6. Discussion

This study is one of its kind which comprehends the humanistic, clinical and economics outcomes of PCI in a tertiary care hospital setup. The results of the study give insights into the current trends in the treatment outcomes in a real world setup. The results of the study are discussed under humanistic, clinical and economic outcomes point of view which also fulfil the objectives of the study. The patients were drawn from rural and urban locations in and around 300 Km radius. The Kasturba hospital is one of the leading hospital catering to the healthcare needs of Karnataka. Other districts like Chikkamagalur, Shimoga, Davanagere, Chitradurga Karwar and Mangalore. In addition there are large number of patients form adjacent states like Goa and Kerala. The hospital has established itself as strategic quality healthcare provider for patients who are critically ill. Demographic distribution involves geographically diverse co-inhabitants, due to lack of scope the details of demographic classification was limited to classical representation such as age, gender, residence, education and occupation.

6.1 Humanistic Outcomes:

HRQoL is an important measure of how a patient feels about his/her health as a whole rather than only relief from the symptoms of disease. The present study used EQ-5D-5L questionnaire consisting of descriptive as well as VAS scoring. The EQ-5D-5L questionnaire was found to be valid and reliable questionnaire in correlation with disease specific questionnaire, while measuring HRQoL among patients with MI (Schweikert et al., 2006). Hence EQ-5D-5L questionnaire was used at baseline as well as four follow ups.

The initial recruitment for BMS group was 180 patients and for DES group it was 200 patients. The review of subjects was done at the 9 month follow-up, which revealed the mortality score 4 and 23 subjects with missed follow-up, ending up with 153 subjects at the end of one year follow-up in BMS arm. Whereas in DES 200 subjects were recruited in the beginning and on review at 9 month the mortality score was found to be 3 and missed follow-up subjects 10 ending up with 187 subjects for the final follow-up. Attrition rate was found to be 15% and 6.5% for BMS and DES groups respectively in our study.

The domain scores of EQ-5D-5L, although similar at baseline, showed an initial increase and a decrease at a later stage for DES group whereas BMS group showed a continuous increase in EQ-5D-5L from baseline to final follow-up. The major difference for DES vis-à-vis BMS
was found to be statistically significant and the difference in improved domain scores for DES is attributed not only due to antiproliferative drugs but also due to psychological confidence. The subjects in DES group feel secured due to perceived benefits attached with expensive stents implanted. There is a need to make a study to know regarding the psychological advantage due to perceived benefits of DES stents.

The mobility of the patient is greatly influenced by the knowledge and instructions given by physicians, nurses and family members following the PCI. Patients are supposed to remain immobile for certain period of time during which the endothelial cells cover the stent and the stent becomes internalised in the blood vessels which ultimately becomes the part of the coronary artery. During this period which may take roughly seven days, the patients are advised to remain immobile and should not involve in strenuous physical activity. In the later weeks there is no such risk caused due to mobility of the patients and they can move freely as the stent is fixed to the blood vessels. In DES due to release of antiproliferative drug, there will not be any abnormal growth of endothelial cells restricting the movement of the blood. These facts are usually explained to the patients following PCI. However, the perception of the patients can be a major guiding factor influencing the mobility of the patients in the post PCI period. The overall mobility increasing trend in DES and decreasing trend in BMS seems to be realistic as it indicates the superiority of DES over BMS after a one year follow-up indicating the value for money with DES.

The self-care problem score measured at different visits varied and at fourth and fifth visits irrespective of the type of stent and the problem scores were found overlapping. The self-care scores explored the patient’s ability to bathe, change the dress and other similar personal care activities. The confusion and lack of confidence with fear of restenosis might be one of the predictors in BMS patients. The age plays a major role in self-care, as aged person is likely to score low as far as the self-care is concerned. Looking at the demographic differences of subjects in BMS and DES, the average age group is higher in DES compared to BMS. Further, in the fourth and fifth visit the problem score for self-care merges and continued in an overlapped fashion (Figure 5.4).

Higher frequency problem scores of usual activity among DES patients compared to decreasing frequency scores for BMS scores for usual activity may look Prima facie the BMS are better than DES during the first to third visit. But at the fourth and fifth visits the frequency problem score with usual activity reaches a plateau indicating no difference at the
end of one year. The difference might have raised due to patient’s age of DES group (60.65 Years) where as it was 57.79 in BMS. The DES patient group had higher percentage score of diabetes (42%) compared to BMS (31%). The higher percentage of diabetes and pill burden may be contributing towards increased problem scores among DES patients for 9 months.

