Original article:

The study of mortality and morbidity associated with major limb amputations and its correlation with HbA1c levels

[1]P Varun Gautam, [2]Manjusha M. Litake

[1]Resident, General Surgery, B.J. Govt. Medical College and Sassoon General Hospital, Pune.

[2]Associate Professor, General Surgery, B.J. Govt. Medical College and Sassoon General Hospital, Pune.

Corresponding author: Dr. P Varun Gautam.

ABSTRACT:

INTRODUCTION: Limb amputation is one of the most ancient of all surgical procedures. A major amputation is the one that is done proximal to the ankle joint in case of a lower limb amputation and proximal to the wrist in case of an upper limb amputation. The following aims to study the morbidity and mortality associated with major limb amputations and to assess the role of HbA1c as a possible indicator of the same.

OBJECTIVES: The objectives of the study include the assessment of the morbidity associated directly with the procedure of amputation, with pre-existing co-morbidities such as Diabetes Mellitus , PVD, etc, to measure the post operative in hospital deaths following major limb amputations and to assess the possible role of HbA1c in predicting the same.

METHODS:100 patients undergoing major limb amputations admitted in the surgical wards of Sassoon General Hospital were assessed as a part of the study.

RESULTS: maximum number of amputations occurring were Below Knee, with Diabetes mellitus and PVD being the two most commonly associated co-morbidities, with wound gape, pus discharge and gangrene of the amputation stump being the common post operative complications, which were more following a BK amputation and in those amputees with pre existing co-morbidities, and post operative mortality and re-amputations were higher in diabetics with deranged HbA1c levels.

CONCLUSION: the study , though small can act as a stepping stone for further large studies with regards to the role of hyperglycemia and HbA1c in predicting the possible outcome following a major limb amputation.

Introduction:

The history of man has been accompanied by trauma, war, and congenital anomalies. Consequently, amputations and deformity have been dealt with, one way or another, throughout the ages (1).Limb amputation is one of the most ancient of all surgical procedures with a history of more than 2500 years dating back to the time of Hippocrates (2,3). A major amputation is the one that is done proximal to the ankle joint in case of a lower limb and proximal to the wrist in case of an upper limb amputation. The present study includes the following major limb amputations .a) Below Knee(BK) amputations, b) Above Knee(AK) amputations, c) knee disarticulation d) Hip disarticulation (hind quarter amputation), e) Below Elbow(BE) amputations, f) Above Elbow(AE) amputations ,g) elbow disarticulation and h)Shoulder disarticulation (forequarter amputations). Complications of amputation may involve the skin, muscle, artery, nerve, joint or bone and might also arise due to improper placement of the prosthesis. Major limb amputations are essentially disfiguring operations

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

that carry a fairly high peri - operative mortality and morbidity .

Peri-operative hyperglycaemia also places the patients at an increased risk for Surgical Site infections (SSI), increased post operative morbidity and mortality (4). HbA1c or Glycated Haemoglobin gives an approximate measure of the blood glucose levels over the past 3 months. There are very few published studies in literature that have tried to assess the correlation between the peri-operative Hyperglycemia levels and the occurrence of post operative morbidity and mortality in patients undergoing major limb amputations. Hence the need of the present study, with HbA1c being used as an indicator of Pre/peri-operative hyperglycemia.

OBJECTIVES:

1 To study the morbidity directly associated with amputations in terms of :
   a) Post operative complications of the amputation stump.
   b) Increased or prolonged duration of hospital stay.
2) To evaluate the morbidity due to the presence of pre- existing co-morbidities (including Diabetes mellitus(DM), Peripheral Vascular Disease(PVD), etc.) in amputees in terms of: Need for revision surgery including reamputations.
3) To measure the number of immediate in hospital post operative deaths.
4) To assess the possible role of HbA1c in predicting the likelihood of complications.

MATERIALS AND METHODS:

Ours was a prospective study conducted over 18 months, which included 100 patients above or equal to the age of 16 years undergoing a major limb amputation due to any cause, selected from the surgical wards of a tertiary care hospital.

- History was obtained in detail & a thorough clinical examination was carried out. Pre operatively present co-morbid conditions such as diabetes mellitus, Peripheral vascular disease (PVD), Ischaemic heart disease (IHD) and hypertension were noted.

Post Operative Period:

The patients were assessed in the post operative period to look for:

1) Features of infection: including presence of fever, raised post operative total leukocyte (WBC) levels.
2) Amputation stump site was examined for: hematoma formation, seroma formation, presence of inflammation, wound gape or suture site dehiscence, pus discharge and presence of stump site gangrene.
3) Post operative random blood sugar levels were measured:
   In case of a known Diabetic: 12 hourly for the duration of the hospital stay.
   If the patient was not a known diabetic: then on post operative day 1 and if found to be normal, was not measured again.
4) Response to physiotherapy was noted and the patients were categorized into three categories:
   a) Ambulant by self
   b) Ambulant with the help of physiotherapy
   c) Non ambulant.

