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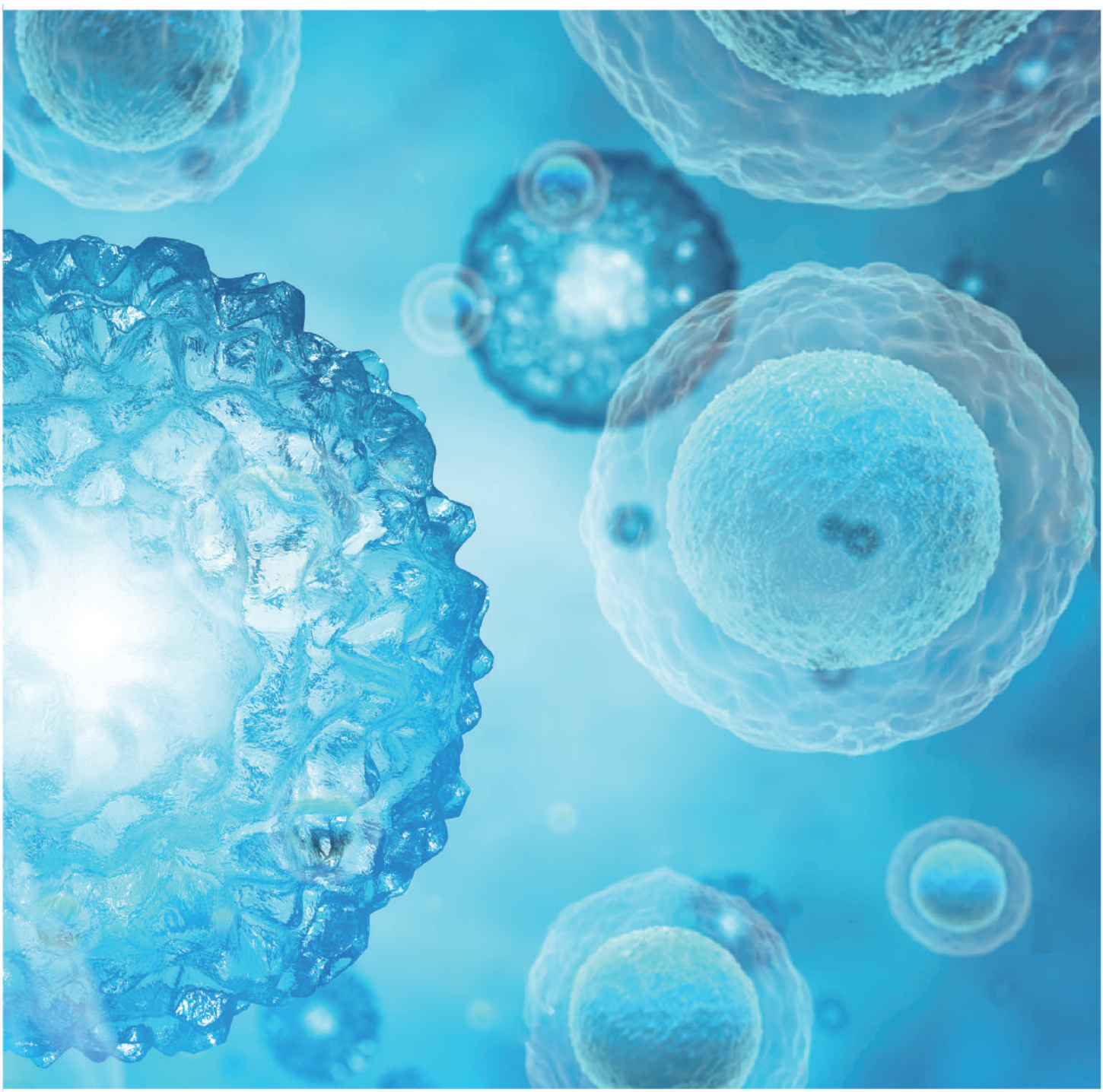

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REVIEW

Review on Thyroid Disorders, Epidemiology and Treatment Methods

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ABSTRACT

Thyroid disorders are commonly overwhelming health conditions reported worldwide. The prevalence of thyroid disorders such as hypothyroidism and hyperthyroidism is increasing in developed and developing countries, including India.This is due to change in traditional foods to Besides low / insufficient iodine intake, smoking, ageing, genetic susceptibility, lifestyle, usage of new medicine, endocrine disrupting chemicals and immune status of an individual are the key determinants for thyroid disorders. This review emphasizes the various disorders of the thyroid gland and, its epidemiology and treatment methods.

1. Introduction

The thyroid gland is a bilobed connected through the isthmus and located in the front of the neck. The thyroid hormones such as triiodothyronine (T3 form) and thyroxine (T4 form) are the secretary products of the thyroid gland. The two hormones which regulate the synthesis and release of thyroid hormones are thyroid-stimulating hormone from the anterior pituitary and thyrotrpin-releasing hormone from hypothalamus [1]. The T3 and T4 hormones of the thyroid gland are essentially required for normal growth and oxidative phosphorylation in all the nucleated cells of the body [2]. The primary thyroid diseases notified commonly are hypothyroidism and hy-perthyroidism due to infections in the thyroid gland. The larger parts, widespread among all the endocrine diseases are thyroid disorders and are prevalent in all countries in-cluding India [3].

Table 1. Iodine intake/deficiency and thyroid disorders

S.No.	Daily intake of iodine/ deficiency	Disorders
1	50 mg	Goitre and is endemic
2	25 mg	inborn hypothyroidism
3	All age groups	Goitre, Hypothyroidism, Impaired mind utility, Augmented defenselessness to nuclear radiation
4	Adult group	Goitre and its complications, Iodine induced hyperthyroidism
5	Child and adoles-cent groups	Augmented infant death, Retarded mind and physical growth
6	Neonate group	Augmented neonatal deaths, Perinatal hypothyroidism, Retarded mind and physical growth
7	*In utero*	Abortions, Stillbirths, Neurologic cretinism, Inborn anomalies, Psychomotor defects and Myxedematous cretinism

The major reason for thyroid dysfunctions reduces intake of iodine. Approximately 1/3rd population resides

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in the iodine deficient areas in the world [4]. The amount of iodine intake shows various thyroid disorders and is presented in the Table 1. Literature from developed countries emphasized the prevalence of various thyroid disorders [5]. About 50, 15, 10, 5 and 3.5% of western population are suffering with thyroid disorders like microscopic nodules, palpable goiters, altered levels of thyroid-stimulating hormone, overt hypothyroidism or hyperthyroidism and occult papillary carcinoma [5].Though countries all over the world initiated the control programmes for thyroid disorders (iodine deficiency diseases), but still many parts of the world its occurrence is reported. Creating awareness among communities living in the different parts of the world is most important. Hence, the present review focused on thyroid disorders, its epidemiology and preventive methods.

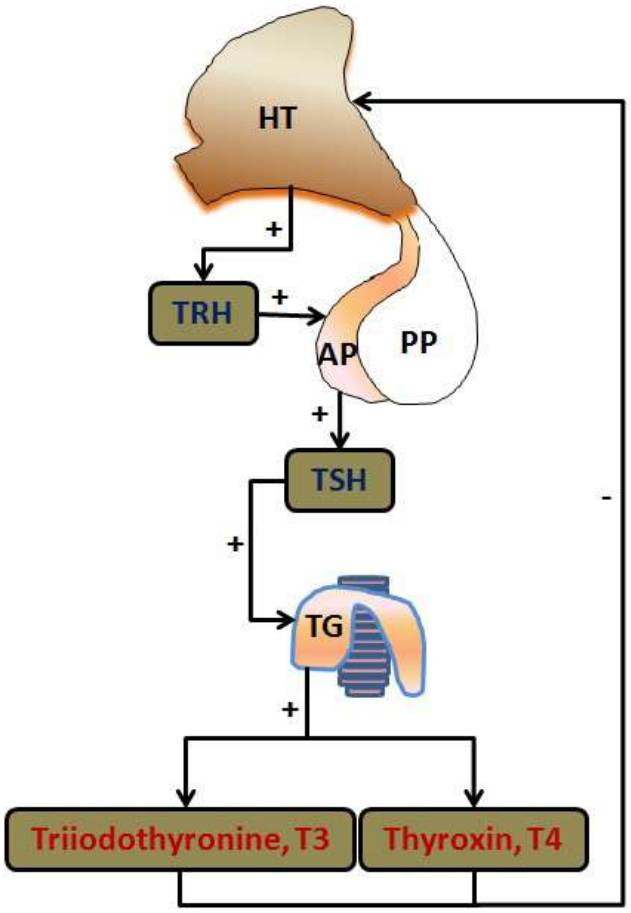

Figure 1. The synthesis and regulation of triiodothyronine and thyroxin from the thyroid gland (TG)

Note:

Where HT: Hypothalamus; AP: Anterior Pituitary; PP: Posterior Pituitary; TRH: Thyrotrophin Releasing Hormone; TSH: Thyroid Stimulating Hormone. '+' and '-' denotes positive and negative regulation respectively.

