ur website www.jaypeebrothers.com, for detailed information on endocrinology books, visit our website www.jaypeebrothers.com

Diabetology

RSSDI

Yearbook of Diabetes 2020

Editor-in-Chief
Sujoy Ghosh

JAYPEE

Content

Section 1: Basic Science

Soumik Goswami, Sreenivasa Murthy L, Rakesh Kumar Sahay, Vijay Viswanathan

1. Liver Iron Concentration is an Independent Risk Factor for the Prediabetic State in β-thalassemia Patients 1
2. Nonalcoholic Fatty Liver Disease, Insulin Resistance, and Ceramides 2
3. Taking a Brown Adipose Tissue to the Chains of Diabetes 4
4. The *TCF7L2* Locus: A Genetic Window into the Pathogenesis of Type 1 and Type 2 Diabetes 5
5. Glycemic Index of Wheat and Rice are Similar when Consumed as Part of a North Indian Mixed Meal 7
6. *MACF1* Gene Variant rs2296172 is Associated with Type 2 Diabetes Susceptibility in Mizo Population from Northeast India 8
7. Copeptin, a Surrogate Marker for Arginine Vasopressin Secretion, is Positively Associated with Glucagon 10
8. PAX Proteins and Their Role in Pancreas 11
9. What has Zinc Transporter 8 Autoimmunity Taught us About Type 1 Diabetes? 13

Section 2: Epidemiology

Chitra Selvan, Jugal Kishor Sharma, Anand Moses, Vijay Kumar Panikar

1. Association of Maternal Lactation with Diabetes and Hypertension: A Systematic Review and Meta-analysis 15
2. Prevalence and Predictors of Osteopenia and Osteoporosis in Patients with Type 2 Diabetes Mellitus: A Cross-sectional Study From a Tertiary Care Institute in North India 16
3. Autoantibody Reversion: Changing Risk Categories in Multiple-autoantibody-positive Individuals 18
4. Incidence and Associations of Chronic Kidney Disease in Community Participants with Diabetes: A 5-year Prospective Analysis of the EXTEND45 Study 19
5. Establishment and Validation of a Risk Prediction Model for Early Diabetic Kidney Disease Based on a Systematic Review and Meta-analysis of 20 Cohorts 21

6. Every Fifth Individual with Type 1 Diabetes Suffers from an Additional Autoimmune Disease: A Finnish Nationwide Study 22
7. Absence of Islet Autoantibodies and Modestly Raised Glucose Values at Diabetes Diagnosis Should Lead to Testing for MODY: Lessons from a 5-year Pediatric Swedish National Cohort Study 24
8. Effect of Age at Menarche on Microvascular Complications Among Women with Type 1 Diabetes 26
9. Geographic Variation and Associated Covariates of Diabetes Prevalence in India 28
10. Sex Differences in the Burden of Type 2 Diabetes and Cardiovascular Risk Across the Life Course 30
11. Incidence of New-onset Diabetes and Post-transplant Metabolic Syndrome after Liver Transplantation - A Prospective Study from South India 31
12. Use of Antihyperglycemic Medications in U.S. Adults: An Analysis of the National Health and Nutrition Examination Survey 33
13. Why are South Asians Prone to Type 2 Diabetes? A Hypothesis Based on Underexplored Pathways 34
14. Prevalence and Clinical Characteristics of Individuals with Newly Detected Lean Diabetes in Tamil Nadu, South India: A Community-based Cross-sectional Study 36
15. Prevalence of Diabetes Mellitus in 2019 Novel Coronavirus: A Meta-analysis 37
16. Vitamin D Supplementation and Prevention of Type 2 Diabetes 38
17. Prognostic Significance of Long-term HbA1c Variability for All-cause Mortality in the ACCORD Trial 40
18. Evaluating the Performance of the Indian Diabetes Risk Score in Different Ethnic Groups 42

Section 3: Comorbidities

Amritava Ghosh, Shalini Jaggi, Mithun Bhartia, Bikash Bhattacharjee

1. Usefulness of Routine Fractional Flow Reserve for Clinical Management of Coronary Artery Disease in Patients with Diabetes 44
2. The Long-term Effects of Metformin on Patients with Type 2 Diabetic Kidney Disease 46
3. Impact of Treating Oral Disease on Preventing Vascular Diseases: A Model-based Cost-effectiveness Analysis of Periodontal Treatment Among Patients with Type 2 Diabetes 48
4. Risk of Rapid Kidney Function Decline, All-cause Mortality, and Major Cardiovascular Events in Nonalbuminuric Chronic Kidney Disease in Type 2 Diabetes 49
5. Performance of Plasma Biomarkers and Diagnostic Panels for Nonalcoholic Steatohepatitis and Advanced Fibrosis in Patients with Type 2 Diabetes 51
6. Time in Range is Associated with Carotid Intima-media Thickness in Type 2 Diabetes 53

Section 4: Complications

Indira Maisnam, Amit Gupta, Neeta Deshpande, Brij Mohan Makkar

1. Reduced Pancreatic Polypeptide Response is Associated with Early Alteration of Glycemic Control in Chronic Pancreatitis 56
2. Young-onset Type 2 Diabetes and Younger Current Age: Increased Susceptibility to Retinopathy in Contrast to other Complications 58
3. Dipeptidyl Peptidase 4 Inhibitors and the Risk of Bullous Pemphigoid among Patients with Type 2 Diabetes 60
4. Seroprevalence and Risk Factors Associated with HBV and HCV Infection among Subjects with Type 2 Diabetes from South India 62
5. Prevalence and Patterns of Cardiac Autonomic Dysfunction in Male Patients with Type 2 Diabetes Mellitus and Chronic Charcot's Neuroarthropathy: A Cross-sectional Study from South India 64
6. Longitudinal Associations between Depression and Diabetes Complications: A Systematic Review and Meta-analysis 66
7. Bone Histomorphometry in Young Patients with Type 2 Diabetes is Affected by Disease Control and Chronic Complications 68
8. Teriparatide [Recombinant Human Parathyroid Hormone (1-34)] Increases Foot Bone Remodeling in Diabetic Chronic Charcot Neuroarthropathy: A Randomized Double-blind Placebo-controled Study 70

