Oral Candida – a marker of the influence of general health on oral health in children up to one year old

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Summary

Oral colonization with Candida in part of new born children represents the start of their oral ecosystem whereby homeostasis is an important defense factor. The aim of the present study is to follow the oral colonization with Candida in new born children and children up to 1 year of age and seek dependence of these microorganisms on the general health status of the children. The study was carried out with 160 children age 0 to 1 year.

Fungi of Candida type are among the first colonizers in oral medium, populating 16.5% of the new born children and reaching 38.46% of the children up to 1 year of age. The type characteristics of oral Candida shows that C. albicans is isolated in 87% of the children. Candida quantities are very different; more then 1/3 of the children with Candida have quantities of 105-106 cells/ml without exhibiting clinical symptoms of oral candidosis. Candida colonises more frequently children with systematic chronical diseases and damages.

The dependence between the general health status of the children and the oral Candida provides reasoning to propose that Candida in oral cavity be accepted as a marker indicating the influence of the general status of the organism on the oral medium.

Key words: microorganisms, fungi, Candida albicans, oral ecosystem, new born, oral biomarkers, oral diagnosis, saliva, thrush.

The diversity in oral ecology, the multiple factors of local and general character characterizing biological medium in the mouth as well as the general health status of the child maintain the equilibrium in the complex and dynamic oral system. All those factors define the thin limits between health and disease of organism of the child, more specifically in the oral cavity. Oral colonization with Candida in part of new born children represents the start of their oral ecosystem whereby homeostasis is an important defense factor. These microorganisms, as part of the resident oral microflora, may become opportunist pathogen and develop diseases called oral candidosis (1, 2, 3, 13). An interesting fact is that not all new born children, having primary oral colonization with Candida, develop a disease. With most children, Candida remains as a part of the resident oral microflora. While literature records consensus on the sequence of oral colonization with Streptococcus of the resident oral microflora, the terms with regard to Candida are different and the question about the perfofmance of their pathogen potential remains unclear (4, 6, 5, 7). The specifics of Candida, whose pathogen potential to the greatest degree depends on the local and general immunity, determined our interest to studying these microorganisms in new born children as well as in children with different general diseases and pathological conditions (8, 9, 10, 11, 12).

The aim of the present study is to follow the oral colonization with Candida in new born children and children up to 1 year of age and seek dependence of these microorganisms on the general health status of the children.

Tascs

1. To investigate the relative ratio of children with oral Candida during the first year after birth;
2. To study the type and quantities of oral Candida in children up to 1 year of age;
3. To study the influence of the general health status of the children and the oral colonization with Candida.

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Material and Methods

'The study was carried out with 160 children age 0 to 1 year, divided in 3 groups:

- **group 1** - 79 new born children, aged 1 to 10 days, from the maternity ward of Second Town Hospital in Sofia and the maternity ward of Hospital in Rousse;

- **group 2** - 42 children, age 10 days to1 year, from the Orphanage in Rousse;

- **group 3** - 39 healthy children, age 10 days to 1 year, from "Children Consultation"- department of a Medical Center in Sofia.

The groups were formed in a way to allow the follow up of oral Candida during the first year of the life of healthy children and of children with different health problems living in various conditions(group nurturing, children damaged during birth as well as healthy children brought up in family atmosphere).

All factors described in literature as risky for oral colonization with Candida and as suspectable to the development of oral Candidosis (Trash) were followed.

We registered data on the health status of the children: height and weight on birth , chronic disease, damage, data on oral candidosis at check, etc. The data were recorded in a specially designed questionnaire and were collected with the active cooperation of pediatricians and parents.

Microbiological investigation:

The material for microbiological study was taken by a sterile tampon from mouth of the children.

The quantitative determination of Candida was done by the method of Gould /Contemporary Medicine, book 5 /2003/.After cultivation for 48 hrs at 35°C the colonies grown were calculated and the microbe number was recorded by the standard table. When in doubt, a microscope sample by Leffere was prepared from the colonies and cell morphology characteristic for the Candida type was sought in parallel cultures of chromagar Candida were prepared from the materials in order to determine the type of Candida kind by cultivation again for 48 hrs at 35°C.

The statistic analysis was done with the help of program SPSS – 15 - Nonparametrics analyse (χ^2); Independent Samples T-Test, Correlation Pearson,s Coeficient.