The percentage frequency problem scores show a wayward trend among DES and BMS subjects. The DES patients show a higher pain/discomfort scores compared to BMS scores until the third visit. In fourth and fifth visit DES percentage frequency problem scores are lower to BMS scores. The main cause due to lower cores of BMS can be attributed to the lower age and patients belonging to lower economic group who mainly comprises of a group of patients who are unskilled and depend upon the physical labour for their livelihood. The BMS patients naturally align to lower cost due to their economic conditions, whereas DES group who are able to afford higher cost of stents are belonging to skilled labour with good educational background. Careful observation of demographic tables give the supporting data for the above discussion.

It is quite natural on the day of angioplasty that the patients may suffer from high anxiety status with depression. The comfort of DES patients over BMS patients is clearly indicated in percentage frequency scores which reduces to 50% from 80% by third visit. The decline in both the groups appear to converge at the third visit however, the anxiety/ depression in DES increases to 70% and BMS to 60% in the fourth visit and converge in fifth visit. Midterm decrease and increase of anxiety and depression in both groups is attributed due to fear of cardiac problems perceived by the patients. The major difference of higher scores in DES than BMS is attributed to the exposure of more information and overthinking due to more leisure among DES patients than BMS patients.

The comparative utility scores and VAS score are presented in Figure 5.8 and Figure 5.9 respectively, which shows almost similar trends. The HRQoL represented as VAS score in the beginning was 60 units in both the groups and shoots between to 75-80. Further, the BMS group of patients does not show the improvement as compared to DES group and it was found to be maximum in the fourth follow-up. The difference was found to be statistically significant as shown by the ANOVA test. The patient in the DES group has sense of psychological comfort with the perception that they have spent more money for drug eluting stents than bare metal stents. The DES group consisting of mostly the skilled labour, has more opportunities to relax and adopt a practice of recommended lifestyle changes which
have a major impact on perceived HRQoL. However BMS patients with less income and having economic burden may feel ‘low’ and report lower scores of overall quality of life perceptions.

In the 6 month BASKET trial done at the University Hospital of Basel, Switzerland it was found that the DES group was having statistically significant humanistic outcomes for both VAS scores and domain scores as compared to BMS group (Kaiser et al., 2005).

In the 18 month follow-up BASKET trial again the significant difference in the HRQoL was seen in DES group as compared to BMS group (Brunner-La Rocca et al., 2007).

In a study done to find the effect of PCI on the HRQoL in patients with stable coronary disease it was reported that there was a statistically significant improvement in the HRQoL among the patients who received PCI compared to medical intervention alone (Weintraub et al., 2008).

In a prospective study done among 1518 patients for a period of one year it was identified that the aginal pain is an important predictor for the HRQoL among the patients undergoing PCI for nonacute myocardial infarction (Spertus et al., 2004).

In an US study among elderly patients undergoing PCI, the HRQoL domain are evaluated and reported that there was an improvement of 51% in physical health, and 29% mental health. This improvement did not change significantly after six months to one year follow-up (Seto et al., 2000).

6.2 Clinical Outcomes

The clinical outcomes of BMS and DES groups are given in Table 5.22, which are considered as baseline data. The BMI of both groups are shown in Figure 5.13. The clinical characteristics have a direct link to risk factors, with comparative account given in Table 5.2. Other important factors, which have profound effect on clinical effect are co-morbid conditions. The risk factors are computed as lifestyle factors, in a numerical scale of 1-5 for which data is given in Table 5.4. The pooled data of lifestyle factors and co-morbidities of both the groups is shown in Figure 5.2.

The analysis of risk factors such as co-morbidity and lifestyle has emerged as major risk factors. The influence of risk factors which are very high includes hypertension, diabetes and
sedentary lifestyle among both the groups. Hypertension, and diabetes are conditions which can be modified by proper management of diseases. The sedentary lifestyle although a major risk factor but does not appeal to the patients or to the providers as an effective intervention. Hence enough efforts in intervention are necessary to motivate the patients to give up sedentary lifestyle, which can play a major difference in morbidity and mortality among DES and BMS groups following the procedure.

