics. The increased incidence of nasal colonization with Staphylococcus aureus in diabetics, combined with reduced pulmonary ciliary clearance in patients with influenza, leads to increased incidence of Staphylococcal pneumonia. So, current guidelines recommend both influenza and pneumococcal vaccines for all diabetic patients[12].

**Tuberculosis and Diabetes Mellitus:**

Diabetics have a risk for increased incidence of tuberculosis and have a more advanced disease at presentation[12]. Reider et al[64] reviewed the epidemiology of tuberculosis in diabetes mellitus based on three large surveys from 1950s and suggested that the relative risk of tuberculosis in individuals with diabetes is 2-3.6 times that in those without diabetes. In a study from Papua New Guinea[65], the frequency of occurrence of tuberculosis in diabetic patients was found to be 11 times the expected rate in the general population. There does not seem to be an increased prevalence of patients in developed countries[14]. There is however, evidence for increased rate of both tuberculosis in diabetes mellitus patients and new diabetes mellitus in tuberculosis patients in Africa[66].

Diabetics have more advanced disease at presentation and also atypical presentations of with greater involvement of the lower lobes, cavitation, pleural effusion and multilobe involvement[12]. While M. tuberculosis used to be a major cause of mortality in diabetic patients, this is no longer the case in developed countries[12]. Diabetes does not alter the basic guidelines for prophylaxis and treatment of tuberculosis, but it is still indication for tuberculosis testing[9].

## Skin and Soft Tissue Infections and Diabetes Mellitus:

Diabetic patients have an increased frequency of deep soft tissue infections, both bacterial and fungal.

## Bacterial Infections:

There is no clear evidence that diabetic patients are more prone to Staphylococcal infections than control subjects[14]. However, Smith JA et al[67] reported in the Lancet that there is evidence for increased nasal carriage of Staphylococcus aureus in diabetic patients, especially those treated with insulin. Patients with well-controlled diabetes do not have an increased risk for infection post operatively[14]. Cluff et al[68] in their study on staphylococcal bacteremia found that the mortality in staphylococcal bacteremia and diabetes is higher than in those without the disease.

## Fungal Infections:

Infection with Candida albicans is believed to be more prevalent in the diabetic population. In a study of 100 diabetic and 100 control subjects by Alteras et al[69], only Candida was detected more frequently in the diabetic group (31% Vs 5%); other fungi including Trichophyton and Epidermophyton were not more prevalent in diabetic patients. Chronic paronychia due to Candida was found in 10% of young diabetic girls as against 3% of normal subjects in a study by Stone et al[70] . Hyperglycemia aids the colonisation of Candida species. Hill et al[71], using a

direct swab technique, found that a level of $HbA_{1C}$ of 12% or greater correlated with yeast colonization.

Mucormycosis relates to a group of fulminant infections caused by Phycomycetes. Infection with these organisms is rare as there is strong innate immunity. The increased risk in diabetics is evident only in those who are debilitated, for example with diabetic ketoacidosis[14]. Batra et al[72]. have reported that about 75% of the patients with mucormycosis have diabetes mellitus. In such patients, the natural inhibitory activity of the patient's serum against the Phycomycetes is lost but can return with insulin treatment.

**Diabetic Ketoacidosis and Infections:**

Various studies have been done in adults to find the incidence of Diabetic Ketoacidosis (DKA) in new onset and established cases, the most common precipitating factor in DKA and to find the cause of mortality in DKA.

Infection has been found to be the most common precipitating factor of DKA in the various studies done in adults. In many case series in adults in the last 20 years, infection was the most common precipitating factor in about 28-43%. However, insulin omission is considered to be the most frequent cause of DKA in children with known diabetes[73].

A study done by Chiang et al[74] to investigate the frequency of viral and bacterial infections in children, who have DKA, showed that bacterial infections

were present in only 13% and viral infections in18%. Among the subgroups of children with established diabetes, bacterial infections were present in 17% and viral infections in 20%.

**Table 3: DKA study – Chiang et al[74]**

| | **Bacterial infections** | **Viral Infections** |
|---|---|---|
| All DKA | 13% | 18% |
| DKA in Established diabetics | 17% | 20% |

A study was done by Matoo et al[75] at Chandigarh among 143 cases of DKA in the age group 8-70 years. 33.5% was new onset DKA and infection was the most common precipitating factor (30%). Omission of insulin was the cause in 20%. Mortality rate was 23.7%.

**Table 4: Summary of DKA studies**

| **Reference** | **Episodes (n)** | **Infection (%)** | **Poor insulin compliance (%)** | **New onset diabetes** |
|---|---|---|---|---|
| Faisch et al[76] | 152 | 43 | 26 | NR |
| Kitabchi et al[77] | 202 | 38 | 28 | 22 |
| Krentz et al[78] | 746 | 28 | 13 | 10 |

**Infections and Glycemic Control:**

Some studies have failed to prove a causal relation ship between hyperglycemia and infections like the study by Wheat LJ[36] published in the Diabetes Care in the year 1980. However, some authors like Moutschen et al[15] suggest that hyperglycemia or the metabolic abnormality is sufficient to explain the immune response in patients responding to infections. They have reported that cells from diabetic patients have reduced chemotaxy, especially when diabetes is poorly controlled. Gin H et al[21]. reported that the bactericidal capacity of the Polymorphonuclear leucocytes, which is decreased in the presence of high blood glucose, normalizes following intensive insulin regime. So, there is evidence both for and against the fact that poor glycemic control predisposes to infections in diabetes mellitus.

It is also true that infections in diabetic patients may worsen the glycemic control. Stress related hyperglycemia causes release of cytokines that affect carbohydrate metabolism. IL -1 and TNF increase net glucose flux and oxidation[79]. In addition, stress causes release of counter regulatory hormones and hence, hyperglycemia. So, poor glycemic control may impair the immune response and cause infections, which in turn may worsen the glycemic status.

# Study Justification

# 4. STUDY JUSTIFICATION

Infections occurring in adult diabetics have been extensively studied but literature does not provide much data on infections in childhood diabetes, especially in India as research data on diabetes in children is scarce. Review of literature shows that infections occur more frequently and with more severity in diabetic patients. It is also seen that they are predisposed to certain specific infections like those of urinary tract and skin. Infections with certain organisms are also found to be more common. Infections may be caused by poor glycemic control and may further hamper the glucose homeostasis. Infections are also found to be the most common precipitating factor in diabetic ketoacidosis, the most frequent diabetic related cause of death in children. There is no data available on the incidence of Hepatitis B infection and tuberculosis in diabetic children. Hence there is an urgent need to study about infections in diabetic children - whether they occur in increased frequency and with more severity. There is also a need to study the role of infections in precipitating diabetic ketoacidosis in children with diabetes mellitus.

