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RESEARCH ARTICLE

PREVALENCE AND RISK FACTORS OF COMMON INFECTIONS IN PATIENTS WITH DIABETES MELLITUS IN SAUDI ARABIA: A SINGLE CENTER STUDY.

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Manuscript Info

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Abstract

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Introduction:-Diabetes mellitus is a common health problem in our country. Diabetic patients are more prone to contract infections, which may lead to increased morbidity and mortality. Identification of those patients at risk can decrease the burden of illness for the patients and our community.

Aim of the study:-To determine the common infections in diabetic patients in our setting and the risk factors for developing these infections.

Subject and methods:-From the period 1st December 2015 to 31st January 2016 three hundred diabetic patients who have the illness for not less than 5 years were interviewed using a prepared questionnaire. Questions included baseline characteristics, comorbidities, infections encountered in the past and complications developed. Data was analyzed using means or ratios as appropriate. A p value of < 0.05 was considered as significant.

Results:-Most of the patients were male (71.3%) with most of them being above 40 years old. The prevalence of infection was (173/300) 57.6%. Bacterial infections were the most common (140/300) 46.7% followed by fungal infections (19/300) 12% and the least were viral infections (14/300) 4.7%. Serious infections constituted 21%. The presence of diabetic complications ($p < 0.0001$) and being hypertensive (p 0.034) were the most significant risk factors for overall infections.

Conclusion:-Although the prevalence of infection is high in diabetic patients. Being hypertensive and the presence of diabetic complications were associated with a higher risk of developing these infections. Knowing these risk factors would help directing the patient management for this group of patients.

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Introduction:-

The incidence of diabetes mellitus (DM) has increased significantly in recent years in several developed and developing countries. A recent study showed a prevalence of 30% in Saudi Arabia (1), which is considered a major health problem leading to human suffering, loss of productivity, and enormous costs. No doubt, diabetic patients are more prone to infections, and few studies have been done on the overall risk of infection in diabetic patients (2). Generally, many factors may contribute to an increased risk of infection among diabetics, which include an increased level of glucose and decreased blood pH values, whichcause impairment in the function of polymorph leukocytes and lymphocytes. This affects humeral immunity, decreases the production of interleukins, decreases tissue perfusion as a result of macrovascular and microvascular complications, and decreases sensation due to diabetic neuropathy, which may cause skin infections. (3,4) Skin and urinary tract are the most common sites infected in DM patients. Staphylococcal, fungal infections, cellulitis, erysipelas, and oral or genital candidal infections are the most common skin infections (4). A few infectionsprimarily affect diabetic patients, such asrhinocerebralmucormycosis, malignant otitis externa, and emphysematous cholecystitis (3). Few studies were done worldwide to estimate the risk of overall infections in patients with DM.One study was a 1999 retrospective cohort study in Canada. It analyzed the rate of infection and/or death in diabetic patients and age-matched groups, with 513,749 in each group. It results showed that diabetic patients have significantly higher rate of infections and infectious disease-related hospitalizations. The most common of which were bacterial infections such as osteomyelitis, pyelonephritis and cystitis, pneumonia, cellulitis, sepsis or peritonitis (2,5). Another study was a prospective cohort study in Netherlands. The study compared 705 adult patients with type 1 DM and 6,712 adult patients with type 2 DM to a control group of 18,911 patients who had hypertension without diabetes. It concluded that upper respiratory tract infections were equally common in the diabetic patients and in the control group. The study also found that patients with types 1 and 2 DM are at increased risk for lower respiratory tract infections, urinary tract infections, and skin and mucous membrane infections (6). On the other hand, in Saudi Arabia, only few studies focused on a single type of infection, such as hepatitis B, hepatitis C and diabetic foot. In 1999 and 2000, a study conducted in Jeddah estimated that 33 out of 234 (14.1%) hepatitis B–positive patients and 35 out of 165 (21.2%) hepatitis C–positive patients are type 2 diabetics (7). Another study in Jeddah on 598 diabetic patients revealed that 11.4% of them had diabetic foot complications such as foot ulcers, gangrenes, and amputations. The author concluded that there is an association between longer diabetes duration, insulin use, low hemoglobin, and diabetic foot complications (8). We aim in our study to identify the common infections in diabetic patients in Al-Madinah region and identify the associated risk factors fordeveloping these infections, aiming to give physicians information that could be used to decrease the rate of certain infectious diseases in diabetic patients.

