



Diabetes Update

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"DIABETES UPDATE"** which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Study of Dapagliflozin on COVID-19 patients with cardiometabolic risk factors: DARE Trial
- Advance prediction model for diabetes patients with high risk of foot ulcer recurrence
- A study on Single-center Experience of Endocrine Dysfunction among COVID-19 Patients.

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

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Study of Dapagliflozin on COVID-19 patients with cardiometabolic risk factors: DARE Trial

Patients with COVID-19 and cardiovascular risk factors have the risk of multi organ failure and slow clinical recovery. Dapagliflozin is an SGLT2 inhibitors reduce the risk of cardiovascular disease by inhibiting pathways which are involved in causing acute illness, thus help in preventing multiorgan failure and improve recovery of COVID-19 patients.

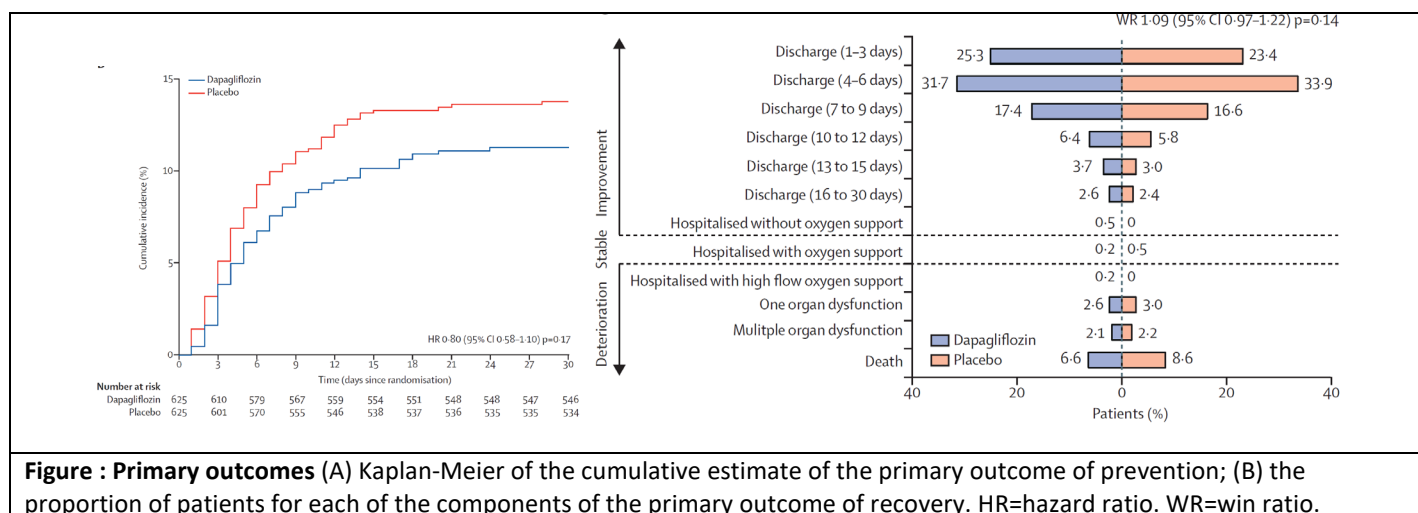
Dapagliflozin in respiratory failure in patients with COVID-19 (DARE-19) trial evaluated the efficacy and safety of dapagliflozin in patients who are hospitalized with COVID-19 and have cardiometabolic risk factors. This study was a multicenter, randomized, double blinded and placebo controlled trial to assess dapagliflozin in hospitalized COVID-19 patients for 30 days. 1273 patients, 18 years of age with atleast one cardiometabolic risk factors were assessed for eligibility. Patients were randomly treated with either 10mg of dapagliflozin once daily orally or matching placebo for 30 days. This trial had dual primary efficacy outcomes.

