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**Managing cardiovascular disease risk in South Asian kidney transplant recipients**

Prasad GVR *et al*. Cardiovascular disease in South Asians

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**Abstract**

South Asians (SA) are at higher cardiovascular risk than other ethnic groups, and SA kidney transplant recipients (SA KTR) are no exception. SA KTR experience increased major adverse cardiovascular events both early and late post-transplantation. Cardiovascular risk management should therefore begin well before transplantation. SA candidates may require aggressive screening for pre-transplant cardiovascular disease (CVD) due to their ethnicity and comorbidities. Recording SA ethnicity during the pre-transplant evaluation may enable programs to better assess cardiovascular risk, thus allowing for earlier targeted peri- and post-transplant intervention to improve cardiovascular outcomes. Diabetes remains the most prominent post-transplant cardiovascular risk factor in SA KTR. Diabetes also clusters with other metabolic syndrome components including lower high-density lipoprotein cholesterol, higher triglycerides, hypertension, and central obesity in this population. Dyslipidemia, metabolic syndrome, and obesity are all significant CVD risk factors in SA KTR, and contribute to increased insulin resistance. Novel biomarkers such as adiponectin, apolipoprotein B, and lipoprotein (a) may be especially important to study in SA KTR. Focused interventions to improve health behaviors involving diet and exercise may especially benefit SA KTR. However, there are few interventional clinical trials specific to the SA population, and none are specific to SA KTR. In all cases, understanding the nuances of managing SA KTR as a distinct post-transplant group, while still screening for and managing each CVD risk factor individually in all patients may help improve the long-term success of all kidney transplant programs catering to multi-ethnic populations.

**Key Words:** Cardiovascular risk; South Asians; Diabetes; Dyslipidemia; Metabolic syndrome; Health behavior; Novel cardiovascular risk factors

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**Core Tip:** South Asian kidney transplant recipients are at higher risk for cardiovascular disease. Aggressive management should begin before transplantation and continue into the post-transplant phase. Each risk factor should be managed individually to reduce cardiovascular risk and improve post-transplant outcomes.

**INTRODUCTION**

Kidney transplantation (KT) provides the highest survival benefit for patients once chronic kidney disease (CKD) progresses to end-stage kidney disease (ESKD)[1]. Registry analyses of KT recipient (KTR) outcomes indicate that cardiovascular disease (CVD) substantially contributes to post-transplant mortality[2]. South Asian (SA) KTR in particular are at higher CVD risk than other population groups[3]. Worldwide experience with post-transplant care in patients of SA origin is increasing[3-5] and as access to KT within SA itself also gradually increases[6], further SA KTR experience will accumulate. According to the Transplantation Society website (accessed February 11, 2019), there were almost 7000 KT performed in India alone. Despite the known higher post-transplant CVD risk in SA[3], preventive and management recommendations for SA KTR have not been made even with available SA-specific general population and CKD population information[7,8]. This review summarizes available literature on CVD in the SA population more generally, and integrates this with post-transplant CVD more specifically so that focused recommendations can be considered to both study and guide CVD management in SA KTR.

**Cardiovascular Disease Incidence and Mortality in South Asians**

South Asia typically refers to the Indian subcontinent (India, Pakistan, Nepal, Bangladesh, Sri Lanka, Bhutan, and Maldives), and these two geographical terms are often used interchangeably. SA have emigrated to many parts of the world. SA ethnicity is a risk factor for CVD, whether SA live in their country of origin or have immigrated to countries outside SA. Within India, SA’s largest country, about 2.8 million people died from CVD in 2016 alone[9]. CVD leads mortality across both urban and rural areas[10]. With improved longevity, CVD prevalence also increased by 4 to 7-fold between 1970 and 2013[11].

Emigrating Indians facilitate comparisons to other ethnic groups in their new countries. Coronary artery disease (CAD) is more incident and prevalent in SA[12]. A review of 124 articles indicates that SA have twice the CAD prevalence compared to age- and sex-adjusted Caucasians[13]. In Canada, the age-standardized incidence of acute myocardial infarction (MI) in SA men was 4.97/1000 population per year compared to 3.29/1000 population per year in Caucasian men[14]. In the United Kingdom, SA were almost four times as likely to report a history of MI compared to other groups[15]. CVD incidence may even be higher as succeeding generations of SA live outside South Asia[16].

SA experience acute MI about 10 years earlier than the global population[17]. In India, the mean age for CAD documented by angiography is 48 years, with one-third of cases occurring under 45 years[18]. Young Indians typically over-represent CAD outside SA, such as in the Middle East[19]. Mortality from CAD in SA is also higher[20] and occurs earlier[21]. Sex-standardized mortality rates from CAD are about 50% higher in SA compared to Caucasians for both men and women[22]. SA have a greater burden of triple-vessel disease and a greater atheroma score[23]. CAD may thus be more incident, prevalent and severe in SA.

How well do such epidemiological studies apply to SA KTR? Death with graft function (DWGF) is a leading cause of late kidney allograft loss, and CVD is its leading cause[24]. Unselected KTR have an annual cardiovascular event rate of 3.5%-5%[25]. Major adverse cardiovascular events (MACE), a term encompassing acute coronary syndrome, coronary revascularization, hospitalization for congestive heart failure and cardiac death, contribute significantly to overall post-transplant morbidity and mortality[24]. A current estimate indicates about 8000 KT are performed across over 267 transplant centres in SA patients annually[6]. KT rates will increase further as deceased donor organ procurement and paired donations increase[6]. Many SA already reside in countries such as Canada, the United States, and the United Kingdom, where KT rates are high and comparisons across ethnic groups will become possible. Therefore, studying and comparing cardiovascular risk factors in SA KTR is worthwhile.

Few studies report post-transplant cardiovascular events in SA. A single-centre study from Canada[3] reported a post-transplant MACE rate of 4.4/100 patient years in SA, compared to 1.31 in Caucasians, 1.16 in blacks, and 1.61 in East Asians (*P* < 0.0001 *vs* each). SA also experienced a greater incidence of post-transplant MACE in the first three months compared to each of the other groups[3]. The pre-transplant prevalence of CVD was similar across ethnic groups. In a study from India, CAD was diagnosed in 28% post-KT, and was a major cause of DWGF for up to 15 years[26]. An evaluation of elderly South Indian KTR found that CVD was a major contributor to the post-transplant mortality rate of 12% over 4 years[27]. The increased cardiovascular risk in SA KTR is thus consistent with that of the corresponding SA general population. CKD per se confers increased CVD risk[28], but to accommodate KT, potential candidates are usually subject to rigorous pre-transplant cardiovascular screening and risk mitigation[29]. Yet focused study of post-transplant CVD risk and mortality in SA KTR is tragically scarce.

In view of the dearth of studies on CVD in SA KTR, it may be helpful to first look at studies relating CKD to CVD more generally. CKD strongly associates with CVD mortality[30]. Low estimates of glomerular filtration rate (eGFR) and albuminuria are multiplicative in populations at risk for CKD, where risk factors include hypertension, diabetes, or CVD, but they are not interactive with respect to all-cause and CVD mortality[31]. In the SA general population the urine albumin-to-creatinine ratio may better estimate CVD risk and mortality[32], although eGFR in SA using existing equations may be inaccurate[33]. Vagueness results in CVD risk estimation when eGFR estimates are inaccurate and the unique post-transplant milieu compounds this vagueness further.

There is a need for awareness that MACE is both more common and more severe in SA KTR, just as during other CKD phases. A pre-transplant history of CVD remains an important risk factor for post-transplant MACE. Well-studied risk factors mirror those of the general population. In a large multi-ethnic sample from Canada that included a substantial number of South Asians, the Framingham Risk Score calculator under-predicted MACE[34]. Few studies examine either traditional or novel cardiovascular risk factors specifically in SA KTR, but managing cardiovascular risk is best targeted to individual risk factors, as with the KTR population as a whole.

**Cardiovascular Disease Screening**

Management of cardiovascular risk begins well before transplantation. Recording SA ethnicity during the pre-transplant evaluation process enables programs to assess cardiovascular risk in greater depth and potentially intervene earlier. Regular pre-transplant screening for CVD remains controversial[35]. Findings from clinical trials regarding CVD screening should be cautiously applied to SA KTR due to their differential risk, unless adequate SA representation in such trials can be ensured. Critical ischemic lesions when detected may be more advanced, and if occurring at a younger age should preclude lower age limits for initial pre-transplant screening. Pre-transplant screening for diabetes incidence and control through an oral glucose tolerance test or HbA1c may permit further focus to managing pre- and post-transplant cardiovascular risk[36].

