Manuscript Submission

Title: Ethical Qualms While Treating Diabetes In Low Resource Areas

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Ethical qualms while treating Diabetes in low resource areas

**Introduction:**

India has the largest number of diabetes in the world. INDIAB study estimates,62 million diabetics in India(prevalence of 7.3%), with higher urban prevalence (11.2%) than rural 5.2%(1).

Jan Swasthya Sahyog (JSS)(People's Health Support Group) runs a rural secondary cum tertiary care hospital situated in central India serving 32 million population from 8 districts with high rates of poverty (72%)(2), illiteracy, undernutrition and infant and maternal mortality than the average Indian population. JSS hospital also serves as a referral center for a comprehensive community health programme in 70 hard to reach forest villages. We see about 20,000 new patients every year requiring secondary or tertiary level care. Diabetes Mellitus constitutes 2.5 % of routine new outpatients. Around 450 new patients get diagnosed to have diabetes in a year. Comparable to urban counterparts, 90% of our patients present during adulthood (type 2) and 10% present during childhood and adolescence (type 1 DM). The median age for type 2 diabetes is just under 50. In contrast to urban counterparts, only a third of type 2 diabetes have a BMI greater than 22.5 Kg/M2 (Indian BMI cutoff for overweight(3)) and over a third have a BMI lower than 18.5 Kg/M2 often referred as 'Lean Diabetes'(4).

Retrospective cohort data analysis of 1023 patients from 2013 to 2016 showed that 793 (78%) patients were on OHA (oral hypoglycemic agents) and 230 (22%) required insulin. 81% of these patients were being treated with metformin as one of the drug(5).

In another prospective random cohort analysis of 250 type 2 diabetes between November 2017 and April 2018, 22% of diabetes had HBA1C of more than 8. The prevalence of complications in them was 14.8 % (95 % confidence interval: 10.2 to 19.4%) for diabetic foot ulcer, late nephropathy (elevated serum creatinine >1.2 mg/dl) 14% and peripheral neuropathy 50 %. (Unpublished Data of JSS Hospital).

Most challenges are structural due to lower socioeconomic status, poor health awareness and poor healthcare infrastructure. Basu et al (6) described under-recognized nature of ethical dilemma in low resource settings focused on drug therapy, we further elaborate structures leading to ethical dilemmas with possible solutions.

Diabetes is a deficiency amongst excess of glucose. Lean diabetes makes us feel that there is a cruel parallel about diabetes at societal and cellular levels. In diabetes, body cells are surrounded by abundant glucose but cannot use it. Similarly, our rural poor live in a country with marked rise in income and material resources, but cannot reap its benefits due to rising socio economic inequity(7). There is an urgent need to improve understanding of barriers to plan and deliver appropriate care to neglected subset of patients.

Some dilemmas are not specific for diabetes only but are also relevant to all chronic illnesses such as how to respect patient autonomy and shared decision making when patient has uncontrolled diabetes and deny close follow up with underlying structural financial and geographical constraints? Should one deny care to those unable to adhere with treatment recommendations or continue treatment while accepting long term micro and macro vascular complications? Should we recommend limiting carbohydrate intake with the awareness of unaffordable protein and fat while 80 % of calories consumed are carbohydrates in patients with BMI of 16 Kg/M2 or lower?

**Challenges in Diagnosis:**

**Classification- Is Lean diabetes a separate class?** Classifying diabetes type clinically is challenging in presence of undernutrition. Often lean diabetes is misclassified as either Type 1 or Type 2 due to difficulty to conclude whether low BMI is a cause or effect. This leads not only to underestimation of the actual burden of lean diabetes but also delays initiation of insulin in them. Some authors propose that these “lean” diabetics represent a separate pathophysiological process than that of classic type 1 and type 2 diabetes while others believe it is a variant of type 2 diabetes(8). Should we call lean diabetes as a separate category when WHO has removed it from current classification(4), different from Maturity onset diabetes of the Young (MODY) ? Should all of these people be investigated for chronic calcific pancreatitis? Classification is important as early starting of insulin in them preserves beta cell function for longer duration. Further studies are needed to study causation and mortality reduction in lean diabetes(9–11).

