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RESEARCH ARTICLE

An Ontology and Rule-Based Clinical Decision Support System for Personalized Nutrition Recommendations in the Neonatal Intensive Care Unit

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ABSTRACT Premature neonates hospitalized in the neonatal intensive care unit (NICU) have high nutritional needs to ensure optimal growth and development. Monitoring adherence to neonatal nutritional guidelines and providing personalized nutritional recommendations are essential for promoting their health. However, ensuring consistent adherence to these guidelines is challenging. To address this, we developed a clinical decision support system using an ontology and rule-based approach to offer personalized nutrition recommendations for preterm infants in the NICU. The Nutrition Recommendation Ontology (NRO) was developed, incorporating 121 classes, 366 axioms, and 157 semantic rules based on standard nutrition guidelines and retrospective data from 601 NICU patients, using a cumulative 8460 patient-days data collected from a single center between 2019-2021. While the ontology represented the conceptual knowledge, the rules encoded the procedural knowledge. The integrated NRO-based system serves as a reasoning engine, enabling the generation of patient-specific feeding recommendations and assisting in identifying deviations from established guidelines. To validate its efficacy, the NRO system was tested on 10 sample case studies and achieved 98% accuracy, as assessed by a panel of neonatologists. Our findings indicate that the NRO-based clinical decision support system can provide accurate personalized nutrition recommendations and assess guideline adherence in the NICU. With further real-world validation, we anticipate that this approach could significantly improve nutrition delivery, prevent malnutrition, and ultimately improve outcomes for preterm infants.

INDEX TERMS Premature neonates, ontology, clinical decision support, semantic, nutrition management.

I. INTRODUCTION

Appropriate nutrition is essential for the growth, development, metabolism, and immunity of preterm neonates [1],

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[2], [3], [4], [5], [6]. Inadequate nutrition in premature neonates hospitalized in the neonatal intensive care unit (NICU) is associated with long-term adverse outcomes such as decreased growth and impaired neurodevelopment [7], [8]. Due to immature gastrointestinal tracts, premature neonates at <34 weeks gestational age are unable to tolerate full enteral nutrition after birth and therefore require parenteral nutrition (PN), which provides intravenous protein (i.e., amino acids), carbohydrates (i.e., dextrose), and lipids to support nutrition [9]. Despite comprehensive nutritional management standards for neonates in the NICU, adherence to guidelines can be a challenge [10]. Potential reasons for nutritional guideline non-adherence include concern for a neonate's clinical status (e.g., sepsis, necrotizing enterocolitis), pre-or post-surgery management (e.g., congenital heart disease, abdominal wall defect), strategies to prevent intestinal injury (e.g., stopping enteral feeds during a blood transfusion), and variation in healthcare provider practice [11], [12]. Other factors that may contribute to guideline deviation include frequent physician schedule variations and challenges in processing large amounts of clinical data from multiple sources [13], [14], [15], [16]. To promote nutritional guideline adherence and improving neonatal outcomes, strategic approaches are needed to properly aggregate and analyze data to facilitate quality and consistent decision-making [17], [18], [19].

A bedside, patient-customized, rule-based clinical decision support (CDS) system for feeding recommendations may further improve decision-making on nutritional management during daily rounds in the NICU [20]. Recent studies have shown the usage of ontologies as part of CDS in adult medicine for the representation of complex clinical conditions and generating patient-specific medication advice in electronic discharge summaries [21]. Ontologies are crucial for healthcare applications because they provide a formal representation of the domain knowledge, which can be used to improve the accuracy and efficiency of healthcare systems [22], [23], [24]. An ontology is a knowledge representation that defines a set of concepts and relationships between those concepts [25]. In CDS systems, ontologies help to limit complexity and organize data into accessible information and knowledge that can be utilized for integration, retrieval, or interoperability [26]. The CDS system leveraging ontologies has assisted physicians in making appropriate decisions regarding antibiotic selection for diabetic patients [27]. Ontology has also been used in hospitalized neonates, including for the automatic generation of textual summaries from NICU data [28]. Similarly, OntoNeo is an ontology that captures the data from the Electronic Medical Records (EMR) related to pregnant women and neonates [29].

In this paper, we present the Nutrition Recommendation Ontology (NRO) engine, an ontology-based recommendation system to represent clinical data (e.g., details related to birth, nutrition, and current health) of neonates admitted to the NICU and recommend the feed volume and feed advancement based on neonate's day of life, risk factors, and morbidities. The NRO framework was developed incorporating standard nutrition guidelines and EMR data. Neonatal experts verified the accuracy of the NRO-based design and patient data were used retrospectively to identify deviation from nutritional recommendations. The NRO provides personalized neonatal health profile recommendations and can act as a clinical decision support tool to assist clinicians in identifying deviations from nutrition guideline adherence.

II. MATERIAL AND METHODS

To develop the NRO, we first extracted data fields from the database tables implemented in iNICU, a neonatal EMR [30]. iNICU is a data solution platform that captures and consolidates bedside clinical data of neonates in the real-time. This data were classified into two types (i) fixed data which represents data points that never changed during the hospital stay such as weight and gestational age at birth (ii) intermittent data which represents data collected periodically during the hospital stay such as day of life, resuscitation details, daily captured abdominal girth, feeding intake, gastric aspirates, vomiting episodes, stool and urine output, and morbidities [31] such as feeding intolerance or necrotizing enterocolitis (NEC), a serious gastrointestinal problem that affects mainly premature neonates.