SA transplant candidates with stable CAD are likely to receive aspirin, but may be at risk for suboptimal utilization of beta blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers, and statins[37]. These medications are commonly used for pre-transplant optimization. However, based on non-SA specific data, initiating a beta-blocker just prior to non-cardiac surgery may prevent perioperative non-fatal MI but increase risk for stroke or death[38]. SA representation in similar clinical trials is needed. Besides screening at a younger age, lower thresholds for blood pressure (BP) treatment may also be required[39]. SA may even be underrepresented in statin trials[40]. In the case of pre-dialysis KT candidates, SA-specific eGFR equations can be explored[41]. Among dialysis modalities, peritoneal dialysis may decrease post-transplant graft dysfunction[42]. In all cases, SA candidates require special attention to pre-transplant cardiovascular risk reduction to optimize post-transplant success.

Despite widely practiced pre-transplant screening, routine screening for post-transplant CVD is rarely practiced by busy transplant programs. Awareness of the increased CVD risk in SA KTR however may allow earlier post-transplant referral to cardiologists and other specialists, and ensure continuity of cardiovascular care from the pre-transplant to the post-transplant phase of CKD. A major role of post-transplant programs is to ensure that CVD risk factors are adequately managed.

**Individual Cardiovascular Risk Factors**

***Diabetes***Diabetes is the most significant cardiovascular disease risk factor in SA KTR[43]. One estimate indicates 87 million Indians will have diabetes by 2030[44]. The crude prevalence of diabetes in a population-based study of 1.3 million Indian adults, based on fasting or random glucose measurement was 7.5%[45]. In a United States study, diabetes prevalence was 17% in SA compared to 8% in non-Hispanic whites[46]. SA demonstrate a higher degree of insulin resistance[47] and early pancreatic β-cell dysfunction[48]. Diabetes in SA also clusters with other metabolic syndrome components such as lower high-density lipoprotein (HDL) cholesterol, higher total-to-HDL cholesterol (HDL-C) ratio, and hypertension[7]. SA are more centrally obese[49], the phenotype of which includes less subcutaneous adipose tissue compared to Caucasians, combined with more deep cutaneous and visceral fat[7]. A body mass index in SA of over 35 kg/m2 associates with increased mortality from CAD[50]. Duration of residence in the United States inversely correlates with being overweight or obese and the likelihood of leading a sedentary lifestyle, while being directly correlative to fruit and vegetable consumption[51].

SA more likely transport an existing diabetes burden to their post-transplant phase. Pre-existing diabetes increases the risk of post-transplant CVD threefold[52]. Significant CAD is detectable by angiography in a third to half of diabetic patients with ESKD[53]. Diabetes in SA is also likely to occur 5-10 years earlier[54], likely increasing post-transplant CVD attributable to diabetes. Post-transplant diabetes mellitus (PTDM) is also increased in SA, with an incidence at median 50 mo higher in SA (35%) compared to Caucasians (10%, *P* < 0.001 for difference)[55]. Calcineurin inhibitors (CNI) and steroids blunt insulin secretion and increase insulin resistance[56] in a population already at higher risk in this milieu of immune stress and ischemia-reperfusion injury[55]. Tacrolimus is generally more diabetogenic than cyclosporine. Differing predisposition to PTDM by CNI type may occur in SA based on the human leukocyte antigens profile[57]. However, there are no studies to prospectively modify PTDM risk in SA KTR.

PTDM portends a worse post-transplant prognosis in SA KTR[58]. There is no proven benefit to avoiding tacrolimus or prednisone to prevent or control diabetes in any population, so immunological concerns primarily should motivate choice of immunosuppressive medication. Glucagon-like peptide 1 receptor agonists (GLP-1RA) may similarly affect glycemia and weight in non-KTR SA, while dipeptidyl peptidase-4 inhibitors may provide greater glycemic benefit[59]. Sodium-glucose transport protein 2 inhibitors (SGLT2i) are safe, and may also provide greater benefit in non-KTR SA compared to Caucasians[59,60]. GLP-1RA and SGLT2i outcome trials demonstrated benefit in some subgroups, although granularity of ethnicity data remains a concern. Linagliptin either as monotherapy or combined with metformin or gliclazide is effective in SA KTR[61].

***Hypertension***Hypertension is also widely prevalent in the SA general population, with one estimate being 25% when defined as systolic BP (SBP) ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic[45]. Even among the youngest adults (18-25 years of age), the prevalence of hypertension was around 12%[45]. Based on echocardiography the left-ventricular mass index and left-ventricle remodeling index are lower in SA compared to Caucasians[62], despite no significant differences between them in electrocardiographic voltage[63]. By contrast, diabetes may impact left ventricular function adversely in SA compared to Caucasians[64].

Similar to diabetes, hypertension is widely prevalent at transplantation, is exacerbated by CNI particularly cyclosporine, and may occur de-novo or worsen as a result of stable or progressive graft dysfunction. A report suggests that each 10 mmHg systolic BP increase relates to an 18% increase in mortality[65]. Although hypertension is widely prevalent among SA, there is no literature to suggest that its risk in SA is increased compared to other ethnic groups, either with or without CKD. Awareness of hypertension is low in India[66], but might be higher in emigrant Indians[67], so one might also expect higher awareness in SA KTR.

There are no BP-lowering trials specific to SA KTR. The AIM-HY-INFORM trial in the United Kingdom plans to recruit one-third SA, using amlodipine, lisinopril, and chlorthalidone in varying combinations[68]. A review of 16 randomized controlled trials with BP outcomes in 1719 SA hypertensive patients showed no significant differences in BP-lowering efficacy among drugs[39]. SA may generally respond to antihypertensive therapy similar to Caucasians[69]. Vitamin D deficiency may also play a role in hypertension[70]. In a sub-analysis of the Anglo-Scandinavian Cardiac Outcomes Trial study, BP response to amlodipine monotherapy, or adding a diuretic to atenolol did not differ significantly by ethnic group. However, adding perindopril to amlodipine resulted in a greater SBP response in SA compared to Caucasians [-6.2 (-10.2 to -2.2) mmHg *vs* -1.7 (-2.8 to -0.7) mmHg][70]. Adherence to ACE inhibitors may be concerning[71].

***Dyslipidemia***SA consistently demonstrate higher triglycerides and lower HDL-C levels, in addition to having more pro-inflammatory small-dense HDL-C even if the HDL-C level is normal[72]. SA also have higher small dense low-density lipoprotein cholesterol (LDL-C)[73] and non-esterified fatty acids[74], indicating a defective insulin response in adipose tissue leading to pancreatic β-cell dysfunction[75]. Apparently normal total cholesterol levels can therefore be quite deceptive to conventional CVD risk assessment in SA KTR.

Dyslipidemia affects almost half of KTR. The association between post-transplant dyslipidemia and CVD may not be as strong as for diabetes and CVD, especially when considering dyslipidemia as a stand-alone risk factor[76]. However, according to one estimate in non-SA populations, a 2 mmol/L increase in LDL-C doubles the risk for MACE[77], while a low level of HDL-C associates with a threefold increase in post-transplant MACE[78]. A composite measure, non-HDL-C may be a powerful predictor of MACE in KTR[79]. Both low HDL-C and hypertriglyceridemia are components of the metabolic syndrome, to which SA are prone[80]. Hypertriglyceridemia is associated with progressive coronary artery calcification[81]. While CVD risk data for metabolic syndrome may be stronger than for dyslipidemia alone and the unique contribution of dyslipidemia in SA KTR is unclear[43], dyslipidemia should not be ignored.

There are no lipid-lowering trials in SA KTR, although statins are effective at lowering both total cholesterol and LDL cholesterol in non-transplant SA populations[82]. There is no difference in lipid-lowering response compared to Caucasians[83]. Statins may also lower BP in KTR population samples with significant SA representation[84]. Statin use in SA KTR requires close monitoring. Rosuvastatin doses should be kept lower in SA due to increased plasma exposure[85].

***Obesity***SA possess a greater waist-to-hip circumference ratio than native United Kingdom populations[86], and SA possess 6% more body fat for a given waist circumference or body mass index (BMI)[87]. In the United States, migrant Indians have greater total abdominal fat and intra-abdominal adipose tissue[88]. Skinfold thickness is also greater, even in children[89]. Increased hepatic steatosis[90], intra-myocellular triglyceride deposition, and adipocyte size in subcutaneous adipose tissue[88], as well as lower skeletal muscle mass[91] are all seen more in SA compared to Caucasians.

A meta-analysis of 165 studies with 1.5 million participants with any stage of CKD failed to demonstrate an association between obesity and mortality in CKD, but sparse data regarding waist and hip measurements did not allow further analyses[92]. However, the increased MACE risk in KTR is real[3] and SA have numerous increased obesity-related CVD risk factors[86-91]. Overweight in SA doubles the risk for CKD, more than for any other ethnic group[93]. In a European study higher age and female sex were associated with more post-transplant obesity, which in turn was associated with increased PTDM and lower eGFR[94], both of which increase CVD risk. An increased waist-to-hip ratio in KTR samples with large SA representation indicates less impact compared to other cardiovascular risk factors[43], but monitoring the waist-to-hip ratio may help motivate positive health behavior.

