The Impact of Sickle Cell Disease on Oral Health-related Quality of Life

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Abstract: Purpose: The purpose of this study was to characterize the impact of sickle cell disease (SCD) on oral health and examine its impact on quality of life. Methods: Fifty-four study subjects were recruited from the sickle cell clinic and 52 control subjects from the adolescent medicine clinic at Nationwide Children’s Hospital, Columbus, Ohio. A dental exam was performed to determine each participant’s caries burden. The Child Oral Health Impact Profile survey was used to assess their oral health-related quality of life (OHRQoL). Results: Most subjects in both the SCD and control groups rated their overall health and oral health as “good” or “excellent.” There was no statistically significant difference in OHRQoL between these groups. Additionally, no significant relationship was found between white blood cell count, medication intake, or the number of sickle cell crises as related to the caries burden. Statistically significant differences were detected in caries burden between the control group and the sickle cell hemoglobin C disease (HbSC) group (P<.02) and between the sickle cell anemia and HbSC subjects (P=.04). Conclusions: Adolescents with sickle cell hemoglobin C disease had fewer caries than peers with sickle cell anemia or controls, though the cause of this finding is not clear. (Pediatr Dent 2014;36:24-8) Received May 1, 2012 | Last Revision October 16, 2012 | Accepted October 22, 2012

KEYWORDS: SICKLE CELL DISEASE, ORAL HEALTH, QUALITY OF LIFE

The Impact of Sickle Cell Disease on Oral Health-related Quality of Life. Sickle cell disease (SCD) is a vascular disorder characterized by chronic, ongoing organ damage that is punctuated by episodes of acutely painful vascular complications.1 It is the most common genetic blood disorder in the United States, affecting approximately 0.3 percent to 1.3 percent of African Americans.2 In addition to its systemic complications, SCD is also associated with changes in the craniofacial bones and oral soft tissues.

Increased demand for erythropoesis may cause compensatory expansion of the marrow spaces of the craniofacial bones. This can lead to changes such as: decreased radiodensity of facial bones; formation of a coarse “stepladder” trabecular appearance due to medullary hypertrophy; maxillary protrusion with flaring of maxillary incisor teeth; thin border of mandible; increased prominence of zygomatic and parietal bones; widened diploic spaces; a thinned calvarium; and vertical trabeculations known as a “hair on end” appearance.3 Compensatory marrow expansion may also cause the skull to exhibit a granular appearance, resembling osteoporosis.4 “Doughnut” lesions of the calvarium may also be observed.5 Mucous membranes tend to exhibit pallor, due to a low hematocrit, and a jaundiced appearance consistent with increased hemolysis.6 Glossitis and gingival enlargement may also be present.7 Facial swelling, mimicking an odontogenic cellulitis, has been reported.8,9 Both bony and soft tissue changes are nonspecific to SCD and may be present in other systemic conditions as well.

There is no conclusive data regarding the caries experience of SCD patients. Nigerian 14- to 33-year-old SCD patients were shown to have a reduced caries experience compared to healthy controls, which was attributed to an avoidance of sweets by most patients.6 O’Rourke and Hawley7 found no difference between caries prevalence or severity of disease between 13- to 45-year-old patients with or without SCD. By contrast, SCD children younger than six years old who were taking daily penicillin were reported to have decreased colonization by Streptococcus mutans and, hence, a lower caries experience vs. healthy subjects not taking antibiotics.9 This difference, however, only existed as long as penicillin was administered. Laurence et al.9 reported that there was no difference in caries experience in six- to 19-year-olds with or without SCD, but the number of decayed, missing, and filled permanent tooth surfaces (DMFS) was higher in SCD adults older than 20 years old vs. controls. Therefore, the conflicting reports about the caries experience of SCD patients warrant further investigation.