Table 2. Iodine intake/deficiency and thyroid disorders

S.No.	Thyroid disorder	Diseases associate with
1	Graves' disease	Thyrotoxicosis/ Hyperthyroidism
2	Toxic nodular goitre 1) Toxic adenoma 2) Toxic multinodulargoiter	
3	Thyroiditis	
4	TSH secreting pituitary tumors	
5	hCG induced hyperthyroidism (gestational and trophoblastic disease associated)	
6	Iodine induced hyperthyroidism (iodine and Amiadarone)	
7	Thyrotoxicosis factita	
8	Goitrous hypothyroidism (Hashimoto's thyroiditis, iodine deficiency and lithium)	Hypothyroidism
9	Congenital hypothyroidism	
10	Atrophic hypothyroidism (Hashimoto's thyroiditis and post ablative)	
11	Central hypothyroidism III. Euthyroid i) Diffuse nontoxic (simple) goitre ii) Nodular thyroid disease (solitary nodule and multinodular) iii) Thyroid neoplasia (follicular adenoma and thyroid malignancy)	
12	Thyroiditis (inflammation in thyroid gland) Postpartum thyroiditis (in women after delivery)	

2. Thyroid Gland, Hormones and Disorders

Small, bilobed structures located in the neck are called thyroid gland (20-25 g) secrets minor (7%) triiodothyronine (T3) and major (93%) thyroxin (T4) hormones from its follicles. It is clear from Guyton and Hall [1] that the biological activity of T3 is 3-5 folds higher than T4. Both of these are much similar to each other in holding two tyrosine amino acids. The difference between these two is holding three iodine atoms in T3 and four iodine atoms in T4 [6]. The regulation of synthesis and secretion of T3 and T4 hormornes is under the control of thyrotrophin (also called thyroid stimulating hormone; TSH) released from the anterior pituitary, which is stimulated by tripeptide releasing hormone/thyrotrophin releasing hormone (TRH) from hypothalamus [1] (Figure 1).

Thyroid hormones, virtually affects each and every cell in the body by stimulating the glucose oxidation enzymes, thereby increases body heat and basic metabolism. The high levels of thyroid hormones increase in the basic metabolic reactions 60 to 100% in body cells, which ultimately increases in the rate of energy production from food, transcript thereby translation and protein degradation. Even the thyroid hormones stimulate many other endocrine hormone synthesis and release. According to Elaine and Maieb [6] fetal growth and development is promoted by T3 and T4 thyroid hormones. The variations in the levels of TSH were identified in thyroidal and non-thyroidal disorders. Low levels of T3 and T4 an indication of primary hypothyroidism induces the release of TSH and increases its serum levels. Whereas in hyperthyroidism elevated T3 and T4 levels through a negative feedback mechanism suppresses the serum TSH levels. In children,

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hypothyroidism reduces skeletal growth (dwarfism) and hyperthyroidism excessive bone growth (gigantism) besides mental retardation in throughout their life in both the cases [1]. The dysfunction of the thyroid gland is associated with various diseases and is mentioned in the Table 2.

Moreover the diagnosis of thyroid disorders is difficult. Pretreatment of these disorders is uncommon due to difficulty in diagnosis of its pre and early stages. Though the simple blood test can determine the levels of thyroid hormone, doctors are suggestive to do this due to the symptoms of this disorder are mimicking with many other diseases. In case of subclinical thyroid malfunctioning is found with no or few hypothyroidism symptoms. Mostly the blood levels of 0.5 to 5 mIU/L TSH were found normal and can be called 'euthyroid', beyond these levels considered as malfunctioning of the thyroid gland. A person with a condition of low/over thyroid function determines the hypo/hyperthyroidism or Grave's disease/ Hashimoto's thyroiditis the autoimmune diseases of the thyroid. Thyroid autoimmune disorders play an unpredictable role in thyroid functioning (Table 3). The best method identifies and treat hyper or hypothyroidism is to maintain periodical blood test reports along with the patient's personal and symptoms history and risk factors.

Table 3. Thyroid autoimmune diseases and their symptoms

S.No.	Antibodies of autoimmune thyroid disease	Symptoms	References
1	**Antibodies of thyroid stimulating hormone receptor**	**Identified in Hashimoto's and Grave's cases with 10 and 90 % respectively.**	[7]
2	**Antibodies of thyroid peroxide**	**Identified in Hashimoto's and Grave's cases with 95 and 70 % respectively.**	[8]
3	**Antibodies of thyroglobulin**	**Identified in Hashimoto's and Grave's cases with 80 and 50 to 70 % respectively.** Elevated in thyroid cancer.	[9]

3. Epidemiology of Thyroid Disorders

The rate of prevalence of hyperthyroidism is increasing day by day. Epidemiology says about 1/3rd of the Indian community is suffering by hyperthyroidism and among these 39% are suffering with goiter [10]. Reported 2.7 and 0.23% of UK women and men respectively is identified with hyperthyroidism [11]. The cases with hyper or hypothyroidism became common in the United States of America. About 12% of people are suffering with the disorder of the thyroid and is increasing drastically though the US Government has taken steps to consume iodized salt throughout the country. The increased occurrence of diffuse goiter is reported in women of pre-menopausal stage and its ratios 4:1 in women and men [12]. The occurrence of hypothyroidism was also reported in countries like Norway, Japan, Denmark and Sweden [13-17]. About 2% of women are suffering with hypothyroidism during pregnancy [18,19]. However still many places in the each and every corner of the world need to be surveyed for exact statistics and prevalence of hypothyroidism.

4. Treatment Methods of Thyroid Disorders

The thyroid Hashimoto requires treatment only the patients who are not having autoimmune antibodies against it. In this case, antibodies are produced for longer periods (years) and facilitates the release of sufficient amount of thyroid hormones. However, it is clear from the literature about more than 80 among 100 suffering with hypothyroidism are needed treatment [20]. The condition where over or low production of thyroid hormones produced are need to be corrected by supplementation of thyroid correction medicine. Thyroid replacement medication is required in case of hypothyroidism and controlling medication for hyperthyroidism. The surgery and/or oral iodine supplementation is the alternative methods for hyperthyroidism. The regulation of cholesterol biosynthesis,the rate of degradation and its receptors are under the control of thyroid gland secretions. The risk of cardiovascular diseases in hypothyroidism patients is high along with body weight. High blood pressure due to increased lipid profiles (LDL and cholesterol) along with homocysteine and C-reactive protein an inflammatory marker is common in hypothyroidism [20]. This condition can be rectified by normalizing the thyroid gland secretions by medication and other means [21].

Whatsoever, the balanced diet with medication can correct the thyroid gland secretions. A number of food components are detrimental to thyroid disorders and they correct the thyroid functions. The balanced diet with the help of a physician can set right the body condition and thyroid function. It is not at all suggestible to decide the own diet by the patient suffering with thyroid disorders. The key nutrients must be included in the diet are iodine, vitamin D, vitamin B12 and selenium. Iodine deficiency is the primary cause of thyroid dysfunction worldwide. The supplementation of iodine play pivotal role in maintaining thyroid function, since it is a component of thyroid hormones (http://ods.od.nih.gov/factsheets/Iodine-QuickFacts) [22]. Iodine supplementation through iodized salt is the best way and is used in all kinds of food making.Anyhow the intake of iodine has its own limitations. Low or high intake of iodine leads complications like Hashimoto's disease [23]. Since the low levels of vitamin D identified

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in all most all patients holding Hashimoto's and Grave's disease, it is found to be one of the causes of thyroid disorders [24]. The richest source of vitamin D is morning and evening sunlight, besides this milk, dairy products, fatty fish, eggs and mushrooms are the potential dietary sources. The other vitamin showing effect on thyroid dysfunction is B12. Its deficiency was identified in thyroid disorders. The dietary source for vitamin B12 is salmon fish, muscle meat, liver, mollusks and sardines. The other food component, the heavy metal selenium a component of thyroid hormones biosynthetic enzymes play crucial role in thyroid function [25]. It is clear from the studies that selenium rich foods such as tuna fish, lobster, crab and Brazil nuts are increasing the selenium levels and corrects the thyroid dysfunctions [26].

There are certain foods can be avoided by patients of thyroid dysfunction. For example the foods release goitrogens are capable to worst the thyroid disorders. Most popularly the vegetables belong to Cruciferae like cauliflower, cabbage and broccoli release goitin (IMFNB) [27]. Isoflavone rich foods (soya based diet) are also rich with goitrogens. In most of the studies the role of goitrogenic foods in thyroid dysfunction is still not clear. The diet of gluten free grains and millets reduces the thyroid function even with iodine rich foods [28]. Another good method to control thyroid dysfunction is by doing systematic exercise every day with the suggestion of a physician. The over or abnormal exercise may cause side effects.

5. Conclusion

The change in the weight, cardiovascular risk, fatigue, change in mood and upset of gastrointestinal are the inimitable challenges identified during thyroid dysfunction. The methods of treatment and diet can alter the thyroid malformations. The iodine, selenium, vitamin D and B12 rich diets are helpful to reduce thyroid dysfunction along, avoiding goitrogens rich, millets and gluten free foods. Proper exercise is an alternative to maintain a healthy body and its condition. Here, conclude by suggesting for patients of thyroid disorders doing all together may normalize their health. The medication along with iodine, vitamin D, B12 and selenium rich diet with low goitrogens and proper exercise may normalize thyroid gland secretions and helps maintaining better health.

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ARTICLE

New Paradigm in Nutrition Practice - Initial Findings From Ntuitive Software

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ABSTRACT

Objective: Nutrition practice in India has generally been confined to pen and paper with little use of algorithms and technology. Nutritionists in practice find it difficult to go beyond macronutrient analysis for dietary intake or diet plans. Since nutrition practice requires lot of data processing, we decided to develop software to aid in these calculations and to empower nutritionist with technology enabled scientific practice using software. Method: Ntuitive software was developed by a team of nutrition experts and technologists over a period of 18 months. Data for nutrient values was sources from IFCT 2017 [6], RDA's were taken from ICMR guidelines and growth charts from IAP publications [7]. Design and coding of the software was done inhouse. Ntuitive database has over 8500 recipes and packed foods and has most of the national and international cuisine items. The software module enables client / patient management, detailed profiling, recording anthropometric data and plotting on WHO and IAP growth charts, recording food allergies and medical condition. The dietary recall be it one day, three day or seven day can be easily recorded and analysis of nutrients can be obtained for the same. The software is hosted on Amazon Web Server and applied as SAAS platform for practice. Result: 800 children and adults underwent analysis and consultation using Ntuitive software. All 189 micronutrients could be calculated using the software and deficiency or excess quantified when compared with RDA. Conclusion: Nutrition practice can be made easy and technology enabled keeping in mind scientific standards. This helps in data collection not just in macro nutrients, but also in micronutrients.