***Metabolic syndrome***

Metabolic syndrome is more prevalent in SA compared to Caucasians[95]. Once the metabolic syndrome develops, SA have a higher blood pressure, serum triglycerides, and fasting insulin levels, along with lower HDL-C levels compared to Caucasians[72]. Insulin resistance, which is the cardinal feature of metabolic syndrome, also occurs at a lower age in SA, occurring often in adolescents[96] and perhaps even at birth[97]. Insulin resistance in turn correlates with adipocyte size[87] and hepatic steatosis[90].

Metabolic syndrome is present in over one-fourth of KTR in India and is associated with female gender and hypertriglyceridemia[98]. Metabolic syndrome increased post-transplant MACE in a population in which SA were over-represented[43]. Metabolic syndrome also increases the risk of graft failure generally, but its contribution to graft loss in SA KTR specifically remains unknown. Nonetheless, metabolic syndrome definitions that contain information on insulin resistance correlate best with post-transplant MACE[43]. Non-diabetic KTR with metabolic syndrome but without diabetes will likely eventually develop diabetes, and metabolic syndrome components can enhance the effect of diabetes on post-transplant MACE. Therefore, it may be helpful to screen for metabolic syndrome components in SA KTR.

***Novel biomarkers***

Only one-third of measured metabolic factors such as insulin resistance, dyslipidemia, and central obesity explain the excess CVD risk that SA face[51]. Novel biomarkers that may correlate with increased CVD include increased serum leptin and C-reactive protein, as well as adiponectin levels that are lower in SA compared to Caucasians despite similar BMI[99]. The correlation between decreased adiponectin and increased insulin resistance is particularly strong for SA[100]. Both total and high molecular weight adiponectin levels are lower in SA KTR[101]. KTR with metabolic syndrome have significantly lower serum adiponectin levels than those without metabolic syndrome. Leptin levels are higher even after adjusting for body fat, suggesting increased adipocyte production[74]. Leptin inversely correlates with adiponectin, increases with decreasing eGFR, and is associated with inflammation[102]. Similar to adiponectin, lectin has not yet been linked to post-transplant MACE.

The association between hs-CRP and mortality in KTR is J-shaped, with both very low and very high levels associated with a two-fold increase risk of post-transplant mortality[103]. Serum homocysteine levels are higher in SA[46]. Although observational studies in CKD suggested homocysteine was associated with increased cardiovascular risk, lowering homocysteine with a multivitamin in the Folic Acid for Vascular Outcome Reduction in Transplantation trial did not improve post-transplant cardiovascular outcomes[104]. Apolipoprotein B (ApoB) predicts new-onset diabetes in KTR samples with a significant proportion of SA[105]. The LDL-C/ApoB ratio and the non-HDL-C/ApoB ratio were both significantly lower in SA than NHANES participants in the United States[106]. Other promising biomarkers in SA include reduced endothelial nitric oxide[107], increased plasminogen–activator inhibitor-1[108], and increased fibrinogen[109], all of which may correlate with insulin resistance.

The greatest attention among novel biomarkers has been given to elevated lipoprotein (a) [Lp(a)] levels[17,72]. Lp(a) levels are largely genetically determined, varying over 1000-fold among individuals and 5-fold across populations. SA have a median Lp(a) concentration of 16 mg/dL compared to 6 mg/dL in Caucasians[99]. Elevated Lp(a) levels associate with vulnerable plaques and culprit lesions in acute coronary syndromes, including premature CAD, correlating with the extent and severity of both acute coronary syndrome, CAD, and coronary artery calcium score[17]. Lp(a) might be the most promising novel biomarker to explain the excess SA CVD risk. Lp(a) levels decrease post-KT[110] despite an increase from cyclosporine[111]. Lp(a) remains a promising biomarker for targeting cardiovascular risk based on data from statin-based lipid-lowering trials[112], but more data in SA KTR are needed.

At the present time there are no interventions confirmed to influence novel biomarkers, which are at best secondary endpoints, but these biomarkers may be useful to monitor post-transplant CVD risk and guide interventions towards more established risk factors. Enriched recruitment of SA in clinical trials that include novel biomarker measurement may ultimately allow their incorporation into post-transplant cardiovascular risk modifying strategies, thereby benefiting all ethnic groups.

***Health behaviors***

Using a composite score that included non-smoking, moderate alcohol intake, physical activity, and fruits and vegetables consumption, the attributable fraction of lack of adherence to positive health behavior for CAD and CVD overall was 63% and 51% in SA, compared to 43% and 28% in Caucasians[113]. Besides ethnicity itself, diet and lifestyle may be particularly important to cardiovascular risk in low- and middle-income countries[114]. Dietary sodium intake in India approximates 3.7 g/d, very similar to the intake in the United States and United Kingdom[115]. SA diets are higher in carbohydrate, saturated fatty acids, trans-fatty acids, and ω-6 polyunsaturated fatty acids content, while being lower in monounsaturated fatty acids and fiber[116]. Vitamin D deficiency is especially common in SA[117].

Physical activity correlates inversely with established cardiovascular risk factors in KTR[118]. SA KTR in particular may be prone to a sedentary lifestyle before transplantation, potentially leading to increased post-surgical recovery times and associated complications. Decreased muscle strength and fatigue can affect post-transplant quality of life, thus emphasizing the need for graded exercise training[119]. SA are also more likely to report joint pain[120], further challenging participation in physical activity.

Physical activity is generally lower in SA, especially SA women. Although walking does not have a significant benefit on lipids, it may benefit insulin levels[121]. Cardiorespiratory fitness in SA is generally lower[122]. Therefore, SA KTR may benefit from more intense focus regarding education on physical activity, as well as structured exercise programs. Such programs will need to be culturally sensitive, especially in multiethnic regions of the world. Exercise training improves maximal exercise capacity, quadriceps muscle strength, health-related quality of life and diastolic BP[123].

Table 1 summarizes the cardinal features of CVD in SA. Table 2 summarizes some recommendations to manage CVD in SA KTR.

**CONCLUSION**

KTR are a group of transplant recipients at higher cardiovascular risk than other KTR groups. This increased risk in SA KTR is consistent with that seen in the corresponding SA general population. SA KTR are at higher risk for MACE both early and late after transplantation. CVD risk management should therefore begin well before transplantation. Recording SA ethnicity during the pre-transplant evaluation process may enable programs to more accurately assess individual cardiovascular risk and allow for earlier intervention to improve both pre-transplant and post-transplant cardiovascular outcomes. Diabetes remains the most prominent post-transplant cardiovascular risk factor, and corresponds to insulin resistance and pancreatic β-cell dysfunction. Hypertension is widely prevalent. Dyslipidemia, metabolic syndrome, and obesity are all significant CVD risk factors in SA KTR, and contribute to increased insulin resistance. Novel biomarkers may be especially important to study in SA KTR. Focused interventions to improve health behaviors in SA KTR may be particularly beneficial. However, there are few clinical trials specific to SA, and none are specific to SA KTR. In all cases, understanding the nuances of managing SA KTR while still approaching each CVD risk factor individually will facilitate improvement in the long-term success of all kidney transplant programs catering to multi-ethnic populations.

**REFERENCES**

1 **Wolfe RA**, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, Held PJ, Port FK. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999; **341**: 1725-1730 [PMID: 10580071 DOI: 10.1056/NEJM199912023412303]

2 **Stoumpos S**, Jardine AG, Mark PB. Cardiovascular morbidity and mortality after kidney transplantation. *Transpl Int* 2015; **28**: 10-21 [PMID: 25081992 DOI: 10.1111/tri.12413]

3 **Prasad GV**, Vangala SK, Silver SA, Wong SC, Huang M, Rapi L, Nash MM, Zaltzman JS. South Asian ethnicity as a risk factor for major adverse cardiovascular events after renal transplantation. *Clin J Am Soc Nephrol* 2011; **6**: 204-211 [PMID: 20884776 DOI: 10.2215/CJN.03100410]

4 **Tonelli M**, Hemmelgarn B, Gill JS, Chou S, Culleton B, Klarenbach S, Manns B, Wiebe N, Gourishankar S; Alberta Kidney Disease Network. Patient and allograft survival of Indo Asian and East Asian dialysis patients treated in Canada. *Kidney Int* 2007; **72**: 499-504 [PMID: 17554253 DOI: 10.1038/sj.ki.5002367]

5 **Loucaidou M**, Prasad S, Van Tromp J, Cairns TD, Griffith M, Hakim N, McLean AG, Palmer A, Papalois V, Taube D. Outcome of renal transplantation in South Asian recipients is similar to that in non-Asians. *Transplantation* 2004; **78**: 1021-1024 [PMID: 15480168 DOI: 10.1097/01.tp.0000136260.11575.cd]

6 **Jha V**, Ur-Rashid H, Agarwal SK, Akhtar SF, Kafle RK, Sheriff R; ISN South Asia Regional Board. The state of nephrology in South Asia. *Kidney Int* 2019; **95**: 31-37 [PMID: 30612598 DOI: 10.1016/j.kint.2018.09.001]