SCD patients tend to have a lower baseline health-related quality of life (HRQoL) than those without the disease. Parents of affected children reported a worse HRQoL in self-esteem, behavior, physical functioning, and overall perception of health than the children themselves reported.10-12 Another study showed that reports from SCD children and their parents regarding physical pain were highly correlated.13 SCD children and concomitant neurobehavioral comorbidities, such as attention deficit hyperactivity disorder (ADHD), also had a worse HRQoL.11 Increased physical pain, internalizing symptoms (ie, depression and anxiety), and disease-related parenting style were all associated with lower HRQoL in SCD adolescents.13 Urban, predominantly African American schoolchildren diagnosed with the disease reported low HRQoL, as early as the second grade.14,15 Socioeconomic distress on both an individual family and a neighborhood or community predicted increased pain and lower HRQoL in SCD patients.16

The Child Oral Health Impact Profile (COHIP) measures self-reported oral health-related quality of life (OHRQoL) in eight- to 15-year-olds using 34 questions in five domains (oral health, functional well-being, social-emotional well-being, school environment, and self-image) and four questions about treatment expectations and global health.17-19 Higher COHIP scores reflect a higher OHRQoL. The survey’s reliability and validity have been established.17,18

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To the best of our knowledge, there are no reported data on OHRQoL in SCD patients. This study's purposes were to: (1) determine the impact of oral health in the quality of life of adolescents with sickle cell disease; (2) assess the caries experience in SCD adolescents; (3) determine whether the number of SCD crises is associated with caries burden; and (4) determine whether caries burden impacts the white blood cell (WBC) count.

**Methods**

This study was approved by the Institutional Review Board at Nationwide Children’s Hospital, Columbus, Ohio. Subjects from the sickle cell and the adolescent medicine clinics were invited to participate if they:

1. were between 10 and 18 years old;
2. had permanent dentition only;
3. were diagnosed with SCD and did not have a painful crisis at the time of the survey (for the study group);
4. had no medical conditions other than SCD that would qualify them as ASA 3 or ASA 4 (ie, ASA 1 and 2 patients only);
5. were willing to do a clinical dental exam;
6. were able to have their blood drawn as part of their clinical visit (for the study group only);
7. were not pregnant;
8. did not have an intellectual disability; and
9. were fluent in English because the survey had not been tested in foreign languages at the time.

After the study consents and assents were obtained, patients were assigned a number by which they were identified in order to protect their confidentiality. Subjects completed COHIP on their own, which was transformed into a sheet that could be processed using an HP scanner (Hewlett-Packard Company, Palo Alto, Calif., USA) and Cardiiff TeleForm software (New England Survey Systems, Brookline, Mass., USA).

COHIP was chosen as the most appropriate tool to assess OHRQoL because its reliability and validity had been previously established, and it was specifically targeted to the age group in the study, whereas other instruments available for measuring OHRQoL were designed for different age groups. COHIP is a 38-question survey designed to measure self-reported OHRQoL in eight- to 15-year-olds. COHIP contains 34 questions to measure OHRQoL in five domains: (1) oral health (10 items); (2) functional well-being (six items); (3) social-emotional well-being (eight items); (4) school environment (four items); and (5) self image (six items). It also contains four questions to assess treatment expectations and global health of the child, which are not used in computing the overall COHIP score. In keeping with the World Health Organization concept that health is more than the absence of disease, the questionnaire contains items to assess both positive and negative aspects of OHRQoL.

Responses for the seven positively worded items (eg, “In the past three months, how often have you been unhappy because of your teeth, mouth, or face?”) were recorded as: “never” = 0; “almost never” = 1; “sometimes” = 2; “fairly often” = 3; and “almost all of the time” = 4. Scoring of the remaining 31 negatively worded items (eg, “In the past three months, how often have you been unhappy or sad because of your teeth, mouth, or face?”) were reversed (“almost all of the time” = 0; “fairly often” = 1; “sometimes” = 2; “almost never” = 3; and “never” = 4).

Higher COHIP scores reflected more positive OHRQoL, while lower scores reflected lower OHRQoL. Subscales scores were calculated by summing the responses of the items specific to the subscale. The overall OHRQoL score was computed by summing the subscales scores. Scores range from zero to 140 for the overall scale.