Subject And Methods:-

The study was carried out in Prince Abdulaziz Bin Majed Bin Abdulaziz Diabetes Care Center in Al-Madinah, Saudi Arabia. We carried out a retrospective cross-sectional study on all diabetic patients who have records in the diabetes care center for at least five years and attending the out-patient clinics in the period from 1st December 2015 to 31st January 2016. We conducted direct interviews using a questionnaire (Appendix 1), including personal and medical history to determine the risk factors, such as age, gender, smoking status, uncontrolled diabetes status, high HbA1c, residency (urban or rural), job, and other comorbid conditions such as hypertension or any end-organ failure or malignancy, and also the type of treatment, such as insulin, oral hypoglycemic drugs, or a combination; it also included asking about the infections that happened to the patients after they had been diagnosed with diabetes.

Data Analysis:-

The gathered data was processed using Statistical Package of Social Sciences version 17 (SPSS version 17 Inc., Chicago, IL, USA). Quantitative data were expressed as means with standard deviations (SD) and medians with inter-quartile ranges (IQR) for normally and abnormally distributed data, as appropriate. Qualitative data were expressed as frequency (numbers) and percentages. Student's t-test was used to test the significance of difference for quantitative variables that follow normal distribution. Chi squares and Fisher'sexact tests were used to test the significance of difference for qualitative variables. A p value of < 0.05 was used as a statistically significant value.

Ethical Considerations:-

Writtenconsent was obtained from Prince Abdulaziz Bin Majed Bin Abdulaziz Diabetes Care Center administration in Madinah.This study was also approved by the ethical committee of the local health authority in Madinah . Moreover, a formal consent was obtained from every patient participating in the study.

Results:-

Table(1) shows a total of 300 diabetic patients attending the Diabetes Center who were included in this study. Of those patients, 34(11.3%) were type 1 DM and 266 (88.7%) were Type 2 DM; there were 214 (71.3%) males and 86 (28.7%) females. Most of the patients were older than 40 years (86.3%), and the majority (92.3%) live in urban areas. Regarding the type of infection, Figure (1) shows that UTI was the most common infection associated with DM (26.3%), followed by skin infection (23%), wound site infection (12.7%), oral candidiasis (7.3%), pneumonia (4.7%), HBV (2%), and HCV (0.7%); the least infections were sepsis, TB, and malignant otitis externa, which had the same percentage (0.3%). In Figure (2), we found that according to the etiology and the presence of serious infections, the most common type of infection was bacterial infection, with 46.7 % of the subjects having at least one episode of bacterial infection, followed by fungal infection (12%), and viral infection (4.7%). However, serious infections (malignant otitis externa, tuberculosis, pneumonia, sepsis, hepatitis B, hepatitis C and/or diabetic foot) constituted 21%. In regard to the socio-demographic risk factors for infection, Table (2) shows that the highest infections rate was in patients less than 20 years old (77.8%), and the lowest was (43.8%) in patients between 20 and 40 years old; females have a higher percentage of infection (66.3%) than males (54.2%), patients who live in suburban areas have the highest percentage of infection (85.7%) while patients who live in urban areas have the lowest percentage (56.3%); divorced patients have the highest percentage of infection (87. 5%) while married patients have the lowest percentage (54.5%); however, none of the socio-demographic factors was statistically significant. In Table (3), we notice that the presence of diabetic complications is statistically highly significant risk factor for infection ($p < 0.0001$); it also was found that 62.7% of the hypertensive patients get infections versus 37.3%, which was statistically significant ($P=0.034$). Table (4) shows the relationship between documented HbA1c levelsand the presence of infection. We find that the majority of patients with high HbA1c values get infections (55.5%). However, this was statistically insignificant. Table (5) shows risk factors for the occurrence of bacterial infection in diabetic patients; it is more common in females (60.5%) compared to males (41.1%) ($P <0.01$). Hypertension and hyperlipidemia were risk factors for having a bacterial infection, as 69.3% of the infected patients were hypertensive ($P=0.001$), and 50.7% had hyperlipidemia ($P= 0.004$), but the presence of diabetic complications was the most significant risk factor ($P < 0.001$) for bacterial infections. In Table (6), we notice that being maleand smoking are significant risk factors for the occurrence of viral infections, with p-values of 0.015 and 0.023, respectively.