7 **Rana A**, de Souza RJ, Kandasamy S, Lear SA, Anand SS. Cardiovascular risk among South Asians living in Canada: a systematic review and meta-analysis. *CMAJ Open* 2014; **2**: E183-E191 [PMID: 25295238 DOI: 10.9778/cmajo.20130064]

8 **Misra A**, Tandon N, Ebrahim S, Sattar N, Alam D, Shrivastava U, Narayan KM, Jafar TH. Diabetes, cardiovascular disease, and chronic kidney disease in South Asia: current status and future directions. *BMJ* 2017; **357**: j1420 [PMID: 28400361 DOI: 10.1136/bmj.j1420]

9 **Xavier D**, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, Gupta R, Joshi P, Kerkar P, Thanikachalam S, Haridas KK, Jaison TM, Naik S, Maity AK, Yusuf S; CREATE registry investigators. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet* 2008; **371**: 1435-1442 [PMID: 18440425 DOI: 10.1016/S0140-6736(08)60623-6]

10 **India State-Level Disease Burden Initiative CVD Collaborators**. The changing patterns of cardiovascular diseases and their risk factors in the states of India: the Global Burden of Disease Study 1990-2016. *Lancet Glob Health* 2018; **6**: e1339-e1351 [PMID: 30219317 DOI: 10.1016/S2214-109X(18)30407-8]

11 **Prabhakaran D**, Jeemon P, Roy A. Cardiovascular Diseases in India: Current Epidemiology and Future Directions. *Circulation* 2016; **133**: 1605-1620 [PMID: 27142605 DOI: 10.1161/CIRCULATIONAHA.114.008729]

12 **Enas EA**, Yusuf S, Mehta JL. Prevalence of coronary artery disease in Asian Indians. *Am J Cardiol* 1992; **70**: 945-949 [PMID: 1529952 DOI: 10.1016/0002-9149(92)90744-j]

13 **Fernando E**, Razak F, Lear SA, Anand SS. Cardiovascular Disease in South Asian Migrants. *Can J Cardiol* 2015; **31**: 1139-1150 [PMID: 26321436 DOI: 10.1016/j.cjca.2015.06.008]

14 **Nijjar AP**, Wang H, Quan H, Khan NA. Ethnic and sex differences in the incidence of hospitalized acute myocardial infarction: British Columbia, Canada 1995-2002. *BMC Cardiovasc Disord* 2010; **10**: 38 [PMID: 20723259 DOI: 10.1186/1471-2261-10-38]

15 **Mather HM**, Chaturvedi N, Fuller JH. Mortality and morbidity from diabetes in South Asians and Europeans: 11-year follow-up of the Southall Diabetes Survey, London, UK. *Diabet Med* 1998; **15**: 53-59 [PMID: 9472864 DOI: 10.1002/(SICI)1096-9136(199801)15:1<53::AID-DIA521>3.0.CO;2-V]

16 **Gupta P**, Gan ATL, Man REK, Fenwick EK, Tham YC, Sabanayagam C, Wong TY, Cheng CY, Lamoureux EL. Risk of Incident Cardiovascular Disease and Cardiovascular Risk Factors in First and Second-Generation Indians: The Singapore Indian Eye Study. *Sci Rep* 2018; **8**: 14805 [PMID: 30287859 DOI: 10.1038/s41598-018-32833-0]

17 **Enas EA**, Varkey B, Dharmarajan TS, Pare G, Bahl VK. Lipoprotein(a): An underrecognized genetic risk factor for malignant coronary artery disease in young Indians. *Indian Heart J* 2019; **71**: 184-198 [PMID: 31543191 DOI: 10.1016/j.ihj.2019.04.007]

18 **Krishnaswami S**, Prasad NK, Jose VJ. A study of lipid levels in Indian patients with coronary arterial disease. *Int J Cardiol* 1989; **24**: 337-345 [PMID: 2788622 DOI: 10.1016/0167-5273(89)90013-2]

19 **Chaikhouni A**, Chouhan L, Pomposiello C, Banna A, Mahrous F, Thomas G, al-Hassan NA, Khalifa S, Jaddan A, Bsata MW. Myocardial infarction in Qatar: the first 2515 patients. *Clin Cardiol* 1993; **16**: 227-230 [PMID: 8443996 DOI: 10.1002/clc.4960160312]

20 **Forouhi NG**, Sattar N, Tillin T, McKeigue PM, Chaturvedi N. Do known risk factors explain the higher coronary heart disease mortality in South Asian compared with European men? Prospective follow-up of the Southall and Brent studies, UK. *Diabetologia* 2006; **49**: 2580-2588 [PMID: 16972045 DOI: 10.1007/s00125-006-0393-2]

21 **Enas EA**, Mehta J. Malignant coronary artery disease in young Asian Indians: thoughts on pathogenesis, prevention, and therapy. Coronary Artery Disease in Asian Indians (CADI) Study. *Clin Cardiol* 1995; **18**: 131-135 [PMID: 7743682 DOI: 10.1002/clc.4960180305]

22 **Sheth T**, Nair C, Nargundkar M, Anand S, Yusuf S. Cardiovascular and cancer mortality among Canadians of European, south Asian and Chinese origin from 1979 to 1993: an analysis of 1.2 million deaths. *CMAJ* 1999; **161**: 132-138 [PMID: 10439820]

23 **Hughes LO**, Raval U, Raftery EB. First myocardial infarctions in Asian and white men. *BMJ* 1989; **298**: 1345-1350 [PMID: 2502249 DOI: 10.1136/bmj.298.6684.1345]

24 **Reuter S**, Reiermann S, Malyar V, Schütte-Nütgen K, Schmidt R, Pavenstädt H, Reinecke H, Suwelack B. A Comparison of Different Algorithms for the Assessment of Cardiovascular Risk in Patients at Waiting List for Kidney Transplantation. *PLoS One* 2016; **11**: e0161927 [PMID: 27768693 DOI: 10.1371/journal.pone.0161927]

25 **Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group**. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant* 2009; **9** **Suppl 3**: S1-155 [PMID: 19845597 DOI: 10.1111/j.1600-6143.2009.02834.x]

26 **Prakash J**, Ghosh B, Singh S, Soni A, Rathore SS. Causes of death in renal transplant recipients with functioning allograft. *Indian J Nephrol* 2012; **22**: 264-268 [PMID: 23162269 DOI: 10.4103/0971-4065.101245]

27 **Mohamed Ali AA**, Abraham G, Khanna P, Reddy YN, Mehrotra A, Mathew M, Sundararaj S, Jasmine R. Renal transplantation in the elderly: South Indian experience. *Int Urol Nephrol* 2011; **43**: 265-271 [PMID: 21203840 DOI: 10.1007/s11255-010-9887-4]

28 **Major RW**, Cheng MRI, Grant RA, Shantikumar S, Xu G, Oozeerally I, Brunskill NJ, Gray LJ. Cardiovascular disease risk factors in chronic kidney disease: A systematic review and meta-analysis. *PLoS One* 2018; **13**: e0192895 [PMID: 29561894 DOI: 10.1371/journal.pone.0192895]

29 **Palepu S**, Prasad GV. Screening for cardiovascular disease before kidney transplantation. *World J Transplant* 2015; **5**: 276-286 [PMID: 26722655 DOI: 10.5500/wjt.v5.i4.276]

30 **Chronic Kidney Disease Prognosis Consortium**, Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE, Coresh J, Gansevoort RT. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010; **375**: 2073-2081 [PMID: 20483451 DOI: 10.1016/S0140-6736(10)60674-5]

31 **van der Velde M**, Matsushita K, Coresh J, Astor BC, Woodward M, Levey A, de Jong P, Gansevoort RT; Chronic Kidney Disease Prognosis Consortium, van der Velde M, Matsushita K, Coresh J, Astor BC, Woodward M, Levey AS, de Jong PE, Gansevoort RT, Levey A, El-Nahas M, Eckardt KU, Kasiske BL, Ninomiya T, Chalmers J, Macmahon S, Tonelli M, Hemmelgarn B, Sacks F, Curhan G, Collins AJ, Li S, Chen SC, Hawaii Cohort KP, Lee BJ, Ishani A, Neaton J, Svendsen K, Mann JF, Yusuf S, Teo KK, Gao P, Nelson RG, Knowler WC, Bilo HJ, Joosten H, Kleefstra N, Groenier KH, Auguste P, Veldhuis K, Wang Y, Camarata L, Thomas B, Manley T. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. *Kidney Int* 2011; **79**: 1341-1352 [PMID: 21307840 DOI: 10.1038/ki.2010.536]

32 **Eastwood SV**, Chaturvedi N, Sattar N, Welsh PI, Hughes AD, Tillin T. Impact of Kidney Function on Cardiovascular Risk and Mortality: A Comparison of South Asian and European Cohorts. *Am J Nephrol* 2019; **50**: 425-433 [PMID: 31665726 DOI: 10.1159/000503873]