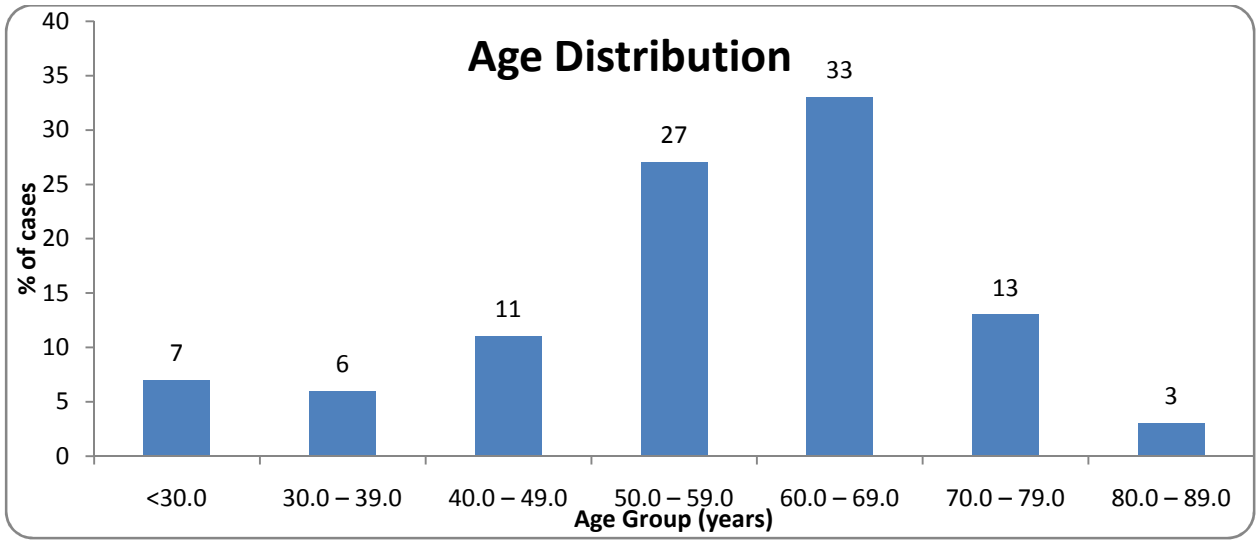
www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

5) Duration of hospital stay was noted.
6) The wound or amputation stump was reassessed at the time of discharge.
7) The total number of in hospital deaths occurring was measured.

OBSERVATIONS:

1) AGE:

Figure 1) Age distribution of the patients studied (n= 100).



The mean ± standard deviation of age of the study group was 56.0 ± 14.7 years.

2) Sex distribution of the patients:

Of 100 cases studied, 80 were males and 20 were females, with the ratio being 4:1.

3) Type of amputation done:

Table 2) showing the different types of amputations done

Type of Amputation	No. of cases (%)
Above Knee (AK)	17
Below Knee (BK)	48
Above Knee (Guillotine)	5
Below Knee (Guillotine)	15
Above Elbow (AE)	2
Below Elbow (BE)	10
Above Elbow (Guillotine)	1
Below Elbow (Guillotine)	2
Total	**100**

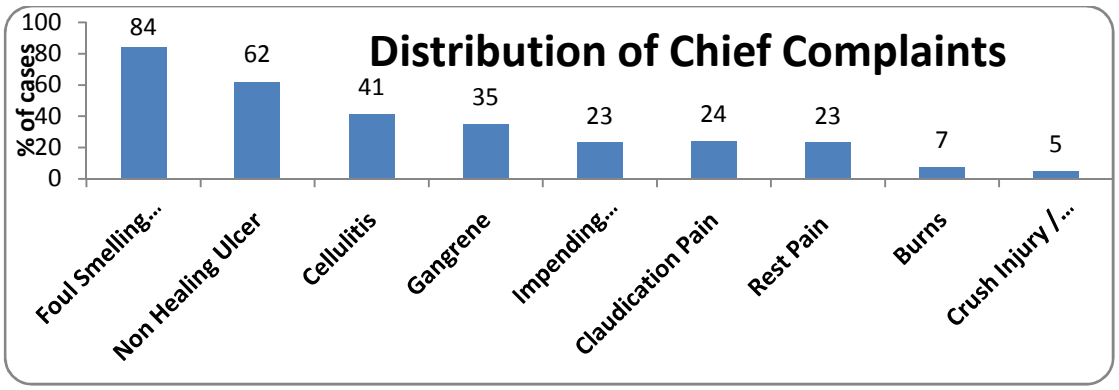
www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

4) Chief Complaints:

Table 3) showing the various chief complaints

Chief Complaints	No. of cases(%)
Foul Smelling Discharge	84
Non Healing Ulcer	62
Cellulitis	41
Gangrene	35
Impending Gangrene	23
Claudication Pain	24
Rest Pain	23
Burns	7
Crush Injury / Trauma	5

Figure 2) showing distribution of the chief complaints.



Only 5 patients with crush injury and 1 with severe burns had a single complaint. All the other patients had a mixture of complaints.