A pediatric dental resident preformed an intraoral exam on each patient using a disposable intraoral mirror and pen light and documented the findings on an exam sheet together with demographic and medical information. For each patient, the age, gender, ethnicity, medical diagnoses, and current medications were determined by reviewing the medical record. The number of sickle cell crises in the past 12 months was determined by reporting from the parent and/or patient. Oral hygiene status (assessed by the presence or absence of gingivitis in the lower anterior quadrant), and caries burden (established by the decayed, extracted, and filled permanent teeth [DMFT] score) were evaluated by the dental resident and recorded. The dental findings were discussed with parents and patients, and those with needs were referred for care. For the sickle cell group, blood was drawn by a clinic staff member to evaluate each patient's white blood cell count as part of their clinical visit.

**Data analysis.** COHIP subscale scores were calculated by adding the responses of the items specific to them. The overall OHRQoL score, which may range from zero to 140, was the sum of all domain scores. Treatment expectation scores and the overall health response were not included in the overall COHIP scale, since these items are relevant only when the survey is used as part of a treatment assessment.

Statistical analysis was performed using SAS 9.1.3 software (SAS Institute Inc, Cary, N.C., USA) with a significance level of P < .05. Frequency, mean, median, and standard deviation were estimated using descriptive statistics. COHIP survey data was normally distributed; therefore, parametric tests were used for analysis. Caries burden data did not follow a normal distribution; thus, nonparametric tests were used to analyze it. Overall and individual subscales of COHIP were compared between groups using linear regression. The responses to specific questions by group were summarized in frequency tables and compared using either a chi-square test or Fisher's exact test for contingency tables with small cell counts.

Summary statistics were used to examine the association between the caries burden, WBC count, and number of SCD crises in the previous year. A negative binomial regression model was used to examine the relationship between SCD type, number of crises, WBC count, and current medications with caries burden (DMFT) as the outcome variable because the DMFT values were not normally distributed.

**Results**

In the SCD group, there were 24 males and 30 females with an average age of 14 years, six months vs. 10 males and 42 females with an average age of 16 years, four months in the control group. Most subjects in both groups were African American (88/106), but there were more Caucasians in the control group. Most subjects in both groups were African American (88/106), but there were more Caucasians in the control group. There was an even distribution in SCD and control groups. There was an even distribution of subjects with sickle cell anemia (HbSS) and sickle cell hemoglobin C disease (HbSC) genotypes (23 individuals each), with eight subjects having other types of SCD (Table 1).

**COHIP findings.** Table 2 shows the total and subscale scores for SCD and control groups and HbSS and HbSC genotypes. There were no statistically significant differences in total COHIP scores or domain scores between SCD and control subjects; HbSS and HbSC subjects; patients older or younger than 15 years old; and races. There were no statistically significant differences in how SCD patients and control patients rated their global health. Overall, 56 percent of SCD patients rated...
their global health as “good” or “excellent,” with only 12 percent rating it as “poor” or “fair.” By comparison, 65 percent of control patients rated their global health as “good” or “excellent,” while only six percent considered it “fair” or “poor.” The only statistically significant finding between genders was that females in both groups reported higher social and emotional well-being ($P<.03$).

**Caries burden impact.** Table 3 shows DMFT relationships among several groups. The only statistically significant differences found were that patients with HbSC had a lower DMFT than individuals with HbSS ($P<.04$) and control subjects ($P<.02$), and patients older than 15 years had a higher DMFT score than younger ones ($P<.001$). There were no significant differences in DMFT between HbSS and control patients ($P=.97$), among races (all $P$-values >.05), or between genders, although females had higher average scores approaching significance ($P=.08$).

No significant relationships were detected between the patients’ caries burden and:
1. the number of SCD crises experienced in the past 12 months ($P>.60$);
2. their WBC count ($P>.72$); and
3. those who reported taking medications vs. those who did not ($P>.84$).

Only five of the subjects were taking hydroxyurea. Twelve of the 56 SCD patients were taking antibiotics at the time of the study (six HbSS patients, five HbSC, and one with another type of SCD). The duration of antibiotic therapy was not assessed in this study.