**Challenges in Treatment:**

**Balancing Intensive Hyperglycemic Control and Risk of Hypoglycemia:**

A large majority of rural adults with diabetes have to perform heavy manual work with varying seasonal schedules and are unable to control their meal content or the timing (due to job profile and expense). Uncontrolled status of meals leads to swings in blood glucose levels from life threatening hypoglycemia to hyperglycemia. Should these people have different glucose or HbA1C targets than those in areas with better access? Fear of hypoglycemia is an important factor affecting care in presence of underlying high glycemic index rice based diet (leading to rapid blood glucose swings), higher risk of skipping of meals, religious fasts, livelihood work demanding intense physical activity, mistakes in dosing of OHA or insulin and higher infection rates in these population. Often we err on the side of accepting risk of long term micro and macrovascular complications than hypoglycemia with the principle of non-maleficence. We do not have evidence if we are doing the right for our patients.

**Frequency of follow Ups:**

We find it difficult to achieve desired glucose control due to patient’s inability of monthly follow ups with financial and geographic barriers. The situation compels us make a difficult choice between accepting patient autonomy of shared decision making with unmet targets of sugar control without clear consensus of unintended consequences of each decision. It makes us wonder about shared decision making guidelines when patients often don’t seem to understand and judge the consequences or even if they understand are forced to choose less than ideal follow up frequency owing to structural factors like poor socio-economic status and accessibility of services.

**Glucose Monitoring Test and Quality Control:**

Blood glucose can be tested either by finger prick glucometer or venous blood colorimetry. Glucometric checks have the advantage of rapidity of results, ease of technique and of being a point of care test but requires regular calibration. Erroneous results showing falsely low sugar if strips are stored above 30 C are reported(12).Glucometers are recommended in temperate climate only if quality control results are in acceptable range with individualized quality control plan. HbA1c testing has the advantage of monitoring sugar control for last 90 days but is expensive, has a reasonably difficult technique for peripheral laboratory services to provide, requires high level of quality control. High prevalence of iron deficiency (falsely increases HbA1C(13)) and hemolytic anemia like sickle cell disease(falsely reduces HbA1C(14)) is common in rural central India makes its interpretation difficult. In a situation where expenses are paid by patients, physicians have to ensure affordable care or expect high default rates and thus face a dilemma in choosing monitoring tool for sugar control. We worry about escalating therapy based on results of glucometric sugar control without regular calibration or HbA1C results with anemia prevalence being 54%(15).

**Challenges around Insulin:**

OHAs (Oral Hypoglycemic Agents) are mainstay for type 2 diabetes, however a large proportion of type 2 and lean patients require insulin in variable doses, sometimes reaching up to 100 IUs a day. We have not been able to find a single satisfactory method of choosing the dose of insulin. Since the overwhelming majority of people consume more than 80% calories as carbohydrates, much higher than published 65 %(16), normal glucose values become difficult to target for. The decision to start insulin in addition to OHAs is painful because of problems related to insulin cost, injection technique, dosing and insulin storage, poor access. In Chhattisgarh and Madhya Pradesh, NPH insulin or Combination (70/30) insulin rarely available in health facilities peripheral to district hospital. Maintaining insulin potency in rural setting without electricity and refrigerator is difficult. Earthen pots storage is a poor option in tropical situations with room temperatures beyond 30 degrees Celsius for some hours each day. Ensuring patient's understanding around injectable devices, dosing, reusing and disposing syringes demands extraordinary nursing and counseling skills.

**Managing uncontrolled Hyperglycemia Requiring High Doses of Insulin:**

For patients with uncontrolled diabetes despite 2 units per Kg body weight of insulin in addition to one or two OHA, we are unsure about their management in low resource setting with costs preventing use of long acting insulin forms.