Table 1:- Sociodemographic characteristics of the study sample.

	Total(n=300)	%
Age (years):		
<20	9	3.0%
20- <40	32	10.7%
40- <60	156	52.0%
60-	103	34.3%
Gender: Male	214	71.3%
Female	86	28.7%
Residence:		
Urban	277	92.3%
Rural	16	5.3%
Suburban	7	2.3%

Table 2:- the occurrence of infection according to the socio-demographic characteristics.

	Total (n=300)	%	Group				p-value
			infection (n=173)		No infection (n=127)		
			No.	%	No.	%	
Age (years):							
<20	9	3.0%	7	77.8%	2	22.2%	
20- <40	32	10.7%	14	43.8%	18	56.3%	0.24
40- <60	156	52.0%	91	58.3%	65	41.7%	
60-	103	34.3%	61	59.2%	42	40.8%	

Gender:							
Male	214	71.3%	116	54.2%	98	45.8%	
Female	86	28.7%	57	66.3%	29	33.7%	0.056
Residence:							
Urban	277	92.3%	156	56.3%	121	43.7%	
Rural	16	5.3%	11	68.8%	5	31.3%	0.195
Suburban	7	2.3%	6	85.7%	1	14.3%	
Marital status:							
Single	28	9.3%	19	67.9%	9	32.1%	0.12
Married	235	78.3%	128	54.5%	107	45.5%	
Widow	29	9.7%	19	65.5%	10	34.5%	
Divorced	8	2.7%	7	87.5%	1	12.5%	

Table 3:- risk factors for occurrence of infection:

Risk factors	Total (n=300)	%	Group				p-value
			infection (n=173)		No infection (n=127)		
			No.	%	No.	%	
Hypertension	177	59.0	111	62.7%	66	37.3%	0.034*
Hyperlipidemia	126	42.0	80	63.5%	46	36.5%	0.82
Hypercholesterolemia	147	49.0	88	59.8%	59	40.2%	0.450
Diabetic Complications	242	80.7	153	63.2%	89	36.8%	<0.0001*
Smoking	44	14.7	28	63.6%	16	36.4%	0.386

**Table 4:-** The relation between HgA1c Level and presence of infection

| HgA1c level	Total (n=190)	%	Group				p-value
			infection (n=100)		No infection (n=90)		
			No.	%	No.	%	
More than 7	144	75.8%	80	55.5%	64	44.5%	0.153
7 or less	46	24.2%	20	43.5%	26	56.5%	

Table 5:- risk factors for occurrence of bacterial infection:

Risk factors	Total (n=300)	%	Group				p-value
			infection (n=140)		No infection (n= 160)		
			No.	%	No.	%	
Age (years): <20	9	3.0%	5	55.6%	4	44.4%	0.668
20- <40	32	10.7%	13	40.6%	19	59.4%	
40- <60	156	52.0%	70	44.9%	86	55.1%	
>60	103	34.3%	52	50.5%	51	49.5%	
Gender: Male	214	71.3%	88	41.1%	126	58.9%	<0.01*
Female	86	28.7%	52	60.5%	34	39.5%	
Smoking	44	14.7%	22	15.7%	22	13.8%	0.631
Hypertension	177	59%	97	69.3%	80	50%	0.001*
Hyperlipidemia	126	42%	71	50.7%	55	34.4%	0.004*
Hypercholesterolemia	147	49%	77	55%	70	43.8%	0.052
Complications	242	80.7%	125	89.3%	117	73.1%	<0.001*

Table 6:- risk factors for occurrence of viral infection:

Risk factors	Total (n=300)	%	Group infection (n=14)		No infection (n= 286)		p-value
			No.	%	No.	%	
Age (years): <20	9	3.0%	0	0.0%	9	100.0%	0.194
20- <40	32	10.7%	0	0.0%	32	100.0%	
40- <60	156	52.0%	11	7.1%	145	92.9%	
>60	103	34.3%	3	2.9%	100	97.1%	
Gender: Male	214	71.3%	14	6.5%	200	93.5%	0.015*
Female	86	28.7%	0	0.0%	86	100.0%	
Smoking	44	14.7%	5	35.7%	39	13.6%	0.023*
Hypertension	177	59%	8	57.1%	169	59.1%	0.885
Hyperlipidemia	126	42%	4	28.6%	122	42.7%	0.297
Hypercholesterolemia	147	49%	5	35.7%	142	49.7%	0.308
Complications	242	80.7%	13	92.9%	229	80.1%	0.237

Figure (1) Presence of infection in the study subject

Figure (2) Presence of infection in the study subject according to etiology and serious infection
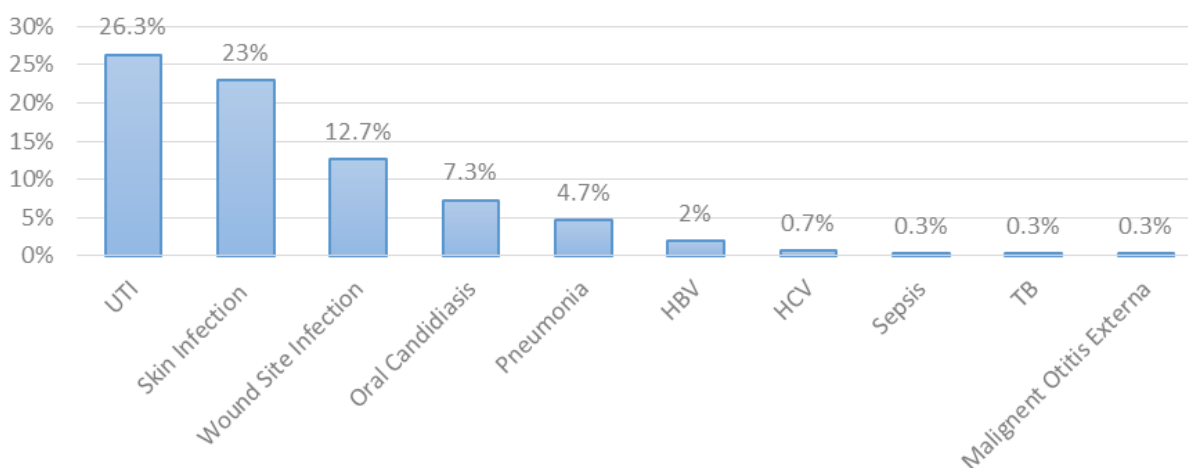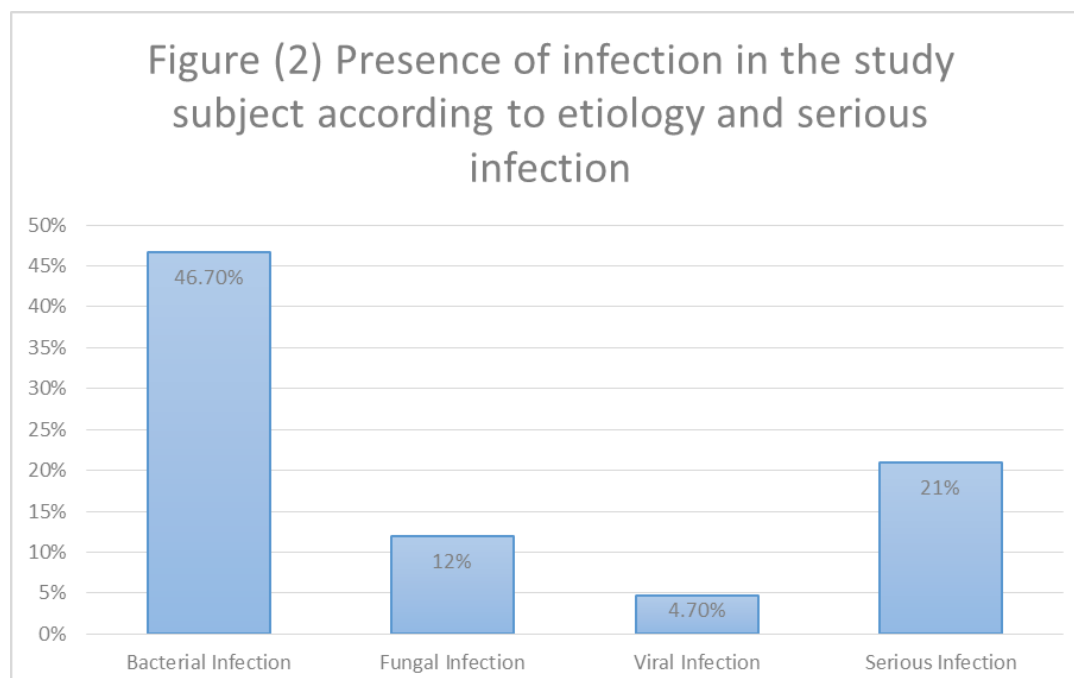
Discussion:-