# Objectives of the Study

# 5. OBJECTIVES OF THE STUDY

1) To identify the incidence of infections in children with Type 1 Diabetes Mellitus.

2) To determine the type and severity of infections.

3) To evaluate the risk factors causing infections in diabetic children.

4) To evaluate the role of infections in precipitating diabetic ketoacidosis in diabetic children.

# Study Methodology

# 6. STUDY METHODOLOGY

**Study Design:**

This study was carried out with a Cohort study design.

**Setting:**

The study was conducted at the Institute of Child Health and Hospital for Children, Madras Medical College, a Tertiary care Children's Hospital in Chennai.

**Study Period**:

It was done during the period of January 2005 – September 2006

**Study Population:**

Children with Diabetes Mellitus attending the Diabetic clinic at the Institute of Child Health and Hospital for Children, Chennai (GROUP 1) were enrolled and an equal number of age and sex matched children without Diabetes mellitus enrolled from the School Health Cell and Immunisation OPD of the Institute of Child Health and Hospital for Children, Chennai as the comparison group (GROUP 2).

**Inclusion Criteria:**

**For Group 1:** Children with Diabetes Mellitus in the age group of 0 – 12 years and registered at the Diabetic clinic at Institute of Child Health and Hospital for Children and on regular follow up and willing to participate in the study.

**For Group 2:** Age and Sex matched children free of Diabetes Mellitus and willing to participate in the study.

**Exclusion criteria:**

- Children with severe PEM (Grade III and Grade IV PEM)
- Children with malignancies like leukaemia, lymphoma
- Children on immunosuppressive drugs or steroids for any reason.
- Children with Renal failure, nephrotic syndrome or any known immunodeficiency states, sickle cell anaemia and recurrent wheeze.

**Sample size:**

There is no data on infections in diabetic children, especially in comparison with normal children. Hence, the sample size was calculated for an expected 20% difference in incidence of infections between the two groups and found to be 112 in each group.

**Manoeuvre:**

The study was conducted at the Institute of Child Health and Hospital for Children between the period of January 2005 and September 2006. The cases were enrolled for the study from the Diabetic clinic at the Institute.

Though 300 patients are registered with the clinic many patients collect their drug (insulin) from a neighbouring government hospital and come only for assessment of glycemic control and complications. The others come for a review once in every 6-8 weeks. So, it was decided to enrol patients who lived in and around Chennai and collected drugs from the clinic and were on a regular follow up. Enrolment was done from April 2006 – June 2006. About 170 children who were on regular follow up were selected and data regarding age of onset, family history of diabetes mellitus, previous hospitalisations and other relevant medical history were collected and anthropometry recorded.

Of these 170 children, 112 children who satisfied the inclusion and exclusion criteria and who were free of infections at the time of enrolment and who were willing to participate in the study were registered. Baseline investigations in the Group 1 included complete blood count, peripheral smear, blood glucose, urine routine, urine culture and sensitivity, Mantoux and chest X ray. These children were advised to come to the clinic for a monthly follow up on Fridays and to meet

the principal investigator. The parents were also encouraged to contact the principal investigator in case of intercurrent infections or hospitalisations.

At the time of monthly follow up, data was collected regarding any intercurrent illness – its type and also severity – i.e., whether it required hospitalisation or not. The children were thoroughly examined and anthropometric measurements were recorded. All infections in the Group 1 were appropriately investigated with complete blood count, peripheral smear, urine routine, urine culture and sensitivity, radiological investigation, culture of body fluids & serological tests. The children were screened for HBsAg after obtaining consent from the patients. For the assessment of glycemic control, $HbA_{1C}$ levels were evaluated once in every 4 months i.e., at 4, 8 and 12 months into the study.

Age and sex matched controls satisfying the inclusion and exclusion criteria and willing to participate in the study were enrolled within 3 days of registering a case, from the School Health Cell and Immunisation OPD of the Institute of Child Health and Hospital for Children, Chennai. Data was recorded regarding a family history of diabetes mellitus and relevant medical illness in these children. Anthropometric measurements were recorded. No baseline investigation was done in this group. These children were followed up monthly at the review OP days on Saturdays at the General OPD for a period of one year. The patients were encouraged to meet the principal investigator in case of intercurrent illness or

hospitalisations. Appropriate investigations were done for these children when they developed infections. They were not tested for HBsAg. Mantoux and Chest X ray were not done. $HbA_{1C}$ was also not done in this group, as it is not relevant.

Both the groups were investigated based on the signs and symptoms of infection only. There was no difference in the intensity of the investigations done in either group.

Any documented infection based on clinical and/or lab investigations was considered as an outcome measure. List of expected infections included Urinary tract infections, Pneumonia, Impetigo, cellulitis, furunculosis and other soft tissue infections, Fungal infections of skin and mucosal membranes, Supportive otitis media, Tonsillitis, Sinusitis, fever > 5 days without or localising symptoms , etc., Simple URI i.e. fever < 5 days duration with or without cough and rhinitis, fever without localising focus of infection and acute watery diarrhoea with a few loose stools lasting for less than three days, all of which did not warrant antimicrobial or antimalarial therapy were documented but were not considered as an outcome. The detailed definitions for infections considered as outcome in this study are as follows:

**Urinary Tract Infection:**

Clinical signs and symptoms of UTI in the form of fever, dysuria, increased frequency of urination, lower abdominal pain and hematuria supported by urine

examination showing pyuria with or without urine culture and sensitivity positivity was considered as UTI.

**Pneumonia:**

Features such as fever, cough, breathlessness, chest pain, preceded by symptoms of upper respiratory infection with clinical evidence in the form of tachypnea, respiratory distress, cyanosis, adventitious breath sounds with increased total WBC count in the range of 15 – 40,000 cells/cu .mm with polymorphic or lymphocytic predominance and a positive CRP, confirmed by radiological evidence of pneumonia in the form of pneumonitis, consolidation, bronchopneumonia with or without pleural effusion and empyema.

**Pharyngitis / Tonsillitis:**

Fever, sore throat, headache, change of voice, dysphagia, with congestion of the tonsils with exudates, enlarged tender anterior cervical lymph nodes supported by increased total WBC count, with polymorphic predominance and a positive CRP confirmed by positive throat swab culture.

**Sinusitis:**

Persistent upper respiratory symptoms of fever, cough, including nasal discharge, headache, pain over the sinuses for 10 – 14 days or severe respiratory symptoms including purulent nasal discharge and a temperature of at least 102° F

for 3 – 4 days, supported by radiological evidence of infection of the sinuses in the form of opacification, mucosal thickening or presence of air fluid levels.

**Otitis Media:**

History of fever, ear pain, irritability, ear discharge supported by otoscopic evidence of infection in the form of two of the three abnormalities 1. White, yellow of amber or blue colour of the tympanic membrane. 2. Opacification of the membrane and 3. Decreased or absent mobility.