**Lean Diabetes:**

The pathogenesis of lean diabetes is multi-theory and the usual standard type 2 diabetes management guidelines are inappropriate for "lean diabetes". Study from west(17) reports diabetes with normal BMI are at risk of higher mortality than obese counterparts with non-cardiac causes. A hospital based Indian study(18) reports ischemic heart disease, infections, nephropathy, stroke and coma as causes of mortality and should be further studied by community based study in low resource area. There is no definite answer about role of weight reduction in lean diabetes and needs to be studied(9). Guidelines about prescribing statins need to be redefined in presence of non-obese (lean) diabetes and higher than normal cardiovascular risk in South Asians than rest of the world coupled with limited access to lipid testing. Research on lean diabetes is almost static since 1991 like many other diseases of poor people.

**Dietary and Lifestyle Advice:**

We find this as the most difficult aspect of diabetes management. It is ironical to advise low carbohydrate diet when it constitutes more than 80% of food, Public Distribution System (PDS) providing mainly carbohydrates containing food items and unaffordable proteins and vegetables for poor patients. We are unsure if physicians should advocate for change in PDS food contents for people with diabetes. Should PDS rethink on its content when high carbohydrates are known to increase the risk of diabetes and other non-communicable diseases in general population as well? The work profile for farmers and farm laborers does not allow them to have frequent and small quantity meals. Also guideline are required for modifying exercises and for optimizing weights in hard working labour population so as to allow physical labor without adverse effects.

**Surgical Care in Diabetes:**

Diabetes patients are more prone to abscesses, carbuncles, cellulitis, necrotizing fasciitis, dry gangrene, pressure ulcers and require combination of knowledge of medicine and surgery. Surgical care in diabetes is expensive requiring longer wound care, antibiotics, longer hospital stay often pushes patients deeper in poverty with significant loss of function. The National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases & Stroke (NPCDCS) does not integrate surgical care with medical care leading to poor care at district hospitals as shared by our patients.

**Opportunistic Infections:**

Preventing life threatening infections for dually immunodeficient patients with uncontrolled diabetes and associated undernutrition is challenging. India being a high burden country for tuberculosis (TB) and uncontrolled diabetes increases tuberculosis risk. We wonder should diabetes be included as a screening criterion like under 5 years for TB contact screening. Nine percent of our tuberculosis patients have diabetes and managing patients with combined disease is challenging technically. Further, clear guideline are required regarding immunization against recurrent pneumonia for this patient population.

**Type 1 Diabetes:**

Teaching self-glucose monitoring with carbohydrates counting is difficult with poor literacy levels of patients, expensive glucose strips and hypoglycemic risks. In our view just free or subsidized insulin is not enough for their care and health system should also think of psychological trauma, physical disability and invest to make them self-sufficient providing school scholarship and professional skill building. Similarly our system needs to be equipped to allow and engage these rural young patients requiring chronic care in monitoring of health facilities, patient based advocacy and peer support for wider benefit and empowerment.

**Diabetes with End Organ Damage:**

A1chieve study from South India(19) reported, complication rate of 23.6% for cardiovascular, 21% for renal and 16% for ophthalmic irreversible damage. All of these patients need care for their complication. Protocol based tertiary care at specialty unit with follow up at nearby health centers can achieve better care near patients home.

**Socio-Economic Factors Complicating Diabetes Care:**

In addition to technical difficulties, socio-economic factors like cost of care, distance from health facilities and stigma are difficult to deal affecting continuity, quality and outcomes of diabetes care**.**

**Cost of Care:**

Diabetes patients spend more than 40 % of total household income on care(20).Chronicity of the diabetic care pushes people below poverty line. Thus far there is no insurance coverage for the outpatient level diabetes care. The National program promises affordable care but medicines are not available below the level of CHC, being prescribed for 1 or 2 weeks per visit resulting in almost equivalent expenditure on travel and opportunity cost. The primary health center (PHC) level is not yet implemented on ground in national diabetes care programme(21). Equipping PHCs for follow up care with free investigations and free medicines would help resolve distance and cost barriers of care access.