To model the complexity of the domain, Web Ontology Language (OWL) was used to create ontologies [32]. The ontology data model was then applied to a set of individual nutritional facts and guidelines to create a knowledge graph [33] – a collection of entities, where the types and the relationships between them are expressed by nodes and edges between these nodes. The architecture of the system illustrating the nutritional management adherence is shown in Figure 1. The EMR data were accessed through pgAdmin software, an Open-Source administration and development platform for PostgreSQL database [34]. The EMR data were categorized as instance data at a particular moment in time. Based on the type of instance data, it was then instantiated to the ontology model via classes, properties, relationships, and individual data. Institution-specific nutrition guidelines from a single center participating NICU were converted to rules (''IF-THEN'' clauses) that computers could ''understand'' and then stored in the rule editor.

An inference engine was used to derive additional assertions using the base statements, ontology information, and rules associated with the system ''reasoner''. A final comprehensive model was created for each neonate.

A. STUDY DESIGN

To identify the adherence to nutritional guidelines, clinical data were collected for 601 neonates admitted to one 22-bed urban level-III NICU study site in India over a period of three years (January 2019 – December 2021). The clinical data were anonymized in accordance with Health Insurance Portability and Accountability Act protocol. The clinical data consisted of (a) fixed variables (b) intermittent variables, and

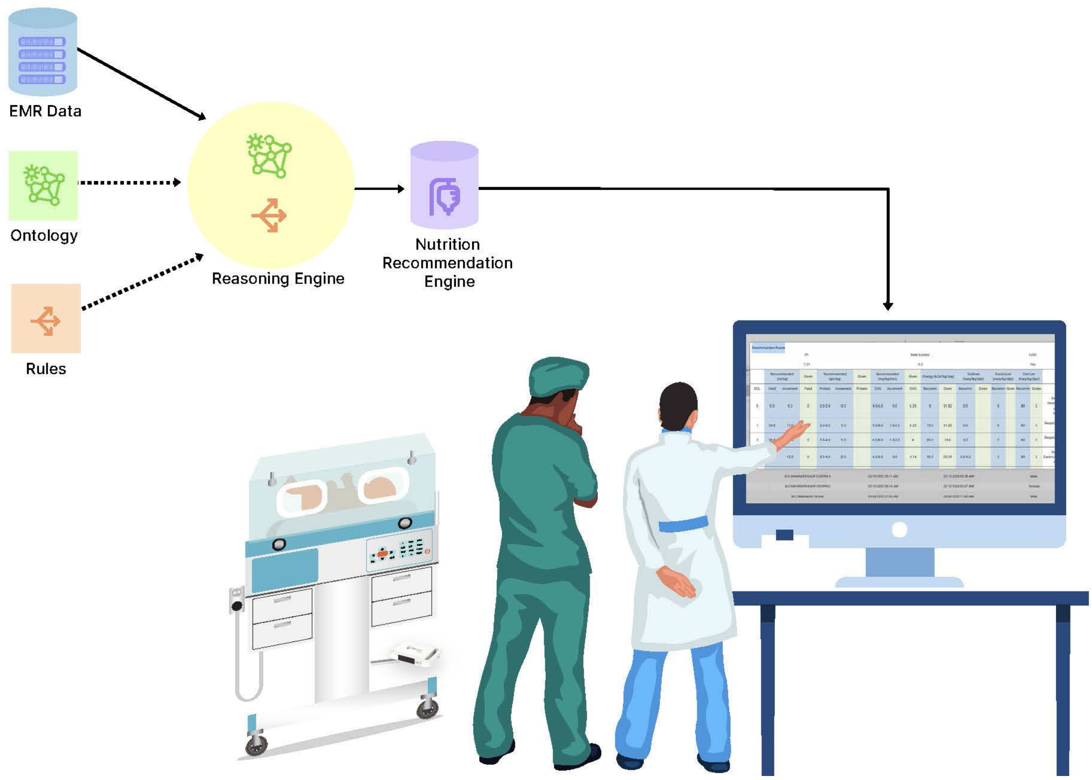

FIGURE 1. **Overall architecture diagram of system illustrating nutritional management adherence.**

(c) clinical diagnoses and morbidity data [30]. All neonates who were admitted within the first 72 hours from birth and who stayed for more than 24 hours from the time of admission were considered for the study. The nutrition orders and health profiles of the neonates were utilized to identify non-adherence to guidelines.

B. NUTRITIONAL GUIDELINES IN DETAIL

A group of three neonatologists (expert panel) with an average of 20 years of clinical experience from different Level III/IV NICUs reviewed NICU-specific nutrition guidelines based on ASPEN recommendations [35], [36]. The nutrition guidelines were analyzed on four elements related to (i)Total Fluid Limit (TFL), (ii) Feed, (iii)Energy,and (iv) Carbohydrate (CHO). There are three scenarios, the neonate can be on (a) only enteral feed, (b) only parenteral feed, and (c) both enteral and parenteral feed. For the babies on only enteral nutrition, only the compliance of feed is checked (one out of the four elements). For the neonates on parenteral nutrition or both enteral and parenteral nutrition, all four elements are checked (details in Table 1). The compliance calculations were done for all the gestational age categories of neonates till their last day of life (DOL) using 5-day intervals. Furthermore, the expert panel was provided with additional details, ''Rules'', pertaining to medication administration, respiratory support, abdominal distension, resuscitation, increased lactate, gastric aspirate color, and more, referred to as ''Risk factors'' which were utilized in generating the recommendations. The NRO engine was then executed on three-year nutrition record data to generate a compliance report.

The following section represents expert panel recommendations.