5) Co-morbidity:

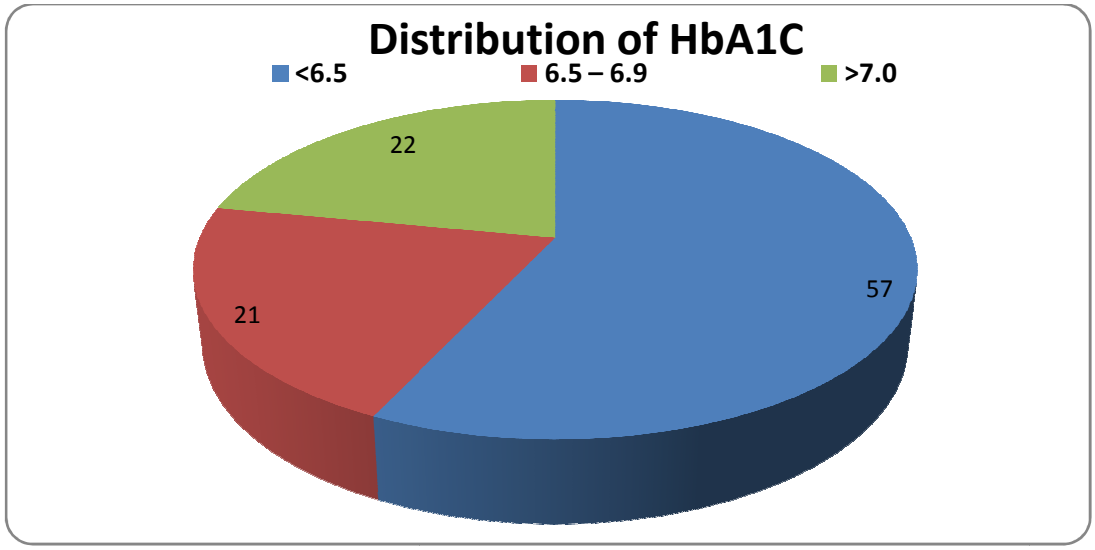
Co-Morbidity	No. of cases(%)
Diabetes mellitus (DM)	30
Peripheral vascular disease (PVD)	23
DM + PVD	29
Others	18
Total	**100**

Table 4) showing the distribution of the different co-morbidities.

6) HbA1c levels:

Of 100 cases studied, 57 cases(%) had HbA1C less than 6.5%, 21(%) had HbA1C between 6.5 – 6.9% and 22 (%) had their HbA1C more than 7.0%.

Figure 3) showing the distribution of HbA1c levels.



7) Distribution of complications according to the type of amputation:

	Hematoma	Seroma	Inflammation	Wound gape	Pus discharge	Stump site gangrene	Revision surgery	Reamputations
Amputation								
Below Knee (BK)	3	0	22	29	33	5	11	7
Above Knee (AK)	0	1	7	11	13	2	5	0
Below Elbow (BE)	0	0	0	1	3	0	0	0
Above Elbow (AE)	0	0	0	0	0	0	0	0

Table 5) showing the distribution of complications according to the type of amputation.

8) The distribution of parameters of post-op morbidity and mortality according to the co-morbidity (n= 100).

Table 6) showing the distribution of complications with each co-morbidity.

		Co-Morbidity				
Parameters	**Details**	**DM (n=30)**	**PVD (n=23)**	**DM + PVD (n=29)**	**Others (n=18)**	**P-value**
Local Complications	Hematoma	3 (10.0)	0	0	0	0.065^{NS}
	Seroma	0	0	0	0	0.999^{NS}
	Inflammation	14 (46.7)	7 (30.4)	8 (27.6)	0	0.008**
	Wound Gape	15 (50.0)	11 (47.8)	12 (41.4)	3 (16.7)	0.119^{NS}
	Pus Discharge	19 (63.3)	12 (52.2)	15 (51.7)	2 (11.1)	0.005**
	Gangrene of Stump	0	3 (13.0)	4 (13.8)	1 (5.6)	0.181^{NS}
Re-Amputation	Revision of stump	5 (16.7)	6 (26.1)	5 (17.2)	0	0.157^{NS}
	Higher level Amputation	1 (3.3)	2 (8.7)	3 (10.3)	1 (5.6)	0.735^{NS}
Response to physiotherapy	Non-Ambulant	8 (26.7)	10 (43.5)	16 (55.2)	5 (27.8)	0.001***
	Ambulant Self	1 (3.3)	3 (13.0)	5 (17.2)	10 (55.6)	
	Ambulant Physio	21 (70.0)	10 (43.5)	8 (27.6)	3 (16.7)	
Duration of hospital stay (Days)	<7 days	7 (23.3)	6 (26.1)	15 (51.7)	11 (61.1)	0.028*
	7 – 14 Days	19 (63.3)	10 (43.5)	10 (34.5)	4 (22.2)	
	>14 Days	4 (13.3)	7 (30.4)	4 (13.8)	3 (16.7)	
Mortality	Alive	27 (90.0)	20 (87.0)	21 (72.4)	16 (88.9)	0.244^{NS}
	Dead	3 (10.0)	3 (13.0)	8 (27.6)	2 (11.1)	

Values are n (% of cases). P-value by Chi-Square test. P-value <0.05 is considered to be statistically significant. *P-value<0.05, **P-value<0.01, ***P-value<0.001, NS: Statistically Non-Significant.