Section 5: Type 1 Diabetes Mellitus

Ajitesh Roy, Archana Sarda, Banshi Saboo, Ch Vasanth Kumar

1. Immune Checkpoint Inhibitor-induced Type 1 Diabetes: A Systematic Review and Meta-analysis 75
2. Serum Urate Lowering with Allopurinol and Kidney Function in Type 1 Diabetes 77
3. Profile of Auto-antibodies (Disease Related and Other) in Children with Type 1 Diabetes 80
4. Biomarker Panels Associated with Progression of Renal Disease in Type 1 Diabetes 82
5. Effect of Continuous Glucose Monitoring on Glycemic Control in Adolescents and Young Adults with Type 1 Diabetes: A Randomized Clinical Trial 84
6. Continuous Glucose Monitoring in People with Type 1 Diabetes on Multiple-dose Injection Therapy: The Relationship between Glycemic Control and Hypoglycemia 86
7. The Efficacy of Technology in Type 1 DM: A Systemic Review, Network Meta-analysis, and Narrative Synthesis 88
8. Use of Sensor-integrated Pump Therapy to Reduce Hypoglycemia in People with Type 1 Diabetes: A Real-world Study in the UK 90

Section 6: Gestational Diabetes Mellitus

Rana Bhattacharjee, Purvi Chawla, Sunil Surajprasad Gupta, Rajeev Chawla

1. Prevention of Gestational Diabetes Mellitus in Overweight or Obese Pregnant Women: A Network Meta-analysis 95
2. Maternal Age and the Risk of Gestational Diabetes Mellitus: A Systematic Review and Meta-analysis of Over 120 Million Participants 96
3. Gestational Diabetes Mellitus in HIV-infected Pregnant Women: A Systematic Review and Meta-analysis 98
4. Continuous Glucose Monitoring in Pregnancy: Importance of Analyzing Temporal Profiles to Understand Clinical Outcomes 99
5. Urinary and Serum Angiogenic Markers in Women with Pre-existing Diabetes During Pregnancy and their Role in Pre-eclampsia Prediction 101

Section 7: Drugs and Therapeutics

Sayantan Ray, Pratap Jethwani, Anuj Maheshwari, Sudhir Bhandari

1. Effect of Dapagliflozin on Worsening Heart Failure and Cardiovascular Death in Patients with Heart Failure with and without Diabetes 105
2. Glycemic Efficacy and Safety of Glucagon-like Peptide-1 Receptor Agonist on Top of Sodium-glucose Cotransporter-2 Inhibitor Treatment Compared to Sodium-glucose Cotransporter-2 Inhibitor Alone: A Systematic Review and Meta-analysis of Randomized Controlled Trials 107
3. Once-weekly Insulin for Type 2 Diabetes without Previous Insulin Treatment 109
4. Efficacy and Safety of the Glucagon Receptor Antagonist RVT-1502 in Type 2 Diabetes Uncontrolled on Metformin Monotherapy: A 12-Week Dose-ranging Study 111
5. Optimization of Metformin in the GRADE Cohort: Effect on Glycemia and Body Weight 113
6. Combined GLP-1, Oxyntomodulin, and Peptide YY Improves Body Weight and Glycemia in Obesity and Prediabetes/Type 2 Diabetes: A Randomized, Single-blinded, Placebo-controlled Study 114
7. Hypoglycemia is Reduced with Use of Inhaled Technosphere® Insulin Relative to Insulin Aspart in Type 1 Diabetes Mellitus 116
8. Systematic Review and Meta-analysis of Clinical Trials Examining the Effect of Hyperbaric Oxygen Therapy in People with Diabetes-related Lower Limb Ulcers 118
9. Oral Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes 119
10. Effects of Probiotic Supplementation during Pregnancy on Metabolic Outcomes: A Systematic Review and Meta-analysis of Randomized Controlled Trials 121
11. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction 122
12. Associations between Metformin Use and Vitamin B12 Levels, Anemia, and Neuropathy in Patients with Diabetes: A Meta-analysis 124
13. Risk of Severe Hypoglycemia and its Impact in Type 2 Diabetes in DEVOTE 126

14. Switching to Degludec is Associated with Reduced Hypoglycemia, Irrespective of Definition Used or Patient Characteristics: Secondary Analysis of the ReFLeCT Prospective, Observational Study 127
15. A Survey of Physician Experience and Treatment Satisfaction using Fast-acting Insulin aspart in People with Type 1 or Type 2 Diabetes 128
16. A Randomized Trial Evaluating the Efficacy and Safety of Fast-acting Insulin Aspart Compared with Insulin Aspart, Both in Combination with Insulin Degludec with or without Metformin, in Adults with Type 2 Diabetes (Onset 9) 130
17. Oral Semaglutide versus Empagliflozin in Patients with Type 2 Diabetes Uncontrolled on Metformin: The PIONEER 2 Trial 131
18. Efficacy, Safety, and Tolerability of Oral Semaglutide versus Placebo Added to Insulin with or without Metformin in Patients with Type 2 Diabetes: The PIONEER 8 Trial 133
19. Effectiveness and Safety of Insulin Glargine 300 U/mL in Insulin-naïve Patients with Type 2 Diabetes after Failure of Oral Therapy in a Real-world Setting 135
20. An Assessment of Physician Reasons for Prescribing Insulin Lispro 200 units/mL in Germany 136
21. Cardiovascular and Kidney Outcomes of Linagliptin Treatment in Older People with Type 2 Diabetes and Established Cardiovascular Disease and/or Kidney Disease: A Prespecified Subgroup Analysis of the Randomized, Placebo-controlled CARMELINA® trial 138
22. Linagliptin and Cardiorenal Outcomes in Asians with Type 2 Diabetes Mellitus and Established Cardiovascular and/or Kidney Disease: Subgroup Analysis of the Randomized CARMELINA® Trial 139
23. Efficacy and Safety of Remogliflozin Etabonate, a New Sodium-glucose Cotransporter-2 Inhibitor, in Patients with Type 2 Diabetes Mellitus: A 24-Week, Randomized, Double-blind, Active-controlled Trial 141
24. An Open-label, Single-period, Two-stage, Single Oral Dose Pharmacokinetic Study of Remogliflozin Etabonate Tablet 100 and 250 mg in Healthy Asian Indian Male Subjects Under Fasting and Fed Conditions 143
25. Efficacy of Empagliflozin on Heart Failure and Renal Outcomes in Patients with Atrial Fibrillation: Data from the EMPA-REG OUTCOME Trial 144
26. Effect of Empagliflozin on Left Ventricular Mass in Patients with Type 2 Diabetes Mellitus and Coronary Artery Disease: The EMPA-HEART CardioLink-6 Randomized Clinical Trial 146
27. Suboptimal Glycemic Control among Subjects with Diabetes Mellitus in India: A Subset Analysis of Cross-sectional Wave-7 (2016) Data from the International Diabetes Management Practices Study (IDMPS) 148
28. A Practitioner's Toolkit for Insulin Motivation in Adults with Type 1 and Type 2 Diabetes Mellitus: Evidence-based Recommendations from an International Expert Panel 149
29. Impact of Baseline Characteristics and Beta-cell Function on the Efficacy and Safety of Subcutaneous Once-weekly Semaglutide: A Patient-level, Pooled Analysis of the SUSTAIN 1-5 Trials 151
30. Efficacy and Safety of Once-weekly Semaglutide versus Daily Canagliflozin as Add-on to Metformin in Patients with Type 2 Diabetes (SUSTAIN 8): A Double-blind, Phase 3b, Randomized Controlled Trial 153