1. Introduction

Nutrition sector is a continuously emerging sector and in today's world technology is rapidly making its way into dietetics practice. It is a fact that technology can radically alter the way nutritionists connect with their clients, discover new clients, and contribute to positive nutrition care. Technology can be a crucial asset in nutrition care if utilised to practice effectively in clinical or hospital settings either at an OPD, IPD or even at a private clinic level.

In many foreign countries like USA, Australia, UK, New Zealand, Canada etc nutritionists have aid to softwares which enhances their skill and are able to deliver better guidance. Nutrition practise in India is majorly limited to calculations using paper and pen. Appointments

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of clients are generally managed either through mail or phones or by maintaining diaries and it becomes difficult to keep a record of them. Even, medical records and follow up of patients at large are maintained on papers. Nutritionists utilise a major portion of their time maintaining and tracking data of their clients. Also, keeping a track of this huge amount of data becomes difficult when practice increases multiple fold.

With diverse flow of patients and clients, it becomes tedious and time consuming to calculate all the nutrient requirements, infact, even macro nutrients for each patient. The dietitian has to be all over google and refer different sources for obtaining authentic information with regards to specific nutrients found in food or nutrient rich specific foods. Easing out the calculations, hassle-free management of clients as well as finding authentic information under one roof will definitely be a boon to the nutritionists as that will save lots of time and resources and help them channelise their energy in providing efficient nutrition care to their clients.

Keeping this in mind, Ntuitive software was created by an expert team of nutritionists and technologists. After reviewing softwares like ESHA [2], Nutrium [1], and NutritIO [3]; it helped the team to develop the software strategically. Taking the international software ESHA [2] as a base, the team could start off with the basic designing of the software keeping the Indian scenario in mind. Nutrium helped in further developing the design which enhanced the way a nutritionist could function on the software [1]. NutritIO, as well became useful to bridge the gap between patient and nutritionist by helping to understand how to converse with each other [3].

Ntuitive is a perfect combination of nutrition and technology simplifying the work of multi-tasking nutritionists. Though similar softwares are present in foreign countries, with diverse culture, eating habits and food found all over India, there was a need to create a software catering to Indian data.

This software serves the purpose of practicing complete nutrition care at a click. Apart from processing a lot of saved data for providing nutrition care, the nutritionist is also able to utilise the same data in doing advanced researches.

2. Methodology

Looking at the urge of creating an all-rounder tool for the nutritionists, a meticulously planned and fully functional software was developed by a team of nutrition experts and technologists over a period of 18 months. Coding language used by technology department were HTML, CSS, Angular JS, Ruby on Rails, PosGres, Java Script, GitHub and AWS Cloud. Data was derived from authentic sources like IFCT (Indian Food Composition Tables) 2017 (for nutrient values) [6], Recommended Dietary Allowance's were taken from ICMR (Indian Council of Medical Research) guidelines and growth charts from IAP (Indian Academy of Pediatrics) publications [7] and World Health Organization [8].

The module of the software was designed to work in perfect coordination with the process of nutrition consultation .The various sections which were designed included:

2.1 Appointment Calendar

The software ensures smooth tracking of upcoming appointments as well as follow-ups and helps in managing clients easily across multiple clinics. The nutritionist can keep a track of patients or clients consulted in different clinics by creating multiple clinics. The patients can be classified into different clinics based on their medical condition.

It ensures that the nutritionist never misses any of the scheduled clients. Through the appointment calendar, it becomes a matter of seconds to handle appointments efficiently.

2.2 Client Management

This shoots out an easy accessible list of clients. Also, helps to segregate clients as per clinics. This functionality is quite useful in searching for a specific client from a huge list.

2.3 Detailed Profiling

Basic Information like Gender, Date of Birth, Height, Weight, BMI (Body Mass Index), Plotting on growth charts, Preferences, Allergies and Medical conditions can be recorded using this feature of the software. Specific Questionnaires can be prepared as per the client or the medical condition handled and utilized accordingly. This information could include fluid requirement, biochemical parameters, temperature, etc. and would be saved in the profile of the client. Multiple such questionnaires can be created which eventually can be very well utilized for analyzing data or could prove beneficial during consultation.

2.4 Recording Food Intake

There is an easy to use calendar interface to maintain food, water and activity records of the client as per date and time. This recall can be for one or multiple days. The clinical or other observations can also be recorded in the notes section for additional information to be associated

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with the client.

2.5 Configuring Recommended Allowances (RDA) of Nutrients

There is an option to choose appropriate and patient specific recommended requirements from the pre-listed formulae for both macro nutrients as well as micronutrients. Nutrition Atlas was referred to understand the range, sources and deficiency of each nutrient [5]. Disease specific nutrient requirement formulae can also be configured easily. The software allows the nutritionist to change the requirement as and when required. The default requirement adheres to Indian Council of Medical Research (ICMR) recommendations.

2.6 Analysis- Day-wise/Meal-wise of the Food Intake

Nutritionists spend most of their time in calculating micronutrients and disease specific nutrients. All 189 nutrients mentioned in IFCT 2017 [6] and NIN (National Institute of Nutrition) [4] is calculated within seconds in Ntuitive. Multiple day recalls can be saved in Ntuitive and analysis can be obtained in a click. In the analysis section, the nutritionist is not only able to understand how much requirements are being met, but the nutritionist can also check the specific food sources from which the nutrients are derived. Detailed nutrient intake analysis across months, weeks, days, meal-times and food items is possible through this section. One can also view aggregated energy distribution charts for all or selected days. There is an option to create custom templates of nutrients for targeted specific analysis. The analysis can also be shared with the client through a shareable link.

2.7 Advanced Diet Planner

It is an experience to create diet plans adhering to RDA by adding foods or nutrient dense ingredients with real time charts. The nutritionist can make multiple menu plans (day-wise) and also meal-wise plans and save it as templates. These could be easily re-used in different combinations and permutations to create unique plan for each client without spending time on calculations. While creating these plans, the nutritionist gets a visual display of how much recommended requirements are met. The nutritionist have an option to provide 7 days diet plan to the clients or generic plans keeping in mind the convenience of the client.

2.8 Curating Specific Guidelines

Nutritionist can make guideline templates using this feature of the software and save it for future use. These guidelines can be based on specific medical condition or some general instructions which need to be given to clients can be generated. Creating multiple templates for guidelines make the consultation speedy. These guidelines could be integrated directly in Client Consultation Interface.

2.9 Client Consultation

For consultation, a special interface is linked which can be utilized by the nutritionist to explain how much recommended requirements are being met. The nutritionist can also show client or patient the sources from where the nutrients are being consumed. This gives the clients a visual representation of their food and nutrient pattern and helps the nutritionist to self-educate the clients.

2.10 Sharing Reports with the Client

Nutrient reports can be generated based on the food intake documented and can be shared to the clients either by sending a message link or on email.

2.11 Information Centre

The most time consuming task is finding which nutrient is present in particular food ingredient or what are the richest sources of a particular nutrient. Ntuitive is a pool of such vital information and it's just a matter of few fractions to browse for the required data. This information is taken from IFCT 2017 [6] and NIN [4]. The nutritionist can find the rich food sources of a particular nutrient or all nutrients present in a particular food ingredient.

2.12 Recipe Database

Ntuitive database has over 8500 recipes and packed foods and has most of the national and international cuisine items. The ntuitive database has recipes which are all standardized recipes created using nutrient values from ICFT 2017 [6] and NIN [4]. With diversity in eating habits, recipes from all over India are found and are being added on day to day basis. The nutritionist can also create new recipes as per their need and share them with others. The software consists of many international ingredients and recipes which are sourced from USDA (United States Department of Agriculture) [9].

The software is cloud based, meaning all the data entered in the software is stored in Amazon Web Server and applied as Software as a Service (SaaS) platform for practice. Hence, there is no limit in saving or creating the data and the data remains safe.

Also, each nutritionist can have their own account.

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Each account information remains confidential and is not shared without the permission of concerned nutritionist.

The software can be used in multi-speciality hospital, with multiple nutritionists functioning and using the software. In this scenario, the chief dietitian can have all the rights to assign the clients to other nutritionist of the team.

After creating the software, we decided to check the functionality and feasibility of the software by conducting nutrition consultation for a sample size of 500 adults and children. The sample populations were residents of Mumbai, Thane and Navi Mumbai. The software was fruitfully utilized right from booking appointments to maintaining the patient profile, to feeding in the food intake as well as for doing final nutrient analysis and final consultation with the clients.

3. Results and Discussion

Nutrition consultation was conducted for a sample size of 500 children and adults using Ntutive Software.

Listed below are the detailed set of observations that we made about how the software was utilized step-wise to manage the entire process of consultation for the sample size mentioned.

3.1 Managing Appointments

The software was first used to manage appointments and first visit of the client. 500 clients could be easily managed using the 'manage appointment feature' of this software. Segregating the clients as per the schools or the clinics was quite easy. One could also search for a specific client easily either by putting up a contact number or search could be even performed by entering the first/last name of the client for locating the client account. Appointments could be added for current date as well as future dates. It thus, proved to be an easy tool to manage the appointments in a systematic manner. Listed below in Figure 1 is the appointment screen wherein all clients could be seen under a respective activity/clinic.