**Table 1. SUBJECT DISTRIBUTION**

<table>
<thead>
<tr>
<th>Genotype*</th>
<th>No. of subjects</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbSS</td>
<td>23</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>HbSC</td>
<td>23</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Other SCD</td>
<td>2</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Total SCD</td>
<td>54</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>Control</td>
<td>52</td>
<td>10</td>
<td>42</td>
</tr>
</tbody>
</table>

* HbSS=sickle cell anemia; HbSC=sickle cell hemoglobin C disease; SCD=sickle cell disease.

**Table 2. TOTAL AND SUBSCALE CHILD ORAL HEALTH IMPACT PROFILE (COHIP) SCORES FOR SICKLE CELL DISEASE (SCD) VS. CONTROL GROUPS AND SICKLE CELL ANEMIA (HbSS) VS. SICKLE CELL HEMOGLOBIN C DISEASE (HbSC) GENOTYPES**

<table>
<thead>
<tr>
<th>COHIP category</th>
<th>SCD mean score</th>
<th>Control mean score</th>
<th>$P$-value</th>
<th>HbSS mean score</th>
<th>HbSC mean score</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total COHIP score</td>
<td>34.6</td>
<td>35.9</td>
<td>.50</td>
<td>37.4</td>
<td>31.5</td>
<td>.10</td>
</tr>
<tr>
<td>Functional well-being</td>
<td>2.9</td>
<td>3.2</td>
<td>.64</td>
<td>3.6</td>
<td>2.2</td>
<td>.46</td>
</tr>
<tr>
<td>Social and emotional well-being</td>
<td>4.6</td>
<td>4.4</td>
<td>.87</td>
<td>6.0</td>
<td>3.7</td>
<td>.41</td>
</tr>
<tr>
<td>School environment</td>
<td>1.2</td>
<td>1.4</td>
<td>.71</td>
<td>1.7</td>
<td>0.9</td>
<td>.45</td>
</tr>
<tr>
<td>Self image</td>
<td>17.0</td>
<td>17.3</td>
<td>.70</td>
<td>17.9</td>
<td>15.6</td>
<td>.21</td>
</tr>
<tr>
<td>Treatment expectancy</td>
<td>4.5</td>
<td>4.1</td>
<td>.42</td>
<td>4.6</td>
<td>4.5</td>
<td>.97</td>
</tr>
<tr>
<td>Total global health scores</td>
<td>5.4</td>
<td>5.6</td>
<td>.46</td>
<td>5.2</td>
<td>5.1</td>
<td>.36</td>
</tr>
</tbody>
</table>

* Higher scores reflect more positive oral health-related quality of life. Total COHIP scores range from 0-140; functional well-being scores range from 0-24; social and emotional well-being scores range from 0-32; school environment scores range from 0-16; self-image scores range from 0-28; treatment expectancy scores range from 0-8; and total global health scores range from 0-8.

**Table 3. COMPARISON OF DECAYED, MISSING, AND FILLED PERMANENT TEETH (DMFT) VALUES AMONG SEVERAL GROUPS**

<table>
<thead>
<tr>
<th>Groups*</th>
<th>No. of subjects</th>
<th>Mean DMFT±(SD)</th>
<th>Median</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>52</td>
<td>2.96±4.10</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>SCD total</td>
<td>54</td>
<td>1.94±2.70</td>
<td>1.0</td>
<td>.10</td>
</tr>
<tr>
<td>Control</td>
<td>52</td>
<td>2.96±4.10</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>HbSS</td>
<td>23</td>
<td>2.91±2.80</td>
<td>2.0</td>
<td>.97</td>
</tr>
<tr>
<td>Control</td>
<td>52</td>
<td>2.96±4.10</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>HbSC</td>
<td>23</td>
<td>1.30±2.70</td>
<td>1.0</td>
<td>&lt;.02†</td>
</tr>
<tr>
<td>HbSS</td>
<td>23</td>
<td>2.91±2.80</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>HbSC</td>
<td>23</td>
<td>1.30±2.70</td>
<td>1.0</td>
<td>.04†</td>
</tr>
<tr>
<td>African American</td>
<td>88</td>
<td>2.27±2.70</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2</td>
<td>0.00±0.00</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>15</td>
<td>3.87±6.50</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1</td>
<td>1.00±NA</td>
<td>1.0</td>
<td>All &gt;.05</td>
</tr>
<tr>
<td>Male</td>
<td>34</td>
<td>1.71±2.20</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>72</td>
<td>2.79±4.00</td>
<td>2.0</td>
<td>.08</td>
</tr>
<tr>
<td>&lt; 15 years of age</td>
<td>35</td>
<td>1.17±1.40</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>&gt; 15 years of age</td>
<td>71</td>
<td>3.07±4.00</td>
<td>2.0</td>
<td>&lt;.001†</td>
</tr>
</tbody>
</table>