This study included 300 diabetic patients who'd had the disease for at least five years. It aimed to identify common infections and their risk factors in this patient population. Most of the participants live in urban settings(277, or 92.3%), which could be due to the accessibility to the center or the fact that the prevalence of diabetes among urbanites is higher than in the rural population, which was examined in an international study that found the prevalence of diabetes to be higher in urban areas than in rural areas (9). Most of our patients have type 2 diabetes, and the overall rate of infections was documented in 57.6% of patients; although this percentage seems high, we infer that it is underestimated as it was reported from the patients while their files were lacking information about their incidence of infection and/or type. In our study, bacterial infection was the most common modality of infection followed by fungal infection and finally viral infection. It might be argued that the rates of viral infections are usually more common than fungal infections in this patient population. A possible explanation is that we may have underestimated the rates of viral infections as we only looked for HBV, HCV, and the herpeszostervirus. Also, the fact that the prevalence of HBV has declined in the last years in Saudi Arabia and that the prevalence of HCV in the general population in Saudi Arabia is only 0.4-1.1% (10) is significant.Furthermore, regarding HZV, a study was done in a dermatology clinic in the eastern region of Saudi Arabia. It showed that only 0.62% out of 22,749 patients who attended the clinic between 1988 and 2006 had HZV (11), which might give an impression that fungal infection is more common than the previous three viral infections in the Saudi community. Moreover,it is believed that fungal infection is more common in diabetics than in the general population (12). Aging, as well as diabetes, decrease the immunity which makes older diabetic patients even more susceptible to serious infections (13).Because the majority of the sample was older than forty and about one-third of them was above sixty,they are expected tohavearelatively high percentage of serious infections. Regarding the risk factors, none of the socio-demographic factors was significant for the overall infection. However, females were affected more than males in overall infection and bacterial infection. This is supported by some studies (14,16) that found more UTI bacterial infections among females.The highest percentage of infection was among patients less than twenty yearswhich could be explained by a study assessed the risk of bacterial infection on type 1 diabetics and an age-matched control group which showed that the diabetic group was more prone to bacterial infection, and it claimed that the cause is the particular association between type 1 diabetes and the impairment of immunity (17). Patients who live in urban areas have the lowest percentage of infection.This may be due to the availability of good sanitation and health care system. The presence of diabetic complications in our study was statistically significantly associated with infection; this is true especially that neuropathy and nephropathy predispose to infection. Moreover, an interesting finding in our study was no significant difference was found regarding the prevalence of infection between those who are controlled or the other patients who are not controlled, and this may document that the presence of diabetes itself is a predictor for infection, which is supported by a study

done on 328 diabetic patients that showed no difference in the mean HgA1c level between infected and non-infected patients. However, those patients showed a significantly higher mean HgA1c level during the time of infection, and the investigators concluded that these high levels are a result rather than a cause of infection (18). On the other hand, other studies (19,20,21) claim that poor glycemic control is a risk for infection, and considering that we excluded 110 of the sample due to the undocumented last HgA1c level in those patients, we cannot tell if there is a particular association between infection and HgA1c level or not. Another interesting finding is that hypertension was also significantly associated with developing the overall infection; this may be explained through a study conducted in patients with denguehemorrhagicfever. They found that hypertension and diabetes are independent risk factors for infection (22). The main limitation in our study is the cross-sectional study design, with its inherit limitations, including recall bias. Also, the lack of a good record system for infection in the diabetic patients in our local center further limited the ability to obtain data. In conclusion, diabetic patients in our community have a high prevalence of infection; while the presence of diabetic complications and hypertension are risk factors for the overall infections, female gender, diabetic complications, hypertension, and hyperlipidemia are risk factors for bacterial infection.