**Pyogenic Infections of Skin:**

Including impetigo, abscess, folliculitis, hydradenitis, cellulitis and ecthyma were diagnosed based on that clinical examination findings, Gram stain and culture positivity of the blister fluid or a moist plaque if present.

**Candidiasis:**

Clinical evidence of candidal infection as oral thrush and genital involvement as itching, pain, dysuria, vulvar erythema, with cheesy exudates, paronychia and onychomycosis with laboratory evidence of candida in the scrapings.

**Septicemia:**

Clinical features suggestive of sepsis supported by evidence of infection in the complete blood count and peripheral smear and a positive CRP confirmed by non-enteric blood culture positivity.

Any other infection encountered was diagnosed as per the clinical features and confirmed by laboratory evidence. The end point for the diagnosis was based on laboratory evidence in the form of culture positivity wherever feasible. However in certain conditions where lab evidence was not possible always (for e.g. Impetigo) definite clinical features were taken as the end point for infection.

**Diabetic Ketoacidosis:**

All the children admitted with diabetic ketoacidosis during the study period (January 2005 – June 2006) were evaluated. Detailed history regarding the clinical features and duration, compliance of insulin and features suggestive of infection were taken. Clinical examination for assessing the hydration status, circulatory status and to identify the focus of infection was done. Baseline investigations included complete blood count, blood sugar, blood urea, serum creatinine and serum electrolytes, urine routine with ketones, urine culture and sensitivity, non-enteric culture and chest X ray. Special additional investigations like culture of body fluids were done as required.

All the children in both the groups completed the one-year follow up period. There were no deaths in either group. The results are discussed subsequently.

# Results

# 7. RESULTS

A total of 112 diabetic children were enrolled in the study. The same number of age and sex matched children who were not the siblings of the study children were identified from the Immunisation OPD and School Health Cell of The Institute of Child Health and Hospital for Children, Chennai were enrolled as the comparison group. Both the groups of children were followed up for a period of one year from the time of enrolment. They were reviewed every month for the presence of infections and the details were documented. The data was analysed using SPSS software Version 11.0 for Windows.

The results of analysis are presented as follows:

**1.Socio - demographic characteristics**

**2.Incidence, type and severity of infections**

**3. Risk factors for infections in diabetic children**

## 7.1.Socio- demographic Characteristics:

These are presented as follows:

Age and Sex

Nutritional status

Family History of diabetes mellitus

Diabetic age in diabetic children

## Age and Sex Distribution of the Study Populations

The age and sex distribution of the study populations is depicted in the following table.

**Table 1: Age and Sex Distribution of the Study populations**

| Age (years) | Group 1* | | Total | Group 2* | | Total |
|---|---|---|---|---|---|---|
| | Males | Females | | Males | Females | |
| < 5 | 6 | 13 | **19** (16.96%) | 6 | 13 | **19** (16.96%) |
| 5-10 | 23 | 31 | **54** (48.21%) | 23 | 31 | **54** (48.21%) |
| > 10 | 15 | 24 | **39** (34.82%) | 15 | 24 | **39** (34.82%) |
| Total | **44** (39.28%) | **68** (60.71%) | **112** | **44** (39.28%) | **68** (60.71%) | **112** |

Group 1 – Diabetic Children

Group 2 – Non Diabetic children

Of the 112 diabetic children enrolled for the study, 54 children (48.21%) were in the age group 5 – 10 years. 39 children (34.82%) and 19 children (16.96%) were in the age group above ten years and less than five years respectively. There were 44 males and 68 females in Group 1 constituting 39.28% and 60.71% respectively. The controls were chosen to be age and sex matched as per the study

design and their age and sex distribution were similar to the diabetic children as revealed by the table.

**Nutritional Status:**

The nutritional status of the study populations is presented as weight, height and Body Mass Index (BMI) percentiles .

**Weight for Age Centiles Distribution:**

The following table shows the weight for age centiles of the study groups.

**Table 2: Weight for Age Centiles Distribution of Group 1 and Group 2:**

| Weight centiles | Group 1 | | | Group 2 | | |
|---|---|---|---|---|---|---|
| | **Males** | **Females** | **Total** | **Males** | **Females** | **Total** |
| < 5 $^{th}$ | 5 | 2 | 7(6.25%) | 9 | 14 | 23(20.53%) |
| 5$^{th}$- 95$^{th}$ | 38 | 66 | 104(92.85%) | 35 | 54 | 89(79.46%) |
| >95$^{th}$ | 1 | 0 | 1(0.89%) | 0 | 0 | 0(0%) |
| **Total** | **44** | **68** | **112** | **44** | **68** | **112** |

In the diabetic group, the weight of 104 children(92.85%)were in the normal range, seven (6.25%) had weight less than the 5 $^{th}$ centile and one(0.89%) had weight above the 95$^{th}$ centile. In the non diabetic group, the weight of 89 children(79.46%)were normal, 23( 20.53%) were less than 5 $^{th}$ centile and none above 95$^{th}$ centile.

**Height for Age Centiles Distribution:**

The following table shows the height for age centiles of the study groups.

**Table 3: Height for Age Centiles Distribution of Group 1 and Group 2**

| Height centiles | Group 1 | | | Group 2 | | |
|---|---|---|---|---|---|---|
| | **Males** | **Females** | **Total** | **Males** | **Females** | **Total** |
| < 5 $^{th}$ | 4 | 4 | 8(7.14%) | 9 | 17 | 26(23.21%) |
| 5$^{th}$- 95$^{th}$ | 39 | 63 | 102(91.07%) | 35 | 51 | 86(76.78%) |
| >95$^{th}$ | 1 | 1 | 2(1.78%) | 0 | 0 | 0 (0%) |
| **Total** | **44** | **68** | **112** | **44** | **68** | **112** |

In the diabetic group, the height of 102 children(91.07%) were in the normal range, eight ( 7.14%) had height less than the 5$^{th}$ centile and two( 1.78%) had height above the 95$^{th}$ centile. In the non-diabetic group, the height of 86 children(76.78%) were normal, 26( 23.21%) were less than 5$^{th}$ centile and none above 95$^{th}$ centile.

**BMI for Age Centiles Distribution:**

The following table shows the BMI for age centiles of the study groups.