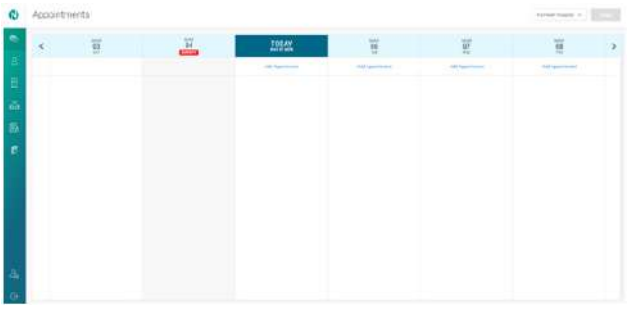

Figure 1. Appointment schedule

Once an appointment was booked, they were seen as shown in figure 2

Figure 2. Scheduled appointments view

With client management as shown in figure 3, it was convenient to visualise the total number of clients. It even gave details of the last appointment and had a tab to schedule new appointment if follow-up was advised for the same client/patient.

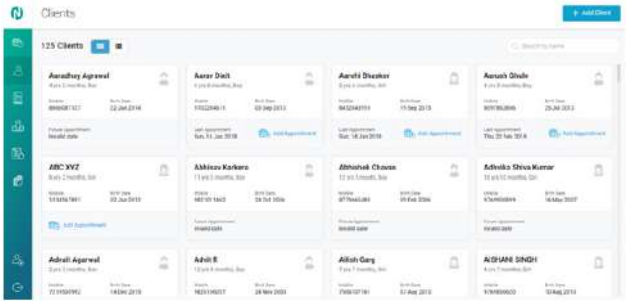

Figure 3. Current data (personal details of the clients/patients)

3.2 Client Profiling

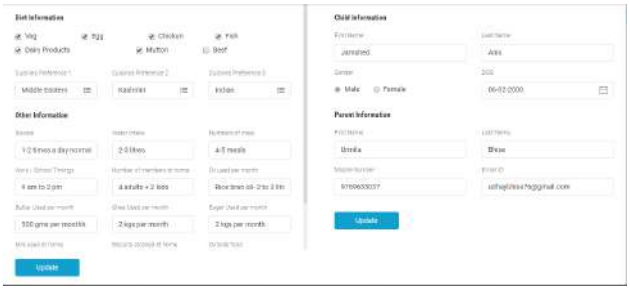

Figure 4. Basic Profiling

Basic profiling information like food and cuisine preferences was recorded. General details like bowel movements, water intake, and monthly consumption of oil, ghee, sugar and butter were also listed. Regular schedule of the clients were recorded along with eating habits.

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Figure 5. Growth charts

Height, weight and BMI of the client or patient were recorded. For pediatric age group, 0-5 years, the height, weight and weight for height were plotted on the World Health Organization (WHO) [8] growth charts and clients between 5-18 years were plotted on Indian Academy of Pediatrics (IAP) [7]. These formulas were in the database which helped achieve easy calculation of the same. Ideal weight of the child was obtained by back calculation of Body Mass Index (BMI) on the system itself and the ideal weight of adults, was obtained by Broca's Index formula. There was a provision to enter height and weight for multiple visits.

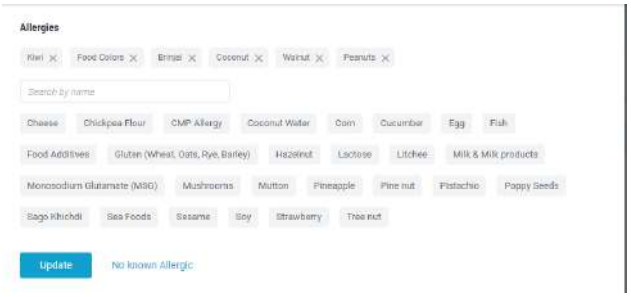

Figure 6. Selection of allergies

Food related allergies also could be selected. This allergies were highlighted as red alerts in the diet plan, which indicated the nutritionist to avoid the recipe having the allergic ingredient while making the diet plans.

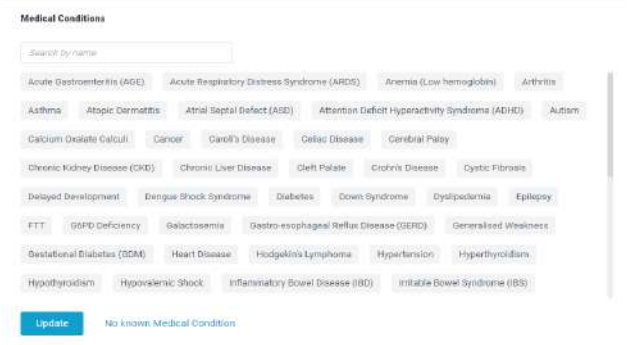

Figure 7. Selection of medical condition

Medical condition can be selected and added as a part of basic profiling.

Figure 8. Selection of questionnaire

Questionnaires could be created and saved with reference of disease or medical condition name. The questionnaire could have biochemical parameters, intake and output questions etc. Below is the image of questionnaire created for fever template.

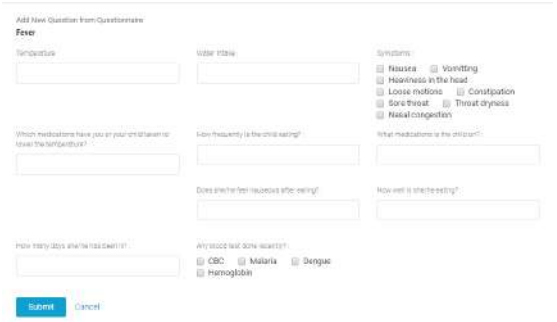

Figure 9. Condition specific questionnaire

Multiple sentences, paragraph, multiple choice can be added while making the questionnaire. This feature assisted us with collecting more information about the client.

3.3 Maintaining Client Food Diary and Notes

The software was quite user-friendly in terms of entering the food recalls for the sample size chosen for multiple days. We took recalls majorly for 7 days, however depending upon the data received, some clients even chose to give data only for 3 days or 5 days. Day-wise meal entries, water intake and activity data for the clients was added using this interface section of the software. There was an option to enter a date, time as well as select a specific recipe from the list of recipes found in the master database. One could choose the quantity and the portion size of the food consumed.

Figure 10 shows steps on selection of a date and selecting from the option of adding meal, water or adding activity for the client.

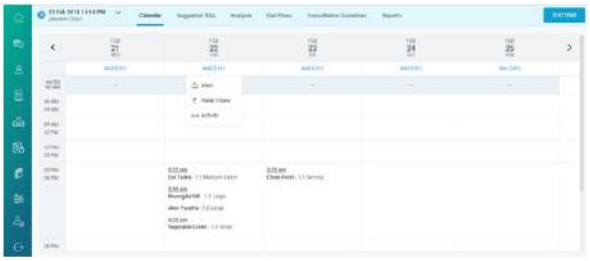

Figure 10. Food diary calendar view

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Further clicking on the meal option, another pop-up box (as shown in Figure 11) to fill the details of the timings, food consumed and the portion size was available. The steps were repeated to add the intake for a full day/ multiple days (as shown in Figure 12)

Figure 11. Selection of food item to fill food diary

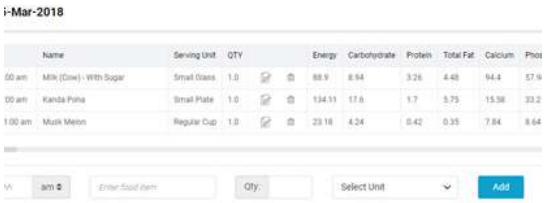

Figure 12. Recording food data

This is how a calendar looked (as in Figure 13) after filling in meal details for 4 days. One could go back and edit meal/water/activity options as per need.

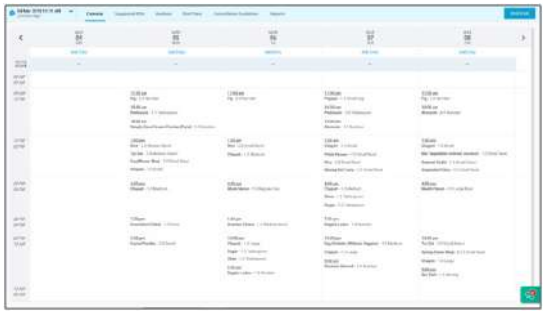

Figure 13. Food diary overview

We could also add different notes about client, their meal patterns and specific requirements in notes as shown in figure 14 below. These notes were quite helpful to add on more information about the client that was utilized appropriately during the diet planning as well as the consultation process.

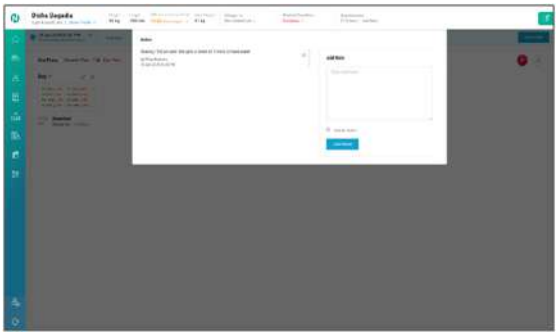

Figure 14. Notes section

3.4 Working on Formulae/Suggested RDA

The default formula set in the database was as per RDA. Suggested RDA is seen in the analysis while comparing client's meal intake. However, formulas/ RDA could be changed/edited as per client case/medical condition by clicking on edit as shown in Figure 15. Being easy to edit the formulae made it ever more easier to generate the analysis at the click of a button.