Conflict of interest:-
The authors declare that they do not have any conflicts of interest to declare.

Acknowledgments:-

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Appendices:-
1-Taibah University
COLLEGE OF MEDICIN   DATE :   /   /
A-Personal Information :

Serial_no = NUMBER:………………
q1-AGE: (   ) less than 20 =1 (   )   20-30 =2 (   ) 31-40 =3 (   ) 41-50 =4 (   ) 51-60 =5 (   ) more than 60 =6
q2-GENDER: ( )male =1   (   )female =2
q3-Occupation: (   ) not working =1   (   )office =2   (   )field =3
q4-Natunality : (   )Saudi =1   If not (   )Arabic =2   (   )not Arabic =3
q5-Residensy :   (   ) urban =1   (   )Rural =2   (   )Sub-urban =3

| q6-Marital status (   )Single =1   (   )married =2   (   )widow =3   (   )divorced =4 |
| q7-Weight:……………….   q8- Height:…...   q9-BMI:………………. |

B- Diabetes History:

| q10-Duration of DM: (   )5-10 =1   (   )11-15 =2   (   )16-20 =3   (   )more than 20 =4 |
| q11-Type: (   )Type 1 =1   (   ) Type 2 =2 |
| q12-Current Treatment :
(   )Oral hypoglycemic drug (   )Insulin (   )Combined oral and insulin(   ) Combined oral drugs |

C- Controlled or Not :

| q13- The last Hg A1c level was :……………………. (Write it down)
if you don't have it answer the following question :
q13 _1 - (   )Do not know =1   (   ) Not done before =2 |
| q14-Regular follow up   (   ) yes =1   (   ) no =2 |
| q15- Taking drugs regularly   (   ) yes   (   ) no |
| q16-Healthy diet   (   ) yes   (   ) no |
| q17-Regular exercise   (   ) yes   (   ) no |

D-Risk factors:

| q18-Smoking   (   ) yes   (   ) no |
| q19-Hypertension   (   ) yes   (   ) no |
| q20-Hyperlipidemia   (   ) yes   (   ) no |
| q21-Hypercholestrolemia   (   ) yes   (   ) no |
| q22-Family history   (   )yes   (   ) no |

E-Chronic Complications :

| Eye complication
q23 (   )Blurred vision   Yes =1   No =2
q24 (   )Cataract   Yes =1   No =2
q25(   )laser therapy   Yes =1   No =2
q26(   )Glaucoma   Yes =1   No =2
q27 (   )Other eye complications   Yes =1   No =2
q27_1 (If yes Write it down) |
| Kidney complications :
q28 (   )Microalbuminuria   Yes =1   No =2
q29 (   ) Chronic kidney disease   Yes =1   No =2
q30(   ) others kidney complications :   Yes =1   No =2
q30_1   (If yes Write it down)   as : (kidney stone) |
| q31-diabetic neuropathy   (   ) yes   (   ) no   Yes =1   No =2 |
| q32-diabetic foot   (   ) yes   (   ) no |
| q33-gangrene   (   ) yes   (   ) no
q33_1 - If yes how it was treated ?
(   )Amputation =1
(   )Self amputation =2
(   ) Other :   =3   (Just type the number) |
| q34-stroke   (   ) yes   (   ) no |
| q35-heart disease (   ) yes   (   ) no
q35_1 - if yes what is it:…………………………….. (If yes Write it down)   As : (MI , tachycardia , angina) |