- The distribution of incidence of local complications such as inflammation and pus discharge differs significantly across four groups of co-morbidity (P-value<0.05 for both).
- The distribution of response to physiotherapy differs significantly across four groups of co-morbidity (P-value<0.001). Significantly higher proportion of cases with Diabetes had higher incidence of ambulant with physiotherapist than the cases with other morbidity (P-value<0.001).
- The distribution of duration of hospital stay differs significantly across four groups of co-morbidity (P-value<0.05).

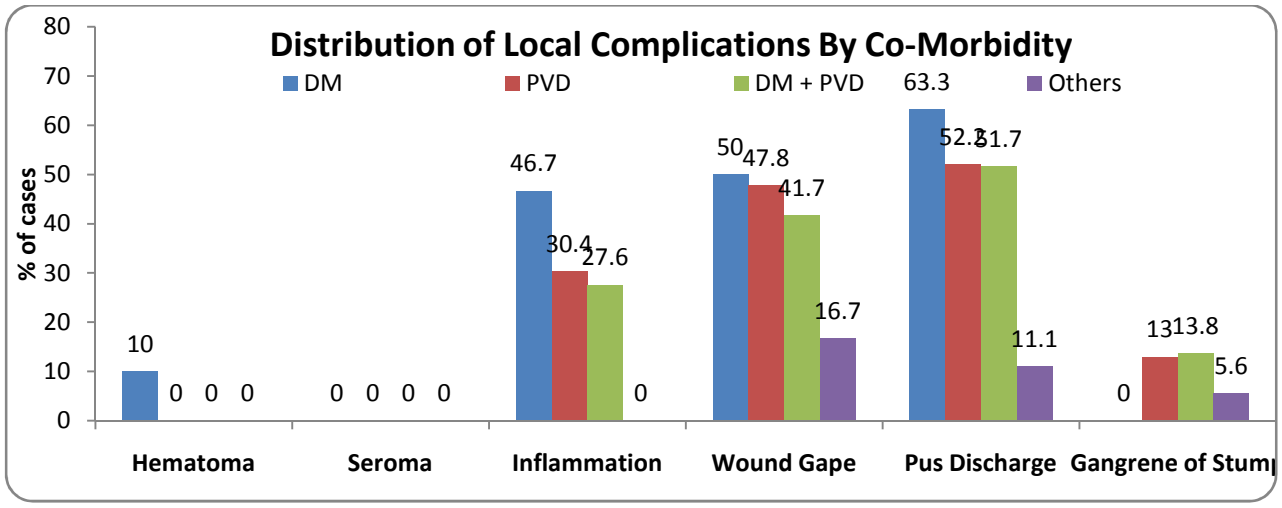


Figure 4) showing the distribution of local complications according to co-morbidity.