33 Erratum. *J Pediatric Infect Dis Soc* 2019; **8**: 586 [PMID: 31639182 DOI: 10.1093/jpids/piz072]

34 **Silver SA**, Huang M, Nash MM, Prasad GV. Framingham risk score and novel cardiovascular risk factors underpredict major adverse cardiac events in kidney transplant recipients. *Transplantation* 2011; **92**: 183-189 [PMID: 21558986 DOI: 10.1097/TP.0b013e31821f303f]

35 **Ying T**, Gill J, Webster A, Kim SJ, Morton R, Klarenbach SW, Kelly P, Ramsay T, Knoll GA, Pilmore H, Hughes G, Herzog CA, Chadban S, Gill JS. Canadian-Australasian Randomised trial of screening kidney transplant candidates for coronary artery disease-A trial protocol for the CARSK study. *Am Heart J* 2019; **214**: 175-183 [PMID: 31228771 DOI: 10.1016/j.ahj.2019.05.008]

36 **Rao N**, Rathi M, Sharma A, Ramachandran R, Kumar V, Kohli HS, Gupta KL, Sakhuja V. Pretransplant HbA1c and Glucose Metabolism Parameters in Predicting Posttransplant Diabetes Mellitus and Their Course in the First 6 Months After Living-Donor Renal Transplant. *Exp Clin Transplant* 2018; **16**: 446-454 [PMID: 29251576 DOI: 10.6002/ect.2017.0020]

37 **Sharma KK**, Mathur M, Gupta R, Guptha S, Roy S, Khedar RS, Gupta N, Gupta R. Epidemiology of cardioprotective pharmacological agent use in stable coronary heart disease. *Indian Heart J* 2013; **65**: 250-255 [PMID: 23809376 DOI: 10.1016/j.ihj.2013.04.019]

38 **Wijeysundera DN**, Duncan D, Nkonde-Price C, Virani SS, Washam JB, Fleischmann KE, Fleisher LA; ACC/AHA Task Force Members. Perioperative beta blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; **130**: 2246-2264 [PMID: 25085964 DOI: 10.1161/CIR.0000000000000104]

39 **Brewster LM**, van Montfrans GA, Oehlers GP, Seedat YK. Systematic review: antihypertensive drug therapy in patients of African and South Asian ethnicity. *Intern Emerg Med* 2016; **11**: 355-374 [PMID: 27026378 DOI: 10.1007/s11739-016-1422-x]

40 **Adams C**, Singh K. Geographic variation in the statin trials: Underrepresentation of Asian populations. *Int J Cardiol* 2020; **316**: 249-251 [PMID: 32682006 DOI: 10.1016/j.ijcard.2020.07.015]

41 **Jessani S**, Levey AS, Bux R, Inker LA, Islam M, Chaturvedi N, Mariat C, Schmid CH, Jafar TH. Estimation of GFR in South Asians: a study from the general population in Pakistan. *Am J Kidney Dis* 2014; **63**: 49-58 [PMID: 24074822 DOI: 10.1053/j.ajkd.2013.07.023]

42 **Pavan KR**, Subhramanyam SV, Karopadi AN, Sinoj KA, Nayak KS. What Is the Best Dialysis Therapy for South Asia: HD or PD? *Contrib Nephrol* 2017; **189**: 71-78 [PMID: 27951552 DOI: 10.1159/000450687]

43 **Prasad GV**, Huang M, Silver SA, Al-Lawati AI, Rapi L, Nash MM, Zaltzman JS. Metabolic syndrome definitions and components in predicting major adverse cardiovascular events after kidney transplantation. *Transpl Int* 2015; **28**: 79-88 [PMID: 25207680 DOI: 10.1111/tri.12450]

44 **Shaw JE**, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract* 2010; **87**: 4-14 [PMID: 19896746 DOI: 10.1016/j.diabres.2009.10.007]

45 **Geldsetzer P**, Manne-Goehler J, Theilmann M, Davies JI, Awasthi A, Vollmer S, Jaacks LM, Bärnighausen T, Atun R. Diabetes and Hypertension in India: A Nationally Representative Study of 1.3 Million Adults. *JAMA Intern Med* 2018; **178**: 363-372 [PMID: 29379964 DOI: 10.1001/jamainternmed.2017.8094]

46 **Misra R**, Patel T, Kotha P, Raji A, Ganda O, Banerji M, Shah V, Vijay K, Mudaliar S, Iyer D, Balasubramanyam A. Prevalence of diabetes, metabolic syndrome, and cardiovascular risk factors in US Asian Indians: results from a national study. *J Diabetes Complications* 2010; **24**: 145-153 [PMID: 19303333 DOI: 10.1016/j.jdiacomp.2009.01.003]

47 **Petersen KF**, Dufour S, Feng J, Befroy D, Dziura J, Dalla Man C, Cobelli C, Shulman GI. Increased prevalence of insulin resistance and nonalcoholic fatty liver disease in Asian-Indian men. *Proc Natl Acad Sci U S A* 2006; **103**: 18273-18277 [PMID: 17114290 DOI: 10.1073/pnas.0608537103]

48 **Motala AA**, Omar MA. Evidence for impaired pancreatic beta cell function in South African Indians with impaired glucose tolerance. *Diabet Med* 1994; **11**: 437-444 [PMID: 8088120 DOI: 10.1111/j.1464-5491.1994.tb00303.x]

49 **Tillin T**, Hughes AD, Mayet J, Whincup P, Sattar N, Forouhi NG, McKeigue PM, Chaturvedi N. The relationship between metabolic risk factors and incident cardiovascular disease in Europeans, South Asians, and African Caribbeans: SABRE (Southall and Brent Revisited) -- a prospective population-based study. *J Am Coll Cardiol* 2013; **61**: 1777-1786 [PMID: 23500273 DOI: 10.1016/j.jacc.2012.12.046]

50 **Chen Y**, Copeland WK, Vedanthan R, Grant E, Lee JE, Gu D, Gupta PC, Ramadas K, Inoue M, Tsugane S, Tamakoshi A, Gao YT, Yuan JM, Shu XO, Ozasa K, Tsuji I, Kakizaki M, Tanaka H, Nishino Y, Chen CJ, Wang R, Yoo KY, Ahn YO, Ahsan H, Pan WH, Chen CS, Pednekar MS, Sauvaget C, Sasazuki S, Yang G, Koh WP, Xiang YB, Ohishi W, Watanabe T, Sugawara Y, Matsuo K, You SL, Park SK, Kim DH, Parvez F, Chuang SY, Ge W, Rolland B, McLerran D, Sinha R, Thornquist M, Kang D, Feng Z, Boffetta P, Zheng W, He J, Potter JD. Association between body mass index and cardiovascular disease mortality in east Asians and south Asians: pooled analysis of prospective data from the Asia Cohort Consortium. *BMJ* 2013; **347**: f5446 [PMID: 24473060 DOI: 10.1136/bmj.f5446]

51 **Bharmal N**, Kaplan RM, Shapiro MF, Mangione CM, Kagawa-Singer M, Wong MD, McCarthy WJ. The association of duration of residence in the United States with cardiovascular disease risk factors among South Asian immigrants. *J Immigr Minor Health* 2015; **17**: 781-790 [PMID: 24380928 DOI: 10.1007/s10903-013-9973-7]

52 **Kasiske BL**, Guijarro C, Massy ZA, Wiederkehr MR, Ma JZ. Cardiovascular disease after renal transplantation. *J Am Soc Nephrol* 1996; **7**: 158-165 [PMID: 8808124]

53 **Ramanathan V**, Goral S, Tanriover B, Feurer ID, Kazancioglu R, Shaffer D, Helderman JH. Screening asymptomatic diabetic patients for coronary artery disease prior to renal transplantation. *Transplantation* 2005; **79**: 1453-1458 [PMID: 15912119 DOI: 10.1097/01.tp.0000164147.60036.67]

54 **Sattar N**, Gill JM. Type 2 diabetes in migrant south Asians: mechanisms, mitigation, and management. *Lancet Diabetes Endocrinol* 2015; **3**: 1004-1016 [PMID: 26489808 DOI: 10.1016/S2213-8587(15)00326-5]

55 **Peracha J**, Nath J, Ready A, Tahir S, Parekh K, Hodson J, Ferro CJ, Borrows R, Sharif A. Risk of post-transplantation diabetes mellitus is greater in South Asian versus Caucasian kidney allograft recipients. *Transpl Int* 2016; **29**: 727-739 [PMID: 27062063 DOI: 10.1111/tri.12782]

56 **Rodrigo E**, Fernández-Fresnedo G, Valero R, Ruiz JC, Piñera C, Palomar R, González-Cotorruelo J, Gómez-Alamillo C, Arias M. New-onset diabetes after kidney transplantation: risk factors. *J Am Soc Nephrol* 2006; **17**: S291-S295 [PMID: 17130277 DOI: 10.1681/ASN.2006080929]

57 **Reddy YN**, Abraham G, Sundaram V, Reddy PP, Mathew M, Nagarajan P, Mehra N, Ramachandran A, Ali AA, Reddy YN. Is there a genetic predisposition to new-onset diabetes after kidney transplantation? *Saudi J Kidney Dis Transpl* 2015; **26**: 1113-1120 [PMID: 26586047 DOI: 10.4103/1319-2442.168558]

