Diabetes Epidemic in South Asians

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I'm delighted to be here. This topic is very much at the center of my heart, as significant numbers of my maternal family members were diabetic. I remember at a very young age when I decided I wanted to be a doctor and find a cure for this disease and that's what motivated me to go into medical school. So I'm going to bring all my passion into prevention of diabetes. I'm so excited to tell you that now we have the armament to really screen the high-risk people, find their risk of diabetes early on and prevent it from developing.

(**Slides #2-5**) So to outline my talk on Diabetes and obesity, the global epidemic, I will first describe prediabetes, which is metabolic syndrome and impaired glucose tolerance, than I'm going to describe how to diagnosis diabetes, the micro and macro vascular complications of diabetes, how to reduce or prevent these complications, the economic burden related to diabetes, and finally the research that is needed in preventing pre-diabetes and diabetes, especially in our South Asian population.

(**Slide #6**) There has been a global epidemic of obesity which accounts for 1.7 billion population, and because of the diabetes and obesity link, actually now the word has been coined, "diabesity." Type 2 diabetes is so much related to obesity, that's why we are discussing obesity here. Worldwide 25% of the population is obese and therefore is at a tremendous risk of developing type 2 diabetes. (**Slide #7**) According to the WHO, in 2005 we have 194 millions population with diabetes. And their prediction is that in the next 20 years, by 2025, we will have almost 330 million diabetics throughout the world and half of them will be Asians and Pacific Islanders. Asians include all kind of Asians, Chinese, Koreans and South East Asians from Indian subcontinent, including Indian, Sri Lankan, Pakistani and Bangladeshi.

Now if you look at the obesity epidemic in the last 20 years according to the CDC, in 1985 we had only 10-15 percent of the population with BMI over 30, which was the definition of obesity. And as you can see now it has reached to almost, 25-30% of the population with BMI over 30. (**Slide #8**) To define obesity in Asians, their BMI is much lower and they have much greater risk of metabolic syndrome and not only adults, we are having more and more kids having the obesity epidemic. And unfortunately we are seeing Type 2 diabetes more and more in these young children. And again, according to the CDC statistics, you can see that in 2002 obesity rate increased to 16-20% in children, which just 20 years ago was 2-3%. Now it's 20%.

According to international diabetes studies, if you look globally the risk of diabetes and impaired glucose tolerance has tremendously increased. In 2003 the statistics shows that people with diabetes in the world were 194 million. There is going to be global epidemic of diabetes in the next 20 years, reaching 330 million populations if nothing is done about it. And the scary part is that for every diabetic that is diagnosed there are two undiagnosed people with impaired glucose tolerance who are at increased risk of developing diabetes. And if we can catch them at an early stage when they have just impaired glucose tolerance and correct it we can avoid this problem of diabetes global epidemic.

Looking at the South Asian population on the Indian subcontinent, currently in India, in 2005 we have about 30 million diabetics and it is predicted to be 80 millions in next 20 years. Another big population is in China, which is also progressing very rapidly towards obesity and diabetes. So there is emerging epidemic of diabetes in children and adults as well. There are some studies, which show that ethnicity is a risk factor. African Americans are disproportionately affected with obesity and they have higher risk of diabetes in their population. Similarly, a study from California showed that in Mexican Americans they had about 31 percent of their children below the age of 17 with diabetes. So the diabetes in children, which used to be Type 1 insulin dependent now we are seeing more and more type 2 diabetes in children.

(**Slide #10**) We have almost 10,000 patients diagnosed each day with diabetes in the US, that is scary. In children it's about 15% of the children who have type 2 diabetes. The risk factors for diabetes besides obesity are older age group. (**Slides #11-13**) This slide shows you that with increasing age we have increasing risks of diabetes. Below age 30 years it's about 2% risk by the time we reach to 70 years it gets to be 12%. We are an aging population in US so as we progress in age we have higher risk of diabetes. Other risks are ethnicity, physical inactivity, environment factors such as diet and psychological or emotional stress. Increasing growth of ethnic population in the US also has increased the risk of diabetes. Physical activity is decreasing with urbanization and new technological improvements. Kids and adults are spending more and more time with computers and TV. And it becomes difficult for us to go and do exercise with the other stresses that we have in our life.