Section 8: Newer Technologies and Future Directions

Partha P Chakraborty, Sanjay Reddy, Jothydev Kesavade, Sanjay Agarwal

1. Effects of Continuous Glucose Monitoring on Metrics of Glycemic Control in Diabetes: A Systematic Review with Meta-analysis of Randomized Controlled Trials 160
2. Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations from the International Consensus on Time in Range 162
3. Diabetes Digital App Technology: Benefits, Challenges, and Recommendations. A Consensus Report by the European Association for the Study of Diabetes (EASD) and the American Diabetes Association (ADA) Diabetes Technology Working Group 163
4. Systematic Review of Randomized Controlled Trials Evaluating Glycemic Efficacy and Patient Satisfaction of Intermittent-scanned Continuous Glucose Monitoring in Patients with Diabetes 165
5. Serum Tenascin-C is Independently Associated with Increased Major Adverse Cardiovascular Events and Death in Individuals with Type 2 Diabetes: A French Prospective Cohort 167
6. Diabetes Screening: Detection and Application of Saliva 1,5-Anhydroglucitol by Liquid Chromatography-mass Spectrometry 168
7. Circulating Retinol-binding Protein 4 is Inversely Associated with Pancreatic β-cell Function Across the Spectrum of Glycemia 170
8. Positioning Time in Range in Diabetes Management 171
9. Neprilysin Inhibition: A New Therapeutic Option for Type 2 Diabetes? 173
10. Early Pregnancy Prediction of Gestational Diabetes Mellitus Risk using Prenatal Screening Biomarkers in Nulliparous Women 174
11. Six-month Randomized, Multicenter Trial of Closed-loop Control in Type 1 Diabetes 176

Index **179**

Section 2: Epidemiology

Chitra Selvan, Jugal Kishor Sharma, Anand Moses, Vijay Kumar Panikar

1. Association of Maternal Lactation with Diabetes and Hypertension: A Systematic Review and Meta-analysis

Ref: Rameez RM, Sadana D, Kaur S, Ahmed T, Patel J, Khan MS, et al. Association of maternal lactation with diabetes and hypertension: A systematic review and meta-analysis. JAMA Netw Open. 2019;2(10):1913401.

ABSTRACT

Importance: In available literature, lactation has been reported to be associated with lower rates of maternal diabetes and hypertension. But these studies have been conducted in relatively small sample size and have shown varied range of strength of association.

Objective: To determine association of lactation with lower risk of diabetes and hypertension among mothers through a systematic review and meta-analysis.

Methodology: Manual search of the references in Ovid MEDLINE, Ovid Embase, Cochrane CENTRAL, and CINAHL databases from inception to July 2018. Studies conducted in adult women specifying at least 12 months of breastfeeding and assessing primary hypertension and diabetes in them were included in the review. The full-text articles in English reporting statistical outcomes as odds ratios were included. A standard spreadsheet template was used to extract the study characteristics independently and the data were pooled using the random-effects model. This review followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guideline for reporting. The main outcomes included diabetes and hypertension.

Results: Out of 1,558 searched studies, six studies met inclusion criteria of association between lactation and diabetes and/or hypertension. The meta-analysis to explore the association between lactation and diabetes included four studies having a total of 206,204 participants. On the other hand, the meta-analysis to explore the association between lactation and hypertension included five studies having a total of 255,271 participants. This meta-analysis showed a relative risk reduction of 30% for diabetes in women reporting 12 months of lactation {pooled odds ratio, 0.70 [95% confidence interval (CI) 0.62–0.78]; $p < 0.001$} and a relative risk reduction of 13% for hypertension [pooled odds ratio, 0.87 (95% CI 0.78–0.97); $p = 0.01$].

Conclusion and relevance: This study demonstrated the benefits of breastfeeding in preventing maternal diabetes and hypertension that can be easily included in daily practice. The lactation may also have a positive impact on cardiovascular outcomes in mothers.

COMMENT

Cardiovascular disease is the most common cause of mortality in women. Diabetes and hypertension are the two important preventable risk factors of cardiovascular disease.

Women also have unique cardiovascular and metabolic stresses in the setting of pregnancy and the puerperium. Lactation has been known to decrease the risk of diabetes and hypertension, but the papers which have studied this association have all been relatively small with disparity in outcomes reported. This meta-analysis and systematic review

JAYPEE BROTHERS

has tried to study the relationship between maternal lactation and risk for diabetes and hypertension.

The four studies included in the meta-analysis for the association between lactation and diabetes had a total of 206,204 participants, and the five studies included in the meta-analysis for the association between lactation and hypertension had a total of 255,271 participants. Thus, one of the biggest advantages of the paper is the large number of participants studied.

Two independent investigators extracted information and were blinded. They included studies that looked at women who breastfed for at least 12 months and reported diabetes and hypertension as outcome.

Breastfeeding for more than 12 months was associated with a relative risk reduction of 30% for diabetes {pooled odds ratio, 0.70 [95% confidence interval (CI) 0.62–0.78]; $p < 0.001$} and a relative risk reduction of 13% for hypertension [pooled odds ratio, 0.87 (95% CI 0.78–0.97); $p = 0.01$].

Interestingly, one of the papers included did also note that exclusive breastfeeding was associated with a lower risk than nonexclusive breastfeeding.

Strength of the paper is the large sample size; they included papers that have looked at breastfeeding for at least 12 months and excluded studies which included gestational diabetes and preeclampsia/eclampsia.