Out of 1250 patients, 50.9% patients had type 2 diabetes, 84.8% patients had hypertension and 15.9% had atherosclerosis, 7.2% heart failure, 6.6% had chronic kidney disease and 92.7% patients were tested positive for COVID-19. The primary outcome of prevention occurred in 11.2% of patients treated with dapagliflozin and 13.8% of patients given with placebo. Worsened organ failure was observed in 10.2% and 6.6% death in dapagliflozin group and in placebo group 12.8% organ failure and 8.6% death. Primary outcome of recovery, 87.5% of patients in dapagliflozin

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group versus 85.1% patients in placebo group had improvement compared with baseline, but both the primary outcome did not show statistical significance. Patients in both dapagliflozin and placebo group showed acute kidney injury and 147 patients had serious adverse events leading to discontinuation of study. Two patients showed diabetic ketoacidosis who had type 2 diabetes.



Patients hospitalized with COVID-19 and having cardiometabolic risk factors, showed that dapagliflozin was not statistically significant and did not reduce the rate of organ dysfunction or clinical recovery or death. In this study, dapagliflozin was well tolerated but no new safety signals were identified.

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Reference: Kosiborod MN, et al.. Lancet Diabetes Endocrinol. 2021 Jul 21:S2213 8587(21)00180-7.

Advance prediction model for diabetes patients with high risk of foot ulcer recurrence

People with diabetes mellitus have common complication of developing foot ulcer. Ulcer recurrence is observed in 12 months in patients who heal from ulcer, which leads to higher risk of infection and amputation, thus prevention of ulcer recurrence is vital. Prediction model can be used in order to provide appropriate treatment, different strategies adequately among the patients. This study aimed to develop and validate prediction model for patients with high risk of foot ulcer recurrence using variety of clinical variables on a diverse group with diabetes.

This study was conducted in multicenter, randomized controlled trial, at home monitoring temperatures of foot to prevent foot ulcer recurrence in diabetes patients. 1411 people were screened for eligibility, out of which 304 subjects were with diabetes, history of foot ulcer and loss of protective sensation (LOS). LOS was examined using 10g Semmes-Weinstein monofilament and tuning fork. Patients were randomly assigned to usual care or enhanced care with follow up time of 18 months which was the primary outcome of the study.

Development of two logistic regression model to detect foot ulcer recurrence; model 1, for any ulcer recurrence and model 2, for plantar foot ulcer recurrence. Model fitting had four stages: 1) Five data sets were

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created using multiple imputations, 2) Selection of potential predictors, 3) Fitting a logistic regression model and 4) To obtain final prediction model. Linear predictor was used to represent the final logistic regression model. 10-fold cross validation was done to validate the prediction model. Model performance was assessed in terms of discrimination; by applying area under the receiver operating characteristic curve (AUC) and calibration using calibration graphs.

126 participants had foot ulcer recurrence in 18 months, with mean time to ulceration of 212 days. 70 participants had plantar foot ulcer recurrence, with mean time to plantar ulceration of 206 days. Model 1; ulcer recurrence, predicted probability was >0.70 the model slightly under estimated the proportion of observed ulcers. The mean AUC of the model was 0.69 and the mean Brier Score was 0.22. Model 2; plantar foot ulcer recurrence, the predicted probability underestimated when 0.30 and slightly overestimated when >0.50 . The mean AUC of the model was 0.66 and the mean Brier score was 0.16.

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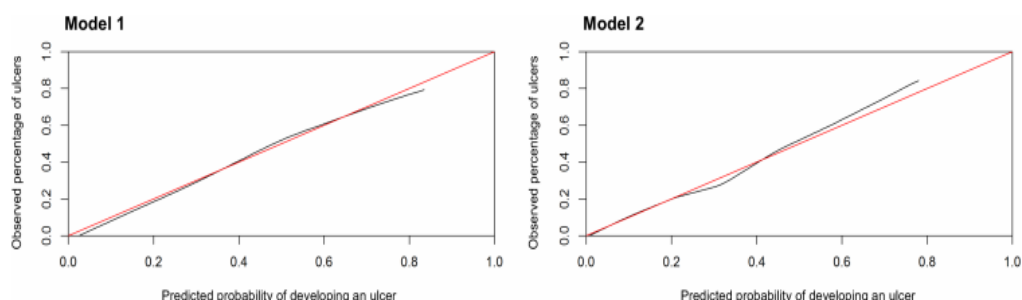


Figure 1: calibration graphs for model 1 (all recurrent for ulcers) and model 2 (all recurrent plantar foot ulcers)