1) ENTERAL NUTRITION

Enteral Nutrition refers to tube feeding wherein the neonate is fed breast milk directly via the stomach or small intestine. This is the preferred form of nutrition wherein the recommended dosage of macro-nutrients (fats, and carbohydrates) present in human milk are given to neonates [37]. The recommended feed volume as per gestational age and day of life are demonstrated in Table 1. The focus in this form of nutrition is on the initial feeding volume and subsequently advancing the same to meet the neonate's nutritional needs.

2) PARENTERAL NUTRITION(PN)

PN is an intravenous administration of nutrition, which may include carbohydrate, fat, minerals and electrolytes, vitamins, and other trace elements for neonates who are unable to absorb enough food through oral feedings (gavage tube feeding or by mouth). The recommended energy, total fluid limit and carbohydrates as per gestational age and day of life are demonstrated in Table 1.

3) RISK FACTORS

In the presence of one or more risk factors, the clinician may hold enteral feeds (referred to as ''nothing by mouth,'' from the Latin, nil per os- NPO) for one day. Risk factors include absent end-diastolic flow per fetal ultrasound (if performed), need for resuscitation at birth (initial steps, O2, Positive Pressure Ventilation (PPV), chest compression), umbilical cord gas lactate greater than 5 mmol/L, respiratory instability (defined as ventilator requirement or increased work of breathing), inotrope administration, surfactant administration, and no stool passed in any 24-hour period [38].

4) MORBIDITIES

Along with the risk factors, there are certain clinical conditions (or signs) wherein the neonate may be NPO for one or more days. The first recommendation was to make the neonate NPO for a few hours in the presence of only one of these signs. The second recommendation was to make the neonate NPO for 24 hours if more than one sign was present. Below signs were considered:

- Feed Intolerance: Feeding intolerance was defined by difficulty in ingestion or digestion of the milk that causes a disruption in the enteral feeding plan due to clinical manifestations [39] such as:
  - Emesis
  - Abdominal distension
  - Bilious or blood-stained gastric aspirates
- NEC: Premature babies are at risk for NEC, a potentially life-threatening gastrointestinal condition characterized by intestinal inflammation and ischemia. The modified Bell staging criteria are used to provide a standardized clinical definition of NEC; these criteria, which are based upon the severity of systemic, intestinal, radiographic, and laboratory findings, are used to diagnose and stage NEC. In general, stages I and II are managed medically, whereas stage III is managed surgically [40], [41].

C. NEONATOLOGISTS VALIDATION

The nutrition guidelines of the NICU, which represent the standard of care at the site, were used as the facts by the NRO engine to generate the recommended nutritional approaches for the preterm neonates. By familiarizing the expert panel with these guidelines, they were able to evaluate the feed recommendations generated by the NRO engine while considering the established clinical reasoning behind them. The expert panel members collectively possessed expertise in various sub-specialties within neonatology, such as clinical informatics, interventional informatics, neurodevelopmental outcomes, and respiratory support. The expert group validated the accuracy of the ontology-based recommendations (NRO engine).

To validate the compliance of these recommendations, the expert panel assessed 10 random neonatal cases and their corresponding recommendations. The cases used for manual validation of NRO included their (i) gestational ages, (ii) birth weights, (iii) diagnoses, such as preterm infants with respiratory distress syndrome and neonates with intrauterine growth restriction, and (iv) maternal details. The maternal details was provided to the expert panel to ensure a holistic understanding of each neonate's background. The neonatologists were also presented with a detailed breakdown of each neonate's clinical progression, including DOL, clinical signs, risk factors, respiratory support requirements (e.g., mechanical ventilation), morbidity information (e.g., sepsis, NEC) and the associated feed recommendations. Considering that feed changes in preterm neonates often occur around DOL 5 [42], the expert panel focused their evaluation on the recommended feeds for DOL 4 and 5. This decision was guided by clinical experience, which indicates that DOL 5 is a critical time point for assessing the appropriateness of feed changes in this population. A total of 300 clinical reviews were analyzed (10 patients $\times$ 2 days (four and five days) $\times$ 5 elements (in EN and PN guidelines) $\times$ 3 (physicians) $=$ 300 reviews). This emphasis was based on the understanding that these specific periods are pivotal for significant nutrition-related decisions in neonatal care. Along with the system-generated compliance report and the expert panel validation, we also present two case studies of neonates to describe the workings of the NRO engine. The case studies include demographic details of the neonate along with DOL, risk factors, clinical signs, and diagnoses. Two case studies out of these 10 were chosen to encompass both the patients needing complex care compared to those with straightforward medical needs, showcasing the NRO engine's applicability in different scenarios (presented in the section on case studies). These detailed case studies underscore how the NRO engine operates based on a neonate's birth profile, ongoing morbidity, risk factors, and clinical signs.

The expert panel carefully examined the alignment of the NRO engine-generated feed recommendations with the participating site's clinical guidelines and critically assessed their suitability for each neonate's condition.

D. NUTRITION ONTOLOGY MAPPING

The process of mapping ontology to EMR data played a vital role in obtaining accurate recommendations. Our initial step involved the specification of classes and their interconnections. For this purpose, we utilized the concepts from UMLS [43] and Galen ontology [44] as a foundation for the class definition. Following the initial step, the next phase involved mapping EMR data to the ontology, resulting in the creation of instances of various classes. Additionally, we establish rules that encompass guideline conditions. Once this mapping and rule creation process was complete, we executed a SPARQL query, enabling us to retrieve recommendations from both ontology and the rules [45].

