The diabetes treatment modality health and social care essay

This is the first population based study on ISS in Mauritius being carried out at the cardiac centre and which examines the incidence of ISS as well as the significance of certain risk factors towards this process. It must be noted that PCI accounts for 70 to 80 percent of all coronary interventions performed (Levin et al, 2000). In our study, all patients have been referred from their respective hospitals or health care centres to the cardiac centre in order to get access to tertiary care for the in-depth treatment of their cardiovascular diseases. Most of them were already being followed for non communicable diseases at their respective hospitals. All patients studied were treated with Bare-metal Stents (BMS).

4. 1 Incidence of ISS among PCI patients

A standard value for incidence of ISS among patients with BMS is normally 20 – 30% (Alcocer et al, 2006) which is relatively higher compared to the 5% incidence obtained in our study. Levine et al obtained 17-25% incidence of ISS after 6 months of successful stent placement while Jorgensen et al affirmed a 12 to 32 % value. However in August 2008, Bainey et al obtained a fairly comparable ISS incidence of 6% out of a highly significant study carried out on 12492 subjects from January 1998 to December 2002 at the University of Alberta in Canada. Regarding Spain, ISS symbolized 6. 3% of the total PCI activity in 2003 and 5. 5% of interventions in 2007 (Baz et al, 2008). There are also extremes of values with 48. 8% incidence of ISS in an Indian study carried out by Mohan and Dhall in the year 2010. However they had a small sample population with 41 BMS subjects out of which 20 experienced ISS. The incidence values obtained at the cardiac centre provides for approximately half of the island as PCI procedures are also

being done in other hospitals as well but this has in no way hindered the validity of our result with an incidence value of 5%, observed for the period of October 2009 to September 2012.

4. 2 Incidence of ISS in diabetic and non diabetic patients

Our studied cohort of ISS patients involved 61 diabetic and 12 non-diabetic patients. In other words, diabetic patients reflected 83. 6% of the ISS population while 16. 4% were non diabetics. The percentage of diabetic patients in the ISS population was 90. 6% for 2009/2010, 76. 5% for 2010/2011 and 79. 2% for 2011/2012 with an average of 82. 1% for the 3 years studied. This value gives us an insight of the high proportion of diabetic patients among the new cases of ISS. As affirmed, DM patients have a less favourable clinical outcome at one year after successful stent placement as compared to patients without DM (Elezi et al, 1998; Onuta et al, 2011). However, most previous studies have limited their epidemiology to the incidence of ISS among PCI subjects and to our knowledge, no known value was available for comparison. In addition, restenosis rate is a popular variable in previous studies and requires the prospective monitoring of the PCI patient where angiography is performed at each one to three months interval to observe the rate of restenosis. This particular aspect was not within reach for our study as a PCI patient performs only one angiography after the PCI procedure at the cardiac centre either for an emergency where the stent is usually obstructed or for a checkup which is done at around one year interval after the procedure. It must also be remembered that the degree of occlusion of the stented vessel is only a visual estimate made by the interventional cardiologist.

4. 3 Mean age of presentation and ethnicity

Our 73 patients of the ISS target group had a mean age of 57. 2 years (±9. 8; range, 34-80). This is a younger population compared to ISS studies like the one carried out in USA by Chen et al in 2006, entitled as ' Bare metal stent restenosis is not a benign clinical entity' with a mean age of 63 years. Alli et al had a study group with a mean age of presentation of 63. 1 years in USA itself. However, the target group of Mohan and Dhall has a mean age of 52 years which may be due to some extent because of the small sample size. In addition, a study in Turkey carried out by Onsel et al had a mean age of ISS presentation of 58. 2 years which is nearly equal to the result we obtained. Furthermore, information on the ethnic group of the subjects was mostly missing from patients' records and hence, the influence of ethnicity was unachievable in this study. Indo-Mauritians are known to be classified amongst those having the highest prevalence of Coronary Heart Diseases and it is of high importance to note that a first evidence of susceptibility loci in Indo-Mauritians that predisposes to coronary heart diseases, type 2 diabetes mellitus and hypertension in the context of metabolic syndrome has been demonstrated in a genomic study carried out by Francke et al in 2001. In addition, past studies do show a particular interest concerning ethnic differences in the expression of angiotensin converting enzyme gene polymorphism and interaction with other genes (Jorgensen et al, 2001). It has been demonstrated that South Asians have a threefold increase of TLR leading to ISS compared to white Europeans (Toor et al, 2011).