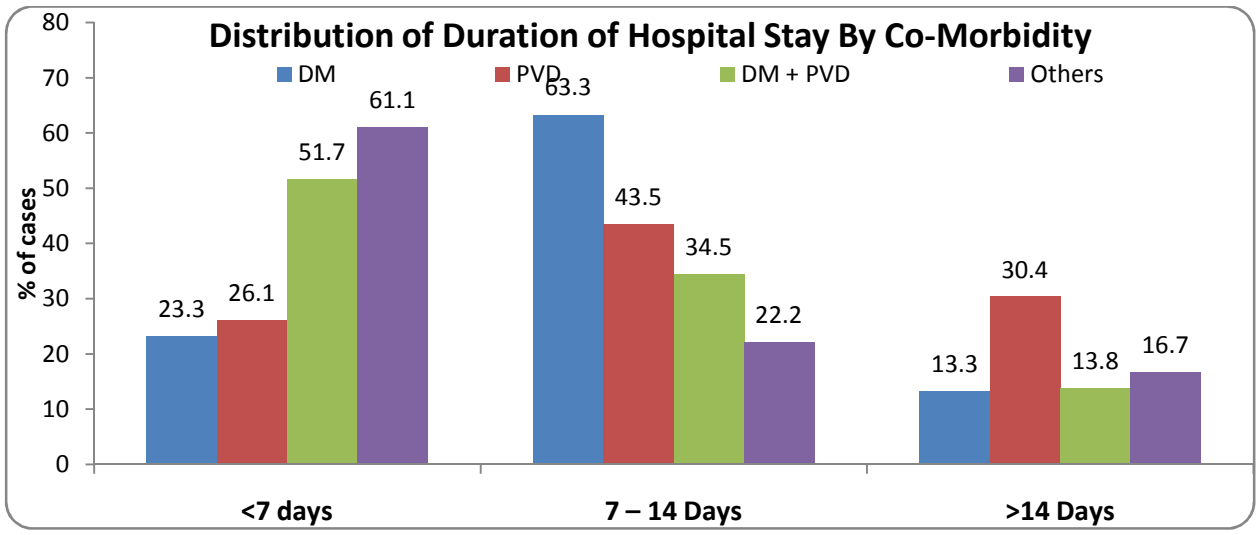
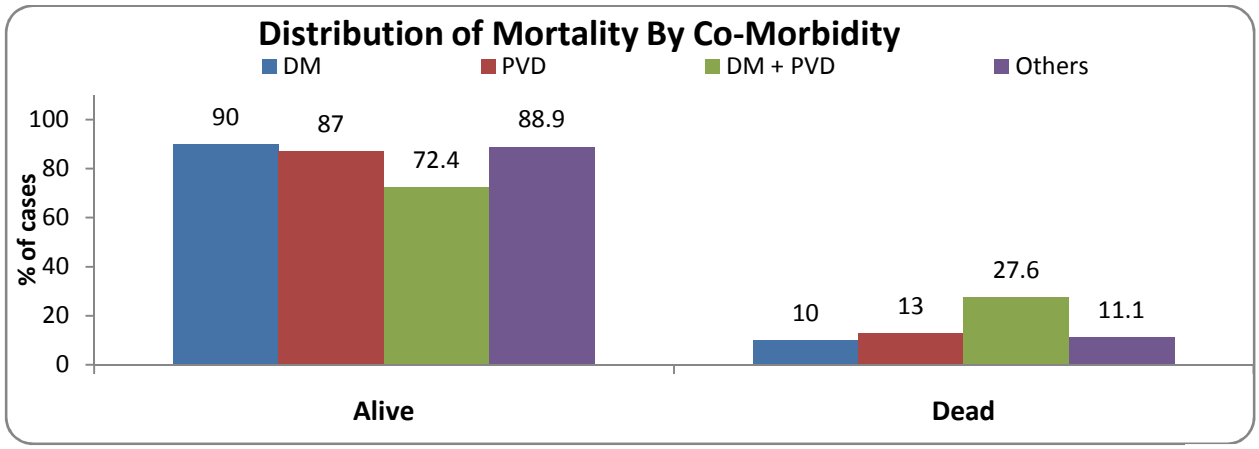


Figure 5) showing the duration of hospital stay according to co-morbidity.

Figure 6) showing distribution of mortality by co-morbidity.



9) The distribution of parameters of post-op morbidity and mortality according to levels of HbA1C (n= 100).

Table 7) showing the complication distribution with different levels of HbA1c.

		HbA1C (%)			P-value		
Parameters	**Details**	**Gr 1 [<6.5 (n=57)]**	**Gr 2 [6.5 – 6.9 (n=21)]**	**Gr 3 [>7.0 (n=22)]**	**Gr 1 v Gr 2**	**Gr 1 v Gr 3**	**Gr 2 v Gr 3**
Local Complications	Hematoma	2 (3.5)	0	1 (4.5)	0.999^{NS}	0.999^{NS}	0.999^{NS}
	Seroma	0	0	0	0.999^{NS}	0.999^{NS}	0.999^{NS}
	Inflammation	14 (24.6)	5 (23.8)	10 (45.5)	0.999^{NS}	0.210^{NS}	0.411^{NS}
	Wound Gape	23 (40.4)	7 (33.3)	11 (50.0)	0.999^{NS}	0.999^{NS}	0.804^{NS}
	Pus Discharge	24 (42.1)	9 (42.9)	15 (68.2)	0.999^{NS}	0.114^{NS}	0.387^{NS}
	Gangrene of Stump	6 (10.5)	1 (4.8)	1 (4.5)	0.999^{NS}	0.999^{NS}	0.999^{NS}
Re-Amputation	Revision of stump	9 (15.8)	3 (14.3)	4 (18.2)	0.999^{NS}	0.999^{NS}	0.999^{NS}
	Higher level Amputation	3 (5.3)	2 (9.5)	2 (9.1)	0.999^{NS}	0.999^{NS}	0.999^{NS}
Response to physiotherapy	Non-Ambulant	21 (36.8)	7 (33.3)	11 (50.0)	0.999^{NS}	0.456^{NS}	0.498^{NS}
	Ambulant Self	13 (22.8)	5 (23.8)	1 (4.5)			
	Ambulant Physio	23 (40.4)	9 (42.9)	10 (45.5)			
Duration of hospital stay (Days)	<7 days	20 (35.1)	11 (52.4)	8 (36.4)	0.897^{NS}	0.999^{NS}	0.999^{NS}
	7 – 14 Days	25 (43.9)	8 (38.1)	10 (45.5)			
	>14 Days	12 (21.1)	2 (9.5)	4 (18.2)			
Mortality	Alive	50 (87.7)	18 (85.7)	16 (72.7)	0.999^{NS}	0.321^{NS}	0.999^{NS}
	Dead	7 (12.3)	3 (14.3)	6 (27.3)			

- **The distribution of incidence of local complications, the need for revision surgery, response to physiotherapy, duration of hospital stay and the incidence of mortality did not differ significantly across three groups of HbA1C (P-value>0.05 for all).**

Figure 7) distribution of local complications according to the HbA1c levels.