**Table 4: BMI for age centiles distribution of Group 1 and Group 2**

| BMI centiles | Group 1 | | | Group 2 | | |
|---|---|---|---|---|---|---|
| | Males | Females | Total | Males | Females | Total |
| Normal | 36 | 61 | 97(86.6%) | 34 | 48 | 82(73.21%) |
| Underweight | 8 | 6 | 14(12.5%) | 8 | 17 | 25(22.32%) |
| Overweight | - | - | - | 2 | 2 | 4(3.57%) |
| Obese | 0 | 1 | 1(0.89%) | 0 | 1 | 1(0.89%) |
| Total | 44 | 68 | 112 | 44 | 68 | 112 |

Of the 112 children in the diabetic group, 97 children(86.6%) were normal, 14 were underweight(12.5%), none were overweight and one was obese(0.89%). Of the 112 non-diabetic children, 82 (73.21%) were normal, 25(22.32%) were underweight, four (3.57%)were overweight and one was obese.

**Family History of Diabetes Mellitus:**

The family history of diabetes mellitus in the children with diabetes mellitus is depicted below.

**Table 5: Family History of Diabetes in Group 1**

| Relation | Male | Female | Total |
|---|---|---|---|
| Mother | 0 | 1 | 1 |
| Father | 1 | 4 | 5 |
| Siblings | 0 | 1 | 1 |
| Other relatives | 12 | 7 | 19 |
| **Total** | **13** | **13** | **26** |

A total of 26 children among the diabetic group had a family history of diabetes, of whom 13 were males and 13 were females. The table above depicts the family history of diabetes in Group 1. None of the children in Group 2 had a positive family history of diabetes.

**Diabetic Age:**

This is analysed as diabetic age less than two years and more than two years.

**Table 6: Diabetic Age Group:**

| Diabetic Age | Number of children | | Total |
|---|---|---|---|
| | Males | Females | |
| <2 years | 18(40.9%) | 27(39.7%) | **45**(40.17%) |
| >2 years | 26(59.09%) | 41(60.29%) | **67**(59.82%) |
| **Total** | **44** | **68** | **112** |

Of the 44 males in Group 1, 18 (40.9%) had a diabetic age less than two years, whereas 26 males (59.09%) had a diabetic age more than two years. Among the females, 41(60.29%) had a diabetic age more than two years, while 27(39.7%) had a diabetic age less than two years. Overall, among the 112 diabetic children, 45children(40.17%)and 67 children (59.82%)had diabetic age less than two years and more than two years respectively.

## 7.2. Incidence of Infections:

In this section , the incidence of infections in the study populations is discussed. Simple URI, Fever without localizing signs lasting less than five days and acute watery diarrhea lasting less than three days were not considered for analysis. The following table shows the number of infected children in both the groups.

**Table 7: Number of children with infections in Group 1 and Group 2**

| No. of children who had infections | Group 1 (N = 112) | | Group 2 (N =112) | | p – value* |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Total no. of children with infections | 56 | 50.5% | 46 | 41.1% | 0.23 |
| Skin infections | 51 | 45.5% | 23 | 20.5% | **0.000** |
| Urinary tract infections | 7 | 6.3% | 0 | - | **0.014** |
| Respiratory Infections | 7 | 6.3% | 22 | 19.6% | **0.005** |

*Chi-square test

Out of the 112 diabetic children, 56 children (50.5%) developed infections during the study period. Out of the 112 controls, 46 children (41.1%)developed infections during the study period. Analysis by Chi- square test, revealed no statistical difference in the total number of infected children between the two groups. However, the presence of individual infections showed a significant difference between the two groups. 51 children (45.5%) of the 112 diabetic

children, developed bacterial and fungal infections of the skin during the study period as against 23 children (20.5%) in the control group. Analysis revealed a statistical significance of p –0.0000. 7(6.3%) of the diabetic children developed Urinary tract infections whereas none in the control group had the same in the one-year follow up period. This again was found to be statistically significant. Analysis of the total respiratory infections in the groups showed that there were only 7 cases (6.3%) among diabetics as against 22 cases (19.6%) in the control group. This also had statistical significance, however with respiratory infections being more in the Group 2.

**Number and Type of Infections in the Study Populations:**

The table below shows the number and type of infections in both the groups.

**Table 8: Type of Infections in Group 1 and Group 2:**

| Infections | Group 1 | Group 2 |
|---|---|---|
| **Respiratory Infections:** | | |
| Pneumonia | 1 | 1 |
| Sinusitis | 1 | 2 |
| Pharyngotonsillitis | 2 | 16 |
| ASOM | 3 | 3 |
| Urinary tract infections | 8 | 0 |
| **Skin and soft tissue infections:** | | |
| Bacterial Infections | 77 | 21 |
| Fungal Infections | 13 | 2 |
| Sepsis | 0 | 0 |
| **TOTAL** | **107** | **45** |

A total of 107 infections were encountered in among the diabetic children during the one-year follow up as against only 45 infections in the normal children during the same period. Of the 107 infections in Group 1, skin and soft tissue infections were the most commonly encountered. A total of 90(84.1%) infections of the skin and soft tissue were seen during the study period. Bacterial infections (71.96%) were more common than fungal (12.14%) of the skin. In Group 2, only 23 (51.1%)

were infections of the skin and soft tissue. Here again, bacterial infections (46.66%) were commoner than fungal (4.44%). A total of eight Urinary tract infections (7.4%) were seen in the diabetic group and none in the control group (0%) during the one-year follow up. There were 22 (48.88%) infections of the respiratory tract in Group 2 as against 7(6.5%) in Group 1.

This table shows that diabetic children had more number of infections when compared to the normal children. Also, infections of the skin and soft tissue and urinary tract were more commonly seen in the diabetic children.

None of the diabetic children tested positive for HBsAg. Though three children had Mantoux positivity, none required treatment with Anti tuberculous therapy.

Also, 27 of the 56 infected diabetic children (48.21%) had more than one infection during the study period, with one child recording a maximum of 10 infections. None in the control group had more than one infection during the study period.

**Infections of the Skin and Soft Tissue:**

Below is shown, the type of skin infections in both the groups.

**Table 9: Type of Skin infections in Group 1 and Group 2:**

| Skin Infections | Group 1 | Group 2 |
|---|---|---|
| **Bacterial infections:** | | |
| Impetigo | 31 (34.4%) | 14 (60.86%) |
| Cellulitis | 10 (11.11%) | 2 (8.7%) |
| Abscess | 18 (20%) | 0 (0%) |
| Furunculosis | 14 (15.56%) | 5 (21.73%) |
| Nail infections | 4 (4.44%) | 0 (0%) |
| **Fungal infections:** | | |
| Dermatophytosis | 3 (3.33%) | 2 (8.7)% |
| Candidal Infections | 10 (11.11%) | 0 (0%) |
| **Total** | **90** | **23** |

In Group 1**,** of the 90 infections of the skin and soft tissue, 77 infections (85.5%) were bacterial and 13(14.4%) were fungal whereas in Group 2, of the total 23 skin infections, 21 infections (91.3%) were bacterial and two were fungal (8.69%). Among the diabetic children, the most common bacterial infection was impetigo (n= 31, 40.25%), followed by abscess (n=18,23.38%). There were 10 episodes of cellulitis (13%). Furunculosis constituted 18.18%( n=14) and nail infections 5.2%( n=4) of the total bacterial skin infections. Of the 18 abscesses encountered, five were at the injection site. Staphylococcus aureus was isolated

from one of the five injection site abscesses (n=1, 20%). and ten of the thirteen abscesses at other sites (n=10,76.9%). Totally 11 cultures (61.1%) were positive of the 18. The rest of the cultures (38.89%) were sterile. Looking at fungal infections in Group 1, Candidal infections were the commonest (n=10,76.92%) and Dermatophytosis constituted the rest (n=3,23.07%).