Results and Discussion

1. Frequency of the oral colonisation with Candida in mouth cavity of new borns and children up to 1 year of age.

The results obtained from the isolated Candida of the mouth cavity of children studied are shown in *Fig. 2.*

Fungi of Candida type were isolated from the mouths of 1/3 of the children immediately after birth and up to 1 year of age. This fact shows that Candida is one of the first microorganisms colonising mouth cavity and participating in the initial formation of the oral ecosystem. The presence of this microorganism and the exhibition of its pathogenic potential during immunodeficancy make it on interesting factor for evaluation of oral medium.

The distribution of Candida carriers in the three groups of children is shown in *Fig.3*

In all three groups of children, Candida is isolated in quite wide limits-from 16,50% in new bourns to 52,40% in the second group and 28,20% in the third group. Groups 2 and 3 comprise children from 10 days to 1 year of age. It turns out that immediately after birth, fungi of Candida type are one of the first microorganisms populating the mouth of the children. During the first month in breast-fed age, children with Candida increase in both groups with dif-

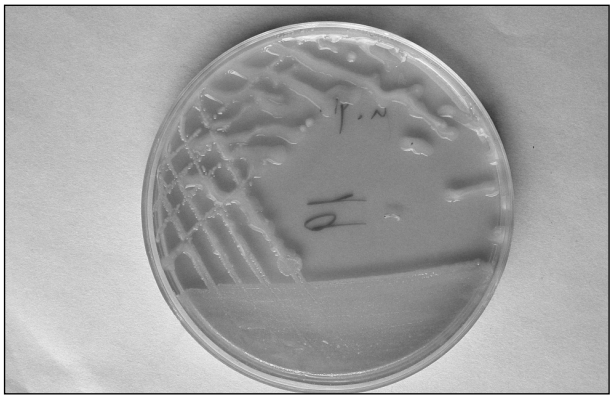

Fig. 1 The colonies grown of oral Candida

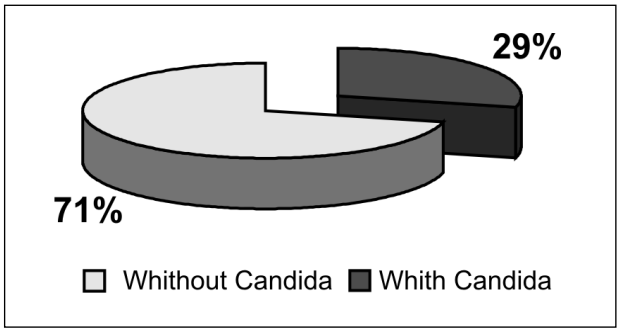

Fig. 2. Isolation of Candida from mouth cavity of new borns and children up to 1 year of age

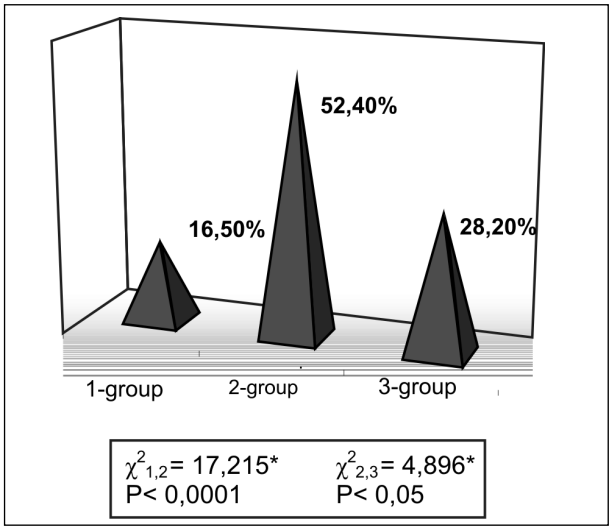

Fig.3 The distribution of Candida carriers in the three groups of children

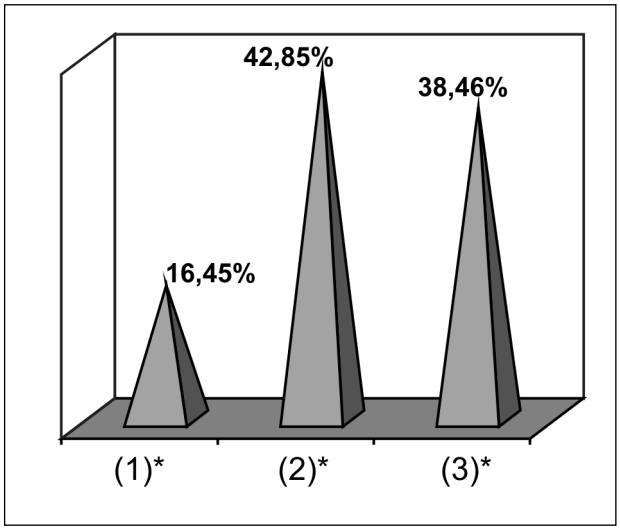

Fig. 4 Age distribution of all children with oral Candida studied

ferent percentage 28,20% for group 3 and 52,40% for group 2. The abrupt increase of children with Candidas from group 1 to group 2 is with high statistical importance (P < 0,0001).