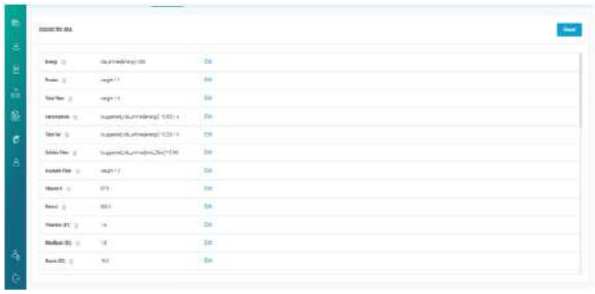

Figure 15. Suggested RDA

3.5 Analysis of the Food recall

Once a multiple day recall of the client is taken, the analysis per day was calculated under Analysis tab. The calculations were based on food items entered during recall. The percentage shown in figure 16, next to the intake, indicated the deficit or excess quantity of the specific nutrient. This analysis was shown for all the 189 nutrients listed in IFCT 2017 [6]. This section could help us keep a tab on the range of nutrients coming from the diet on a daily basis.

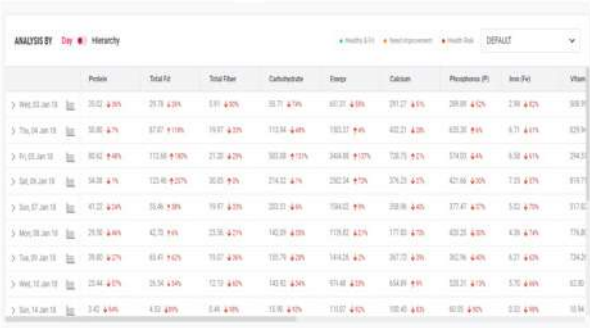

Figure 16. Food diary analysis

Further this could be divided also into meal wise and food wise calculation on clicking the drop-down arrow. as shown in figure 17. That helps the nutritionist to study meal wise and food wise distribution of nutrients.

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Figure 17. Meal wise analysis

The nutritionist could also select the number of days and find out how much requirement the client is meeting. Only specific days could also be selected from a whole lot entered to analyze nutrient ranges in a particular period.

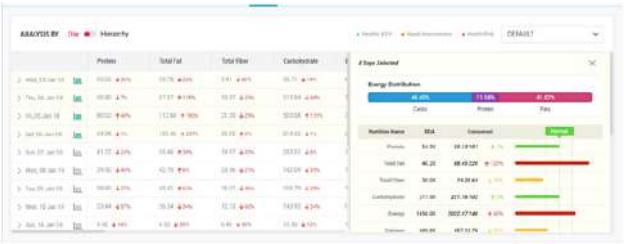

Figure 18 Analysis in comparison with RDA

The graphical representation can be obtained for one or more days. Figure 18 shows graphical representation for 4 days.

3.6 Diet Planning

Effective diet Plans could be created quite easily for the clients along with real time correlation with RDA using Ntuitive.

Meal wise diet plan entries could be done with suggested individual food item along with serving size and simultaneously nutrient's value could be checked for individual food item compared to RDA value as shown in figure 19.

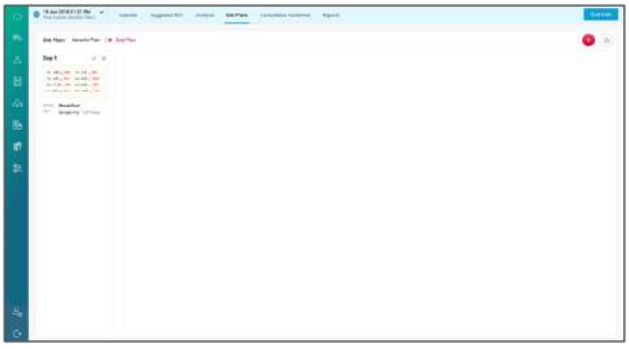

Figure 19. Creating Day wise diet plans

Diet plan could also be customised based on disease specific nutrient calculations by clicking on 'Default' (shown in figure 20).

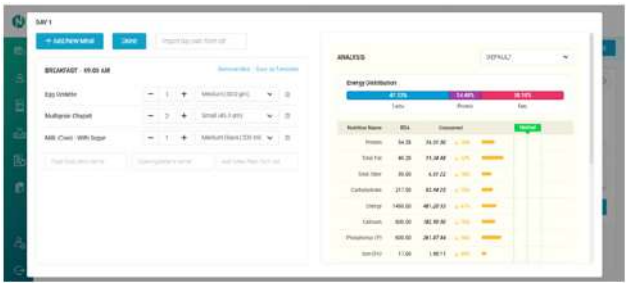

Figure 20. Entering meals in the diet plan (Left) and nutrients values (right)

Meal plan templates could be saved by making a meal plan and then saving it as 'Save as Template' along with adding a name to the meal plan. Examples of template name can be Protein Rich Breakfast, Low Carbohydrate Snack, etc. List of saved meal plans could also be viewed as shown in figure 21.

Figure 21. Sample Meal Plans

Entire Day Plans could be created and saved as templates too. To make a new day plan, click on 'Add Day Plan' and give the desired name of the template as shown in figure 22. Example- Lactose Free Diet, Ketogenic Diet, Low Carbohydrate Diet, etc.

Figure 22. Sample Day Plans

The option to save Meal Plans and Day Plans as template was a boon as one could easily replicate individual client based diet plans extracting these saved templates.

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Diet plans made could be saved in .pdf format and mailed to the client or could be printed and given to the client as a hard copy.

3.7 Curating Consultation Guidelines

This section helped the nutritionist to prepare structured guidelines based on individual nutrients. These could be tailor-made for the specific client based on the food diary analysis, food habits, activity level, food allergies/intolerances and medical conditions, if any (collated during basic profiling).

Guidelines could be created either by creating templates and saving them to edit later and utilise specific to case of the client (as displayed in figure 23)

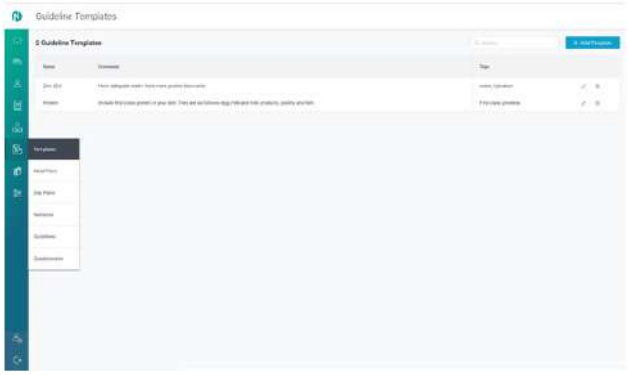

Figure 23. Guidelines templates

or they could be directly written in the client profile after analysing the report (as in figure 24)

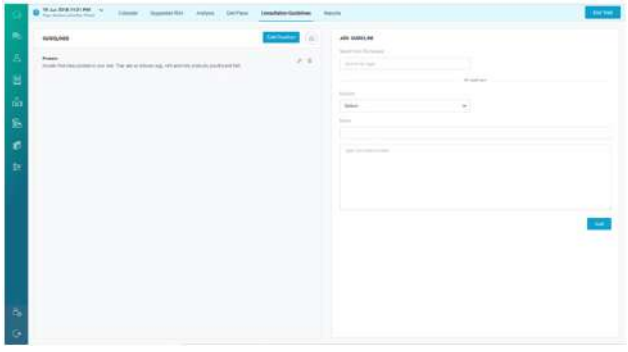

Figure 24. Final Guidelines

These saved guidelines can be referred to during one-to one consultations as they are integrated directly in client consultation interface or could also be shared with the client by clicking on 'Print icon' option at the top of the tab as seen in the figure 24.

One could also select individual nutrient and write guidelines pertaining to that nutrient by clicking on 'Nutrient' option to create nutrient specific guidelines as shown in figure 25 and figure 26.

Thus, a lot of time was invested in creating templates and later quickly editing them to make them more client specific.

Figure 25. Nutrient wise guidelines

Figure 26. Nutrient wise guidelines

3.8 Generating Reports and Client Consultation Interface

Reports tab (refer figure 27) was one of the most important tabs since it showed the total nutrient analysis of a client's recall. This tab helped to understand which macronutrient or micronutrient the client is deficient or excess with. On the basis of these findings, one could create guidelines or new diet plans for the client.