The Xavier et al., has created a registry of ACS patients in 2008 to study the treatment and outcomes in India (Xavier et al., 2008). This study compared the distribution of patient population for STEMI and NSTEMI among western countries and India. Further, the study reported 70 percent STEMI prevalence in India, a strikingly different trend compared to west. The reason for high rates of STEMI in India is attributed to poor access to facilities, due to socioeconomic causes. In our study we have also observed high rate of STEMI than NSTEMI. As STEMI is a condition where complete blockade of a vessel leading to heart failure, needs an aggressive treatment with thrombolytic like streptokinase whereas NSTEMI there is a partial blockade. The patient pool in our study was a combination of urban and rural population. The patients from rural population comprised mainly of farmers and fishermen having irregular occupation and income. Their income was mainly dependent on monsoon and income earned out of agricultural produce. The results strongly reinforce the role of economic background being one of the predictor for high rate of STEMI among Indian rural patients.

The consolidated major clinical outcomes are recorded in Table 5.23 for MI, ST and death. The percentages of the MI, ST and death appear to show no difference and also the chi-square test indicated that there is no statistical significance between groups (Figure 5.12). Jensen et al. has reported a study in which they have compared the clinical outcomes of BMS patients with DES patients. Results in the study Prima facie do not show any superiority over BMS group in terms of MI, ST and mortality (Jensen et al., 2007). In our study also we have similar results without any statistical significance which was confirmed by Chi-square test.

Tu et al. in a Canadian study in cohort of 3791 patients reported that the DES were effective in reducing the need for target vessel revascularisations and without significantly affecting rate of death or MI (Tu et al., 2007).

A meta-analysis of 22 RCTs and 34 observational studies have concluded that in RCTs there was no debatable reduction in overall mortality and MI associated with DES in comparison
to BMS. But the same study reported significant reductions in target vessel revascularisation. Whereas in observational studies it reported significant reduction in all three clinical outcomes (Kirtane et al., 2009).

Mauri et al., have done hierarchical classification of stents across RCTs to comparatively evaluate the ST among the DES and BMS. In their study they have concluded that ST did not differ significantly among patients with DES as compared to BMS (Mauri et al., 2007).

In a study done with Swedish Coronary Angiography and Angioplasty Registry involving 13,738 patients treated with BMS and 6033 patients treated with DES followed-up for 3 years, it was concluded that DES were associated with increased risk of death and this trend increases after the initial 6 month follow-up (Lagerqvist et al., 2007).

Dawkins et al. in a prospective, multicentre, double-blind randomised trial reported that there was no significant difference between DES and BMS in terms of mortality and MI but they have found comparable reduction in restenosis (Dawkins et al., 2005).

### 6.3 Economic Outcomes

The sponsorship for healthcare services involves variety of modes starting from complete out of pocket, partial reimbursement support, and complete reimbursement. The out of pocket expenditure is highly prevalent and is about 30 percent of the total household income among the patients suffering from CVD in India (Rao et al., 2011). The subjects belong to diverse economic background. Some of them are very rich and have sufficient financial resources making economic burden of treatment is insignificant. The middle class and people above poverty line are the people who have limited financial resources. To these subjects the cost of treatment shall affect the economic status, pushing them towards economic distress. These people usually live in urban areas, employed, and have a regular monthly income meeting their expenses. The third category of people are below poverty line, who are labour class, earn their livelihood by daily wage systems and does not have proper secured regular income. The farmers also are the special class which are more or less similar to the labour class excluding the rich landlords who have a reserve economic background.

The middle class comprises of urbanites and persons who are working as an employee in a private or public enterprises. Many of the urbanites are covered by health insurance schemes, like ESI, Medicare or private health insurance. The labour class is also covered partially by central and state health schemes like Yashashvini for farmers, Sampoorna Suraksha etc.
The Indian healthcare system and funding for healthcare have remained as an individual responsibility by regulators and law makers. The health insurance although essential, has hardly able to cover a quarter of the population. The basic infrastructure of unified databank linked to social security schemes is one of the proposed agenda of the government. The government along with private insurance companies are offering variety of schemes. However patients are put to hardship as they fail to understand the details and conditions of health insurance policy. The reimbursement becomes a challenge for the patients who depend upon health insurance funding.

The major cost of treatment of PCI intervention can be divided into hospitalisation costs, cost of the stents, cost of the medicines post discharge and cost on hospital visits. The insurance coverage usually includes hospital charges with or without medicine charge while the patient is in the hospital. The stents are not usually covered by insurance scheme except in government schemes where subsidy is provided for the stent cost. The overall burden for the patient, irrespective of economic category, includes hospital charges, stent cost and cost of medicine in the post discharge period. The usual medicines prescribed following PCI discharge are anticoagulants, statins and co-morbidity specific drugs for hypertension and diabetes.