58 **Kumar S**, Sanyal D, Das P, Bhattacharjee K, Rungta R. An observational prospective study to evaluate the outcomes of new onset diabetes after renal transplantation (NODAT) in a tertiary care centre in eastern India. *Diabetes Res Clin Pract* 2020; **159**: 107948 [PMID: 31778745 DOI: 10.1016/j.diabres.2019.107948]

59 **Ghouri N**, Javed H, Sattar N. Pharmacological Management of Diabetes for Reducing Glucose Levels and Cardiovascular Disease Risk: What Evidence in South Asians? *Curr Diabetes Rev* 2020 [PMID: 33371853 DOI: 10.2174/1573399817666201228120725]

60 **Shah M**, Virani Z, Rajput P, Shah B. Efficacy and Safety of Canagliflozin in Kidney Transplant Patients. *Indian J Nephrol* 2019; **29**: 278-281 [PMID: 31423063 DOI: 10.4103/ijn.IJN\_2\_18]

61 **Sanyal D**, Biswas M, Chaudhari N. Long-term efficacy and safety of anti-hyperglycaemic agents in new-onset diabetes after transplant: Results from outpatient-based 1-year follow-up and a brief review of treatment options. *Diabetes Metab Syndr* 2021; **15**: 13-19 [PMID: 33278690 DOI: 10.1016/j.dsx.2020.11.019]

62 **Park CM**, March K, Ghosh AK, Jones S, Coady E, Tuson C, Francis D, Mayet J, Tillin T, Chaturvedi N, Hughes AD. Left-ventricular structure in the Southall And Brent REvisited (SABRE) study: explaining ethnic differences. *Hypertension* 2013; **61**: 1014-1020 [PMID: 23478098 DOI: 10.1161/HYPERTENSIONAHA.111.00610]

63 **Spencer CG**, Beevers DG, Lip GY. Ethnic differences in left ventricular size and the prevalence of left ventricular hypertrophy among hypertensive patients vary with electrocardiographic criteria. *J Hum Hypertens* 2004; **18**: 631-636 [PMID: 15071486 DOI: 10.1038/sj.jhh.1001713]

64 **Park CM**, Tillin T, March K, Ghosh AK, Jones S, Wright A, Heasman J, Francis D, Sattar N, Mayet J, Chaturvedi N, Hughes AD. Hyperglycemia has a greater impact on left ventricle function in South Asians than in Europeans. *Diabetes Care* 2014; **37**: 1124-1131 [PMID: 24241789 DOI: 10.2337/dc13-1864]

65 **Kasiske BL**, Anjum S, Shah R, Skogen J, Kandaswamy C, Danielson B, O'Shaughnessy EA, Dahl DC, Silkensen JR, Sahadevan M, Snyder JJ. Hypertension after kidney transplantation. *Am J Kidney Dis* 2004; **43**: 1071-1081 [PMID: 15168388 DOI: 10.1053/j.ajkd.2004.03.013]

66 **Anchala R**, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, Prabhakaran D. Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. *J Hypertens* 2014; **32**: 1170-1177 [PMID: 24621804 DOI: 10.1097/HJH.0000000000000146]

67 **Yip W**, Wong TY, Jonas JB, Zheng Y, Lamoureux EL, Nangia V, Sabanayagam C. Prevalence, awareness, and control of hypertension among Asian Indians living in urban Singapore and rural India. *J Hypertens* 2013; **31**: 1539-1546 [PMID: 23666423 DOI: 10.1097/HJH.0b013e328361d52b]

68 **Mukhtar O**, Cheriyan J, Cockcroft JR, Collier D, Coulson JM, Dasgupta I, Faconti L, Glover M, Heagerty AM, Khong TK, Lip GYH, Mander AP, Marchong MN, Martin U, McDonnell BJ, McEniery CM, Padmanabhan S, Saxena M, Sever PJ, Shiel JI, Wych J, Chowienczyk PJ, Wilkinson IB. A randomized controlled crossover trial evaluating differential responses to antihypertensive drugs (used as mono- or dual therapy) on the basis of ethnicity: The comparIsoN oF Optimal Hypertension RegiMens; part of the Ancestry Informative Markers in HYpertension program-AIM-HY INFORM trial. *Am Heart J* 2018; **204**: 102-108 [PMID: 30092411 DOI: 10.1016/j.ahj.2018.05.006]

69 **Islam AK**, Majumder AA. Hypertension in Bangladesh: a review. *Indian Heart J* 2012; **64**: 319-323 [PMID: 22664819 DOI: 10.1016/S0019-4832(12)60096-0]

70 **Gupta AK**, Poulter NR, Dobson J, Eldridge S, Cappuccio FP, Caulfield M, Collier D, Cruickshank JK, Sever PS, Feder G; ASCOT. Ethnic differences in blood pressure response to first and second-line antihypertensive therapies in patients randomized in the ASCOT Trial. *Am J Hypertens* 2010; **23**: 1023-1030 [PMID: 20725056 DOI: 10.1038/ajh.2010.105]

71 **Lai EJ**, Grubisic M, Palepu A, Quan H, King KM, Khan NA. Cardiac medication prescribing and adherence after acute myocardial infarction in Chinese and South Asian Canadian patients. *BMC Cardiovasc Disord* 2011; **11**: 56 [PMID: 21923931 DOI: 10.1186/1471-2261-11-56]

72 **Ajjan R**, Carter AM, Somani R, Kain K, Grant PJ. Ethnic differences in cardiovascular risk factors in healthy Caucasian and South Asian individuals with the metabolic syndrome. *J Thromb Haemost* 2007; **5**: 754-760 [PMID: 17408409 DOI: 10.1111/j.1538-7836.2007.02434.x]

73 **Misra A**, Khurana L. Obesity-related non-communicable diseases: South Asians vs White Caucasians. *Int J Obes (Lond)* 2011; **35**: 167-187 [PMID: 20644557 DOI: 10.1038/ijo.2010.135]

74 **Abate N**, Chandalia M, Snell PG, Grundy SM. Adipose tissue metabolites and insulin resistance in nondiabetic Asian Indian men. *J Clin Endocrinol Metab* 2004; **89**: 2750-2755 [PMID: 15181053 DOI: 10.1210/jc.2003-031843]

75 **Zhou YP**, Grill V. Long term exposure to fatty acids and ketones inhibits B-cell functions in human pancreatic islets of Langerhans. *J Clin Endocrinol Metab* 1995; **80**: 1584-1590 [PMID: 7745004 DOI: 10.1210/jcem.80.5.7745004]

76 **Agarwal A**, Prasad GV. Post-transplant dyslipidemia: Mechanisms, diagnosis and management. *World J Transplant* 2016; **6**: 125-134 [PMID: 27011910 DOI: 10.5500/wjt.v6.i1.125]

77 **Soveri I**, Holdaas H, Jardine A, Gimpelewicz C, Staffler B, Fellström B. Renal transplant dysfunction--importance quantified in comparison with traditional risk factors for cardiovascular disease and mortality. *Nephrol Dial Transplant* 2006; **21**: 2282-2289 [PMID: 16574686 DOI: 10.1093/ndt/gfl095]

78 **Barn K**, Laftavi M, Pierce D, Ying C, Boden WE, Pankewycz O. Low levels of high-density lipoprotein cholesterol: an independent risk factor for late adverse cardiovascular events in renal transplant recipients. *Transpl Int* 2010; **23**: 574-579 [PMID: 20003032 DOI: 10.1111/j.1432-2277.2009.01021.x]

79 **Holme I**, Fellstrom B, Jardine A, Holdaas H. Comparison of predictive ability of lipoprotein components to that of traditional risk factors of coronary events in renal transplant recipients. *Atherosclerosis* 2010; **208**: 234-239 [PMID: 19596331 DOI: 10.1016/j.atherosclerosis.2009.06.020]

80 **Ram CV**, Farmer JA. Metabolic syndrome in South Asians. *J Clin Hypertens (Greenwich)* 2012; **14**: 561-565 [PMID: 22863165 DOI: 10.1111/j.1751-7176.2012.00652.x]

81 **Seyahi N**, Cebi D, Altiparmak MR, Akman C, Ataman R, Pekmezci S, Serdengecti K. Progression of coronary artery calcification in renal transplant recipients. *Nephrol Dial Transplant* 2012; **27**: 2101-2107 [PMID: 21965591 DOI: 10.1093/ndt/gfr558]

82 **Patwardhan VG**, Mughal ZM, Padidela R, Chiplonkar SA, Khadilkar VV, Khadilkar AV. To study impact of treatment with Rosuvastatin versus Atorvastatin on 25 hydroxy Vitamin D concentrations among adult Indian men- a randomized control trial. *Indian J Pharmacol* 2020; **52**: 365-371 [PMID: 33283767 DOI: 10.4103/ijp.IJP\_93\_18]