Limitation of the meta-analysis is that none of the four studies which were included in the systematic review was randomized controlled trial. Second limitation of the paper is the fact that the history of lactation and breastfeeding duration were from self-reported questionnaires and interviews. The intervening years could have potentially brought in a recall bias. None of the studies included in the analyses reported blinding. The duration of follow-up was variable in the included studies. The authors included only those papers which reported the results of the association between lactation and diabetes and hypertension as odds ratio and excluded those papers which reported results in relative risk or hazard ratio but they went on to do a subanalysis of these papers whose findings corroborated with the papers included in the main analysis.

Breastfeeding for longer than 12 months was associated with a 30% lower risk of diabetes and a 13% lower risk of hypertension in mothers after adjusting for confounding variables. The prenatal and antenatal period is an important opportunity to educate women about lifestyle interventions that may protect their health in the future. Given the low-risk nature of this intervention, educating mothers about the potential benefits of breastfeeding for their cardiovascular health can be easily introduced into clinical practice when addressing prevention of cardiovascular outcomes in women.

Future research could be focused on a randomized controlled trial which provides a uniform protocol of lifestyle changes including exercise, eating, and weight management and after matching for factors such as family history, age, and body mass index (BMI), the risk reduction of lactation on diabetes and hypertension can be studied for longer period of follow-up and even beyond menopause.

2. Prevalence and Predictors of Osteopenia and Osteoporosis in Patients with Type 2 Diabetes Mellitus: A Cross-sectional Study From a Tertiary Care Institute in North India

Ref: Aleti S, Pal R, Dutta P, Dhibar DP, Prakash M, Khandelwal N, Dhiman V, et al. Prevalence and predictors of osteopenia and osteoporosis in patients with type 2 diabetes mellitus: a cross-sectional study from a tertiary care institute in North India. Int J Diabet Dev Ctries. 2020;40:262-8.

JAYPEE BROTHERS

ABSTRACT

Background: Patients with type 2 diabetes mellitus (T2DM) have an increased risk of hip and vertebral fractures. The increased fracture risk has largely been attributed to poor bone quality and microarchitecture. The contribution of bone quantity, measured as areal bone mineral density (BMD), to the risk of fracture, is variable with most studies showing an increase in BMD in T2DM. The present study was undertaken to find out the prevalence of osteoporosis and osteopenia (based on BMD) in a cohort of patients with T2DM and delineate the possible modifiable and nonmodifiable risk factors.

Methods: In this cross-sectional observational study, 252 otherwise ostensibly healthy patients with T2DM underwent dual-energy X-ray absorptiometry (DEXA) scan. Osteoporosis and osteopenia were defined based on T-scores. The effects of modifiable and nonmodifiable risk factors on BMD and osteoporosis were assessed.

Results: The mean age of the cohort was 59.9 years with a male:female (M:F) ratio 2.9:3.4. The mean BMD at the lumbar spine and hip was 0.892 g/cm^2 and 0.715 g/cm^2, respectively. Males had significantly higher BMD at both the sites compared to females. The prevalence of osteoporosis and osteopenia was 33% and 40%, respectively. Female gender, increasing age, normal body mass index (BMI), low serum 25-hydroxyvitamin D, and use of pioglitazone were significantly associated with the risk of osteoporosis.

Conclusion: The prevalence of osteoporosis and osteopenia in patients with T2DM is high. Female gender, increasing age, normal BMI, low serum 25-hydroxyvitamin D, and pioglitazone use further increase the risk of osteoporosis.

COMMENT

Type 2 diabetes mellitus (T2DM), apart from contributing to micro- and macrovascular disease, also exerts a detrimental effect on bone health with moderately increased risk of hip and vertebral fractures. Hip and vertebral fractures not only contribute to significant morbidity but also independently predict mortality. The increased risk of fractures in T2DM is multifactorial with changes both in bone quality and microarchitecture. Bone quantity as measured by bone mineral density (BMD) in individuals with T2DM has been controversial with some studies showing increased BMD while others showing reduced BMD. The present study attempted to find out the prevalence of osteoporosis and osteopenia based on BMD in individuals with T2DM and to identify possible modifiable and nonmodifiable risk factors.

Individuals aged 50 years and above with T2DM for more than 5 years were included. Interestingly, individuals who are on calcium and vitamin D supplements were excluded. Hologic 6 machine was used to do the dual-energy X-ray absorptiometry (DEXA) scan to assess BMD and the World Health Organization (WHO) definition was used to diagnose osteoporosis and osteopenia.

Body mass index (BMI) had a positive correlation with both lumbar spine and hip BMD. Similarly, 25-hydroxy vitamin D had a positive correlation with lumbar and hip BMD. Normal BMI (18.5–22.9 kg/m^2) was associated with an odds ratio of 3.9 for having osteoporosis compared to obese subjects. Pioglitazone was significantly associated with osteoporosis with an odds ratio of 10.6 into confidence interval of 3.8–29.3 with *p* value being significant.

Diabetes duration, presence of nephropathy, or degree of glycemic control over the past 1 year did not have any significant effect on BMD or prevalence of osteoporosis. Female gender and increasing age were associated with risk of having osteoporosis.

The limitations of the study are the absence of an age and BMI-matched control group. It is also a cross-sectional study with no follow-up data on fracture incidence. Men and women both included in the study, which could have affected results. Lastly, attempts to study

JAYPEE BROTHERS

bone quality along with BMD with the use of trabecular bone score would have added value to the study, considering in T2DM, bone quality is affected more than mineral density.

In summary, the study demonstrates the high prevalence of osteoporosis and osteopenia (33% and 40 %) in patients with T2DM in India and reinforces the fact that BMD is actually decreased and not increased. Bone health must be added in all attempts made to provide comprehensive care for patients with T2DM.

3. Autoantibody Reversion: Changing Risk Categories in Multiple-autoantibody-positive Individuals

Ref: So M, O'Rourke C, Bahnson HT, Greenbaum CJ, Speake C. Autoantibody reversion: changing risk categories in multiple-antibody-positive individuals. Diabetes Care. 2020;43(4):913-17.

ABSTRACT

Objective: The majority of individuals with two or more islet autoantibodies progress to clinical type 1 diabetes mellitus (T1DM). Nevertheless, in certain individuals, autoantibodies are lost later on. Here, we aimed to determine the occurrence of autoantibody loss (reversion) in multiple-autoantibody-positive subjects and to determine the relationship between reversion and progression to clinical disease.