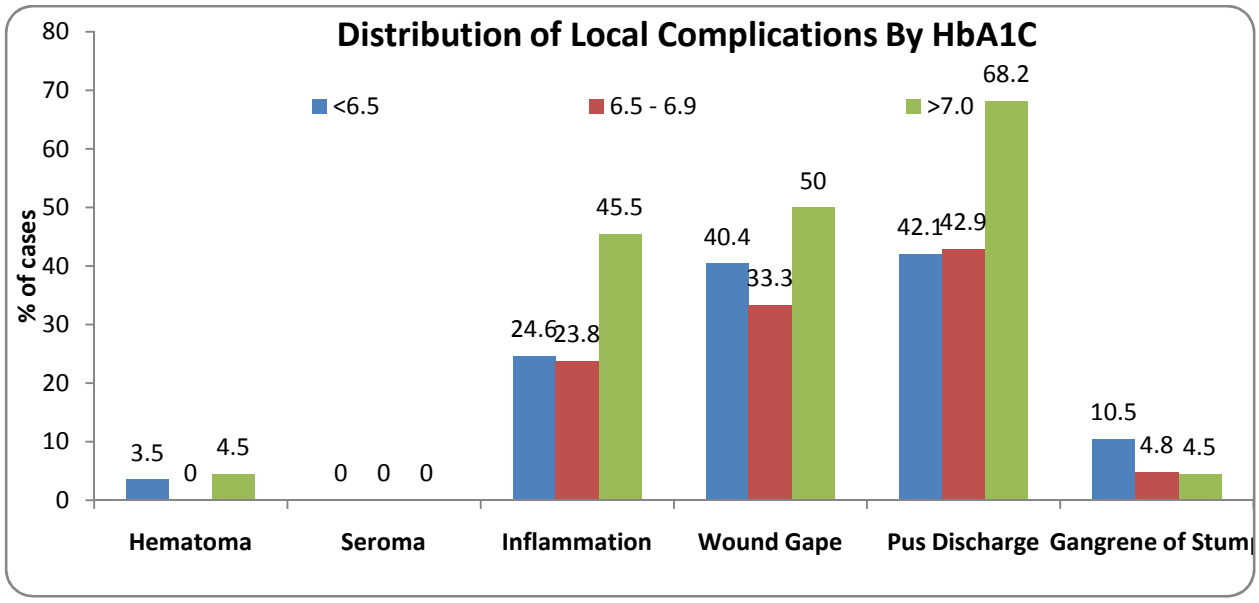
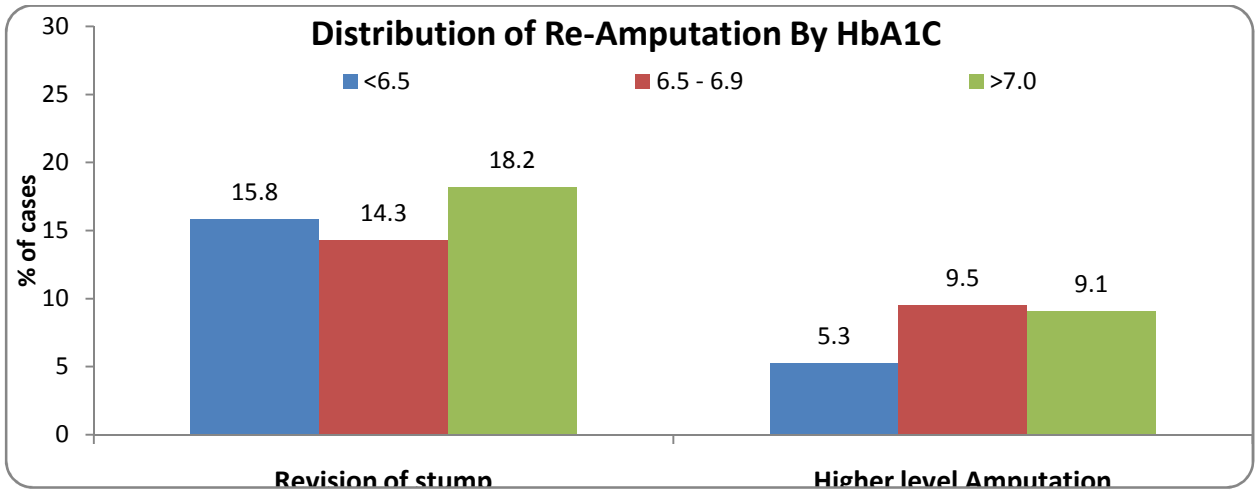


Figure 8) distribution of revision surgery according to HbA1c levels.



10) The distribution of parameters of post-op morbidity and mortality between Cases with Diabetes + HbA1C<6.5% and Cases with Diabetes +HbA1C>6.5% with respect to levels of HbA1C (n= 59).

Table 8) showing variation in the post operative morbidity and mortality within the two subgroups of Diabetics(one with a controlled HbA1c level and the other with a deranged HbA1c level).