83 **Gupta M**, Braga MF, Teoh H, Tsigoulis M, Verma S. Statin effects on LDL and HDL cholesterol in South Asian and white populations. *J Clin Pharmacol* 2009; **49**: 831-837 [PMID: 19398601 DOI: 10.1177/0091270009334376]

84 **Prasad GV**, Ahmed A, Nash MM, Zaltzman JS. Blood pressure reduction with HMG-CoA reductase inhibitors in renal transplant recipients. *Kidney Int* 2003; **63**: 360-364 [PMID: 12472804 DOI: 10.1046/j.1523-1755.2003.00742.x]

85 **Lee E**, Ryan S, Birmingham B, Zalikowski J, March R, Ambrose H, Moore R, Lee C, Chen Y, Schneck D. Rosuvastatin pharmacokinetics and pharmacogenetics in white and Asian subjects residing in the same environment. *Clin Pharmacol Ther* 2005; **78**: 330-341 [PMID: 16198652 DOI: 10.1016/j.clpt.2005.06.013]

86 **Lean ME**, Han TS, Bush H, Anderson AS, Bradby H, Williams R. Ethnic differences in anthropometric and lifestyle measures related to coronary heart disease risk between South Asian, Italian and general-population British women living in the west of Scotland. *Int J Obes Relat Metab Disord* 2001; **25**: 1800-1805 [PMID: 11781761 DOI: 10.1038/sj.ijo.0801823]

87 **Chandalia M**, Lin P, Seenivasan T, Livingston EH, Snell PG, Grundy SM, Abate N. Insulin resistance and body fat distribution in South Asian men compared to Caucasian men. *PLoS One* 2007; **2**: e812 [PMID: 17726542 DOI: 10.1371/journal.pone.0000812]

88 **Raji A**, Seely EW, Arky RA, Simonson DC. Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. *J Clin Endocrinol Metab* 2001; **86**: 5366-5371 [PMID: 11701707 DOI: 10.1210/jcem.86.11.7992]

89 **Peters J**, Ulijaszek SJ. Population and sex differences in arm circumference and skinfold thicknesses among Indo-Pakistani children living in the East Midlands of Britain. *Ann Hum Biol* 1992; **19**: 17-22 [PMID: 1734819 DOI: 10.1080/03014469200001882]

90 **Albracht-Schulte K**, Rosairo S, Ramalingam L, Wijetunge S, Ratnayake R, Kotakadeniya H, Dawson JA, Kalupahana NS, Moustaid-Moussa N. Obesity, adipocyte hypertrophy, fasting glucose, and resistin are potential contributors to nonalcoholic fatty liver disease in South Asian women. *Diabetes Metab Syndr Obes* 2019; **12**: 863-872 [PMID: 31354322 DOI: 10.2147/DMSO.S203937]

91 **Rush EC**, Freitas I, Plank LD. Body size, body composition and fat distribution: comparative analysis of European, Maori, Pacific Island and Asian Indian adults. *Br J Nutr* 2009; **102**: 632-641 [PMID: 19203416 DOI: 10.1017/S0007114508207221]

92 **Ladhani M**, Craig JC, Irving M, Clayton PA, Wong G. Obesity and the risk of cardiovascular and all-cause mortality in chronic kidney disease: a systematic review and meta-analysis. *Nephrol Dial Transplant* 2017; **32**: 439-449 [PMID: 27190330 DOI: 10.1093/ndt/gfw075]

93 **Owusu Adjah ES**, Bellary S, Hanif W, Patel K, Khunti K, Paul SK. Prevalence and incidence of complications at diagnosis of T2DM and during follow-up by BMI and ethnicity: a matched case-control analysis. *Cardiovasc Diabetol* 2018; **17**: 70 [PMID: 29764436 DOI: 10.1186/s12933-018-0712-1]

94 **Nöhre M**, Schieffer E, Hanke A, Pape L, Schiffer L, Schiffer M, de Zwaan M. Obesity After Kidney Transplantation-Results of a KTx360°Substudy. *Front Psychiatry* 2020; **11**: 399 [PMID: 32457669 DOI: 10.3389/fpsyt.2020.00399]

95 **Unwin N**, Bhopal R, Hayes L, White M, Patel S, Ragoobirsingh D, Alberti G. A comparison of the new international diabetes federation definition of metabolic syndrome to WHO and NCEP definitions in Chinese, European and South Asian origin adults. *Ethn Dis* 2007; **17**: 522-528 [PMID: 17985508]

96 **Ehtisham S**, Crabtree N, Clark P, Shaw N, Barrett T. Ethnic differences in insulin resistance and body composition in United Kingdom adolescents. *J Clin Endocrinol Metab* 2005; **90**: 3963-3969 [PMID: 15840754 DOI: 10.1210/jc.2004-2001]

97 **Yajnik CS**, Lubree HG, Rege SS, Naik SS, Deshpande JA, Deshpande SS, Joglekar CV, Yudkin JS. Adiposity and hyperinsulinemia in Indians are present at birth. *J Clin Endocrinol Metab* 2002; **87**: 5575-5580 [PMID: 12466355 DOI: 10.1210/jc.2002-020434]

98 **Banerjee D**, Chitalia N, Raja R, Bhandara T, Poulikakos D, Jha V. Metabolic syndrome in chronic kidney disease and renal transplant patients in North India. *Int Urol Nephrol* 2012; **44**: 937-943 [PMID: 21660424 DOI: 10.1007/s11255-011-9998-6]

99 **Palaniappan L**, Garg A, Enas E, Lewis H, Bari S, Gulati M, Flores C, Mathur A, Molina C, Narula J, Rahman S, Leng J, Gany F. South Asian Cardiovascular Disease & Cancer Risk: Genetics & Pathophysiology. *J Community Health* 2018; **43**: 1100-1114 [PMID: 29948525 DOI: 10.1007/s10900-018-0527-8]

100 **Mente A**, Razak F, Blankenberg S, Vuksan V, Davis AD, Miller R, Teo K, Gerstein H, Sharma AM, Yusuf S, Anand SS; Study of the Health Assessment And Risk Evaluation; Study of the Health Assessment And Risk Evaluation in Aboriginal Peoples Investigators. Ethnic variation in adiponectin and leptin levels and their association with adiposity and insulin resistance. *Diabetes Care* 2010; **33**: 1629-1634 [PMID: 20413520 DOI: 10.2337/dc09-1392]

101 **Prasad GV**, Vorobeichik L, Nash MM, Huang M, Rapi L, Maguire G, Mamdani M, Yan AT, Connelly PW. Lower total and percent of high-molecular-weight adiponectin concentration in South Asian kidney transplant recipients. *Clin Kidney J* 2012; **5**: 124-129 [PMID: 24744849 DOI: 10.1093/ckj/sfs033]

102 **Nagy K**, Nagaraju SP, Rhee CM, Mathe Z, Molnar MZ. Adipocytokines in renal transplant recipients. *Clin Kidney J* 2016; **9**: 359-373 [PMID: 27274819 DOI: 10.1093/ckj/sfv156]

103 **Winkelmayer WC**, Schaeffner ES, Chandraker A, Kramar R, Rumpold H, Sunder-Plassmann G, Födinger M. A J-shaped association between high-sensitivity C-reactive protein and mortality in kidney transplant recipients. *Transpl Int* 2007; **20**: 505-511 [PMID: 17362474 DOI: 10.1111/j.1432-2277.2007.00472.x]

104 **Bostom AG**, Carpenter MA, Kusek JW, Levey AS, Hunsicker L, Pfeffer MA, Selhub J, Jacques PF, Cole E, Gravens-Mueller L, House AA, Kew C, McKenney JL, Pacheco-Silva A, Pesavento T, Pirsch J, Smith S, Solomon S, Weir M. Homocysteine-lowering and cardiovascular disease outcomes in kidney transplant recipients: primary results from the Folic Acid for Vascular Outcome Reduction in Transplantation trial. *Circulation* 2011; **123**: 1763-1770 [PMID: 21482964 DOI: 10.1161/CIRCULATIONAHA.110.000588]

105 **Malyala R**, Rapi L, Nash MM, Prasad GVR. Serum Apolipoprotein B and A1 Concentrations Predict Late-Onset Posttransplant Diabetes Mellitus in Prevalent Adult Kidney Transplant Recipients. *Can J Kidney Health Dis* 2019; **6**: 2054358119850536 [PMID: 31205732 DOI: 10.1177/2054358119850536]

106 **Singh K**, Thanassoulis G, Dufresne L, Nguyen A, Gupta R, Narayan KV, Tandon N, Sniderman A, Prabhakaran D. A Comparison of Lipids and apoB in Asian Indians and Americans. *Glob Heart* 2021; **16**: 7 [PMID: 33598387 DOI: 10.5334/gh.882]

107 **Chambers JC**, McGregor A, Jean-Marie J, Kooner JS. Abnormalities of vascular endothelial function may contribute to increased coronary heart disease risk in UK Indian Asians. *Heart* 1999; **81**: 501-504 [PMID: 10212168 DOI: 10.1136/hrt.81.5.501]