Research design and methods: Multiple-autoantibody-positive individuals participating in TrialNet Pathway to Prevention Study were analyzed for reversion and the effect of reversion on progression to clinical disease was determined using a Cox regression analysis.

Results: Out of 3,284 multiple-autoantibody-positive individuals, reversion occurred in 134 (4.1%) and was linked with decreased incidence of clinical T1DM. Reversion occurred more commonly with older age, lesser autoantibody titers, and fewer positive autoantibodies.

Conclusion: Even though reversion of multiple-autoantibody positivity is rare, when it happens, the risk of progression to clinical disease is decreased. This observation suggests unidentified mechanisms triggering immune remission in some individuals.

COMMENT

Islet autoantibodies are tested as a measure to distinguish type 1 diabetes mellitus (T1DM) from other forms of diabetes and to predict disease progression. Large scale prospective studies of relatives of individuals with T1DM revealed that nearly all individuals with two or more autoantibodies progressed to clinical diabetes. Some individuals noticed autoantibody titer levels dropping below threshold for positivity. The implication of this loss of multiple autoantibodies (reversion) on disease development is not known so this study was designed to evaluate the same.

Through TrialNet Pathway to Prevention Study, two lakh and more relatives of subjects with T1DM were screened for autoantibodies between 2004 and 2018. Multiple-autoantibody positivity was defined as two or more islet autoantibodies confirmed on two occasions within 12 months; the antibodies included are islet cell antibody (ICA) insulin antibody (IAA) GAD antibody (GAD) or zinc transporter.

Reverters were defined as an individual who demonstrated a loss of multiple-autoantibody positivity to one or zero autoantibodies on two consecutive encounters within 12 months.

JAYPEE BROTHERS

Reverters were more likely to be older at the time of confirmed multiple-autoantibody positivity (19.4 vs. 13.1 years) with longer follow-up (5.2 vs. 2.1 years) and also had a lower number of autoantibodies (2.1 vs. 3.1). On the basis of univariate Cox model, each additional positive autoantibody decreases the risk of reversion by a factor of five. They also had a lower titer of autoantibodies as compared to maintainers.

Among reverters, ICAs were most likely to be lost, with 85 of the 87 (98%) who started with a positive ICA losing positivity. In contrast, reverters were unlikely to lose glutamic acid decarboxylase antibodies (GADAs), with only 19/129 (15%) reverters who had GADAs losing GADA positivity.

Estimated cumulative 5-year risk of T1DM was 42% for maintainers and 11% for the reporters with a confidence interval of 6–18%.

During follow-up, 41 of 134 (31%) reverters regained multiple-autoantibody status. There was no significant difference in diabetes incidence ($p = 0.99$) between the reverters who regained their multiple-autoantibody status (7/41, 17%) and those who did not (16/93, 17%). Nor was there a significant difference in distribution of autoantibody titers.

Strength of the study is to understand that there could be reversion of autoantibodies and this point might be relevant while recruiting individuals, especially for prevention trials.

Hide a group of individuals in home reversional multiple-autoantibodies and disease progression can be studied to find a mechanistic link of the pathophysiology of T1DM.

The limitation of the study is that it only looked at multiple-autoantibodies as against single autoantibodies or no antibodies.

4. Incidence and Associations of Chronic Kidney Disease in Community Participants with Diabetes: A 5-Year Prospective Analysis of the EXTEND45 Study

Ref: Sukkar L, Kang A, Hockham C, Young T, Jun M, Foote C, et al. Incidence and associations of chronic kidney disease in community participants with diabetes: a 5-year prospective analysis of the EXTEND45 study. Diabetes Care. 2020;43(5):982-90.

ABSTRACT

Objective: We intended to determine the incidence of and factors related with an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 in people with diabetes.

Research design and methods: We identified diabetic individuals in the EXTEND45 (EXamining ouTcomEs in chroNic Disease in the 45 and Up Study), a population-based cohort study (2006–2014) that connected the Sax Institute's 45 and Up Study cohort to community laboratory and administrative data in New South Wales, Australia. The outcome of the study was the first eGFR measurement <60 mL/min/1.73 m^2 documented during the follow-up period. Participants with eGFR <60 mL/min/1.73 m^2 at baseline were excluded. Poisson regression was used to calculate the incidence of eGFR <60 mL/min/1.73 m^2 and multivariable Cox regression was performed to examine factors associated with the outcome of the study.

Results: Out of 9,313 participants with diabetes, 2,106 (22.6%) developed incident eGFR <60 mL/min/1.73 m^2 over a median follow-up time of 5.7 years (interquartile range, 3.0–5.9 years). The incidence rate of eGFR <60 mL/min/1.73 m^2 per 100 person-years was 6.0 [95% confidence interval (CI) 5.7–6.3] overall, 1.5 (1.3–1.9) in individuals aged 45–54 years, 3.7 (3.4–4.0) for 55–64 year olds, 7.6 (7.1–8.1) for 65–74 year olds, 15.0 (13.0–16.0) for 75–84 year olds, and 26.0 (22.0–32.0) for those aged 85 years and above. A fully adjusted multivariable model showed an independent association of the incidence with

JAYPEE BROTHERS

age (hazard ratio 1.23 per 5-year increase; 95% CI 1.19–1.26), geography (outer regional and remote vs. major city: 1.36; 1.17–1.58), obesity (obese class III vs. normal: 1.44; 1.16–1.80), and the existence of hypertension (1.52; 1.33–1.73), coronary heart disease (1.13; 1.02–1.24), cancer (1.30; 1.14–1.50), and depression/anxiety (1.14; 1.01–1.27).

Conclusion: The incidence of an eGFR <60 mL/min/1.73 m^2 was high in people with diabetes. Older age, remoteness of residence, and the presence of various comorbidities were associated with greater incidence.

COMMENT

The leading cause of chronic kidney disease (CKD) worldwide is the presence of diabetes and CKD leads to increased risk of cardiovascular death and disease. Identifying individuals with diabetes who are at increased risk of developing CKD is a key step to develop preventive strategies for improving health outcomes in this high-risk population.

EXTEND45 (EXamining ouTcomEs in chroNic Disease in the 45 and Up Study) is a large population-based cohort built on Sax Institute's 45 and Up Study, a prospective cohort of residents aged 45 years or older in the state of New South Wales, Australia.

Follow-up data was collected from health and administrative databases. CKD-Epidemiology Collaboration (CKD-EPI) equation was used to calculate estimated glomerular filtration rate (eGFR). Among the 9,313 participants with diabetes, hypertension was present in 73.4% in hypercholesterolemia and 65.8%.