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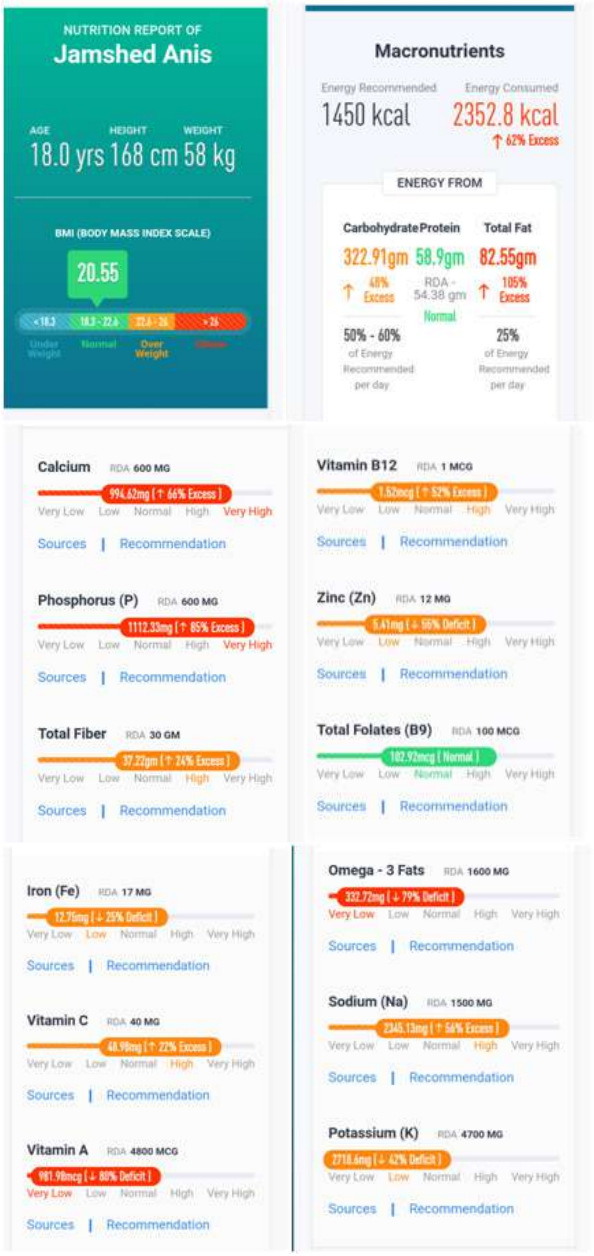

Figure 27. Mobile report

If any of the nutrients displays deficit/excess, one may choose to view the sources of food from the individual's diet which contribute to that nutrient. The values or percentage of excess and deficit of each nutrient are set by referring values given by ASPEN guidelines. These nutrient values are derived from the food consumed by the client, taking into consideration the absorption of each nutrient in different food groups.

To view the individual nutrient sources, click on the right side of the report which opens up a consultation interface as seen in figure 28 and 29 to check which foods contribute to which amount of the selected nutrient.

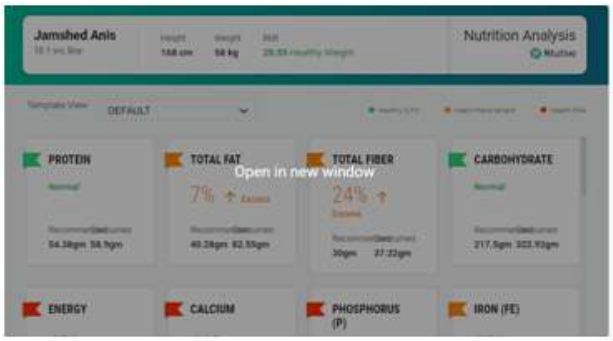

Figure 28. Nutrient wise consumed sources

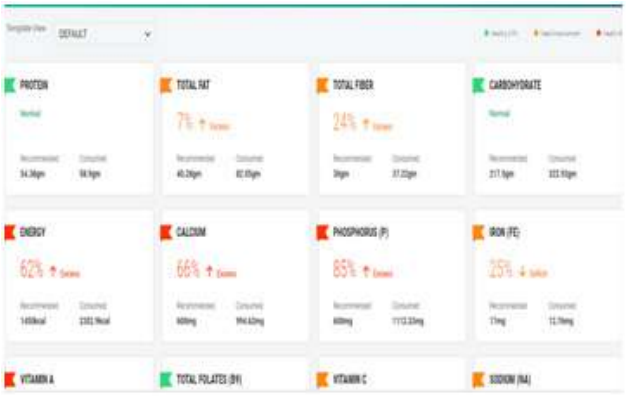

Figure 29. Nutrientwise Food Sources

One can also choose the nutrient whose sources want to be viewed by clicking on the nutrient. Figure 30 shows the sources of nutrient. This can be easily transmitted to the client during consultation. This gives the client a reality check of the food sources and their exact nutrients being consumed which further assists in smooth consultation process and making the client understand where the diet should be exactly worked on.

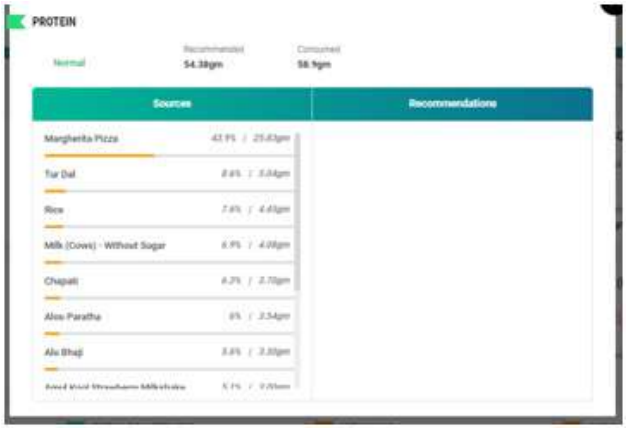

Figure 30. Food sources

Disease specific nutrients and nutrient related sources could also be viewed using the 'Template View 'option shown in figure 31 on top of the sources screen to select

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a specific disease and view only the disease specific nutrient and nutrient related sources. This certainly took off a burden off our shoulders to easily concentrate on more case-specific nutrients specially for certain disease related clients from the huge sample size

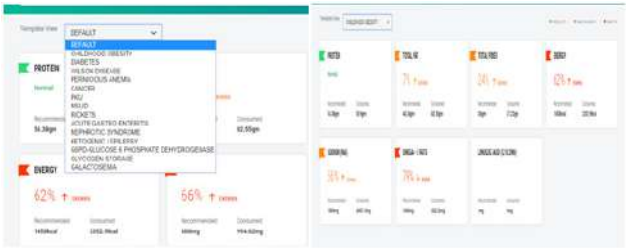

Figure 31. Condition Specific Nutrients

3.9 Knowledge Centre

This section could also be referred to as information pool since it includes sources and RDA of definite nutrients as well as specific ingredients all at one junction. Select a specific ingredient or nutrient to find more about it at the click of a button.

(1) Nutrient Knowledge Centre:

Total 189 nutrients are listed in knowledge centre as seen in figure 32

Figure 32. Knowledge Center

Each nutrient has information listed about its chemical nature, functions, rich food sources, cause of deficiency, treatment, toxicity, digestion and absorption, signs and symptoms, RDA for different age groups and ingredients with grammage of that specific nutrient as seen in figure 33.

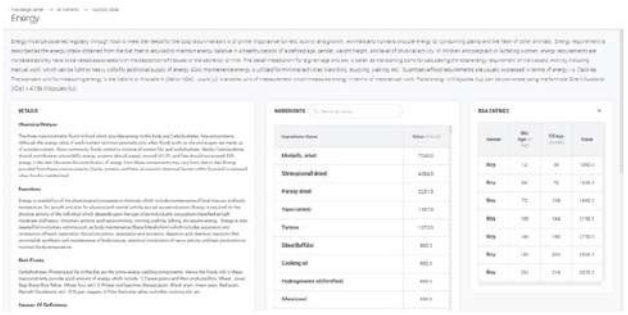

Figure 33. Knowledge center

(2) Ingredient Knowledge Centre:

Around 800 ingredients from IFCT [6], NIN [4] and USDA [9] are present in the ingredient sheet. A gist of ingredients can be seen in figure 34.

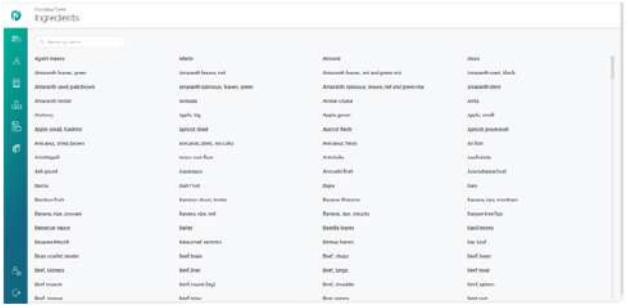

Figure 34. Knowledge center

Each ingredient as shown in figure 35 displays information about the nutrient content, summary, benefits, caution, recommended in and not recommended in. Along with it, a list of recipes present from the master recipe database which has the ingredient is displayed.

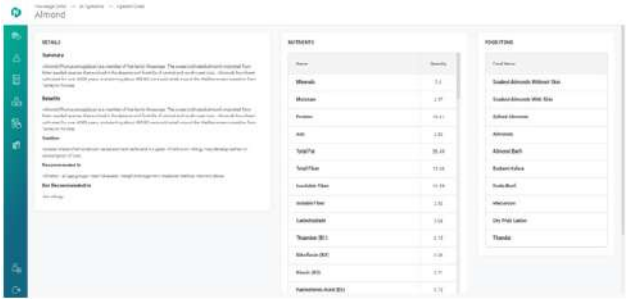

Figure 35. Knowledge Center

We could calculate all 189 micronutrients for 500 children and adults who underwent analysis and consultation using the functionalities of these Ntuitive software and deficiency or excess could be quantified when compared with RDA.

With the help of the functionalities of the software, the data could be accessed at any point of time and the nutritionist got a chance to view the entire case. The most tedious and time consuming tasks saved on quite an amount of time with the help of the software, especially the calculations for the diet plan and the client consultation interface which enhanced the consultation quality.

4. Summary and Conclusion

Nutrition practice can be made easy and technology enabled keeping in mind scientific standards. A walk-through of the entire software makes one realise how dietetics practice can become much easier. Quality amount of time can be devoted by the nutritionist in providing nutrition care to the clients rather than spending time on

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calculations or maintaining records. This not only helps in easy data collection of macro nutrients, but also of micronutrients. Managing a huge chunk of clients and maintaining accessibility to their information is much easier with this software coming in practice.

Loaded with information, the functionalities of this software definitely makes it a ready-reckoner for every working nutritionist in the dietetic fraternity as it can be used to enhance the knowledge and skills of the nutritionist. With the practical difficulties faced by the practising nutritionist, this software is like a boon saving time, enhancing the skills as well as taking the dietetic practice to a different level.