TABLE 1. Recommended total (parenteral + enteral) nutrition as per the guidelines from the NICU study site.

Gestation Age	Advancement	26 weeks	26- 27+ 6/7 weeks	28- 29+6/7 weeks	30- 31+6/7 weeks	32-34+6/7 weeks	>35 weeks
Feed (ml/kg/day)	Initial	12	12	12	60-80	60-80	60
	Subsequent daily advancement	12	12	20	20	20-30	20-30
	Feeding volume advanced until volume reaches maximum of 150 ml/kg/day						
Energy (kcal/kg/day)	Initial	60	60	70	70	70	70
	Subsequent daily advancement	10	10	10	10	10	10
	Goal requirement	90-110	90-110	90-110	90-110	110	110
Total fluid limit(ml/kg/day)	Initial	80-100	80	80	60	60	60
	Subsequent daily advancement	20	20	20	20	20	20
	Goal requirement	150	150	150	150	150	150
Carbohydrates (gm/kg/day)	Initial	4-6	4-6	4-6	4-6	4-6	4-6
	Subsequent daily advancement	1-2	1-2	1-2	1-2	1-2	1-2
	Goal Requirement	6-8	6-8	6-8	6-8	6-8	6-8
	The goal is to reach 6-8 instead of 8-10 since more hyperglycemia cases were seen						

The details provided below offer more information about the ontology and rules utilized in this context.

1) SPECIFYING THE CLASSES

The ontology captures neonatal clinical information using class, property, objects, and instances. Classes describe concepts in the domain. Major concepts and relationships of the high-level ontology are shown in Figure 2. The following are some main concepts or classes.

- *Neonate*, describing a summary of all the information pertaining to the patient. It is the main class of the ontology because other classes are directly or indirectly linked with this class. All the neonates in the EMR will be the instance of this class. It is connected with other classes like *PhysicalSign, DiagnosticInvestigation* etc., through various properties as described below.
- *DiagnosticInvestigation*, describing the laboratory and radiological investigation of the neonate like blood culture, abdominal X-ray, and others. It has two subclasses, i.e., Laboratory and Radiological investigation.
- *FeedType*, describing the feed related information of neonates. It has two subclasses, Enteral and Parenteral feeds.
- *PhysicalSign*, represents objective evidence of a disease such as abdominal distension, fever or vomit.

2) SPECIFYING THE AXIOMS

Axioms refer to statements that capture the relationship between the classes. Axioms can describe various aspects, including class hierarchies, relationships between classes or individuals, property characteristics, domain and range restrictions, cardinality constraints, and logical implications. Table 2 shows a few examples of axioms used in NRO. First axiom indicates that *FormulaMilk* is a subclass of *MilkType*, i.e., every instance of *FormulaMilk* class also belongs to *MilkType* class. Second axiom is an existential restriction which states that every neonate has at least one physical sign. Third axiom is a class assertion which defines that individual *X-RayAbdominStatusTest* is an instance of the class *RadiologyInvestigation*. Fourth specifies a *disjointness* axiom stating that no individual can be at the same time an instance of both *HumanMilk* and *FormulaMilk* classes. Last axiom shows an equivalent axiom which states that all instances of class *CHIL:HumanMilk* and *UMLS:C0026140* are semantically equivalent to each other.

3) SPECIFYING THE RELATIONSHIPS

There are two types of properties (relationships) in the ontology - object and data properties. Object properties connect two individuals, while data properties connect individuals with literals. Some example of data property and object properties from NRE are:

- Galen:Neonate *CHIL:hasDayOfLife: xsd:integer*
  - The neonate has data property ''day of life'' whose expected value is integer.
- Galen:Neonate *CHIL:hasRespiratoryDistress xsd:boolean*
  - The neonate has data property respiratory distress whose expected value is true or false.
- Galen:Neonate *CHIL:hasPhysicalSign CHIL:PhysicalSign*
  - An instance of Neonate is connected to an instance of PhysicalSign through the hasPhysicalSign object property.
- Galen:Neonate *CHIL:hasParenteralFeed CHIL:ParenteralFeed*
  - An instance of Neonate is related to an instance of the class ParenteralFeed through the object property hasParenteralFeed.

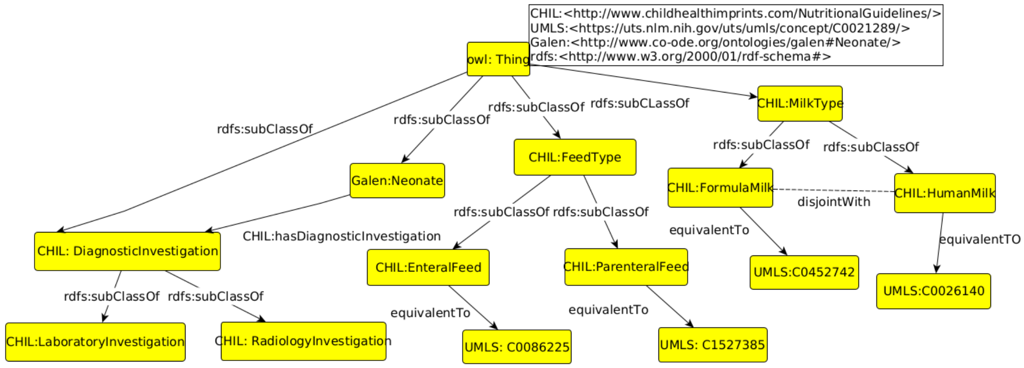

FIGURE 2. High-level diagram of nutrition guideline ontology.

TABLE 2. Description of axioms used in ontology.