In this Australian population-based cohort of participants with diabetes aged 45 years and over, the age-adjusted incidence rates of eGFR <60 mL/min/1.73m^2 were six new cases per 100 person-years between 2006 and 2014, which is much higher than previously reported incidence rates. This high incidence could be explained by the fact that the cohort was 5–10 years older than other cohorts and also that this is real world clinical data from multiple sources.

Advancing age was found to be the strongest association of CKD in diabetes, followed by obesity and the presence of hypertension.

The social economic marker such as living remotely was an independent risk factor for greater incident CKD probably attributable to poorer access to health care. The study found no sex difference in the risk of CKD in those with diabetes.

History of cancer at baseline as well as baseline depression and anxiety predicted incident disease and these are interesting findings which have been observed before.

The strength of the study is the large number of the population in the real world set-up followed up for up to 5.7 years.

The first limitation of the study is the fact that the inclusion criteria only measured one creatinine in the 3 years prior to recruitment, the second important limitation is the fact that only eGFR was used to classify CKD and not albuminuria. The third limitation is the age of inclusion of individuals in this was only 45 years and higher. The type of diabetes was not specified. Yet the study is relevant in identifying factors which could potentially identify individuals with a higher risk of progression of eGFR decline and design interventions to mitigate the same.

JAYPEE BROTHERS

5. Establishment and Validation of a Risk Prediction Model for Early Diabetic Kidney Disease Based on a Systematic Review and Meta-analysis of 20 Cohorts

Ref: Jiang W, Wang J, Shen X, Lu W, Wang Y, Li W, et al. Establishment and validation of a risk prediction model for early diabetic kidney disease based on a systematic review and meta-analysis of 20 Cohorts. Diabetes Care. 2020;43(4):925-33.

ABSTRACT

Background: Clinical outcome of diabetic kidney disease (DKD) can be improved by identifying patients at high risk.

Purpose: To establish a model for predicting DKD.

Data sources: The derivation cohort was from a meta-analysis. The validation cohort was from a Chinese cohort.

Study selection: We selected cohort studies that reported risk factors of DKD with their corresponding risk ratios (RRs) in patients with type 2 diabetes mellitus (T2DM). Their estimated baseline glomerular filtration rate (eGFR) was ≥60 mL/min/1.73 m^2 and urinary albumin-to-creatinine ratio (UACR) was <30 mg/g.

Data extraction: Only statistically significant risk factors were included in our DKD risk prediction model.

Data synthesis: Twenty cohorts including 41,271 patients with (T2DM) were included in our meta-analysis. Statistically significant risk factors were age, body mass index (BMI), smoking, diabetic retinopathy, hemoglobin A1c (HbA1c), systolic blood pressure (SBP), high-density lipoprotein (HDL) cholesterol, triglycerides (TGs), UACR, and eGFR. All, except eGFR, were included in the study because of the significant heterogeneity seen in eGFR among various studies. Risk factors were scored according to their weightage, with 37.0 being the highest score. Model validation was done in an external cohort with a median follow-up of 2.9 years. A cutoff value of 16 was selected with a sensitivity of 0.847 and a specificity of 0.677.

Limitations: A huge heterogeneity among studies involving eGFR was observed. So, more studies are needed to establish it as a risk factor of DKD.

Conclusion: High-risk patients of DKD can be easily predicted using this simple tool of DKD risk prediction model consisting of nine risk factors.

COMMENT

Diabetic kidney disease (DKD) is a major microvascular complication of diabetes with high prevalence, mortality, and treatment cost. Yet, there is low awareness and poor effective prevention and treatment strategy. Since most early predictive markers of DKD are difficult to promote in clinical practice due to high cost and/or stability, we have to rely on a comprehensive assessment of other risk factors which could potentially provide a window for intervention in high-risk individuals for preventing DKD.

The derivation cohort came from a systematic review and meta-analysis of 14 prospective cohorts and 6 retrospective cohorts. These 20 cohorts were identified by searching electronic databases. In total, 41,271 patients with type 2 diabetes mellitus (T2DM) from Europe, Asia, and America with an estimated glomerular filtration rate (eGFR) of

JAYPEE BROTHERS

>60 mL/min/1.73 m^2 and urine albumin-to-creatinine ratio (UACR) <30 mg/g in baseline were included.

The validation cohort came from Tianjin Medical University Metabolic Disease Hospital and included 380 patients with T2DM who are followed up for at least 12 months.

The outcomes included were the occurrence of an eGFR <60 mL/min/1.73 m^2 or UACR ratio >30 mg/g for more than 3 months caused by diabetes.

The estimated incidence of DKD was approximately 29.1% in a derivation cohort and 25.8% in the validation cohort.

Of the 19 risk factors identified in the systematic review and meta-analysis, 10 risk factors were associated with the onset of DKD. These factors, followed by the respective pooled risk ratios (RRs), were age (1.09), body mass index (BMI) (1.07), diabetic retinopathy (DR) (1.72), smoking (1.49), HbA1c (1.17), systolic blood pressure (SBP) (1.03), high-density lipoprotein cholesterol (HDL-C) (0.75), triglycerides (TGs) (1.15), UACR (1.25), and eGFR (2.20). These factors are essentially consistent with the risk factors traditionally associated with DKD, further verifying that age and harmful lifestyle, together with poor glycemia, blood pressure, and plasma lipid control, initiate DKD. Except for age, most of these risk factors are modifiable, which is particularly important for DKD prevention.

Age, smoking, and TG were the most powerful baseline risk factors for detecting DKD in this systematic review and meta-analysis. With age incremented by 5–10 years, the risk for DKD was increased by 38%. The risk for DKD increased by 49% in patients with diabetes who smoked. TG increased by 1 mmol/L and the risk for DKD increased by 42%. With HDL-C increased by 1 mmol/L, the risk for DKD was reduced by 22%. For every 1% increase in HbA1c, the risk for DKD increased by 17%. With SBP increased by 10–20 mm Hg, the risk of DKD increased by 21%.

The risk of DKD increased by 16% when BMI increased by 5 kg/m^2 while patients with DR had their risk of DKD increased by 31%.

The limitations of the study are: First, the method of systematic review and meta-analysis was heterogeneous due to differences in research design and method as well as different race and sex compositions of the cohorts in included studies.