Some populations are disproportionately affected as they age. (**Slide #14**) In this NHANES study compared to white population, which by the time they are 70's have diabetes rate of 10-12 percent, up to 15 percent at age 80. It is 35-40 percent in African Americans, Cubans, Mexican and Puerto Ricans. Asians, which is not described in this slide, also follow the same pattern as Mexican American and Puerto Rican. Dr. Arora had also mentioned in his

slides. We are reaching almost 35 to 40 percent risk of developing in elderly. Asian Indians fall in between these two groups with 25-30 percent risk of diabetes.

This is the first US study from Alabama on Asian Indians. They studied over 1046 immigrants Asian Indian people in the community and found that the Asian Indians had much higher risk of diabetes compared to the white and Hispanic. We need similar studies in other geographic areas.

(**Slide #15**) This slide is from the International Diabetes Federation, and this shows that as the population moves from rural areas to the urban area, and it is across the board, you know that when the rural population moves to urban areas their risk of diabetes increases from 3-5 percent to almost 15, 20 up to 25 percent. So it is the lifestyle changes like poor diet, lack of physical exercise and psychological stresses of moving to new place away from family that is leading to this increasing risk of diabetes.

(**Slide #16**) According to WHO in 2005 the population with diabetes is 194 million, with the way that obesity is progressing, in next 20 yrs it will be reaching 330 million and half of them will be Asian and Pacific Islanders. China is also going to have the highest rise in the diabetes prevalence, followed closely by India. (**Slide #17**) Type 2 diabetes is the disorder where we have elevated blood glucose, resulting from defective insulin secretion and defective insulin action and a combination of the two. Diabetes is significantly associated with macrovascular complications, which Dr. Arora alluded to with cardiovascular death. And that is why we put so much emphasis on reducing the risk of diabetes so as to prevent complications related to micro and macrovascular disease and premature death.

Now we have two huge studies DCCT and UKPDS and I want the audience to be aware that DCCT was study in type 1 diabetics and the UKPDS was a study in type 2 diabetes. And they did those studies to prove that with tight control of glucose we can reverse the diabetic complications. Later I'll go into more details about those studies.

(**Slides #18-22**) But just to give you information on what makes the diagnosis of diabetes, normally the fasting blood sugar should be less than 110. And diabetes is diagnosed if your fasting blood glucose is over 126. So any blood sugar in between 110 and 126 is impaired fasting glucose. Two hour postprandial blood glucose less than 140 is normal and over 200 is diabetic range. And any blood sugar in between 140 and 200 is impaired glucose tolerance. Now this impaired fasting glucose and impaired glucose tolerance is what we call pre-diabetes. And we have NIH data, a diabetes prevention trial DPP, in which they took the patients who had

impaired glucose tolerance or high risk of diabetes and reduced their development of diabetes with diet and exercise.

So what are the risks? What is the pathophysiology behind type 2 diabetes? We know that certain genes make us more susceptible to have impaired insulin secretion, and genes which have impaired insulin sensitivity combined with environmental factors such as poor nutrition in early fetal growth can affect size of fetal pancreas and beta cell reserve especially in the second and third trimester if fetus is deprived of the nutrients or is born preterm or is small for gestational age with smaller pancreatic beta cell reserve when exposed to high load of nutrients in adult life has significantly greater risk of developing impaired glucose tolerance and type 2 diabetes.

Once the person has defective pancreatic insulin secretion and also the impaired glucose uptake by the muscle or the fat cell, and increased endogenous production of glucose from the liver, that then causes hyperglycemia and development of diabetes. (**Slide #23**) If you see this next graph, it tells us that before the person develops diabetes there are subtle things going on almost ten years prior to onset of diabetes. Once the person develops obesity or have the metabolic syndrome and has increase in the visceral fat, the pendulum starts from there. (**Slide #24**) There is progressive destruction of the beta cells of the pancreas. Initially that person presents with postprandial rise in the glucose. By the time they present with diabetes they already have 90% destruction of their pancreas. So if we want to preserve beta cell of pancreas and secretion of the insulin, we have to reverse the process where the visceral obesity starts so that we can prevent the cardiovascular complications. Both in the DCCT and the UKPDS studies, they have shown that the diabetic control reverses the microvascular complications, such as the retinopathy, nephropathy and neuropathy. But they do not show reversal in the cardiovascular complications. Cardiovascular complications start when the visceral obesity starts. You have development of atherosclerosis and visceral fat is what causes the increase in the inflammatory markers of atherosclerosis, which is interleukin-6 and CRP and all that Dr. Arora just mentioned.