Serial Number	Description Logic	Example(Functional style syntax in OWL)
1	$A \sqsubseteq B$	*subClassOf(CHIL:FormulaMilk CHIL:MilkType)*
2	$A \sqsubseteq \exists R.B$	*subClassOf(Galen:Neonate someValuesFrom(CHIL:hasPhysicalSign CHIL:PhysicalSign))*
3	$a \in A$	*classAssertion(CHIL:X-RayAbdominStatusTest CHIL:RadiologyInvestigation)*
4	$A \sqcap B \equiv \Phi$	*DisjointClasses(CHIL:HumanMilk CHIL:FormulaMilk)*
5	$C1 \equiv C2$	*EquivalentClasses(CHIL:HumanMilk UMLS:C0026140)*

4) SPECIFYING THE RULES

Rules are defined as instructions that dictate actions based on specific conditions or criteria. Rules are created using logical expression and attributes. These attributes could include basic data like gestational age, day of life, birth weight, and current health conditions of neonates such as feeding intolerance, sepsis, or necrotizing enterocolitis. If a neonate's basic details and condition matched with the pre-conditions of the rules expressed within these logical expressions, then a conclusion (assertion)was reached.

Figure 3 shows an example of Jena [46] grammar representing a NPO recommendation when a neonate demonstrates signs of feeding intolerance. The example comprises two rules. The first rule specifies that for any neonate if the property *hasAbdominalDistension* is true, or the property *hasGastricAspirateAbnormalColor* is true, or *hasX-RayAbdomenStatus* is *abnormal* is true, or *hasvomit* is true, the neonate qualifies for the *hasFeedIntolerance* condition If the consequence of the first rule causes the second rule to be active, then the neonate qualifies for feed intolerance and the recommendation is to withhold feeds (i.e., NPO).

5) ONTOLOGY MODEL

The Ontology model was created after execution of rules containing all the asserted facts. This model contains instance information mapped with initial ontology and feed recommendation details as per the execution of rules. SPARQL query language was used to get the feed recommendation of specific neonates [47]. In this way, the NRO based engine created recommendations by exploiting knowledge related to neonates such as neonates' day of life, gestation, conditions such as Feed Intolerance, NEC, or any signs such as emesis, lethargy, or more.

III. RESULTS

A total of 121 classes, 366 axioms, and approximately 157 semantic rules were included in the NRO framework to represent knowledge relevant to nutrition guidelines. Data of 601 infants accounting for 8460 patient days from a single NICU site who met enrollment criteria were analyzed from January 2019 to December 2021 (patient characteristics shown in Table 3). The NRO engine was implemented on daily nutrition data from 601 neonates to identify any