4. 4 Diabetes treatment modality

The majority of our ISS subjects (57 patients) were on oral drugs - Metformin and Glicazide while 4 were on insulin injections and 12 were non diabetics. Indeed, stenting of native coronary arteries in DM patients is independent of the treatment modality for DM while some affirm that its effect on ISS has not been elucidated yet (Schofer et al, 2000; Choi et al, 2004).

4. 5 Cardiac events

75. 3% of our subjects presented with angina while 24. 7% patients had a myocardial infarction. This is in line with the values obtained by Bainey et al in August 2007 with 77. 5% presenting with angina while 18. 5% had an MI. Assali et al reported 53. 7% patients with angina using the PRESTO database while Chen et al demonstrated 26. 7% patients with angina and 9. 5% patients with MI. Eventually the study of Steinberg et al showed a low death rate and MI in the following 6 months after PCI with BMS. He reported 3. 3% of death cases, 6. 7% of MI cases and 74. 1% of angina cases in a sample of 2539 subjects. These variations in values may be influenced by veiled factors like degree of adherence to medications and other lifestyle factors.

4. 6 Target vessel

In our study, 69. 9% patients experienced ISS in the left anterior descending artery, 20. 5% in the right coronary artery while 9. 6% had an occluded stent in the left circumflex artery. Known as " end circulation", coronary arteries represent the exclusive source of blood supply to the myocardium thus making their blockage critical to the heart (MedBanner, 2012). As shown above, the LAD is mostly occluded (Kastrati et al, 1997) and this is because it

provides the major blood supply to the interventricular septum where stenosis usually leads to injury or infarction of the conduction system (Atlas of Human Cardiac Anatomy, 2012). Being proved as predictors, artery tortuosity and small vessel diameter definitely alters the ISS process (Zegers et al, 2007; Zhou et al, 2011).

4. 7 Balloon pressure

In our study, subjects were initially stented with balloon pressures ranging from 8 to 19 atmospheres before the occurrence of ISS. High-pressure stent deployment leaves us with a better lumen while it may also initiate tissue hyperplasia from the wounded vessel wall. Dirshinger et al established that ISS is not dependent on the balloon pressure, which is the opposite of what we expected to have. They contrasted for all angiographic and clinical indexes of restenosis between the high- and low-pressure arms. However, they were unable to find the link between vessel injury during stenting and the hyperplastic response which followed (Dirshinger et al, 1999). Shiran et al affirm that the residual lumen stenosis remains high even after using an elevated balloon pressure and this is due to remaining neointimal tissue in the stent and important tissue reinvasion following ISS treatment.

4. 8 Risk factors for ISS

In our study, risk factors like diabetes mellitus, hypercholesterolemia, smoking and male gender were found to be significant according to the □2 test performed while hypertension did not influence the ISS population. From the linear regression model, the contribution of these risk factors was 52% for diabetes mellitus, 24% for hypercholesterolemia and 12% for smoking.

4. 8. 1 Diabetes mellitus

Our study demonstrated not only a very strong correlation between DM and ISS (p-value= 0. 000) but also DM as the major contributor amongst the different risk factors while Carrozza et al demonstrated that DM does not necessarily accelerate ISS. According to the tradition, DM has always been a major risk factor for ISS development in PCI patients (Settler et al, 2006; Sheen et al, 2004; Gilbert et al, 2004), irrespective of the type of stent used (Smith et al, 2002; Scheen et al, 2004). In line with our result, Kastrati et al in 1997 and Mehran et al in 1999 demonstrated DM being a major predictor of ISS. This is because DM increases coagulability of blood, thus accelerating smooth muscle cell growth and producing higher shear rates (Liu et al, 1989; Schneider et al, 1993). Concerning the United States, Abbott et al demonstrated that DM patients formed 33. 3% of the PCI cohort in 2007 and this value is on a constant rise. Furthermore, DM provides for a higher restenosis tendency, poorer outcomes of coronary artery diseases and a higher threat of MI and eventual cardiac death (Cutlip et al, 2004; Lee et al, 2006). Indeed, DM patients possess a two to four fold increase in risk of cardiovascular diseases when compared to non diabetics (Kitoga et al, 2007). Concerning the duration of DM, it has been proved in rats that long term type 1 DM encourages the development of ISS (Onuta et al, 2011).