The difference between group 1 and group 3 is not so drastic indicating a tendency to increase which is moore smooth and closer to data cited in literature (1). Although different studies cite wide range of Candida carries in children (25% - 75%), it is clear that young age favourable for colonization with oral Candida which under certain conditions may become a source for the development of oral candidosis (13).

1.2. Distribution by age of children with oral Candida.

The children were divided in three age groups *(figure 4):*

- (1)* from 1st to 10th day (period of new born);
- (2)* from 10th day to six months (early breast-fed period);
- (3)* from 6 months to 1 year (late breast-fed period).

During the first several days after birth 16,45% of the children become Candida carries. The number of the children with Candida doubles up to the 6th month, and drops slightly after that, and at about 1 year of age the children with Candida represent 38,46% of all the children studied in that age group. The difference between the children with oral Candida during the first days and the children breast –fed up to 6 months is statistically important (P < 0,0001). The first 6 months is the period when most children become an object of colonization with oral Candida because of the unstable immunity and acidic oral medium maintained when the child is fed primary with milk food most often by breast feeding.

2. Study of the type and quantities of oral Candid in children up to 1 year of age

2.1 Type characteristic of fungi of Candida kind in new born and children up to 1 year of age.

It showed be noted that only tree types of Candida have been found to colonise the oral cavity of new born children and children up to 1 year of age: 87% of the children carry C. albicans and the rest distribute 8.7% of C. globrata and 4.3% of C. tropicalis. The last two types have been isolated from children of group 2 (raised in orphanage). The pathogenic potential of these type of Candida is greater and depends on the secreting hydrolythic enzymes with expressed protease activity, adhesive properties, ability to form hyphal forms and their genotype characteristics.

All this, determines the pathogenic potential of the different types of Candida and their different characteristics which may mutate for various individuals and under changing risky conditions

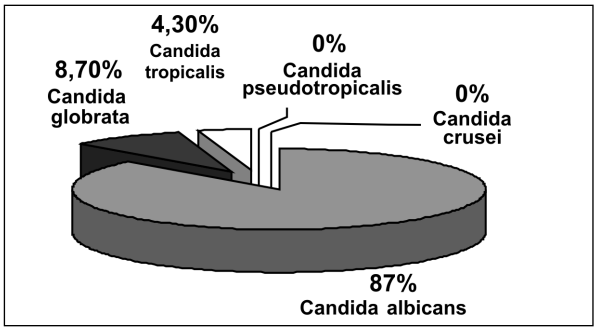

Fig. 5. Different types of Candida isolated from the mouths of children studied

2.2. Quantitative characteristics of Candida in the oral cavity of children studied

The quantitative characteristics of Candida shows that close to 1/3 of the children with oral Candida have my 10^4 cells per ml. The number of children with Candida under this quantity (10^3 < 10^3) as well as the children with quantities of 10^5 and 10^6 is equal. They are distributed approximately uniformly *(table 1).*

It is interesting to note the fact that 30.6% of all children with Candida studied show quantities of 10^5-10^6 cells/ml. which is accepted in the clinic as sufficient for the development of oral Candidosis and is indicative for proving the disease. This is demonstrated in *Fig. 6.*

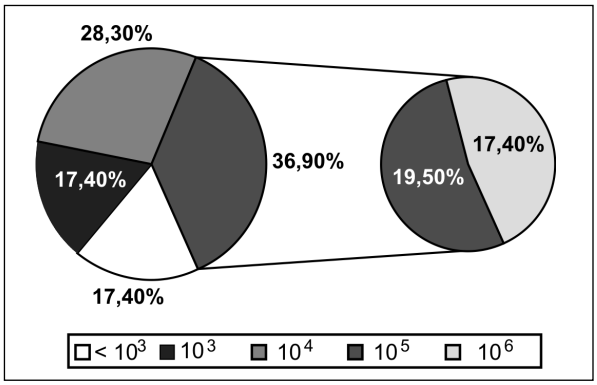

Fig. 6. Quantitative characteristics of Candida in the oral cavity of children studied