		Group		
Parameters	**Details**	**DM + HbA1C<6.5% (n=18)**	**DM + HbA1C>6.5% (n=41)**	**P-value**
Local Complications	Hematoma	2 (11.1)	1 (2.4)	0.218^{NS}
	Seroma	0	0	0.999^{NS}
	Inflammation	8 (44.4)	14 (34.1)	0.451^{NS}
	Wound Gape	10 (55.6)	17 (41.5)	0.317^{NS}
	Pus Discharge	11 (61.1)	23 (56.1)	0.720^{NS}
	Gangrene of Stump	2 (11.1)	2 (4.9)	0.578^{NS}
Re-Amputation	Revision of stump	4 (22.2)	6 (14.6)	0.475^{NS}
	Higher level Amputation	1 (5.6)	3 (7.3)	0.999^{NS}
Response to physiotherapy	Non-Ambulant	6 (33.3)	18 (43.9)	0.101^{NS}
	Ambulant Self	0	6 (14.6)	
	Ambulant Physio	12 (66.7)	17 (41.5)	
Duration of hospital stay (Days)	<7 days	4 (22.2)	18 (43.9)	0.284^{NS}
	7 – 14 Days	11 (61.1)	18 (43.9)	
	>14 Days	3 (16.7)	5 (12.2)	
Mortality	Alive	16 (88.9)	32 (78.0)	0.476^{NS}
	Dead	2 (11.1)	9 (22.0)	

- The distribution of incidence of local complications, need for revision surgery, response to physiotherapy, duration of hospital stay and the incidence of mortality did not differ significantly between diabetes cases with and without good glycaemic control (P-value>0.05 for all).

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

DISCUSSION:

The present study aims to assess the morbidity and the mortality associated with major limb amputations due to the amputation itself, due to pre-existing co-morbidities including Diabetes Mellitus(DM) and Peripheral Vascular Disease(PVD) . It also tries to assess the possible relation between peri-operative hyperglycaemia and post operative morbidity and mortality.

The ratio of the number of males to female amputees in our study was found to be 4:1(80 males to 20 females). This is consistent with the study conducted by Lombardo et al (5), who showed that male sex was at a higher risk of LEAs than females and advanced age played a very significant role in the incidence of LEAs, and males present a much higher age than females. The mean age of occurrence of an amputation in our study was 56 years with no significant correlation between advancing age and the occurrence of an amputation.

The most common complaint remained an infected ulcer with pus discharge, followed by cellulitis. This is in contrast to the study conducted by Lipsky et al (6), where the most common presentation remained cellulitis in about 80 % of the patients followed by an infected ulcer in about 16%. They also stated that more than about one fifth of patients who presented with a diabetic foot ended up having an amputation . The variation in the chief complaint could possibly be attributed to the variation in the demography of the two study populations.

The ratio of the AK to the BK amputation was found to be 0.349 (22 AK amputations when compared to 63 BK amputations). This was comparable to the study conducted by Aulivola et al (7), in which 959 patients who underwent lower extremity amputations were compared and it was found that the ratio of the AK to the BK amputation was found to be 0.362.

The incidence of local wound complications was highest in lower limb amputees with maximum complications being seen in Below Knee amputees. This was comparable to a study by Ploeg et al(8), who observed that the occurrence of local complications was more in those patients who had undergone a Below Knee(BK) amputation,with wound infection being the most common complication.

In our study , it was observed that revision surgery was required in 25.39% (16 out of 63 cases) of the BK amputees, and in 22.73%(7 out of 22 cases) of the AK amputees.This is in accordance to the study conducted by Aulivola et al (7), who found that the need for revision surgery was more in BK amputees, with about 18.4% needing a revision surgery or re-amputation.

The rate of conversion of a BK amputation to an AK amputation in our study was 11.11% (7 out of 63 cases), with that in study conducted by Aulivola et al (7), being around 9.4 % and in that by Ploeg et al (8) being 14.3 %.

Post operative Morbidity and Mortality and pre-existing Co-morbidity:

Diabetes Mellitus and Peripheral Vascular Disease (PVD) were the two main co-morbidities that were associated with lower limb amputations. A study conducted by Kristensen et al(9), found that PVD as a co morbidity was most commonly associated with lower extremity amputations and that the rates of complications and mortality was significantly higher in amputees with pre-existing PVD.

In our study, the occurrence of post operative inflammation (46.7% of the cases), wound gape (50% of the cases) and pus discharge (63.3% of the cases)

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

was found to be higher in patients with pre-existing Diabetes ,whereas post operative gangrene of the amputation stump was found to be higher in patients having pre-existing combination of Diabetes with PVD. (13.8% versus 13% in patients with only PVD). This was similar to a study conducted by Moulik et al (10), who found that co-existing of DM and PVD worsened the prognosis following a major limb amputation.

The need for revision of the amputation stump in our study, was found to be higher in patients with pre-existing PVD (26.1%), whereas the need of re-amputation was found to be higher in patients with combination of pre-existing Diabetes Mellitus with PVD (10.3%).There was no statistical significance among the different groups of co-morbidities with regards to the revision surgery.