The commonest bacterial infection in Group 2 was impetigo (n=14,66.67%). The number of furunculosis and cellulitis seen were five (23.8%) and two (9.52%) respectively. All fungal infections were Dermatophytal infections (n=2,100%). No Candidal infection was seen.

**Infections of the Urinary Tract:**

The organisms causing urinary tract infections in Group 1 is shown below. There were no urinary tract infections in Group 2 during the study period.

**Table 10: Organisms causing urinary tract infections in Group 1**

| Organism | Number |
|---|---|
| E.coli | 4(50%) |
| Klebsiella | 3(37.5%) |
| Pseudomonas aeruginosa | 1(12.5%) |
| Total | **8** |

Of the eight urinary tract infections in Group 1, four (50%) were caused by E.coli, and three by Klebsiella (37.5%). One child admitted with Diabetic ketoacidosis had urinary tract infection with Pseudomonas aeruginosa (12.5%).

**Severity of Infections:**

Severity of infections was assessed in our study by the need for hospitalisation. There were three admissions in Group 1 for infections, which included leptospirosis, urinary tract infection and abscess of both the thighs. Of the 14 children admitted for Diabetic Ketoacidosis, five children had associated infections. It could not be assessed if the infections in these children posed an independent risk factor for hospitalisation. None in the control group had any hospitalisations.

## 7.3 Risk Factor Analysis for Infections in Children with Diabetes Mellitus:

Risk factor analysis was done for children with diabetes mellitus based on the following:

**1.Socio-demographic factors:**

- **Age**
- **Sex**
- **Diabetic age and**
- **Nutritional status (BMI).**

**2. Glycemic control (Mean $HbA_{1C}$)**

**3. Presence of Diabetic Ketoacidosis (DKA)**

Risk factor analysis was done for incidence of total infections and for incidence of specific infections like skin and soft tissue, respiratory tract and urinary tract. The correlation between infections and diabetic ketoacidosis was also analysed.

**Analysis of Risk Factors for Total Infections :**

The risk factor analysis for total infections in diabetic children is discussed below.

**Table 11: Analysis of risk factors for total infections**

| | N | % | Total Infections | | | | p-value* |
|---|---|---|---|---|---|---|---|
| | | | Yes | | No | | |
| | | | n | % | n | % | |
| **Age** | | | | | | | |
| < 5 years | 19 | 17.0 | 10 | 52.6 | 9 | 47.4 | |
| 5 - 10 years | 54 | 48.2 | 27 | 50.0 | 27 | 50.0 | |
| > 10 years | 39 | 34.8 | 19 | 48.7 | 20 | 51.3 | 0.96 |
| **Sex** | | | | | | | |
| Male | 44 | 39.3 | 21 | 47.7 | 23 | 52.3 | |
| Female | 68 | 60.7 | 35 | 51.5 | 33 | 48.5 | 0.85 |
| **Diabetic age** | | | | | | | |
| <=2 years | 45 | 40.2 | 20 | 44.4 | 25 | 55.6 | |
| > 2 years | 67 | 59.8 | 36 | 53.7 | 31 | 46.3 | 0.44 |
| **Nutrition:** | | | | | | | |
| Normal | 97 | 86.6 | 49 | 50.5 | 48 | 49.5 | |
| Under weight | 14 | 12.5 | 6 | 42.9 | 8 | 57.1 | 0.52 |
| Overweight | - | - | - | - | - | - | |
| Obese | 1 | 0.9 | 1 | 100.0 | - | - | |

*Chi-square test

The incidence of total infections in the diabetic children were analysed with respect to age as age less than 5 years, 5-10years and more than 10 years. Of the 19 children in the Under 5 group, 10(52.6%) had infections. 27of the 54 children (50%) in the age group 5-10 years and 19 of the 39 children (48.7%) of age more than 12 years had infections . Analysis by Chi- square test, showed no statistical significance. Of the 44 males with diabetes, 21 (47.7%) had infections and 35 of the 68 females (51.5%) had infections. Statistical analysis showed no significant

correlation with sex. There were 45 children with diabetic age less than 2 years, of whom 20(44.4%) had infections .36 of the 67 children (53.7%) with diabetic age more than 2 years had infections. This again was not statistically significant. Of the 97 children with normal nutrition, 49 (50.5%) had infections and 48 (49.5%) had no infections. Six of the14 underweight children (42.1%) had infections and eight (57.1%) did not. The one obese child (100%)had no infection. No statistical significance was noted.

**Glycemic Status and Occurrence of Total Infections:**

The influence of glycemic status on the occurrence of total infections is shown below.

**Table 12: Mean $HbA_{1C}$ Level and Occurrence of Total Infections**

| | **All diabetic children** | **Occurrence of Total Infections** | | **p-value** |
|---|---|---|---|---|
| | | **Had Infection** | **No infection** | |
| **Mean $HbA_{1C}$** | 11.7 ± 3.1 | 13 ± 2.9 | 10.5 ± 2.8 | **0.00**$^{+}$ |

+ Two sample t-test

Mean $HbA_{1C}$ in the study population was 11.7 ±3.1. It was higher in the infected children group, with a mean of 13± 2.9, when compared to the non-infected diabetics (10.5±2.8). This was found to be statistically significant when analysed by the two-sample test.

**Analysis of Risk Factors for Skin Infections:**

The risk factor analysis for skin infections in diabetic children is discussed below.