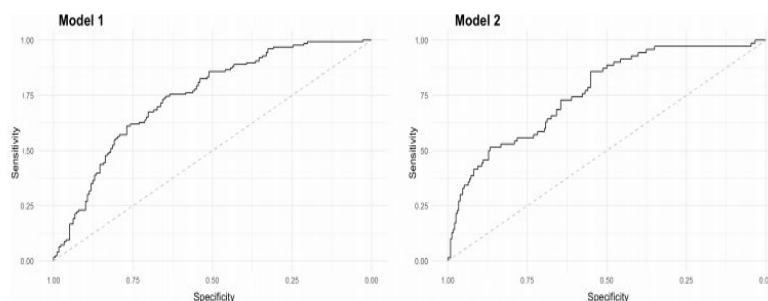


Figure 2: AUC for model 1 (all recurrent foot ulcers) and model 2 (all recurrent plantar foot ulcers)

The validated prediction models contain easy-to obtain modifiable and non-modifiable variables and built from diverse group of people. It stratifies and help determine who should be treated intensively with the objective on preventing foot ulcer recurrence in diabetes patients.

Reference: Aan de Stegge WB, et al. Development of a prediction model for foot ulcer recurrence in people with diabetes using easy-to-obtain clinical variables. BMJ Open Diabetes Res Care. 2021 Jul;9(1):e002257.

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A study on Single-center Experience of Endocrine Dysfunction among COVID-19 Patients.

Coronavirus disease 2019 (COVID-19) belongs to Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV2) family. Many reports showed that COVID-19 had a predilection for multisystem, especially endocrine system by activating inflammatory and cytokine pathways.

The comprehensive studies to assess the relationship between endocrine system and COVID-19 remains unexplored. Hence this study aimed in evaluating hormones released from pituitary, thyroid and adrenal gland in COVID-19 patients admitted at Tertiary care hospital at Jodhpur. Endocrine profiling among COVID-19 patients was done at ALL India Institute of Medical Sciences from 15 May to 30 June 2020. 235 patients, above 18 years of age admitted with COVID-19 after the confirmation by RT-PCR.

Thyroid function was assessed by free triiodothyronine (FT3), free tetraiodothyronine (FT4) and thyroid stimulating hormone (TSH). Prolactin levels were counted in to evaluate pituitary function. Adrenal function was assessed by basal cortisol and 1hr post-intramuscular adrenocorticotrophic hormone (ACTH) cortisol. All hormones from adrenal gland was analyzed by chemiluminescent immunoassay and C-reactive protein(hs-CRP) was measured by immune-turbidimetric test.