So if we want to bring the pendulum back and reduce the cardiovascular morbidity and mortality I think we have to start from the beginning when the visceral fat is starting to build up and obesity is developing. We need to think ahead – we have a lot of work ahead of us. And we have many people who are going to just pick up from here and go and start proposing all the people about diet and nutrition and exercise.

So just to mention in the developmental stage of diabetes postprandial glycemia is the first event that occurs and then later fasting hyperglycemic develops. So when they have significant obesity, and they develop insulin resistance this than produces more insulin and that insulin acts as a growth hormone, which makes the person gain more and more weight.

To diagnose insulin resistance in an obese individual we have to look at the glucose and insulin ratio, which is called as homeostatic model of insulin resistance, a mathematical calculation with which you can find out whether somebody has insulin resistance or not. All obesity is the not the same. We have one fourth of the globe with obesity but not everyone who is obese develops diabetes. So we have to identify the people who are at risk for developing diabetes. And the way we can do it is just do a fasting glucose and insulin ratio. If you get fasting plasma glucose level multiply it with insulin level and than divide it with 405, if the ratio is more than 1.6 that leads to the diagnosis of insulin resistance and you can find out about the homa model. It's given in the literature. So that's where we have to start. When the person starts to get obese we have to identify their risk by doing the insulin resistance evaluation in them and try to reverse their insulin resistance with behavior modification, diet, exercise, stress reduction.

(**Slide #25**) Now looking at this diabetes among South Asians in the US, and UK there are certain studies that have already been published. And Dr. Jay has also mentioned these studies. (**Slide #26**) One US study from Hawaii showed that different ethnic groups such as Asian, Hawaiian, Filipino, Chinese, Japanese and Koreans, all have shown that compared to US populations Asians have twice the risk of developing diabetes. And in UK studies of Indian, Pakistani and Bangladeshi population have shown four to five times greater incidence of developing diabetes as compared to UK population. So there is something with this ethnic group that when they move to west either UK, or US it increases their risk of developing diabetes. (**Slide #27**) And this slide just shows that compared to the white population, Asians have higher risk of developing diabetes, which increases to 2-4 fold, almost from five percent to 20 percent, if you move to a location in the Western Hemisphere, possibly due to change in their diet. So there is something in the water here that makes a person develop obesity and diabetes. And the European study similarly shows the risk of diabetes in South Asians is about 4-5 times as high as Europeans. And around 25 percent of the Indo-Asians in the UK suffer from type 2 diabetes. It develops almost ten years earlier than in European and US white populations. And as Dr. Arora mentioned, that heart attacks occurs ten years earlier than the European population and kidney disease also because of their earlier onset of diabetes. Kidney disease, as well as heart diseases,

are much more common in South Asians. And they have a higher risk for metabolic syndrome even in children, as you see, I mean these children are going to be adults soon and have an earlier risk of heart disease. So we have to make an effort to stop it here.

(**Slide #28**) So what are the risk factors? If somebody with a family history of diabetes or has high BMI (over 25, for the Western population), but for Asians BMI over 23, have certain racial background such as African American, Native American and Asian Americans are at much higher risk of developing diabetes. If they have gestational diabetes with babies over 9 pounds, if they have hypertension, if they have low HDL, or have high triglycerides or polycystic ovary syndrome they are at high risk. I'm seeing more and more young Asian girls come to me with menstrual irregularities have polycystic ovary disease because of their insulin resistance. And that is where you can make the dent, when you catch them at that age, than you can avoid diabetes and its complications with diet and exercise. Physical inactivity and poor diet is causing the problem of obesity and impaired glucose. Once we identify these factors we're going to have to do something about it.