**Table 13: Analysis of Risk Factors for Skin Infections:**

| | N | % | Skin Infections | | | | p-value* |
|---|---|---|---|---|---|---|---|
| | | | Yes | | No | | |
| | | | n | % | n | % | |
| **Age** | | | | | | | |
| < 5 years | 19 | 17.0 | 10 | 52.6 | 9 | 47.4 | |
| 5 - 10 years | 54 | 48.2 | 25 | 46.3 | 29 | 53.7 | |
| > 10 years | 39 | 34.8 | 16 | 41.0 | 23 | 59.0 | 0.70 |
| **Sex** | | | | | | | |
| Male | 44 | 39.3 | 19 | 43.2 | 25 | 56.8 | |
| Female | 68 | 60.7 | 32 | 47.1 | 36 | 52.9 | 0.70 |
| **Diabetic age** | | | | | | | |
| <=2 years | 45 | 40.2 | 19 | 42.2 | 26 | 57.8 | |
| > 2 years | 67 | 59.8 | 32 | 47.8 | 35 | 52.2 | 0.70 |
| **Nutrition:** | | | | | | | |
| Normal | 97 | 86.6 | 44 | 45.4 | 53 | 54.6 | |
| Under weight | 14 | 12.5 | 6 | 42.9 | 8 | 57.1 | |
| Overweight | - | - | - | - | - | - | |
| Obese | 1 | 0.9 | 1 | 100.0 | - | - | 0.54 |

*Chi-square test

The number of children with skin infections were analysed age wise as less than 5 years, 5- 10 years and more than 10 years.10 of 19children under 5 years, 25 of 54 children (46.3%) between 5 and10 years and 16 of 39children (41%) above 10 years had skin infections with no statistical significance. 19 of 44 male diabetics

(43.2%) and 32 of 68(47.1%) female diabetics had skin infections, which again failed to show any statistical significance. Diabetic age again, did not seem to affect the incidence of skin infections as 19 of 45 (42.2%)children with diabetic age <2 years had skin infections as against 32 of 67 (47.8%)children with diabetic age >2 years. Of the 97 children with normal nutrition, 44 (45.4%) had skin infections whereas 53 (54.6%) did not. Six of the 14 underweight children (42.1%) had skin infections and eight (57.1%) did not. The one obese child (100%) was infected. No statistical significance was noted.

**Glycemic Status and Skin Infections:**

The influence of glycemic status on the occurrence of skin infections is shown below.

**Table 14: Mean $HbA_{1C}$ Level and Skin Infections**

| | **All Diabetic Children** | **Skin Infections** | | **p-value**[+] |
|---|---|---|---|---|
| | | **Had Infection** | **No infection** | |
| **Mean $HbA_{1C}$** | 11.7 ± 3.1 | 13.1 ± 2.8 | 10.6 ± 2.9 | **0.00** |

+ Two sample t-test

The glycemic status however did affect the occurrence, with greater $HbA_{1C}$ levels of 13.1±2.8 being associated with skin infections. In the non-infected group, the mean $HbA_{1C}$ was 10.6±2.9.

**Analysis of Risk Factors for Respiratory Infections:**

The risk factor analysis for respiratory infections in diabetic children is discussed below.

**Table 15: Analysis of risk factors for Respiratory infections in Group 1:**

| | N | % | Respiratory Infections | | | | p-value* |
|---|---|---|---|---|---|---|---|
| | | | Yes | | No | | |
| | | | n | % | n | % | |
| **Age** | | | | | | | |
| < 5 years | 19 | 17.0 | 1 | 5.3 | 18 | 94.7 | |
| 5 - 10 years | 54 | 48.2 | 4 | 7.4 | 50 | 92.6 | |
| > 10 years | 39 | 34.8 | 2 | 5.1 | 37 | 94.9 | 0.89 |
| **Sex** | | | | | | | |
| Male | 44 | 39.3 | 5 | 11.4 | 39 | 88.6 | |
| Female | 68 | 60.7 | 2 | 2.9 | 66 | 97.1 | 0.11 |
| **Diabetic age** | | | | | | | |
| <=2 years | 45 | 40.2 | 2 | 4.4 | 43 | 95.6 | |
| > 2 years | 67 | 59.8 | 5 | 7.5 | 62 | 92.5 | 0.70 |
| **Nutrition:** | | | | | | | |
| Normal | 97 | 86.6 | 7 | 7.2 | 90 | 92.8 | |
| Under weight | 14 | 12.5 | - | - | 14 | 100.0 | |
| Overweight | - | - | - | - | - | - | |
| Obese | 1 | 0.9 | - | - | 1 | 100.0 | 0.56 |

* Chi-square test

Of the total 7 children with respiratory infections, one was less than 5 years old (5.3%), four were between 5-10 years (7.4%) and one was more than 10 years (5.1%). Age, did not seem to affect the incidence of respiratory infections when

analysed statistically. 5 males (11.4%)and two females (2.9%) had respiratory tract infections .Sex again, did not have any effect on the incidence of respiratory infections. 2 children (4.4%) with diabetic age less than 2 years and 5 children (7.5%)with diabetic age more than 2 years had respiratory infections with no statistical significance. Of the 97 children with normal nutrition, 7(7.2%) had respiratory infections whereas 90 (92.8%) did not. None of the underweight or obese children were infected. No statistical significance was noted.

**Glycemic Status and Respiratory Infections:**

The influence of glycemic status on the occurrence of respiratory infections is shown below.

**Table 16: Mean $HbA_{1C}$ level and Respiratory infections**

| | **All diabetic children** | **Respiratory Infections** | | **p-value**[+] |
|---|---|---|---|---|
| | | **Had Infection** | **No infection** | |
| **Mean $HbA_{1C}$** | 11.7 ± 3.1 | 12.7 ± 3.7 | 11.7 ± 3.1 | 0.40 |

+ Two sample t-test

Mean $HbA_{1C}$ also showed no difference between the diabetic children with respiratory infections (Mean $HbA_{1C}$ 12.7±3.7) and those without (11.7±3.1).

**Analysis of Risk Factors for Urinary Tract Infections:**

The risk factor analysis for urinary tract infections in diabetic children is discussed below.

**Table 17: Analysis of Risk Factors for Urinary Tract Infections :**

| | N | % | Urinary Tract Infections | | | | p-value+ |
|---|---|---|---|---|---|---|---|
| | | | Yes | | No | | |
| | | | n | % | n | % | |
| **Age** | | | | | | | |
| < 5 years | 19 | 17.0 | 2 | 10.5 | 17 | 89.5 | |
| 5 – 10 years | 54 | 48.2 | 2 | 3.7 | 52 | 96.3 | |
| > 10 years | 39 | 34.8 | 3 | 7.7 | 36 | 92.3 | 0.52 |
| **Sex** | | | | | | | |
| Male | 44 | 39.3 | 2 | 4.5 | 42 | 95.5 | |
| Female | 68 | 60.7 | 5 | 7.4 | 63 | 92.6 | 0.70 |
| **Diabetic age** | | | | | | | |
| <=2 years | 45 | 40.2 | 5 | 11.1 | 40 | 88.9 | |
| > 2 years | 67 | 59.8 | 2 | 3.0 | 65 | 97.0 | 0.12 |
| *Nutrition* | | | | | | | |
| Normal | 97 | 86.6 | 7 | 7.2 | 90 | 92.8 | |
| Under weight | 14 | 12.5 | - | - | 14 | 100.0 | |
| Overweight | - | - | - | - | - | - | |
| Obese | 1 | 0.9 | - | - | 1 | 100.0 | 0.56 |

* Chi-square test

Of the eight diabetic children with urinary tract infections, two (10.5%)were in the age group less than five years, two (3.7%) in the age groups 5- 10 years and three (7.7%) in the age group more than 10 years. No statistical significance for

age was noted. There were two males (4.5%) and five females (7.4%) with no statistical significance for sex. Five of the children had diabetic age less than two years (11.1%) and two had a diabetic age more than two years (3%). This was also not found to be significant statistically. Of the 97 children with normal nutrition, 7(7.2%) had urinary tract infections whereas 90 (92.8%) did not. None of the underweight or obese children were infected. No statistical significance was noted.

