ABSTRACT

Physician estimate of the patient's oral medication adherence level has a poor predictive value. A valid and reliable tool to measure oral medication adherence among type 2 diabetes mellitus (DM) which can be used in a busy clinic setting is an unaddressed need. Adherence to oral medication among type 2 DM patients is low. Hence, simple interventions to improve adherence which can be integrated into the existing health care system should be explored.

The "Model Adherence to Medicine" (MAM) questionnaire was developed with the evidence from the literature review, key informant interviews with key stakeholders of medication dispensing, and five in-depth interviews with purposively chosen DM patients. Answers were developed in a five-point Likert scale which scored from 1-5 and the possible range of the total score of the questionnaire is 15-73.

A descriptive cross-sectional study was carried out among adult patients with type 2 DM who attended clinics in District General Hospital (DGH) Gampaha from March 2016 – April 2016 to validate MAM. A sample of 150 patients was recruited consecutively to test the criterion and construct validity. The criterion was the composite index of pill count, recital dosage and the regular clinic attendance. Sensitivity and the specificity with 95% Confidence Intervals (CI) were established. Construct validity of MAM was assessed by convergent, discriminative validity and exploratory factor analysis (EFA) Results were analyzed by Spearmen correlation and Man Whitney U test with p values.

Optimal cut off point to discriminate high from average adherence to DM medication among adult patients was 70; ≤ 70 denotes average adherence while >70 high adherence. Area Under Curve (AUC) was 0.87 (95% CI 0.81 – 0.93). MAM score >70 denotes high while ≤70 average adherence. It has a sensitivity of 72.5% (95 % CI 58 – 83.7%) specificity of 92.9% (95% CI 85.5 – 96.9%) with a positive likelihood ratio of 10.2. EFA yielded four factors; sick role behavior, autonomy, forgetfulness and barriers. Spearmen correlation between MAM score with the variables tested were moderate; pill count r=0.39 (p=0.01),

recital dosage r= 0.54 (p=0.001), recall screen for doses missed r=-0.52 (p<0.001) and pills missed r= -0.48 (p<0.001). The ability of the score of the MAM to discriminate between the groups of self-reported adherence (u= 811.5, p<0.01), the presence of symptoms of hypo/hyperglycaemia (u=3012, p<0.01) and adequate long term glycaemic control was (U=372, p<0.001) satisfactory.

A clinic-based descriptive cross-sectional study was carried out to describe adherence to oral medication using the validated tool among patients with type 2 DM in Colombo North Teaching Hospital (CNTH), Ragama from July 2016 to September 2016. Multistage stratified cluster sampling was done to recruit 950 outpatient clinic attendees. Results were expressed as percentages and CI. The level of high adherence to medication among adult DM type 2 patients who attended outpatient clinics in CNTH was 35.9% (95% CI- 32.8 - 39%) while male had (37.1%, 95% CI - 31.1 – 43.4) and female had (35.5%, 95% CI - 31.9 – 39.1). Clinic defaulters had high adherence level of 37.5%, 95% CI- 32.4 – 42.8).

A clinic-based unmatched case-control study was carried out among patients with type 2 DM in CNTH from July 2016 to September 2016 to determine the factors associated with adherence to medication. Multi-stage stratified cluster sampling was done to recruit 950 participants with 341 cases and 609 controls. Cases had high adherence while controls had average adherence as categorized by MAM. Five validated interviewer-administered questionnaires to measure health literacy, numeracy, beliefs, knowledge about DM and medication, basic socio-demographic and seeking alternative treatment were used in data collection. Results were expressed as Adjusted Odds Ratios (AOR) and CI. Multivariate logistic regression was performed.

There were 10 independent factors associated with high adherence to medication among adult type 2 DM patients who attended outpatient clinics in CNTH. Duration of diabetes ≥5 years (AOR 1.4, 95% CI 1.05-1.87) , normal Body Mass Index (BMI) (AOR 1.63, 95% CI 1.21-2.2), high numeracy skills (AOR 1.59, 95% CI 1.19-2.13) , never visiting an alternative treatment provider (AOR 2.83, 95% CI 1.66-4.81), obtaining medicine from private pharmacy (AOR 2.04, 95% CI 1.35-3.08), and satisfied about the time spent with the doctor during the consultation (AOR 1.85, 95% CI 1.06-3.22) were positively associated with high adherence. Perceived suffering of side effects (AOR 0.47, 95% CI

0.32 – 0.69) positive family history for DM in a sibling (AOR 0.65, 95% CI 0.43 – 0.97), feeling unfit (AOR 0.51, 95% CI 0.38 – 0.68), and blurred vision (AOR 0.73, 95% CI 0.55 – 0.98) were negatively associated with high adherence.