(**Slide #29**) Now we want to discuss metabolic syndrome definition for south Asians. As Dr. Arora had mentioned previously, that waist circumference for males over 40 and for females over 35 makes the diagnosis of metabolic syndrome associated with elevated blood pressure over 130/86, the triglyceride is over 150 mg/dl, HDL is less than 44 mg/dl in men and less than 50mg/dl for a woman, their fasting blood sugar over 110. And if they have three of these five they have metabolic syndrome, which is a precursor of diabetes but for Asian it is four inches less for waist circumference for both males and females as compared to White Caucasians.

(**Slide #30**) When we talk about waist circumference what do we mean by that? This waist circumference differentiates the two different types of obesity. The apple or male type android obesity is what causes insulin resistance instead of pear or female gynecoid type obesity. If you have increased fat around your viscera this fat is metabolically different than if you have the female type, which is the gynecoid obesity in the gluteal area, which is around the hip. So waist circumference is always defined as metabolic syndrome type obesity where you have hypertrophy of the fat, not the hyperplasia. In hyperplasia these are small fat cells and are insulin sensitive. But hypertrophied cells are insulin resistant. (**Slide #31**) If you look at the CAT scan of the patients with diabetes you will see this visceral fat in significant amount compared to the normal. Now that's where we get fooled when we look at the Asians although they may look very thin, but if you do the CAT scan on them you find that the whole viscera is loaded with the fat.

(**Slide #32**) So metabolic syndrome in Asians is estimated to be about 50% of the population as compared to 25% of the American population. And that is what causes all this increased risk of diabetes and cardiovascular death in Asians. Compared to Caucasian children, South Asian children demonstrate higher levels of insulin and insulin resistance. (**Slide #33**) And screening and prevention has to be started from a very young age. Prevention has to started ten years earlier, so that they don't develop atherosclerosis and cardiovascular risk. So our job is to identify these patients who are at high risk and have insulin resistance to help them reduce the burden of coronary artery disease. South Asians have increased prevalence of coronary artery disease compared to Caucasians, and also the leading cause of death among South Asians in the US is cardiovascular. The incidence of end stage renal disease also is high in South Asians. Dr. Brenner a leading Nephrologist says that we are born with a certain amount of nephrons in our kidneys and if the salt and fat load is increased then these nephrons start to fail. So it's the same situation with pancreatic beta cells that if we have small pancreas and small kidneys, and load of the blood pressure and lipids is high, that we're bound to fail sooner. A study in Hong Kong based Chinese says that the treatment of high cholesterol can reduce risk of heart disease with use of statin and aspirin.

(**Slide #34**) Asian Indians in the US account for about 1.6 million population. We just heard about New Jersey data on south Asians, but this is the whole US data. There are several myths about Asian Indians that they are highly educated professionals and rich but only 34% of Asian Indians are professionals, which means 66% are not professionals. Not everybody who is Asian is really financially well off. Nearly half of the Asians live below poverty level and have no health insurance. Many Asians even though they're lifelong vegetarians, still have high incidence of coronary artery disease due to increase consumption of saturated fat. So besides the weight and the diet, there are genetic factors also, which are causing added risk of coronary artery disease.

(**Slide #35**) So to reduce the complications and excess cardiovascular mortality among south Asians, I think we need to educate the south Asian population about the increase risk and how to reduce or avoid this risk with diet and lifestyle modification. And you have to increase the awareness among the South Asians regarding their risk of diabetes and pre-diabetes and early screening, if we want to make some strides into preventing diabetes and cardiovascular disease. And we have to eliminate the misconception that because they are vegetarian, and they may look normal in weight, I see it all the time that a person may look very normal by their weight, you know. But that is a misconception that their BMI and waist circumference is normal. Smoking

is another big risk factor, which needs to be reduced, and also the blood pressure. Diabetes and blood pressure are silent killers. And unless a person comes in contact with a healthcare provider, they are not going to find out if they have diabetes or high blood pressure or high cholesterol. And sometimes we find out ten years after they have diabetes, when they present with cardiovascular or neurological or renal complications to the physician's attention. So unless they go for screening they won't be able to find out that they have any of these risks.