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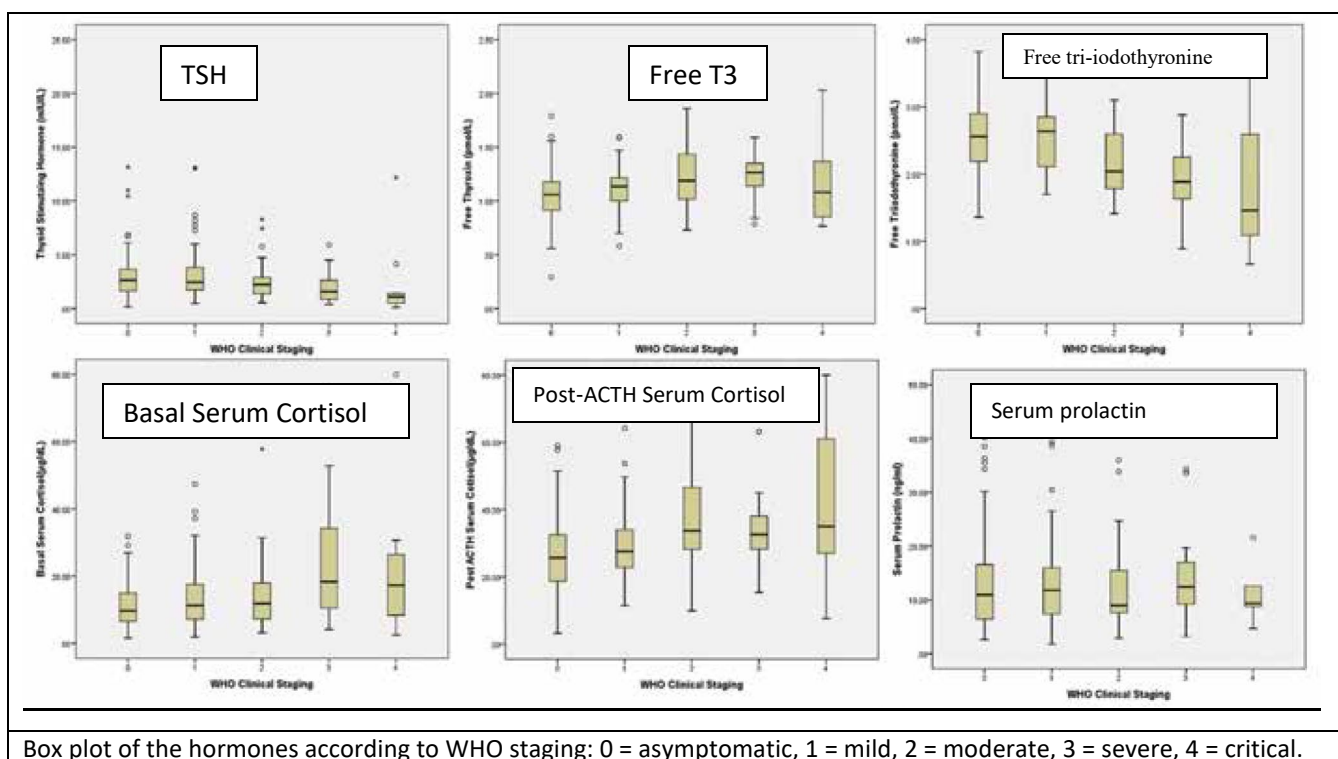
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Patients with normal FT3, FT4 and TSH were considered as euthyroid, with the range of 11.5-22.7 pmol/L, 3.5-6.2 pmol/L and 0.35-5.5 mIU/L. Primary hypothyroidism was defined <11.5 pmol/L low FT4 and >5.5 mIU/L high TSH and subclinical hypothyroidism by FT4 within normal range. Adrenal insufficiency with basal cortisol was <3 µg/dl or 1 hr post-ACTH cortisol was µg/dl and <9 µg/dl of delta cortisol. Hyperprolactinemia was observed as >20 ng/ml in males and >30ng/ml in non-pregnant females. The statistical significance of all hormones was calculated by non-parametric Kruskal-Wallis test and the data were compared by Chi-square test. The correlation between serum cortisol, interleukin-6 and hs-CRP was done by using Pearson correlation coefficient.

9.8% patients had moderate disease, 14% had severe disease, 94.5% had recovered and discharge and there were 5.5% death. 91 patients, 38.5% had <3 mg/L of hs-CRP and 84 patients had hs-CRP levels >10mg/L. The level of serum hs-CRP raises with increase in severity. 47 patients had high level of IL6, >100 pg/ml. Adrenal insufficiency was present in 14% of asymptomatic or mildly symptomatic patients. Among patients, mean cortisol levels were 13.9 ± µg/dl and post-ACTH cortisol levels were 29.5 ± 13.0 µg/dl. Both basal and post-ACTH cortisol levels increased significantly with severity. Mean values of FT3, FT4 and TSH was 3.69 ± 0.9 pmol/L, 14.2 ± 3.9 pmol/L and 3.6 ± 7.0 mIU/L. Serum FT3 and TSH declined from asymptomatic to severe groups and serum FT4 increased among severity groups. Twenty-one patients had hyperprolactinemia and two patients had very high serum prolactin levels. Mean value of prolactin levels were 152 ± 16.9 µg/L and did not differ between survivors and non-survivors.

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Endocrine dysfunctions such as adrenal insufficiency, low T3, low TSH level and hyperprolactinemia commonly occurred in COVID-19 patients.

Reference: Kumar B, et al. Endocrine dysfunction among patients with COVID-19: A single-center experience from a tertiary hospital in India. Indian J Endocr Metab 2021;25:14-9



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