With the help of the software, the Ntuitive was successful in testing the nutritional assessment of 800 children and adults. The time spent on taking recall and getting the nutrition analysis was merely few minutes. All 189 nutrients were calculated with statistics of how requirements are being achieved. Based on their analysis weekly plans were provided to clients which were specific to their needs and customized. As the nutritionist can view the requirements achieved while planning, it became very easy to create multiple plans for them. Lastly, during consultation, with technological appeal, it became easy for client to understand where are they lacking and where they need to improve.

Thus the goal of improving the lifestyle and medical condition was achieved with easy, innovative and scientific aid of Ntuitive software.

Acknowledgement

The need of technology for nutrition was always there, but it would not have been possible without the vision of CEO Dr Arbinder Singal, Fitterfly technologies and Mr. Shailesh Gupta. A heartwarming thank you to Mr. Jayesh Sawant, Technology head and his team for leading the technology development. With the help of Nutrition team, the software could be tested and launched for mass practice.

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ARTICLE

Relation of Urobilinogen Presence Resence in the Selection of Food (SALTY or Sweet)?

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ABSTRACT

The total amount of 100 subjects were contributed in this review and all were the students who are studying in Bahauddin Zakariya University Multan, Pakistan. The bilirubin is metabolized in the gut which produced a colorless pigment known as urobilinogen. It is by-product of bilirubin which is used to break down the red blood cells in hemolysis. Salty food contains usually more minerals and vitamins while sweet food is enriched with carbohydrates, water and many other fats soluble substances. Every person has a unique taste according to their taste buds. A questionnaire based was made to relate the urobilinogen with the food (salty or sweet). Urinalysis is a method which is used to measure the urobilinogen in urine. It was concluded that there is a scientific relation between the presence of urobilinogen in urine with eating of salty or sugary food. Table no. 1 represents that urobilinogen play important role in the choice of eating either salty food more or sweet.

1. Introduction

The bilirubin is metabolized in the gut which produced a colorless pigment known as urobilinogen. Bilirubin is yellowish substance which helps to breakdown the red blood cells called hemolysis. Some of the urobilinogen is expelled out via feces while the remaining is reabsorbed in the normal blood circulation and eliminated in urine. In obstructive jaundice, the bilirubin fails to reach to the bowel due to which urobilinogen is not excreted out through urine. The level of urobilinogen is increased in jaundice condition. There are many tests are available which can be used to detect the obstructive jaundice. The regular urobilinogen range is beneath 17 mol/L. When the values are in between of 0 – 8 mg/dl it considered as normal. When the values get higher or lower than the normal it may be a symptom of abnormal condition. When the level of urobilinogen get increases so, it enhances the more break down of red blood cells, hematoma formation, poisoning and many liver cirrhosis. This elevated urobilinogen level may be due to many different bacterial, medical and parasite infections. The balance between the production and the breaking of red blood cells always maintained but with the increased level of urobilinogen then it may lose balance. If urobilinogen level decreased, it means that there may be a blockage of bile duct or the failure of bilirubin or also due to enzymatic jaundice or some drugs which are responsible to decrease the urobilinogen by making urine acidic.

Food is a basic need of every organisms for the gain of energy and nutrition's. It may be present in the form of solid and liquid there are also many kinds of food like

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salty, savory and sweet etc. Salty food contains usually more minerals and vitamins while sweet food is enriched with carbohydrates, water and many other fats soluble substances. Every person has a unique taste according to their taste buds. Taste buds are responsible for our selection to like either salty food more or sweet. Taste buds respond with the respect of our genes that are composed of specific combinations. If we contain sweet tooth, we want to crave more sugary food. But if we are in stress or any anxiety then we want to eat more salty food like snacks and chips etc. environment also play important in the selection of food.

Objective of current study was to make a relation between the presence of urobilinogen with the likeliness of salty or sweet food.

2. Materials and Methods

The total amount of 100 subjects were contributed in this review and all were the students who are studying in Bahauddin Zakariya University Multan, Pakistan. A questionnaire based was made to relate the urobilinogen with the food (salty or sweet). Subjects were asked the question in two sections whether they like more sweet food or salty and according to their taste they must write their urobilinogen value. Urinalysis is a method which is used to measure the urobilinogen in urine. First, wash your hands and clean the genital area. Now collect the urine in a container under a urine stream. Now dip the specially treated urine dipstick in the urine sample just for 2 second. The strip color changes compared with the chart. If the strip color changes are dense it means much urobilinogen is present in urine. By this procedure, the data is collected one by one of every subject.

Statistical analysis was performed by using MS Excel.

3. Results and Discussion

Table 1. Males and females having urobilinogen in their urine love to eat more salty food over sugary or more sugary food over salty

Male				Female			
Salty likeliness		Sugary likeliness		Salty likeliness		Sugary likeliness	
0.1	1	0.1	1	0.1	1	0.1	1
2%	11%	0%	3%	24%	23%	4%	3%

In table 1, 2% of males having 0.1 urobilinogen value were interested in eating salty food and 11% of the males with 1 urobilinogen also said they like salty to eat. 3% of the males with 1 urobilinogen value prefer to eat sugary food. 24% of the females having 0.1 urobilinogen value and 23% of the females with 1 urobilinogen loves to eat salty food while 4 % of the females have 0.1 and 3% of the females with 1 urobilinogen said they cherish more sugary food in meal. 24% of the females favors to eat more salty food due to which they have 0.1 urobilinogen in their urine. It means ratio of urobilinogen in urine affected the choice of liking more salty food or sugary food.

Table 2. Males and females who do not have urobilinogen in their urine prefer to eat more salty food over sugary and more sugary food over salty

Male		Female	
Salty lover	Sweet lover	Salty lover	Sweet lover
5%	1%	8%	1%

In Table 2, 5% of the males replied they love salty food and 1% males said they cherish more sugary food. On other hand, 8% of the females said they desire to eat salty food and 1% of the females said they love to eat more sweet food.

4. Conclusion

It was concluded that there is a scientific relation between the presence of urobilinogen in urine with eating of salty food because the value of urobilinogen was more in salty. It represents that urobilinogen play important role in the choice of eating either salty food more or sweet.

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ARTICLE

Novel *StAR* Gene Mutation Identified in a Moroccan Patient with Lipoid Congenital Adrenal Hyperplasia

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ABSTRACT

Congenital Adrenal Hyperplasia (CAH) is an autosomal recessive condition that results from the deficiency of one of the steroidogenesis enzymes responsible for cortisol biosynthesis. In the majority of cases, CAH is caused by 21-hydroxylase deficiency. More rarely, the deficiency concerns 11b-hydroxylase, 3b-hydroxysteroid dehydrogenase, 17hydroxylase, or exceptionally *StAR* and P450 oxydoreductase. Here, we report the case of a 3 year and 4 months old male child, born from a consanguineous marriage who presented at 15 months old with the salt-loss syndrome. Physical examination found generalized melanoderma, micropenis and bilateral cryptorchidism. Biological assessment at the time of diagnosis revealed hyponatremia, hyperkalemia, functional renal failure, hypoglycemia, low blood cortisol level, and high blood level of ACTH, suggesting primary adrenal insufficiency. The patient presented also with the abnormality of sexual differentiation with a 46 XY karyotype, testosteronemia level was low at the baseline and after HCG stimulation, pelvic ultrasound and Magnetic Raisonance Imaging (MRI) showed bilateral testicular atrophy in the inguinal position. The genetic study revealed a likely pathogenic homozygous variant in the *StAR* (steroidogenic acute regulatory) gene.
Therapeutically, our patient was hydrated by saline solution and treated with hydrocortisone and fludrocortisone, then benefited from a surgical testicular correction marked by a favorable evolution. Although mutations in *StAR* gene are rare, they can be responsible for the defect in the early stage of steroidogenesis and therefore cause a deficiency in adrenal and sexual hormones biosynthesis.

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1.Introduction

Congenital Adrenal Hyperplasia (CAH) is the result of an adrenal enzymatic block. Depending on the deficient enzyme, the biosynthesis of one or more hormones and sometimes an excess of synthesis of other hormones can occur. CAH is a genetic condition of autosomal recessive inheritance, commonly caused by 21-hydroxylase enzymatic deficiency [1]. Steroidogenic acute regulatory deficiency (*StAR*) is responsible for a rare and severe form of CAH where its incidence in the general population remains unknown. To date, only Eighty-five cases from Japanese, Korean and Palestinian cohorts have been published in the literature [1]. Here, we report a patient with a defect in the adrenal and sexual hormones secondary to a mutation of the *StAR* gene highlighting the epidemiological, genetic, and phenotypic aspects of *StAR* gene mutations.

2. Case Report

3 years and 4 months old boy, born to a family with first degree consanguineous marriage. His siblings do not present any related health problem. The past medical history of his mother is marked with two incidents of spontaneous abortions.

Our patient was initially hospitalized at the age of 15 months old for several episodes of acute dehydration aggravated by convulsive tonic-clonic seizures and complicated by a coma. Physical examination in admission revealed an acute dehydration associated with generalized melanoderma, micropenis, and bilateral cryptorchidism (Figure1) Laboratory analysis revealed a salt-loss syndrome with sodium levels of 113.1 mEq /l (139 mEql normal), high natriuresis to 112 mEq/l,potassium levels of 6.28 meq/l (3.5 – 5,2 mEq/l), a functional acute renal failure and hypoglycaemia at 0, 50 g/L, evoking primary adrenal insufficiency which was confirmed by a low level of 8 a.m. cortisol at 72 ng / ml (40-200 ng/l) and a high level of adrenocorticotropic hormone (ACTH) at 1250 µg / ml (10.3- 48, 3 µg/ml).