4. 8. 2 Hypertension

Our study provided a p-value of 0. 087 which brought us to the conclusion that there is no significant association between ISS and HBP. Such an observation was noted from the chi squared test because in addition of our ISS group, even the control group had a large proportion of subjects with

HBP, hence making this variable unimportant towards ISS. Even in intracranial atherosclerotic diseases, Dubow et al found no association between HBP and ISS. One of the contributing factors towards the high prevalence of HBP in the Mauritian population goes to our eating habits. The Mauritius salt intake study of 2012 reported that 83. 2% of Mauritians aged 30-59 years old consumed more than 5g of salt daily, which is 60% higher than the recommended guidelines of the WHO. Each person consumes an average of 7. 9g of salt daily where men were larger consumers and 37. 9% of the whole population of Mauritius Island was hypertensive. It is alarming to note that more than 20% of the adult population consumed levels of salt accounting to a 10 fold higher than the required level (Le Défi Plus, 2012).

4. 8. 3 Hypercholesterolemia

In our study population, a strong correlation was obtained between ISS and hypercholesterolemia with a p-value of 0. 000 where hypercholesterolemia stands for a 24% contribution among the relevant risk factors. Lemos et al reported similar findings in 2004 by studying 27 lesions of restenosis. Predictors of ISS were studied and researchers found a strong association with serum High Density Lipoprotein (Sukhija et al, 2007; McDermid, 2007). Higher HDL values were related with a lower incidence of ISS where the comparable p-value obtained was 0. 011 (Sukhija et al, 2007). Another study by Shigematsu et al shows elevated serum malondialdehyde-modified low-density lipoprotein level as an effective risk factor for ISS in diabetic patients. This high level might be a result of metabolic abnormalities caused by diabetes and may behave like a growth factor for neointimal tissues within the implanted stent (Shigematsu et al, 2007). Even on a study involving atherosclerotic rabbits, hypercholesterolemia was proven to be a significant factor towards ISS (Tominaga et al, 1993). However, Vignali et al found no link between ISS and serum cholesterol levels. As affirmed by Herdeg et al, hypercholesterolemia indeed increases smooth muscle cell proliferation in the medial and intimal walls of the vessel and it also promotes inflammatory infiltrates around the stent struts (Herdeg et al, 2003).

4. 8. 4 Smoking

With a p-value of 0. 001 in our study, smoking has been considered as an important risk factor towards ISS. In an Iranian study concerning the effect of folic acid on ISS, researchers came across the fact that smoking was strongly

linked with ISS having a p-value of 0. 009 (Namazi et al, 2006). In contrast, Cohen et al studied 5682 patients for the impact of smoking on restenosis after PCI where they found that smoking reduces TLR rate, thus not influencing restenosis (Cohen et al, 2001). Comparing with intracranial arteries, even there, smoking has no influence on ISS but history of smoking do play a role in triggering ischemic stroke or transient ischemic attack in the stented vessels (Dubow et al, 2011). In an article of science daily, Dr Schillinger affirmed that smoking decreases restenosis rate following his research on 650 patients. With his research team, they deduced that bringing carbon monoxide to the site of the occlusion could be a hopeful concept and they suggest that further studies needs to be done concerning the therapeutic use of carbon monoxide in reducing restenosis rate (Schillinger et al, 2004). In addition, Gulesserian et al tried to combine genetic and conventional risk factors of restenosis by studying the Heme Oxygenase-1 Gene Promoter Polymorphism – involved in generating endogenous antioxidant bilirubin and carbon monoxide where both have anti-inflammatory and antiproliferative effects. Eventually they concluded that the effect of this gene polymorphism as a genetic risk factor is attenuated in smokers (Gulesserian et al, 2005). As stated before, measurement of restenosis rate was not within our reach for this study due to inadequate angiographic reports required for calculating this variable. Our result reflects the importance of lifestyle modification with smoking being the third most prominent risk factor influencing ISS in the Mauritian population.