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@prefix CHIL: <http://www.childhealthimprints.com/NutritionalGuidelines/>.
[FeedIntoleranceRule1: (?a    CHIL:hasAbdominalDistension "true"^^data type:),
                       (?a    CHIL:hasGastricAspirateAbnormalColor "true"),
                       (?a    CHIL:hasXRayAbdominStatus ?d), listEqual(?d,"Abnormal)
                       (?a  CHIL:hasVomit "true")
                       -> (?a    CHIL:hasFeedIntolerance "true") ]
[FeedIntoleranceRule2: (?a    CHIL:hasFeedIntolerance "true")
                       -> (?a  CHIL:hasNPO  "true")
 [FeedRule: (?a  type:   Galen:Neonate)  ( ?a CHIL:hasGestationalAgeAtBirth ?c),
            lessThan(?c, 32.0),ge(?c,30.0),
            noValue(?a   CHIL:hasFeedIntolerance),
            noValue(?a  CHIL:hasNPO),
            (?a    CHIL:hasDayOfLife    ?d), equal(?d,6)
             -> (?a CHIL:hasInitialFeedingVolume  "180"), (?a CHIL:hasInitialFeedingAdvancement   "0" )]
```

FIGURE 3. An example of rule with an if and then condition.

deviation from the nutritional guideline recommendations. The anonymized database was queried to obtain daily EN and PN administration data. The neonatal nutrition record was considered compliant if the administered feed met requirements based on the neonate's gestational age, day of age, risk factors, clinical signs, and morbidities. The adherence was calculated based on (i) Feed, (ii) Energy, (iii) Total Fluid Limit (TFL), and (iv) Carbohydrate (CHO). The adherence was checked for all gestation groups and as an example, Tables 4 and 5 demonstrate the NRO adherence percentage in neonates from the 25-31 weeks and 31-34 weeks gestational age categories of neonates. Of the 576 infants whose final diagnosis did not include feeding intolerance, NEC, and sepsis, 48% were compliant with the recommendation engine, while all the remaining 25 infants who were either diagnosed with feeding intolerance or NEC or sepsis or in combination were not compliant with the recommendation engine. For Extremely Low Birth Weight (ELBW) and Very Low Birth Weight (VLBW) (weight < 1500 grams) infants, the nutrition administration was not compliant with the recommendations on the initial DOL; however, adherence improved with the increasing DOL. Additionally, 10 case studies and 100 recommendations were presented to a panel of four neonatologists. The recommendations of the neonatologists were concordant with 98% of the NRO nutritional guideline recommendations (Table 6). The adherence reported across all gestational categories (de-identified) is provided in CSV format along with code.

IV. CASE STUDIES

In Table 7 and Table 8, we present two case studies illustrating the accuracy of the NRO engine. These case studies were chosen, each offering a distinct perspective on the engine's capabilities. The first case study represents a medically complex scenario involving a male infant born at 27+3 weeks of gestation. This premature baby underwent many medical challenges throughout his 77 day stay in NICU, encompassing respiratory distress syndrome, recurring apneic episodes, elevated bilirubin levels leading to hyperbilirubinemia, suspected sepsis, and the advanced stage III retinopathy of prematurity (ROP). In contrast, the second case study represents a simpler medical scenario, involving a female infant born at 32+2 weeks of gestation. This infant's NICU stay, spanning 15 days, primarily centered on respiratory issues, specifically the respiratory distress syndrome and episodes of apnea. Throughout her stay, she received enteral feeds as part of her care plan. To demonstrate the accuracy of the NRO engine, we highlighted the total number of mismatches, along with the two primary reasons for these discrepancies, over the span of the neonate's length of stay. Figure 4 represents the difference between infant's NRO recommended versus administered feed, carbohydrates, and energy at the bedside for the first case study.

V. DISCUSSION

The current study demonstrates that an ontology and rule-based CDS system has the potential to provide real-time personalized nutrition recommendations and identify adherence to guidelines. Such capabilities can promote optimal nutrient intake to avoid growth failure and support improved outcomes in preterm infants. Analysis of the 601-patient dataset found 48% compliance with NRO recommendations in patients without major morbidities, indicating substantial room for improvement in guideline adherence.

Nutrition requirements for preterm infants and the effects of malnutrition are well-established [48], but the challenge lies in ensuring favorable delivery of nutrients in the NICU setting. Suboptimal nutrition can lead to growth failure and other negative health outcomes [49]. This emphasizes the

TABLE 3. Baseline data of the NICU study site.

Fields	<26 weeks	26- 27+ 6/7 weeks	28- 29+6/7 weeks	30- 31+6/7 weeks	32-34+6/7 weeks	>35 weeks
Number of infants[b]	1	24	48	83	298	147
Length of Stay (days)[a]	75.0(-)	63.3(12.1)	38.0(11.2)	24.0(9.6)	8.1(5.3)	5.9(4.3)
Gestational age (weeks)[a]	25.9 (-)	26.8(0.7)	29.3(0.6)	31.0(0.6)	33.3(0.7)	37.0(1.3)
Birth Weight(grams)[a]	650.0 (-)	953.8(194.8)	1159.0(235.1)	1448.1(292.3)	1913.6(367.3)	2626.1(646.1)