Other laboratory workup showed a low basal testosteronemia at 0.03 ng/ml then at 1.01ng / ml (0.03-0.32) after stimulation with Human Chorionic Gonadotropin Hormone (HCG). Noteworthy that this patient's karyotype was normal with 46 XY.

Pelvic ultrasound and pelvic MRI showed bilateral testicular atrophy in the inguinal position. This clinical presentation with double deficiency in adrenal and sex hormones, triggered after obtaining an informed consent from parents a genetic study that revealed the absence of mutations in *SF1* gene (steroidogenic factor 1) and *DAX1* gene (DSS-AHC critical area on the X chromosome, gene 1) and the presence of a likely pathogenic homozygous variant in the *StAR* gene.

The mutation was detected at position number 41 of the coding region of the gene with transposition of Adenine to Cytosine c.41A> C resulting in a missense variant in the proteic sequence replacing Tyrosine with Serine. This variant p.Tyr14Ser affects a very conserved amino acid and In Silico predictive tools (SIFT, TASTER mutation and Polypen-2) confirmed its deleterious aspect (Figure 2).

Our patient was treated with intravenous hydrocortisone, relayed by oral hydrocortisone at 30 mg/m^2, after correction of acute dehydration, with progressive graduation at 15 mg /m^2 per day, associated with fludrocortsione at 50 µg per day. Surgical treatment on the ascending testicle has been performed. The evolution was marked three years later by the appearance of right cervical lymphadenopathy with a positive tuberculin skin test > 20 mm ,and lymph node biopsy revealed tuberculous lymphadenitis with no histological sign of malignancy; for which the patient was put on antituberculosis treatment with a favorable evolution.

Figure 1. micropenis and absence of testicles in scrotal palpation

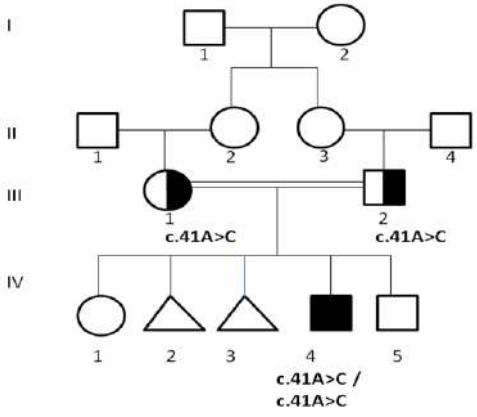

Figure 2. Pedigree presenting the genetic finding in the patient family

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Haplotypes:

a: **Mutation c.41A>C or p.Tyr14Ser corresponding to exon 1 of StAR gene**

b: Normal*

c: Normal*

d: **Mutation c.41A>C or p.Tyr14Ser corresponding to exon 1 of STAR gene**

Note: * Normal: this chromosome does not carry mutations detected in the sick child.

Father: a-**b**

Mother: **c-d**

Sick child: a-**d**

Sister: **b-c**

Brother: not studied

3. Discussion

Cholesterol is an important part of cellular membranes and is the substrate for biosynthesis of steroids, oxysterols and bile acids. Moreover , the mechanisms directing cholesterol trafficking inside cell gaived more attention through the discovery of the steroidogenic acute regulatory protein *StAR* [1].

StAR is expressed in the adrenals and gonads, but not in the placenta.Congenital lipoid adrenal hyperplasia, a rare and severe disorder of human steroidogenesis, results from mutations in *StAR*, providing a *StAR* knockout of nature that has provided key insights into its activity. Cell biology experiments show that *StAR* moves large amounts of cholesterol from the outer to the inner mitochondrial membrane, but acts exclusively on the outer membrane [2].

Cholesterol will then be supported by the CYP11A1 protein (P450scc) involved in the first stage of adrenal and testicular steroidogenesis.

3.1 The Role of STAR

StAR acts exclusively on the outer mitochondrial membrane to bind cholesterol and is inactivated when imported into the mitochondria [3]. This process is important in the regulation of steroidogenesis.

StAR gene mutations have now been described less than 200 patients with lipoid CAH, mostly from Japanese cohorts. In most studies the reported patients were siblings, or they were born from consanguineous marriages [4]. The present study is the first one to identify the *StAR* Mutation c.41A>C in a patient of Moroccan ancestry. Noteworthy, that in Moroccan patients the most frequent etiology of congenital adrenal hyperplasia is a 21-hydroxylase deficiency.

StAR missense mutations causing lipoid CAH are mostly concentrated from exons 5–7. Whereas in our case it was located in the exon 1 .Deletion of only ten carboxyl-terminal amino acids reduces *StAR* activity by half, and deletion of only 28 carboxyl-terminal amino acids deletes all activity [5]. The small number of missense mutations that cause lipoid CAH all lie between amino acids 169 and 275 [6]. In the absence of *StAR* expression, steroidogenic cells still produce 10–14% pregnenolone [1].

In general, mutations in the *StAR* gene usually lead to a classic form of the disease characterized by early onset adrenal insufficiency and gonadal failure, the latter showing gender dimorphism both in severity and in time of onset. [7,8,9].

An attenuated form of the disease, "non-classic lipoid CAH," is caused by mutations in which 10–25% of normal *StAR* activity is retained [6,10]. These patients typically experience adrenal insufficiency several years after infancy and the 46,XY individuals may masculinize normally, and mineralocorticoid secretion may be minimally affected [11]. In our patient, a mutation of the *StAR* gene was detected in the homozygous state and confirmed by sequencing using the Sanger method and the family study. This c.41A> C or p.Tyr14Ser mutation affects a conserved amino acid up to C. elegans (12 species studied) and gives a serine amino acid with a very large chemical difference [Grantham distribution: 144 (0 - 215)]

As shown in the pedigree (Figure 2), both the father and the mother are healthy carriers of the mutation. The eldest daughter is mutation free, while our patient is homozygous for the mutation. The little brother and the rest of the family members were not explored. The association with tuberculous lymphadenitis would only be fortuitous since Morocco is a country of endemic tuberculosis, with an annual incidence of 92/100 000 [12].

3.2 Physiopathological of CAH due to StAR Mutation

StAR promotes steroidogenesis by increasing the movement of cholesterol into mitochondria, but in the absence of *StAR*, steroidogenic cells still make small amounts of steroids by StAR-independent steroidogenesis [3,6,13]. This observation led to the two-hit model of lipoid CAH [13] (Figure 3).

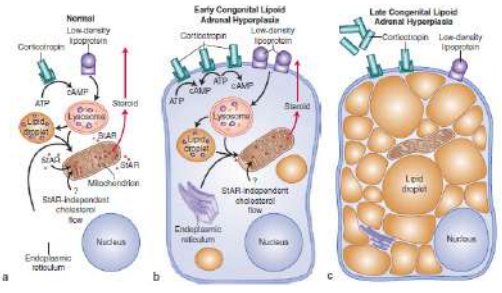

Figure 3. Two-hit model of congenital lipoid adrenal hyperplasia (lipoid CAH) " image slightly modified from Himangshu SN Engl J Med 1996; 335:1870-1879"

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Note:

a. *In normal adrenal cells, cholesterol is primarily derived from low-density lipoproteins, and the rate-limiting step in steroidogenesis is movement of cholesterol from the outer mitochondrial membrane (OMM) to the inner mitochondrial membrane (IMM).*

b. *Early in lipoid CAH, StAR independent steroidogenesis moves small amounts of cholesterol into mitochondria, yielding sub-normal steroidogenesis; adrenocorticotropic hormone (ACTH) secretion increases, stimulating further accumulation of cholesteryl esters in lipid droplets.*

c. *As lipids accumulate, they damage the cell through physical engorgement and by the action of cholesterol auto-oxidation products; steroidogenic capacity is destroyed, but tropic stimulation continues. Ovarian follicular cells remain unstimulated and undamaged until puberty, when small amounts of estradiol are produced, as in b, causing phenotypic feminization, with infertility and hypergonadotropic hypogonadism [14].*

This explains the phenotypic aspect of our patient and the delayed onset of symptoms until the age of 3 years and 4 months.

3.3 Diagnostic of CAH due to StAR Mutation

Lipoid CAH patients have normal external female genitalia either with XX or KY karyotype which makes it easy to differentiate them from XX patients with 21-hydroxylase deficiency who are virilized. In the other hand Lipoid CAH patients harbor low level of all steroid hormones, while 21-hydroxylase deficient patients show high level of 21-deoxysteroids and 17-hydroxyprogesterone. Our patient with lipoid CAH also demonstrated low level 17-hydroxyprogeterone of less than 0.3 ng/ml which ruled out the possibility of a 21 hydroxylase enzymatic block.

3b-hydrxysteroid dehydrogenase (3bHSD) deficiency caused by high level of 17-hydroxypregnenolone is a differential for lipoid CAH. In our case; and although the 17-hydroxypregnenolone assay was not performed, the normal dehydroepiandrostendione sulfate (SDHEA) findings excluded the diagnosis of 3bHSD deficiency.

The differentiation between lipoid CAH and congenital adrenal hypoplasia with a normal looking XY female genitalia is considered another clinical challenge that might be addressed by imaging; showing absent adrenal glands in congenital adrenal hypoplasia.

4. Conclusion

In the Moroccan population, the high frequency of consanguineous marriage uncovers several genetic conditions masked in the context of less consanguinity. Therefore, genetic screening should be recommended in high-risk families in order to decrease the occurrence of the genetic conditions and meanwhile prevents its complications that may be life-threatening. The present case report with acute adrenal insufficiency secondary to *StAR* gene mutation is an example of the critical importance of presymptomatic genetic diagnosis.

Declaration of interest

The authors declare that there is no conflict of interest.

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