**Glycemic Status and Urinary Tract infections:**

The influence of glycemic status on the occurrence of urinary tract infections is shown below.

**Table 18: Mean $HbA_{1C}$ level and Urinary tract in**fections

| | **All diabetic children** | **Urinary Tract Infections** | | **p-value**[+] |
|---|---|---|---|---|
| | | **Had Infection** | **No infection** | |
| **Mean $HbA_{1C}$** | 11.7 ± 3.1 | 10.8 ± 2.9 | 11.8 ± 3.1 | 0.40 |

+ Two sample t-test

The mean $HbA_{1C}$ was 10.8 ± 2.9 in the diabetic group with urinary tract infections and was 11.8 ± 3.1 in the diabetic group with no urinary tract infections. Glycemic status did not show any statistically significant association with urinary tract infections in the diabetic group.

**Infections and Diabetic Ketoacidosis:**

The correlation between infections and Diabetic Ketoacidosis is presented below.

**Table 19: Association between Infections and Diabetic Ketoacidosis (DKA)**

| | DKA present | No DKA |
|---|---|---|
| **Infections present** | 5 | 51 |
| **No Infections** | 9 | 47 |

Of the 112 diabetic children enrolled in the study, 14 developed Diabetic Ketoacidosis during the study period, of which five were associated with infections. Analysis showed no significant correlation between infections and Diabetic Ketoacidosis. (p value = 0.25)

**Infections and Severity of diabetic ketoacidosis:**

Of the 14 children admitted with diabetic ketoacidosis during the study period, five had infections.

**Table 20: Infections and Severity of diabetic ketoacidosis**

| | N | % | Infections | | | | p-value |
|---|---|---|---|---|---|---|---|
| | | | Yes | | No | | |
| | | | n | % | n | % | |
| **Severity** | | | | | | | |
| Mild | 9 | 64.3 | 3 | 33.3 | 6 | 66.7 | |
| Moderate | 5 | 35.7 | 2 | 40.0 | 3 | 60.0 | 1.00* |
| **Shock** | | | | | | | |
| Yes | 8 | 57.1 | 3 | 37.5 | 5 | 62.5 | |
| No | 6 | 42.9 | 2 | 33.3 | 4 | 66.7 | 1.00* |
| **Insulin infusion duration (Hours)** | 20 ± 18 | | 24 ± 24 | | 17 ± 15 | | 0.61+ |
| **Subcutaneous insulin duration (Hours)** | 68 ± 43 | | 46 ± 36 | | 80 ± 43 | | 0.19+ |
| **Days of hospital stay** | 6 ± 4 | | 4 ± 2 | | 7 ± 5 | | 0.44+ |

* Chi-square test + Mann-Whitney U test

The severity of DKA was assessed as mild, moderate and severe based on the pH and mental status as per the table in Nelson's textbook of pediatrics (17th edition , Pg 1954).

**SEVERITY OF DKA**

| | **Venous pH** | **Clinical** |
|---|---|---|
| Normal | 7.35 – 7.45 | No change |
| Mild DKA | 7.25 – 7.35 | Fatigued |
| Moderate DKA | 7.15 – 7.25 | Kussmaul's respiration, sleepy, arousable |
| Severe | < 7.15 | Kussmaul or depressed respiration, depressed sensorium to coma. |

Other factors like shock, duration of insulin infusion, duration of subcutaneous insulin administered and duration of hospitalisation was compared between the children with infections and diabetic ketoacidosis and children with diabetic ketoacidosis only.

As is evident from the table, none of the factors achieved any statistical significance, implying that the presence of infections did not alter the severity of diabetic ketoacidosis. Though the mean duration of hospital stay was higher in the non-infected group when compared to the infected group, it also did not achieve any statistical significance. Probably, other risk factors like poor compliance may need to be assessed to find the cause for this seemingly increased duration of hospitalisation in the non-infected group. This aspect, though outside the purview of this study, may form the basis for future studies in diabetic ketoacidosis

# Summary of the Study

# 8. SUMMARY OF THE STUDY

At the end of a one-year follow up period, it is seen that the number of infections are more common in the diabetic children than in the normal children. Though the actual number of infected children in both the group is not very different between the groups, it is seen that the number of times a diabetic child got infected is more than the number of times a normal child got infected during the same one year follow up period, i.e.; whenever a diabetic child got infected it had a tendency to have recurrent infections which was not so in the case of normal children. It is also seen that infections of the skin and soft tissue and urinary tract are more common in the diabetic children than in the normal children whereas respiratory tract infections are more common in the normal children. While three children in the diabetic group were hospitalized for infections, in addition to five children with infections and diabetic ketoacidosis, none of the normal children were hospitalized for infections. None of the diabetic children in the study suffered from Hepatitis B infection or tuberculosis.

Analysis of risk factors for infections shows that the incidence of total infections is not affected by age, sex, nutritional status or diabetic age, but poor glycemic control predisposes to an increased number of total infections in the infected children. Similarly, the incidence of skin, respiratory, and urinary tract infections is not affected by age, sex, nutritional status or diabetic age. The

incidence of skin infections is affected by the glycemic status, with poor glycemic control predisposing to more infections of the skin and soft tissue. However, incidence of urinary tract infections and respiratory tract infections is not affected by the glycemic status.

In our study, no correlation has been found between infections and Diabetic ketoacidosis or its severity.

# Discussion

# 9. DISCUSSION

## Comparison with Other Studies and Literature Review:

Most of the studies on infections in diabetes mellitus have been done only in adults with either Type 2 or Type 1 diabetes. There is paucity of data on infections in diabetes mellitus in children. Review of the literature shows that, people with diabetes mellitus have incompletely defined abnormalities of the cell mediated immunity, phagocytic function, hyperglycemia and diminished vascularisation all of which leads to an increased incidence and frequency of infections in these patients[1]. In fact, the World health Organisation lists diabetes as a secondary immunodeficiency disease[13]. There is also evidence to support the concept that hyperglycemia per se or the metabolic abnormality in diabetes is sufficient to explain the impaired immune response in patients responding to infections[15]. It is also true that infections in diabetic patients may worsen the glycemic control[12, 79]. So, poor glycemic control may impair the immune response and cause infections, which in turn may worsen the glycemic status, and, hence, these children with poor glycemic control have recurrent infections.