F-Previous infection:

| q36-Malignant Otitis Externa   (   ) yes =1   (   ) no =2
q36_1 If yes: Duration:………………….. q36_3 Hospitalized   (   )yes=1   (   )no=2
q36_2 Treatment:……………………… as (cream , surgery , ointment , antibiotic) |
| q37 -Frunculosis(   ) yes   (   ) no |

q37_1 If yes: Duration:………………….. q37_2 Treatment:………………………	q37_3 Hospitalized ( )yes ( )no
q38 – RhinocerebralMucormycosis( ) yes ( ) no q38_1 If yes: Duration:………………….. q38_2 Treatment:………………………	q38_3 Hospitalized ( )yes ( )no
q39- Oral Candiasis( ) yes ( ) no q39_1 If yes: Duration:………………….. q39_2 Treatment:………………………	q39_3 Hospitalized ( )yes ( )no
q40 –Pneumonia( ) yes ( ) no q40_1 If yes: Duration:………………….. q40_2 Treatment:………………………	q40_3 Hospitalized ( )yes ( )no
q41 TB ( ) yes ( ) no q41_1 If yes: Duration:………………….. q41_2 Treatment:………………………	q41_3 Hospitalized ( )yes ( )no

q42 -HBV ( ) yes ( ) no q42_1 If yes: Duration:………………….. q42_2 Treatment:………………………	q42_3 Hospitalized ( )yes ( )no
q43 HCV ( ) yes ( ) no q43_1 If yes: Duration:………………….. q43_2 Treatment:………………………	q43_3 Hospitalized ( )yes ( )no
q44 Emphysema Cholecystitis ( ) yes ( ) no q44_1 If yes: Duration:………………….. q44_2 Treatment:………………………	q44_3 Hospitalized ( )yes ( )no
q45-UTI ( ) yes ( ) no q45_1 If yes: Duration:………………….. q45_2 Treatment:………………………	q45_3 Hospitalized ( )yes ( )no
q46 -Pyelonephritis ( ) yes ( ) no q46_1 If yes: Duration:………………….. q46_2 Treatment:………………………	q46_3 Hospitalized ( )yes ( )no

q47 –Intertrigo ( ) yes ( ) no q47_1 If yes: Duration:………………….. q47_2 Treatment:………………………	q47_3 Hospitalized ( )yes ( )no
q48 - Herpes Zoster ( ) yes ( ) no q48_1 If yes: Duration:………………….. q48_2 Treatment:………………………	q48_3 Hospitalized ( )yes ( )no
q49- Erysipelas( ) yes ( ) no q49_1 If yes: Duration:………………….. q49_2 Treatment:………………………	q49_3 Hospitalized ( )yes ( )no
q50-Cellulitis ( ) yes ( ) no q50_1 If yes: Duration:………………….. q50_3 Treatment:………………………	q50_3 Hospitalized ( )yes ( )no
q51 -Folliculitis ( ) yes ( ) no q51_1 If yes: Duration:………………….. q51_2 Treatment:………………………	q51_3 Hospitalized ( )yes ( )no
q52 –Abscess( ) yes ( ) no q52_1 If yes: Duration:………………….. q52_2 Treatment:………………………	q52_3Hospitalized ( )yes ( )no

q53-Pertonitis ( ) yes ( ) no q53_1 If yes: Duration:………………….. q53_2 Treatment:………………………	q53_3 Hospitalized ( )yes ( )no
q54 -Sepsis ( ) yes ( ) no q54_1 If yes: Duration:…………………..	q54_3 Hospitalized ( )yes ( )no

q54_3 Treatment:………………………
q55 -Wound site infection ( )yes ( )no q55_1 If yes: Duration:………………..   q55_3 Hospitalized ( )yes ( )no q55_2 Treatment:………………………
q56 -Others ( )yes =1 ( )no =2 q56_1 ………………… q56_2 If yes: Duration:………………..   q56_4Hospitalized ( )yes ( )no q56_3 Treatment:………………………

G-Distress:-

q57 -Not feeling motivated to keep up my diabetes self management ( ) yes ( ) no
q58 -Feeling that I will end up with complication no matter what ( ) yes ( ) no

H-Vaccination History:-

q59 - Influenza vaccine was taken in the last year ( )yes ( )no
q60 -Pneumococcal vaccine   ( )yes ( )no