Our study was only concerned with the in hospital morbidity and mortality and hence the long term need for re-amputations could not be commented upon.

More number of non ambulant patients was found in the group with combination of pre-existing DM and PVD (55.2% of the cases), whereas more number of patients who were ambulant with physiotherapy was found in the group with pre-existing DM only (70% of the cases). The importance of our study lies in the fact that not many studies have previously tried to assess the co-relation of pre-existing Co-morbidity with response to physiotherapy in amputees

The mean duration of post operative hospital stay in Diabetics was 10.9 days, in those with pre-existing PVD was11.83 days and with combined (DM + PVD) was 8.63 days. This is in contrast to a study conducted by Currie et al(11), who observed that Diabetics had a longer duration of post operative hospital stay when compared to amputees with other co-morbidities.(mean duration of 15.5 days versus 8.4 days in amputees with other co-morbidities). The mean duration of post operative hospital stay overall in our study was 10.38 days with a standard deviation of 7.49.

The mortality rates were also found to be relatively higher in amputees with pre-existing combined (DM + PVD). (27.59 % in this group as compared to 10% in amputees with only pre-existing DM and 13.04% in amputees with only pre-existing PVD).

HYPERGLYCEMIA:

Patients were divided into three groups based on the levels of HbA1c as a) <6.5, b) between 6.5 to 6.9. c) >7.0

It was observed that the occurrence of local complications (45.5% of the cases of inflammation, 50 % of the cases of wound gape and 68.2 % of the cases of pus discharge), revision of stump (18.2 %), percentage of non ambulant patients and mortality (27%) was higher in amputees with an HbA1c level more than 7.

This was in relation to a study conducted by Dronge et al (12), who found that Good preoperative glycemic control (HbA1c levels <7%) was associated with a decrease in infectious complications across a variety of surgical procedures, witha p-value of 0.007(statistically significant).

Conclusion:

- The occurrence of Below Knee amputations is more common when compared to Above Knee amputations.
- BK amputations are associated with more peri-operative complications when compared to other forms of major limb amputations. The increased incidence of local complications could possibly be attributed to impaired microscopic

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

circulation at the level of amputation stump following a BK amputation .

- Diabetes mellitus and PVD are among the two most common co-morbidities associated with major limb amputations.
- The presence of pre-existing co-morbidity worsens the post operative outcome, with increase in the post operative local complications, the need for revision surgery and increased death rates.
- Peri-operative hyperglycemia as can be assessed by HbA1c levels is usually associated with an increased post operative morbidity and mortality.
- More studies with a larger sample size are needed to validate the above mentioned point.

References:

1) Vanderwerker EE., a Breif review of the history of amputations and prostheses: ACPOC: ICIB,1976; 5:5.

2) Van der Meij W: K N: No leg to stand on. Historical relation between amputations. Surgery and Prostheseology 1995; 1:1–256.

3) Paudel B, Shrestha BK, Banskota AK: Two faces of major lower limb amputations. Kathmandu University Medical Journal 2005; 3(11):212–216.

4) Akbari CM, Saouaf R, Barnhill DF, et al. Endothelium dependant vasodilation is impaired in both micro- and macrocirculation during acute hyperglycemia. JVasc Surg 1998; 28: 687-94.

5) Lombardo FL, Maggini M, De Bellis A, Seghieri G, Anichini R. Lower Extremity Amputations in Persons with and without Diabetes in Italy: 2001–2010. Herder C, ed. PLoS ONE. 2014; 9(1).

6) Lipsky et al. Developing and validating a risk score for lower-extremity amputation in patients hospitalized for a diabetic foot infection. Diabetes Care 2011; 34:1695-1700.

7) Aulivola B, Hile CN, Hamdan AD, Sheahan MG, Veraldi JR,Skillman JJ et al. Major lower extremity amputation: outcome of a modern series. Arch Surg 2004; 139(4):395–399.

8) Ploeg, A.J. et al.Contemporary Series of Morbidity and Mortality after Lower limb Amputation. European Journal of Vascular and Endovascular Surgery 2005; 9(6):633 – 637.

9) Kristensen TM et al. An enhanced treatment program with markedly reduced mortality after a transtibial or higher non-traumatic lower extremity amputation: A single-center comparison of 129 amputations with historical and national controls. Acta Orthopaedica 2016; 87(3):1-6 .

10) Probal K. Moulik, Robert Mtonga, Geoffrey V. Gill. "Amputation and Mortality in New-Onset Diabetic Foot Ulcers Stratified by Etiology":Diabetes Care Feb 2003; 26(2) :491-494.

11) Currie CJ, Morgan CL, Peters JR.The epidemiology and cost of inpatient care for peripheral vascular disease, infection, neuropathy, and ulceration in diabetes.Diabetes Care. 1998 Jan; 21(1):42-8.

12) Dronge AS, Perkal MF, Kancir S, Concato J, Aslan M, Rosenthal RA. Long-term Glycemic Control and Postoperative Infectious Complications. Arch Surg. 2006; 141(4):375-380.