As observed by Smitherman et al.[51] our study also shows that infections occur with greater frequency and severity than in non- diabetics. Greenwood et al.[52] in their study found an increased frequency of skin infections, notably,

furunculosis, erysipelas, and carbuncle. In our study also diabetic patients had more number of skin and soft tissue and urinary tract infections. Bacterial infections of the skin were more common than fungal. However impetigo was the commonest bacterial infection in our study among the diabetic population. Abscesses and nail infections were more commonly seen in the diabetic population. Staphylococcus aureus was the commonest organism isolated. There is no clear evidence for increased incidence of Staphylococcal infections in diabetics, though the risk of increased nasal[61] and skin colonization[39] by the same is noted, especially for those on insulin therapy.

As seen in the study by Alteras et al.[69], Candida was more common in the diabetics than non –diabetics (11.11%Vs 0%) whereas their study showed a difference of 31% Vs 5%. Dermatophytosis was not more common in the diabetics than in the non diabetics (3.33% Vs 8.75%) as observed in the study by Alteras as well.

E.coli was the most commonly isolated organism causing urinary tract infection in our study (50%) followed by Klebsiella(37.5%).Nirmal Joshi[12] says that E.coli is the commonest organism causing urinary tract infection. This was also observed in the study by Lye et al[57] where they noted that that though E.coli was the commonest pathogen causing urinary tract infection in diabetics, they had a significant risk of acquiring Klebsiella infection both in the community and in the

hospital. Our study also shows that, Klebsiella is the next most common pathogen causing urinary tract infection in diabetics. One child admitted with Diabetic ketoacidosis grew Pseudomonas aeruginosa, which again could be explained by the hospitalisation.

Respiratory infections were not more commonly seen in the diabetic group as compared to the normal children. As seen in the Woodhead study[58], the incidence of pneumonia is not higher in diabetic children. In our study, no serious respiratory infections were encountered as quoted in the studies by Fine et al.[59] and Koziel et al.[60] probably because of seeking health care early and lack of exposure to certain organisms said to be associated with increased morbidity and mortality in diabetics, such as Legionella and influenza. Also, respiratory infections were significantly more common in the normal children with the risk of spread from one to another. None of the diabetic children in our study had tuberculosis. This is in contrast to the study by Reider et al.[64] which suggested that the relative risk of tuberculosis in individuals with diabetes is 2-3.6 times that in those without diabetes. Again , in a study from Papua New Guinea[65], the frequency of occurrence of tuberculosis in diabetic patients was found to be 11 times the expected rate in the general population. However all these were done on adults with diabetes and probably more studies would be needed to find the prevalence of tuberculosis in diabetes mellitus in children. Again the incidence of HBsAg was not found to be

increased. Fraser et al.[46] only found an association with chronic Hepatitis C virus infection and not chronic Hepatitis B virus infection.

A number of in vitro studies done by Moutschen et al.[15] and Gin H et al.[21]have proved the impaired immune response in poorly controlled diabetes. Our study has established that poor glycemic control does lead on to infections in diabetic children, especially of the skin and soft tissue.

No correlation between infections and diabetic ketoacidosis was noted. Poor compliance is the most common precipitating factor for diabetic ketoacidosis in children as per literature. The study by Chiang et al.[74] also shows that children with diabetic ketoacidosis are not commonly associated with infections.

# Conclusion

# 10. CONCLUSIONS

- ✓ Infections occur more frequently in diabetic patients and with more severity.
- ✓ Diabetic children are more prone to infections of the skin and urinary tract when compared to normal children.
- ✓ None of the diabetic children in our study suffered from tuberculosis.
- ✓ None of the diabetic children in our study had Hepatitis B Virus infection.
- ✓ Poor glycemic control predisposes to infections in diabetic children, especially of the skin and soft tissues.
- ✓ There is no correlation between infections and diabetic ketoacidosis or its severity in children with diabetes.

*Maintaining good glycemic control could prevent infections in children with diabetes mellitus. Hence, there is an urgent need to create awareness in children with diabetes and their parents regarding maintenance of good glycemic control.*

# Annexure - i

**Data Entry Form for Registration of Group 1:**

## S.no

Name Age Sex

Address

Date of Registration

Family history of Diabetes mellitus:

Diabetic age as on registration

## Previous hospitalisations: Y /N

Diagnosis:

Other medical illnesses :

**Clinical Examination:**

Height (cm): Weight (kg): BMI:

**Baseline Investigations:**

Total count: Differential count : Peripheral smear :

Urine : Albumin Sugar Deposits

Urine C/S :

Mantoux Chest X ray:

HBsAg :

$HbA_{1c}$ : 1 2 3

**Data Entry Form for Registration of Group 2:**

S.No

Name

Age

Sex

Address

Date of Registration

Family history of Diabetes mellitus:

Medical History:

Clinical Examination:

Height (cm):

Weight (kg):

BMI:

**Follow up Visits – Data entry form for Groups 1 and 2:**

Date: S.no: Visit number :

Height (cm): Weight(kg) : BMI :

Complaints: Nil / Fever/ Cough/ breathlessness/diarrhea/vomiting/ Skin infection/ dysuria/ itching over genitals/injection site injection/ ear discharge/convulsions/ altered sensorium/ others.

Duration of illness:

Examination: HR RR BP Temp

CVS RS P/A CNS

ENT SKIN

Severity of illness: treated as op/ip

Investigations:

TC DC PS

Blood Glucose (Group 1):

Urine R/E:

Urine Culture and sensitivity:

Non Enteric Culture and sensitivity:

Body Fluids Culture and sensitivity:

Radiological investigations: X rays USG

Final diagnosis: Duration of Hospitalisation:

**Proforma for children with Diabetic Ketoacidosis:**

Complaints:

Duration :

**Examination:** HR RR BP Temp

CVS RS P/A CNS

SKIN ENT

Focus of Sepsis:

**Features of DKA:**

1.Dehydration : Y/N

2.Acidotic features: Y/N

3. Shock : Y/N

**Predisposing Factors :**Infections/ Poor compliance/ none

**Investigations:**

**TC DC PS**

B.Sugar S.electrolytes B.urea S.creatinine

pH :

Urine R/E

Urine Culture and sensitivity:

Non Enteric Culture and sensitivity:

Chest x- ray : Others :

Duration of insulin infusion (hrs):

Duration of subcutaneous insulin(hrs):

Duration of Hospitalisation(days):

Final diagnosis:

Outcome:

# Annexure – ii

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