A cluster randomized controlled trial was carried out to determine the effectiveness of combined practitioner and patient-focused intervention to enhance adherence to medication among adult type 2 DM patients who attended outpatient clinics in CNTH from March 2017 to November 2017. The study population included patients with average adherence, as measured by MAM. Stratified simple randomization was done to select three clusters in each arm. The intervention group consisted of 91 and the control group of 85 patients who were recruited consecutively. Pre-tested practitioner and patients focused intervention package was delivered to the intervention group while the control group received usual care. Intervention package included health education (HE) to patients and practitioner sensitization about the adherence status of the patient. The primary outcome was the mean score of MAM six months after the intervention. Data were collected using validated interviewer-administered questionnaires and collectors were kept blind to the intervention status of the group. Results were expressed as mean difference and relative risks (RR) with CI. Mean difference of MAM scores six months after the intervention was 3.58 (95% CI 2.17 - 4.99, $p<0.001$). RR of intervention group for no dose adjustment was (2.75, 95% CI 1.13–6.7), short term glycaemic control (2.01, 95% CI 1.09 – 3.69) knowledge about DM/complications (4.33, 95% CI 1.85 – 10.17). ETU admissions 0.03 (95% CI 0.01 – 0.26) and first contact care provider visits 0.14 (95% CI 0.07 – 0.28) were reduced.

Clinic- based unmatched case-control study was carried out to identify the risk factors for high adherence in CNTH from July 2016 to September 2016. Cases were patients with high adherence while controls were average adherence. Consecutive patients were recruited until 273 sample size was reached in each group. Five validated interviewadministered questionnaires to measure health literacy, numeracy, beliefs, knowledge about DM and medication, basic socio-demographic and seeking alternative treatment were used in data collection. An additional questionnaire was used to collect data on operationalized predictors for the development of the model. Reference criterion was high adherence. The model was built using multiple logistic regression and was tested for discrimination and calibration.

There were six predictors in the model; BMI (Kg/m2), positive family history for DM, visiting an alternative treatment provider, usual place of getting medicine, symptoms and health education on DM and complications. Calibration of the model was Hosmer Lemeshow Goodness of fit test was P=0.89, $\chi 2$= 2.93, df=8. Discrimination of the model was AUC 0.67 (95 CI % 0.62 – 0.73), p<0.001.

The developed model with six predictors was externally validated in a clinic-based descriptive cross-sectional study in Base Hospital (BH), Kiribathgoda in February 2019. Reference criterion was the high adherence while test criterion was the developed model. A sample of 140 DM patients who were on medication for more than one year was recruited consecutively. An interviewer-administered questionnaire which included the details of re operationalized six predictors were used in data collection. The model was built using multiple logistic regression and tested for discrimination and calibration. Calibration of the model demonstrated a Hosmer Leme show Goodness of fit test p=0.76, $\chi 2$ of 4.97 with df= 8. AUC was 0 .72 (95% CI - 0.63 -0.81), p<0.001.

Conclusions and recommendations

MAM was a simple, valid and reliable questionnaire with a high clinical significance in diagnosing level of adherence to oral DM medication. Approximately one-third of the clinic attendees have high adherence to DM medication which was suboptimal. Seven modifiable determinants of low adherence were identified in the present study; Body Mass Index (BMI), numeracy skills, visiting an alternative treatment provider, current herbal medicine use, obtaining medicine from a private pharmacy, receiving health education regarding DM, and time spent with the doctor during the consultation. Combined practitioner and patients focused intervention was effective in improving adherence, disease, and therapy-related outcomes. The developed model with six predictors had good predictive performance and performed well in internal and external validation. MAM is recommended to be used in the clinical research setting. Interventions to promote factors associated with high adherence in clinic setting should be incorporated into the current busy clinic setting. Readjustment and upgrading of the developed model should be done in a wider geographical context with the inclusion of a rural population.