It should be noted that none of the children showed clinical characteristics of oral candidosis on check. Only 8 of the children with Candida from the group of the new born developed later pseudomembranous candidosis (thrush). More then 1/3 of the children in group 3 (healthy children) have quantities of Candida in the order of 10^5-10^6.This is an age when the risk period of new born children is over come and the children exhibit normal for the age growth and development. According to information from the mothers these children have not suffered thrush in their breast feeding period. Based that data as well as other numerous observations made by us for greater quantities of Candida and lack of oral pathology the conclusion has to be made the quantitative evaluation is not sufficient to state that Candida is the reason for oral candidosis. Therefore the quantitative evaluation of Candida should not be accepted unanemously as an indicator for clinically expressed oral candidosis. The clinical evaluation of such type of disease should be complex incorporating besides the quantity and type of Candida, an evaluation as well of the various factors of risk needed for the development of the disease and the presence of a typical clinical finding.

3. Dependence of children's health status and oral colonisation with Candida

Oral health depends on individual's general health. Oral medium is influenced both by local as well as by factors of systematic character. The favorable medium for colonisation the oral microorganisms including oral Candida is created under the action of all these factors. The general diseases and damages at birth influence the non stable and non ripe oral system. The characterisation of the heath status of small children is a necessary step in studying all the factors that could be of importance for the early colonisation with oral Candida.

3.1. Health status of the children studied

The health status of the children studied and the influence of the general status of a new born child on the colonisation with Candida as well as the manifestation of its pathogen potential is an important part of the evaluation of the risk medium for colonisation of these microorganisms in human oraganism. Part of the children studied have defferent diseases, distributed in three groups in the table below.

Table 1. *Quantities of Candida isolated from the mouths of children studied by groups*

Quantity of Candida (cells/ml)	**Group 1 – new born (1-10 days)**	**Group 2 - from orphanage (10 days – 1 year)**	**Group 3 - from med. consultation (10days-1 year)**	**total**	
				number	**%**
< 10^3	3	5	0	8	17,4
10^3	3	5	0	8	17,4
10^4	3	6	4	13	28,3
10^5	2	3	4	9	19,5
10^6	2	3	3	8	17,4
total	13	22	11	46	100

Table 2. *Frequency of diseases of new borns of children studied*

groups	with disease		without disease		total	
	n	%	n	%	n	%
1-group	14	17,7	65	82,3	79	100
2-group	29	69,0	13	31,0	42	100
3-group	5	12,8	34	87,2	39	100
total	48	30	11	270	160	100
χ^2 P	$\chi^2_{1,2}$ =31,534* P< 0,0001		$\chi^2_{1,3}$=0,46 P> 0,05		$\chi^2_{2,3}$=26,249* P< 0,0001	

30% of the children have been born after complicated pregnancy, problems at delivery, most often premature delivery and have obtained temporary or permanent damages. 2/3 of the children are in group 2 - left after birth and raised in orphanage. The relative share of the children with general diseases in this group is distinguished by statistically notable difference from the other two groups (P < 0,0001). Much diversified pathology is observed in the children studied shown in the *table 3.*

Children studied are characterised by total of 86 cases of different pathological conditions and diseases of new born children. They can be grouped in several directions; 1/3 of the complication are connected with premature birth. The second 1/3 is equally distributed among the following complications: asphyxis at birth, intrauterine hypotrophy and anaemia of the new born child. The last 1/3 comprises different more rarely met pathological conditions of a permanent character: malformation of the central neurvous system and retarded development, others connected with infections (Enterococci, Klebsiela, E.coli) as well as neonatal sepsis, congenital defects- slit of the lips, heart damages, neonatal hypoglycaemia, cryptorchismus, etc.

It can be noted that some of the children combine several diseases. In contrast to the children of groups 1 and 3, where diseases are more rare and only one disease is observed, 1/2 of the children in group 2 suffer four of the described complication and diseases. The other children in group 2 equally suffer 3 and 2 diseases, and only five children of this group show one type of damage of the new born *(table 4).*

Table 3*. Types and frequency of diseases and pathological conditions after birth in the children studied*