4. 8. 5 Male gender

Our □2 test showed male gender as a significant risk factor with p-value of 0. 013 but in our linear regression model, this variable was not strong enough to be statistically significant. Even Kitoga et al identified male gender as a predictor of ISS. Controversially, Mohan and Dhall concluded that females had a higher restenosis rate than males while Jacobs et al showed that ISS is independent of gender. The role of gender as a contributor to ISS has long been debated. Normally, women have a lower risk of ISS compared to men (Mehilli et al, 2003). A plausible explanation to our result is the protective role of estrogen in delaying atherosclerosis and reducing the response of vessel wall to damage (Rossouw, 2002). Estrogen decreases the oxidative rate of degradation of arterial wall nitric oxide, encourages prostacyclin formation and reduces thromboxane A2 and endothelin-I synthesis, thus enhancing vasodilatation of unhealthy coronary arteries and restraining the inflammatory response to balloon-injury (Mikkola et al, 1995; Chen et al, 1996). Estrogen also accelerates endothelial cell growth, increasing the accessibility of nitric oxide and altering cellular migration after coronary intervention to prevent restenosis (Cornwell et al, 1994; Dai-Do et al, 1996). Alternatively, reduced plasminogen activator inhibitor type-1 levels and augmented plasmin activity causes estrogen to increase expression of matrix metalloprothroteinase-9, hence preventing the accumulation of extracellular matrix (Rossouw, 2002).

4. 9 Strengths and limitations of the study

The strength of our study lies in the fact that the database available at the cardiac centre for PCI patients was large enough such that a random sample

derived from it was adequate to allow for statistical analyses. Sufficient data has been collected so as to be able to meet up with our aims and objectives. Furthermore, list of patients available for study from the record's office was counter checked with the entries made at the angiography department for improved accuracy of collected data. We also confined our study to those variables with comprehensive and prospectively recorded data. Hence, a comparatively good result of the incidence value of ISS among PCI subjects has been achieved. On the other hand, the ISS sample population was available as from October 2009 and before that, there was no registry made for ISS cases at the cardiac centre. Hence, we were unable to extend our study before October 2009. Accurate information on the duration of diabetes was missing from patient's records and we were unable to study this important variable. This is because the cardiac centre offers tertiary care while detailed monitoring of NCDs' are performed at the patient's nearby AHC or hospital. Moreover, no data was available on the control of risk factors analyzed in the previous chapter. This might have influenced the association of the risk factors with ISS. Comparing results in different types of lesions and different types of patients from the non-randomised ISS group and the randomized control group may be somewhat imprecise. In addition, lack of information concerning hormone replacement therapy in females is a limitation particularly in this study where male gender showed some significance towards ISS. It is known that estrogen plays a vital role in delaying ISS and the mean age of the study population indicates that most of the females might have surely reached menopause. Eventually, data collected from the cardiac centre stands for PCI patients of around half of the

island and might probably not be a paragon of the whole Mauritian

population.

5. Conclusion and recommendation

In the present era, DM patients referred for PCI remains one of the major

challenges for interventional cardiologists. In addition of demonstrating the

incidence of ISS in the PCI population and the percentage of DM patients in

the ISS cohort, this study also highlights the fact that DM,

hypercholesterolemia and smoking are three most powerful predictors of ISS

in the studied Mauritian cohort. Mauritius is ranked as the third country

concerning the percentage of diabetic population (News on Sunday, 2011)

and on top of that, DM has been proved to be the major risk factor for ISS in

our study. As Dr. Gunness mentioned, " The result of bad lifestyle on cardiac

patients is all too evident at the cardiac centre" (Jugernauth, 2012). Hence,

waiting for the progress towards DES technology is important but more

essential is to adopt a systemic approach in improving hyperglycemia,

insulin resistance, hypercholesterolemia and also to encourage tobacco

cessation so as to minimize the occurrence of ISS in PCI patients.

Importantly, further studies needs to be carried out on factors like duration

of plavix treatment and the different brands of BMS being used for a better

enfolding of this issue of ISS in the Mauritian population. It is also high time

that we shift to DES in patients with BMS stenosis for a better outcome.

While are still using the BMS, other countries are on the verge of shifting

from DES to the promising Bioresorbable Vascular Scaffolds (BVS) which are

still under trial. However, the challenge to treat ISS in the DES era will then

be the oncoming frontier of interventional cardiology. It goes without saying

that even today; ISS remains the Achilles' heels of interventional cardiology.