Birth Head Circumference(cm)[a]	-	25.0(1.7)	27.2(1.7)	28.2(2.2)	31.0(2.0)	33.0(2.1)
Mothers Age (years)[a]	37.0(-)	32.0(2.3)	33.1(5.0)	32.2(4.1)	32.6(5.8)	31.4(4.4)
In vitro fertilization [b]	0 (0%)	15 (62.5%)	27 (56.25%)	47 (56.63%)	150 (50.34%)	22 (14.97%)
Natural[b]	1(100%)	9 (37.5%)	17 (35.42%)	29 (34.94%)	115 (38.59%)	107 (72.79%)
Unknown [b]	0 (0%)	0 (0%)	4 (8.33%)	7 (8.43%)	33 (11.07%)	18 (12.24%)
Male [b]	0 (0%)	18 (75.0%)	30 (62.5%)	50 (60.24%)	177 (59.4%)	88 (59.86%)
One Min APGAR [a]	6.0(-)	7.0(1.4)	7.0(0.9)	7.6(0.8)	7.7(0.8)	7.9(1.0)
Five Min APGAR [a]	7.0(-)	8.4(0.9)	8.3(0.9)	8.7(0.6)	8.8(0.5)	8.9(0.6)
Vaginal Delivery [b]	0 (0%)	3 (12.5%)	1 (2.08%)	6 (7.23%)	7 (2.35%)	16 (10.88%)
Cesarean section [b]	1 (100%)	21 (87.5%)	47 (97.92%)	77 (92.77%)	291 (97.65%)	131 (89.12%)
InBorn [b]	1 (100%)	22 (91.76%)	40 (83.33%)	70 (84.34%)	232 (77.85%)	124 (84.35%)
Hyperbilirubinemia [b]	1 (100%)	20 (83.33%)	45 (93.75%)	69 (83.13%)	124 (41.61%)	62 (42.18%)
Sepsis [b]	1 (100%)	17 (70.83%)	19 (39.58%)	13 (15.66%)	11 (3.69%)	9 (6.12%)
Respiratory Distress Syndrome [b]	1 (100%)	14 (58.33%)	18 (37.5%)	18 (21.69%)	17 (5.7%)	17 (11.56%)
Multiple Pregnancy (Twins/ Triplets) [b]	1 (100%)	14 (58.33%)	28 (58.33%)	41 (49.4%)	191 (64.09%)	20 (13.61%)
Antenatal Steroids [b]	1 (100%)	20 (83.33%)	42 (87.5%)	67 (80.72%)	230 (77.18%)	23 (15.65%)
Feeding Intolerance [b]	0 (0%)	4 (16.67%)	7 (14.58%)	2 (2.41%)	4 (1.34%)	5 (3.4%)
Necrotizing Enterocolitis [b]	0 (0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.68%)
Hypoglycemia[b]	0 (0%)	0 (0.0%)	1 (2.08%)	0 (0.0%)	3 (1.01%)	15 (10.2%)
Bronchopulmonary Dysplasia [b]	1 (100%)	17 (70.83%)	6 (12.5%)	0 1 (1.2%)	0 (0.0%)	0 (0.0%)
Intraventricular Hemorrhage [b]	0 (0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retinopathy of Prematurity [b]	1 (100%)	13 (54.17%)	20 (41.67%)	6 (7.23%)	3 (1.01%)	1 (0.68%)
Mechanical Ventilation(days) [a]	4.1 (-)	2.9(1.9)	3.7(4.1)	1.7(1.9)	2.1(1.6)	2.4(1.2)
Time to reach birth weight (days) [a]	17.0(-)	23.4(16.3)	15.6(3.3)	11.9(4.8)	2.7(4.4)	1.4(3.6)
Time to reach full feeds (days) [a]	17.3 (-)	21.9(9.4)	13.4(5.3)	9.7(5.3)	2.3(3.8)	0.9(3.6)
TPN [b]	1 (100%)	24 (100.0%)	48 (100.0%)	71 (85.54%)	109 (36.58%)	65 (44.22%)
Duration of TPN (days)[a]	16.6(-)	12.8(7.2)	10.4(5.7)	5.0(3.5)	1.3(2.2)	1.7(4.1)
Proportion of Human Milk* $* a$	76.9 (-)	71.6(30.4)	63.0(34.9)	57.1(38.4)	24.4(29.1)	33.0(30.9))
Time to start Human milk fortifier(days) [a]	27.4 (-)	12.7(4.4)	9.9(4.4)	7.2(2.9)	5.9(2.3)	9.4(8.7)
EN compliance(Feed volume) [a]	80.0%	86.9%	81.9%	88.9%	94.1%	88.4%
EN & PN compliance(Energy) [a]	78.6%	81.4%	73.3%	75.5%	61.8%	37.2%
PN compliance(Carbohydrates) [a]	96%	91.6%	87.3%	88.1%	92.1%	87.8%

** Human milk / (Human Milk + Formula Milk) * 100 ; APGAR: appearance, pulse, grimace, activity, and respiration; TPN: Total Parenteral Nutrition; EN: Enteral Nutrition ; PN: Parenteral Nutrition

a - Mean (standard deviation).

b - Count (percentage within that class)

TABLE 4. Gestation-wise (28-29+6/7weeks) distribution of TFL, energy,feed,and CHO adherence percentage along with the count of babies who received enteral feed.

DOL	Count	TFL adherence(%)	Feed adherence(%)	Energy adherence(%)	CHO adherence(%)
0	47	2.13	100	0	97.87
5	48	97.92	17.39	14.58	41.6
10	48	95.83	70.21	77.08	89.5
15	48	93.75	89.13	85.42	100
20	47	97.87	95.45	87.23	95
25	45	100	88.64	88.89	88.8
30	28	100	89.29	89.29	*NA*
35	23	100	95.45	91.3	*NA*
40	13	100	92.31	92.31	*NA*
45	10	100	100	100	*NA*
50	6	100	83.33	100	*NA*
55	3	100	100	100	*NA*

DOL:Day Of Life; TFL: Total Fluid Limit ; CHO: Carbohydrate
NA : IV dextrose fluid was discontinued with full enteral feeding.

TABLE 5. Gestation-wise (32-34+6/7weeks) distribution of TFL, energy,feed,and CHO adherence percentage along with the count of babies who received electrolytes.

DOL	Count	TFL adherence(%)	Feed adherence(%)	Energy adherence(%)	CHO adherence(%)
0	298	25.17	100	0.38	97.2
5	200	90	63.96	72.22	90.2
10	94	98.94	88.3	96.81	97.1
15	32	100	96.88	100	*NA*
20	9	100	100	100	*NA*
25	3	100	100	100	*NA*
30	2	100	100	100	*NA*
35	1	100	100	100	*NA*

DOL:Day Of Life; TFL: Total Fluid Limit ; CHO: Carbohydrate
NA : IV dextrose fluid was discontinued with full enteral feeding.

pressing need for strategies to improve guideline adherence, such as the real-time, personalized decision support system we have investigated, which may help prevent malnutrition during the neonatal period.

TABLE 6. Accuracy of nutrition recommendation ontology engine.

10 Cases studies with 100 corresponding recommendations		
Verification Type	Total recommendations	Accuracy
Enteral Nutrition	84	95.2%
Parenteral Nutrition	36	100%
Enteral & Parenteral Nutrition	120	96.7%

TABLE 7. Patient demographics, day of life wise morbidities and summary of compliance for Use case 1.

Patient demographics : Male, birth weight 640 grams, gestational age of 27 weeks and 3 days, Delivered via cesarean for maternal hypertension and signs of fetal stress from umbilical Doppler assessment.			
Morbidity profile : prematurity , respiratory distress syndrome, instances of apnea episodes, hyperbilirubinemia, suspected sepsis, and retinopathy of prematurity stage III in the left eye.			