* SCD=sickle cell disease; HbSS=sickle cell anemia; HbSC=sickle cell hemoglobin C disease.
† Statistically significant ($P<.05$).

**Discussion**

It is noteworthy that our sample comprised an equal number of HbSS and HbSC subjects, since, in the United States, approximately two thirds (1:601) of affected individuals have HbSS while only one third (1:1,127) have HbSC. The explanation may reside in the fact that central Ohio has a high number of individuals from Ghana, where HbSC disease is more prevalent.

This study found that SCD adolescents had an ORRQoL similar to control subjects. Interestingly, the SCD and control groups also rated their global health similarly. These results are somewhat surprising, as SCD patients clearly face a great health challenge. The lack of a significant difference could be explained in part as patient selection bias. Only patients who were not currently experiencing pain crises attended the SCD outpatient clinic and were recruited for the study, while patients admitted for pain crises and other acute complications were excluded. Thus, it is possible that patients who reported “good health” actually simply meant absence of acute pain. By contrast, many control patients reported having seasonal allergies, asthma, ADHD, depression, hypertension, and migraines, for which they were seeking treatment in the adolescent medicine clinic.

Due to the fact that this study was conducted in a hospital setting, many control patients were being treated for non-life-threatening illnesses; thus, data was collected for both ASA 1 and ASA 2 control patients. Thirty-one of them had medical conditions that would have classified them as ASA 2 (eg, asthma, hypertension, and gastroesophageal reflux disease [GERD]). On the other hand, half of the study patients also had concomitant non-life-threatening illnesses that would have placed them in an ASA 2 category if they did not have SCD. These conditions may have influenced the perception of HRQoL by both groups. Furthermore, the multidisciplinary care and close follow-up provided to SCD patients seems to have been effective in decreasing the impact of the disease in their everyday life, consequently leading them to report a good HRQoL.
Broder et al.\(^8\) reported that 13- to 15-year-olds had lower COHIP scores than 11- to 13-year-olds. Since the survey has only been validated in children up to age 15 years old and our study used it through 18 years old, there was concern that our results could be skewed by older subjects reporting a decreased OHRQoL vs. younger subjects. Our study, however, found that there were no significant differences in overall or subscale COHIP scores between the different age groups. Furthermore, the same authors suggested that African American subjects tended to report lower COHIP scores than Caucasians, which was not supported by our study.

Females in both groups were found to have significantly higher social and emotional well-being than males (\(P = .03\)), in contrast to a study of 58 SCD children in which females, older children, and patients with more disease-related complications had lower HRQoL.\(^2\) This finding also disagrees with other studies suggesting that females affected with chronic illnesses report a lower HRQoL.\(^2\), \(^2\) In our study, females were also found to have higher scores for total COHIP, functional well-being, school environment, and global health, although they were not statistically significant. The trends were strong enough to suggest, however, that, with a larger sample size, significant differences may have been detectable.

Physical differences between males and females with SCD may explain the fact that females had a higher social and emotional well-being in this study. SCD adolescents have been shown to progress through puberty slower than their healthy peers, with males particularly being significantly shorter than controls, which could, at least temporarily, affect their self-image and self-confidence.\(^2\) SCD males also report a higher number of days experiencing crises and utilizing health care services,\(^2\) which may have lowered their perception of well-being.