Diseases	Group 1		Group2		Group3		total	
	n	%	n	%	n	%	n	%
Cryptorchism	0	0	1	2,4	0	0	1	1,26
Anaemia	1	1,3	6	14,3	1	2,6	8	10,12
Retarded development	0	0	3	7,1	0	0	3	3,79
Heart noise	2	2,5	1	2,4	0	0	3	3,79
Escherichia coli	0	0	1	2,4	1	2,6	2	2,52
Malformations of CNS	0	0	5	11,9	0	0	5	6,32
Prematurely born child	8	10,1	14	33,3	3	7,7	25	31,64
Asphyxia	3	3,8	9	21,4	0	0	12	15,18
Hypotrophia intrauterine	2	2,5	7	16,7	0	0	9	11,39
Sepsis neonatalis	0	0	2	4,8	0	0	2	2,52
Chealin-membrane disease	0	0	3	7,1	0	0	3	3,79
Cheiloschisis	0	0	3	7,1	0	0	3	3,79
Hyphoglycemia neonatalis	1	1,3	0	0	0	0	1	1,26
Polycithaemia	2	2,5	1	2,4	0	0	3	3,79
Enterococcus and Klebsiela	0	0	2	4,8	0	0	4	5,06
Aspiration syndrom	1	1,3	3	7,1	0	0	4	5,06

Table 4. *Combination of different diseases of the new born children in the three groups studied*

	Frequency of disease	Combination of different disease
Group 1	14 cases of single disease	14 with 1 disease
Group 2	50 cases of diseases in different combinations	15 children with 4 diseases 4 children with 3 diseases 5 children with 2 diseases 5 children with 1 disease
Group 3	5 cases of single disease	5 children with 1 disease

The characteristics thus made on the general health status of children studied shows that children of groups 1 and 3 suffer more rarely complications during womb development and birth. In contrast, children from group 2 are strongly damaged due to problems during pregnancy, womb development and birth.

Numerous studies indicate early transmission of Candida in mouth cavity for children with congenital malformations, congenital heart diseases, problems at delivery and premature born children (2, 5, 7). These factors are risky also for the development of candidosis particularly dangerous for damaged children living in closed environment. Hospital social facilities and other similar institutions are indicated as a risk factor for maintaining oral colonisation with Candida. Without being accepted as causes for interhospital infections, Candida is a part of the resident oral microflora, disseminating and invasive candidosis and sepsises with possible lethal out come may develop in children with damages, prematurely born after invasive therapeutical interventions, or children subject to central venous catheter, etc. The struggle with these infections is very difficult because it is hard to envisage the transition of these microorganisms from resident to opportunistic pathogens. This however looks very easy for organisms in the time of the risky after-birth period especially for prematurely born children.

For this reason we sought a connection between the oral transmission with Candida and children with damages.

General health status and oral colonisation with Candida

The main risk factors for oral colonisation with Candida are connected with multiple health problems and diseases, congenital anomalies which influence the immunity and indirectly the colonisation with Candida. We studied this dependence and the results are summarized in the *table below.*

Table 5. *Candida and disease of new born child for all children studied*

	without Candida	**with Candida**	**total**
without disease	93	19	112
with disease	21	27	48
total	114	46	160
χ^2 P Pearson Correlation (PC)	$\chi^2 = 25{,}315$ P < 0,0001 PC= 0,398*		

When comparing children with diseases and children without diseases with regard to the presence or absence of Candida in their oral medium, one observes a statistically notable difference between the too groups(P < 0,0001) as well as a good correlation between Candida and general diseases of the children studied (PC=0,398). This fact is a confirmation of the close relation between the general health condition of the children and the oral colonisation with Candida.

This provides the reasoning to propose that the evaluation of the oral risk medium for children includes as a risk marker of the general health status, the presence or absence of oral Candida- an objective parameter which together with numerous other characteristics of evaluation of the risky oral medium, could provide information of the influence of the general status on the oral medium of new born children and children up to 1 year of age.

Conclusions

1. Fungi of Candida type are among the first colonizers in oral medium, populating 16.5% of the new born children and reaching 38.46% of the children up to 1 year of age;

2. The type characteristics of oral Candida shows that C. albicans is isolated in 87% of the children;

3. Candida quantities are very different; more then 1/3 of the children with Candida have quantities of 105-106 cells/ml without exhibiting clinical symptoms of oral candidosis;

4. Candida colonises more frequently children with systematic chronical diseases and damages;

Candida is one of the early inhabitants of the oral ecosystem, and the possibility for colonisation increases for children with general diseases and children with system damages obtained at birth. The dependence between the general health status of the children and the oral Candida provides reasoning to propose that Candida in oral cavity be accepted as a marker indicating the influence of the general status of the organism on the oral medium.

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