Second, the derivation cohort consisted of about 80% white patients and 20% Asian patients, leaving out some of the ethnicities with higher risk for DKD incidence (for instance, black and Hispanic patients). Third, amongst the Asians included, they were predominantly Chinese and the Chinese cutoffs for BMI were used in the risk prediction model making the model difficult to generalize to all Asians.

Fourth, a median follow-up period of 2.9 years may be insufficient follow-up for incidence of DKD validation cohort.

Yet, a simple DKD risk prediction model was developed using age, BMI, smoking, presence of diabetic retinopathy, HbA1c, SBP, TGs, HDL, and UACR which could identify individuals at risk for progression of kidney disease with high sensitivity and specificity, highlighting the importance of grouping use of risk prediction models.

6. Every Fifth Individual with Type 1 Diabetes Suffers from an Additional Autoimmune Disease: A Finnish Nationwide Study

Ref: Mäkimattila S, Harjutsalo V, Forsblom C, Groop PH, FinnDiane Study Group. Every fifth individual with type 1 diabetes suffers from an additional autoimmune disease: A Finnish nationwide study. Diabetes Care. 2020;43(5):1041-47.

JAYPEE BROTHERS

ABSTRACT

Objective: To quantify the risk of coexisting autoimmune diseases (ADs) in type 1 diabetic adults of Finland.

Research design and methods: A total of 4,758 participants of Finnish Diabetic Nephropathy (FinnDiane) Study and 12,710 nondiabetic control individuals were enrolled for this study. Identification of the ADs like thyroid-related disorders, Addison disease, celiac disease, and atrophic gastritis was done with the help of Finnish nationwide health registries (1970–2015).

Results: The median duration of diabetes was 35.5 (26.5–44.0) years while the median age of the participants at the end of follow-up was 51.4 (interquartile range 42.6–60.1) years. 31.6% of women and 14.9% of men had at least one coexisting AD (overall 22.8%). The odds ratios (ORs) for hypothyroidism, hyperthyroidism, celiac disease, Addison disease, and atrophic gastritis were 3.43 [95% confidence interval (CI) 3.09–3.81], 2.98 (2.27–3.90), 4.64 (3.71–5.81), 24.13 (5.60–104.03), and 5.08 (3.15–8.18), respectively, in the participants compared to control group. The corresponding ORs for women compared with men were 2.96 (2.53–3.47), 2.83 (1.87–4.28), 1.52 (1.15–2.02), 2.22 (0.83–5.91), and 1.36 (0.77–2.39), respectively. Late onset of type 1 diabetes mellitus (T1DM) and ageing is associated with increased risk of hypothyroidism, while young age at onset of T1DM increased the risk of celiac disease.

Conclusion: The results of our study, which is one of the largest studies conducted in Finland, highlight the importance of screening of individuals with T1DM for risk of ADs.

COMMENT

Autoimmune disorders share common genetic factors and immunologic processes and hence, often coexist within the same individual and families. In individuals with type 1 diabetes mellitus (T1DM), celiac disease and hypothyroidism are the most frequently observed additional autoimmune disease (AD) amongst 80 different others. Although common genetic background is the main factor determining high prevalence of additional AD in individuals with T1DM, shared environmental or other pathological mechanisms cannot be ruled out. Finland has the highest incidence of T1DM in children (62.5 per 100,000) and is among the countries with the highest incidence of celiac disease in young adults (31 per 100,000) in the world.

This study aimed to quantify the excess risk of ADs in adult individuals with long-term T1DM compared with sex and age match control individuals without T1DM.

Autoimmune diseases were identified by linking the data with the Finnish nationwide health registry and prescription patterns of 4,758 individuals with T1DM in the Finnish Diabetic Nephropathy study cohort and 12,000 age and sex match control individuals without T1DM.

About 2,523 (53%) were diagnosed with T1DM under 15 years of age, and the median duration of diabetes was 35.5 (26.5–44.0) years. There were 1,245 additional ADs that were identified in 1,087 individuals with T1DM. The most prevalent AD on top of T1DM was hypothyroidism (n = 859, 18.1%) followed by celiac disease (n = 207, 4.4%), hyperthyroidism (n = 112, 2.4%), atrophic gastritis (n = 49, 1.0%), and Addison disease (n = 18, 0.4%).

There was a female preponderance for all ADs, although this was not significant for atrophic gastritis. It was most conspicuous for hyperthyroidism where the proportion of women reached 71.4%. Women were also more likely to develop multiple ADs with a prevalence of 31.6% compared with 14.9% in men ($p < 0.0001$). Individuals with hypothyroidism were older, had a longer duration of diabetes, and had a lower body weight but higher body mass index (BMI) (adjusted for sex) than those without any additional AD. Alongside female predominance, the individuals with hyperthyroidism more often had a history of

JAYPEE BROTHERS

smoking. Individuals with Addison disease had a worse lipid profile, lower high-density lipoprotein (HDL) cholesterol, and a tendency to higher triglyceride concentrations. Individuals with celiac disease had lower age at onset and longer duration of diabetes as well as lower body weight and BMI.

Of T1DM individuals, 937 (19.7%) had only one additional AD, 143 (3.0%) had two, 6 (0.13%) had three, and one patient (0.02%) had four ADs together with T1DM. The most prevalent combination was hypothyroidism and celiac disease. Although Addison disease was not a frequent AD, 16 out of 18 (89%) clustered with another AD and mostly with hypothyroidism (78%). Similarly, 53% of the cases of atrophic gastritis clustered with hypothyroidism.

The risk of hypothyroidism increased 1.7% [95% confidence interval (CI) 0.9–2.5%, $p < 0.0001$] by each increasing year of age at onset of diabetes. The risk increased 1.3% (0.7–2.0%, $p < 0.0001$) by year of age. Opposite to hypothyroidism, the risk of celiac disease was 1.5% (95% CI 0.1–3.0%, $p = 0.048$) higher for each decreasing year of age at onset of diabetes.

The highest risk was seen in those with an age at diagnosis of diabetes under 10 years compared with all other individuals with T1DM with an odds ratio (OR) of 1.38 (1.02–1.85, $p = 0.03$), but thereafter, the risk leveled off.

The main strength of the study is the large cohort of well-characterized patients with T1DM during a long diabetes duration with age and sex match controls. The limitations of the study are that it is a registry-based study with absence of clinical data and baseline, and also the fact that the age of onset of ADs is not determined.