(**Slide #36**) Now this slide shows the DPP study from NIH, which had over 3000 participants, which showed that diet and exercise with lifestyle modification there was 58% reduction in the incidence of diabetes. So there is a significant improvement just with the diet and exercise alone. And metformin, an insulin sensitizer only had a 31% reduction. So I think we should overemphasize diet and exercise and underemphasize drugs.

So I was just going to quickly in two minutes summarize about treatment for diabetes, which is not the goal. The goal is the prevention. (**Slide #37**) But treatment is important. Diet and exercise always come on the top. (**Slide #38**) And there are many drugs available and we are getting more drugs approved by FDA. (**Slide #39**) Again, different drugs work on different parameters and they all have same goal, to lower the blood sugar, weather it is insulin or different oral agents, monotherapy or combination therapy. (**Slides #40-44**) I think most of the people have denial about their diabetes control and they want to stay on oral agents, even if they are in poor diabetes control and don't want to go on insulin, and now more and more studies are coming out that insulin therapy, you know, can achieve the target much faster and the goal of achievement of metabolic target should be the fasting blood glucose level to be close to 100 mg/dl and post prandial level close to 140mg/dl, blood pressure goal of less than 130 over 80 mm of Hg, cholesterol LDL goal which can still be lowered in diabetics to less than 70, triglyceride less than 150, and HDL more than 45. (**Slides #45-50**) And A1C goal of 6. A1C is closely monitored. Normal A1C is 5. Studies have shown such as DCCT and UK-PDS, that lowering A1C lowers microvascular complication 7.5 and above had increasing risk of complications, but risk of macrovascular complications between A1C of 5 to 6.5 cardiovascular mortality progressively worsens with higher A1C. (**Slides #51-54**) So if you want to really null the complication of cardiovascular disease you have to get as close to normal A1C as possible. And this is basically to show you that one percent drop in the A1C can significantly reduce the risk of micro vascular complications. The goal should be to keep the A1C below six and the fasting blood sugar should be as close to normal as possible, less than 110, and postprandial should be less than 140. That should be our goal. So we have to be very aggressive with glucose

control, blood pressure and cholesterol control. (**Slides #55-57**) Risk of death is related to the A1C level. So if you want to lower the risk, as the A1C goes up over 7, you know, risk is double. So we have to bring it down to close to 5 or 5.5 if possible. (**Slides #58-59**) And cardiovascular mortality for each increment in the fasting blood sugar there is a higher risk of cardiovascular mortality from 5 to 15 to 20 percent with each quartile of elevation in the blood sugar. Again, the goal should be to keep the blood sugar below 110 to keep the mortality down.

So basically, to lower the risk of micro and macrovascular complications, we have to tighten control. Otherwise the economic burden is going to be tremendous, as we know that poor glycemic control causes significant increase in the risk of cardiovascular mortality. (**Slides #60-63**) And we are spending billions of dollars, and if you look at that in billions, we have spent this year 132 billion dollars for care of diabetic patients. And by 2025 or 2030 that will reach to 200 billion if we don't do anything about it. So lifetime cost of taking care of complications is significant in diabetic patients.

(**Slide #66**) So in summary, pre-diabetes and type 2 diabetes is very common, but a serious disease, and must be screened early and managed aggressively. The goal of therapy is to lower insulin level and waist circumference with diet and exercise in pre-diabetics and diabetes to normalize or near normalize the blood glucose levels. And patient education is key to success. With diet and exercise, early and aggressive pharmacologic intervention, to achieve better glycemic control, better blood pressure control and better lipid control is a must to reduce complications. And the recent therapies advances include improvement in existing classes of drugs, and we are seeing more and more newer classes, which are improving the glycemic and blood pressure control to reduce these complications.

(**Slide #67**) Now what our future research needs? We need to screen them early, starting at younger ages, like the age of 30, and we need leadership to bring this problem of South Asians to the public and we need more research to understand the cardiovascular mortality in South Asians and diabetes, and we need to spread the current available information that we have to educate the South Asians so that we can reduce the risk.