This study found that HbSS adolescents had a similar caries experience compared to control subjects, but HbSC individuals had a decreased caries experience vs. control subjects (\(P < .02\)) and HbSS peers (\(P = .04\)). Although not statistically significant, this study also found that SCD adolescents had a lower caries experience than control subjects, which is consistent with a study by Laurence et al.\(^8\) Several factors may have contributed to this. First, pediatric dental residents rotate weekly in the SCD clinic and provide anticipatory oral health guidance to families and patients from an early age, which may have led its staff to become more sensitized to the importance of oral health. On the other hand, the pediatric dental service is not involved in the adolescent clinic. Moreover, frequent water consumption is recommended to all SCD patients to avoid dehydration, which may precipitate a pain crisis. Patients are provided water bottles and given permission to drink from them throughout the school day, which could potentially expose them to more fluoride than the control subjects, thus increasing their protection against dental disease.

In this study, HbSC patients had a significantly decreased caries experience statistically vs. control subjects and patients with other types of SCD. Because HbSS and HbSC patients have been subjected to the same early anticipatory guidance, extended antibiotic exposure, and possible increased fluoride intake, the discrepancy in the caries experience between the two groups begs an explanation. One may speculate that:

1. The severity of HbSS disease may make oral health a lesser priority for the affected patients.
2. HbSS individuals may have a higher exposure to pain and other medications with high sugar content.
3. Dental providers may be less willing to treat HbSS children, given their disease severity.

The finding that patients older than 15 years old had more dental caries than younger subjects was not surprising, considering that the former have more teeth that have been present for a longer period of time, putting them at higher risk for disease.

The fact that no significant relationship between the patients’ number of SCD crises, WBC count, medication usage, and caries burden was found has to be taken with caution, because active dental disease was not analyzed separately from previously treated caries. Thus, it is possible that active disease could actually have a relationship with these parameters. Additionally, some SCD subjects were taking hydroxyurea, which can lower the WBC count, thus masking our findings.

This study has several limitations. First, many control patients had chronic illnesses, such as asthma, ADHD, and GERD, which may confound the ability to distinguish between “healthy” controls and “disease” subjects. Secondly, dental radiographs were not obtained; thus, curious lesions that can only be detected radiographically were missed. Thirdly, during data collection, components of the caries burden index (DMFT) were not separated, making it impossible to differentiate the burden of active disease from the treated disease. Fourthly, patient recall bias may have affected reporting of oral health concerns and the number of crises experienced during the previous year. Additionally, the sample size was small, and the adolescent medicine patients may not have had the same exposure to dental disease prevention as the SCD patients did. Consequently, a larger multicenter trial with healthier controls is warranted. Furthermore, comparing adolescents seen in a sickle cell clinic with a dental component to those without it would be interesting to measure the specific impact of dental residents attending medical specialty clinics.

**Conclusions**

Based on this study’s results, the following conclusions can be made:

1. Sickle cell disease adolescents have a similar oral health-related quality of life compared to healthy subjects, as measured by the Child Oral Health Impact Profile.
2. Adolescents with sickle cell anemia have a similar caries experience compared to healthy subjects.
3. Adolescents with sickle cell hemoglobin C disease have a decreased caries experience compared to healthy subjects (\(P < .02\)) and sickle cell anemia peers (\(P = .04\)).
4. The frequency of sickle cell crises is not associated with the patient’s caries burden.
5. The white blood cell count is not associated with the patient’s caries burden.
6. Patients taking medications were not found to have a similar caries experience to those who were not taking medications.
7. Females reported a statistically significant (\(P = .03\)) higher social and emotional well-being than males.
8. Patients who were at least 15 years old had a significantly higher decayed, missing, and filled permanent teeth than patients younger than 15 years old (\(P < .001\)).

**Acknowledgment**

Funding for this study was provided by Nationwide Children’s Hospital Intramural Research (grant no. 240809).

**References**