**Distance**

26 % of our patients travel more than 100 kilometers for diabetes treatment. We find distance from health facilities a common reason for default. Patients get trapped in vicious cause and effect cycle of poverty and diabetes. Almost all diabetes defaulters require costly emergency and/or inpatient care for complications. Should we have active follow ups by VHW (village Health Worker) for such patients similar to TB? Costing studies would help to understand cost-effectiveness of active follow up approach for health systems.

**Social Stigma and Discrimination:**

We often come across social discrimination and stigma associated with diabetes leading to cessation of treatment. Children with type 1 diabetes often drop out of schools or hostels because of the teacher advising parents to not send the child to school for the fear of hypoglycemic seizures. Young women presenting with DKA due to discontinued insulin after marriage is not uncommon. Patients often miss their insulin doses when they have to travel outside their home to stay with relatives to avoid stigma. A health system should prevent and protect social discrimination especially for type 1 diabetes for marriage, domestic violence attributed to pregnancy related complications, inability to do equally hard physical labour as normal individual?

**Diabetes Control Programme:**

With current diabetes programme, we need further studies to answer about how far should communitization of care of diabetes should reach- at VHW, PHC or CHC for better compliance without harm? With the onset of diabetes at earlier age, what age group cut offs should be used for population screening in addition to opportunistic screening? How should we handle prediabetes when follow up is not guaranteed? Which method should be used for mass screening? Is our system capable of handling all diagnosed based on screening if mass screening is offered? Should we investigate all pregnant women in non-obese environment for gestational diabetes screening? Can we task share care of diabetes with mid-level health workers or nurses and patient support groups for diabetes on ethical principles?

**Diabetes Education and Support Groups:**

Good patient education material is not available in most vernacular languages. Running peer support groups is one effective strategy in diabetes care(22). They are difficult to organize and get ignored in a resource poor setting. People with skills of counselling are not available where they are needed the most and the task of counselling is left with already burdened doctors and nurses. NPCDCS is currently using mDiabetes (23) with only text messages, scope of which can be expanded to voice interactive apps and IVRs for uneducated diabetes patients and caregivers. There is a need to bridge the evidence gap for its development and implementation. Mobile technology can also be used to engage and support existing patients to form peer support groups.

**Nurse Led Model of Multidisciplinary Integrated Care:**

Technically, management of diabetes is complex, especially the complications. It requires a multidisciplinary approach with physicians, nurse, counselor, dermatologist, ophthalmologist, dietician and often a surgeon. Few cases of diabetes and certain diabetes syndromes may require face to face or tele-consultation with an endocrinologist. In the current national programme NPCDCS , specialist care is available at district level and above. We need to have well tested protocols, continued rather than just one time training, continuous guidance for peripheral health workers using mobile technology and referral services for surgical needs in diabetes to compensate for lack of multidisciplinary teams. We need to learn from countries like Rwanda and South Africa (24,25) to aim and achieve nurse led model of NCD care.

**Possible Solutions:**

Diabetes education material should be available in local vernacular language. Peer support groups can play a big role in education and improving treatment compliance. Better training materials and protocols with increased frequency of training for the ground level staff with mobile technology support for telemedicine and continuous learning should be focused upon. Glucometers used for blood glucose testing should be routinely calibrated and monitored. Communitisation of care would be possible with case managers, including PHC in care of diabetes and ensured availability of free OHA and Insulin with at least 3 monthly refills. Pathogenesis of lean diabetes and its treatment needs further research. Further evidence needs to be generated for large scale use of mobile technology, interactive voice records (IVRs), peer support groups, active diabetes follow up and nurses led NCD clinics in India.

**Conclusions**

Diabetes care in low resource and rural areas is compromised by barriers of access and finances leading to physician ethical dilemmas. NPCDCS for diabetes needs restructuring to contain these barriers via communitization of care to include PHC level NCD clinics, task shifting to nurses, health workers by set protocols, continuous training and use of telemedicine and mobile technology so as to allow more physician time and research for complicated cases. Non physician health workers can be utilized better to handle this epidemic.

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