Course of Stay : - Phototherapy for 3 days due to hyperbilirubinemia.. - Three courses of antibiotics for suspected sepsis - Laser therapy to treat retinopathy of prematurity - Respiratory support via mechanical ventilation, continuous positive airway pressure, and high flow nasal cannula - Multiple instances of absent stool passage and abnormal gastric aspirates			
Number of recommendations	Number of mismatches	Reason 1	Reason 2
322	56	The unit is non compliant to institutional guidelines for Total Fluid limit and Energy	NRO lacks the rules for restarting the feeds post NPO

Compared to full-term infants, preterm ones have more substantial nutritional needs to promote optimal growth. Despite numerous existing strategies, growth failure remains a critical issue. A retrospective study by Silvia et al assessed variations in practice, compliance with guidelines for energy and amino acids intake, and postnatal growth in infants born between 30-33 weeks [14]. They discovered that the nutrition provided often fails to meet international guidelines, leading to significant rates of extra-uterine growth restriction. Various strategies–including education, improved nursing documentation, EMR modification, documentation audits with personalized feedback, and the use of digital scribes–have proven effective in enhancing adherence to clinical guidelines [50], [51], [52]. However, the efficacy of using real-time, personalized recommendation tools at the bedside for assessing adherence remains uncertain and therefore warrants further study. Following their thorough evaluation and validation process, the neonatologists in the expert panel reached a unanimous agreement, endorsing the feed recommendations generated by the NRO engine.

TABLE 8. Patient demographics, DOL wise morbidities and summary of compliance for Use case 2.

Patient demographics : Female, birth weight 1645 grams, gestational age of 32 weeks and 2 days, delivered via cesarean section Maternal Medical Disease - Hypothyroidism			
Morbidity profile : prematurity , respiratory distress syndrome, instances of apnea episodes			
Course of Stay : - Continuous Positive Airway Pressure (CPAP) respiratory support.			
Number of recommendations	Number of mismatches	Reason 1	Reason 2
60	18	The unit is compliant to institutional guidelines for Enteral Feed	NRO engine demonstrates its highest efficacy in uncomplicated medical scenarios

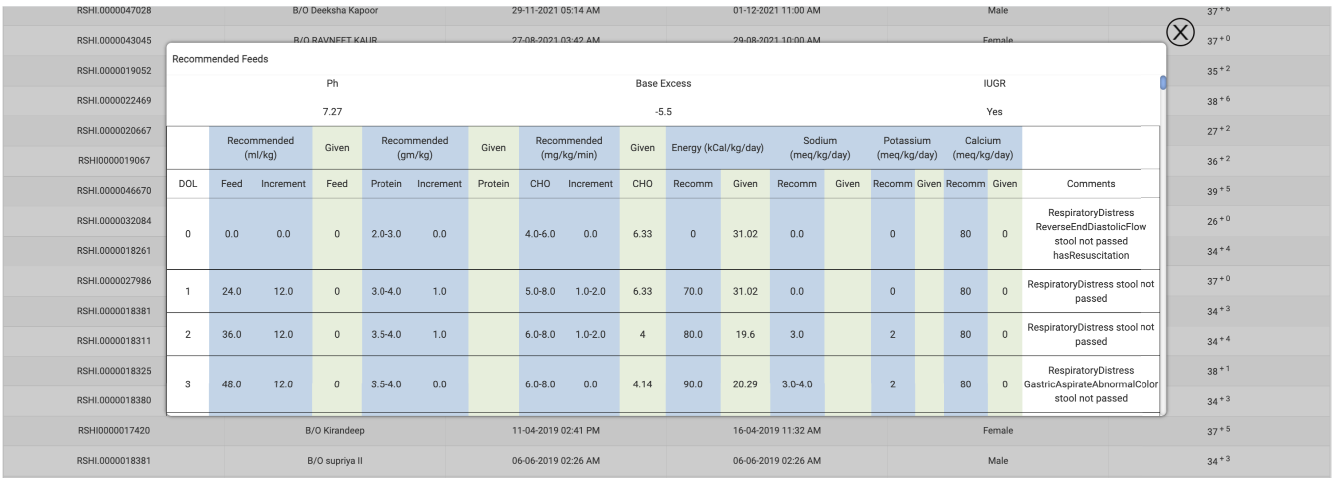

FIGURE 4. Tabulated representation of recommended versus administered nutrition at bedside.

This consensus reflects their high level of confidence in the accuracy and appropriateness of the NRO engine's recommendations.

The present study has several limitations. One limitation of this approach is that the feed recommendations generated by the NRO engine were based solely on the participating site's clinical guidelines [53]. As a result, the applicability of these recommendations may be limited to the specific practices and protocols followed at the site [54]. Therefore, caution should be exercised when generalizing these findings to other clinical settings. To address the limitation mentioned above, the next important step is to broaden the range of clinical guidelines that inform the NRO engine's feed recommendations. By incorporating a diverse set of guidelines from multiple institutions and expert consensus, the engine can encompass a wider range of clinical practices. This expansion would contribute to increasing the generalizability and relevance of the NRO engine's recommendations in various neonatal care settings. A further limitation is that the NRO engine is still evolving, and does not incorporate other nutrients such as lipids and protein. The future models will need to consider overall nutrition and medical co-morbidities that may impact feeding tolerance or NPO status (e.g., sepsis, neurological injury, metabolic acidosis).

Despite these limitations, the ontology and rule-based clinical decision support system offers promise for enhancing nutrition in the NICU, where optimal intake is essential for preterm infants' growth and development. By tailoring recommendations to each infant's unique needs, this system can potentially counter the risk for malnutrition. The next steps for real-world implementation would include further evaluating the system across diverse neonatal populations and NICU settings, integrating recommendations into clinical workflows, monitoring the impact on growth and developmental outcomes, and addressing barriers like technology acceptance and adherence to nutrition goals using this system.

VI. CODE AVAILABILITY

The code that underpins the ontology is openly available. The drive containing the code used to generate the ontology, nutrition guidelines, rules, queries (SPARQL), and Java code is available. The repository is https://github.com/kracr/nicu-nutrition-kb/blob/master/nutrition_guideline_ontology.owl. The README file has all the script-related comments and other steps for executing the code.

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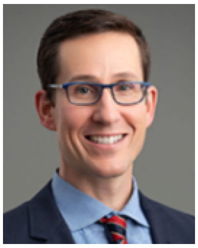

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