In conclusion, this nationwide study showed that 22.8% of individuals with T1DM have an additional AD. Hypothyroidism, celiac disease, and hyperthyroidism are the most prevalent ADs. Late onset of T1DM and ageing increases the risk of hypothyroidism. Screening for celiac disease is important during childhood, since age 10 years at onset of T1DM but not ageing, per se, increases the risk of celiac disease. ADs should be screened throughout life equally for both sexes and more often in those with a family history of T1DM.

7. Absence of Islet Autoantibodies and Modestly Raised Glucose Values at Diabetes Diagnosis Should Lead to Testing for MODY: Lessons from a 5-year Pediatric Swedish National Cohort Study

Ref: Carlsson A, Shepherd M, Ellard S, Weedon M, Lernmark Å, Forsander G, et al. Absence of Islet Autoantibodies and Modestly Raised Glucose Values at Diabetes Diagnosis Should Lead to Testing for MODY: Lessons From a 5-Year Pediatric Swedish National Cohort Study. Diabetes Care. 2020;43(1):82-9.

ABSTRACT

Objective: To identify the discriminatory factors for maturity onset diabetes of the young (MODY) in the pediatric population at the time of diagnosis of diabetes.

Research design and methods: A total of 3,933 Swedish patients, aged 1–18 years, from a national consecutive prospective cohort were enrolled for the study. Clinical data and other information related to islet autoantibodies [glutamic acid decarboxylase (GAD) insulinoma antigen-2 (IA-2), zinc transporter-8 (ZnT8), and insulin autoantibodies (IAAs)], human leukocyte antigens (HLAs) type, and C-peptide were collected at diagnosis. Confirmation for MODY was done by glucokinase (GCK), hepatocyte nuclear factor-1A (HNF1A), and HNF4A sequencing.

JAYPEE BROTHERS

Results: Discriminatory factors for MODY at diagnosis included four islet autoantibody negativity (100% vs. 11% not-known MODY; $p = 2 \times 10^{-44}$), hemoglobin A1c (HbA1c) [7.0% vs. 10.7% (53 vs. 93 mmol/mol); $p = 1 \times 10^{-20}$], plasma glucose (11.7 vs. 26.7 mmol/L; $p = 3 \times 10^{-19}$), parental diabetes (63% vs. 12%; $p = 1 \times 10^{-15}$), and diabetic ketoacidosis (0% vs. 15%; $p = 0.001$). Detection rate for MODY was 15% in islet autoantibody-negative patients, and 49% in islet autoantibody-negative patients having HbA1c <7.5% (58 mmol/mol) at diagnosis. On follow-up, the 46 patients with MODY showed good glycemic control, having an HbA1c level of 6.4% (47 mmol/mol).

Conclusion: Absence of all islet autoantibodies and modest hyperglycemia [HbA1c <7.5% (58 mmol/mol)], at the diagnosis of pediatric diabetes, should prompt the clinician to test for GCK, HNF1A, and HNF4A MODY. Testing all patients negative for four islet autoantibodies is an effective strategy for not missing MODY but will result in a lower detection rate.

COMMENT

Maturity onset diabetes of the young (MODY) is noninsulin dependent, dominantly inherited monogenic variant of diabetes which is diagnosed in young age typically. It has been recognized that management of MODY is different from type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). MODY is found to be accountable for 1–2% of pediatric diabetes but misdiagnosis results in unnecessary treatment of many young people with insulin resulting in delay in diagnosis of MODY. The most common subtypes of MODY or glucose kinase MODY does not require any treatment whereas other two subtypes, i.e., hepatocyte nuclear factor-1A (HNF1A) MODY and HNF4A MODY are optimally treated with low-dose sulfonylureas in case therapy is needed.

Islet autoantiantibodies can be useful in diagnosis of MODY, non-T1DM. These antibodies are detected in 90% of pediatric cases of T1DM but are rarely detected in MODY, i.e., only 1% of cases which are similar to healthy population. In routine clinical practice, comprehensive islet autoantibody testing of all four subtypes—antibodies against glutamic acid decarboxylase (GAD), insulinoma antigen-2 (IA-2A), zinc transporter-8 (ZNT8A), and insulin autoantibodies (IAA)—is not performed. The present study was carried out in a pediatric national cohort with the aim to characterize discriminatory clinical features of the most common types of MODY in diagnosis of diabetes.

This study, i.e., better diabetes diagnosis study (BOD), was carried out from May 2005 to December 2010 in 42 hospital pediatric clinics in Sweden. Total 3,933 eligible pediatric patients were included in the study cohort with the mean age of 10.1 years at the time of diagnosis and 45% being female.

The study reported 88% of patients to be positive for at least one islet autoantibody. Anti-glutamic acid decarboxylase antibody (GADA) alone were reported negative in 49% patients. 17% of patients were reported to be negative for GADA and IA-2A; 13% for GADA, IA-2A, and ZNT8A; and 12% with all the four autoantibodies.

It was found that MODY was not identified in any autoantibody-positive patient.

The characteristic clinical feature of MODY and diagnosis was found to be absence of islet autoantibodies. Additionally, lower HbA1c (7% vs. 10.7%), parental diabetes (63% vs. 12%), and not having DKA (0 out of 46 vs. 601 out of 3,887) $p < 0.001$ were other keys discriminating features.

Maturity onset diabetes of the young was detected in 45% of the islet autoantibodies-negative patients who were tested on clinicians request. Whereas it was detected in 5% of the autoantibody-negative patients who were tested genetically as part of this research project.

Glucokinase (GCK) MODY subtype was detected in 63%, HNF1A MODY subtype in 22%, and HNF4A MODY subtype in 15%.

JAYPEE BROTHERS

for detailed information on endocrinology books, visit our website www.jaypeebrothers.com, for detailed information on endoc

RSSDI *Yearbook of* Diabetes 2020

Salient Features

- RSSDI (Research Society for the Study of Diabetes in India) Yearbook 2020 is a collection of carefully chosen articles from various peer reviewed journals published over the last 1 year.
- The topics included are of relevance to practicing physicians, diabetologists, and endocrinologists.
- The book has eight sections covering basic science, epidemiology, comorbidities, complications, type 1 diabetes mellitus, gestational diabetes, therapeutics, and newer technologies.
- For each article, the authors have provided background information, key learning points, strengths and limitations of the study, and a "take home" message for the readership. Each article is accompanied by detailed references for further reading.

Printed in India

Available at all medical bookstores
or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Daryaganj, New Delhi - 110 002, INDIA
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
DIABETOLOGY

ISBN 978-93-90595-28-0