108 **Juhan-Vague I**, Thompson SG, Jespersen J. Involvement of the hemostatic system in the insulin resistance syndrome. A study of 1500 patients with angina pectoris. The ECAT Angina Pectoris Study Group. *Arterioscler Thromb* 1993; **13**: 1865-1873 [PMID: 8241109 DOI: 10.1161/01.atv.13.12.1865]

109 **Kain K**, Catto AJ, Grant PJ. Impaired fibrinolysis and increased fibrinogen levels in South Asian subjects. *Atherosclerosis* 2001; **156**: 457-461 [PMID: 11395044 DOI: 10.1016/s0021-9150(00)00684-5]

110 **Kerschdorfer L**, König P, Neyer U, Bösmüller C, Lhotta K, Auinger M, Hohenegger M, Riegler P, Margreiter R, Utermann G, Dieplinger H, Kronenberg F. Lipoprotein(a) plasma concentrations after renal transplantation: a prospective evaluation after 4 years of follow-up. *Atherosclerosis* 1999; **144**: 381-391 [PMID: 10407499 DOI: 10.1016/s0021-9150(99)00014-3]

111 **Brown JH**, Murphy BG, Douglas AF, Short CD, Bhatnagar D, Mackness MI, Hunt LP, Doherty CC, Durrington PN. Influence of immunosuppressive therapy on lipoprotein(a) and other lipoproteins following renal transplantation. *Nephron* 1997; **75**: 277-282 [PMID: 9069448 DOI: 10.1159/000189549]

112 **Willeit P**, Ridker PM, Nestel PJ, Simes J, Tonkin AM, Pedersen TR, Schwartz GG, Olsson AG, Colhoun HM, Kronenberg F, Drechsler C, Wanner C, Mora S, Lesogor A, Tsimikas S. Baseline and on-statin treatment lipoprotein(a) levels for prediction of cardiovascular events: individual patient-data meta-analysis of statin outcome trials. *Lancet* 2018; **392**: 1311-1320 [PMID: 30293769 DOI: 10.1016/S0140-6736(18)31652-0]

113 **Eriksen A**, Tillin T, O'Connor L, Brage S, Hughes A, Mayet J, McKeigue P, Whincup P, Chaturvedi N, Forouhi NG. The impact of health behaviours on incident cardiovascular disease in Europeans and South Asians--a prospective analysis in the UK SABRE study. *PLoS One* 2015; **10**: e0117364 [PMID: 25730129 DOI: 10.1371/journal.pone.0117364]

114 **Anand S**, Bradshaw C, Prabhakaran D. Prevention and management of CVD in LMICs: why do ethnicity, culture, and context matter? *BMC Med* 2020; **18**: 7 [PMID: 31973762 DOI: 10.1186/s12916-019-1480-9]

115 **Powles J**, Fahimi S, Micha R, Khatibzadeh S, Shi P, Ezzati M, Engell RE, Lim SS, Danaei G, Mozaffarian D; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCoDE). Global, regional and national sodium intakes in 1990 and 2010: a systematic analysis of 24 h urinary sodium excretion and dietary surveys worldwide. *BMJ Open* 2013; **3**: e003733 [PMID: 24366578 DOI: 10.1136/bmjopen-2013-003733]

116 **Misra A**, Khurana L, Isharwal S, Bhardwaj S. South Asian diets and insulin resistance. *Br J Nutr* 2009; **101**: 465-473 [PMID: 18842159 DOI: 10.1017/S0007114508073649]

117 **Darling AL**. Vitamin D deficiency in western dwelling South Asian populations: an unrecognised epidemic. *Proc Nutr Soc* 2020; **79**: 259-271 [PMID: 32046797 DOI: 10.1017/S0029665120000063]

118 **Kang AW**, Garber CE, Eaton CB, Risica PM, Bostom AG. Physical Activity and Cardiovascular Risk among Kidney Transplant Patients. *Med Sci Sports Exerc* 2019; **51**: 1154-1161 [PMID: 30629045 DOI: 10.1249/MSS.0000000000001886]

119 **Senthil Kumar TG**, Soundararajan P, Maiya AG, Ravi A. Effects of graded exercise training on functional capacity, muscle strength, and fatigue after renal transplantation: a randomized controlled trial. *Saudi J Kidney Dis Transpl* 2020; **31**: 100-108 [PMID: 32129202 DOI: 10.4103/1319-2442.279929]

120 **Brown SA**, Tyrer FC, Clarke AL, Lloyd-Davies LH, Stein AG, Tarrant C, Burton JO, Smith AC. Symptom burden in patients with chronic kidney disease not requiring renal replacement therapy. *Clin Kidney J* 2017; **10**: 788-796 [PMID: 29225808 DOI: 10.1093/ckj/sfx057]

121 **Yates T**, Edwardson CL, Celis-Morales C, Biddle SJH, Bodicoat D, Davies MJ, Esliger D, Henson J, Kazi A, Khunti K, Sattar N, Sinclair AJ, Rowlands A, Velayudhan L, Zaccardi F, Gill JMR. Metabolic Effects of Breaking Prolonged Sitting With Standing or Light Walking in Older South Asians and White Europeans: A Randomized Acute Study. *J Gerontol A Biol Sci Med Sci* 2020; **75**: 139-146 [PMID: 30403772 DOI: 10.1093/gerona/gly252]

122 **Ghouri N**, Purves D, McConnachie A, Wilson J, Gill JM, Sattar N. Lower cardiorespiratory fitness contributes to increased insulin resistance and fasting glycaemia in middle-aged South Asian compared with European men living in the UK. *Diabetologia* 2013; **56**: 2238-2249 [PMID: 23811809 DOI: 10.1007/s00125-013-2969-y]

123 **Janaudis-Ferreira T**, Tansey CM, Mathur S, Blydt-Hansen T, Lamoureaux J, Räkel A, de Sousa Maia NP, Bussières A, Ahmed S, Boruff J. The effects of exercise training in adult solid organ transplant recipients: A systematic review and meta-analysis. *Transpl Int* 2021 [PMID: 33608971 DOI: 10.1111/tri.13848]

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**Table 1 Features of cardiovascular disease particular to South Asians when compared to other ethnic groups**

|  |  |  |
| --- | --- | --- |
| **Epidemiology** | **Clinical Features** | **Laboratory Features** |
| ↑ Prevalence, ↑ mortality | ↑ Type 2 diabetes | ↑ Serum triglycerides |
| ↓ Age at presentation, ↓ age at mortality | ↓ Hypertension awareness | ↓ Serum HDL cholesterol |
| ↑ Severity by angiography | ↑ Central obesity | ↑ Small-dense HDL cholesterol |
| ↑ Difficult revascularization | ↑ Intra-abdominal adiposity | ↑ Small-dense LDL cholesterol |
| ↑ Carbohydrate intake | ↑ Insulin resistance | ↓ Serum total and high molecular weight adiponectin |
| ↑ Saturated fat intake | ↓ Age at pancreatic β-cell dysfunction | ↑ Serum leptin |
| ↓ Physical activity | ↑ Fatty liver | ↑ Serum homocysteine |
|  | ↑ Metabolic syndrome | ↑ Vitamin D deficiency |
|  | ↓ Left ventricular mass index | ↓ Non-HDL-cholesterol/apolipoprotein B ratio |
|  | ↓ Skeletal muscle mass | ↓ Endothelial NO |
|  | ↓ Accurate estimate of glomerular filtration rate | ↑ Lipoprotein (a) |
|  |  | ↑ Fibrinogen |

HDL: High-density lipoprotein; LDL: Low-density lipoprotein; NO: Nitric oxide.

**Table 2 Possible interventions to manage cardiovascular risk in South Asian kidney transplant recipients**

|  |  |  |
| --- | --- | --- |
| **Pre-transplant** | **Post-transplant** | |
| No lower age limit for screening | Diabetes | Screen for post-transplant diabetes |
| Consider earlier cardiologist referral |  | Consider using any oral antihyperglycemic including newer agents |
| Use oral glucose tolerance test/HbA1c | Hypertension | Consider using any antihypertensive agent |
| Maximize cardioprotective medication |  | Consider vitamin D deficiency |
|  |  | Monitor for adherence |
|  | Dyslipidemia | Recognize that lipid profiles do not necessarily reflect increased cardiovascular risk |
|  |  | Monitor HDL cholesterol and triglycerides |
|  |  | Recognize potential for increased exposure from standard statin doses |
|  | Obesity and metabolic syndrome | Monitor waist-hip ratio |
|  |  | Target counseling about potential weight gain and abdominal girth increase even if body mass index is normal |
|  |  | Screen for presence of metabolic syndrome |
|  |  | Target interventions to individual components of metabolic syndrome |
|  | Health behavior | Decrease carbohydrate and saturated fat intake |
|  |  | Increase monounsaturated fat and fiber intake |
|  |  | Implement structured, graded exercise programs |

HbA1c: Glycosylated hemoglobin; HDL: High-density lipoprotein.