A detailed treatment cost data for BMS and DES patients are given in Table 5.25. All the data is subjected to Mann-Whitney, test which showed P value less than 0.001 for 95 percent confidence intervals. The data is subjected to cost consequence analysis in which total cost, VAS score along with percentages of episodes of MI, ST and mortality are compared for BMS and DES subjects, which is given in Table 5.26.

Cost effectiveness ratio for BMS and DES is calculated against HRQoL (VAS score), MI prevented, ST prevented and life saved, which is given in Table 5.27. The QALY is calculated for the data of 4th follow-up is computed in Table 5.28. The incremental cost effectiveness for one unit of QALY, VAS score gained, MI prevented, ST prevented and life saved is computed in Table 5.29.

The cost consequence analysis clearly indicates the DES subjects have paid almost near double the money and the result of VAS score is statistically significant than BMS patients. The other parameters remain more or less same except the mortality. This data emphasises that DES subjects pay more money than the BMS subjects with the consequence of an
improved HRQoL and also reduction in death. The outcomes observed may be due to complex inputs like unmeasured clinical and psychological inputs.

The cost effectiveness ratio keeps DES at high price compared to BMS group in terms of VAS scores, MI prevented, ST prevented and life saved. It is beyond doubt that DES patients spend almost double the amount to have comparable outcomes with BMS group. The computation of QALY with a difference of 0.24 clearly indicates about the high value of DES subjects over BMS subjects.

The ICER analysis highlights the value ratio of DES versus BMS costs which a patient has to pay per one unit of gained/ prevented/ saved values. The QALY take into account HRQoL experienced in each treatment groups. It gives a justification point for the expenditure on DES procedure. Now the policy maker has to decide how much money is available and can be allocated for gaining one unit of gained / prevented / saved parameters. The patient can also be informed regarding the values achievable for extra investment made. The data is of much value for designing the suitable health insurance products to the patients.

The increase in number of patients reporting to hospitals for angina and MI has increased to an epidemic scale in recent years. With lack of knowledge, along with lifestyle changes has increased the casualty of cardiac ailments. The immediate treatment requirement has pressurised the burden of healthcare system on all stakeholders beginning form patients to providers and government. There is no alternative to overcome this condition after the diagnosis. Among the available alternatives PCI is most popular due to least intervention compared to open heart surgery. A developing country like India has resource scarcity and needs. To be proactive in promotion of social issues like public health education. The current study establishes the fact that the DES intervention does offer perceived HRQoL advantage over BMS option, which is a little costlier than BMS. Clinically, DES and BMS derive almost equal benefits at the end of one year.

The Basel Stent Cost Effectiveness Trial done on 826 patients treated with BMS and DES showed that the mean cost of DES was €10,544 compared to BMS cost of €9,639. The study also reported the ICER of 18311 to avoid one major event, and cost per QALY gained was more than €50,000. The study concluded that the use of DES in all patients is less cost effective in real world setting (Kaiser et al., 2005).
Hill et al. in their systematic review involving 25 RCTs, of which 17 RCTs compared DES to BMS have reported cost effectiveness results. The study revealed that calculated cost per QALY was higher (£183,000–562,000) and outside the range of acceptability and it suggested the use of DES in subgroup of patients having the high risks of requiring reintervention (Hill et al., 2007).

Cohen et al. in their SIRUS trial involving sirolimus eluting stents with 1058 patients having complex coronary stenosis, evaluated costs for a period of one year follow-up. The ICER for DES was found to be $1650 per repeat revascularization event avoided or $27,540 per quality-adjusted year of life gained (Cohen et al., 2004).

The 18 month follow-up BASKET trial carried out to find out ICER, calculated an ICER of €64,732 to prevent one major adverse cardiac event, and of €40,467 per QALY gained. It also concluded that if used in all patients, the DES are not good value for money (Brunner-La Rocca et al., 2007).

A study involving 12 month audit data analysis of 2884 UK patients utilised economic modelling to estimate the cost-utility ratio reported that, the threshold price premium justifying 90% substitution of conventional stents was estimated to be £112 (US$212, €162) for sirolimus stents or £89 (US$167, €130) for paclitaxel stents (Bagust et al., 2006).